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## List of Ph.D. Theses (with abstract)



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## **Department of Biology Sciences**

**SNX27-retromer assembly directs MT1-MMP trafficking to invadopodia and promotes breast cancer metastasis**

**Priyanka Sharma**

**Supervisor: Dr. Sunando Datta**

**Department of Biological Sciences**

**Accession No.: T00145**

**Abstract**

Tumor metastasis involves a complex sequence of events that facilitate the movement of tumor cells by breaking the underlying extracellular matrix (ECM). It is composed of macromolecules, mainly proteins that are packed densely like mesh-fibers and hence act as a physical barrier for the cellular movement. To move across the ECM, specialized actin-rich membrane protrusive structures named invadopodia are formed by the metastatic cells. Proteases that can degrade components of ECM are recycled from intracellular compartments to invadopodia for efficient degradation. This research work was aimed to study the molecular machinery governing recycling of the proteases and thus facilitate cancer cell invasion.

In the metastatic breast cancer cell line, MDA-MB-231, we found that retromer regulates the matrix invasion activity in association with sorting nexin 27 by recycling matrix metalloprotease, MT1-MMP on the cell surface. Also, MT2-MMP, another most abundantly expressed MMP, was found to be invadopodia associated in this cell line and contributes to its invasive potential. Although MT1 and MT2-MMP showed a high degree of colocalization, they were located on the distinct endosomal domains when analyzed by super-resolution microscopy. TIRF microscope-based analysis revealed that retromer and SNX27 could selectively recycle MT1-MMP but not MT2-MMP. They phenocopied each other in facilitating matrix degradation and associating with MT1-MMP.

Furthermore, the *in vitro* interaction studies via pull-down and Isothermal Titration Calorimetry revealed that both SNX27 and retromer could directly interact with MT1-MMP. However, in the *in silico* analysis, among retromer and its family members, SNX27 was found to be overexpressed or profoundly altered in the patients having invasive breast cancer. In Xenograft based studies, SCID mice engrafted with SNX27 knockout cell line showed prolonged survival, suggesting possible implication for over-expression of the sorting nexin in tumor samples. These findings highlight a novel role of sorting machinery in the breast cancer cell invasion via trafficking proteases.

**Identification of molecular chaperones having neuron-specific functions; roles beyond protein folding and aggregate remodelling**

**Raut Sandeep Shrikrishna**

**Supervisor: Dr. Chandan Sahi**

**Department of Biological Sciences**

**Accession No.: T00138**

**Abstract**

Molecular Chaperones are at the centre of proteostasis network (PN) and are indispensable for protein folding and aggregation remodelling functions. Besides de novo protein folding, chaperones also assist in clearance of terminally misfolded and cytotoxic protein aggregates. Compared to other cells, dealing with proteostatic imbalance is a bigger challenge for non-mitotic cells like neurons. Accumulation of toxic proteins in neurons has been linked to altered neuronal function, synapse loss and the onset of neurodegenerative diseases (NDDs). Consistent with this, several chaperones have been found to be differentially expressed in neurons; however, their function is largely unknown. This thesis describes identification of Drosophila chaperones with crucial neuronal functions. We identified a total 95 chaperones belonging to seven different families. Ubiquitin RNAi mediated knockdown revealed that about 50% of the chaperones are essential in Drosophila. Eye-specific and neuron-specific knockdown of essential chaperones identifies the ones that regulate eye and NMJ morphogenesis. The neuron-specific knockdown of essential chaperones along with immunocytochemistry and behavioural assays identifies nine chaperones crucial for neuromorphogenesis in Drosophila. Some of these chaperones are linked to mitochondrial biogenesis and import, cytoskeletal organization, intra-cellular protein-trafficking and RNA splicing. Together, our data presents the first classification and comprehensive analysis of Drosophila chaperones. Outcome of the screen reported here provide a useful resource for further elucidating the role of individual chaperones in Drosophila eye morphogenesis and synaptic development. One of the candidate chaperone that was crucial for viability as well as eye and NMJ development was, CG17187. CG17187 is an ortholog of Cwc23, an essential J-protein and a known splicing factor in *Saccharomyces cerevisiae*. However, CG17187 along with most of the orthologs of Cwc23, failed to rescue *cwc23Δ*, suggesting functional divergence amongst these orthologs. Besides, acquisition of RNA recognition functional divergence amongst these orthologs. Besides, Acquisition of RNA recognition motif (RRM) at their C-terminus in some eukaryotic orthologs, their ability to bind RNA might provide additional functional diversity or robustness to the J-protein/Hsp70 machine in

spliceosomal remodelling processes. Cwc23 recruits Ntr 1, a G-patch protein, which further interacts with Prp43, a DExD/H RNA helicase to facilitate spliceosomal disassembly. In-silico analysis supported by yeast complementation and yeast two-hybrid data presents a case of co-evolution of the spliceosome disassembly triad in eukaryotes.

**Elucidating the Role of Human Gut Microbiome in Health and Disease Using Next Generation Sequencing and Computational Approaches**

**Darshan Bharatkumar Dhakan**

**Supervisor: Dr. Vineet Kumar Sharma**

**Department of Biological Sciences**

**Accession No.: T00136**

**Abstract**

During the last decade, the role of human gut microbiome has been associated with the health and well-being of human individuals. Recent advances in next generation sequencing have provided the necessary impetus leading to the sudden spurt in the number of studies and reports profiling the human gut microbiome. The microbiome is associated with the essential human physiological processes such as development, immunity, neural regulation, mood swings, digestion of food and metabolic regulation. During my PhD tenure I have been involved in understanding the changes in gut microbiome composition with diet, location, lifestyle and other pathophysiological conditions. In order to understand these variations and its functional consequences on the human health we carried out large-scale microbiome profiling of Indian gut microbiome using multi-omic approaches. The study reveals *Prevotella* to be the key species associated with Indian gut microbiome when compared to datasets from other countries across the globe. The use of multi-omics approach which includes metabolomics analysis of faecal and serum samples helped in deciphering the role of *Prevotella* in regulation of key metabolites associated with human health.

I was also involved in few studies to investigate the role of microbial dysbiosis in disease conditions such as tuberculosis and autism. Both these studies revealed important insights in the microbiome-immune cross talk and gut-brain axis. The study of microbiome composition in patients suffering from tuberculosis and those undergoing antibiotic treatment identified short chain fatty acid (SCFA) producing microbes such as *Faecalibacterium prausnitzii* to be associated with TB gut. Important functional mechanisms of this association were derived from this study which could play key role in the survival of *Mycobacterium tuberculosis*. The study of variations in microbial composition in autistic children also provided significant insights into the role of lactobacillus species in modulating the behaviour. The association of lactic acid producing microbes with autism was identified showing

key association of species from this group in aggravating the disease. The work presented in this thesis provides the thorough analysis of above mentioned studies and gives better understanding of microbiome in human health and disease.

**Critical for Periplakin SUMOylation in the efficient re-organization of Keratin intermediate filament network**

**Mansi Gujrati**

**Supervisor: Dr. Ram Kumar Mishra**

**Department of Biological Sciences**

**Accession No.: T00134**

The interplay of numerous architectural proteins is crucial for the coordination of efficient cellular cytoskeleton assembly, its movement, and maintenance of tissue integrity. Plakins serve as adaptors inter-connecting cytoskeletal intermediate filaments and affect its reorganization during migration, differentiation, and response to stress. Periplakin (PPL) an important plakin family protein interacts specifically with intermediate filament proteins K8, K18, and vimentin via its C-terminal linker domain. Post-translational modifications (PTM's) provide a versatile way to regulate the dynamics of protein-protein interactions. SUMOylation is a reversible PTM, which is essential in most organisms, and affects virtually all types of diverse cellular processes.

In my graduate study, I have attempted to characterize PPL as a bona fide SUMO substrate and decipher functional consequences of its SUMOylation. This thesis describes for the first time, that PPL is SUMOylated at a conserved lysine in its linker domain (K1646) preferentially by SUMO1. Further, stresses perturbing intermediate-filament and cytoskeletal architecture induce hyper-SUMOylation of PPL. Strikingly, exogenous over-expression of a non-SUMOylatable PPL mutant (K1646R) induces aberrant bundling and loose network interconnections of the keratin filaments. Live recording of cells expressing the K1646R mutant highlighted the enhanced sensitivity of keratin filament collapse upon phosphatase inhibition.

Altogether, the study in this thesis revealed that periplakin is modified by SUMO1 in the C-terminal tail. Various cellular stresses enhanced SUMOylation of Periplakin and expression of the non-SUMOylatable form of periplakin in cells induced perturbation in keratin filament organization. An important finding from this study established periplakin SUMOylation as a novel mechanism for regulating keratin filament dynamics.

**Key Words:** SUMOylation, Periplakin, Intermediate filament, Keratin, and Stress.

## **Assessing the Functional Roles of Human and Environment-associated Microbiomes usinf Next-Generation Sequencing**

**Rituja Saxena**

**Supervisor: Dr. Vineet Kumar Sharma**

**Department of Biological Sciences**

**Accession No.: T00126**

## **Abstract**

Microorganisms are ubiquitously associated with the environment, humans and other organisms, and are known to play a significant role in human health and well-being. Metagenomics is the culture-independent genomic analysis of microbes using the next-generation sequencing technology, which has been known to play a pivotal role in unravelling the genetic information underlying the environment and human-associated microbiome. During my graduate research, I have focussed on assessing the functional roles of scalp and oral microbiome, which has revealed interesting findings. The comparison of healthy and dandruff scalp microbiome revealed a new potential role of bacterial commensals in supplying the host with nutrients essential for a healthy scalp. It also showed the high abundance of yet uncharacterised *Malassezia* sp. in the dandruff scalp, whose characterization seems to be imperative in designing novel anti-dandruff therapies. Additionally, a 16-weeks long time-course study was also performed, which suggested an apparent beneficial effect of coconut oil on the scalp microbiome. Among the various types of cancers, oral cancer ranks among the three most prevalent cancers in India, with Bhopal contributing the maximum number of cases per year, attributable to the exposure to risk factors such as tobacco consumption and lack of early-stage diagnosis. The oral microbiome of oral cancer patients in Bhopal was examined and compared to the healthy oral microbiome in tobacco-consuming and non-consuming groups. The results revealed drastic differences in the abundance of bacterial communities between the groups and showed significant associations between oral bacterial communities and oral cancer.

I was also involved in the metagenomic study of two different hot springs from central India, which revealed the presence of hydrocarbon degrading thermophiles and their pathways essential for survival in extreme environments. The culture-based analysis from the environmental samples, resulted in the characterization of the hitherto unknown novel species and genomes. This thesis presents the results obtained from the analysis of the above-mentioned metagenomic projects. Metagenomics proves to be promising in the identification of novel genes, genomes, and pathways, which hold tremendous application in human health and medicine, bioremediation and in industrial biotechnology.

**Keywords:** Metagenomics, Next-generation sequencing, Microbiome and Genomes.

**Study of oncogenic role of PAK2 and HNRNPA2B1 in head and neck cancer**

**Amit Gupta**

**Supervisor: Dr. Sanjeev Shukla**

**Department of Biological Sciences**

**Accession No.: T00130**

**Abstract**

Cancer is widely perceived as a heterogeneous group of disorders with markedly different biological properties, like immortality, tissue invasion, migration, angiogenesis and metastasis commonly known as hallmark of cancer [1]. These hallmarks of cancer appear with successive accumulation of genetic and epigenetic alterations. The epigenetic regulation of gene expression helps in the maintenance of normal cellular homeostasis; however, perturbation of these regulations has been evidenced with oncogenesis. Since the epigenetic regulations are guided by the activity of chromatin associated/binding proteins (CAPs), we hypothesized that these proteins might play an important role in oncogenesis.

In order to identify the deregulated CAPs, we performed in silico analysis wherein we analyzed seven head and neck cancer microarray profiles and found consistent upregulation of p21 activated kinase (PAK2) which was cross-validated in head and neck cancer tumor samples. The molecular study identified that PAK2 promotes increased activation of  $\beta$ -catenin, which in turn, favor the upregulation of c-Myc. Furthermore, the c-Myc binds at Pyruvate Kinase (*PKM2*) promoter region and leads to elevated expression of *PKM2*, consequentially, promotes the aerobic glycolysis also known as Warburg effect in head and neck cancer cells (HNCCs). We identified that the axis of PAK2-cMyc-PKM2 is critical for HNC cells growth [2].

In addition, we have also investigated the role of a chromatin-associated protein as well as splicing factor, HNRNPA2B1 in head and neck tumorigenesis. The upregulation of hnRNPA2B1 was observed in head and neck tumor samples. We found that the HNRNPA2B1 regulates the MST1R splicing and give rise to cancer-specific isoform in head and neck cancer cells. Furthermore, the presence of MST1R cancer-specific isoform correlates with the activation of Akt/PKB signaling and promotes epithelial to

mesenchymal transition. Conclusively, we showed that the PAK2 and HNRNPA2B1 are critical regulators of head and neck oncogenesis and targeting these molecules may help in the better management of head and neck cancer.

**Distinct Conformational Preferences of a Pore Forming Protein: Molecular Mechanism and  
Peptide Engineering**

**Muralikrishna Lella**

**Supervisor: Dr. R. Mahalakshmi**

**Department of Biological Sciences**

## Accession No.: T00129

### Abstract

Protein sequences that defy the first principles of secondary structure prediction and attain two different folds are of interest in peptide engineering. Such proteins, aptly named metamorphic proteins, decrease the conformational constraint by increasing flexibility in the secondary structure and thereby result in efficient functionality. This study identifies the occurrence of metamorphic behavior in the transmembrane domains of Mycobacteriophage D29 holin. Holins are phage-encoded transmembrane proteins expressed by the host cell during bacteriophage infection. Holins kill the host cell by forming a pore in the membrane. Conventionally, the molecular switch in the regulation and physical basis of pore formation is mediated by the interaction of the active holin with its regulatory counterpart, antiholin. However, Mycobacteriophage D29, which infects and kills *Mycobacterium* sp., possesses the holin protein, but its antiholin counterpart is absent. How the Mycobacteriophage D29 holin is kept inactive and regulated in the absence of an antiholin was not known. In this study, we have structurally and functionally characterized the first and second transmembrane domains of D29 holin, namely **TM1** and **TM2**. We find that **TM1** undergoes a lipid-dependent  $\alpha$ -helix  $\leftrightarrow$   $\beta$ -hairpin conformational switch, which is mediated by a centrally positioned proline residue. The conformational switch is responsible for the controlled **TM1** self-association in the lipid membrane. Furthermore, **TM2** samples three secondary structures, namely  $\alpha$ -helix, PPII-like conformation, and random coil structure, depending on its microenvironment. We propose that the structural alteration in **TM1** and **TM2** of D29 holin presents itself as a holin self-regulatory mechanism, and its implications are discussed in the context of holin function. **TM1** and **TM2** are also the longest known chameleonic sequences identified so far. We have also successfully redesigned the membrane disruption property of **TM1** into specific nanopore ion channels using a sequence reversal strategy. Our strategy for peptide engineering to obtain nanopore channels can pave the way for better bio-based design of controlled nanopores, using only natural amino acids.

**Key words:** Metamorphic proteins, Holin, Transmembrane peptide, Conformational switch, Peptide nanopores

**Assessing the Functional Roles of Human and Environment-associated Microbiomes using Next-Generation Sequencing**

**Rituja Saxena**

**Supervisor: Dr. Vineet Kumar Sharma**

**Department of Biological Sciences**

## **Accession No.: T00126**

### **Abstract**

Microorganisms are ubiquitously associated with the environment, humans and other organisms, and are known to play a significant role in human health and well-being. Metagenomics is the culture-independent genomic analysis of microbes using the next-generation sequencing technology, which has been known to play a pivotal role in unravelling the genetic information underlying the environment and human-associated microbiome. During my graduate research, I have focussed on assessing the functional roles of scalp and oral microbiome, which has revealed interesting findings. The comparison of healthy and dandruff scalp microbiome revealed a new potential role of bacterial commensals in supplying the host with nutrients essential for a healthy scalp. It also showed the high abundance of yet uncharacterised *Malassezia* sp. in the dandruff scalp, whose characterization seems to be imperative in designing novel anti-dandruff therapies. Additionally, a 16-weeks long time-course study was also performed, which suggested an apparent beneficial effect of coconut oil on the scalp microbiome. Among the various types of cancers, oral cancer ranks among the three most prevalent cancers in India, with Bhopal contributing the maximum number of cases per year, attributable to the exposure to risk factors such as tobacco consumption and lack of early-stage diagnosis. The oral microbiome of oral cancer patients in Bhopal was examined and compared to the healthy oral microbiome in tobacco-consuming and non-consuming groups. The results revealed drastic differences in the abundance of bacterial communities between the groups and showed significant associations between oral bacterial communities and oral cancer.

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**Keywords:** Metagenomics, Next-generation sequencing, Microbiome and Genomes.

**Evolutionary conservation and emerging functional diversity of the cytosolic Hsp70: J protein chaperone network in plants**

**Amit Kumar Verma**

**Supervisor: Dr. Chandan Sahi**

**Department of Biological Sciences**

**Accession No.: T00122**

**Abstract**

J protein are ubiquitous and among the most versatile chaperones found in all living organisms. They work with partner Hsp70s to perform a wide array of cellular functions, including a variety of stress associated and housekeeping chaperones functions. The Hsp70:J protein machines play important role in fine tuning the cellular protein quality control in all organism under normal as well as stress conditions. Compared to their Hsp70 partners, the number of J proteins has dramatically increased in eukaryotes including plants which underline the requirement of highly complex and robust Hsp70: J protein networks in different sub-cellular compartments. Although ubiquitous, the functional specificity and complexity of the plant Hsp70: J protein network has not been studied. Cytoplasm is the hub for most diverse cellular processes, thus requires efficient chaperone surveillance systems for the maintenance of the functional proteome. Consistent with this, the Hsp70: J Protein network is most complex in the cytosol. In this study, we made an attempt to map the cytosolic/nuclear J protein network in model plant *Arabidopsis thaliana*. We employed the yeast genetic tools and bioinformatic approaches to explore the functional conservation and evolution of cytosolic J proteins in *Arabidopsis*. We show that although the functional specificities of most plant J proteins are maintained across long evolutionary timescales, the Hsp70: J protein network in the *A. Thaliana* cytosol is incredibly complex. We identified plant J proteins that are involved in crucial cellular processes such as cellular protein quality control, endocytosis, translation, diphthamide biosynthesis, ribosome biogenesis and aggregate remodelling. Further, we also show that besides the number, regulatory differences, neo and sub-functionalization as well as combinatorial interaction between J proteins is further expanding the Hsp70: J protein networks in eukaryotes including plants thus resulting into unprecedented functionalization diversity of the Hsp70: J protein network.

**Functional Specificity of Caj1: a class II J Protein in *Saccharomyces cerevisiae***

**Neha Dobriyal**

**Supervisor: Dr. Chandan Sahi**

**Department of Biological Sciences**

## **Accession No.: T00120**

All living cells have a robust protein quality control ( PQC) machinery that ensures proper folding, stability as well as degradation of terminally mis-folded proteins. Molecular chaperones, especially the Hsp70: J protein system, along with the ubiquitin proteasome machinery play a central role in regulating cellular protein homeostasis. An equally robust surveillance system operates at the plasma membrane as well that affects proper sorting, folding as well as regulated endocytic degradation of membrane proteins. However, although plausible, a definitive role of the Hsp70:J protein machine in plasma membrane PQC is not known. Caj1, one of the cytosolic class II J protein in *Saccharomyces cerevisiae* was identified as a lipid binding protein using a nanodisrupt pull-down assay. Caj1 shows specificity towards phosphatidic acid and its lipid binding activity is important *in vivo*. We show that Caj1 regulates plasma membrane protein homeostasis. While a deletion of Caj1 mis-localizes membrane proteins to the vacuoles, a modest increase in cellular Caj1 levels stabilizes proteins in the yeast plasma membrane, suggesting specificity of Caj1 in regulating plasma membrane protein quality control (pmPQC). Additionally, Caj1 over-expression also resulted into cell cycle defects in budding yeast, a phenotype that was suppressed by co-over-expression of UB14. This suggests that dosage imbalance of Caj1 could be affecting turnover of cell cycle genes resulting into G2/M arrest. A whole genome dosage suppressor screen identified genes such as LOCI, ERG26, DOM34, HATI, ECM15 and MET14, which when co-over-expressed, suppressed the dominant phenotypes of Caj1, preliminary microarray analysis data suggest that Caj1 differentially regulates expression of various genes and a major chunk of these genes are related to ribosome biogenesis/functions. Put together, our results indicate that Caj1 is potentially involved in several pairwise interactions and could be involved in multiple functions, specifically the ubiquitin-mediated protein turnover pathway in *S. cerevisiae*.

**Keywords :** Chaperone, Hsp70, Hsp40, J protein, J-domain, Caj1, plasma membrane, proteostasis, membrane proteins, pseudohyphal growth.

## **Host miRNA suppresses H5N1 influenza virus replication by targeting host and viral gene**

**Ashish Kumar**

**Supervisor: Dr. Himanshu Kumar**

**Department of Biological Sciences**

## **Accession No.: T00114**

The highly pathogenic avian influenza A virus (HPAIV) pose a pandemic threat due to zoonotic transmission to humans. The high degree of genetic shift and reassortment has evolved the avian influenza virus in such a way that the virus acquired resistance against various anti-viral drugs and therapeutic antibodies. HPAI infection cause severe respiratory illness by progression of pneumonia in avian and mammalian host, including humans. From 2003-2017, H5N1 HPA1 has caused 453 human deaths from 859 cases reported leading to a high mortality rate of 52.74%. Recently, there had been increasing number of evidences that host encoding small non-coding RNAs (miRNAs) interact with the genome of RNA viruses and inhibit viral replication. Thus these miRNAs could prove to be a potential candidate for controlling viral replication via interaction with viral transcripta or genome. Here we show that expression of cellular miRNA, Mir-324- 5p downregulate in response to infection with RNA virus, H5N1. Also, mir-324-5p directly target the polymerase subunit PB1 of HN1 influenza virus in a sequence specific manner and degrades the viral RNA in host cells. Reduced expression of PB1 by miR-324-5p leads to severe reduction in HN replication. In addition, transcriptome analysis reveal that miR-324-5p enhance the expression of Type-I, Type-III infections, and interferons-inducible genes(ISGs) by targeting CUEDC2, the negative regulator of JAK-STAT pathway. Altogether, these findings highlights that miR-324-5p plays a crucial role in host defence against H5N1 by targeting viral PB1 and host CUEDC2 to inhibit H5N1 replication.

**Functional Insights into Genomes and Metagenomes through Integrative Omics and Machine Learning Approaches**

**Ankit Gupta**

**Supervisor: Dr. Vineet Kumar Sharma**

**Department of Biological Sciences**

## **Accession No.: T00113**

### **Abstract**

Recent advancements in high-throughput sequencing technologies have enabled us to access the genetic and functional information inherent in individual genomes and metagenomes. Several large-scale global efforts are underway for the characterization of genomes, and complex microbiomes such as the human gut microbiome, which plays a key role in the well-being of the host. The understanding of the human gut microbiome holds unprecedented potential in disease diagnostics and therapeutics. Colorectal carcinoma is one such disease which is associated with gut dysbiosis and its incidence is increasing in India. Hence, the taxonomic, functional and metabolic dysbiosis in colorectal carcinoma in the India population was examined using multi-omics approaches and potential microbial markers such as microbial genes and metabolites, which can be used for the early-stage detection of colorectal cancer were identified. However, the major bottleneck for any such large scale metagenomic analysis is the unavailability of efficient computational methods for functional analysis and also for the comparative analysis of healthy and diseased microbiomes. For this task, a unique tool ‘MP3’ using machine learning to predict and compare complete and partial pathogenic proteins from genomic and metagenomic datasets was developed. Similarly, ‘MicroTAXI’ was developed for the ab-initio taxonomic classification using proteome information of the genome. Another challenge was to recover assembled genomes from metagenomic data, for which a unique ‘Binning-Assembly’ approach for the reconstruction of bacterial and viral genomes from a fragmented pool of genome ‘metagenome’ was developed.

With the advent of next-generation sequencing technologies, sequences of thousand of genomes are revealed which also ensures to facilitate the identification of novel biofuel enzymes and greenhouse gas mitigating properties. Hence, a database ‘Biofuel1DB’ and prediction tool ‘Benz’ was constructed for enzymes involved in biofuels production, along with genome-scale metabolic modelling of methanotrophs for utilizing them as biofuels and to mitigate greenhouse gases. With the efficient and cost effective high-throughput sequencing technologies, Not only prokaryotic but also a large number of eukaryotic genome sequences are also increasingly becoming available. Hence, the genomic analysis of higher eukaryotes was carried out in which the main aim was to decipher the genomic clues underlying the unique phenotype of pracock using comparative genomics and evolutionary analysis.

**Structural and thermodynamic studies on metal binding proteins from Entamoeba histolytica**

**Rupali Yadav**

**Supervisor: Dr. Sunado Datta**

**Department of Biological Sciences**

**Accession No.: T00107**

## Abstract

The protozoan parasite, *Entamoeba histolytica* is a frequent cause of dysentery and liver abscess in humans with a major predominance in the developing countries. The invasive property of the parasite relies on its potential to kill the host cells and ability to degrade host extracellular matrix and metastasize to extra-intestinal tissues, such as liver. All these processes are crucial for the establishment of infection which begins with the adhesion of amoeba with the host cells. Hgl, heavy subunit of Gal/GalNAc lectin has been demonstrated to mediate amoebic adhesion to host cell via its carbohydrate recognition domain which could be further modulated by calcium binding. The ability of the parasite to degrade the host extracellular matrix depends on the secretion of the various cysteine proteases which is regulated by retromer complexes. Mammalian retromer is a peripheral membrane protein complex having two sub-complexes, a membrane recognizing SNX complex and cargo recognition Vps sub-complex which consists of Vps26, Vps35 and Vps29. The smallest subunit of sub-complex, Vps29 consists of the metallo-phosphatase fold. The role of metal in Vps29 is in quest; its metal binding mutants have been reported to affect the localization of the retromer complex in human cells. The present work is aimed to study the molecular basis of metal-binding and its functional consequences in (i) EhCRD, Carbohydrate recognition domain of Hgl and EhVps29, Vacuolar protein sorting 29.

In this study, we demonstrated that EhCRD is calcium-binding protein but not a C-type lectin. To further decipher the role of calcium in carbohydrate binding and host cell adhesion, biophysical and cell based studies were carried out. We further show that carbohydrate recognition domain of the lectin binds to calcium through DPN motif. Mutation of Calcium binding motif did not show any effect on the CHO cell adhesion to the amoeba but it completely abolishes its agglutination property. The results suggest that EhCRD Exhibits calcium dependent as well as independent properties.

We have also investigated the structural and functional implication of metal binding to EhVps29. We show that EhVps29 preferentially bind to zinc and is localized on the phagosomes in *Entamoeba histolytica*. Although the mutations at the metal I binding site in EhVps29 lead to reduction in affinity for zinc, its sub-cellular localization remains unaltered. We further show that the retromer mediated regulation of cysteine protease secretion is independent of the metal binding property of Vps29. The crystal structure of EhVps29 reveals that the metal coordination in EhVps is distinct from typical metallo-phosphatases and its mammalian homologs. Based on the crystal structure of wild type EhVps29, its complexes with zinc ion, single(D62A) and double mutant (D62A/H86A), we propose that

the metal positions are highly conserved and can be occupied with water in the absence of metal suggesting its importance in maintaining the structural integrity of the protein.

In conclusion , the present thesis described the differential role of metals in two metal binding proteins from the parasite which are implicated in its pathogenesis

**Study of DNA methylation-mediated regulation of PKM splicing in breast cancer**

**Smriti Singh**

**Supervisor: Dr. Sanjeev Shukla**

**Department of Biological Sciences**

## **Accession No.: T00106**

### **Abstract**

The cancer cells thrive on glucose by converting it to lactate at the end of glycolysis. The phenomenon is known as aerobic glycolysis or Warburg effect and promotes the growth of the cancer cells. The alternative spliced isoform Pyruvate kinase M2 (*PKM2*) contributes to the Warburg effect by promoting aerobic glycolysis whereas *PKM1* isoform promotes oxidative phosphorylation. The *PKM* gene contains two mutually exclusive exons, exon 9 and 10 which are alternative included in the final transcript to give rise to *PKM1* and *PKM2* isoform respectively. In this study, we report that the intragenic DNA methylation-mediated binding of BORIS (Brother of regulator of imprinted sites) at the alternative exon of Pyruvate Kinase (*PKM*) is associated with cancer-specific splicing that promotes Warburg effect and breast cancer progression. Interestingly, inhibition of DNA methylation or *BROIS* depletion of CRISPR/Cas9-mediated deletion of BORIS binding site leads to splicing switch from cancer-specific *PKM2* to normal *PKM1* isoform. This results in the reversal of Warburg effect and inhibition of breast cancer cell growth, which may serve as a useful approach to inhibit the growth of breast cancer cells. Importantly, our results show that in addition to *PKM* splicing, BORIS also regulated alternative splicing of several genes in a DNA methylation-dependent manner. Our findings highlight the role of intragenic DNA methylation and DNA binding protein, *BORIS*, in cancer-specific splicing and its role in tumorigenesis.

## **Essential Role of HCMV in Oncogenesis through Evasion of Host Innate Immunity**

**Puja Kumari**

**Supervisor: Dr. Himanshu Kumar**

**Department of Biological Sciences**

**Accession No.: T00105****Abstract**

Since the first knowledge of cancer in 2<sup>nd</sup> centuray, it has been a burden to affected individuals, their family and health care systems as well. Cancer is a multifactorial disease and virus-mediated carcinogenesis is one of the crucial factors, which is poorly understood. The DNA and RNA viruses both, are known to cause cancer, and together they contribute to 15-20% of all human cancers. Human cytomegalovirus (HCMV) is a human-herpesvirus and its structural components have been evidenced to be associated with cancer of different tissue origin, however role of HCMV in cancer remains unexplored. Here, HCMV deubiquitinase encoded by tegument protein pUL48, has been identified as playing a key role in carcinogenesis. Using deubiquitinase sufficient-and deficient-HCMV, it has been shown taht HCMV deubiquitinase is a key in inducing oncogenic properties through upregulation of several anti-apoptotic genes and dowbregulation of several pro-apoptotic genes. Further investigations revealed that HCMV-deubiquitinase acquires pro-tumor functions through inhibiting PRR-mediated type I interferon synthesis via deubiquitination of key signalling molecules of innate-immune pathway. This new role of HCMV deubiquitinase in inhibition of innate-immunity is found in accordance with deubiquitinases of many viruses and other HCMVproteins. Taken together, the results of my work suggest that HCMV infection may promote oncogenesis by inhibiting host innate-immunity and tha inhibitor for the viral deubiquitinases may help in combating virus-mediated oncogenesis.

**Biophysical Determinants of Transmembrane  $\beta$ -barrel Folding and Stability****Deepti Chaturvedi****Supervisor: Dr. R Mahalakshmi**

## **Department of Biological Sciences**

**Accession No.: T00104**

### **Abstract**

Transmembrane  $\beta$ -barrels are involved in a repertoire of functions such as membrane maintenance, small molecule and protein transport, bacterial virulence, and antibiotic resistance. The partitioning free energy of hydrophobic residues is believed to be important contributor of  $\beta$ -barrels stability. However, the molecular nature of these forces and the involvement of other factors such as protein-lipid interactions are poorly understood. With the Escherichia coli 8-stranded outer membrane protein X (OmpX) as our working model, we identify molecular factors that determine the folding and stability of transmembrane  $\beta$ -barrels. Particularly, we identify determinants of  $\beta$ -barrels folding at the residue level, examine strand contributions and study the importance/contribution of the lipid environment to  $\beta$ -barrels energetic.

Interface aromatics play an important role in the folding of membrane proteins. Using spectroscopic methods, we assign an anchoring role for Trp76 of OmpX in  $\beta$ -barrels folding. We also identify the importance of Trp140 in conferring global thermal and chemical stability of OmpX. Further, we deduce the folding pathway for  $\beta$ -barrels assembly. Based on these findings, we further investigated the importance of interface tryptophans on OmpX stability. We find that Tyr and Phe are favourable choices at the solvent-membrane interface and the transmembrane region respectively, for rapid folding of the OmpX barrel in both micelles and bicelles as well as for the post-folding  $\beta$ -barrels stability. Our findings contradict the evolutionary requirement (selection) of Trp at these positions, providing us with novel insight on why proteins with lowered stability were evolutionarily retained. In similar lines, we have deduced the dramatic influence of interface methionines on OmpX folding and stability.

Our findings showcase the dramatic influences of influence of interfacial Transmembrane as well as extra-membranous residues on the measured energetic of 8-stranded  $\beta$ -barrels.

**Keywords:** Outer Membrane Protein X, transmembrane  $\beta$ -barrels folding, membrane-solvent interface, kinetic stability.

**Molecular insights into the function of lysozyme domain of mycobacteriophage D29 peptidoglycan hydrolase**

**Himanshu Joshi**

**Supervisor: Dr. Vikas Jain**  
**Department of Biological Sciences**

**Accession No.: T00100**

## **ABSTRACT**

*Mycobacterium tuberculosis* (Mtb) has posed a grave threat to the global healthcare for decades. Although antibiotics have helped to curtail Mtb related fatalities, the emergence of drug resistant bacteria has warranted the search for newer potent drugs and therapeutics. Mycobacteriophages in this regards present a unique avenue for the development of new generation therapeutics. During the mycobacteriophage life cycles, concerted and timely action of three phage-encoded proteins viz. Holin, Lysin A, and Lysin B lead to the disruption of cytoplasmic memberane, cell wall, and outer mycolic acid layer of mycobacteria, respectively. This ultimately leads to host cell rupture.

In this study, we present an in-depth analysis of the structure relationship of the lysozyme domain (LD) of the *Mycobacterium* D29-encoded endolysin, Lysin A. LD demonstrates peptidoglycan hydrolaseactivity aganist both gram-positive *Micrococcus lysodeiktics* and Gram-negative E. Coli. We adopted a novel strategy to identify keyresidues involved in the activity of LD. Replacement of these residues with Ala or other amino acids results in loss of activity and/or stability. Interestingly, these residues were also found to be evolutionarily conserved. Thus we were able to successfully map the active site of the enzyme by *in vitro*, *in vivo* and in silico experiments and show how mutations affect the enzyme active site. Additionally, using LD protein, we have developed a novel method expedite the protein purification process from both high-throughput as well as large-scale culture. The protein of interest that is co-expressed with the LD can be easily isolated and purified from a large-scale culture.

We thus present LD as a potent candidate for developing phage-based broad spectrum therapeutics as well as a novel tool in recombinant DNA technology application.

**Keywords:** Mycobacteria, bacteriophage, endolysin, peptidoglycan, lysozyme, site-direkte mutagenesis, enzyme inactivation, recombinant protein, membrane permeabilization

**Regulation of Synaptic Morphogenesis and Function by membrane Deforming Proteins at the Drosophila Neuromuscular Junction**

**Bhagaban Mallik**

**Supervisor: Dr. Vimlesh Kumar**

**Department of Biological Sciences**

**Accession No.: T00096**

## **ABSTRACT**

Synapses are specialized junctions that allow efficient communication between neurons and their postsynaptic targets. During development, synapses undergo morphological differentiation which involves a change in the underlying cytoskeleton as well as membrane remodeling. Several signaling proteins have been identified which contain modules that can regulate cytoskeleton as well as induce membrane dynamics. Among these, Bin-Amphiphysin-Rvs (BAR) domain-containing proteins with their membrane deforming properties have emerged as key players in shaping up neuronal morphology. Very little progress has been made towards understanding the function mediated by the BAR family proteins and the signaling pathways still remain elusive. In this thesis, I have attempted to understand the role of BAR family proteins in the context of synaptic signaling.

Following an RNAi mediated genetic screening approach in *Drosophila*, led to the identification of one such protein, islet cell autoantigen 69 kDa (ICA69) protein which affects synaptic development at the neuromuscular junction (NMJ). Besides, this study also showed that *Drosophila* ICA69 colocalizes with  $\alpha$ -Spectrin at the NMJ and the conserved N-BAR domain of ICA69 deforms liposomes *in vitro*. Full-length ICA69 and the ICAC but not the N-BAR domain of ICA69 induces filopodia in cultured cells. Further, consistent with its cytoskeleton regulatory role, ICA69 mutants show reduced  $\alpha$ -Spectrin immunoreactivity at the larval NMJ. Manipulating levels of ICA69 or its interactor PICK1 alters the synaptic level of ionotropic glutamate receptors (iGluRs). Moreover, reducing PICK1 or Rab2 levels phenocopies ICA69 mutation. Interestingly, Rab2 regulates not only synaptic iGluR but also ICA69 levels. To summarize, the results from this study highlight the role of the ICA69 in NMJ organization through a pathway that involves PICK1 and Rab2, and Rab2 functions genetically upstream of ICA69 and regulates NMJ organization and targeting/retention of iGluRs by regulating ICA69 levels.

**Keywords:**

Neuromuscular junction, ICA69, BAR domain,  $\alpha$ -Spectrin, Rab2, Glutamate recept

**Development of Computational models and algorithms for designing of novel microbiome-based therapeutics**

**Ashok Kumar Sharma**

**Supervisor: Dr. Vineet Kumar Sharma**

**Department of Biological Sciences**

**Accession No.: T00089**

Our understanding of the human microbiome has enhanced significantly with rapid advancements in sequencing technology and availability of various computational tools. The population-specific difference in human microbiome due to diet, geographical location, age etc. Play a key role in determining human health and metabolism and the gut microbiome dysbiosis is often found to be associated with various metabolic diseases. Microbiome studies also suggest that differences in gut microbiome can drastically alter the therapeutic outcomes of ingested drugs, which is one of the reasons for their different responses in different individuals. Thus, a precise knowledge of the complete microbial potential is required such as identification of taxonomic, functional and metabolic biomarkers in a given microbiome, and prediction of the gut microbes, which can directly and/or indirectly affect the efficacy and toxicity of drug molecules. Therefore, development of highly accurate and robust computational approaches will be very helpful in determining the microbial insights from large-scale omics data.

To explore the microbial potential in an environment, an efficient and accurate taxonomic classifier named ‘16S Classifier’ and an orthology-based functional classifier named ‘Wood’ were developed. To study the association of microbes with critical diseases, 16S rRNA and metabolomic analyses were performed using fecal samples from patients of autism spectrum disorder and colorectal cancer. Furthermore, novel methods such as ‘HyPe’ for the identification of novel peptidoglycan hydrolases, and BioFin for the prediction of novel anti-microbial and anti-biofilm peptides/proteins, were developed for the identification and designing of novel alternatives to antibiotics. To understand the functional role of gut microbes and to predict the microbial enzymes responsible for the metabolism of xenobiotic/drug molecules, a novel approach ‘DrugBug’ was developed by integrating machine learning and

chemoinformatics approaches. The metabolism of FDA-approved drugs was predicted using DrugBug and the results were compiles as a comprehensive database. DrugBug predicted metabolism of amphetamine was validates using structural and experimental methods. Further, ‘ToxiM’ tool was developed to predict the toxicity of the metabolites. The above work provies novel machine learning-based tools for metagenomic analysis and provide new insights on the microbiome-mediated xenobiotic metabolism. Taken together, the developed methods and approaches would be very useful in designing novel and efeciecnt microbiom-based therapeutics.

**Implication of Budding Yeast as a Model Organism for Understanding the Chemical-Genetics and Functional Toxicogenomics**

**Upendar Rao Golla**

**Supervisor: Dr. Raghuvir Singh Tomar**

**Department of Biological Sciences**

**Accession No.: T00066**

Eukaryotes have their genome in the compacted form of chromatin. The dynamics in chromatin structure is facilitated by epigenetic modifications on both the DNA and histone proteins. These modifications are reversibly influenced by one's lifestyle and in response to a variety of environmental cues and stress, for modulating the gene expression at innumerable locations throughout the genome and thus to achieve cellular adaptation and survival. The unique genetic tools, high degree of conservation with more complex organisms, and modern genome-wide '-omics' approaches (transcriptomics/proteomics/chemogenomics) have implied budding yeast *Saccharomyces cerevisiae* as a privileged model organism for exploring the biological targets and mechanisms of action of pollutants and various bioactive molecules. In this thesis, I have focused on investigating the molecular targets and mode of action of Acrolein (using its precursor Allyl alcohol), a

very common environmental pollutant; Valproic acid (VA), a histone deacetylase inhibitor as well as an anticancer molecule; and KP1019, a lead ruthenium-based anticancer drug underway clinical trials using *S. cerevisiae* as a model organism through global transcriptomics and chemical genetics approaches. Genome-wide microarray analysis upon treatment with a sublethal dose of Allyl alcohol (AA), VA, and KP1019 has evidenced transcriptional regulation of the yeast genome significantly. Subsequent functional enrichment analysis of AA, VA, and KP1019 transcriptome revealed that the genes belonging to diverse cellular processes such as cell cycle, DNA damage repair, metal homeostasis, lipid biosynthesis and metabolism, stress response, ribosomal biogenesis, metabolism, macromolecules biosynthesis and metabolism, transcription regulation, meiosis, cell morphogenesis, and transport were regulated differentially. Furthermore, I have identified several new molecular targets that were required for Acrolein/AA, VA, and KP1019 tolerance through genetic screening approach. In particular, the detailed biochemical and genetic analysis of different pathways including redox homeostasis, DNA damage repair, cell wall integrity, metal homeostasis, lipid homeostasis, and gametogenesis that were targeted by these xenobiotics (Acrolein/AA, VA, and KP1019) have revealed their comprehensive mode of action. Notably, my findings also have established the role of histone tails in mediating Acrolein toxicity and suggested the use of both pyrazole and ethanol as probable antidotes

for AA intoxication. For the first time, my study findings demonstrated the reproductive toxicity of AA/Acrolein using the yeast gametogenesis (spermatogenesis) model. I have also revealed that VA exhibits its effect by modulating the MAP Kinase signaling, both mitochondrial and ER architecture and functions. Besides, I have also found that the effects of VA were neutralized in cells lacking lipid droplets. I have also demonstrated that KP1019 treatment induces the accumulation of neutral lipids (lipid droplets) in both the yeast and human (HeLa) cells. Furthermore, the comprehensive findings obtained in yeast have disclosed that the anticancer efficiency of KP1019 can be augmented by various metal ions, whereas neutralized by iron ion, reducing agents (GSH/NAC), osmotic stabilizer (sorbitol) and ethanolamine (precursor of the Kennedy pathway). I have also employed yeast synthetic histone H3/H4 library to identify critical histone residues required for potentiating or neutralizing the anticancer efficiency of KP1019. Altogether, these findings in budding yeast strengthened our current knowledge and facilitated the prediction of biomarkers for toxicity assessment, therapeutic targets along with their detoxification approaches. In summary, these studies favour the use of toxicogenomics and chemical-genetic approaches in yeast for investigating the mode of action of bioactive molecules, pollutants, and toxicants.

**Keywords:** Budding yeast, DNA damage repair, Epigenetics, Genetic targets, Stress response, and Transcriptomics.

**Biochemical characterization of histone H3 clipping by chicken liver H3 specific protease: Clipping is regulated by structure of histone H3 and inhibitor, stefin B**

**Sakshi Chauhan**

**Supervisor: Dr. Raghuvir Singh Tomar**

**Department of Biological Sciences**

**Accession No: T00061**

Structure of chromatin is highly dynamic as it has to allow interaction of various proteins to regulate DNA replication, transcription, repair, and recombination etc. There are various mechanisms which regulate dynamic nature of the chromatin such as DNA methylation, chromatin remodeling, histone post-translational modifications, histone variants and clipping of histone tails etc. The significance of ATP-dependent chromatin remodeling and post-translational modifications of histones is well established. However, the cellular function as well as regulation of proteolytic processing of histones is still not clear. Few studies have reported clipping of histone proteins in yeast, chicken and mammals. For example; Cathepsin L-dependent clipping of histone H3 occurs in mouse which is required for differentiation of stem cells. In chicken, glutamate dehydrogenase has been identified as a protease for age dependent clipping of histone H3 in liver and PRB1 in yeast.

Despite these studies, mechanism, substrate specificity and physiological significance of this epigenetic process are still not clear. We have studied the role of histone H3 and the inhibitor, stefin B in clipping of H3 by ‘chicken liver H3 specific protease’. We have further characterized the clipping sites in histone H3 and mechanism of inhibition by stefin B. By employing site-directed mutagenesis and *in vitro* biochemical assays, we have identified QVVAG region and C-terminus of stefin B protein to be very crucial for inhibition of the protease activity. In addition to stefin B, stefin A and cystatin C were found to act as weak and strong inhibitor, respectively. We also observed that ‘chicken liver H3 protease’ (Glutamate dehydrogenase) creates three distinct clipping sites in recombinant human histone H3. However, post-translationally modified histone H3 (isolated from chicken brain and *S. cerevisiae* wild-type cells) showed different clipping pattern. Furthermore the clipping activity was also found to be regulated by N-terminal tail and globular domain of histone H3. Altogether, our biochemical studies have revealed three distinct clipping sites in recombinant human histone H3 and their regulation by the structure of histone H3, histone modifications marks and stefin B. **Keywords:** Histone H3, stefin B, chicken liver H3 protease, histone clipping.

**Molecular insights into the structural stability and biological activity of T4 bacteriophage DNA polymerase processivity factor**

**Manika Indrajit Singh**

**Supervisor: Dr. Vikas Jain**

**Department of Biological Sciences**

**Accession No.: T00059**

The well-coordinated efforts of DNA polymerase (DNAP) and the accessory proteins result in the replication of DNA of an organism with high fidelity (errorless synthesis) and processivity (number of nucleotide added before ‘falling-off’). Although DNAPs inherently have high fidelity, they require sliding clamp protein to enhance their processivity. Sliding clamps are ring-shaped proteins that encircle DNA and function as DNA polymerase processivity factor. They are ubiquitously present in all living organisms. Notwithstanding their high significance, the molecular details of clamps pertaining to the factors contributing to their stability are presently lacking. Thus we chose to study one such clamp protein from T4 bacteriophage, gp45. gp45 is a homotrimeric molecule that not only assists in DNA replication, but also moonlights as a transcription factor.

In this study, we have carried out a detailed characterization of gp45 to understand the role of structural hallmarks and molecular interactions involved in stability and functioning of the protein. Several biochemical and biophysical tools have helped us discover that the two domains present in gp45 display asymmetric characteristics. While the C-terminal domain shows stability and rigidity, we find that the N-terminal domain is unstable and flexible, which probably confers easy loading and stability on DNA. Our findings explain how gp45 acts as a highly dynamic clamp whose stability is governed by subunit interface interactions. Tryptophan scanning mutagenesis experiments with gp45 allow us to conclude that the C-terminal domain of the protein undergoes a global conformational change while unfolding and adopts a molten globule state before complete denaturation. We demonstrate for the first time that protein’s molten globule state could be visualized on Blue-Native PAGE and could also be trapped *in vitro* under native conditions, thus opening avenues for studying on-pathway folding/unfolding intermediates.

Very interestingly, two domains display an intermolecular cross-talk that governs structural stability and biological activity in gp45. Furthermore, we were able to uncouple the two biological activities of gp45 – replication and transcription – by means of sitedirected mutagenesis; two of the mutations render

gp45 inactive for T4 phage late promoter transcription, whereas strand-displacement DNA replication ability remains unaltered. We believe that our data will help in understanding the clamps behavior at molecular level to use them as drug target to combat bacterial infections and cancer by directly targeting the DNA replication.

**Keywords:**

DNA polymerase processivity factor; protein stability; protein denaturation; circular dichroism (CD); fluorescence anisotropy; in vitro transcription; DNA replication; bluenative PAGE; dry molten globule; tryptophan scanning mutagenesis.

**Genetic Analysis of AP2 Adapter Function in Synaptic Transmission and Growth Signaling at the  
Drosophila Neuromuscular Junction**

**Saumitra Dey Choudhury**

**Supervisor: Dr. Vimlesh Kumar**

**Department of Biological Sciences**

**Accession No.: T00054**

Synapses are the sites of specialized contact between neurons. To sustain neurotransmission, synaptic vesicles (SVs) with their associated proteins must be recycled locally at synapses. Clathrin-mediated endocytosis which requires AP2 adapter is the most well studied form of endocytosis at synapses. The requirement of clathrin during intense nerve firing is however debatable due to the slower time scale of its recruitment. Defects in synaptic vesicle retrieval also lead to synaptic growth defects which is a consequence of aberration in growth signaling. Synaptic growth is an interplay of different molecular signaling events mediated by different pathways, viz. the Bone Morphogenetic Protein (BMP), Wnt and Mitogen Activated Protein (MAP) kinase pathways. Although significant progress has been made towards understanding these pathways, the cross talks among them still remain elusive.

This thesis describes the isolation and functional characterization of a Drosophila mutation that drastically altered synaptic development. This mutant was named *angur* and was mapped to  $\sigma 2$ -adaptin, the smallest sub-unit of the AP2 complex.  $\sigma 2$ -adaptin mutants exhibited prolonged synaptic fatigue under high frequency nerve stimulation indicating the requirement of this complex in regenerating synaptic vesicles during high frequency nerve firing. Besides, this study also showed that  $\sigma 2$ -adaptin is an obligate partner of the AP2 complex as evidenced by the reduction in synaptic levels of other sub-units of the complex and clathrin.  $\sigma 2$ - adaptin mutants also exhibited deregulated BMP and MAP kinase signaling. An important finding from this study is the severe reduction of a neuronal E3 Ubiquitin ligase, Highwire in  $\sigma 2$ -adaptin mutants. Further, the suppression of the mutant  $\sigma 2$ -adaptin phenotype by expressing various MAP kinase pathway components indicate that this signaling module is perturbed in the absence of AP2 mediated endocytosis. Interestingly, this work showed that *endo* and *synj* mutants have reduced Highwire levels, thus indicating a general underlying theme explaining the growth defects in these endocytic mutants. To summarize, the results from this study highlight the role of the AP2

complex in generating vesicles during high frequency nerve stimulation and uncovers the cross talk among signaling modules that regulate synaptic growth at the Drosophila neuromuscular junction.

**Key words:** angur, synapse, Drosophila, signaling, pMAD, Highwire

# **Molecular Regulators of Human VDAC-2 Scaffold Stability and Function Svetlana**

**Rajkumar Maurya**

**Supervisor: Dr. R. Mahalakshmi**

**Department of Biological Science**

**Accession No.: T00039**

The voltage-dependent anion channel (VDAC), aptly called as “governor of mitochondrial bioenergetics” is the workforce of mitochondrial transport. The elaborate tie-up of mitochondria with the apoptotic pathway makes VDAC a major player in regulating cell death. In the recent years, VDAC isoform-2 (VDAC-2) has gained considerable interest due to its anti-apoptotic behaviour, which contrasts the pro-apoptotic role of VDAC-1. While preliminary functional insight on the differences between the two isoforms is available, the differences at the molecular level that confer contrasting properties to two proteins that share > 75% sequence identity is not known. This study uses multifaceted biophysical techniques and carefully constructed mutant libraries to gain better access into the nature of protein-micelle and protein-protein interactions, channel activity, and barrel topology of human VDAC-2. Using the Cys-less mutant of hVDAC-2, we show the contribution of hVDAC-2 cysteines in promoting barrelinicelle interactions at the cost of barrel rigidity and channel activity. We demonstrate for the first time that the unique N-terminal 11-residue stretch is crucial to drive correct refolding of the barrel, and imparts scaffold stabilization and better voltage sensing. We also show that the N-helix itself is crucial for channel activity as well as for maintaining barrel topology and thermodynamic stability. Our findings have demonstrated the evolutionary relevance of the N-terminal 11-residues of hVDAC-2 in the context of cysteine conservation. Additionally, we show the importance of interfacial tryptophans in the stabilization of the hVDAC-2 barrel. Furthermore, using *in silico* approaches, we have shown that 16-C chain length lipid stabilizes the hVDAC-2 barrel. Our work represents a breakthrough in the field of mitochondrial porins and also contributes significantly to the hitherto poorly understood family of eukaryotic membrane proteins. Our findings will have immense implications in understanding mitochondria – membrane protein function and regulation, and will open newer perspectives on apoptosis.

**Keywords:** Scaffold Stability, Human Vdac-2, Thermodynamics, Cysteine Conservation and Anti-Apoptotic Behavior.

**Understanding the Molecular Basis of Holin-Mediated Bacterial Cell Death:  
Dissection of the Phage-Encoded Membrane Pore Forming Protein**

**Soumya Kamilla**

**Supervisor: Dr. Vikas Jain**

**Department of Biological Science**

**Accession No.: T00035**

Majority of the lytic bacteriophages have developed a holin-mediated lysis mechanism to release themselves from the host bacterium after multiplying in them. The bacterial lysis by the phage is a well planned and timely event that involves phage-encoded peptidoglycan hydrolase (endolysin) and a pore forming protein (holin). Holins are phage encoded small transmembrane proteins, which accumulate in the cell membrane and homo-oligomerize to form membrane lesions. These holes allow the phage-encoded endolysins to access the bacterial peptidoglycan resulting in its disruption leading to host cell lysis and virion release. The present study involves a detailed characterization of the D29 mycobacteriophage holin and the molecular mechanism of its functioning. Molecular dissection of gp11 that codes for holin, by making several deletions reveal that shortening of holin from its C-terminus results in diminished cytotoxicity and leads to smaller hole formation. Interestingly, the two transmembrane domains (TMDs) present at the Nterminus of holin are incapable of integrating into the cytoplasmic membrane and do not show toxicity. However, the fusion of two TMDs and a small C-terminal region that bears the coiled-coil motif result in restoration of the cell killing ability of the protein. We further show that the second TMD is dispensable in protein toxicity, since its deletion does not abolish holin-mediated cell death. We conclude that holin's C-terminal region is necessary but not sufficient for toxicity. These results shed light on a yet undiscovered role of holin's C-terminal region that will help in understanding the mechanism of holinmediated membrane perforation in mycobacteriophage. Our results also uncover the role of proline-glycine dipeptide motif in TMD1. Finally we were able to abolish the holin toxicity by carrying out Gly to Asp substitution in the putative loop region of the protein. We believe that our data obtained for holin will help us understand in greater detail this family of proteins.

**Keywords:** Cell Death, Peptidoglycan Hydrolase, Bacterial Peptidoglycan and Mycobacteriophage

# **Essential Role of Anti-Viral Innate Immune Pathways against Cancer**

**Sushil Kumar**

**Supervisor: Dr. Himanshu Kumar**

**Department of Biological Science**

**Accession No.: T00032**

RIG-I and MDA5 are RLR receptors recognize the virus and dsRNA analog polyIC to initiate a signaling cascade through IPS-1-IRF3-IRF7 signaling axis produces various cytokines to inhibit the viral replication. IPS-1, interferon promoter stimulator-1 (also known as MAVS, VISA, and CARDIF) is a single known adaptor molecule of RLR antiviral pathway. PolyIC transfection and Newcastle Disease Virus (NDV) infection (polyIC/NDV) are known to activate RLR receptors, which is being used in cancer therapy. However, the role of RLR/IPS-1 or its dependent type-I-Interferons in anticancer activity is poorly understood. Colony formation assay checked the anticancer activity of polyIC/NDV or transient expression of IPS-1 in various cell lines such as IMR32, MDAMB-231, MCF10A, and HEK293T, wound healing assay, cell death, invasion assay and anchorage-independent cell growth assay. To explore the molecular mechanism, we screened the change in expression of various apoptotic genes in shRNA- mediated knockdown of IPS-1, IRF3 and IRF7 in MDAMB-231 cells upon polyIC-transfection. PolyIC transfection and NDV infection up-regulate the apoptotic gene TRAIL and down-regulate the anti-apoptotic genes BCL2, BIRC3, and PRKCE to facilitate the death of cancer cells. Furthermore, stable knockdown of IPS-1, IRF3 or IRF7 in IFN-nonresponsive MDAMB-231 cancer cells show reduced the anticancer activity of RLR pathway. Collectively, our study suggests that antiviral pathway RLR/IPS -1 axis induces type-I-Interferons dependent extrinsic anticancer activity, as well as it induces intrinsic anticancer activity through upregulation of TRAIL and the down-regulation of the anti-apoptotic genes BCL2, BIRC3, and PRKCE. This basic knowledge can be translated to improve the efficacy of oncolytic virus and application of polyIC in cancer treatments.

**Keywords:** Anti Viral, Viral Replication, Polyic Transfection and Newcastle Disease Virus.

**Biochemical and X-Ray Crystallographic Studies on EhrabX3, a Novel Gtpase from  
Entamoeba Histolytica with Tandem G-Domains**

**Mintu Chandra**

**Supervisor: Dr. Sunando Datta**

**Department of Biological Science**

**Accession No.: T00028**

The enteric protozoan parasite, Entamoeba histolytica, the causative agent of amoebic dysentery, liver abscess and colitis, exploits its vesicular trafficking machinery for survival and virulence. Members of the Rab family of GTPases, with a single nucleotide binding G-domain, play a key role in the vesicular transport. EhRabX3, a catalytically inefficient amoebic Rab protein, is unique among the Ras superfamily of GTPases due to presence of tandem G-domains. A combination of biochemical and micro-calorimetric studies revealed that EhRabX3 binds to a single guanine nucleotide through its N-terminal Gdomain.Unlike most of the Ras super family members, the nucleotide dissociation from EhRabX3 is independent of Mg<sup>2+</sup>. EhRabX3 is extremely sluggish in hydrolyzing GTP and that could be attributed to its atypical nucleotide binding pocket. It harbours substitutions at two positions that confer oncogenicity to Ras due to impaired GTP hydrolysis. Engineering these residues to the conserved counterparts enhanced its GTPase activity by at least 20 fold. In contrast to the most of the Ras superfamily members, EhRabX3 lacks the prenylation motif. Indirect immunofluorescence and biochemical fractionation demonstrated that the protein is distributed all over the cytosol in amoebic trophozoites. In an attempt to understand how the individual GTPase domain influences the overall action of EhRabX3, the crystal structures of GTP-bound EhRabX3 and its fast hydrolyzing mutant in GDP-bound form have been determined at 2.8 and 3.1 Å resolutions, respectively. Consistent with the biochemical observations, only the Nterminal G-domain showed nucleotide bound to its active site. The crystal structure of EhRabX3 revealed how the two G-domains are oriented with respect to each other through a short linker. The structural differences at the conserved functional motifs due to unusual amino acid substitutions could possibly explain the low catalytic efficiency of EhRabX3. Viii Moreover, the existence of an intra-molecular disulfide bond between the Cys39 and Cys163 in EhRabX3 is found to be critical for maintaining the structural integrity and function of this unique Rab protein. Collectively this unique ancient GTPase exhibits a striking evolutionary divergence from the other super family members. Structure-guided functional investigation of cysteine mutants could provide the physiological implications of the disulfide bond and allow us to design potential inhibitors for the better treatment of intestinal amebiasis

**Keywords:** Crystallographic, Entamoeba Histolytica, Amoebic Dysentery and Liver Abscess.

**Host Mirna-Mediated Regulation of Antiviral Innate Immunity through Synergistic  
Regulation of RIG-I and Influenza Virus Replication**

**Harshad Ingle**

**Supervisor: Dr. Himanshu Kumar**

**Department of Biological Science**

**Accession No.: T00026**

Mammals have evolved to contain specialized receptors for sensing the invading pathogen. The cytosolic RIG-I-like receptors (RLRs), Retinoic-acid inducible gene-I (RIG-I) and melanoma differentiation gene 5 (MDA5) sense the RNA moiety of the viruses and initiates the innate antiviral responses through the production of type I and III interferons (IFNs) and inflammatory cytokines. The signaling through RIG -I is therefore tightly regulated to provide optimum innate immune responses for host defense. Several post-translational modification of RIG- I for regulation of antiviral responses has been reported, however, post-transcriptional gene regulation remains unclear. Non-coding RNAs such as microRNAs (miRNAs) are vital post-transcriptional switches responsible for dynamic changes in gene expression and fine tuning the biological processes including innate antiviral responses. Here we show that miR- 485-5p directly targets the host sensor RIG-I to suppress the antiviral response and enhance viral replication. Inhibition of miR-485 expression severely reduced the replication of Newcastle Disease virus and influenza virus (H5N1). Additionally, miR- 485-5p bound to H5N1 polymerase basic (PB)1 in a sequence specific manner, causing a severe inhibition in H5N1 replication. Furthermore, there exists a dose-dependent bi - specificity of miR-485; at low dose of H5N1 infection RIG -I is targeted whereas at a higher viral burden the target shifts to PB1. Such posttranscriptional gene regulation of RIG-I and inhibition of PB1 highlights the dual role of miR-485 in maintaining homeostasis and restricting influenza virus infection.

**Keywords:** Retinoic-Acid Inducible Gene-I, Influenza Virus and Disease virus.

# **Geometry and Impact of Cross-Strand Aromatic Interactions in Designed Beta-Hairpin Peptides**

**Kamlesh Madhusudan Makwana**

**Supervisor: Dr. R. Mahalakshmi**

**Department of Biological Science**

**Accession No.: T00024**

Understanding the fundamental principle behind how a linear polypeptide chain attains its compact three-dimensional structure is a basic question that has attracted interest with its increasing correlation to several diseases caused by protein misfolding, i.e., proteotoxic stress. The folded conformation of a protein is adopted and stabilized by physical forces such as hydrophobic, electrostatic and several covalent and non-covalent interactions. Design and study of synthetic peptides that adopt defined secondary structures can allow us to dissect such physical forces, in isolation. Of the non-covalent interactions among protein side chains, aromatic-aromatic interaction is a well-known mechanism for stabilizing the protein hydrophobic core. However, the mode and packing geometry of aromatic interactions, and consequences of spatial positioning of aromatic pairs on the structural scaffold and scaffold stability, is not clearly understood. Here, using synthetic peptides that adopt  $\beta$ -sheet and  $\beta$ -hairpin structures, extensive NMR and CD-based studies have been carried out on the nature, geometries and strengths of aromatic-aromatic interactions. This investigation has provided the new insight that the stabilizing role of aromatic interactions is dependent on its stereoposition, and less favoured geometries can be rescued by C- H...pi interactions. This has led to the identification of a novel strategy for capping peptide  $\beta$ -hairpins by the use of N-terminal D-amino acids. For the first time, a structure-reactivity relationship has also been identified for Trp-Trp cross-linking, with the cross-link resulting in the formation of highly thermostable stapled peptide  $\beta$ -hairpins and  $\alpha$ -helix. The findings from this study can serve as important selection criteria in the design of stable peptide bionanomaterials and in the design of novel peptide-based amyloid inhibitors. Particularly, the simplistic generation of stapled peptide  $\beta$ -hairpins and  $\alpha$ -helix can find versatile applications in peptide-based drug discovery, with the proposed strategy readily applicable to improving peptide bioavailability.

**Keywords:**  $\beta$ -sheet,  $\beta$ -hairpin,  $\alpha$ -helix, N-terminal and D-amino.

# **Role of small GTPase Rab21 in extracellular matrix invasion by *Entamoeba histolytica***

**Merlyn Emmanuel**

**Supervisor: Dr. Sunando Datta**

**Department of Biological Science**

**Accession No.: T00022**

Extracellular matrix invasion is a protease dependent function where cell movement is coupled with active protease secretion and subsequent cell body translocation which is marked by dynamic actin cytoskeleton reorganization. Matrix remodeling and invasion can be observed in the single-celled protozoan parasite, *E. histolytica* during host tissue destruction in severe cases of infections and during the development of multicellular organisms. It is also an established hallmark of cancer metastasis. Invasion is a complex process where cells migrate in response to various extracellular cues that can be in the form of the extracellular matrix (ECM) itself, or growth factors (GFs). These cues are sensed with the help of cell surface receptors, such as integrins and growth factor receptors (GFRs), respectively. During cancer metastasis, tumor cells extensively degrade the surrounding ECM. This degradative capacity is by virtue of actin rich ventral, protrusive structures called "invadosomes." They act as focalized secretion ports for matrix metalloproteinases (MMPs) and activity hubs for integrins and GFRs. Together, these surface molecules alter a battery of intracellular signaling cascades leading to sustained cell migration and invasion. Therefore, the spatiotemporal distribution of MMPs and integrins during cell invasion is tightly regulated. The details of the route followed by these molecules are still elusive and hence pose an open question in the field. In the recent past Rabs, master regulators of vesicular trafficking in eukaryotes have taken the center stage as they are up-regulated in different cancers and regulate the trafficking of MMPs and integrins during the process of invasion. We have tried to decipher the role of Rab5 subfamily of protein, Rab21 in matrix invasion. We have used *E. histolytica* as our preferred model systems and employed various tools like quantitative cell-based imaging, siRNA mediated knock down and in vitro invasion and matrix degradation assays to address our question.

**Keywords:** Extracellular Matrix, Histolytica, Growth Factor and Metalloproteinases.

# **Interplay of Rab7 Gtpase and SNX Proteins in Retromer Mediated Endosomal Sorting**

**Amulya Priya**

**Supervisor: Dr. Sunando Datta**

**Department Of Biological Science**

**Accession No.: T00021**

The endosomal protein sorting machineries play vital roles in diverse physiologically important cellular processes such as cell to cell signalling, nutrient uptake, immune response, autophagy and many other phenomena. Many of the core membrane sorting apparatus is conserved in evolution, for example, the retromer complex. Retromer plays an instrumental role in maintaining an active pool of trans-membrane receptors in the Golgi by recycling them from endosomes. The defect in the recycling process results in the degradation of the receptors in the lysosomes or its increased localization to the cell surface and thereby resulting in a range of neurodegenerative disorders. The retromer mediated function depends on its recruitment from the cytosol to specific endosomal domains. Thus, the present study aimed at deciphering the molecular mechanism of the recruitment of the retromer complex which would significantly aid our understanding of the underlying endo-lysosomal dynamics and associated disease phenotypes. The retromer complex is composed of two distinct sub-complexes, a membrane recognizing, Sorting Nexins (SNX) complex and a cargo recognizing, Vacuolar protein sorting (Vps) complex (Vps35/Vps26/Vps29). The core retromer Vps sub-complex does not have intrinsic membrane binding ability and therefore relies on the association with sorting nexins or the interaction with small GTPase, Rab7 for the endosomal recruitment. The goal of this study was to investigate the role of the individual Vps components in Rab7-mediated recruitment of the core retromer trimeric complex. Here, by in vitro biophysical measurements we showed direct interaction of Rab7 with Vps35 and Vps26. We elucidated a novel mechanism in which Vps26 and Vps35 directly interact with small GTPase Rab7 in a cooperative manner to recruit retromer to late endosomes. In this study, we attempted to identify the spatio-temporal involvement of SNX family members in the recruitment of the core retromer trimeric complex along the endosomal maturation pathway and their implication in endosome to Golgi retrieval of cation independent mannose-6-phosphate receptor involved in the sorting of acid hydrolases to lysosomes. Here, we have used RNAi based loss of function screen to identify the novel sorting nexins involved in this process. Using this screen, we identified two proteins, SNX12 and SNX32 that when suppressed induced a phenotype similar to that observed upon suppression of known retromer components.

**Keywords:** Signalling, Nutrient Uptake, Immune Response, Autophagy and Sorting Nexins.

**Dissection of Phage Endolysin: Molecular Insight into The Function And Regulation Of  
Mycobacterium Phage Peptidoglycan Hydrolase**

**Amol Arunrao Pohane**

**Suprvior: Dr. Vikas Jain**

**Department of Biological Science**

**Accession No.: T00014**

Mycobacterium tuberculosis has always been recognized as one of the most successful pathogens known to mankind. With the emergence of drug resistant bacteria, the need of the hour is to discover alternative mechanism to restrict the growth of this organism. Mycobacterium phages, or more commonly termed as mycobacteriophages, in this regards serve as wonderful option and a detailed study of the mechanism employed by thesis agents. Upon infection, mycobacteriophages produce lysins that catalyze bacterial cell wall peptidoglycan hydrolysis and mycolic acid lyer breakdown of the host resulting in bacteril cell reture and virus release. It is this property of lysins that makes them extremely significant. We have carried out a detailed molecular dissection of mycobacteriphage D29 lysine in order to gain insight into the function and regulation. By constructing several versions of the protein, we show that the D29 lysin harbours two catalytic domins in its N-terminal region and a cell wall binding domain at its C-terminus. While the catalytic domains are active in E. coli, the wild type protein is seen to be inactive. Our data suggest that the inactivity in the protein is ensued by the C-terminal cell wall binding domain that interacts with the N-terminal region. This interaction occurs intramolecularly and is mediated by a stretch of amino acids present between the domains. Our experiments have also demonstrated that the cell wall binding domain binds specifically with the M. smegmatis and M. tuberculosis cell wall peptidoglycan. We believe that the knowledge obtained from our experiments with D29 Lysin A will immensely help in the bioengineering of endolysins with narrow or broad spectrum antimicrobials efficacy.

**Keywords:** Endolysin, Lysin, Mycobacteriphage and Drug Design.

**Identification of Sen1 as Regulator of Stress Response in *Saccharomyces Cerevisiae***  
**Vikash Singh**

**Supervisor: Dr. Raghuvir Singh Tomar**

**Department of Biological Science**

**Accession No.: T00013**

Diverse phenotypes are shown by an organism when they face environmental stresses. These phenotypes are the result of activation of several stress response pathways leading to the expression or repression of various genes. The yeast *Saccharomyces cerevisiae*, an organism that permits genetic manipulations, has become a model to study how eukaryotic cells respond to stress at the molecular level. The relative simplicity of studying cellular functions in yeast combined with its relevance to higher organisms makes it a very powerful “model organism” for study. This thesis reports the identification of Sen1 a RNA/DNA helicase in *Saccharomyces cerevisiae*, as a regulator of stress response. We demonstrated the role of Sen1p and the cell wall integrity (CWI) signalling pathway in expression of flocculation genes; FLO1, FLO5, FLO9, and FLO10. We have shown coordination among Sen1, RNA processing and degradation machinery in the expression of Flo genes. We have reported role of CWI signalling pathway in the basal level expression of Flo genes. We have also reported that Sen1p regulates the expression of ribonucleotide reductase RNR1 gene, suggesting that Sen1p is required for cell protection against DNA damage. This thesis also reports the identification of biological pathways targeted by the anticancer drug KP1019. KP1019 comprise a class of ruthenium compounds having promising anticancer activity. Our results revealed that, KP1019 evicts histones from mononucleosome and interacts specifically with histone H3. We have also shown that KP1019 treatment causes induction of RNR genes and degradation of Sml1p. We have found that KP1019 causes dose dependent cell arrest in the S-phase of cell cycle. Furthermore, we have demonstrated for the first time that the yeast mitogen activated protein (MAP) kinase Hog1 is essential for the cells in response to KP1019. In summary, KP1019 targets histone proteins, with important consequences for DNA damage responses, epigenetics and Hog1 pathway. In brief, our work on *S. cerevisiae* strongly suggests that these reports can be deduced to understand the stress response pathways in higher eukaryotes including mammalian systems.

**Keywords:** *Saccharomyces Cerevisiae*, Drug Design, *Saccharomyces Cerevisiae*, Cell Protection and Deoxyribo Nucleic Acid.

**Genetic and Genomic Studies to Understand the Stress Response in Budding Yeast**

**Saccharomyces Cerevisiae**

**Gajendra Kumar Azad**

**Supervisor: Dr. Raghuvir Singh Tomar**

**Department of Biological Science**

**Accession No.: T00006**

To survive from the environmental challenges, cells have developed different mechanisms to sense the external stimuli and convert them into appropriate cellular response. The yeast *saccharomyces cerevisiae*, an organism that permits genetic manipulations, has become a model to study how eukaryotic cells respond to stress at the molecular level. Studies in yeast have discovered multiple transcriptional regulatory proteins that mediate tolerance to stresses. We have simulated stress in yeast cells, either genetically or pharmacologically, in an attempt to elucidate the mechanisms involved in the cell's response to stress conditions. This thesis reports the role of yeast transcription factor Rap1 in the maintenance of cell wall homeostasis. Previously, Rap1 was shown to be the key transactivator of over 300 co-regulated genes, including the ribosomal protein and glycolytic enzyme-encoding genes. Our present work extended the earlier observation by identifying the cell wall stress response genes as the novel target of Rap1. Moreover, this thesis also reports the characterization of histone H3 clipping protease under the nutritional starvation (sporulation phase). While attempting to identify H3 protease we also noticed for the first time the presence of h2a proteolytic activity in yeast. Additionally, we have also studied the stress response triggered by yeast cells upon treatment with several pharmacological agents including curcumin, ebselen, chloroquine and isocyanates. We have used *in vivo*, *in vitro* as well as biochemical and genetic methods to identify the pathways targeted by these agents. Our experimental evidence indicates that exposure of these agents to yeast cells triggers alteration in chromatin structure and function, redox homeostasis, cell wall structure and osmotic balance, additionally, similar kind of response was also observed in human cells. In summary, our work on *S. cerevisiae* strongly suggests that these observations can be summary to understand the stress response pathways in higher eukaryotes including mammalian systems.

**Keywords:** Genetic, Genomic, Redox Homeostasis, Pharmacological and Curcumin.

# **Identification and Characterization of Histone H3 Tail Clipping Protease**

**Papita Mandal**

**Supervisor: Dr. Raghuvir S. Tomar**

**Department of Biological Science**

**Accession No.: T00005**

Chromatin is a dynamic structure that responds to different stimuli to regulate fundamental biological processes such as DNA replication, transcription, recombination, etc. To promote all these DNA dependent metabolic processes, chromatin undergoes different types of epigenetic alterations such as exchange of DNA methylation, incorporation of histone variants in nucleosomes, chromatin remodelling, post translational modifications of histones including proteolytic processing of histone tails. Evolutionary conserved histone proteins play a very important role in the regulation of eukaryotic gene expression by undergoing post translational modifications within the tail regions. Clipping of histone tails has been reported in several organisms. However, the significance and regulation of histone tail clipping in tissue-specific gene expression and development remain unclear. I have studied *in vivo* tissue-specific and age-dependent clipping of histone H3 tail in adult chicken liver. By utilizing different biochemical approaches I identified glutamate dehydrogenase (GDH) as the H3 specific protease from liver tissue extract. Edman sequencing revealed that GDH cleaves H3 at two distinct sites between K23-A24 and K27-S28. Free H3 is more preferred substrate of GDH compared to nucleosomal H3. The nuclear and ER-associated monomeric GDH is responsible for the protease activity, whereas, the mitochondrial matrix-associated homohexameric GDH does not show clipping. H3 protease activity of GDH is regulated by different factors such as, conformational changes in GDH, chromatin conformation, histone tail modifications and a cysteine protease inhibitor stefin B. An unanticipated outcome of this study was the implication of GDH in an epigenetic process with which it had never been known to be associated. The correlation of this epigenetic mark as well as its modifier with aging will eventually lead to better understanding in the regulation of gene expression during development, aging, and age associated diseases.

**Keywords:** Chromatin, Epigenetic Alteration, Histone Tail Clipping, H3 Protease, Glutamate Dehydrogenase and Stefin B.

**Department of Chemistry**

# **N-heterocycle synthesis and remote functionalizations via Pd-catalysis**

**Gaurav Saini**

**Supervisor: Dr. Manmohan Kapur**

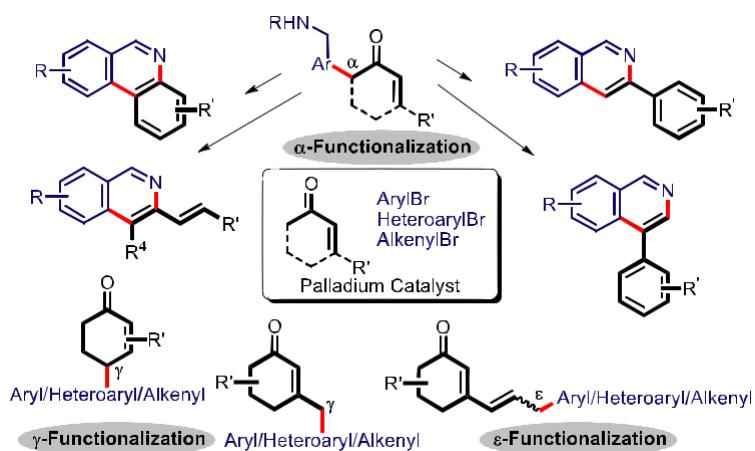
**DEPARTMENT OF CHEMISTRY**

**Accession No.: T00148**

## **Abstract**

A cross-coupling reaction is one of the fundamental organic transformations in which two or more fragments are joined together with the aid of a transition metal catalyst. Transition metal-catalyzed  $\alpha$ -arylation of enolizable carbonyl compounds is a versatile reaction of tremendous synthetic utility. This reaction belongs to a rare class of cross-coupling reactions that form a  $sp^2$ - $sp^3$  C-C bond.<sup>1</sup> Isoquinolines are one of the most significant scaffolds in natural products, material sciences, paints, and dye industries. We developed a two-step, one-pot methodology in which different classes of isoquinolines and phenanthridines have been accessed with the regioselective palladium-catalyzed  $\alpha$ -arylation of silylenol ethers of enones, ketones, and aldehydes followed by acid-mediated deprotection, annulation, and aromatization.<sup>2</sup>

Apart from proximal functionalization, remote functionalization *via* the formation of a C-C bond is one of the most challenging aspects of synthetic organic chemistry.<sup>3</sup> Biologically relevant molecules or pharmaceutical drugs can be derived from commercially available sources by carbon–carbon bond formation *via* remote functionalization. Recently we have developed a remote functionalization strategy with the utilization of palladium-catalyzed  $\gamma$ - and  $\varepsilon$ -arylations of silyl-dienol and trienol ethers of unblocked enones and  $\pi$ -extended enones.<sup>4</sup>



# Lysine Directed Single-Site Precision Engineering of Native Proteins

Dattatraya Gautam Rawale

Supervisor: Dr. Vishal Rai

**DEPARTMENT OF CHEMISTRY**

**Accession No.: T00149**

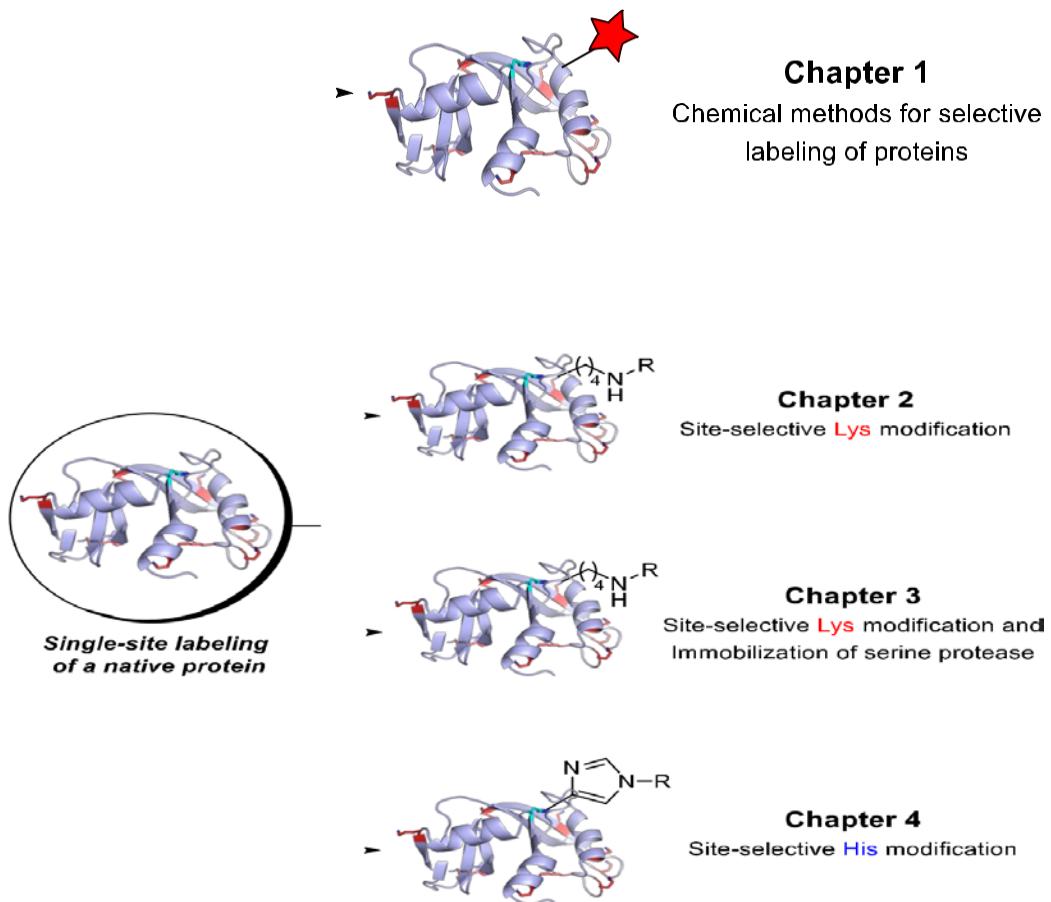
## Abstract

Proteins are outstanding biomolecules with remarkable diversity in their structure and function. Chemical methods for protein modification and attachment of synthetic probes enable the understanding of these attributes. The single-site labeling of proteins with engineered unnatural amino acids, peptide fragments, or recognition motifs for enzymes is highly remarkable. However, this technology does not apply to a large segment of the proteome. Recently, chemical methods for the decoration of native proteins have drawn more attention. Mostly, these methods are incapable to deliver selective protein labeling. Rarely, low-frequency residues such as cysteine, tyrosine, and tryptophan have allowed chemoselective labeling. The N-terminus  $\alpha$ -amine have also rendered a few ingenious methods. Outside N-terminus, Protein-ligand interaction direct labeling has been able to inspire partial success. Chemical platforms that can enable precise single-site labeling of native proteins would have to defy long-standing dogma about their lack of selectivity. On the brighter side, they hold immense possibilities if we can resolve the associated challenges. In this direction, we invested a systematic effort and developed chemical methodologies that enable chemoselective and site-selective labeling of native proteins.

During my doctoral research (Chapters 1-4), I have explored the development of new chemical methodologies for site-selective labeling of native proteins and monoclonal antibodies (mAbs). We solved the challenges related to chemoselectivity, and site-selectivity. In this process, we developed a *residue-specific methodology* for the labeling of *N-terminus Gly* of proteins. The remarkable efficiency and N-Gly selectivity remain undeterred even with a complex mixture of proteins derived from cell lysates. Further, we developed the linchpin directed modification (**LDM<sup>TM</sup>**) for single-site labeling of native proteins. The LDM platform enables modular *single-site labeling of a His residue*. Moreover, it allows us to label a residue irrespective of its position in the reactivity order. Later, we extended the LDM technology to address the single-site targeting of a high-frequency Lys residue. The mild physiological reaction conditions of LDM empower it for the engineering of proteases, an enzyme with high self-degradation propensity. It

delivers single-site ordered immobilization of a serine protease to give enhanced thermal stability, reduced auto-digestion, and recyclability. Besides, we learned that the chemoselectivity of an electrophile is a non-conserved parameter in protein chemistry. However, such promiscuous electrophiles can be regulated through proximal control to render the precision engineering of proteins. The functional group installed during bioconjugation opens the potential for bio-orthogonal late-stage transformations. A few examples include the installation of an affinity tag, NMR tag, fluorophore, and toxins. These chemical technologies are operationally simple and deliver analytically pure single-site tagged proteins/mAbs. Further, we demonstrated that the LDM platform provides homogeneous antibody-drug conjugates (ADCs). These ADCs exhibit highly selective anti-proliferative activity towards the breast cancer cells and compares well with Kadcyla, an FDA approved drug.

**Keywords:** Protein, Chemoselective, Site-selective, Residue specific, Linchpin, immobilization



**Organocatalytic Asymmetric Construction of Benzospiroketal, Benzodiquinane and Benzospirononane**

**Abhisek Midya**

**Supervisor: Dr. Prasanta Ghorai**

**DEPARTMENT OF CHEMISTRY**

**Accession No.: T00143**

**Abstract**

**Organocatalytic Asymmetric Construction of Benzospiroketal, Benzodiquinane and Benzospirononane**

**Abhisek Midya**

**Supervisor: Dr. Prasanta Ghorai**

**DEPARTMENT OF CHEMISTRY**

**Accession No.: T00143**

**Abstract**

Organocatalysis prevails the asymmetric synthesis over the last decade onwards, beginning with iminium-enamine catalysis and continuing the development at its full phase, with bifunctional H-bonding catalysis. Regardless of many advanced name reactions, Michael reaction (carba-/oxa-Michael) receives the attention of synthetic chemist, in the way to construct complex cyclic cores resembling natural scaffold. In this talk, I will introduce keto tethered ortho-formyl chalcones and its other variants as substrates, emerging with new reactivity to formulate the key fused- and spiro-cyclic substructures. Here, I am mainly going to focus on discussing, the asymmetric oxa-/carba-Michael strategies for the construction of benzospiroketals, benzodiquinane, and benzospirononane using both bifunctional H-bonding and iminium-enamine catalysis which provided an excellent enantio- and diastereoselectivity of the oxa-/carba-cycles. The detailing starts with benzospiroketal synthesis using alkoxyboronate spiroketallisation and oxa-Michael reaction of peroxy hemiacetals. Next, the synthesis of

benzodiquinane and benzospirononane, containing multiple stereocenters one of which is an all-carbon quaternary stereocenter, have been developed using reductive carba-Michael addition cascade.

**Keywords:** Iminium-enamine catalysis, bifunctional hydrogen bonding catalysis, Michael reaction (carba-/oxa-Michael), keto-tethered ortho-formyl chalcones, all-carbon quaternary stereocenter, oxa-spirocycles, spiro- and fused carbacycles.

**Annulative  $\pi$  -Extension ( APEX) with Metal-N-Heterocyclic Carbene  
Templates: A Unique Strategy toward New Classes of Cationic Polycyclic  
Heteroarenes**

**Champak Dutta**

**Supervisor: Dr. Joyanta Choudhury**

**DEPARTMENT OF CHEMISTRY**

**Accession No.: T00142**

**Abstract**

Beyond the well-known unique ligand property of metal-templated NHCs (NHC = N-heterocyclic carbene), a new facet of these species has been revealed recently and found to be of significant interest in catalysis and materials research. This new aspect features unprecedented chemistry of Rh-NHC backbone which was made active in *catalytic intermolecular annulation* of imidazolium motifs with internal alkynes leading to the synthesis of a variety of highly conjugated, cationic and annulated organic molecules.

Based on the above background, the primary aim of the present thesis work was to address the quest of (a) new class of '*azolium*' substrates suitable for above strategy, (b) new annulation pattern suitable for variable optoelectronic property of the products, and

= new catalyst system conducive for such type of challenging annulation reactions. The first question is successfully addressed *via* demonstrating the Rh(III)-catalyzed annulation strategy on N,S-heterocyclic carbene (NSHC) motifs accessed from

thiazolium compounds, thus forming a new class of doubly doped thiazoloquinolinium scaffolds with tunable fluorescence and electronic properties. Next, an interesting bimodal ‘*rollover annulation*’ pattern was developed using heteroaryl-imidazolium motifs with the Rh(III) catalyst system showing annulation *via* reductive elimination and alkenylation *via* protodemetalation process. Finally, a new alternative catalyst system based on Co(III) replacing Rh(III) was discovered, which was found to catalyze an interesting C–N annulation pattern *via* the involvement of unprecedented ‘protic-NHC–Co(III)’ templates.

**[Key words:** *N-Heterocyclic carbene, C–H bond activation, annulation, rollover, mechanistic investigation, protic NHC]*

## **Unravelling the Role of Polymorphism and Interaction Topology towards a Quantitative Assessment of Intermolecular Interactions in Molecular Crystals**

**Subhrajyoti Bhandary**

**Supervisor: Dr. Deepak Chopra**

**DEPARTMENT OF CHEMISTRY**

**Accession No.: T00141**

### **Abstract**

This thesis highlights the crucial role of different competitive and cooperative intermolecular interactions in promoting the structural diversity in crystalline molecular solids and their properties. In particular, the occurrence of multiple crystalline phases of any given molecule (polymorphs), including crystallization with guest solvent molecules (solvates), having distinct physicochemical and material properties are observed to tune the structure–function relationships at the molecular level.

The extensive crystallization screening in a library of small molecules containing halogenated *N*-ethynylphenylbenamides has resulted in the formation of different crystal polymorphs, and solvates of the unique guest hexafluorobenzene. In the current work, the dynamic nature of crystal polymorphism was evaluated in terms of *single-crystal-to-single-crystal* polymorphic phase transition induced by hydrophobic silicone oil and rapid desolvation of the guest solvent hexafluorobenzene in various fluoro-substituted compounds. The inclusion chemistry of various substituted *N*-ethynylphenylbenamides host was also explored based on the features of host–guest stacking interactions. Furthermore, nanoindentation study was performed to understand the role of structure on the observed mechanical properties (hardness and elastic modulus) in the crystalline polymorphs of *meta*-fluorinated *N*-ethynylphenylbenamide and the solvates of two biologically promising dihydropyrimidine analogues. Finally, the obtained crystal structure landscape of the unsubstituted molecule, namely, *N*-ethynylphenylbenamide, was experimentally mapped through the method of chemical modification of the parent compound and the device of polymorph formation. The solid-state structural landscape was further investigated with inputs from the quantitative analysis of the interaction topological landscape via the approach of energy frameworks, which was also validated through the method of crystal structure prediction.

**Precision in modification and analysis of proteins by targeting amine and carboxylic acid**

**Rohith Singudas**

**Supervisor: Dr. Vishal rai**

**DEPARTMENT OF CHEMISTRY**

**Accession No.: T00140**

**Abstract**

The post-translational modifications of biomolecules such as acylation, phosphorylation and methylation are used by nature in regulating key functions like signaling, trafficking, and other biological processes. This inspires chemists in driving the development of technologies with a predictable and coordinated modification of natural processes. The recombinant proteins with mutated reactive motifs or point mutations have also strengthened the site-specific functional diversification. Single-site labeling has mostly been dependent on the chemoenzymatic methods, site-directed mutagenesis and amber codon suppression. In recent years, a few chemical methods were developed for single-site installation of probes in a native protein. But, despite the vast progress in the field of bioconjugation chemistry, scientists still face many challenges for the development

of complementary reactions for the site-selective chemical modification of proteins that are mild, efficient, and robust. A chemical technology that can deliver single-site labeling of endogenous proteins would be ideal to meet these requirements. The challenge in the identification of a site with unique reactivity emerges from the abundance of functional groups with similar reactivity. It is complicated further by the presence of multiple copies of each residue. Additionally, chemical labeling of the protein requires experimental conditions that would not perturb the structure and function of a protein.

This thesis details my efforts toward the chemical methodologies for selective modification of the amine and carboxylic acid residue and their unambiguous characterisation in native proteins. In chapter 1, In this regard, we have developed a phthalimidation protocol that addresses the above challenges and delivers single-site modification of N-terminus  $\alpha$ -amine. The tunable reactivity of the amphoteric intermediate under mild reaction conditions is the key to success. In chapter 2, we developed a method for single-site modification of carboxylic acid. Contrary to amine, it is a daunting task to achieve even chemoselectivity in this case. We developed a strategy that re-defines the reactivity landscape of protein to enable the single-site labeling of carboxylic acid. Here, the functional group participates in a multi-component reaction sequence where both intramolecular and intermolecular irreversible pathways can deliver the desired product. This chemical platform allows the single-site installation of the  $^{19}\text{F}$ -NMR probe and a fluorophore.

The lack of unambiguous characterization tools for protein bioconjugates has been one of the bottlenecks in the field. In chapter 3 to address this, we developed the analytical sensitivity booster that enhances the peptide detection up to attomolar

concentration in mass spectrometry (MS). In turn, it allows a remarkable improvement in peptide mapping. Also, it delivers simplified and enhanced

detection of peptide fragments in the MS-MS. Overall, it provides a tool for thorough analysis of proteins, antibodies, and their bioconjugates.

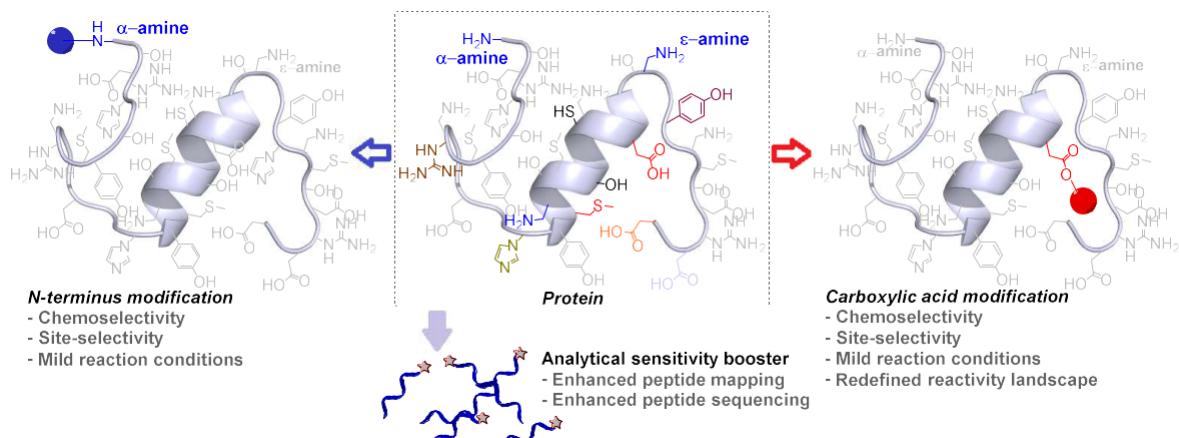


Figure. Reactivity, selectivity, and analysis of proteins.

Chapter 1: Selective methods for amine and carboxylic acid labeling of proteins and their analysis

Chapter 2: A phthalimidation protocol that follows protein defined parameters

Chapter 3: Single-site labeling of carboxylic acid in native proteins through a switchable multicomponent reaction

Chapter 4: Sensitivity booster for mass detection enables unambiguous analysis of peptides, proteins, antibodies, and protein bioconjugates

**Transition metal-based Porous Heterogeneous Electrocatalysts for Oxygen Evolution Reaction**

**Priyajit Jash**

**Supervisor: Dr. Amit Paul**

**DEPARTMENT OF CHEMISTRY**

**Accession No.: T00135**

**Abstract**

This thesis work is directed towards the fabrication of first row transition metal-based nanomaterials and their electrocatalytic enhancement for water oxidation (WO). This thesis is divided into seven chapters.

**Chapter 1** introduces the current scenario of global energy crisis and the sustainable hydrogen fuel production towards the clean energy storage using renewable energy sources like water splitting. It focused on the oxygen evolution reaction (OER) which is the main bottleneck in controlling the energy efficiency of hydrogen production, featuring its complexity and slow kinetics for overall water splitting. Thus a literature overview for the design of various catalysts fabrication and their catalytic performances for the enhancement of OER reaction rates have been discussed. At the end, scope of the thesis was emphasized wherein new approaches have been proposed to improve the catalytic efficiency.

**Chapter 2** discusses the experimental and characterization techniques along with the significance of several OER activity parameters.

**Chapter 3** discusses the synthesis of new precatalysts, cobalt phosphonates (**CoOP**) for electrocatalytic WO by utilizing a novel tetra-constituent assembly of  $\text{CoCl}_2 \cdot 6\text{H}_2\text{O}$ , nitrilotris (methylene) triphosphonic acid (NMPA), pluronic F127 surfactant as soft template, and polyvinyl alcohol (PVA) as co-surfactant. The **CoOP** spheres consist with two distinct types of pores. Morphological studies like transmission electron microscopy (TEM) revealed the formation of large nanocages in the spheres (pore diameter: 20–60 nm) owing to the removal of pluronic F127 and the existence of narrow micro/mesopores (pore diameter: 1.5–5 nm) on their walls due to removal of PVA. The composition and phase purity were undertaken using FT-IR spectroscopy, energy dispersive X-ray spectroscopy (EDAX), X-ray photoelectron spectroscopy (XPS) and powder X-ray diffraction (PXRD). Brunauer–Emmett–Teller (BET) isotherm experiments exposed the contribution of micro/mesopores increased gradually with increasing concentration of PVA (0.5, 10 and 15 wt. %). The increasing population of pores was reflected in their electrocatalytic

performances which were probed through cyclic voltammogram (CV). The best catalyst (**CoOP-15**) exhibited a mass activity of  $44.1 \text{ A g}^{-1}$  and turnover frequency (TOF) of  $0.0162 \text{ s}^{-1}$ .

**Chapter 4** discusses the exploration of **Co<sub>3</sub>O<sub>4</sub>** based nanomaterials for OER, prepared via previous work surfactant directed soft-templating strategy using non-ionic pluronic F127 and ionic octadecyl trimethylammonium bromide (OTAB). The study displayed high BET surface area of **Co<sub>3</sub>O<sub>4</sub>** synthesized from pluronic F127 having narrow mesopores in an unrestricted fashion with sheet like morphology (revealed through TEM). However, **Co<sub>3</sub>O<sub>4</sub>** made from OTAB provided pores in a restricted manner with low intensity of mesopores, spherical morphology having less surface area. The chemical composition and phase purity were studied by FT-IR, XPS and PXRD analysis. Furthermore, utilizing electrochemical techniques such as CV, potential dependent electrochemical impedance spectroscopy (EIS) etc., we unravel their reactivity and the role of morphology which resulted differences in physical processes towards OER.

**Chapter 5** discusses, the synthesis of mesoporous nanomaterials (**Co<sub>3</sub>O<sub>4</sub>**, **NiO** and  $\beta$ -**Ni(OH)<sub>2</sub>**) using the previous concept of pluronic F127 as template and their mass loading dependent electrochemical efficacy within a loading span from  $0.065 \text{ mg cm}^{-2}$  to  $0.4 \text{ mg cm}^{-2}$  on the electrode surface. We have optimized  $0.1 \text{ mg cm}^{-2}$  mass loading gives the highest intrinsic activity parameters value like TOF, mass and specific activity. Beyond that amount of loading, those intrinsic activities had been started to decrease, whereas geometric

activity parameter like overpotential, current density and Tafel slope was increased. This work also revealed that **Co<sub>3</sub>O<sub>4</sub>** showed the better catalytic performances than **NiO** and **β-Ni(OH)<sub>2</sub>** although having less surface area.

**Chapter 6** discusses the substantial improvement of electronic conductivity for OER through the synthesis of **α-Co(OH)<sub>2</sub>** using rock salt and its transformation to translucent single layer (SL) **Co(OH)<sub>2</sub>** nanosheet by liquid phase exfoliation. The single layer surface thickness and morphologies were characterized by atomic force microscopy (AFM), scanning electron microscopy (SEM) and also through TEM. Light scattering tyndall effect proved the transparent colloidal nature of the exfoliated material. The **SL-Co(OH)<sub>2</sub>** exhibited excellent mass activity of  $153.8 \text{ A g}^{-1}$  and  $0.146 \text{ s}^{-1}$  TOF value.

**Chapter 7** discusses the future possibilities of this thesis work.

## **Homometallic Corrole-Porphyrin-Corrole Triads: Synthesis, Characterization and Application**

**Jyoti Rai**

**Supervisor: Dr. Jeyaraman Sankar**

**DEPARTMENT OF CHEMISTRY**

**Accession No.: T00133**

### **Abstract**

**Chapter 1:** Metal complexes of synthetic porphyrin and corroles with a core structure resembling that of the iron porphyrin core of cytochrome P450, have gained enormous attention in the field of catalysis. This is due to their promising activity as oxidation catalysts mimicking cytochrome P450. In biological processes, catalysis is usually executed in a series of different reaction centers. To achieve such a molecular catalyst, there is a need to assemble reaction centers having varied properties into a single molecular entity. With this aim, the complexes having both porphyrin and corrole moieties linked directly and having various metal centres at the core, have been synthesized, studied and utilized in some catalytic transformations like oxidation reaction and hydrogen atom transfer reaction.

**Chapter 2:** The detailed instrumentation and experimental methods have been explained.

**Chapter 3:** Manganese complex of *meso-meso* linked corrole-porphyrin-corrole triad was synthesized and characterized. Beside single crystal X-ray diffraction structure of free base corrole-porphyrin-corrole triad and its manganese complex, three more new manganese complexes have been characterized structurally. Noticeable changes were observed in the corrole-porphyrin-corrole triad structure after metalation with manganese. All the three macrocyclic rings have manganese in Mn(III) state due to the presence of chlorine as an axial ligand in porphyrin and DMF as neutral axial ligand in corrole. Further, all reported manganese complexes were investigated for catalytic epoxidation of alkenes. Initial results with styrene shows the superior catalytic potential of manganese triad complex as an oxidation catalyst.

**Chapter 4:** Cobalt complex of the corrole-porphyrin-corrole triad was synthesized and characterized. Spectral behavior of the cobalt triad was studied in different solvents. In order to explore and study the effect of different metal centers on catalytic epoxidation of alkenes, epoxidation of various alkenes was carried out using synthesized cobalt porphyrin, cobalt corrole and cobalt corrole-porphyrin-corrole triad complexes as catalysts. With a few alkenes, cobalt triad showed almost complete conversion to the respective epoxide and the behavior was found to be different from manganese triad as an oxidation catalyst. In addition to this, hydrogen atom transfer reaction was also studied

using 9,10-dihydroanthracene to generate anthracene using an oxidant, where cobalt triad shows excellent catalytic activity.

**Chapter 5:** In continuation of the work on the studies of properties of metalated corrole-porphyrin-corrole triads and their utilization in catalytic organic transformations, copper complex of the triad was synthesized and studied. Copper corrole units in the triad show the noninnocence of the corrole macrocyclic unit which are demonstrated by variable temperature NMR and EPR spectroscopy techniques. Copper triad and also copper dyad of the porphyrin-corrole hybrids are structurally characterized by their crystal structures which reveal important information about their geometry. Finally, in the ongoing attempts of their utilization in some organic transformations, we found an important result regarding catalytic N-N coupling of carbazoles.

**Chapter 6:** From the present studies it is found that the catalytic activity of the directly linked macrocycles is superior as compared to the monomers as observed in the catalytic

epoxidation and hydrogen atom transfer reactions. Currently, efforts are dedicated to study the mechanisms and some novel catalytic transformations using these macrocycles with different metals and to synthesize some new hybrids exhibiting porphyrin and corroles.

**C-terminal Modified Amphiphilic L-Phenylalanine Derivatives: Anticancer and Templates for Gold Nanoassemblies**

**Bhagat Somnath Dharmaraj**

**Supervisor: Dr. Aasheesh Srivastava**

**DEPARTMENT OF CHEMISTRY**

**Accession No.: T00131**

**Abstract**

This thesis reports the design and applications of molecularly concise self-assembling Phenylalanine (Phe) derivatives and their utility as enzyme inhibitors and templates for AuNPs. A common feature of the molecules prepared in this thesis is the utilization of rotationally flexible aromatic residues as the N-protecting groups for Phe. We hypothesized that the rotational flexibility inherent in these molecules would allow access to versatile properties such as self-assembly and therapeutics. This hypothesis is tested through the preparation of different derivatives by modifying the C-terminus of

amino acids. The results obtained from these investigations have been divided into the following chapters.

**Chapter 1** introduces the modification of L-Phe C-terminal end along with a literature review of diverse self-assemblies formed by these compounds and their use for drug-delivery or as anticancer agents. A review on the **(i)** self-assembly of Phe-containing peptides along with different definitions and classification of hydrogels. **(ii)** single amino acid-based hydrogelator **(iii)** Phe derived dipeptides based hydrogelators **(iv)** stimuli-responsive hydrogelation by Phe containing peptides, **(v)** peptide metallohydrogels, **(vi)** enzyme triggered hydrogelation of small peptides, **(vii)** L-Phe as prodrugs are also presented.

**Chapter 2A** describes the design and synthesis of hydrophobic amino acids derivatives and exploring their isoform-selective inhibition of histone deacetylase (HDAC) enzyme. This screening identified two potent derivatives viz. an L-Nap-Phe-hydroxamic acid (L-NapF-NHOH) and an L-Nap-Ile-hydroxamic acid (L-NapI-NHOH) that exhibited sub-100 nM 50% inhibitory concentration ( $IC_{50}$ ) values for HDAC isoforms 6 and 2, respectively.

Chirality at the amino acid center influenced the HDAC inhibition potency L-NapF-NHOH was ca. 5x more potent inhibitor of HDAC6 than its optical antipode prepared

from D-Phe (D-NapF-NHOH). (Further, L-NapF-NHOH and L-NapI-NHOH were found to exert additive action on lung cancer cells that overexpress both HDAC2 and HDAC6.)

Compound L-NapF-NHOH was active against cancer cells of breast, cervical and mouth origin, with 50% cytotoxicity concentration ( $CC_{50}$ ) values <300 nM in all cases. It retained its efficacy in cell-cultures and on 3D multicellular tumor spheroids(MCTS). The ex-vivo anti-cancer efficacy of L-NapF-NHOH was also established on multicellular tumor spheroids of breast cancer (MCF-7). Combination therapy of L-NapF-NHOH and L-NapI-NHOH achieved  $CC_{50}$  values of ~100 nM on lung cancer cells. Thus, this chapter reports

structurally simple derivatives of Phe and Ileu that show potent and isoform-selective HDAC inhibition activity for epigenetic regulation of cancer.

**Chapter 2B** describes the hydrogelation behavior of L-NapF-NHOH, which results in optically transparent hydrogels above 0.8 mg/ml. The hydroxamic acid residue plays multiple roles viz. giving drug-like properties and imparting strong self-assembly propensity to L-NapF-NHOH. These hydrogels release L-NapF-NHOH molecules in a sustained manner that lead to selective anticancer activity due to HDAC6 inhibition.

**Chapter 3** introduces the use of self-assemblies formed by NapF-OH to create nanoassemblies of gold nanoparticles (AuNPs). The fibrillar assemblies of Nap-Phe undergo rapid conversion into nano-sized globules upon adding of HAuCl<sub>4</sub>. Further, over a period a few hours, spontaneous reduction of HAuCl<sub>4</sub> to AuNPs occurs throughout a few hours. These morphological transformations, as well as the gold reduction, is not observed in heavy water (D<sub>2</sub>O). The gold reduction process in water was investigated with the help of cyclic voltammetry. The 2, 7-dichlorofluorescein diacetate (DCF-DA) and Amplex Red assays were performed for detection and quantification of hydroxyl radicals produced from the NapF-Au(III) complex in water. The catalytic property of Au(0) nanoassemblies was demonstrated by reducing aromatic nitro compounds. The gold complex was used to reduce the aromatic nitro compounds such as 4-nitrophenol via proton-coupled electron transfer (PCET) mechanism.

**Chapter 4** explored the self-assembly and hydrogelation properties of L-Phe derivatives having a rotationally flexible and aromatic 1-naphthaleneacetyl moiety as the N-protecting group, while the carboxylic acid residue was converted into an amide by reaction with different amines such as hydrazine (L-NapF-Hz), ethylenediamine (L-NapF-EDA), 3-aminopropylimidazole (L-NapF-API) and hydroxyethylamine (L-NapF-HEA). All the derivatives were nicely dissolved in hot water, and the subsequent cooling of these sols had varied outcomes. Out of these, L-NapF-Hz and L-NapF-EDA, yielded optically clear

supramolecular hydrogels, while for others such as L-NapF-API and L-NapF-HEA, precipitates were obtained upon cooling. FESEM revealed diverse morphologies such as rigid rods, helical nanofibers, and spherulites, which were obtained from these

**compounds. Circular dichroism spectroscopy revealed  $\pi-\pi$  stacking as one of the critical intermolecular interactions dictating the self-assembly.** Stable hydrogels entrapping the anticancer drug doxorubicin were obtained with L-NapF-EDA hydrogels.

**In appendix,** we describe a prodrug approach towards improving its selectivity for delivering HDACi drugs such as vorinostat (SAHA) for cancer cells, we exemplify a novel SAHA prodrug (SAHA-OBP) that gets activated in the presence of H<sub>2</sub>O<sub>2</sub>, a reactive oxygen species (ROS) known to be overexpressed in cancer cells was designed and synthesized. The high endogenous ROS content in cancer cells triggers rapid removal of the OBP cap to release active SAHA. The SAHA-OBP prodrug demonstrates selective activity against multiple cancer cell lines such as HeLa, MCF-7, MDA-MB-231 and B16-F10 while remaining benign to non-cancer cells such as HEK-293T. The downstream effects of SAHA released from SAHA-OBP in cancer cells are the induction of apoptosis. SAHA-OBP was also effective in multicellular tumor spheroids (MCTS).

## **Catalysis by proteins and their site-selective bioconjugation**

**Pralhad Namdev Joshi**

**Supervisor: Dr. Vishal Rai**

**DEPARTMENT OF CHEMISTRY**

**Accession No.: T00132**

### **Abstract**

Several enzymes exhibit catalytic efficiency in the chemical reactions beyond their portfolio of natural bio-transformations. The expansion in the area of protein-mediated catalysis could open the gateway for new chemical technologies. In natural systems, the enzymes regulate the modification of another protein. We debated that we could harness the specificity of such a model in protein bioconjugation. If successful, it can create a *platform for protein-directed protein modification*. In the long run, it could also enable the identification of interacting domains of two protein molecules in its assembly.

The precise engineering of native proteins and installation of probes is gaining attention from the areas spanning across Chemistry and Biology. The requirement of tools for

biophysical investigations, imaging, and therapeutics provide the thrust to this demand. The unnatural amino acid or recognition motif placed in a protein during its expression could render selectively engineered proteins. As expected, these routes are not applicable to a huge repository of native proteins. The precise labeling of native proteins is challenging due to the presence of a large pool of nucleophilic amino acids. Fishing out a single residue would require a method to exhibit chemoselectivity and site-selectivity. Besides, the methodologies must operate within mild reaction conditions.

In *chapter 1*, we have reviewed the role of protein as a biocatalyst and a substrate in bioconjugation. In the first part, we have discussed the use of proteins as catalysts. Importantly, we have highlighted their promiscuity where the classical activation modes catalyse the non-natural chemical transformations. In the second part of *chapter 1*, we have discussed how proteins serve as a substrate in a chemical reaction. We have presented the challenges offered by a plethora of nucleophilic residues that has kept the precision technologies elusive. In *chapter 2*, we discovered a set of features in a protein that enables nucleophilic catalysis in a model reaction, i.e., Morita-Baylis-Holman (MBH) reaction. Here, the low-order soluble protein self-assembly is critical for the success of organic transformation. In *chapter 3*, we have discussed the single-site labeling of native proteins at His residue and its application in late-stage functionalization. Also, we have demonstrated that the modification provides the platform for metal-free purification of His-tagged proteins. In *chapter 4*, we have used the knowledge of chapters 2 and 3 to show that protein-protein interaction can render precise engineering of proteins. The methodology highlights the utility of the protein as a nucleophilic catalyst and a substrate in one reaction.

**Chapter 1:** Proteins as catalyst and substrate in chemical transformations

**Chapter 2:** Protein self-assembly induces promiscuous nucleophilic biocatalysis in Morita-Baylis-Hillman (MBH) reaction

**Chapter 3:** Single-site labeling of histidine in proteins, on-demand reversibility, and traceless metal-free protein purification

**Chapter 4:** Protein-protein interaction enabled multicomponent reaction delivers chemoselective and site-selective labeling of native proteins

**Tailoring the noncovalent assemblies of molecules: development of materials with tunable fluorescence**

**Pragyan Pallavi**

**Supervisor: Dr. Abhijit Patra**

**DEPARTMENT OF CHEMISTRY**

**Accession No.: T00128**

**Abstract**

Fluorescent molecular probes with tunable emission both in solution and solid state have attracted a significant attention over last few decades owing to their immense application in low-cost memory and display devices, sensors, switches, cellular and sub-cellular imaging. Thus, the fabrication of tunable fluorescent materials, especially with the feature of white-light emission, has become the growing interest of the scientific community. The optical and electronic properties of  $\pi$ -conjugated molecules are governed not only by the chemical structure but also by the intra- and intermolecular interactions. Several fluorophores show strong florescence in solution. But, the  $\pi$ - $\pi$  stacking in the crystalline

state leads to delocalization of excitons resulting in quenching of the fluorescence due to the non-radiative deactivation in the solid state. It retards the utility of the molecular fluorescent probes in solid-state sensing, switching, and device applications. It is possible to improve the fluorescence quantum yield in solid-state employing judicious design strategy. Nonetheless, fabrication of such molecular probes with desirable optoelectronic properties is not easily attainable. Hence, it is quite important to understand the underlying mechanism and design strategy for the development of tunable fluorescent materials capable of exhibiting strong fluorescence both in solution and solid state including white-light emission. Chemical bonding and molecular interactions are the two leading parameters for the alteration of the photophysics of an excited state probe. In this context, the basic understanding of the role of chemical bonding and strong and weak intra- and intermolecular interactions is a prerequisite for the development of molecular materials with excellent photophysical properties and task-specific applications.

Herein, in this dissertation, we have employed the role of non-covalent self-organized assemblies using micellar and porous polymer scaffold to obtain tunable fluorescence leading to strong white-light emission in an aqueous medium. We also demonstrate the approach to circumvent the issue of concentration quenching of fluorescence in the solid state. The balance between the intra- and intermolecular interactions lead to a drastic change in emission properties. The specific themes developed in each chapter are also briefly conveyed below.

**Chapter 1** A brief introduction is presented to various kinds of fluorophores highlighting the role of molecular interactions on their photophysical properties and applications. This is followed by a discussion on various non-covalent interactions including intra- and

intermolecular hydrogen bonding,  $\pi$ - $\pi$  stacking, van der Waals interactions, etc. that have a strong impact on the excited-state behavior of a molecular fluorescent probe. A special emphasis is paid to the design and fabrication of all-organic white-light emitting materials. General strategies to develop molecular materials exhibiting strong fluorescence in the solid state are also delineated. Finally, the salient features of the subsequent chapters in the thesis are outlined.

**Chapter 2** In this chapter, we have discussed pyrido[1,2-*a*]indoles as a new class of functional molecules exhibiting strong emission in solution. Both emission color and intensity could be tuned by the variation of substitution. One of the derivatives, 6,7,8,9-tetrapropylpyrido-[1,2-*a*]indole-10-carbaldehyde (TPIC) with cyan fluorescence exhibits

quantum yield of 80% in DMSO, however it is nonfluorescent in aqueous medium or in aggregated state. The non-covalent approach of self-organized assembly of micelles was employed for the improvement of solubility and fluorescence enhancement of TPIC in an aqueous medium. The strategy of the dipole-dipole interaction through micelle-mediated energy transfer from TPIC to Nile red (energy acceptor) was employed to obtain ‘an all-organic’-based white-light emitting materials with high quantum efficiency.

**Chapter 3** In this chapter, a fluorescent porous organic polymer (tetraphenylcyclopentadiene and benzothiadiazole based solution-processable conjugated porous organic polymer, TPDC-BZ) was employed as a scaffold for effective encapsulation of multiple fluorescent dyes. The facile energy transfer between encapsulated dyes and TPDC-BZ polymer in aqueous dispersion led to white-light emission with quantum yield of 33%. Further, the strategy of noncovalent assembly was used to obtain the white-light emission in solid substrate. The WLE gel and free-standing transparent thin film were fabricated.

**Chapetr 4** Intra- and intermolecular hydrogen bonding is a non-covalent interaction which has a significant effect on the molecular packing which eventually alters the photophysical properties of fluorophores. The subtle balance between the intra- and intermolecular hydrogen bonding and  $\pi-\pi$  stacking can lead to solid-state fluorescence. Herein, we have employed the concept of excited-state intramolecular proton transfer (ESIPT) for the development of a solid-state emitter. However, most of the ESIPT-based fluorophores exhibit weak emission in the solid state limiting the scope of real-time applications. Addressing such issues, herein, we have presented a tripod like molecular architecture (TGHB) employing a simple one-step Schiff base condensation between triaminoguanidinium chloride and 3,5-di-*tert*-butyl-2-hydroxybenzaldehyde. The restriction of intramolecular rotation and eventually suppressing the nonradiative deactivation, led to remarkable enhancement of fluorescence quantum yield of TGHB in solid state by 1600-times compared to that of the solution. TGHB was demonstrated as a rewritable and self-erasable fluorescent platform having promising scope as molecular ink with multiple times ‘write-erase-write’ cycles.

**Chapter 5** In this chapter, I have summarized the various work presented in the thesis towards the development of tunable fluorescent materials. The highlights of the work include (i) fabrication of all-organic white-light emitting assembly with a very high quantum efficiency in an aqueous medium using micellar scaffold, (ii) demonstration of porous organic polymer as a light-harvesting antenna for the encapsulation of multiple

fluorescent aromatics, and (iii) development of a new fluorescent platform with ‘write-erase-write’ function employing excited state intramolecular proton transfer.

In the concluding section, I delineate some of the important avenues for exploration in the future. Micelles or polymer nanoparticles have been explored extensively for the encapsulation of the hydrophobic drug molecules. The prime challenge is the selectivity and fast response of the probe. Considering the environmental disposal perspective, the use of non-toxic materials is also important. To circumvent the above issues, the development of motion-based molecular probes that selectively release the drug at a specific site is needed. The design strategy of biocompatible polymeric nanotubes through layer by layer assembly is proposed. The loading and release of the drug molecules can be achieved by fine-tuning of non-covalent interactions in the presence of external stimuli. The proposed idea of drug-carrying nanovehicles will serve the purpose of targeted drug delivery with fast response time and can also be a potential testbed for motion-based sensing of analytes

# **Aldehyde enabled site-selective protein modification and purification**

**Landa Purushottam**

**Supervisor: Dr. Vishal Rai**

**DEPARTMENT OF CHEMISTRY**

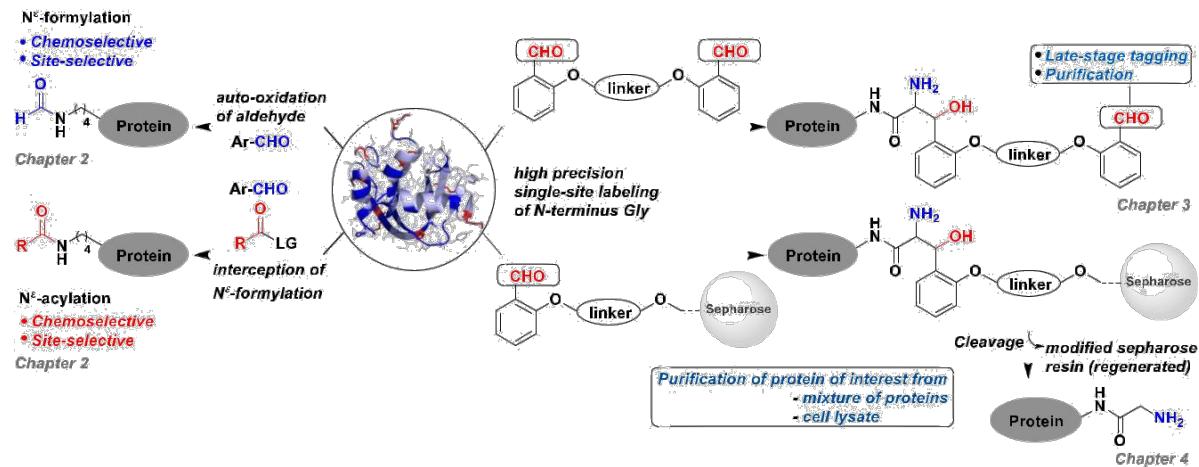
**Accession No.: T00125**

## **Abstract**

The protein labeling methods provide the essential toolbox for biophysical investigations, cell imaging, and protein-based therapeutics. Selective attachment of tags such as affinity probes, fluorophores, and potent cytotoxins plays a vital role in attaining the desired function. The advantages of single-site labeling were explored and established through pre-engineered proteins with un-natural amino acid or a peptide fragment. However, this technology does not extend to the native proteins. In recent years, chemical methods for functionalization of native proteins have drawn extensive attention. Typically, these methods are considered incapable of enabling single-site labeling of proteins. A chemical technology that can deliver single-site labeling of endogenous proteins would be ideal to meet these requirements. The challenge in the identification of a site with unique reactivity emerges from the abundance of functional groups with similar reactivity. It is complicated further by the presence of multiple copies of each residue. Additionally, chemical labeling of the protein requires experimental conditions that would not perturb the structure and function of a protein. Such methods could also provide access to analytically pure proteins that are indispensable for insight to protein's structure, posttranslational modifications, and function. Affinity tag-based approach is the most widely accepted methodology for the purification of proteins. However, selective binding of proteins poses a considerable challenge as they offer a plethora of competing sites with similar potential for interaction.

This thesis details my efforts toward the chemical methodologies for selective modification of the amine residue in native proteins. In *chapter 1*, we have highlighted the methodologies that target amines for the labeling of un-engineered proteins. The discussion highlights the challenges that are responsible for the lack of selectivity in the existing methods. In *chapters 2 and 3* we have discussed our chemical-platforms that offer a single-site modification of proteins under physiological conditions. Besides, such methods can create opportunities for the separation and purification of proteins. In this perspective, the success would require tag-specific capture and release of a protein under mild conditions. In *chapter 4* we discuss our

Gly-tag technology for covalent, selective, and reversible immobilization of a protein containing a single Gly residue at the N-terminus.



**Chapter 1:** Amine selective methods for protein modification and purification

**Chapter 2:** Chemoselective and site-selective peptide and native protein modification enabled by aldehyde auto-oxidation

**Chapter 3:** Single-site glycine-specific labeling of proteins

**Chapter 4:** Gly-tag for metal-free protein purification

# **Exploring Solid State Diversity in Molecular Crystals**

**Pradip Kumar Mondal**

**Supervisor: Dr. Deepak Chopra**

**DEPARTMENT OF CHEMISTRY**

**Accession No.: T00124**

## **Abstract**

This thesis reports the synthesis, crystallization, and investigation of polymorphism/co-crystals/salts in molecules containing organic fluorine and a systematic exploration of its participation in different intermolecular interactions. This includes the quantitative characterization of new supramolecular synthons involving fluorine atoms and the crystal structure landscape (via Crystal Structure Prediction) of conformationally flexible di- and tetra-fluorinated benzanilides. It covers the utilization of PIXEL energy calculations and Atoms in Molecule (AIM) analysis in the study of interactions involving organic fluorine. The crystal chemistry of the investigated compounds, highlight that in the presence of a strong hydrogen bond, additional secondary intermolecular interactions, involving organic fluorine, *namely* C–H $\cdots$ F<sub>sp2/sp3</sub>, C–F<sub>sp2/sp3</sub> $\cdots$ F<sub>sp2/sp3</sub>–C, and C–F<sub>sp2/sp3</sub>(*l.p.*) $\cdots$  $\pi$  play a very pivotal role in the overall formation of crystalline solids. The work in this thesis also involves the quantitative investigation of the structural, thermal, and mechanical properties (the utility of nanoindentation in crystal engineering) of polymorphs in a fluorinated amide.

Furthermore, the structural diversity in the drug Riluzole, obtained via cocrystallization with different carboxylic acids and pyridine derivatives acting as co-formers has been explored. This work has resulted in the formation of cocrystals, a cocrystal polymorph, and salts. This study also captures the *metastable* state during the spontaneous and reversible Single-Crystal-to-Single-Crystal phase transition via a conformational change in the riluzolium oxalate salt. *In situ* cryo-crystallization study, on –F and –CF<sub>3</sub> substituted anilines, by Optical Heating and Crystallization Device constitutes a key study in the examination of different intermolecular interactions in compounds which are liquids at room temperature. This is further extended to understand the role of halogens (Cl or Br or I) involved in the formation of different intermolecular interactions and the observation of the existence of isostructurality in the crystal packing of –CF<sub>3</sub> and halogen substituted benzanilides

**Total Synthesis of the Proposed Structure of Mycobactin J and Transition Metal-Catalyzed Directed C-H dienylation**

**Chiranjit Ghosh**

**Supervisor: Dr. Manmohan Kapur**

**DEPARTMENT OF CHEMISTRY**

**Accession No.: T00123**

**Abstract**

According to the World Health Organization (WHO), Tuberculosis (TB) is one of the world's most predominant diseases currently. Almost one-fourth of the global population is affected by TB and the assassin bacterium responsible for this is *Mycobacterium tuberculosis* (MTB) and which is one of the top 10 death-causing diseases worldwide, mainly in the third world countries. For the treatment of TB, the available drugs are increasingly becoming less efficient for MDR patients because the MTB bacteria acquires drug resistance through genetic mutations or via certain intracellular process and there is therefore a need to devise new methods and approaches to defeat this bacterium. Considerable research is focused on metabolites of *Mycobacterium* sp. and the development of credible drug delivery systems is the main focus of such research. Siderophores containing hydroxamic acid residues are the key system for survival of *Mycobacterium* sp. Mycobactins (metabolites of *Mycobacterium* sp.), formobactin, nocobactin, amamistatin and lasso peptides such as lariatins are some of such metabolites. Depending upon chemical structures, mycobactins show either growth promotion or inhibition activity. Among all the naturally occurring mycobactins, Mycobactin J (MJ) is the only commercially available with relatively most complex structure in its family and this drew our attention for its total synthesis. In this dissertation, the first streamlined total synthesis of the proposed structure of MJ is presented, with extensive elaboration. This work, features novel chemistry for keeping the Z-form of long chain fatty acid intact until the synthetic endeavour is over. Along with this, the other key features are the biomimetic construction of the chiral oxazoline building block and maintaining a protecting group-free phenol moiety throughout the synthesis. During the synthesis, we have worked out the most suitable pathway among the other possible pathways, which are elaborated in this Thesis.

Organic compounds contain several C-H bonds, and the site-selective functionalization of these bonds results in new organic materials *via* new synthetic methodologies. In C-H bond functionalization methodologies, the proper choice of coupling partners and suitable catalyst systems, leads to divergence in outcomes. Allenes are one such type of coupling partner and are a highly valuable synthetic precursors in synthetic organic chemistry, leading to a variety of interesting

transformations when treated with organometallic moieties derived from the C-H activation step. Under coordinating group-directed, transition metal-catalyzed C-H functionalization, presence of substituents alters the allene's reactivity and leads to a wide range of step-economical chemical reactions. In the second part of the Thesis, a Rh-catalyzed C-H dienylation of anilides with allenes is described. The present work studies the C-H dienylation of anilides to produce highly unsaturated, conjugated and electronically-biased olefins with good efficiency, along with detailed mechanistic investigations. We have explored the application of the dienylated product for the synthesis of polycyclic compounds as well as substituted indoles in this dissertation.

**Keywords:** Tuberculosis, Peptide based Natural Products, Mycobactin, C-H Functionalization, Rhodium catalysis, Allenes.

**Fluorescent Molecular Tweezers Based on Pyridine-2,6-dicarboxamide (PDC)  
Framework: Sensing and Photophysical Aspects**

**Rajesh Kumar**

**Supervisor: Dr. Aasheesh Srivastava**

**DEPARTMENT OF CHEMISTRY**

**Accession No.: T00121**

**Abstract**

This thesis reports the rational design and synthesis of novel molecular tweezers that act as selective hosts for inorganic and organic guests. The key features of these tweezers are: (i) the use of pyridine-2, 6- dicarboxamide (PDC) scaffold as the central motif,(ii) the utilization of fluorescent residues as the reporter units, and (iii) employment of flexible or rigid linkers to control the dynamic behaviour of tweezers by external stimuli such as solvents, pH, anions and neutral guests, We hypothesized that the unique positioning of the amide, amine and imine groups would modulate the conformational aspects, non-covalent interactions and molecular self-assembly of these molecules. This hypothesis was tested through the design and preparation of diverse derivatives. The investigations on these systems have been segmented into the four chapters of the thesis.

The **first chapter** gives a brief review of the supramolecular chemistry of cyclic and acyclic receptors including molecular tweezers. It covers the historical development of the field and the importance of non-covalent interactions exemplified by selected host-guest systems reported previously. Thereafter, literature examples by molecular tweezers containing Pyridine-2,6-dicarboxamide (PDC) scaffold are discussed. The conformational aspects, helical structures and reversible supramolecular self-assembly of PDC-based molecular tweezers are mentioned. Towards the end of this chapter, the challenges related to the design of novel molecular tweezers, PDC based foldamers and their metal-complexes for C-H activation are highlighted.

The **second chapter** describes a PDC-based fluorescent molecular tweezer (**FMT**) with flexible linkers connecting pyrene reporter residues to **PDC** unit. **FMT** exhibited selective binding with dihydrogen phosphate anions through H-bonding in a water-organic solvent. Anion-binding induced structural changes in **FMT** that transform the original monomer-like pyrene emission to excimer emission. The anion binding was quantified through UV-vis and fluorescence spectroscopies. **FMT** was found to be selective for tetrahedral oxyanions such as bisulphate and dihydrogen phosphate. The limit of detection of dihydrogen phosphate by **FMT** using fluorescence was 13 nM. **FMT** also showed aggregation-induced emission (AIE)

And photoinduced electron transfer (PET) Process. Addition of a red emitter like perylene monoimide (PMI) led to dihydrogen phosphate-responsive white light emission ( WLE).

**Part A of the third chapter**, details the design and investigations into a conformationally rigid fluorescent molecular tweezer, “heli(aza)cene” (**HAC**) with structurally similar arms. **HAC** adopts helical conformation stabilized by bifurcated intramolecular H-Bonding between amide and imine groups present in it. Crystal structure showed the presence of both *P*- and *M*- type helices. **HAC** retains its helical conformation both in solubilised as well as in solid state. The electronically different arms showed charge-transfer interactions ( CTI) – both of intramolecular ( between pyrene and phenylenediamine (PDA) residues of the opposite arms of (**HAC**) as well as of intermolecular ( between the pyrene residues of adjacent **HAC** molecules) **nature**. **HAC** molecules formed homochiral helices in solid state due to self-sorting phenomena arising from CTI. The electronic band gap of **HAC** could be tuned by using lewis and bronsted acids, both in solution as well as in the solid state of **HAC**. Thus, this molecular tweezer is a primary example of a  $\pi$ -layered helical molecule exhibiting tunable intra-/intermolecular CTI characteristics.

**Part B of the third chapter** describes soluble aggregates sof **HAC** (**HACsa**) in chlorinated organic solvents that demonstrated unprecedeted selectivity in interaction with the planar electron deficient organic guest (**PEDOG**) molecule, 1,2,4,5-tetracyanobenzene(TCNB). The TCNB PEDOG intercalated within **HACsa** driven by both hydrogen (H)-bonding as well as charge-tranfer interactions(CTI) with the host ( **HAC**). The binding affinity (*K<sub>a</sub>*) of TCNB with **HACsa** was found from <sup>1</sup>H NMR studies to be  $2 \times 10^3 \text{ M}^{-1}$ .The CTI between TCNB and **HACsa** led to strong color changes from yellow to red both in solution as well as in solid state. Single crystal analyses of **HACsa** TCNB complex showed strong structural rearrangement in **HACsa** from homochiral helices to heterochiral C<sub>2</sub>-double helix in the complex ( **HACsa TCNB**). The host (**HAC**) also showed changes in its conformation as the guest intercalated within its soluble assemblies . The structural rearrangements of the molecules in the crystal were also reflected in morphological changes from micro-belts to square-bipyramids structures. Complex showed the near-infrared emission as well as the high life-time of the excited state in the solid state. The complexation between **HACsa** and TCNB was fully reversed by using non-chlorinated solvents, diluting as well as heating.

The fourth chapter highlights future aspects of the work carried out in this thesis.

**Transition Metal-Catalyzed Synthesis and Functionalization of Nitrogen Heterocycles  
*via C-H Bond Activation***

**Gangam Srikanth Kumar**

**Supervisor: Dr. Manmohan Kapur**

**DEPARTMENT OF CHEMISTRY**

**Accession No.: T00119**

**Abstract**

Transition metal-catalyzed C-H bond functionalization for the synthesis of various heterocyclic scaffolds has received much attention in recent years owing to their tremendous application in the synthesis of natural products and active pharmaceutical ingredients. Despite the advances of C-H functionalization, development of the synthesis of nitrogen heterocycles with readily available coupling partners remains to be explored. The main objective of this dissertation is development of regiodivergent C-H functionalization strategies for the synthesis of heterocycles with the high atom and step-economy. Detailed mechanistic studies have also been carried out to understand the feasible pathway for the transformations.

Controlling multiple outcomes within a substrate is of enormous significance, as it provides an invaluable tool for predicting, targeting and switching the precise site of reactivity in the late-stage functionalization of a vast range of biologically relevant organic scaffolds. In this regard, allylic alcohols are regarded as a privileged class of coupling partners in C-H functionalization, as they are capable of selectively undergoing multiple reaction pathways to afford diverse products. We have successfully explored the reactivity of the allylic alcohols in the transition metal catalyzed, directed C-H functionalizations by employing them as allylating agents and alkylating agents in a region-divergent fashion to access diverse products. The reactivity of allylic alcohol is tuned to undergo C-H allylation and C-H alkylation pathways selectively by using different directing groups. We successfully employed the use of allylic alcohols in C-H functionalization as an alternative to the prefunctionalized coupling partners such as enones and other preactivated allylating agents. We have also carried out the detailed mechanistic investigations of these transformations to gain key insights into the plausible reaction mechanism.

The merging of C-H functionalizations with other efficient and sustainable approaches like multicomponent reactions or cascade transformations would be an ideal tool in organic synthesis for rapid construction of molecular complexity from a simple starting material. We

have successfully developed a step-efficient ruthenium-catalyzed,oxazolinly1 assisted C-H functionalization involving a three-component casede cyclization for the synthesis of isoquinolinones *via* a metal carbene migratory insertion. This work addresses the challenges associated in this field on using transition metal other than the rhodium. Detailed mechanistic investigations reveal interesting insights on the mode of transformation, involving reversible C-H activation, migratory insertion of hte diazo compound and cascade cyclization as the key step of the transformation.

**Keywords :** C-H activation, Transition-metal Catalysi, Directing group, allylic alcohols, Carbene-migratory insertion, Site-Selectivity.

**Synthesis of functionalized Perylenemonoimides with tailored electro-optical properties and their applications in sensing, white-light emission and memory devices**

**Vikas Sharma**

**Supervisor: Dr. Apurba Lal Koner**

**DEPARTMENT OF CHEMISTRY**

**Accession No.: T00117**

**Abstract**

**Chapter 1:** In this chapter, I will provide a brief introduction of the research work carried out during my doctoral study. This includes the motivation behind the study, the background of the fields and the objective of the work done. The introduction will detail mainly the synthetic aspects related to the functionalization of perylenemonoimides ( PMIs). Furthermore, some interesting applications of PMI derivatives will be demonstrated.

**Chapter 2:** The synthesis of *peri*-functionalized perylenemonoimide dyes containing an electron-donating aromatic and polyaromatic group *via* Suzuki coupling reaction will be discussed in the chapter. Later, the photophysical properties of the synthesized dyes are extensively investigated using various spectroscopic techniques. The introduction of electron-donating substituent's at *peri*-position shows a pronounced effect on emission properties of PNI derivatives. Electrochemical measurement suggest that the *peri*- functionalization of PMI dyes make the reduction much more facile compared to unsubstituted PMI dyes. Furthermore, an efficient and selective fluorescence quenching strategy was developed *via* a photo-induced electron-transfer process from electron-rich aromatic amines to the synthesized PMIs.

**Chapter 3A:** This chapter describes the development of a simple, rapid and an efficient microwave irradiation-assisted Sonogashira-coupling protocol. The reaction time decreases 2-3 orders of magnitude than conventional coupling method and provides an access to the *peri*- arylalkynyl perylenemonomide dye derivatives with a moderate to good yield. Further, we have investigated the optoelectronic properties of the dye derivatives, providing an insight on the push-pull effect of the electron-rich aryl and polyaryl groups through the perylene core. Moreover, we have investigated the effect of extended  $\pi$ -conjugation over carbon-carbon triple bonds.

**Chapter 3B:** This chapter demonstrates the tuning of optical properties of PMI derivative by truncating its intramolecular electronic communication *via* non-covalent nano-assembling. A

large  $\pi$ -surface area containing rigid alkyne-phenanthrene appended PMI is synthesized to realize this effect. Solvent-dependent photophysical studies indicate that the probe is aggregation prone and both the monomeric and aggregated forms are distinctly fluorescent. Serendipitously, upon aging only in dry and freshly distilled THF the optical properties of the molecule changes drastically. In the absence of any external stimuli, only upon aging the probe displays an intermedial white-light emission with most desired CIF chromaticity index ( 0.33, 0.33) using only a single-component *via* non-covalent nano-assembly of alkyne-phenanthrene conjugated perylenemonoimide ( PMIAP) are demonstrated.

**Chapter 4A:** describe a facile bromination reaction at PMI dye leading to tetrabrominated PMI. A series of tetra-substituted PMI was synthesized by substituting the *tetra*-brominated PMI with different electron-rich moieties. Later, the tetra-brominated PMI was region-selectively substituted at the *bay*-positions, followed by annulations with sulphur and selenium at the *peri*-position. The optical and electrochemical properties of the dye derivatives provided an insight into the push-pull effect *via* the electron-rich donors through the perylene core. Finally, the semiconducting property of these derivatives was utilized for the development of bistable organic film for switchable memory applications.

**Chapter 4B:** In this chapter, a new class of sulphur annulated *bay*-substituted PMI dye abbreviated as PMISS has exhibited a visual color change from blue to pink associated with the appearance of strong yellowish fluorescent color in solution upon reacting with peroxide present in THF, 1, 4-dioxane. We were able to detect the benzoyl peroxide at a relatively lower concentration of peroxide ( limit of detection = 0.2  $\mu$ M) at room temperature within an hour. Interestingly, the peroxide has been detected by PMISS within 10 minutes at a higher temperature because of much more reactivity of peroxide and lower activation energy at high temperature.

**Chapter 5:** A brief summary of the research work presented in this thesis will be outlined together with the future research prospect.

**Transition-Metal-Free Synthesis of Diaryl Acetamides, Disulfides, and Unsymmetrical Organochalcogenyl Indoles**

**Vandana Rathore**

**Supervisor: Professor Sangit Kumar**

**DEPARTMENT OF CHEMISTRY**

**Accession No.: T00116**

Development of carbon-chalcogen (S/Se/Te) and carbom-carbon bond formation represents a key step for the construction of a broad range of organic molecules, which are prevalent moiety in pharmaceutical, medicinal chemistry, and biology. Therefore, towards this direction, transition metal (TM) –free and main group chemistry especially, organochalcogen catalytic approaches have attracted attention in recent time, which avoid toxic transition-metal catalysts and makes more environmentally benign process.

This PhD thesis mainly focused on carbon-carbon, carbon-chalcogen, abd chalcogen-chalcogen bond formation. Also understanding the reaction mechanism has been studied multinuclear ( $^1\text{H}$ , $^{77}\text{Se}$ ) NMR, mass spectrometry, electron paramagnetic resonance, cyclic voltammetry. In some of the proposed reaction mechanism, steps involved also corroborated by density functional theory (DFT). Herein, we have discussed an oxidative cross coupling protocol for the synthesis of unsymmetrical diaryl acetamides and its synthetic applications towards indoles, benzofurans, benzophenones, and xanthenes. Then, we have demonstrated aerial oxidation of organothiols to respective disulfides in the presence of organoselenium catalyst, which mimics sulphhydryl oxidase and glutathione peroxidase ( GPx) enzymes for oxidation by oxygen and hydrogen peroxide, respectively, into disulfide. Here , we have shown that the synthesized organodiselenide can activate arrial oxygen towards oxidation of thiols. We have developed a mild visible light induced method for direct C(sp<sup>2</sup>)-H functionalization to access 3-chalcogenyl indole.

**Keywords:** Transition-metal free coupling reactions; C-H functionalization; Organoselenium compounds; Activation of oxygen; Thiol oxidation; sulphhydryl oxidase; Organochalcogenyl idoles; Radical pathways.

**Experimental and Computational Methods towards a Quantitative Understanding of  $\sigma$  and  $\pi$ -hole Directed Interactions**

**Rahul Shukla**

**Supervisor: Dr. Deepak Chopra**

**DEPARTMENT OF CHEMISTRY**

**Accession No.: T00115**

This thesis reports the crystallographic and theoretical investigation on the nature and role of different  $\sigma$  and  $\pi$ -hole directed interactions. Depending on the nature of the electron acceptor atom during the formation of these interaction,  $\sigma$  and  $\pi$ -hole interactions are categorized into Tetrel Bond ( Group 16 elements) and Halogen Bond (Group 17 elements). These interaction are observed to be comparable with the well-known Hydrogen Bond in terms of nature and characteristics and hence warrant a detailed analysis. Apart from studying the nature of different interactions individually, this work also focussed on the investigation of cooperativity between different  $\sigma$  and  $\pi$ -hole interactions. In this thesis, I have studied these interactions in gas phase neutral molecular system, as well as in the solid-state. The nature and characteristics of different intramolecular and intermolecular interactions were delineated in terms of interactions energies and topological analysis. The  $\sigma$  and  $\pi$ -hole interactions present in the crystal structures in the study were primarily investigated through high-resolution experimental and theoretical X-ray electron density analysis. This dissertation shows that the  $\sigma$  and  $\pi$ -hole interactions are highly stabilised interactions and can be efficiently used the designing of molecular solid with desirable properties.

**Keywords:**  $\sigma$ -hole interaction,  $\pi$ -hole interaction, electron density analysis topological analysis.

**Asymmetric Approach to Naturally Occurring Alkaloids Sharing 3a,3a'-Bis-Pyrrolo[2,3-b]indoline and Benzofuroindoline**

**K. Naresh Babu**

**Supervisor: Dr. Alakesh Bisai**

**DEPARTMENT OF CHEMISTRY**

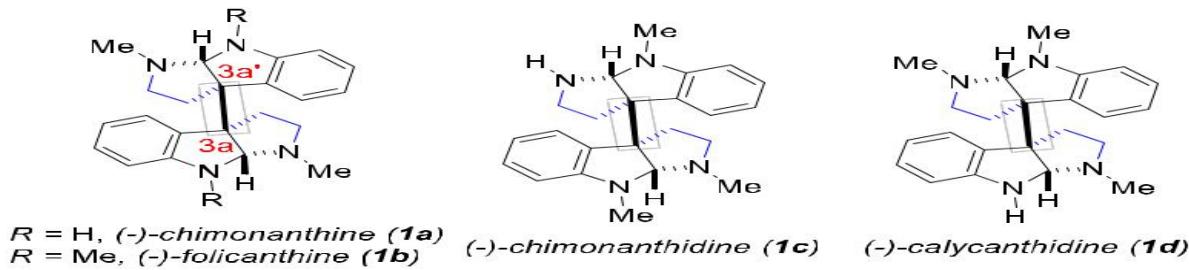
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**ABSTRACT**

The thesis entitled "**Asymmetric Approach to Naturally Occurring Alkaloids Sharing 3a,3a'-Bis-Pyrrolo[2,3-b]indoline and Benzofuroindoline**" is divided into four chapters viz chapters 1, 2, 3 and 4.

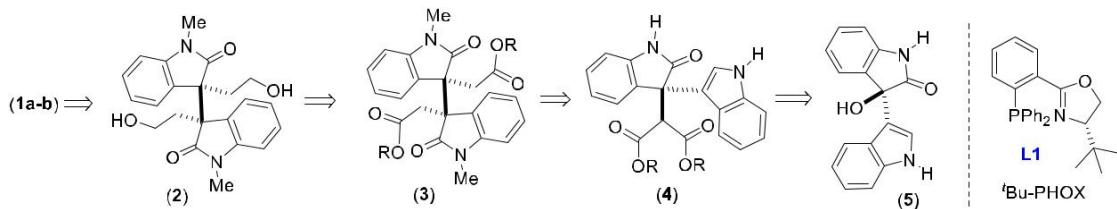
**Chapter 1** entitled "**Synthetic Approaches to the Bis-hexahydropyrroloindoline Alkaloids: The Literature Overview**" is a review of asymmetric construction of vicinal all-carbon quaternary stereogenic centers in the context of synthesis approaches to the bis-hexahydropyrroloindoline alkaloids such as chimonanthine (**1a**), folicanthine (**1b**), chimonanthidine (**1c**), calycanthidine (**1d**) (Figure 1). We have included here significant conceptual literature reports on total synthesis of naturally occurring and biologically active bis-hexahydropyrroloindoline alkaloid (Figure 1). These alkaloids having architecturally interesting staructural motifs with C<sub>2</sub>-symmetry (in case of **1a-b**) and share four contiguous stereocenters. Among all the four stereocenters, two of them are all-carbon quaternary stereogenic centers situated at the vicinal (1,2-position) position (see, 3a, 3a'-position shown in **1a-b**). Most importantly these are having pyrrolindino[2,3-b]-indoline with elongated C3a-C3a' sigma bond that is labile even at mild conditions. In

addition to their intriguing architecture, few congeners of this family exhibits interesting biological properties such as antagonists of neurokinin 1 receptors, exhibit potent anticancer activities, cytotoxic activities to HeLa cell lines, antibacterial, analgesic etc. Given their important biological activities in addition to structural challenges, all the literature reports are particularly centered on the asymmetric construction of vicinal all-carbon quaternary stereogenic centers.



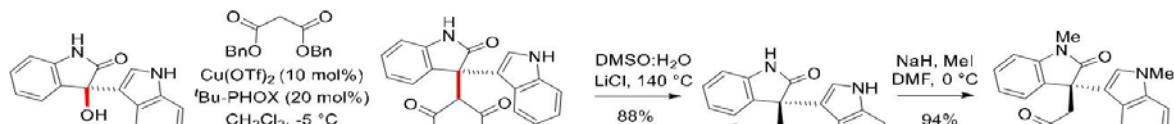
**Figure 1:** Representatives of bis-pyrollindino[2,3-*b*]-indoline alkaloids **1a-d**

**Chapter 2** entitled "**Development of Enantioselective Malonate Addition onto 3-Hydroxy 2-Oxindoles: Application in the Synthesis of Dimeric Pyrroloindoline Alkaloids**" deals with the asymmetric formal total synthesis of (*-*)-folicanthine **1b** via a key Cu(II)-<sup>t</sup>Bu-PHOX-catalyzed enantioselective malonate addition onto 3-hydroxy 2-oxindoles. Our retrosynthetic plan is shown in scheme 1, where we would like to approach to C<sub>2</sub>-symmetric diol (*-*)-**2** from C<sub>2</sub>-symmetric ester (*-*)-**3**.



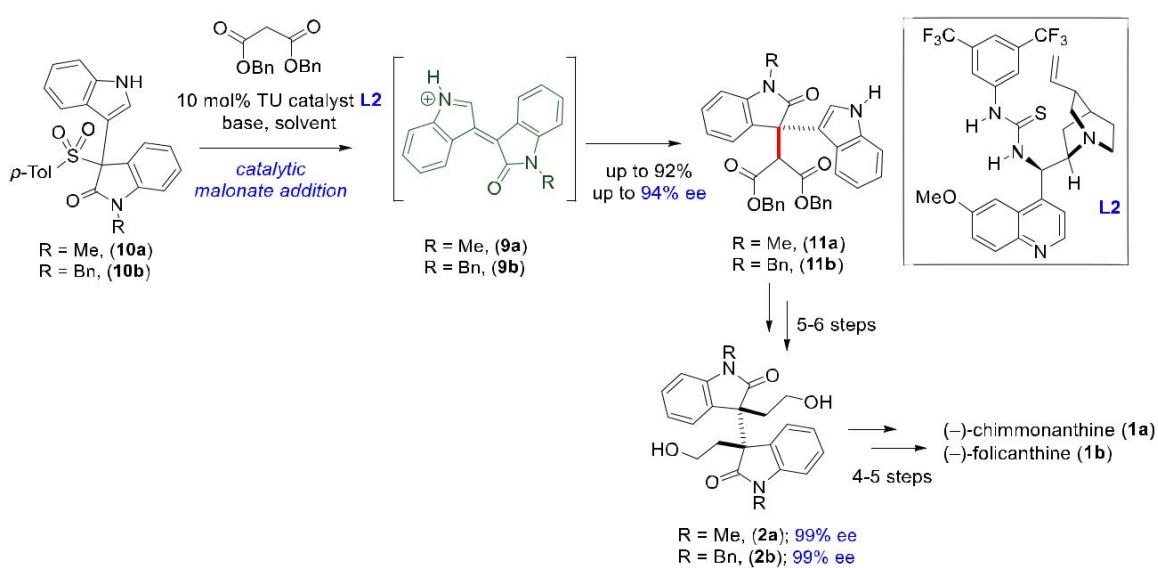
**Scheme 1.** Retrosynthetic analysis of (*-*)-folicanthine [*(-)*-**1b**].

It was envisioned that (*-*)-**3** can be synthesized from enantioenriched (*R*)-**4** via few steps synthetic elaboration (Scheme 1). We envision that (*R*)-**4** having an all-carbon quaternary stereocenter at the pseudobenzylidic position can be obtained via a catalytic enantioselective malonate addition on 3-hydroxy 2-oxindole **5** utilizing Cu(II)-<sup>t</sup>Bu-PHOX as an active catalyst (Scheme 1). As per our hypothesis, we succeeded in the stereoconvergent construction of enantioselective all-carbon quaternary centres using Cu(II)-<sup>t</sup>Bu-PHOX-catalyzed enantioselective malonate addition onto 3-hydroxy 2-oxindoles of type ( $\pm$ )-**5a** (Scheme 2). This strategy afforded product (*R*)-**4a** in high chemical yields with 99% ee. Utilizing aforementioned strategy we have completed formal total synthesis (*-*)-folicanthine **1b** (Scheme 2).



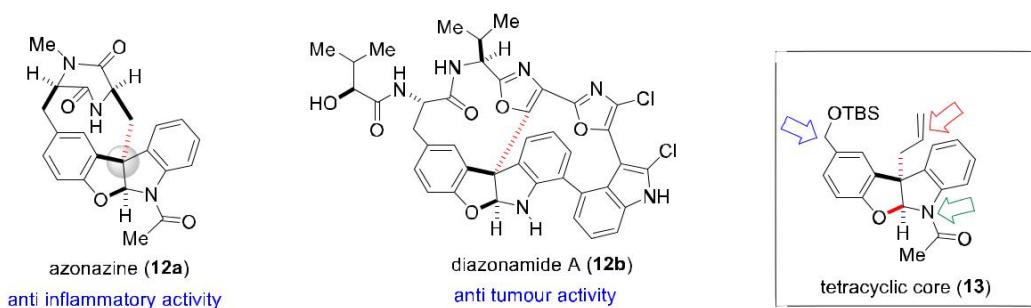
**Scheme 2.** Formal total synthesis of (*-*)-folicanthine [(*-*)-**1b**].

**Chapter 3** entitled "Development of Enantioselective Malonate Addition onto 3-Sulfonyl 2-Oxindoles: Application in the Synthesis of Dimeric Pyrroloindoline Alkaloids" deals with the catalytic asymmetric malonate addition onto 3-sulfonyl 2-oxindoles **10a-b** (Scheme 3). In this chapter, we hypothesized that TU-catalyzed enantioselective malonate addition onto *in situ* generated **9a-b** intermediates from 3-sulfonyl 2-oxindoles **10a-b** could afford enantioenriched products **11a-b** (Scheme 3). In fact, we have succeeded such transformation to afford a product (*R*)-**11a-b** with high enantioselectivities (up to 94% ee) in the presence of TU-catalyst **L2** (Scheme 3). The application of aforementioned strategy has been shown by formal total syntheses of (*-*)-chimonanthine [(*-*)-**1a**] and (*-*)-folicanthine [(*-*)-**1b**] in a few steps from **11a-b** (Scheme 3).



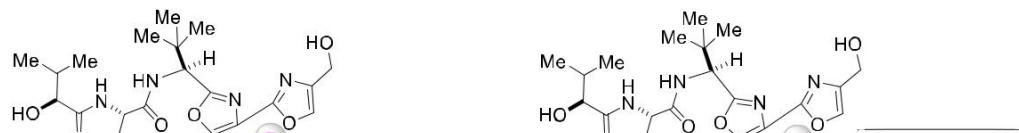
**Scheme 3.** Formal total synthesis of (*-*)-chimonanthine (**1a**) and (*-*)-folicanthine (**1b**).

**Chapter 4** entitled "Catalytic Enantioselective Decarboxylative Allylation of Allyl-2-indolyl Carbonates: Asymmetric Synthesis of Benzofuroindoline Core" describes the asymmetric synthetic approaches to core structure of azonazine (**12a**) and diazonamide A (**12b**). Azonazine (**12a**) is an architecturally interesting indole alkaloid isolated (2010) from = Hawaiian marine sediment-derived fungus *Aspergillus insulicola*. Azonazine (**12a**) possess a unique hexacyclic dipeptide structure (Figure 4) and has a similar tetracyclic core as present in diazonamide A (**12b**), which was isolated earlier in 2004. Oncology reports suggest that azonazine (**12a**) exhibited anti-inflammatory activity by inhibiting NF- $\kappa$ B = luciferase ( $IC_{50}$  8.37  $\mu$ M) and nitrite production ( $IC_{50}$  13.70  $\mu$ M) but was less potent than the standard celastrol ( $IC_{50}$  0.3  $\mu$ M). On the other hand, diazonamide A (**12b**) was reported to be a potent antimitotic agent, exhibiting low nanomolar  $GI_{50}$  values towards a diverse panel of human cancer cell lines.



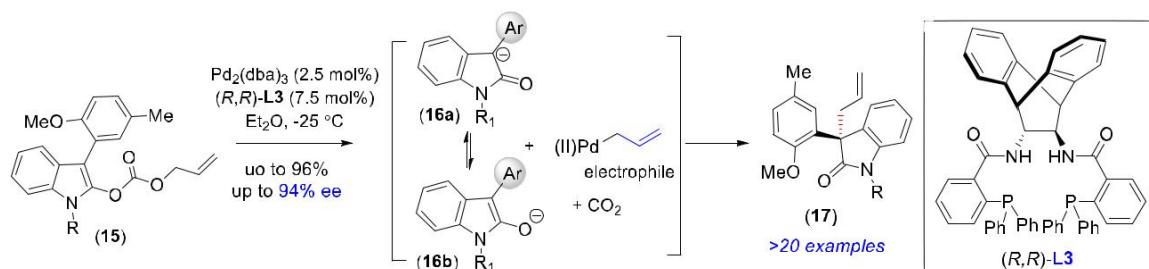
**Figure 4.** Azonazine (**12a**) and diazonamide (**12b**) sharing similar type tetracyclic core.

Because of its high bioactivity of diazonamide A (**12b**), various synthetic analogues such as DZ 2384 (**14a**) and DZ 2384D (**14b**) [diastereomers of **14**] were studied extensively (Figure 5). Importantly, the preclinical oncology study identifying the novel mechanism of action of its new synthetic diazonamide compound, DZ-2384 (**14a**), show that a distinct mode of binding to a classic therapeutic site in tubulin translates into superior anti-tumor activity and safety, including lack of neurotoxicity , with pre-clinical proof of concept in a wide range of cancers including triple-negative breast cancer and pancreatic cancer. The study highlights distinct structural features of DZ-2384 (**14a**) binding to tubulin that help preserve the cell microtubular infrastructure of neurons and non-dividing cells, resulting in lower toxicity. These oncology studies clearly suggest that there is a strong demand for the strategies to synthesize enatioenriched tetracyclic core [such as **13**] similar to that of azonazine (**12a**) and diazonamide (**12b**).



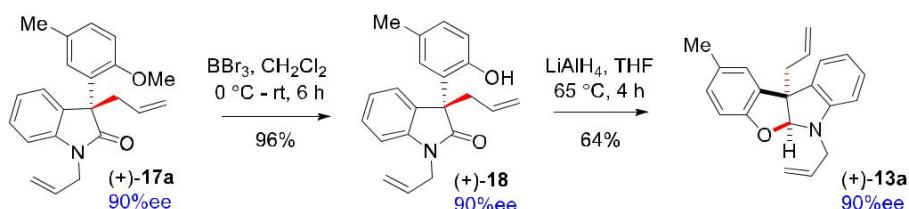
**Figure 5:** Synthetic analogues of diazonamide A (**12b**) [DZ 2384 (**14a**) and DZ 2384D (**14b**) are diastereomers].

Towards these targets, we have developed efficient catalytic enantioselective decarboxylative allylation (DcA) of allyl-2-indolyl carbonates **15** in the presence of catalytic Pd(0)-**L3** via the intermediacy of **16a-b** (Scheme 4). This reaction afforded a variety of enantioenriched 2-oxindoles [such as **17**] sharing an all-carbon quaternary stereocenter at the pseudobenzylic position.



**Scheme 4:** Synthesis of tetracyclic core **13** via intermediate **25**.

Interestingly, a variety of 2-oxindoles **17** with C3-quaternary stereogenic center have been synthesized in high enantiopurity (up to 94% ee) under additive free condition. Utilizing this method, an effective strategy for enantioenriched tetracyclic core (**13**) related to azonazine (**12a**), diazonamide (**12b**), and DZ-2384 (**14a**) has been achieved.



**Scheme 5:** Synthesis of tetracyclic core **(+)-13a** via reductive cyclization

Towards this end, 2-oixindole **17a** sharing an all-carbon quaternary stereocenter at the pseudobenzylic position was reacted with  $\text{BBr}_3$  to affect demethylation to furnish *p*-cresol

derivative **18** in 96% yield (Scheme 5). Finally, a reductive cyclization of **18** was performed using LiAlH<sub>4</sub> to afford tetracyclic core (+)-**13a** in 64% yield (Scheme 5).

**Total Syntheses of *Amaryllidaceae* Alkaloids Sharing *cis*-3a-Aryloctahydroindole Skeleton**

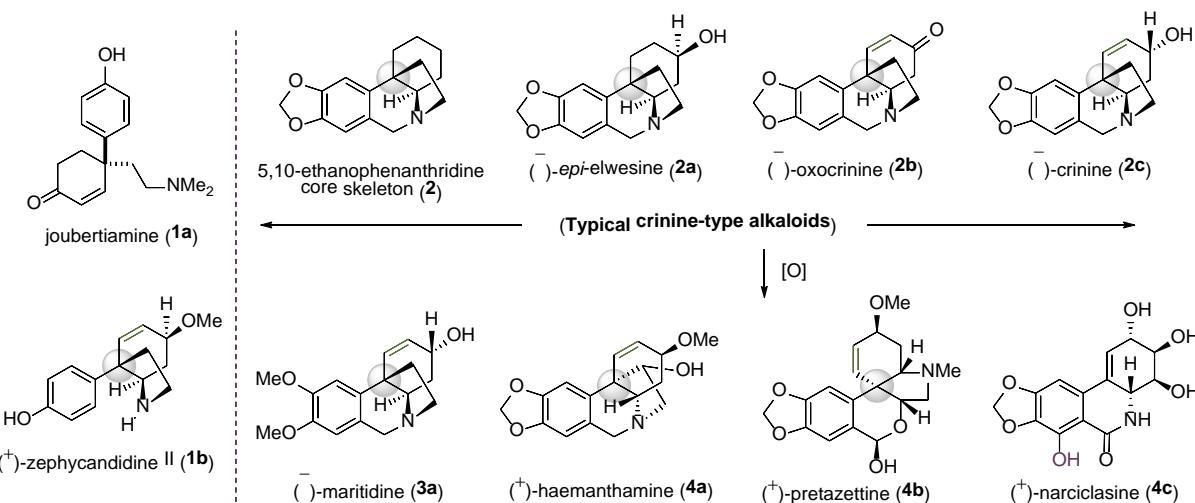
**Mrinal Kanti Das**

**Supervisor: Dr. Alakesh Bisai**

**DEPARTMENT OF CHEMISTRY**

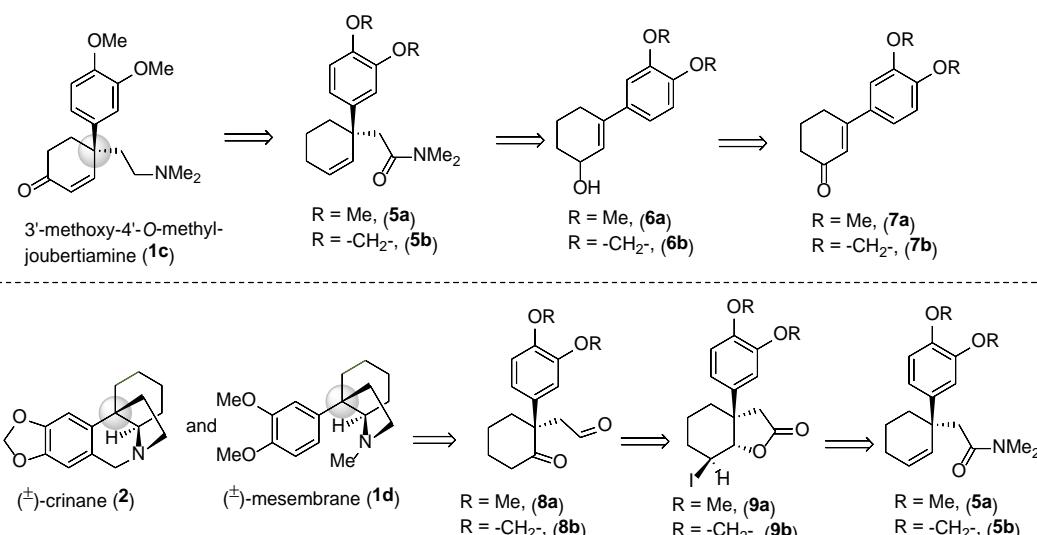
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*Amaryllidaceae* alkaloids (Figure 1) have long attracted the attention of synthetic chemists due to their significant bioactivities such as antitumor, antiviral, and anti-acetylcholinesterase activities, and the fascinating diversity of their structures. This thesis entitled "**Asymmetric Total Syntheses of *Amaryllidaceae* Alkaloids Sharing *cis*-3a-Aryloctahydroindole Skeleton**" is divided into four chapters namely Chapters 1, 2, 3 and 4. **Chapter 1** entitled "**Literature Overview of *Amaryllidaceae* Alkaloids: History, Occurrence, and Synthetic Approaches**" is a review of the *Amaryllidaceae* alkaloids, where most of the important syntheses are described. Over the past three decades, many have been isolated, screened for different biological activities, and synthesized by many research groups. Some elegant literature reports describing total syntheses of naturally occurring and biologically active *Amaryllidaceae* alkaloids have been discussed in this chapter.



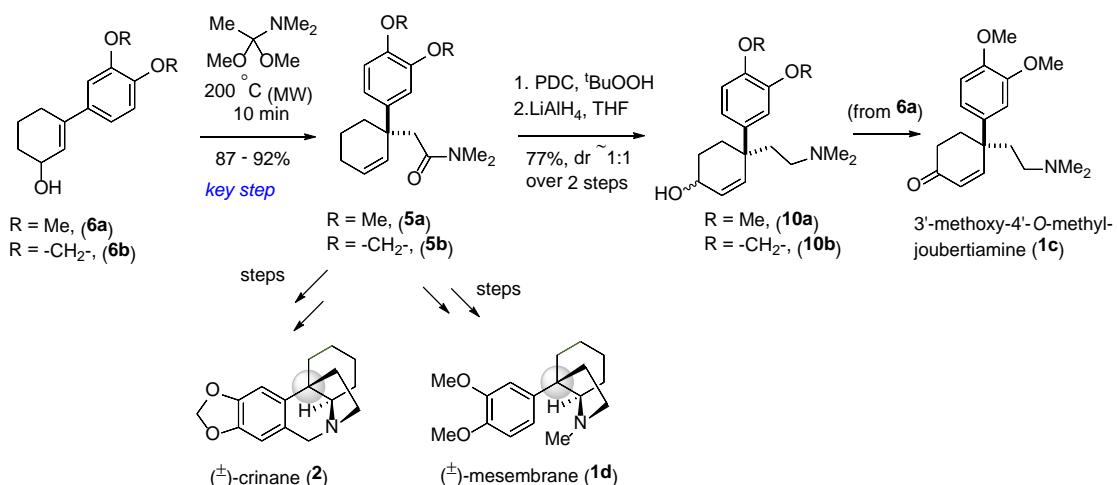
**Figure 1:** Representatives of *Amaryllidaceae* alkaloids.

**Chapter 2** of this thesis entitled "**Expedited Approach to *Amaryllidaceae* Alkaloids via a Key Eschenmoser-Claisen Rearrangement of 3-Aryl-2-cyclohexene-1-ol**" discuss unified total synthesis of *Amaryllidaceae* alkaloids following an efficient Key Eschenmoser-Claisen Rearrangement of 3-aryl 2-cyclohexene-1-ol. Retrosynthetically, it was envisioned that the advanced intermediate ketoaldehyde **8a-b** would lead to a unified pathway to access both mesembrane (**1d**) and crinane (**2**) type alkaloids (Scheme 2). Utilizing reactions shown in Scheme 3, collective total syntheses of *Amaryllidaceae* alkaloids, ( $\pm$ )-mesembrane (**1d**) and ( $\pm$ )-crinane (**2**) have been achieved. It is also believed that this method extendable to alkaloids of other structural types of *Amaryllidaceae* alkaloids.



**Scheme 2:** Retrosynthetic analysis of *Amaryllidaceae* alkaloids.

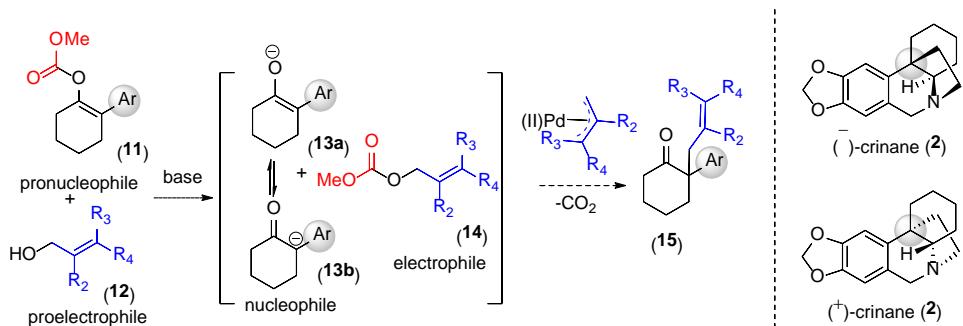
Importantly, as allylic alcohols of the type **6a-b** could easily be accessed in enantioenriched form employing catalytic CBS (Corey-Bakshi-Shibata) reduction, this strategy could be nicely adapted for unified asymmetric total syntheses of *Amaryllidaceae* alkaloids.



**Scheme 3:** Amaryllidaceae alkaloids via a key Eschenmoser-Claisen rearrangement.

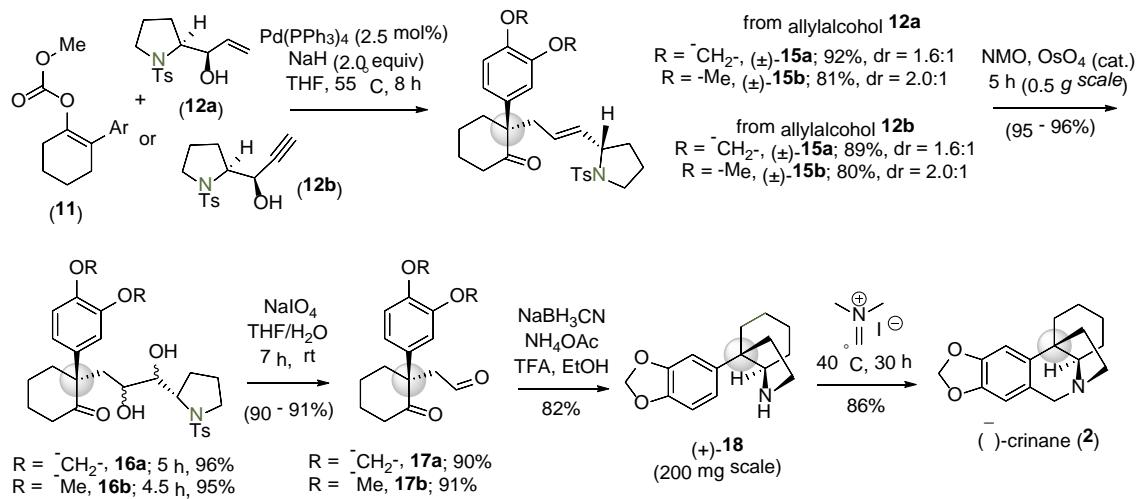
Chapter 3 of this thesis entitled "Development of Pd(0)-Catalyzed Deacylative Alkylation (DaA) of Enolcarbonates: Total Synthesis of (+)- and (−)-Crinane" discuss about the development of Pd(0)-catalyzed deacylative alkylations using commercially available allylalcohols. The hypothesis of deacylative allylations (DaA) of enolcarbonate 2 is shown in Scheme 2. It was argued that an allylic alkoxide may induce a deacylative process of aryl substituted enolcarbonate 11 to form carbanion 13b as active intermediate *via* enolate 13a (Scheme 4). Carbanion 13b would then react with Pd(II)- $\square$ -allyl complex generated *in situ* by

reaction of allyl acetate and Pd(0) to furnish various 2-arylated cyclohexanones 15 bearing an all-carbon quaternary center at the pseudobenzyllic position (Scheme 4).



**Scheme 4:** Our hypothesis of Pd(0)-catalyzed deacylative allylation (DaA).

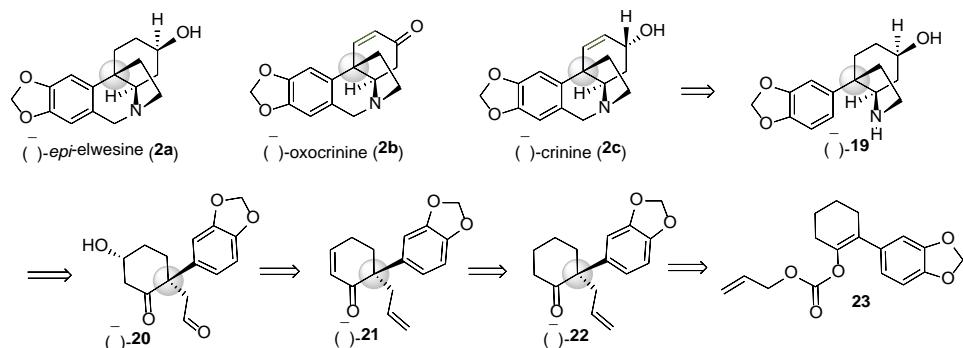
Utilizing reaction sequencece as shown in Scheme 5, total syntheses of ( $\square$ )-crinane (**2**) and ( $\square$ )-crinane (*ent*-**2**) was also accomplished from DaA of enolcarbonate **11** with other antipodes of **12a-b** following similar reactions as shown in Scheme 5.



**Scheme 5:** Total syntheses of *Amaryllidaceae* alkaloids ( $\square$ )- and ( $\square$ )-Crinane.

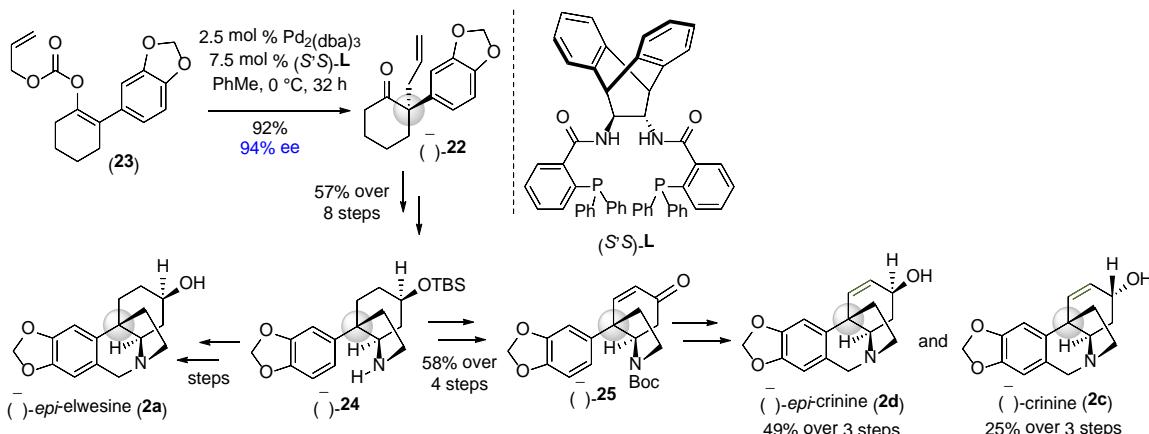
Chapter 4 of this thesis entitled "**Unified Total Syntheses of Naturally Ocurring Amaryllidaceae Alkaloids via Catalytic Asymmetric Decarboxylative Allylations (DcA) of Enolcarponates**" discuss *Amaryllidaceae* alkaloids share *cis*-3a-aryloctahydroindole structure and display vicinal all carbon quaternary and tertiary carbon stereocenters with a fused pyrrolidine ring. Importantly, both antipodes of *Amaryllidaceae* alkaloids [such as ( $\square$ )-crinine (**2c**) vs (+)-vittatine (**2f**) and ( $\square$ )-*epi*-crinine (**2d**) vs (+)-*epi*-vittatine (**2e**)] are isolated from Nature. It was envisioned that *cis*-3a-aryloctahydroindole scaffold **19** of *Amaryllidaceae* alkaloids could be obtained from cyclohexanone **22** via the intermediate enone **21**, which in

turn, could be accessed from an efficient Pd(0)-catalyzed decarboxylative allylation reaction of enolcarbonates **23** (Scheme 6).



**Scheme 6:** Retrosynthetic analysis via a key decarboxylative allylation (DcA) strategy.

Exhaustive optimization using 2.5 mol %  $\text{Pd}_2(\text{dba})_3$  in combination with 7.5 mol % of **L** in toluene at -10 °C afforded **22** in 96% yield and 92% ee. With this result in hand, first asymmetric total synthesis of natural ( $\square$ )-*epi*-elwesine (**1b**) was achieved from ( $\square$ )-**22**. Further, with ( $\square$ )-**22** in hand, collective total synthesis of other *Amaryllidaceae* alkaloids having levorotation was undertaken.



**Scheme 7:** Total syntheses of ( $\square$ )-*epi*-elwesine (**2a**), ( $\square$ )-*epi*-crinine (**2f**) and ( $\square$ )-crinine (**2c**).

Utilizing reaction sequence as shown in Scheme 7, collective total syntheses of naturally occurring *Amaryllidaceae* alkaloids having levorotation, such as ( $\square$ )-crinine (**2c**), ( $\square$ )-*epi*-crinine (**2d**) and ( $\square$ )-oxocrinine (**2b**). Furthermore, ( $\square$ )-**22** in hand [synthesized using (*R,R*)-**L**], total syntheses of (+)-vittatine (**2f**) and (+)-*epi*-vittatine (**2e**) were completed.

### Single-site labelling of lysine in native proteins through multicomponent approach

**Maheshwerreddy Chilamari**

**Supervisor: Dr. Vishal Rai**

**DEPARTMENT OF CHEMISTRY**

**Accession No.: T00110**

The methods for selective labelling of proteins are desired for harnessing their potential in biophysics, biochemistry, and therapeutics. The installation of the probe or drug at a specific site gives an opportunity to understand the biological processes like post-translational modification and protein-protein interactions. Recent outstanding success in this direction has been the access to antibody-drugconjugates for directed therapeutics in cancer treatment. The site-selective labelling of protein was achieved by utilizing the enzymatic methods, site-directed mutagenesis, and nonsense codon suppression methods. However, these methods are not applicable to the huge repository of native proteins. It would require us to understand the

organic chemistry with proteins and develop parameters to govern the selectivity of chemical transformations. The challenge in the identification of a unique site emerges from the abundance of functional groups with similar reactivity. It is complicated further by the presence of multiple copies of each residue. Additionally, chemical labelling of the protein requires experimental conditions that would not perturb the structure and function of a protein.

This thesis details my efforts toward the chemical methodologies for selective modification of single Lys residue in native proteins through a multicomponent approach. In chapter 1, we have given an overview of the challenges related to chemical methods for protein bi conjugation and notable contributions in the area. In chapter 2 and 3, we have discussed the multicomponent approaches that offer single-site installation of propargyl and aminophosphonate groups to a Lys residue. In both the methodologies, the selective labelling of one ε-amine is achieved in a pool of nucleophilic residues, α-amine, and several copies of ε-amine. These results validate that a chemical transformation can distinguish subtle differences in the reactivity of protein backbone residues. Lastly, we discussed a modular linchpin directed methodology (Chapter 4) for the modification of Lys. This approach is independent of the reactivity order of Lys residues. These methods deliver orthogonal tagging of a protein with the probe of interest. They also enable synthesis of antibody-drug conjugates for directed cancer therapeutics.

**Chapter 2:** Site-selective modification of native proteins using the A3 coupling reactions

**Chapter 3:** site-selective labelling of lysine through phospha-Mannich reaction

**Chapter 4:** Linchpin directed single-site labelling of lysine in native proteins

**Electrochemical Methodology Development and Heterogeneous Water Oxidation by  
Transition Metal-Based Systems**

**Debarati Roy Chowdhury**

**Supervisor: Dr. Amit Paul**

**DEPARTMENT OF CHEMISTRY**

**Accession No.: T00109**

The thesis describes the development of the methodology for kinetic analysis and synthesis of nonmaterial's and tuning their properties for improving their catalytic activity towards oxygen evolution reaction. This thesis is divided into six chapters.

**Chapter 1** introduces the basic of electron transfer and the importance of determining the stability of higher oxidation state in various aspects of electrochemistry . It also focussed on the significance of water oxidation reaction for energy generation and storage. The mechanism and hurdles of oxygen evolution reaction (OER), and the various types of

catalysts that can be used to reduce the kinetic barrier of the reaction, have been discussed. Moreover, the parameters used to judge the catalytic performance, and literature reports on various strategies those are used to tune the properties of the catalyst for enhanced oxygen evolution reaction have been focused. At the end , the scope of the thesis elaborated.

**Chapter 2** explains the electrochemical techniques and other characterization techniques that have been used throughout the thesis work.

**Chapter 3** discusses an integrated electrochemical methodology composed of cyclic voltammetry and chronoamperometry for the determination of the stability of in-situ generated higher oxidation state of a molecular complex. The study found that the decomposition of ferrocenium cation followed the first-order kinetics in the presence of ambient oxygen and water. Using this methodology the half-lives and its derivatives, was determined. The new methodology was validated by performing difference concentrations of ferrocene, varable scan rates in cyclic voltammetry, different time periods of amperometry, and in-situ spectroelectrochemistry.

**Chapter 4** describes the electrodeposition of iron oxyhydroxide thin films from different precursors of ferrocene in nonaqueous medium. The film was characterized by using several spectroscopic techniques such as X-ray photoelectron spectroscopy ( XPS), Raman, etc. XPS and Raman confirmed the formation of iron oxyhydroxide. The morphology of the material deposited was characterized by scanning electron microscopy (SEM). It revealed the formation of nanoparticle. The as- prepared films exhibited remarkable catalytic activity towardsOER under alkaline and near-neutral condition for prolonged period.The impact of precursor on the morphology, and finally on the catalytic performance of the material was also studied.

**Chapter 5** discusses the synthesis of nanoporous cobalt borate catalysts for OER and impact of its surface area and pore volume on catalytic property. Cobalt borate was synthesized using a novel soft templating approach aided by the tri-constituent assembly of  $\text{CoCl}_2\text{-}6\text{H}_2\text{O}$ , boric acid (  $\text{H}_3\text{BO}_3$  ) and F127 in aqueous medium. The concentration of  $\text{CoCl}_2\text{-}6\text{H}_2\text{O}$ : and  $\text{H}_3\text{BO}_3$  have been varied ( while maintaining a constant molar ratio of  $6\text{H}_2\text{O}$ : and  $\text{H}_3\text{BO}_3$  as 1:2) by keeping the concentration of other constituent same.Nitrogen adsorption-desorption studies showed the surface area and pore volume increased significantly with increasing  $\text{CoCl}_2$  and  $\text{H}_3\text{BO}_3$  content with respect to F127 from CoB 12 to CoB22 ( where the number indicates the molar ratio of  $\text{H}_3\text{BO}_3$  to F127). It also indicated the presence of both micropore/small mesopore ( 1.5-5.4 nm) as well as large mesopore ( 7-8

nm) in cobalt borate materials. Transmission electron microscopy (TEM) image revealed the formation of a mesoporous network. The materials showed significant catalytic activity for heterogeneous water oxidation with an overpotential of 310 mV and a turn-over frequency of 0.02 s<sup>-1</sup> in alkaline medium. The turn-over frequency followed an increasing trend with increasing CoCl<sub>2</sub> and H<sub>3</sub>BO<sub>3</sub> content, reaching a maximum at the optimal H<sub>2</sub>O:CoCl<sub>2</sub>:H<sub>3</sub>BO<sub>3</sub>:F127 molar ratio of 3:11:22:1. The study showed the impact of increasing porosity as well as the surface area of the catalyst for enhancing the catalytic activity for OER. A systematic strategy has been developed to tune surface area and pore volume of transition metal-based catalyst to enhance the efficiency which should prove advantageous for the preparation of non-precious transition metal-based catalyst.

**Chapter 6** highlights few possible future perspectives of the thesis.

**Stereo-electronically Tuneable and Stimuli-Switchable Organometallic Complexes for Transfer Hydrogenation, Hydrogenation and Dehydrogenation Catalysis: Toward Reseable Energy-Storage and Delivery**

**Shrivats Semwal**

**Supervisor: Dr. Joyanta Choudhury**

**DEPARTMENT OF CHEMISTRY**

**Accession No.: T00108**

**Abstract**

Transition metal hydrides ( M-H) play important role in wide of chemical reactions involving ( transfer) hydrogenation and dehydrogenation. Easy transfer of hydride ion (hydricity) is expected to increase the overall rate of a (transfer) hydrogenation reaction, Provided metal hydrides are involved in the rate-limiting step of the catalytic cycles. Similarly, in hydrogenation catalysis, facile cleavage of dihydrogen ( H<sub>2</sub>) to form metal-hydride ( M-H) intermediates is considered a crucial step within the catalytic cycles. Accordingly, innovative

ligand design to promote bifunctional metal-ligand cooperative( MLC) mechanism for H-H bond breaking is of central focus in this research area. In the realated but reverse process-dehydrogenation of various hydrogen-reach ( organic) substrates, initial Y-H ( Y= C, N, O etc.) activation steps leading to the formation of M-H are the key to following H<sub>2</sub> –releasing processes. Homogeneous catalysis provides opportunity of tuning ligand backbone in order to optimize sterro-electronic influence at the catalytic metal center to achieve better hydride transfer. The first part of the thesis deals with this important issued in the context of transfer hydrogenation catalysis with five- and six-membered cyclometalated iridium-NHC ( NHC = N-heterocyclic carbine) complexes. The investigation reveales that there exists an interesting multidimensional synergy among relevant stereoelectronic factors present within the metal complexes - ya angle, bite angle, ligand electronic , as well as aelectronic of the metal, to govern the hydride doner ability ( hydricity) of the complexes during catalysis. Thus the Six-membered chelate complexes having small yaw and large bite angles, strong donor ligand, and electron-rich metal. Were found to be better catalysts than their five-membered analogues. In the second part of the thesis, hydrogenation and dehydrogenation reactions were explored by extending the application of the emerging class of stimuli-responsive artificial switchable catalysts. A novel type of pH-driven” molecular coordination switch” was developed with Ir- and Ru-NHC-based complexes. These pH-switchable catalysts were applied for hydrogenation and dehydrogenative coupling of imines and amines respectively. Finally , this type of switchable hydrogenation/dehydrogenation application was extended toward developing an efficient reversible chemical hydrogen-storage/delivery system based on the greenhouse gas ( GHG) CO<sub>2</sub> and its hydrogenated counterpart, formic acid ( FA, HCO<sub>2</sub>H).

**C-H Bond functionalization of Ferrocene and Oxindoles: Synthesis of  
Organochalcogenides and benzofuro- and Indolo-indoles**

**MOH. Sattar**

**Supervisor: Professor Sangit Kumar**

**DEPARTMENT OF CHEMISTRY**

**Accession No.: T00102**

**Abstract**

Functionalized ferrocene have attracted considerable interest in catalysis as ligands, bioactive molecules and other applications.<sup>1</sup> The commonly used methodologies for ferrocene functionalization are FriedalCrafts type electrophilic reactions and C-H metalation by stoichiometric amount of alkali metals followed by electrophilic substitution reactions.<sup>1b</sup> The limited substrate scope, high reactivity and handling of alkali metals are the main hurdles for the ferrocene derivatization. Transition metal (TM)- catalyzed directed C-H bond functionalization of ferrocene are highly demanding and reliable strategies due to less waste and easily accessible reaction conditions.<sup>2</sup> Here, in my thesis work, I will show the directed arylation and alkylation of ferrocene by using aryl, alkyl halides and toluene as a coupling

partners.3a-b All chalcogenation such as sulfination, selenation and telluration of ferroceneamide to access mono and di chalcogenated ferroceneamide have been achieved. Further, the sequential chalcogenation of ferroceneamide have achieved with dichalcogenides as a coupling partner using copper salt. 3c-d Apart from this, in continuation of TM free conditions, a base mediated cross coupling reaction of oxindole with nitrobenzene and styrene to access important 3-substituted and 3,3- disubstituted oxindoles have been utilized<sup>4</sup>

## **Divergent Reactivity of Diazoenals in the Construction of N/O-Heterocycles**

**Lad Bapurao Sudam**

**Supervisor: Dr. Sreenivas katukojvala**

**DEPARTMENT OF CHEMISTRY**

**Accession No.: T00101**

### **Abstract**

My research work mainly focused on the diverse reactivity of diazoenal compounds in the synthesis of heterocyclic compounds. The details for the same are described in five-part of the thesis. Chapter 1 gives a short overview of diazo carbonyl compounds, as well as the design, synthesis, and application of diazoenal compounds in heterocycle syntheses. The catalyst dependent reactivity of diazoenal is described in two parts of the second chapter. The first part 2A involves the tetra-substituted furan synthesis by Rh(III)-carbenoid formation *via*[3+2] annulations of keto diazoenal with  $\beta$ -dicarbonyl compound in presences of Rh(III)/Ag(I) catalyst. The strategy further utilized for the synthesis of valuable furan-3-yl pyrazole and nitro derivatives. The Second part 2B demonstrate the [2+3] annulations of diazoenal with  $\beta$ -dicarbonyl compound in presence of In(OTf)<sub>3</sub> for the tri-substituted furans. The reaction involves an aldol condensation followed by cyclization. The methodology was

applied for the synthesis of furan substituted acrylic acid used in herbicides and fungicides. The chapter 3 consists of indole fused 1,3-oxazepine synthesis by Rh(II)-catalyzed [4+3] annulations of diazoenial and 3-substituted 2-oxindole. The chapter 4 of the thesis involves  $\alpha,\beta$ -unsaturated aldonitrone synthesis and its application for the construction of valuable isoxazolidine derivatives *via* 1,3-dipolar cycloaddition under catalyst-free condition. The isoxazolidines were further modified into pyrrolidine derivatives by reductive ring cleavage. The last part of the thesis explains the Cu(I)-catalyzed [4+2] benzannulation of N-substituted pyrroles with diazoenial to indole derivatives.

**Keywords:** diazoenals,  $\beta$ -dicarbonyl compound furan, annulations, aldonitrone, pyrazole, 1,3-dipolar cycloaddition, isoxazolidine, indole.

**Enantio- and Diastereoselective Synthesis of substituted oxa-Spirocycles by Utilizing Hydrogen Bond Donor Based Bifunctional Organocatalysts**

**Reddy Rajasekhar Reddy**

**Supervisor: Dr. Prasanta Ghorai**

**DEPARTMENT OF CHEMISTRY**

**Accession No.: T00099**

**Abstract**

oxa-Michael addition is providing efficient access to oxygen-containing heterocycles in organic synthesis. Oxa-Cycles which are attached to carbocycle in a spiro fashion often found in many natural products such as aculeatin A-D, ophiobolin, scilla scilloside E-1 and laurentristich-4-ol. Moreover, these oxa-spirocyclic motifs were also found in many biologically important molecules and are used as antimalarial drugs and TACE inhibitors. Despite their importance, most of the methods to achieve motifs are achiral or from chiral synthons. Reports for asymmetric synthesis of such motifs scarce in the literature. The major hurdle associated with the asymmetric synthesis of these molecules via oxa-michael addition is the use of tertiary alcohols as a nucleophil. Because of their reduced nucleophilicity due to crowding at  $\alpha$ -position and formation of ethe with  $\alpha$ -stereocenters. We have developed

strategies for the synthesis of oxa-spirocycles through an oxa-Michael addition of hindered tertiary alcohols as a key step by utilizing cinchona alkaloid bases squaramide bifunctional catalysts. Using this strategy, we achieved the enantio- and diastereoselective synthesis of sterically hindered tetrahydro-furans, - pyrans and spiroketal attached to a cyclohexadienone moiety in spiro fashion with excellent selectivities. Further on desymmetrization of keto-bis-enones with malononitrile by utilizing quinine derived amino-squaramide bifunctional organocatalyst gave the 1-oxa-spirocycles and spiroisobenzofurans with excellent selectivities.

**Keywords:** Hindered tertiary alcohols, oxa-Michael addition, hindered ethers with  $\alpha$ -stereocenters, bifunctional hydrogen bonding catalysts, oxa-spirocycles.

## **Total Syntheses of Icetaxane Diterpenoids via Benzoheptannulation Strategy**

**Amarchand Parida**

**Supervisor: Dr. Alakesh Bisai**

**DEPARTMENT OF CHEMISTRY**

**Accession No.: T00098**

## **ABSTRACT**

**Enantio-selective Synthesis of Isochromenes, lactones, and Dihydroisoquinolines using  
Quinine Derived Squaramide Catalyst**

**Biswajit Parhi**

**Supervisor: Dr. Prasanta Ghorai**

**DEPARTMENT OF CHEMISTRY**

**Accession No.: T00097**

**ABSTRACT**

The Intramolecular Hetero-Michael strategy remains a very good tool for synthesizing the heterocycles. In nature, the chiral oxa- and aza-cycles are more explored than other heterocycles. So, we focused to synthesize chiral oxa- and aza-cycles via intramolecular oxa- and aza- Michael strategy respectively. There were few reports available for the synthesis of chiral oxa- and aza-cycles by using covalent organocatalysis. But reports for the synthesis of these moieties by using non-covalent catalyst through hetero-Michael strategy are less in number because of rapid self-cyclization.

We explored the chemistry of IOM addition on highly deficient chalcone by using non-covalent catalyst like quinine derived squaramide catalyst, we hypothesized and succeeded to develop a unified strategy which involves an IOM of in-situ generated enols by using

quinine derived squaramide catalyst to synthesize chiral isochromene moieties with high enantioselectivity. We also functionalized the alkene functionality present in these moieties to get the substituted isochroman moieties with moderate to high diastereoselectivity with the retention of enantioselectivity.

After IOM of enols, we focused to synthesize a verity of lactones which follow a cascade IOM of in-situ generated per-oxy hemiacetal followed by DeLaMare fragmentation. By this strategy, we synthesized 1-Isochromanone, 3-Isochromanone, Phthalides and  $\gamma$ -lactones with high enantio-selectivity and high yield. Also, we apply this strategy to synthesize the precursor of n-Butylated Phthalide (NBT) and  $\gamma$ -heptalactone with high enantioselectivity and good yield.

And finally, we developed a unified strategy to synthesize chiral Dihydroisoquinoline moiety with high enantioselectivity and high yield, which follow an IAM (Intra-molecular Aza -Michael) addition of in-situ generated enamine. This strategy can be utilized to synthesize many biological active chiral dihydroisoquinoline moieties by following easy synthetic transformation.

**Modulating Acid-Base and Photophysical Properties of Drugs Using  
Cucurbit[7]uril**

**Faluguni Chandra**

**Supervisor: Dr. Apurba Lal Koner**

**DEPARTMENT OF CHEMISTRY**

**Accession No.: T00095**

**ABSTRACT**

**Chapter 1** will be the introduction to the research work done during my Ph.D. study including the fundamentals of supramolecular chemistry, discussion about self assembly processes and various types of water-soluble macrocyclic host molecules, bio-compatibility, and objectives of the thesis work. The thesis work. The thesis is mainly describing cucurbit[7] and its applications on modulation of acid-base and photophysical properties of three well-known fluorescent drug molecules.

**Chapter 2** will provide an overview of instrumentation and methods which I have used in my thesis research work. This includes mainly ultraviolet-visible(UV-Vis) spectroscopy, steady-state fluorescence spectroscopy, time –resolved fluorescence, host-guest binding model and synthesis of CB7.

**Chapter 3** is dealing with small fluorescent drug mimic 6-propanoyl-2-(N,N-dimethylamino)naphthalene(PRO), which is an *intramolecular charge transfer*(ICT) dye. Small drug molecules adn other important metabolities are delivered *via* a suitable carrier through a specific receptor protein. The process is highly-coordinated as well as associated with complexationi induces properties of deliverable molecules. We tried to mimic the drug delivery process to know how the carrier protein relocates the drug molecule from macrocyclic host cavity to its binding pocket and also alter the acid-base properties along with photophysical properties. Bovine and human serum albumin(BSA and HSA) were used as a model carrier protein which can snath out PRO molecule from water-soluble macrocyclic CB7 nanocavity at physiological conditions. We have investigated the delivery of a drug molecule from a nanocavity to carrier proteins with a fluorescence-based bio-supramolecular relocation assay. A encapsulation. large supramolecular pKa shift value from 2.3 units was observed upon CB7 shows a significant fluorescence enhancement followed by a 35 nm blue shift in the emission maxima.

**Chapter 4** describes the non-covalent approach of tuning photophysical properties via competitive disassembling of aggregated prodan using different sizeable water-soluble host molecules. The competitive process has been monitored using fluorescence spectroscopic techniques. A competitive disassembling of a self-assembles  $\gamma$ -CD•(PRO)<sub>2</sub> host-guest complex by Heptakis-(2,6-di-O-methyl)  $\beta$ -Cyclodextrin( DOM-  $\beta$ -CD) and CB7 in water to achieve novel optical novel optical properties of the encapsulated guest has been demonstrated. The complexation emissive properties and different binding strength of prodan with different water-soluble host molecules allow us to establish disassembling of its aggregates and the formation of 1:1 complexes with CB7 and DOM-  $\beta$ -CD.

**Chapter 5** is dealing the investigation of acid-base and photophysical properties of antimalarial drug quinine using CB7. The poor water-solubility of the cinchona based alkaloid quinine, resulting in weak and irregular absorption by body upon oral administration. Job's plot, steady-state, and time-resolved pf two CB7 Macrocycles with one quinine molecule. The binding affinity of dicationic quinine with CB7 is one order of magnitude higher than the mono-cationic quinine. Such differential binding results in one unit pKa shift in the ground-state of the quinoline ring. Interestingly, we have obtained two acid-dissociation constants, one for quinoline ring nitrogen and the other for quinuclidine nitrogen using fluorescence spectroscopy. In the excited-state, we have found that 1.1 units pKa shift for quinoline ring and 1.9 units shift for the quinuclidine moiety. A large fluorescence lifetime enhancement, as well as time- resolved anisotropy of quinine ,was observed upon encapsulation with CB7. The host-guest complexation study of quinine with CB7 can be applied to reduce phototoxicity and increases the solubility.

**Chapter 6** describes CB7 complexation of 9H-pyrido[3,4-b]-indole (NHM), which belongs to the class of naturally occurring alkaloids and used as an anxiety control and memory-enhancing drug with a pKa value at near-neutral pH. The acid-base and photophysical properties of NHM are shown to be modulated upon encapsulation with CB7. In this part of the research, along with CB7, I have used three different surfactants e.g., sodium dodecyl sulphate (SDS), cetyltrimethylammonium bromide (CTAB) , and triton X-100 (TX-100) for modulating acid-base and photophysical properties of NHM. The protonated and neutral forms of NMH interact very differently with micelles and CB7. The binding constant of protonated form was 1000 times more rather than non-protonated one with CB7. In this work, we have also demonstrated 105 times solubility enhancement at pH 2.8 using CB7.

**Conjugated porous organic polymers:  
Fluorescence-based sensing, photocatalysis and energy storage**

**Arnab Biswas**

**Supervisor: Dr. Abhijit Patra**

**DEPARTMENT OF CHEMISTRY**

**Accession No.: T00094**

**ABSTRACT**

Porous materials have become an active field of research over the past few decades due to their immense application ranging from gas storage, gas and liquid separation, catalysis to sensing and energy storage, gas and liquid separation, catalysis to sensing and energy storage. Porous are of different kinds such as activated carbons, zeolites, metal-organic framework (MOFs), covalent organic frameworks ( COFs) and porous organic polymers ( POPs). Zelites, activated carbons and MOFs have been investigated quite extensively in the last few decades. However, in recent times conjugated porous organic polymers (CPOPs) have emerged as a new class of functional materials. The CPOPs have drawn much attention to the scientific community because of the high thermal and physicochemical stability in addition to the permanent porous nature. CPOPs contain extended  $\pi$ -electron conjugation and thus become more advantageous compared to the other porous materials in the fields of light harvesting and optoelectronic applications. Even through several studies appeared in recent years, the solution processability of these network polymers remains a challenge.

In this thesis work, we have attempted to address the solubility issue of conjugated porous organic polymers and explore in detail the structure-property relationship of these novel class of materials in fluorescence –based sensing, photocatalysis and energy storage. We provide a brief outline of the specific themes developed in each chapter.

**Chapter 1** A brief introduction is presented to various kinds of porous materials highlighting their emergence and relevance. This is followed by a discussion on the origin of porosity in porous organic polymers and their advantages. An overview of the historical perspectives and the various classes of porous organic polymers are discussed. A special emphasis is paid to their application in gas storage and separation, catalysis energy storage and sensing.

**Chapter 2** In this chapter, we have discussed the design principle and fabrication of porous organic polymers in the form of powder, the solution in common organic solvents and nanoparticles by

using a novel core of tetraphenyl-5,5-dioctylcyclopentadiene (TPDC). The fine-tuning of reaction conditions involving tetrakis(4-bromophenyl)-5,5-dioctylcyclopentadiene and diethynylbenzene (DB) led to the formation of TPDC based polymers in three different forms. The POPs were thermally stable and the porosity of these materials was investigated by nitrogen sorption measurements at 77K. The detailed photophysical properties of the solution-processable POP and the aqueous dispersion of nanoparticles were explored by absorption and steady-state and time-resolved fluorescence spectroscopy. The nitroaromatics sensing was carried out using a set of 30 closely related analytes such as nitrophenols, nitrotoluenes, nitroanilines, nitobenzenes, and quinones. Nitroanilines were found to be the most efficient quenchers in contrast to the extensively studied picric acid, which is unprecedented among POPs. The rigorous spectroscopic investigations coupled with computational studies provided new insights into the underlying photophysical phenomenon of fluorescence quenching. We observed that the electron-deficient nature of nitroaromatics is not the sole governing factor responsible for fluorescence quenching.

**Chapter 3** This chapter deals with the fabrication and properties of a series of CPOPs based on boron dipyrromethene (BODIPY) core. The variation of the substituents in the meso position of BODIPY core and the fine-tuning of Songashira polycondensation reaction with 1,3,5-triethynylbenzene led to the development of CPOPs with a wide range of surface area and porosity. A ten-fold increase in BET surface area from  $73\text{ m}^2\text{ g}^{-1}$  to  $1010\text{ m}^2\text{ g}^{-1}$  was obtained. Simultaneously, the porosity was changed from mesoporous to ultra-microporous. The gas adsorption studies of the polymers revealed a high uptake of CO<sub>2</sub> and H<sub>2</sub>. Electron paramagnetic resonance (EPR) studies revealed the generation of singlet oxygen upon photoexcitation of these polymers. We explored the CPOPs developed in this study as a heterogeneous photocatalyst for oxidation of thioanisole. The calcination of one of the CPOPs resulted in porous carbon which was found to exhibit an appreciable specific capacitance.

**Chapter 4** This chapter describes the fabrication and characterizations of a solution-processable CPOP based on a flexible core comprised of carbazole and BODIPY. The polymer was obtained by palladium(0)-catalyzed (A<sub>4</sub> + B<sub>2</sub>) type Suzuki-Miyaura polycondensation reaction between the boronic ester of bicarbazole octane and diiodo derivative of BODIPY. The resultant polymer Cz-BDP is soluble in common organic solvents having a moderate BET surface area. Cz-BDP is red fluorescent and generates the reactive oxygen species (ROS) upon exposure to visible light. It was explored for a visible light-driven photooxidation of benzylamine.

**Chapter 5** In this chapter, we propose new directions towards (i) the fabrication of soluble POPs having tunable emission and (ii) CPOPs for high supercapacitive energy storage. The cyan fluorescent POPs with TPDC core presented in the second chapter was fabricated using diethynylbenzene (DB) as comonomer. Employing tetraphenylethylene (TPE) and benzothiadiazole (Bz) as comonomers, we obtained TPDC-TPE and TPDC-Bz, respectively, as green and orange

fluorescent soluble polymers. Pyrene based CPOPs were fabricated by palladium-catalyzed Buchwald-Hartwig cross-coupling reaction. The resultant polymers were found to exhibit high specific capacitance in its pristine form. The highest specific capacitance by pyrene based CPOP was found to be  $\sim 456 \text{ F g}^{-1}$ . These polymers also exhibited high cyclic stability promising for device application.

In the subsequent section, we summarize the various work presented in the thesis towards the development of multifunctional porous organic polymers. The highlights of the work include (i) fabrication of TPDC based fluorescent soluble POPs and the detailed exploration of nitroaromatics sensing, (ii) BODIPY based POPs with tunable surface area and porosity for photocatalysis and energy storage, (iii) BODIPY-carbazole based solution-processable POP as a visible light-driven photocatalyst for organic transformation.

In the concluding section, some of the important avenues for the exploration in future is delineated. Application of the strongly fluorescent POPs developed in the present study in organic photovoltaic devices and fabrication of novel metal-organic hybrid materials with improved optical attributes are some of the interesting avenues to be explored further

# Asymmetric Construction of oxygen Containing Heterocyclic Moieties and Alkylation of Nitrogen Heterocycles

Arnab Biswas

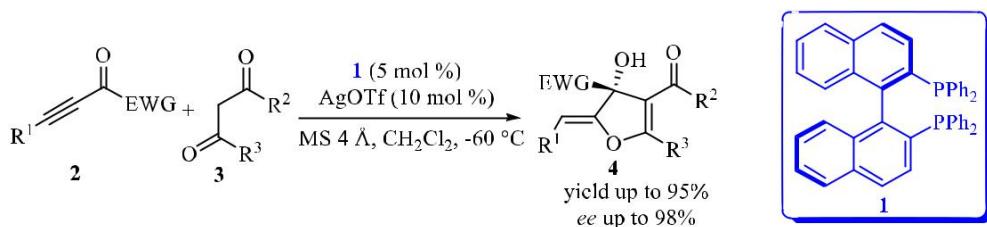
Supervisor: Professor Vinod K. Singh

DEPARTMENT OF CHEMISTRY

Accession No.: T00093

## ABSTRACT

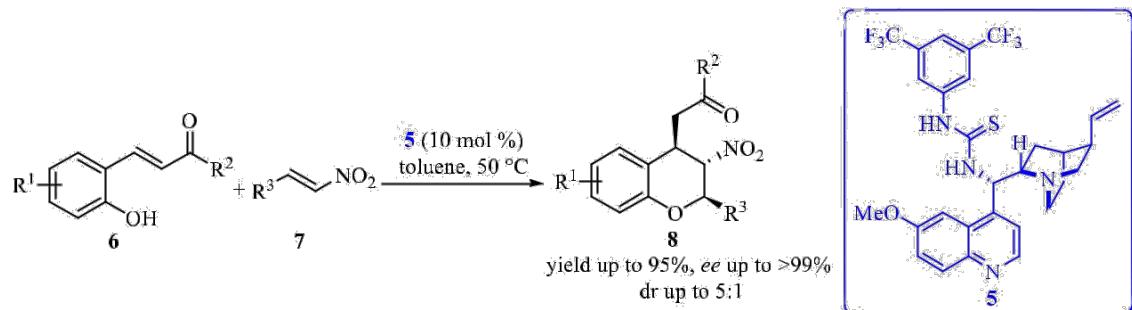
This thesis is divided into three chapters. **Chapter I** deals with the construction of the biologically important dihydrofurans which are of immense significance as various compounds of therapeutic value contain this scaffold. Though the scientific fraternity has made substantial contributions towards construction of this moiety in an enantioselective fashion, the majority of reports focus on use of organocatalysts. The principal objective of the work was to develop an asymmetric protocol for construction of dihydrofuran in a single step employing metal catalysis. The asymmetric ‘interrupted Feist-Bénary’ reaction was successfully developed by utilizing activated yrones **2** and 1,3-dicarbonyl compounds **3** as precursors to dihydrofurans (Scheme 1). A combination of silver salt (AgOTf) and bisphosphine ligand **1** (*R*-BINAP) as the chiral catalyst afforded the enantioenriched dihydrofurans with high yields (up to 95%) and excellent enantioselectivities (up to 98% ee).



Scheme 1

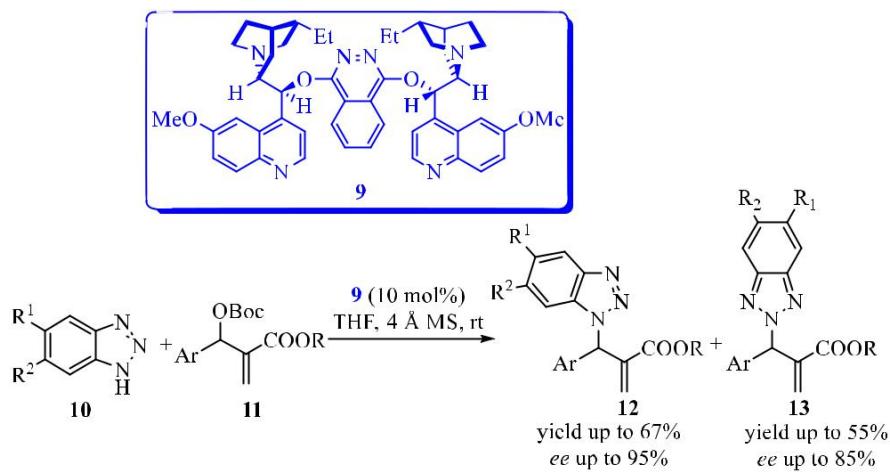
**Chapter II** emphasizes on enantioselective synthesis of chromans, which are ubiquitous heterocyclic architectures found in many natural products and biologically active compounds. The majority of reports on synthesis of these class of heterocycles have concentrated on using proline derived catalysts for enantioselective construction of this moiety. In this context, an additive free and efficient catalytic methodology employing the oxa-Michael reaction and H-bonding bifunctional thiourea organocatalysts **5** was devised for enantioselective construction of the chroman core. Using *ortho*-hydroxychalcones **6** and  $\beta$ -nitroalkenes **7** as templates for the double Michael reaction sequence, the

enantioenriched chroman was assembled in a single-pot with excellent yields (up to 95%), diastereoselectivities (up to 5:1) and enantioselectivities (up to >99% *ee*, Scheme 2).



**Scheme 2**

**Chapter III** describes an organocatalytic method for synthesis of substituted benzotriazoles by means of an asymmetric substitution reaction. Benzotriazoles and triazoles are prominent cores which are present in compounds of pharmaceutical value. Among various synthetic protocols involving substitution reactions between nitrogen nucleophiles with Morita-Baylis-Hillman (MBH) carbonates, the allylation of benzotriazole **10** with Morita-Baylis-Hillman (MBH) carbonates **11** is unique as it furnishes both the regioisomeric benzotriazole derivatives. Under optimized reaction conditions, the modified *cinchona* alkaloid organocatalyst  $(DHQD)_2PHAL$  **9** furnished both the regioisomeric *1H* and *2H* benzotriazole derivatives in good yields (up to 67% and 55% respectively) and high enantioselectivities (up to 95% and 85% *ee* respectively, Scheme 3). The synthetic utility of the benzotriazole derivatives has been demonstrated by synthetic manipulations of the functional groups.



**Scheme 3**

**Keywords:** Silver catalysts, Interrupted Feist-Bénary, Oxa-Michael reaction, Bifunctional thiourea, Allylation, Regioisomeric.

# **Organocatalytic, Enantio-and Diastereoselective Synthesis of Oxa- and Carbocycles**

**Sanjay Maity**

**Supervisor: Dr. Prasanta Ghorai**

**DEPARTMENT OF CHEMISTRY**

**Accession No.: T00092**

In the era of modern organic chemistry, asymmetric synthesis become the main stream in research to provide chiral molecules which has tremendous application in drug molecules and natural products having biological significance. Beside the metal and enzyme catalysis, organocatalysis become the third pillar in asymmetric synthesis for its exceptional advancement. The inherent robust nature make them to survive in all conditions provided by the modern chemistry. The excellent tolerance towards moisture and air as well as metal or organic contaminant, the organocatalysis offers a high level of consistency in organic transformation. These uniqueness steer them to sustain in multistep processes such as cascade/domino, multicomponent reaction, cycloaddition reactions etc.

The most fundamental way to construct oxa- and carbocycles in asymmetric pathway is the intramolecular oxa- and carba-Michael addition, respectively, by using chiral organocatalysts. These oxa- and carbo-cycles, specially, di-hydroisobenzofuran, isochroman, fused carbocycles etc. present in variety of natural product and drug molecules. Generally, covalent and non-covalent organocatalysis are the important tools in asymmetric synthesis to address diverse range of problems in a very efficient way. Keeping this in mind, previously our group addressed a fundamental problem regarding rapid self-cyclization in asymmetric intramolecular oxa-Michael addition and design a catalytic asymmetric system for that to afford enantio- and diastereoselective oxa-cycles with efficient yield.

In continuation, an asymmetric intramolecular oxa-Michael reaction has been developed by supressing the rapid self-cyclization of carboxylic acid using peroxyhemiacetal as a masked carboxylic acid.

Further, a development of chemoselectivity between 1,2- vs 1,4- addition in asymmetric nucleophilic addition to a multifunctional substrate, *ortho*-formyl chalcone is demonstrated using bi-functional chiral organocatalysis.

Moreover we developed an asymmetric C-C bond formation *via* organocatalytic pathway. Using both covalent and non-covalent mode of activation together we address the alternative path for Rauhut-Currier adduct of  $\beta,\beta$ -di-substituted enones as these are very reluctant for this type of reaction to afford fused carbocycles.

**Keywords:** organocatalysis, asymmetric synthesis, oxa-Michael, chemoselectivity, 1,2- vs 1,4-addition, fused carbocycles, RC adduct, dienamine catalysis

**Weakly-Coordinating Directing Groups in Transition Metal Catalyzed C-H  
Functionalization**

**RIKI DAS**

**Supervisor: Dr. Manmohan Kapur**

**DEPARTMENT OF CHEMISTRY**

**Accession No.: T00091**

The C-H bond can be viewed as a ubiquitous functional group in organic molecules. The conversion of unactivated C-H bonds into carbon-carbon or carbon-heteroatom bonds is the most significant conclusion of the transition metal catalyzed C-H activation process. In this scenario, employment of Lewis-basic directing groups has opened up new avenues to achieve site-selectivity in transition metal catalyzed C-H functionalization.

This Thesis is mainly focused on the transition metal catalyzed site-selective C-H functionalizations with the employment of weakly-coordinating directing groups. Detailed mechanistic studies have also been carried out to understand the feasible pathway for the transformations.

We successfully devised a new approach to control the outcome of C-H olefination reactions by just tweaking the substrate design, resulting in the development of a new class of Weinreb amides, wherein we were able to circumvent the reductive-destruction of the Weinreb amide framework, thereby retaining its synthetic utility.

Benzyl nitriles, Weinreb amides and anilides were developed as weakly-coordinating directing groups in palladium-catalyzed proximal C-H halogenations. Mechanistic investigations brought out interesting aspects with regard to the mode of C-H functionalization. This work also led to a rapid assembly of the phenanthridone skeleton. In a work pertaining to site-selective C-H olefination of  $\pi$ -deficient heterocycles, switching site-selectivity within a single substrate was successfully achieved, indirectly proving the two different pathways operating in the palladium and ruthenium catalyzed reactions. Here too, studies related to the mechanistic aspects brought out the difference in the mode of C-H metallation of quinolines and isoquinolines.

**Keywords:** C-H Activation, Directing group, Weak Coordination, Site-selectivity, Transition metal catalysis.

**Peripheral Functionalization,  $\pi$ -Expansion and Innocence of Corroles:  
Structure, Photophysical and Electrochemical Investigations**

**BIJU BASUMATARY**

**Supervisor: Dr. Jeyaraman Sankar**

**DEPARTMENT OF CHEMISTRY**

**Accession No.: T00090**

**Chapter 1:** The corrole macrocycle structurally resembles to that of  $\text{Co}^{\text{II}}$ -chelating corrin ring of Vitamin-B<sub>12</sub> and infact, Vitamin B<sub>12</sub> was the inspiration behind its first synthetic attempt in 1965 by Johnson and Kay. It is a contracted porphyrinoid having a 2,2'-bipyrrolic unit and three inner NH hydrogens. The rich and intriguing properties of corrole remained largely unexplored until the development of efficient methodologies for the synthesis of *meso*-arylcorroles in the late nineties. It exhibits many intriguing properties such as higher UV-Vis absorption coefficient and emission quantum yield, easy functionalization, ability to stabilize metal in higher oxidation state, higher acidic inner NH hydrogens and non-innocent character. A perusal of literature points out that the study on electronic perturbation caused by the chromophoric functionalization of corroles is comparatively less explored. In this thesis, we present some classical advance to this direction.

**Chapter 2:** The detailed experimental and computational techniques have been explained  
**Chapter 3, Part-A:** Design, synthesis and photophysical properties of *meso*/ $\beta$ -linked [3H]corrole-BODIPY and  $\text{Cu}^{\text{II}}$ corrole-BODIPY dyads have been explained. The compounds were characterized with  $^1\text{H}$ ,  $^{11}\text{B}$ ,  $^{19}\text{F}$  NMR, high resolution mass spectrometry and single crystal X-ray diffraction. The corrole and BODIPY fragments maintained respective ground state electronic isolation despite their connection through a single bond, due to a tilted orientation as observed by single crystal X-ray diffraction studies and as noted from UV-Vis absorption and electrochemical studies. Notably, the [3H]corrole-BODIPY exhibits complete fluorescence quenching due to photoinduced-electron transfer to a low lying charge separated state. Interestingly, the emission was regained upon addition of DBU due to the deprotonation of corrole. The “turn on” fluorescence behaviour and the presence of acidic NH hydrogens were further exploited toward basic anion sensing utility. The  $\text{Cu}^{\text{II}}$ Corrole-BODIPY dyad exhibits temperature-dependent paramagnetic behaviour as observed in the variable temperature  $^1\text{H}$  NMR due to the presence of thermally accessible ferromagnetically coupled  $\text{Cu}^{\text{II}}$ corrole- $\pi$ -cation radical.

**Chapter 3, Part-B:** Design, synthesis and photophysical properties of  $\beta$ /*meso*-linked  $\text{Ga}^{\text{III}}$ corrole-BODIPY triad have been explained. The compound was characterized with

<sup>1</sup>H, <sup>11</sup>B, <sup>19</sup>F NMR, high resolution mass spectrometry and single crystal X-ray diffraction. Anchoring a BODIPY moiety through the *meso*-position onto  $\beta$ -positions of Ga<sup>III</sup> corrole facilitated photoinduced electron transfer (PeT) in polar solvents. The corrole centred emission was observed in relatively low-polar solvents ( $\epsilon = 1.89 \leftrightarrow 9.41$ ) but readily quenched in high-polar solvents ( $\epsilon = 20.7 \leftrightarrow 48.9$ ). As the solvent polarity increases, Gibbs free energy for the electron transfer ( $\Delta G_{eT}$ ) values tend towards negative from +0.21 eV (THF)  $\leftrightarrow$  -0.23 eV (DMSO), and PeT becomes thermodynamically feasible in high-polar solvents. This result corroborated the quenching of corrole-centred emission in Ga<sup>III</sup> corrole-BODIPY triad in polar solvents. Interestingly, the Ga<sup>III</sup> corrole-BODIPY triad crystallized as two solvatomorphic forms, *viz.*, monoclinic and orthorhombic.

**Chapter 4:** The  $\pi$ -expansion of Ga<sup>III</sup>-corrole via 2,7  $\beta$ -pyrrolic positions of corrole gave an internally C-linked doubly N-confused [Ga<sup>III</sup>]hexaphyrin and heterobimetallic [Ga<sup>III</sup>/Rh<sup>I</sup>]hexaphyrin. All the compounds were characterized by <sup>1</sup>H, <sup>11</sup>B, <sup>19</sup>F NMR, high resolution mass spectrometry and single crystal X-ray diffraction. The <sup>1</sup>H NMR and electronic structure based on nucleus-independent chemical shift (NICS), anisotropy induced-current density (AICD), harmonic oscillator model of aromaticity (HOMA) and harmonic oscillator stabilization energy (HOSE) calculation suggested substantially localized aromatic character of [18]Ga<sup>III</sup>-corrole and a very weak aromatic contribution of [26]hexaphyrin. The local aromaticity was further supported from typical Ga<sup>III</sup>-corrole centered emission ( $\lambda_{emis} = 605, 660$  nm,  $\Phi_{absolute} = 1.3\%$ ) and strongly deshielded <sup>1</sup>H NMR resonance of  $\beta$ -pyrrolic hydrogen of [18]Ga<sup>III</sup>-corrole unit.

**Chapter 5:** The existence of a full-fledged non-innocent Ga<sup>III</sup>-corrole radical was unambiguously proved for the first time which revealed the [17]  $\pi$ -electron conjugated (or antiaromatic) radical. One-electron oxidation of a Ga<sup>III</sup>-corrole with N(4-BrC<sub>6</sub>H<sub>4</sub>)<sub>3</sub>SbCl<sub>6</sub> (Magic Blue) resulted in an air stable non-innocent Ga<sup>III</sup>-corrole radical. The single crystal X-ray crystallography of 2,17-bisformyl-5,10,15-tris(pentafluorophenyl)corrolato gallium(III)(chloride) radical revealed delocalization of the unpaired electron, which was further confirmed by electron spin resonance (ESR) spectroscopy and spin density distribution plot. The singly occupied Kohn-Sham orbitals (SOMOs) and spin density distribution plot are entirely distributed over the whole  $\pi$ -system of corrole ligand with no contribution from Ga<sup>III</sup> centre. Thus, suggested a full-fledged non-innocent [(corrolato<sup>2-</sup>)Ga<sup>III</sup>-Cl] complex rather than partially non-innocent [{(corrolato<sup>3-</sup>)(Ga<sup>III</sup>)<sup>•</sup>-Cl}] or a [(corrolato<sup>3-</sup>)(Ga<sup>IV</sup>)<sup>•</sup>-Cl] complex. In addition, the nucleus independent chemical shift (NICS), anisotropy induced-current density (AICD) and harmonic oscillator model of aromaticity (HOMA) supported a [17]  $\pi$ -electron conjugated (or antiaromatic) radical.

**Fluorogenic probe for formulation, cancer detection, bioconjugation,  
measuring polarity inside cellular organelle and removal of stress**

**KAUSHIK PAL**

**Supervisor: Dr. Apurba Lal Koner**

**DEPARTMENT OF CHEMISTRY**

**Accession No.: T00087**

This thesis work is highly multidisciplinary and layered in several aspects of drug formulation, organic chemistry, chemical biology, spectroscopy, and fluorescence microscopy. After the discovery of fluorescent materials, it is passing through an enormous evolution from finding new material to their applications. Herein, the report starts with the formulation of drug and food-additive by macrocyclic molecule cyclodextrin (CD). An environment sensitive intramolecular charge transfer (ICT) dye dapoxyl sodium sulfonate (DSS) has utilized as the reporter molecule because it shows substantial variation in fluorescence signal inside CD than that of in the bulk water. Employing indicator displacement assay (IDA) the efficacy of CD as the formulator of twelve drug (ibuprofen, paracetamol, methyl salicylate, salicylic acid, aspirin, piroxicam, resazurin, thiamphenicol, chloramphenicol, ampicillin, kanamycin, and sorbic acid) and seven food additives (monosodium glutamate, *trans*-ferulic acid, *p*-coumaric acid, gallic acid and its methyl, ethyl and propyl ester derivatives) are investigated. Later, the extension of the application of environment-sensitive ICT probes was done *via*. design and synthesis of a new class of single and two-photon active multifunctional and multicolor small fluorescent molecule. After structural and photophysical characterization the bioconjugation ability of multifunctional probe was successfully examined with protein and DNA. Subsequently, the mitochondria and endoplasmic reticulum (ER) specific probes were utilized to determining the polarity inside them. Many regulated biochemical processes are take place inside mitochondria and ER, and the fate of any chemical reaction highly govern by the polarity so, the polarity inside those cellular organelles is a fundamental question to be asked. The polarity inside mitochondria was turned out like MeCN and in case of ER, a mixture of CHCl<sub>3</sub> and CH<sub>2</sub>Cl<sub>2</sub>. After the synthesis of protein the proper processing of them happens inside ER. In stressed condition malfunction of ER can leads to many undesired effects on the living system. Followed by the previous work, an ER targeting two-photon active fluorogenic probe was designed and successfully utilized for the removal of stress because of reactive oxygen species and formaldehyde. In the final section, we have extend the application of specific fluorescent probe in the field

of cancer therapy. During malignancy, many cell-surface proteins get overexpressed hence they are potential target for cancer therapeutics. We have distinguished the cell-surface receptor (biotin and folate) positive and negative cell *via.* receptor-mediated endocytosis.

**Role of Surfactants in Drug Delivery and Protein Unfolding/ Refolding Dynamics : A Spectroscopy and Calorimetric Approach**

**Ramakanta Mondal**

**Supervisor: Dr. Saptarshi Mukherjee**

**DEPARTMENT OF CHEMISTRY**

**Accession No.: T00086**

In the present thesis, various aspects of self-assembled amphiphilic surfactant systems have been investigated using spectroscopic and calorimetric approaches. The interactions of a potent cancer cell photosensitizer namely, norharmane (NHM) with niosome vesicles, a model system for cell membrane which is composed by non-ionic surfactant TritonX 100 and cholesterol have been investigated in details. The contrasting effects of temperature and extrinsically added salt (NaCl) on niosome-bound drug (NHM) have been meticulously explored. Additionally, releasing of niosome-encapsulated drug (NHM) through inclusion complex formation by the addition of  $\beta$ -cyclodextrin as a potential supramolecular host has been investigated. The binding interaction of a model drug, phenoxyfranin (PSF) with Pluronic block copolymer (F127), both in the presence and absence of the anionic surfactant, sodium dodecyl sulfate (SDS) has been monitored. SDS form mixed-micelles with F127 and therefore we have quantitatively estimated the percentage drug bound in the mixed micellar system, which can be used as a potential carrier for drug delivery. The binding and associated thermodynamic properties due to the interactions have been estimated by calorimetric methods.

Mixed micellar systems have been employed to study unfolding and refolding dynamics of a biologically relevant protein, human serum albumin (HSA). Spectroscopic approaches have been used to show the sequential unfolding of HSA rendered by the addition of SDS. We found that the addition of Pluronic block copolymer P123 assist in refolding the unfolded HSA by the sequestration of SDS from the protein scaffolds due to the formation of mixed-micelle. The structural transitions of human hemoglobin (Hb) have been explored by the addition of bile salt (sodium deoxycholate, NaDC) in three different pHs. Our results conclusively establish the fact that bile salt induced the unfolding process of the protein (Hb) at pH 7.4 and 9.0. On the other hand the contrasting results were observed at pH 3.2, where acid induced unfolded protein turns to its native-like conformation by the addition of bile salts.

# **Carbon Based Materials for Energy Storage Application: Improving the Science of Energy**

**Chander Pratap Singh**

**Supervisor: Dr. Amit Paul**

**DEPARTMENT OF CHEMISTRY**

**Accession No.: T00085**

This thesis work is directed towarded the development of new methods for synthesis and activation of carbon based material and subsequently demonstration of these materials for energy storage. The key focus is to improve the science of energy storage. This thesis is divided into six chapters.

**Chapter 1** introduction the ubiquitous of carbon atoms from chemical compounds to living organism and its existing carbon allotropes and nanostructures. Literature survey on properties, synthesis and applications for energy storage devices of carbon nanostructures materials such as grapheme, activated carbon has been discussed. At the end, the scope of thesis highlighted wherein new strategies have been suggested to improve the energy storage.

**Chapter 2** discusses the optimized protocols for the synthesis and activation of carbon based materials used throughout thesis work. Experimental techniques and fabrication of electrodes and materials have been discussed.

**Chapter 3** discusses the synthesis of highly conducting reduced grapheme via low temperature chemically assisted exfoliation by using formic acid and its supercapacitor application. The composition of reduced graphene was characterized by using spectroscopy techniques power X-ray diffraction (PXRD), Raman and FT-IR. The morphology and thermal stability of different materials were characterized by scanning electron microscopy ( SEM), transmission electron microscopy ( TEM) and thermal gravimetric analysis (TGA). Electrical conductivity of reduced grapheme was measured by using four probe method and further, material has been tested for super capacitor application by using electrochemical techniques such as cyclic voltammetry ( CV) , chronopotentiometry ( CP) and electrochemical impedance spectroscopy ( EIS).

**Chapter 4** in continuation with the previous work, oxygen functionalized ( hydroxyl and carbonyl enriched ) few-layer grapheme ( OFG) has been synthesized by optimizing reaction parameters and it was used for proton conduction and super capacitor application.

# **Spectroscopic Investigations of Organized Assemblies Having Biological Significances**

**Nirmal Kumar Das**

**Supervisor: Professor Saptarshi Mukherjee**

**DEPARTMENT OF CHEMISTRY**

**Accession No.: T00084**

In this thesis, I have explored different self-organized assemblies using several spectroscopic and microscopic approaches and demonstrated suitable applications. I have studied temperature induced morphological transitions from native to unfolded aggregated states of Human Serum Albumin (HSA) using intrinsic fluorophore Tryptophan 214 (Trp214) as well as synthesized bio-active probe, 3-pyrazolyl 2-pyrazoline (PZ). Time-resolved FRET has been employed to elucidate structural transition of HSA as function of temperature. We have employed Atomic Force Microscopy (AFM) to establish that at elevated temperature, ~70°C, HSA undergoes self-assembly to form fibrillar structures. We have demonstrated that binding of Bovine Serum Albumin (BSA) to the cationic surfactant, Dodecyl Trimethyl Ammonium Bromide (DTAB) is dynamic in nature. The estimated binding is not strong as evident from weak complex formation of BSA-DTAB. The interactions of the cationic photo-sensitizer, Cresyl Violet (CV) in anionic (Sodium Dodecyl Sulfate, SDS), cationic (DTAB) and neutral (Triton X, TX-100) micellar systems have been explored. The ensemble average molecular interactions of CV into the different micellar assemblies have been substantiated at single molecule level using Fluorescence Correlation Spectroscopy (FCS). Using FCS measurements, we have shown for the first time that micelles with entrapped CV serve as efficient and versatile metal ion sensors. SDS micelle-entrapped CV effectively detects  $\text{Cu}^{2+}$  ions, while DTAB micelle-entrapped CV selectively detects  $\text{Hg}^{2+}$  ions.

We have been successful in developing optimized synthetic protocol for the synthesis of glutathione protected blue emitting Copper nanoclusters (CuNCs). These luminescent CuNCs exhibit enhanced photo-stability and significant quantum yields (QY). Our non-toxic and bio-compatible CuNCs primarily localize in nuclear membranes of the different cancerous cells (cervical cancer HeLa, breast cancer MDAMB-231 and lung cancer A549) and can thus serve as potential nuclear membrane markers. The synthesized CuNCs act as label-free  $\text{Fe}^{3+}$  ion sensors as these effectively detect  $\text{Fe}^{3+}$  ions in solution as well as human hemoglobin. The interactions of the CuNCs with HSA gives rise to the formation of a “protein-corona”, which influences controlled bio-reactivity in enzymes/proteins inside the cells. The associated thermodynamic and binding parameters have been estimated by

spectroscopic and ITC studies. Finally, FCS data substantiate the emergence of new “protein-corona” like assemblies thereby resulting in slower translational diffusion motions and concomitant rise of the hydrodynamic diameters.

**Functionalization of Olefins by Sulfur Based Catalyst/Reagents:  
Application in Asymmetric-Bromolactonization and Oxy-trifluoromethylation**

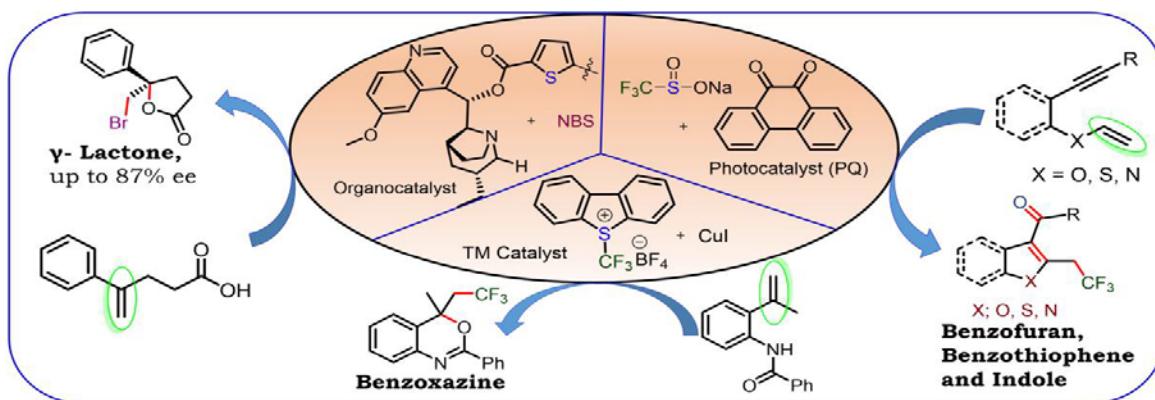
Sadhan Jana

Supervisor: Dr. Sangit Kumar

**DEPARTMENT OF CHEMISTRY**

**Accession No.: T00083**

Chalcogens are Lewis base; in particular, selenides and sulfides are useful catalysts to activate halogens in electrophilic halogenation of olefins. This approach has advantage in a number of electrophilic halogenation reactions such as halolactonization, haloetherification and polyene cyclization etc. However, catalytic, asymmetric bromofunctionalization of alkene is challenging.



The presence of C–F bonds in organic molecules has a profound effect on properties such as lipophilicity, permeability and metabolic stability so that more than 20% of the current approved drugs contain at least one fluorine atom. Although, several approaches have appeared to incorporate  $-\text{CF}_3$  in organic molecules due to their applicability in different fields. However, double bonds are privileged starting materials, as they are also amenable to flexible functionalization.

This PhD thesis describes towards efficient, green and sustainable routes for the synthesis of various heterocycles by using sulfur based organocatalyst and trifluoromethylating reagents.

**Keywords:** Olefines functionalization; asymmetric reaction; bromolactones; trifluoromethylation reaction; benzoxazines; benzofurans, benzothiophenes, indoles; organosulfur; copper-catalyzed reaction; photocatalysis; radical pathways, carbonylation, DFT calculations.

# Total Syntheses of Naturally Occurring Clavine Alkaloids

Saikat Chaudhuri

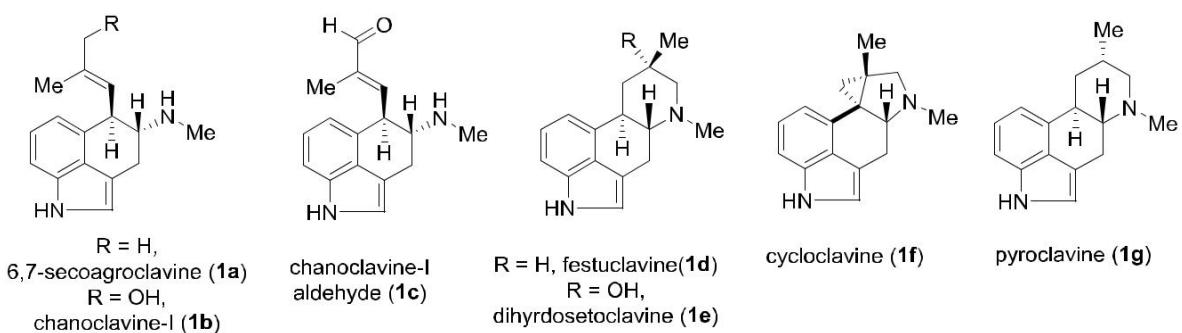
Supervisor: Dr. Alakesh Bisai

DEPARTMENT OF CHEMISTRY

Accession No.: T00082

Clavine family of ergot alkaloids (Figure 1) has a long-lasting and significant impact on both human health as well as agriculture. They were first documented as notorious poisons, stemming from the Middle Ages in central Europe, where consumption of ergot alkaloid contaminated cereal grains led to epidemics of ergotism (also known as St. Anthony's fire) resulting in about ten thousands of fatalities. The synthetic analogues of ergot alkaloids exhibit physiological activities, such as treatment for stopping postnatal bleeding, Parkinson's disease and others. Therefore, concise synthetic strategies to these alkaloids are not only interesting from academic stand point, but also provide the opportunity further to test their biological potentials. This thesis entitled “**Total Syntheses of Naturally Occurring Clavine Alkaloids**” is divided into four chapters namely **Chapters I, II, III and IV**.

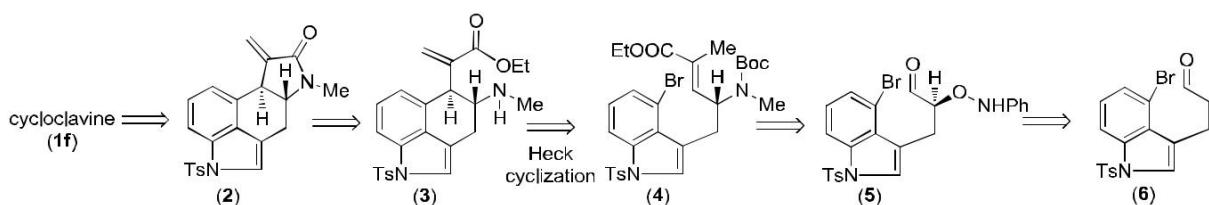
**Chapter I** entitled “**Literature Overview of Clavine Alkaloids: History, Occurrence, and Synthetic Approaches**” is a review of clavine alkaloids and their isolation from various sources. Clavine alkaloids possess architecturally interesting tricyclic, tetracyclic and pentacyclic structural motifs with vicinal stereocenters, with few congeners containing remote stereocenters, such as **1d-g** (Figure 1). Out of these, cycloclavine (**1e**) contain three contiguous stereocentre with a challenging vicinal tetra substituted cyclopropane ring. Some elegant literature reports describing total syntheses of naturally occurring and biologically active clavine alkaloids (Figure 1) have been discussed in this chapter.



**Figure 1:** Representatives of clavine alkaloids

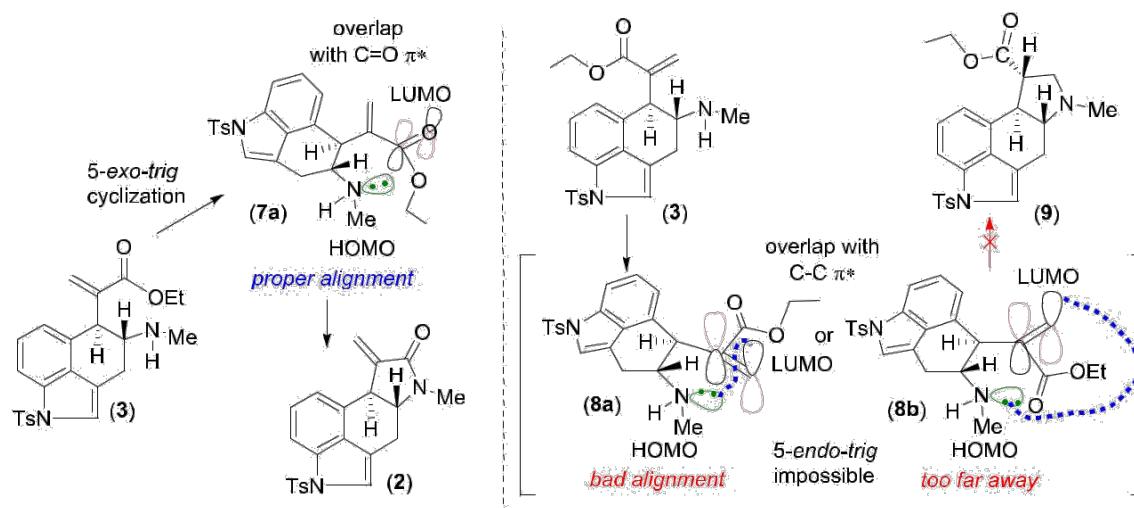
Although a large number of synthetic strategies are reported in the literature, out of which majority of the reports are in racemic form and only a few are reported in asymmetric fashion via chiral pool strategy. Therefore, there is a need for development of efficient catalytic enantioselective strategies for total syntheses of clavine alkaloids, in order to access both naturally occurring as well as unnatural analogues for further biological investigation.

**Chapter II** of this thesis entitled “**Total Syntheses of Cycloclavine via a Highly Diastereoselective Heck Cyclization**” deals with the formal total synthesis of cycloclavine. Retrosynthetically, it was envisioned that cycloclavine (**1f**) can be synthesized from an advanced enantiopure intermediate  $\alpha,\beta$ -unsaturated amide **2** (Scheme 1) via isomerisation followed by reduction of amide functionality and cyclopropanation. Compound **2** can be accessed from  $\alpha,\beta$ -unsaturated ester **3**, which could be, in fact, common intermediate for clavine alkaloids shown in Figure 1.



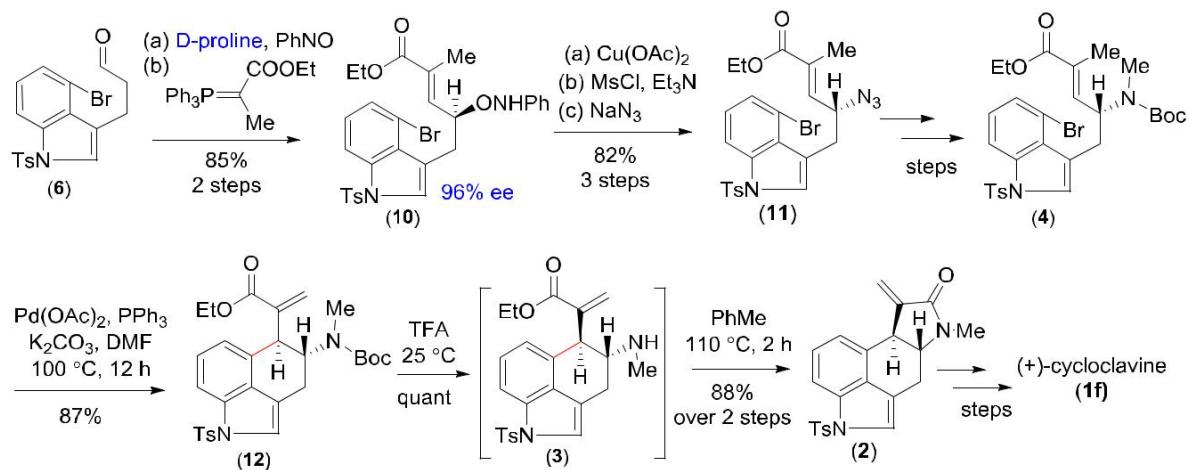
**Scheme 1:** Retrosynthetic analysis of cycloclavine.

It was argued that, ester **3** has the potential to afford two different tetracyclic intermediates, such as **2** and **9** (Scheme 2). A *5-exo-trig* cyclization of **3** can provide access to  $\alpha,\beta$ -unsaturated amide **2** (amide formation), on the other hand **3** can also afford ester **9** essentially following a *5-endo-trig* cyclization (*aza*-Michael reaction). As the secondary amine (HOMO) and C=O  $\pi^*$  (LUMO) are with proper alignment (see orbital representation in **7a**), a *5-exo-trig* cyclization of **3** would be facile to afford tetracyclic amide **2** (Scheme 2), whereas, a *5-endo-trig* cyclization of **3** would not be possible because of bad alignment of secondary amine (HOMO) and C=C  $\pi^*$  (LUMO) (see orbital representation of intermediates **8a** and **8b**) (Scheme 2). Therefore, a selective cyclization under an optimized condition would be utmost challenging and worth performing.



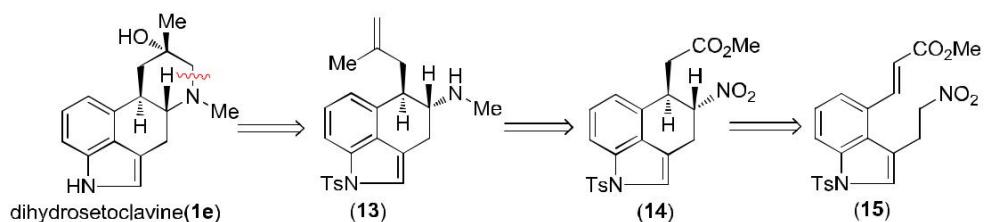
**Scheme 2:** 5-*exo*-trig versus 5-*endo*-trig cyclization of  $\alpha,\beta$ -unsaturated ester **3**.

On the basis of previous reports, it was decided to investigate the potential of proline catalyzed  $\alpha$ -oxyamination reaction in asymmetric total synthesis of cycloclavine (Figure 1). Towards this, 3-indolyl-propanaldehyde **6** was reacted under catalytic enantioselective  $\alpha$ - $\omega$  xyamination reaction with nitrosobenzene in the presence of 10 mol% D-proline (Scheme 3). This reaction afforded  $\alpha$ -oxyaminated aldehyde intermediate, which was immediately reacted with a stabilized Wittig, prepared from 2-bromo ethylpropionate, to afford compound **10** in 85% over 2 steps and with 96% ee. With enantioenriched **10** in hand, formal total synthesis of cycloclavine was achieved following a key 5-*exo*-trig cyclization (Scheme 3).



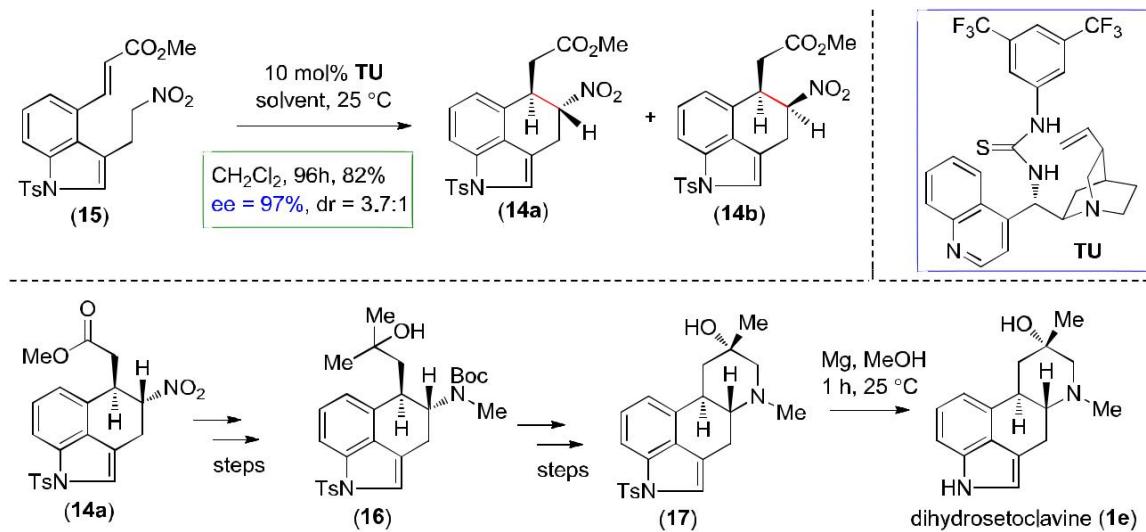
**Scheme 3:** Enantioselective formal synthesis of cycloclavine.

Further, construction of vicinal stereocentres in diastereo- and enantioselective fashion is one of the most challenging aspects in the synthesis of complex molecules. In this regard, **Chapter III** of this thesis entitled “**Total Synthesis of Dihydrosetoclavine via a Key Thio-Urea Catalyzed Nitro-Michael Reaction**”, describes the asymmetric total synthesis of dihydrosetoclavine (**1e**) following a thio-urea catalyzed C-C bond-forming process.



**Scheme 4:** Retrosynthetic analysis of dihydrosetoclavine (**1e**).

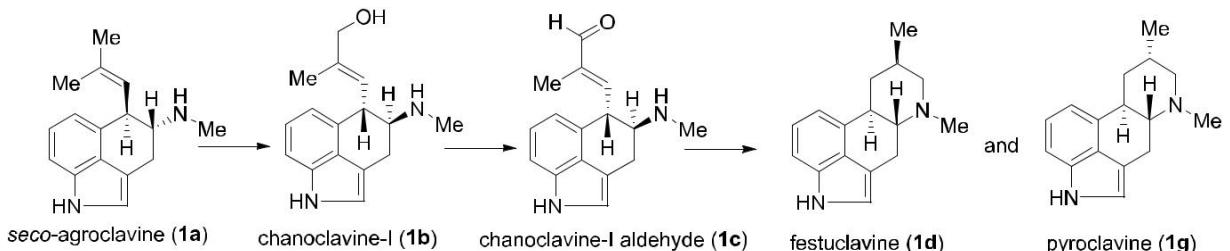
Retrosynthetically, it was envisioned that dihydrosetoclavine could be accessed from **13** via key C-N bond formation following synthetic manipulations, which in turn could be synthesized from enantioenriched **14** having vicinal stereocenter (Scheme 4). Enantioenriched **14** could be obtained from a key thio-urea catalyzed intramolecular diastereo- and enantioselective nitro-Michael reaction of **15**.



**Scheme 5:** Total synthesis of dihydrosetoclavine (**1e**).

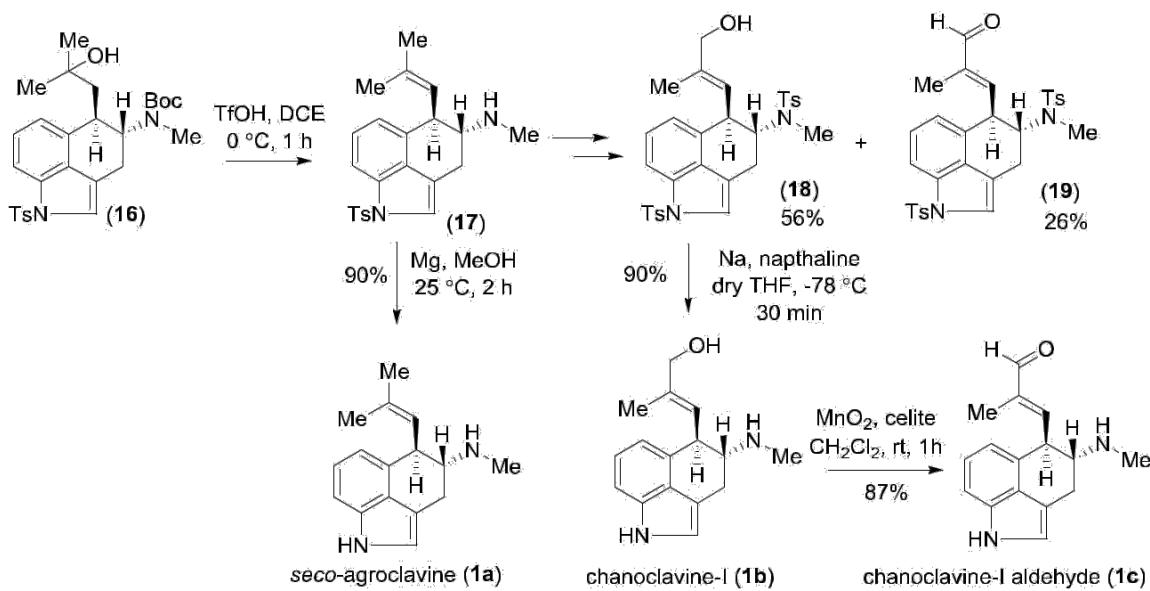
Therefore, an intramolecular thio-urea (TU) catalyzed diastereo- and enantioselective Michael reaction of **15** was developed to afford **14a** and **14b** in 3.7:1 dr with 97% ee of major diastereomer (Scheme 5). Following few synthetic manipulations, total synthesis of dihydrosetoclavine (**1e**) via tetracycle **17** was completed in few steps. It is noteworthy that, the unnatural antipode of **1e** i.e. *ent*-dihydrosetoclavine (*ent*-**1e**) was also synthesized from *ent*-**14a**. The later was prepared from a TU catalyzed intramolecular nitro-Michael reaction of **15** using pseudo enantiomeric catalyst **L** with similar efficiency.

Biosynthetic proposal of natural products often provide the opportunity for concise total synthesis in laboratory (also known as ‘*Nature Inspired Strategy*’). In this context, **Chapter IV** of this thesis entitled “**Biomimetic Total Syntheses of Festuclavine and Pyroclavine from *seco*-Agroclavine**” deals with total syntheses of tetracyclic clavine alkaloids mimicking a biogenetic path way (Scheme 6). It was argued that, being the simplest congener of clavine family, *seco*-agroclavine (**1a**) can be explored for asymmetric total syntheses of all clavine based alkaloids.



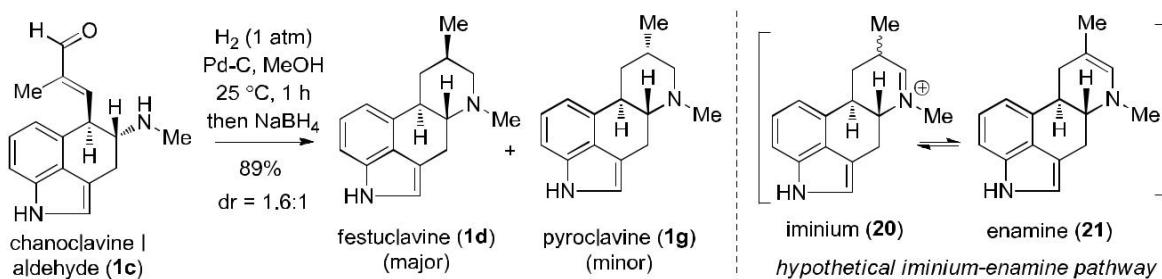
**Scheme 6:** Hypothesis inspired from a biosynthesis proposal.

With above hypothesis, a regioselective Saytzev elimination (over Hoffmann elimination) of tertiary alcohol **16** was carried out in presence of triflic acid to obtain (*R,R*)-**17** in exclusive manner (Scheme 7). The later was then oxidized to provide allylalcohol **18** following a regioselective allylic oxidation. This strategy ensured total syntheses of *seco*-agroclavine (**1a**), chanoclavine I (**1b**), and chanoclavine I aldehyde (**1c**) as per steps shown in scheme 7.



**Scheme 7:** Total syntheses of *seco*-agroclavine (**1a**), chanoclavines I (**1b**) and I aldehyde (**1c**).

With the synthesis of chanoclavine I aldehyde (**1c**) secured, it was hydrogenated to access festuclavine (**1d**) and pyroclavine (**1g**) following a biomimetic proposal (Scheme 8). This one-pot cascade featured a hydrogenation, and iminium-enamine tautomerization (see, iminium **20** and enamine **21** in scheme 8), followed by reduction to afford festuclavine (**1d**) in 54% and pyroclavine (**1g**) in 35% isolated yields (Scheme 8).



**Scheme 8:** Biomimetic total syntheses of festuclavine (**1d**) and pyroclavine (**1g**) through the intermediacy of iminium **20** and enamine **21**.

**Total Syntheses of 3a, 3a'-Bis-Pyrrolo[2,3- b]indoline Alkaloids via the Development of Catalytic Deacylative Alkylation (DaA)**

**NIVESH KUMAR**

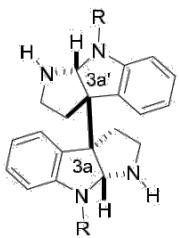
**Supervisor: Dr. Alakesh Bisai**

**DEPARTMENT OF CHEMISTRY**

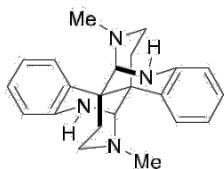
**Accession No.: T00081**

The tricyclic pyrrolidino[2,3-*b*]indoline, with an all-carbon quaternary stereogenic center at the pseudobenzylic C-3 position, is the fundamental building block of naturally occurring cyclotryptamine alkaloids. This ring system is found exclusively in the *cis*-configuration, presumably because of the higher level of ring strain in the *trans*-stereoisomer. In dimeric cyclotryptamine alkaloids, individual *cis*-pyrrolidino [2,3-*b*]indoline units are linked at their pseudobenzylic positions. This thesis is divided into four chapters *viz* chapters I, II, III and IV.

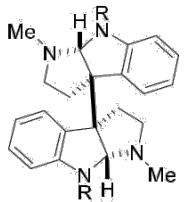
**Chapter I** entitled "**Synthetic Approaches to the 3a,3a'-Bis-Pyrrolo[2,3-*b*]indoline Alkaloids: The Literature Overview**" is a review of the synthetic approaches to the dimeric cyclotryptamine alkaloids sharing 3a,3a'-bis-pyrollindino[2,3-*b*]-indoline structure (Figure 1). The linkage of two *cis*-pyrrolidino [2,3-*b*]indoline units affords a 3a,3a'-bispyrrolidino[2,3-*b*]indoline (**1a-b**), thereby creating challenging vicinal all-carbon quaternary centers. These naturally occurring alkaloids possess architecturally complex structural motifs with C<sub>1</sub>-symmetry, such as *meso*-chimonanthine (**meso-1a**) and *meso*-folicanthine (**meso-1b**), sharing four contiguous stereogenic centers. Among all the four stereocenters, two of them are all-carbon quaternary stereogenic centers situated at the vicinal position (3a, 3a' shown in **1a-b**). Interestingly, there are alkaloids isolated from Nature, can also possess C<sub>2</sub>-symmetry in their structural motifs, leading to active isomers, such as (-)-chimonanthine (**1a**) and (-)-folicanthine (**1b**). In addition, *meso*-calycanthine (**meso-2a**) has also been isolated from various species, which is biogenetically arising from an acid catalysed isomerization of *meso*-chimonanthine (**meso-1a**). Along the similar line, (+)-calycanthine (**2a**) is assumed to be arising from an acid catalysed isomerization of (-)-chimonanthine (**1a**). In addition to their intriguing architecture, few congeners of this family exhibit interesting biological properties. Some conceptual literature reports focussing on the total synthesis of naturally occurring and biologically active alkaloids (Figure 1) have been discussed in this chapter.



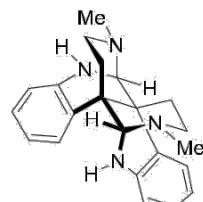
R = H, *meso*-chimonanthine (**1a**)  
R = Me, *meso*-folicanthine (**1b**)



*meso*-calycanthine (**2a**)



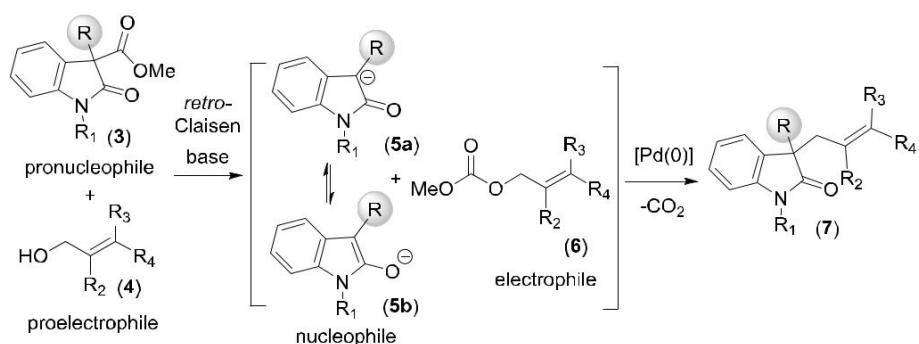
R = H, (-)-chimonanthine (**1a**)  
R = Me, (-)-folicanthine (**1b**)



(+)-calycanthine (**2a**)

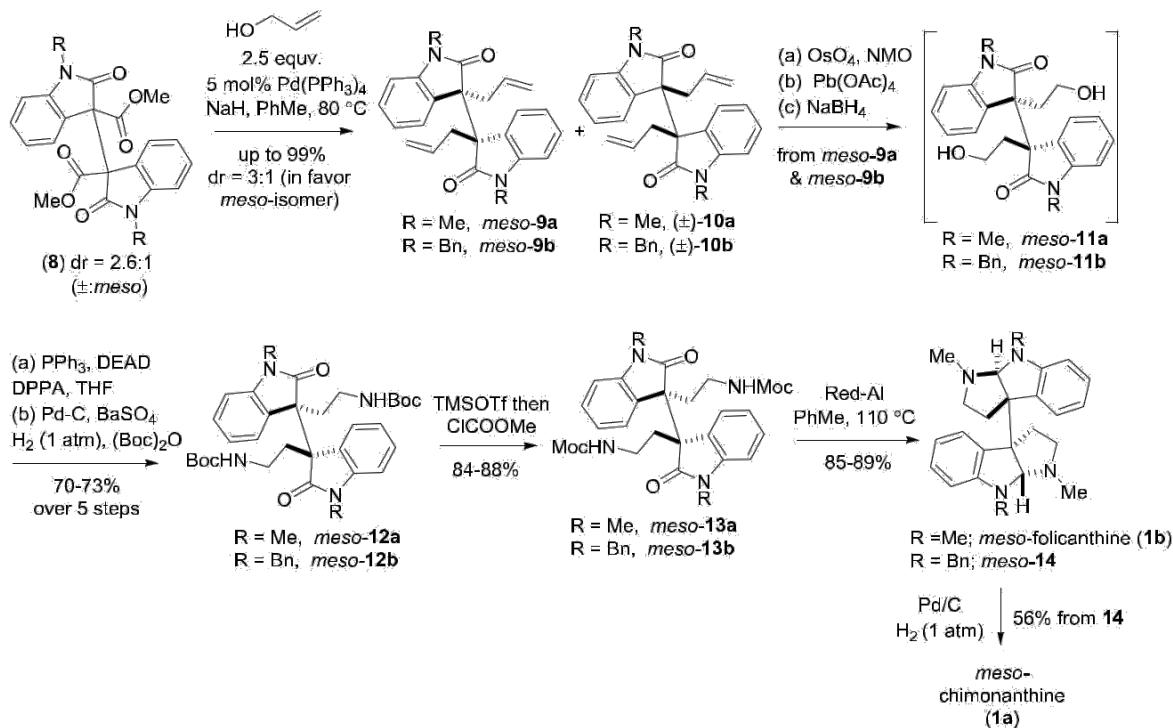
**Figure 1:** Representatives of dimeric cyclotryptamine alkaloids.

**Chapter II** entitled "**Development of Catalytic Deacylative Alkylation (DaA) of 3-Acyl-2-Oxindoles: Total Synthesis of *meso*-Folicanthine and *meso*-Chimonanthine**" deals with the deacylative approaches to *meso*-chimonanthine (*meso*-**1a**) and *meso*-folicanthine (*meso*-**1b**) *via* a key Pd-catalyzed deacylative allylation (DaA) strategy. It was envisioned that an allylic alkoxide (in situ prepared from **4**) may induce a *retro*-Claisen condensation of an appropriately substituted 2-oxindole **3** to form enolate **5b** as active intermediate *via* carbanion **5a** (Scheme 1). This enolate **5** would then react with Pd(II)- $\pi$ -allyl complex generated *in situ* by reaction of allyl acetate **6** and Pd(0) to furnish various 2-oxindoles **7** with a quaternary center at the pseudobenzylidene position.



**Scheme 1:** Deacylative alkylations (DaA) *via* *retro*-Claisen strategy.

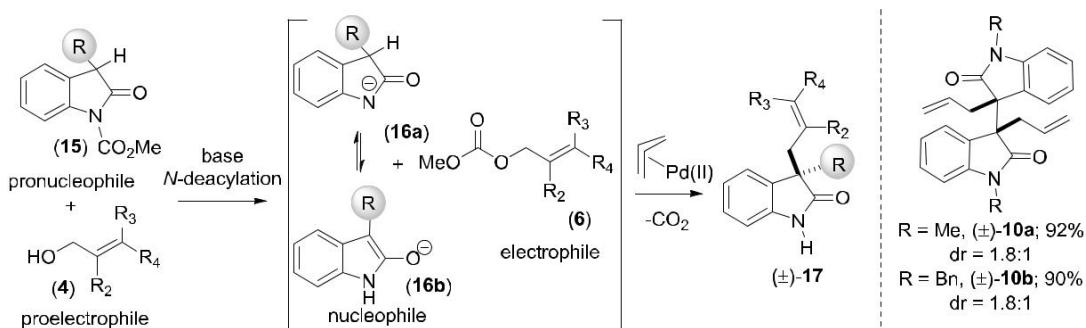
Further, it was succeeded in the stereoconvergent construction of vicinal stereogenic all-carbon quaternary centers using double deacylative alkylation (DaA) of a bisester **8** possessing ( $\pm$ ) and *meso*-diastereomers (dr = 2.6:1) (Scheme 2). This strategy afforded C<sub>1</sub>-symmetric products *meso*-**9** over the ( $\pm$ )-**10** with moderate diastereoselectivity (dr up to 3:1). Utilizing aforementioned strategy it was completed total synthesis of *meso*-chimonanthine (*meso*-**1a**) and *meso*-folicanthine (*meso*-**1b**) (Scheme 2).



**Scheme 2:** *meso*-chimonanthine (*meso*-**1a**) and *meso*-folicanthine (*meso*-**1b**).

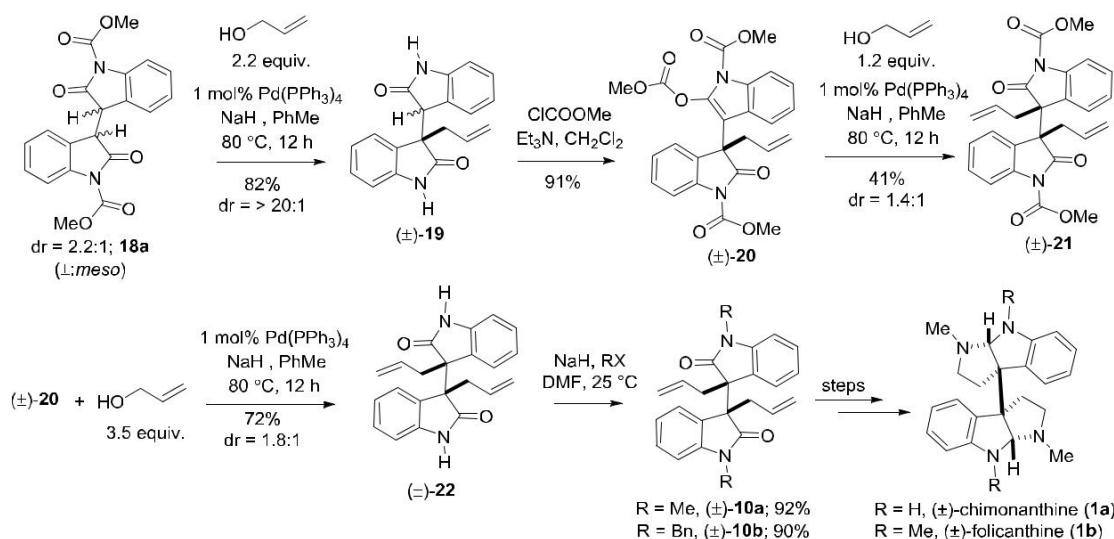
Chapter III entitled "Development of Pd(0)-Catalyzed Chemoselective Deacylative Alkylation (DaA) of *N*-Acyl-2-oxindoles: Formal Total Synthesis of (±)-Folicanthine and (±)-Chimonanthine" describes a highly chemoselective C-C bond forming reaction *via* deacylative alkylations of compound **15** (Scheme 3). In this chapter, it was hypothesized that Pd(0)-catalyzed deacylative allylation of *N*-acyl-2-oxindole **15** *via* coupling of *in situ* generated nucleophiles of type **16** with allyl electrophiles **6** can lead to the advanced intermediates **10a-b**, essentially providing the opportunity for the formal total synthesis of (±)-chimonanthine (**1a**) and (±)-folicanthine (**1b**). Following exhaustive optimization, it was found that Pd(0)-catalyzed deacylative allylations of *N*-acyl-3-substituted 2-oxindoles **15** *via* *in situ* generated electrophiles [Pd-π allyl complex] can be envisioned for the synthesis of a variety of 2-oxindoles **17** with C-3 quaternary centers. Gratifyingly, this alkylation process is found to be highly chemoselective in nature, where a C-C bond formation is completely predominant over a C-N bond formation (Scheme 3). Further, it was explored deacylative sequential allylations of dimeric *N*-acyl-2-oxindole **18a** [ratio of (±) and *meso*-diastereomers is 2.2:1] with 2.2 equiv. of allyl alcohol under the optimized condition (Scheme 4). However, efforts towards this direction led to only monoallylated product **19** in 82% with excellent diastereoselectivity (dr = >20:1), and it didn't observe bis-alkylation in this case. Therefore, we thought of elaborating compound

= for a synthetic approach to C<sub>2</sub>-symmetric pyrrolidino [2,3-*b*]indoline structures. Towards this, compound **19** was reacted with methylchloroformate to furnish ( $\pm$ )-**20** (Scheme 4).



**Scheme 3:** Our hypothesis of deacylative alkylation (DaA) for *N*-acyl-2-oxindoles.

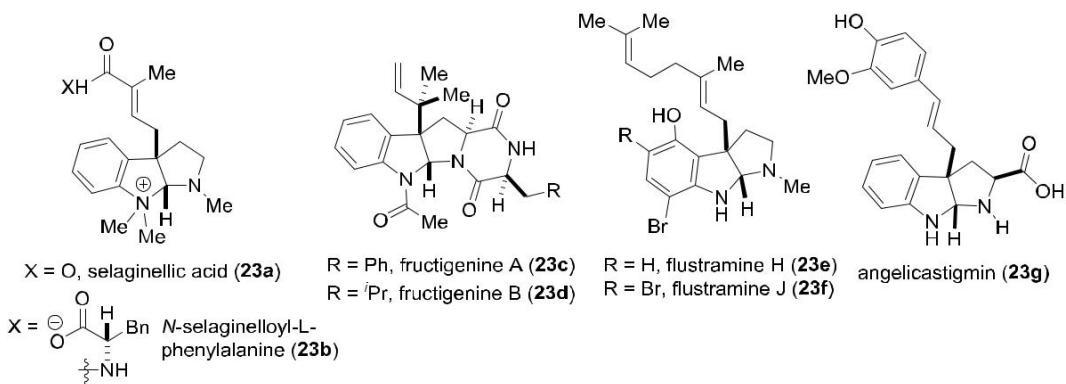
The latter was further treated under chemoselective DaA in the presence of 1.2 equiv. of allylalcohol to afford **21** with 1.4:1 diastereoselectivity, where *N*-methoxycarbonyl groups were intact. Interestingly, compound **20** can follow sequential deacylative allylations with 3.5 equiv. of allylalcohol to furnish bis-allylated compound **22** in 72% with 1.8:1 diastereoselectivity. Compound **22** was further alkylated to afford **10a-b**, en route to formal total syntheses of ( $\pm$ )-chimonanthine (**1a**) and ( $\pm$ )-folicanthine (**1b**) (Scheme 4).



**Scheme 4:** Formal total synthesis of ( $\pm$ )-chimonanthine (**1a**) and ( $\pm$ )-folicanthine (**1b**).

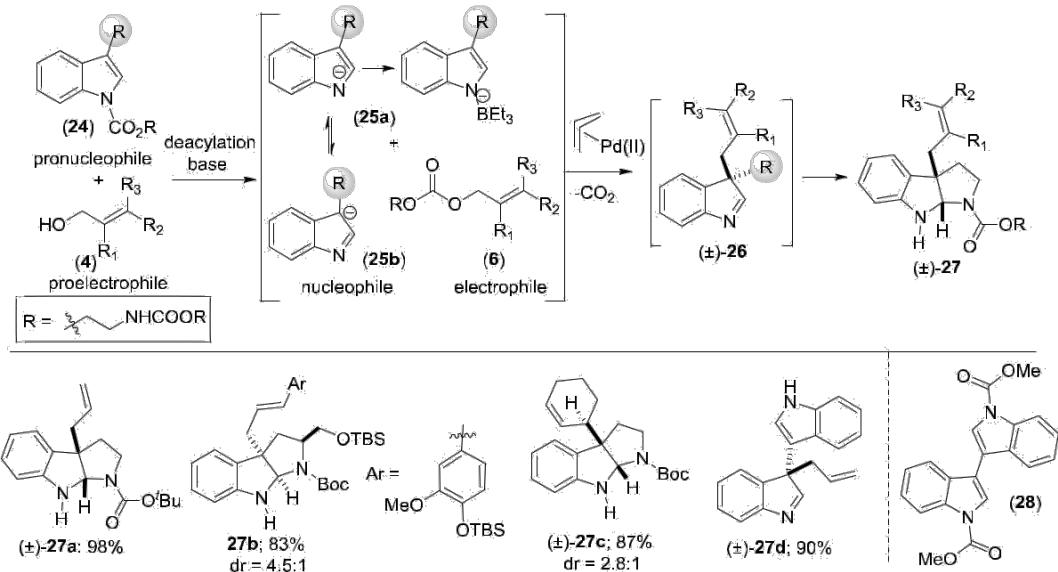
**Chapter IV** entitled "Catalytic Deacylative Alkylation of *N*-Acyl-3-substituted Indoles: Expedient Syntheses of C(3)-Quaternary Hexahydropyrrolo[2,3-*b*]indole Alkaloids" deals with a one-pot catalytic approach to the hexahydropyrrolo[2,3-*b*]indoles

embedded with the C-3 quaternary center from *N*-acyl 3-substituted indoles (**24**). A wide range of hexahydropyrroloindolines (Figure 2) sharing a prenyl (3,3 dimethylallyl) functionality at the pseudobenzylidic position, such as selaginellic acid (such as **23a**), *N*-selaginelloyl-L-phenylalanine (**23b**) are isolated from various species. In addition, there are a number of alkaloids sharing a *reverse*-prenyl group at C-3 quaternary center (such as **23c-d**), and a geranyl group at the quaternary center (such as **23e-f**). Recently, hexahydropyrrolo[2,3-*b*]indoline with a substituted cinnamyl group at the C-3 position, such as angelicastigmin (**23g**, has also been isolated from the root of *Angelica polymorpha* maxim.



**Figure 2:** Representatives of dimeric cyclotryptamine alkaloids.

Therefore, in search for a unified approach to these hexahydropyrrolo[2,3-*b*]indoles embedded with the C-3 quaternary center, exploration of catalytic chemoselective synthesis of hexahydropyrrolo[2,3-*b*]indoles embedded with the C-3 quaternary center from *N*-acyl 3-substituted indoles (**24**) has been investigated. The reaction furnishes adducts **27a-d** displaying high regiocontrol, chemoselectivity for the indole C-3 position, and diastereocontrol in the course of installing vicinal tertiary/quaternary centers (see, **27c**). Later, a one-pot synthesis of enantioenriched pyrroloindolines sharing a cinnamyl group at the C-3 position was also explored for a synthetic approach to angelicastigmin (**23g**). This reaction afforded enantiopure pyrroloindoline **27b** (linear as a sole product over branch) in 83% yield with 4.5:1 dr (Scheme 5).



**Scheme 5:** Deacylative alkylations (DaA) of 3-substituted *N*-alkoxycarbonyl indoles.

Further utilization of this methodology for the synthetic approaches to 3a,3a'-bis-pyrrolo[2,3-*b*]indoline alkaloids, such as ( $\pm$ )-chimonanthine (**1a**) and ( $\pm$ )-folicanthine (**1b**) was undertaken. Towards this, to the surprise, *N,N'*-bis-methoxycarbonyl protected indole **28** afforded monoallylated product **27d** in 90%, where only single allylation took place. Therefore, it was elaborated intermediate **27d** for accessing C<sub>2</sub>-symmetric dimeric 2-oxindoles through a diastereoselective process as described in Chapter III.

**Modulating Anti-microbial and Drug Delivery Potential of Polymers with  
Amine Pendants**

**Prabhusrinivas Yavvari**

**Supervisor : Dr. Aasheesh Srivastava**

**Department of Chemistry**

**Accession No.: T00080**

Amines play prominent role in modulating the membrane or surface interactions of many Biomacromolecules such as antimicrobial peptides or polymer based nanoparticles used for lysing bacterial membranes or for delivering therapeutic payloads into mammalian cells. The ability of the amines to show hydrogen bonding and electrostatic interactions, help synthetic macromolecular systems to permeabilize the bacterial and mammalian cell membranes. This thesis explores biomedical applications such as anti-mycobacterial activity along with drug and gene delivery through chemical modification of synthetic and semi-synthetic polymers endowed with amine pendants.

**Chapter 1** introduces the role of amines in influencing physico-chemical properties of biomaterials. It emphasizes the use of biodegradable polymers constituting amines, in preparing a wide range of biomaterials to fulfil various needs in biomedical applications. This chapter also discusses the literature review of biodegradable amine based polymers used for antibacterial or drug delivery applications. This chapter offers a basic perception of the work presented in the current thesis, discussed in the fore-coming chapters.

**Chapter 2** discusses the design and synthesis of polyaspartamide polymers containing amine pendants with varied degrees of methylation. When explored for their anti-microbial potential, these polymers displayed profound influence of the extent of alkylation of amine pendants on their potency and selectivity. High derivatization and the induction of a hard cationic charge on amine pendants resulted in achieving high potency and high selectivity targeting mycobacterial species over other bacterial strains and mammalian cells. This study helps in understanding the role of amine constituted in biomaterials.

**Chapter 3** discusses the preparation of poly-aspartamide polymers having quaternary amine pendants with variable alkyl residues for use in gene delivery applications. A combination of hard cationic charge and optimal hydrophobicity in the polymer made it highly efficient in delivering the anionic nucleic acid payload into variety of mammalian cells. To subdue the

membrane toxicity of polymers having long alkyl residues attached to them, the polymer-siRNA/pDNA complexes were further mixed with anionic poly-aspartate solution to form polyelectrolyte complexes (PECs). These PECs displayed enhanced shelf lives in addition to offering resistance to degrading effects of nucleic acids, induced by nucleases or serum or pH extremities. The resulting PECs were able to show transfection of the gene therapeutics *in vivo* through oral mode of administration with a very high efficacy.

**Chapter 4** details the preparation of amphiphilic drug delivery systems from poly-succinimide precursor by employing hydrophobic as well as hydrophilic soft charged amines to form cationic nano-aggregates in aqueous solutions. These cationic systems were utilized to entrap high amounts of hydrophobic drug Curcumin (Cur). A clear correlation between the length of alkyl pendants present in the polymer and its ability to entrap Cur was noted. In addition to forming stable dispersions with high drug entrapment efficiency, the aqueous suspensions of the polymers formed poly-electrolyte complexes (PECs) when mixed with aqueous solutions of anionic sodium poly-aspartate (SPA). The PEC formation resulted in high compatibility with the mammalian cell membranes while increasing their ability to deliver the Cur more selectivity towards cancerous cells over non-cancerous mammalian cells resulting in enhanced therapeutic effect.

**Chapter 5** discusses the chemical modification of the amine residues present in natural biopolymer chitosan with catechol groups in order to prepare coordinatively cross-linked hydrogels for localized delivery of multiple anti-cancer drugs at tumor site. Appending catechol moieties onto the inherent glucosamine moieties of chitosan using reductive amination offered a unique advantage of retaining the cationic nature of chitosan independent of the extent of catechol derivatisation. The addition of Fe(III) to the aqueous solutions of these catechol derivatized chitosan polymer yielded hydrogels even at acidic pH. Owing to the reversible Fe(III)-catechol complexation, the hydrogels showed high injectability and self-healing ability. The hydrogel network helped in entrapping multitude of anticancer drugs with sustained drug releasing properties. Drug entrapped gels, when injected into tumor bearing mice, displayed enhanced anti-tumor efficacy and lower toxicity when compared to the injection of drug combination through intravenous modes of administration, leading to higher survival rates of mice.

**Exploring Photophysics of Solvatochromic 2,3-Naphthalimide Dyes with Potential in  
Fluorescence Sensing**

**Suman Mallick**

**Supervisor: Dr. Apurba Lal Koner**

**Department of Chemistry**

**Accession No.: T00078**

**Chapter 1** describes the brief background of this presented work. General concepts about the excited properties of intramolecular charge transfer (ICT) dyes have discussed briefly. Also some relevant examples of ICT dyes and naphthalimide dyes are illustrated briefly with various applications.

**Chapter 2** contains the experimental methods, data analysis, instruments used for the work and the synthetic protocols.

**Chapter 3** represents spectroscopic investigation of small, non-charged diethyl 6-(dimethylamino)naphthalene-2,3-dicarboxylate (DMNDC) by UV-Visible, steady-state, and time-resolved fluorescence spectroscopy. These studies reveal a series of interesting photophysical properties. The photophysical properties of DMNDC originate from the intrinsic intramolecular charge-transfer (ICT) state, leading to various applications. Emission maxima and Stokes shift of DMNDC show a very good correlation with  $E_T(30)$  solvent polarity scale for a series of different polarity solvents, thus confirms its excellent environment sensitivity. DMNDC has been found to be an exceptionally suitable probe for determining critical micelle concentration (CMC) by probing self-organization processes of five different types of surfactants with structural diversity. Along with this, this small sized electroneutral, and excellent solvatochromic fluorescent properties of DMNDC was employed for deciphering the number of hydrophobic binding pockets and their local microenvironment present in Bovine Serum Albumin (BSA).

**Chapter 4a** is based on the detection of biogenic amines accurately at nanomolar concentration. It claims urgent interest due to their crucial roles in different biological process and also for their toxicity. A 2,3-Naphthalimide dye (DMN-Anh) with an anhydride moiety shows an efficient fast ratiometric optical response towards the primary and biogenic amines in a quantitative manner at submicromolar concentration at room temperature. Primary and biogenic amines can be detected easily and accurately at nanomolar concentration. The dye DMN-Anh also shows additional ability to discriminate between primary, secondary and tertiary amines by using both UV-Visible and

fluorescence spectroscopy. The amine detection mechanism by the dye was based on a simple nucleophilic addition reaction by the amines with the anhydride functional group, was proved by NMR and mass spectrometry also.

**Chapter 4b** demonstrates solvent mediated nucleophilic reactions like alcoholysis and hydrolysis of DMN-Anh probe using optical methods (UV-Vis and fluorescence spectroscopy) in variety of alcohols and in bio-mimetic environments like micelles, macrocyclic host and protein nanocavities. Rate of the solvolysis reaction of DMN-Anh in alcohols is found to be dependent with the alkyl chains length. The rate of the hydrolysis of DMN-Anh at physiological condition (pH 7.4, at 25 °C) was very slow but the rate of the same reaction in similar condition was significantly enhanced in presence of micelles and protein (BSA). Thus, this type of fundamental kinetic analysis on the bio-mimetic solvolysis reactions could be helpful to design novel probe-drug conjugate for their efficient control-release and function.

**Chapter 5a** represents the aggregation induced emission (AIE) studies of a new synthesized 2,3-Naphthalimide based environment sensitive dye, 6-(Dimethylamino)-2-butyl-1H-benzo[f]isoindole-1,3(2H)-dione (DMN-Bu). The dye shows unprecedented AIE properties in water at neutral pH at submicromolar concentration. While, the aggregated dye molecules can be deaggregated efficiently by employing Cyclodextrin derivatives, which also reveals the H-aggregation nature of the dye molecules. Along with that, by a supramolecular approach, a reversible tuning of aggregation-induced optical properties using Cyclodextrin-assisted encapsulation is presented. This method opens up the possibility of tuning the optical properties of other aggregation prone dye molecules in water by varying the cavity size of macrocyclic host molecule.

**Chapter 5b** describes surfactants-induced tuning of the AIE properties of DMN-Bu, an environment sensitive 2,3-substituted naphthalimide dye, at neutral pH. The detailed investigation of the photophysical properties of DMN-Bu in water in presence of the surfactants above their micellar concentration by following the excitation spectrum compared to its absorption spectra reveals the transformation of the H-aggregates of the dye to the monomeric form. Following the emission properties of DMN-Bu dye aggregates to its monomeric form, was utilized to estimate the critical micelle concentration (CMC) of the ionic surfactants. Employing a supramolecular approach, *i.e.*, by removal of the surfactant molecules from the system upon host-guest complexation with  $\alpha$ -cyclodextrin, the aggregation-deaggregation properties of the dye molecules has been made reversible.

**Chapter 6** illustrates a brief summary of the work done in this thesis and a short outline to my future plans discussing about scope of the work can be further performed in the same area.

**Exploring Protein-Drug and Protein-Surfactant Interactions by Spectroscopic and  
Calorimetric Approaches**

**Narayani Ghosh**

**Supervisor: Dr. Saptarshi Mukherjee**

**Department of Chemistry**

**Accession No.: T00077**

This thesis reports the binding interaction of potential antibacterial drugs Chloramphenicol (Clp) and Norfloxacin (NOF) with various transport proteins and the molecular level understanding of how anionic and neutral surfactants interact with plasma protein in terms of not only deciphering the modulations of protein structure and function but also exploring the underlying binding forces. The binding of the drugs, Clp and NOF to the protein  $\beta$ -Lactoglobulin ( $\beta$ LG) quenches the intrinsic fluorescence of  $\beta$ LG and the mechanism of quenching was proved to be mainly static in nature. However, the Clp- $\beta$ LG binding constant is found to vary proportionately with temperature. This anomalous result is explained on the basis of the Arrhenius theory which states that the rate constant varies proportionally with temperature. The thermodynamic parameters for the NOF- $\beta$ LG binding phenomenon as-evaluated on the basis of van't Hoff relationship reveal the predominance of electrostatic/ionic interactions underlying the binding process. However, thermodynamic data as- estimated by ITC study suggests the major role of hydrophobic interactions in the Clp- $\beta$ LG binding. The binding interaction of NOF with HSA is also investigated here. Spectroscopic results unravel the zwitterionic to cationic prototropic transformation of NOF accompanying the binding with HSA. However, a key finding of the present work lies in deciphering the thermodynamics of the interaction which displays serendipitous evidence for the involvement of more than one type of binding forces (hydrophobic and electrostatic) underlying the NOF-HSA interaction. The addition of a series of bile salts having varying polarity (Sodium Deoxycholate, Sodium Cholate, and Sodium Taurocholate) to HSA have been shown to occur via a sequential manner via three distinct stages. The spectroscopic and calorimetric techniques conclusively establish the fact that the hydrophobicity of the bile salts seems to be the principal factor in governing the interaction of the bile salts with HSA. The binding interaction of non-ionic surfactant Tween 40 and Tween 80 (TW40 and TW80) to HSA has been also studied by spectroscopic and thermodynamic methods. It is shown that the HSA-Tween interaction does not occur in a step-wise manner unlike the cases with ionic surfactants like SDS. Our ITC experiments substantiate that the interaction is entropically unfavorable and enthalpically favorable (i.e., mainly driven by weak forces like van der Waals/hydrogen bonding interactions).

# **Investigation of Magnetic Anisotropy and Slow Magnetic Relaxation in Cobalt(II) Based SingleIon Magnets**

**Amit Kumar Mondal**

**Supervisor : Dr. Sanjit Konar**

**Department of Chemistry**

**Accession No.: T00076**

Chapter 1 describes the brief background to this presented work. All the general concepts behind those magnetic properties are discussed briefly. Also some relevant examples of lanthanide and transition metal based single-molecule magnets (SMMs) or single-ion magnets (SIMs) are illustrated briefly with the proper comparison. Chapter 2 describes quantitative magnetostructural investigations for tetrahedral CoII complexes based on P-donor ligand. For the first time, the heavy atom effect was explored in the series of tetrahedral CoII complexes CoLX<sub>2</sub> (X= NCS (1), Cl (2), Br (3) and I (4); L= 9,9-dimethyl -4,5-bis(diphenylphosphino) xanthenes) based on P-donor ligand and it has been reported that ligands with heavy and soft main group donor atoms are able to decrease the anisotropy of the metal complexes. Detailed dc and ac magnetic susceptibility measurements divulge the existence of field induced slow magnetic relaxation behavior of the CoII centres with an easy-axis type magnetic anisotropy. The differences in ligand field strength imposed by the terminal ligands result in modulating the single ion anisotropy (D) of complex 1-4. A correlation between the zero-field splitting and angular distortion parameters of tetrahedral CoII complexes has been revealed. To elucidate the role of intermolecular interactions between adjacent CoII centres in the magnetic relaxation behavior a diamagnetic isostructural ZnII analogue (5) was synthesized and magnetic behavior was examined. Chapter 3A represents the investigation of the effects of ligand field strength around the metal ion as well as its geometry on magnetic anisotropy of pentacoordinated CoII complexes using a combined experimental and theoretical approach. For that, a strategic design and synthesis of two new penta-coordinate CoII complexes [Co(bbp)Cl<sub>2</sub>]·(MeOH) (1) and [Co(bbp)(NCS)<sub>2</sub>] (2) (bbp = 2,6-bis(2-benzimidazolyl)pyridine) has been achieved by employing the planar tridentate coordination environment of the ligand in conjunction with two accommodating terminal ligands (i.e. chloride and thiocyanate). Detailed dc and ac measurements disclose the occurrence of field induced slow magnetic relaxation behavior of CoII centres with an easy-plane magnetic anisotropy. A quantitative estimation of ZFS parameters have been successfully performed using density functional theory (DFT) method. Both the sign and magnitude of D are prophesied remarkably well by this theoretical approach. The DFT calculations also reveal that the  $\alpha \rightarrow \beta$  (SOMO-SOMO) excitation contributes almost entirely to the total ZFS values for both complexes. It is worth noting that the excitation pertaining to the most positive contribution to the ZFS parameter is the  $d_{xy} \rightarrow d_{x^2-y^2}$  excitation for complex 1, whereas for complex 2 it is the  $d_{z^2} \rightarrow d_{x^2-y^2}$  excitation. Chapter 3B is based on the reports of two pentacoordinated CoII -P4X1 single ion magnets (SIMs) based on P-donor ligand. Despite the similarity between nitrogen and phosphorus, the usage of P-donor ligand to produce CoII pentacoordinated SIMs has not been reported. This work reports the first example of pentacoordinated CoII -P4X1 single ion magnets (SIMs) based on P-donor ligand. The tetradeinate ligand tris[2- (diphenylphosphino)ethyl]phosphine (PP3) allows the obtention of the isostructural square pyramidal [Co(PP3)Cl]·ClO<sub>4</sub> (1) and [Co(PP3)Br]·ClO<sub>4</sub> (2) complexes. The tripodal PP3 ligand coordinates in a tetradeinate fashion, with one of the P atoms occupying the axial position, while the fifth position is taken by the halide ion (X = Cl (1) and Br (2)).

The geometry at the CoII centre is best described as distorted square pyramidal; the calculated  $\tau$  values for 1 and 2 are 0.331 and 0.354, respectively. Additional SHAPE analysis also confirms that both the complexes can be better described as square pyramidal (1.14 and 1.41 for 1 and 2) than as trigonal bipyramidal (3.31 and 3.29 for 1 and 2). Detailed dc and ac magnetic susceptibility measurements reveal the presence of field induced slow magnetic relaxation behavior of the high spin penta-coordinate CoII centres with an easyplane magnetic anisotropy. A quantitative estimation of ZFS parameters has been effectively achieved using detailed ab initio theory calculation and D and E values are in good agreement with those obtained from the experimental fit. Both complexes show field-induced slow magnetic relaxation behaviours with effective energy barriers of 37.8 K and 34.5 K, respectively. The investigation also reveals the influence of metal coordination geometry on the magnetic anisotropy of CoII SIMs. Chapter 4 describes the possibility of controlling the easy plane magnetic anisotropy of seven coordinate CoII complexes by modulation of coordination environment. The differences at axial coordination position result in the different symmetry and strength of local ligand-field of the CoII ions, and results in fine tuning of the single ion magnetic anisotropy parameter (D). For this purpose, a class of three pentagonal-bipyramidal complexes with formulae  $[\text{Co}(\text{H4daps})(\text{OMe})_2]$  (1),  $[\text{Co}(\text{H4daps})(\text{NCS})(\text{MeOH})] \cdot (\text{ClO}_4) \cdot (\text{MeOH})$  (2) and  $[\text{Co}(\text{H4daps})(\text{NCS})_2] \cdot (\text{MeOH})_2$  (3) were synthesized ( $\text{H4daps} = 2,6\text{-bis}(1\text{-salicyloylhydrazonoethyl})$  pyridine). Whereas the equatorial surroundings remain very similar to each other, the axial positions are ix successively modified from O to N donor ligand in a systematic way. Detailed dc and ac magnetic susceptibility measurements reveal presence of large easy-plane magnetic anisotropy and field induced slow magnetic relaxation behavior. Both experimental and ab initio theoretical calculations display that the easy-plane magnetic anisotropy of these pentagonal-bipyramidal CoII complexes is maintained upon variation of the axial ligands. Nevertheless, the magnitude of the D value can be increased by heavier and harder donor atoms. As per our knowledge, the axial zfs parameter for complex 1 was found to be the highest value reported so far among seven-coordinate CoII system. In order to elucidate the role of intermolecular interactions between adjacent CoII centres in the magnetic relaxation behavior, a diamagnetic isostructural ZnII analogue (4) was synthesized and magnetic behavior was examined. Chapter 5 describes the overall summary and conclusion of the present thesis work. In addition, the future outlook of this research related to transition metal based single-ion magnets (3d-SIMs) has been also described.

# **Towards Multi-BODIPY Macrocycles: Syntheses and Applications**

**Adiki Raja Sekhar**

**Supervisor: Dr. Jeyaraman Sankar**

**Department of Chemistry**

**Accession No.: T00075**

**Chapter 1:** Boron insertion into tetrapyrrolic units like porphyrin and corrole shows unprecedented coordination and electronic properties. Boron in expanded porphyrin analogues observed unusual Huckel and Möbius topological aromatic and antiaromatic systems. For this, it would be interesting to investigate a bottom-up approach installing boron in small precursor and then expand the cyclic core to achieve boron-bound macrocycle for optoelectronic properties and aromaticity.

**Chapter 2:** The detailed instrumentation and experimental methods have been explained.

**Chapter 3A:** The first examples of small molecular zwitterionic BODIPYs were synthesized by a simple aromatic nucleophilic substitution reaction of highly reactive dihalo-BODIPYs. The novel molecules were characterized through NMR and mass analysis. Zwitterionic nature of these BODIPYs has been thoroughly probed through single crystal diffraction studies. The effect of ionic character on boron geometrical arrangement was calculated by a couple of geometrical calculations. The optoelectronic behaviour of zwitterionic BODIPYs was documented in high polar solvents, and it was supported by theoretical calculations. Electronic conjugation and aromatic character have been investigated by NMR, NICS (0) and XRD analysis.

**Chapter 3B:** A novel methodology was developed to prepare  $\alpha$ -amino BODIPY through a simple aromatic nucleophilic substitution ( $S_N\text{-Ar}$ ) reaction by cleavage of carbon-nitrogen bond in tertiary amines without any external catalyst. Resultant amino BODIPY structures were elucidated through NMR, mass and XRD analysis studies. Cleavage of the C-N bond at room temperature was supported by QST3 theoretical calculations and validated through frequency calculations.

**Chapter 4:** Boron-bound expanded porphyrinoid was synthesized from simple BODIPY precursor via bipyrrolic conjugated spacer. Dimerization of pyrrole-appended BODIPY derivative yields an unprecedented 2, 3-pyrrolic connective octapyrrolic expanded porphyrin. This unusual connectivity offers the macrocycle to adopt a Möbius topology. Solid state structure and electronic properties indicate a  $30\pi$ -electronic conjugation. NMR, NIR absorption, quenched emission and perturbed frontier orbitals all point that the current molecule is the first example of a non-aromatic octaphyrin

(1.0.0.0.1.2.0) with a Mobius twist.

**Chapter 5:** In the journey towards macrocycle preparation, a considerable number of BODIPYs were prepared and characterized. Among these, a few are exhibiting solubility in high polar solvents while maintaining their fluorescence properties. I focused on the screening of these synthetic BODIPYs towards the bio-imagining application. Oxo-and Imino-BODIPY demonstrated specificity towards globular part in yeast strains. Amino and terabutylammonium oxo- BODIPYs are specifically targeted to Endoplasmic Reticulum (**ER**) of live and fixed mammalian HeLa cells. It was further supported by colocalization experiment with commercial ER- red tracker.

**Chapter 6:** From the observations, it can be concluded that the choice of the topology of delocalization is a driving force for identifying a new class of interesting  $\pi$ -conjugated molecules. Currently, effort are devoted to understanding the structure and property of some novel boron-bound novel macrocycles.

**A Quantitative Investigation of Intermolecular Interactions in the Solid State in Multi-functional  
Organic Compounds**

**Dhananjay Dey**

**Supervisor: Dr. Deepak Chopra**

**Department of Chemistry**

**Accession No.: T00074**

This thesis reports the crystallographic and theoretical investigation on the nature and role of different intermolecular interactions which is responsible for assembly of the molecules in the solid state. The ability to predict and control the formation of supramolecular assembly involving organic fluorine into ordered networks is now well-recognized in the context of crystal engineering. In this regard, a large library of molecules containing organic fluorine have been synthesized, crystallized and investigated for polymorphism and a systematic exploration of the participation of the fluorine atom in the formation of different supramolecular motifs has been studied both experimentally and theoretically. The understanding of the cooperative effects of various structural motifs associated with the presence of different intermolecular interactions involving organic fluorine has been investigated in a series of fluorinated benzoyl chlorides (liquids at room temperature, determined via *in situ* cryocrystallization), N-phenyl benzimidamides, trifluoromethylated phenyl hydrazones and phenyl benzoates. In this study, the crystal structures are analyzed based on the molecular conformation and the supramolecular architectures in the absence or presence of any strong H-bonds. All the supramolecular building blocks associated with similar or different intermolecular interactions were analyzed in terms of their nature and energetics using PIXEL and QTAIM Method. Hirshfeld surface analysis and associated fingerprint plots helps to understand the similarities and the differences between the two polymorphic forms as well as two isostructural compounds.

**Tween-Mediated Synthesis of Novel Nanoarchitectures of Mesoporous Oxide Materials for Applications in Energy and Medicine**

**Qysar Maqbool**

**Supervisor: Dr. Aasheesh Srivastava**

**Department of Chemistry**

**Accession No: T00072**

This thesis explores the use of polyoxyethylene-based Tween surfactants to prepare a variety of mesoporous oxide nanomaterials such as magnetite, manganese dioxide and silica and is divided into five chapters. Chapter 1 introduces the reader to oxide nanomaterials with particular emphasis on solution-phase synthesis routes by bottom up chemistry approach. The importance of oxide nanomaterials with respect to the applications related to energy and environment as well as biomedical purpose is discussed after synthesis methods. At last, the importance of this thesis is highlighted in broader scope to prepare new nanoarchitectures of mesoporous oxide materials using Tween-mediated synthesis. In Chapter 2, a modified solvothermal synthesis to prepare uniform spheroidal magnetite nanoassemblies (SMNAs) using Tween surfactants is discussed. The morphology of the synthesized materials was characterized by scanning electron microscopy (SEM) and transmission electron microscopy (TEM). The composition and phase analysis was done by FT-IR spectroscopy, energy dispersive X-ray spectroscopy (EDS) analysis and powder X-ray diffraction (PXRD). Magnetic properties of the SMNAs were probed using SQUID magnetometer and electrochemical properties were studied by cyclic voltammetry (CV), galvanostatic charge/discharge and electrochemical impedance spectroscopy (EIS) experiments. The importance of minute amounts of water required for synthesis of these SMNAs is the highlight of the work and has been studied using Karl Fischer titration. These SMNAs were mesoporous (studied by N<sub>2</sub> sorption isotherm), possesses high magnetic moment even at room temperature and were dispersible in ethanol for longer periods (observed for weeks) in absence of external magnetic field. Chapter 3 details the hydrothermal synthesis of two novel morphologies of robust mesoporous MnO<sub>2</sub> nanomaterials, viz. nano “Koosh balls” (MnO<sub>2</sub>-KBs) and “wormlike” nanotubes (MnO<sub>2</sub>-NWs) using Tween 20 surfactant. The morphological studies on the obtained materials were done using SEM and TEM. The composition and phase purity studies were undertaken using EDS, Raman scattering and PXRD. The surface area and pore characteristics were studied by analysis of N<sub>2</sub> adsorptiondesorption isotherms.

Electrochemical properties were probed through CV, galvanostatic charge/discharge and EIS

experiments. It was found that MnO<sub>2</sub>-KBs outperformed MnO<sub>2</sub>-NWs as electrode material for supercapacitor application. The viii reason for this observation was explored through a range of studies that showed enhanced charge transport and storage through the tubular connections of MnO<sub>2</sub>- KBs. In Chapter 4, a modified Stöber method is detailed to prepare highly uniform and water-dispersible mesoporous silica nanospheres (MSNs) with wormhole-like porosity by using small quantities of Tween 20. The obtained materials were characterized by SEM, TEM and DLS for morphological studies and size distribution. The porosity studies were done using N<sub>2</sub> adsorption-desorption experiments as well as TEM. The chemical composition was studied by FT-IR spectroscopy. The amorphous nature was established by PXRD and low-angle XRD was used to study pore ordering in the obtained mesoporous materials. The complete elimination of cytotoxic mesopore-directing agents such as CTAB and block copolymers for synthesizing highly monodisperse MSNs is an important aspect of this work. Further, these MSNs took up hydrophobic and less bioavailable compound curcumin from aqueous dispersions and delivered it intracellularly into cancer cells with high efficiency. Clathrin-independent but caveolae- and lipid raft-mediated uptake pathways were found to be dominant in uptake mechanism for curcumin-loaded MSNs. In Chapter 5, a new protocol to synthesize black TiO<sub>2</sub> microspheres (TiO<sub>2</sub>-B) through ammonia treatment is discussed. The highlight of this protocol is that it does not require the use of hydrogen at elevated temperatures to obtain black TiO<sub>2</sub>. HRTEM studies hinted towards the formation of anatase material with well-defined crystallinity, which was confirmed by PXRD studies. TiO<sub>2</sub>-B showed panchromatic absorption features across UV-vis-NIR wavelength in diffuse reflectance analysis. The composition of the materials reported in this chapter was studied by IR spectroscopy as well as X-ray photoelectron spectroscopy (XPS). Raman scattering was done to analyze changes at molecular level in the black anatase microspheres. Bulk characterization techniques like electron paramagnetic resonance (EPR) spectroscopy and magnetization studies (by SQUID magnetometer) were used to conclude that single-electron-trapped oxygen vacancies (V<sub>O</sub>) are primarily the reason for this observed black color.

**Keywords:** Tween-Mediated, Nanoarchitectures, Mesoporous, Oxide

Materials, Energy and Medicine, PhD Thesis

**Developing a Unique Reactivity of N-Heterocyclic Carbene (NHC)–Metal Template in C–H Activation-Annulation Catalysis: Synthetic and Mechanistic Studies**

**Ranjeesh T. K.**

**Supervisor: Joyanta Choudhury**

**Department of Chemistry**

**Accession No: T00071**

The tremendous success of N-heterocyclic carbenes (NHCs) in homogeneous catalysis portrays a true reflection of their unique stereoelectronic properties, strong metal–C(NHC) bonding, and excellent stability of the metal complexes toward heat, air and moisture. In fact, the robust and inert metal–C(NHC) backbone is considered as a key factor to provide the opportunity for exploring catalytic reactions without any self-transformative unproductive side reaction. In this thesis work, a new and unique reactivity of the metal–C(NHC) motif has been developed and explored in the field of C–H activation/functionalization catalysis.

At first, a preliminary study will be presented toward the understanding of the directing group (DG) property of NHC ligand as well as the influence of pyridine-metal coordination during the C–H bond activation of pyridine backbone. As catalytic direct C–H functionalization of pyridine backbone is a challenging research area, the above understanding was further applied to develop a new rhodium(III)-catalyzed protocol for C–H activation and functionalization of poorly reactive pyridine backbones with the aid of in-built NHC ligand. This protocol highlights a novel conjugative action of NHC ligands as a DG as well as a *functionalizing* group. This chemistry was also demonstrated successfully for catalytic non-aromatic C–H activation and subsequent annulation of various vinylic-group substituted imidazolium substrates with internal alkynes. This newly developed catalytic protocol enables easy synthesis of imidazo[1,2-*a*]quinolinium, imidazo-[1,2-*a*][1,6]naphthyridinium, and imidazo[1,2-*a*]pyridinium architectures which might be useful in pharmaceutical industry, or as abnormal NHC ligands or as organic emitters. Thereafter, a detailed mechanistic investigation of this type of transformations which unravel the crucial competition of two C–H bonds (imidazolium and aryl C–H) and two M–C bonds (M–CNHC and M–Caryl) in establishing the rate-limiting step and the alkyne-insertion regioselectivity in the reaction will be discussed. Lastly, the potential of the metal–C(NHC) template has been explored on chelating pyridyl-imidazole substrates to develop a novel switchable C–C annulation/C–N annulation protocol, via exquisite reactivity control of the metal-complex

intermediates. The developed chemistry and the associated mechanistic insights should be useful in understanding similar C–H activation processes in general which are topical in the area of catalysis.

**Key words:** N-Heterocyclic carbene, directing group, C–H bond activation, annulation, mechanistic investigation

**Palladium(II)-NHC Complexes for Aromatic C–H Functionalization Catalysis: From Homogeneous to Heterogeneous Regime**

**Moumita Mondal**

**Supervisor: Dr. Joyanta Choudhury**

**Department of Chemistry**

**Accession No.: T00069**

The selective functionalization of unactivated arene and alkane C–H bonds to valuable organic derivatives has been a challenging research area in organometallic catalysis for a long time. In this context, more recently, the oxidative functionalization approach, involving high-valent palladium intermediates (Pd(IV) and Pd(III)) in the catalytic cycles, has attracted considerable attention owing to its successful demonstration in the halogenation, acetoxylation and other functionalization reactions of alkanes and arenes. The key to the success of the above oxidative catalysis is the stability of high-valent palladium species (e.g., Pd(IV)) in the catalytic cycles under oxidizing (and acidic) conditions. The stereoelectronic properties of the ancillary ligands play an important role in stabilizing such high oxidation states of the metal centre. In the field of N-heterocyclic carbene (NHC) chemistry, one of the major focuses has been in the design of new carbenic architectures to offer diverse stereoelectronic properties for fulfilling a plethora of desired functions, including the one described above. Toward this direction, Choudhury group has been motivated for developing robust and efficient C–H activation/functionalization catalysts based on NHC ligand framework. In present thesis work, efforts have been made to develop efficient and robust Pd–NHC-based complexes for aromatic C–H activation catalysis. At first, the strategy of utilizing bisNHC-chelated palladium(II) complexes was explored for catalytic oxidative acetoxylation and halogenation of arene C–H bonds. Mechanistic investigation suggested that the catalytic activity was compromised to some extent but it resulted in more robust backbone. Next, upon ligand modification and „structure-activity“ correlation studies, a relatively simpler, mono-NHC palladium(II) complex was developed which appeared to be a highly efficient and robust catalyst for the reaction. This finding is significant in the context of a limited number of efficient candidates available in the library of non-directed arene C–H acetoxylation catalysts reported so far. In the end, the mono-NHC palladium(II) catalyst was further modified to anchor on polymeric platforms to accomplish catalytic aromatic halogenation reaction in single-site heterogeneous manner. The developed chemistry and associated mechanistic investigations enriched the chemistry of high-valent catalysis with NHCmetal motifs

# Iodine and Organoselenium Assisted Intramolecular Cyclization Reactions: Synthesis of Normal and Medium-Sized Heterocycles

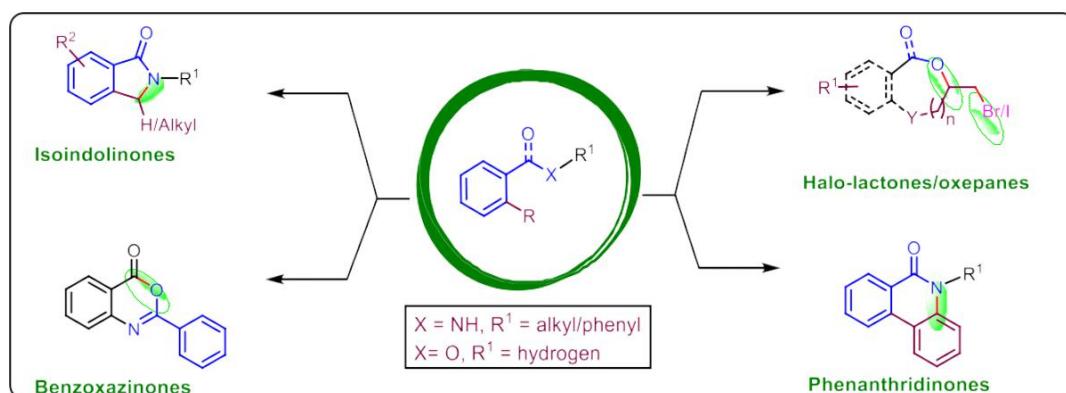
Ajay Verma

Supervisor: Dr. Sangit Kumar

Department of Chemistry

Accession No.: T00067

**ABSTRACT :** Organoselenium compounds used as efficient catalysts for the oxidation and electrophilic halogenation reactions of alkenes; as selenium enhances the electrophilic nature of halogen. Notably, halogen-mediated coupling reactions have emerged as an alternative to transition metal approaches for the C—H functionalization. However, selective C—H functionalization in these reactions brings a new challenge in the present era. Efforts are made to find a suitable iodine reagent, the radical initiator with the combination of appropriate base and solvent to address the challenges associated with selective functionalization of C(sp<sup>3</sup>)—H and C(sp<sup>2</sup>)—H bonds.



This PhD thesis describes the synthesis and mechanistic understanding of an important class of heterocyclic compounds namely bromolactone, bromo-oxepanes, benzoxazinones, isoindolinones, and phenanthridinones. The synthesis has been achieved by the readily available and inexpensive reagents and catalysts. Synthesis of medium sized halolactones and bromo-oxepanes has been achieved by a co-catalytic system consisting of substituted diarylselenide and DMAP at 0 oC. Benzoxazinones, isoindolinones, and phenanthridinones have been accomplished using molecular iodine with the combination of organic peroxide under heating conditions. Overall research work concentrates around the functionalization of unfunctionalized C—H bonds of various substituted carbonyl compounds and subsequently provide the various biologically relevant nitrogen and oxygen-founded heterocycles.

**Keywords:** Coupling reaction; benzoxazinones; isoindolinones; phenanthridinones; halolactones; oxepanes; organoselenium; iodine-mediated reaction; C—H functionalization; co-catalysis; radical pathways, carbonylation, DFT calculations.

**Keywords:** Budding yeast, DNA damage repair, Epigenetics, Genetic targets, Stress response, and Transcriptomics.

**Expedient Access to Isoindolinones and Tetrahydroisoquinolines (THIQs) via Catalytic  
Asymmetric Mannich-Type Reactions**

**Arun Suneja**

**Supervisor : Prof. Vinod K. Singh**

**Department of Chemistry**

**Accession No.: T00064**

**ABSTRACT:** This thesis is divided into three chapters. Chapter 1 deals with a highly efficient Ni-catalyzed one-pot three-component domino homoallylation/lactamization for the stereoselective synthesis of isoindolinones as well as isoquinolinones applying a common catalytic route. Isoindolinones and tetrahydroisoquinolines (THIQs) are important heterocyclic compounds from a synthetic perspective. Moreover, C-3 substituted isoindolinones are useful advanced intermediates in the synthesis of a variety of pharmaceuticals and complex natural products. Similarly, C-1 substituted tetrahydroisoquinolines (THIQs) also exist widely in many naturally occurring alkaloids. Due to their interesting biological activities, the asymmetric synthesis of such structural motifs has drawn considerable attention from the scientific community. In this chapter, we have disclosed an expeditious access to isoindolinones and isoquinolinones following a domino Ni-catalyzed highly stereo- and regioselective homoallylation of aldimines of o-formyl benzoates using 1,3-conjugated dienes promoted by Et<sub>2</sub>Zn. The salient features of this process are the highly regio- and stereoselective nature to provide the 1,3-syn-selective products. The reaction completes at room temperature and has wide substrate scope with electron-donating and -withdrawing functionality.

**Chapter 2** describes an unprecedented CuI – i-Pr-pybox-diPh catalyzed enantioselective alkynylation/lactamization cascade for the synthesis of diversely substituted isoindolinones of immense biological importance. The cascade involves one C–C and two C–N bond formation in one-pot under operationally simple, additive-free reaction conditions in good to excellent yields. Moreover, we utilized this unified approach for the asymmetric syntheses of medicinally important isoindolinones such as (S)-PD 172938, (R)-JM 1232 and related compounds. The aforementioned strategy was further utilized for the enantioselective synthesis of C-1 substituted THIQs, which could serve as an advanced intermediate for the synthesis of a variety of THIQs-based alkaloids.

**Chapter 3** demonstrates an efficient route to pharmacologically interesting isoindolinone-based  $\alpha$ -amino phosphonates via asymmetric hydrophosphonylation of N-acyl ketimines. Enantiomerically enriched  $\alpha$ -amino phosphonates and phosphonic acids are considered as important surrogates for  $\alpha$ -amino acids with an impressive diversity of biological activities. Therefore, stereoselective synthesis of  $\alpha$ -amino phosphonate viii embedded with isoindolinone motif would be challenging in the context of drug discovery. In this chapter, we have reported the BINOL-derived chiral phosphoric acid catalyzed hydrophosphonylation of in situ generated ketimines under ambient conditions for the first time, to the best of our knowledge. The reaction proceeds smoothly at ambient temperature affording a variety of  $\alpha$ -amino phosphonates with a quaternary stereogenic center embedded in the isoindolinone motif. The usefulness of this protocol has also been illustrated by the synthesis of optically active  $\alpha$ -amino phosphonic acid,  $\alpha$ -amino phosphonate monoester, and other valuable synthetic intermediates based on isoindolinones.

**Keywords:** Isoindolinones, Tetrahydroisoquinolines (THIQs), Homoallylation/ Lactamization, Alkynylation/Lactamization,  $\alpha$ -Amino Phosphonates

# **Single-Site Labeling of Native Proteins**

**Srinivasa Rao Adusumalli**

**Supervisor: Dr. Vishal Rai**

**Department of Chemistry**

**Accession No: T00063**

The growing interest in single-site labeling of protein has emerged from the necessity to understand and regulate their structure and function. Selective attachment of tags such as affinity probes, fluorophores, and potent cytotoxins plays a vital role in attaining the desired function. The advantages of single-site labeling were explored and established through pre-engineered proteins with un-natural amino acid or a peptide fragment. However, this technology does not extend to the native proteins. In recent years, chemical methods for functionalization of native proteins have drawn extensive attention. Typically, these methods are considered incapable of enabling single-site labeling of proteins. Occasionally, chemoselective labeling of low-frequency residues such as Cys, Tyr, and Trp have allowed single-site labeling. The N-terminus  $\alpha$ -amine or specific residues have also rendered a few capable methods. Beyond N-terminus, ligand-protein interaction driven labeling has been able to inspire partial success. The selective reaction of a single residue amongst competing nucleophilic residues (chemoselectivity) and its multiple copies (site-selectivity) is non-trivial. However, these attributes are essential for a chemical platform that can enable single-site labeling of native proteins. On the brighter side, such technologies can initiate a research front with immense possibilities if we can resolve the associated challenges. In this perspective, we invested a systematic effort to understand the behaviour of proteins as a multifunctional organic compound in chemical reactions.

In my doctoral thesis (chapters 1-4), I discussed our efforts toward achieving the single-site labeling of native proteins. It includes our current understanding of basic parameters associated with the organic chemistry of proteins. We addressed the challenges related to reaction kinetics, chemoselectivity, and site-selectivity. The functional group installed by single-site labeling opens up the potential for diversity-oriented bio-orthogonal transformations. We demonstrated the installation of an affinity tag, NMR tag, and a fluorophore. Our chemical technologies are operationally simple and allow efficient purification of the labeled protein. Finally, we have discussed the modular linchpin directed modification (LDM) approach for labeling of His and Lys residues on the surface of Protein.

**Keywords:** Single-Site, Native Proteins, Labeling, PhD Thesis

**ABSTRACT** The selective functionalization of unactivated arene and alkane C–H bonds to valuable organic derivatives has been a challenging research area in organometallic catalysis for a long time. In this context, more recently, the oxidative functionalization approach, involving high-valent palladium intermediates (Pd(IV) and Pd(III)) in the catalytic cycles, has attracted considerable attention owing to its successful demonstration in the halogenation, acetoxylation and other functionalization reactions of alkanes and arenes. The key to the success of the above oxidative catalysis is the stability of high-valent palladium species (e.g., Pd(IV)) in the catalytic cycles under oxidizing (and acidic) conditions. The stereoelectronic properties of the ancillary ligands play an important role in stabilizing such high oxidation states of the metal centre. In the field of N-heterocyclic carbene (NHC) chemistry, one of the major focuses has been in the design of new carbenic architectures to offer diverse stereoelectronic properties for fulfilling a plethora of desired functions, including the one described above. Toward this direction, Choudhury group has been motivated for developing robust and efficient C–H activation/functionalization catalysts based on NHC ligand framework. In present thesis work, efforts have been made to develop efficient and robust Pd–NHC-based complexes for aromatic C–H activation catalysis. At first, the strategy of utilizing bisNHC-chelated palladium(II) complexes was explored for catalytic oxidative acetoxylation and halogenation of arene C–H bonds. Mechanistic investigation suggested that the catalytic activity was compromised to some extent but it resulted in more robust backbone. Next, upon ligand modification and „structure-activity“ correlation studies, a relatively simpler, mono-NHC palladium(II) complex was developed which appeared to be a highly efficient and robust catalyst for the reaction. This finding is significant in the context of a limited number of efficient candidates available in the library of non-directed arene C–H acetoxylation catalysts reported so far. In the end, the mono-NHC palladium(II) catalyst was further modified to anchor on polymeric platforms to accomplish catalytic aromatic halogenation reaction in single-site heterogeneous manner. The developed chemistry and associated mechanistic investigations enriched the chemistry of high-valent catalysis with NHCmetal motifs.

# **Transition-Metal Catalyzed and Transition-Metal Free Synthesis of Heterocyclic and Carbocyclic Molecules**

**Md. Rehan**

**Supervisor: Dr. Prasanta Ghorai**

**Department of Chemistry**

**Accession No.: T00062**

The cinnamyl derivatives are important precursors in organic synthesis with several possibilities for further functionalization of the double bond. Anilines and phenols with  $\pi$ -activated alkyl substitution represent recurring structural motifs in bioactive molecules with pharmaceutical relevance and also the precursors of many heterocycles. In this regard, Friedel-Crafts reactions are amongst the most efficient carbon-carbon bond forming processes by which the incorporation of alkyl substituents on aromatic rings occurs. Despite the tremendous progress of Friedel-Crafts alkylations, very rare success has been documented where anilines and phenols are directly being used with respect to arene counterpart.

Therefore, direct C-alkylation of anilines and phenols attracted more attention in recent years. During my doctoral studies, I have developed a new strategy for the direct FriedelCrafts reaction of phenols and anilines with  $\pi$ -activated alcohols for the making of a carbon-carbon bond. Further, the strategy applied for the synthesis of substituted 2-benzyl benzo[b]furan starting from ortho-cinnamylphenols via palladium catalyzed oxidative cycloisomerization pathway and for the KOtBu/DMSO mediated synthesis of substituted quinoline starting from ortho-cinnamylanilines. In this protocol, we have also demonstrated a one-pot sequential synthesis of benzo[b]furan starting from corresponding phenols and substituted cinnamyl alcohols. The one-pot sequential synthesis of quinoline was also demonstrated, starting from the corresponding anilines and substituted cinnamyl alcohols. We have also developed a transition-metal-free synthesis of homo- and hetero-1, 2, 4-triarylbenzene, starting from the corresponding cinnamyl alcohol and  $\alpha,\gamma$ -diaryl propanones. The salient feature of this strategy involves the sequential hydride transfer, regiospecific condensation, regiospecific dearylation, and aromatization under metal-free reaction conditions here we have further demonstrated the synthesis of unsymmetrically substituted triphenylenes by oxidative coupling of the synthesized 1,2,4-triarylbenzene. Further, the same strategy we have applied for the epoxidation of propargyl alcohols and for the synthesis 5-hydroxy-4,5-dihydro-pyrazole from the same propargyl alcohol under transition-metal-free reaction condition

**Keywords:** Transition-Metal, Carbocyclic Molecules,  $\alpha,\gamma$ -diaryl and Friedel-Crafts alkylations.,

**Enantioselective Synthesis of Substituted oxa Heterocycles via Intramolecular oxa-Michael Reaction of Alkoxyboronate Utilizing Cinchona Alkaloid Based Organocatalysts**

**Barnala Ravindra**

**Supervisor : Dr. Prasanta Ghorai**

**Department of Chemistry**

**Accession No.: T00060**

**ABSTRACT** oxa-Michael addition is one of the most widely applied and versatile methods in organic synthesis, providing an efficient access to oxygen-containing heterocycles which are often found within the natural products. However, in spite of the progress achieved, there exist still few drawbacks for the development of asymmetric variants of intramolecular oxaMichael addition reactions arising mainly because of the rapid uncatalysed cyclizations resulting in racemic product. On the other hand oxygen containing heterocycles such as Chiral 1-and 1,1-disubstituted-1,3-(di)hydroisobenzofurans and 1- and 3-substituted isochromans are important scaffolds that are commonly found in many molecular targets, including the natural product pestacin as well as molecules of fascinating pharmaceutical relevance such as citalopram and bioactive molecules sonepiprazole (U-101387), a selective Dopamine D4 receptor antagonist. Furthermore, 3-substituted isochromans can also be the immediate precursors for 3-substituted 3,4-dihydroisocoumarins and 1,3- disubstituted isochromans, which are the key moieties in biologically active molecules.

Despite their importance, although substantial progress has been achieved for the achiral synthesis of 1-substituted isochromans, methods for the catalytic enantioselective synthesis of substituted isobenzofurans and 3-substituted isochromans are scarce. Surprisingly all the existing methods for the synthesis of the 1-substituted isochromans relied primarily on nucleophilic additions to a prochiral cyclic oxocarbenium ion intermediate. The absence of corresponding enantioselective variants for the synthesis of such compounds can be attributed to the problems resulting from self-cyclization and reversibility issues.

We have developed an “oxa-Michael addition via alkoxyboronate intermediate” strategy to avoid the undesired self-cyclization utilizing cinchona alkaloid based squaramide bifunctional catalysts. Using this strategy, we achieved the enantioselective synthesis of various oxo-heterocycles from stable starting materials at ambient reaction conditions.

**Keywords:** alkoxyboronate, oxa-Michael, Cinchona alkaloids, Hydrogen bonding catalysis, Unsaturated oxo-heterocycles, boron activation

**Carbon-Carbon and Carbon-Chalcogen Bond Construction: Access to  $\beta$ -  
(Nitroaryl)-indoles, Dithioacetals and Ebselenol Antioxidants**

**Shailesh Kumar**

**Supervisor Dr. Sangit Kumar**

**Department of Chemistry**

**Accession No. T00058**

The formation of carbon-carbon and carbon-chalcogen (S/Se) bonds by atom-economical and environmentally benign conditions is highly desirable. Here, we have described the formation of carbon-carbon bond by oxidative cross coupling of two C-H bonds under transition-metal-free conditions. Also, construction of carbon-chalcogen bond from C-H bond and diorgano dichalcogenides precursors has been discussed. Application of synthesized organochalcogens as antioxidant and their biological activities have been studied by various model assays. Aryl-indoles and their analogues represent a large number of biologically important compounds such as binedaline, fluvastatin drugs, fragrances, agrochemicals and conducting polymers. Therefore, synthesis of aryl-indoles has drawn much attention and several methodologies have been developed. Herein, we have discussed an oxidative coupling method where unprotected indoles react with inexpensive nitroarenes to form respective  $\beta$ - (nitroaryl)-indoles. Further, we explored the synthetic utility of  $\beta$ -(2/4-nitro-aryl)-indoles for the synthesis of indoloindoles, biindoles and  $\beta$ -(2/4-amino-aryl)-indoles. A plausible mechanism has been proposed on the basis of control experiments. Next, we have developed a synthetic method for the synthesis of dithioacetals, an important class of organic molecules, through C(sp<sup>3</sup>)-H functionalization by coupling of nitrotoluenes with disulfides. The synthesized dithioacetals has been further transformed into 4- nitrobenzaldehyde and 7- dithiocetalindole. We have also prepared and structurally characterized ebselenols antioxidant. The synthesized ebselenols were evaluated for their capacity to inhibit azoinitiated peroxidation of linoleic acid in a two-phase chlorobenzene/water system. They behaved in a regenerable, multifunctional manner and quenched three peroxy radicals (n = 3) more efficiently than  $\alpha$ -tocopherol (n = 2). Also, they acted as better mimics of the glutathione peroxidase enzymes than ebselen. In the presence of

ebselenols, the production of ROS/RNS were considerably reduced in human mononuclear cells quantified by chemiluminiscence assay and they were observed to have minimal toxicity at concentration of 25  $\mu$ M in MC3T3-cells. A plausible mechanism for regeneration of ebselenols has been proposed on the basis of EPR experiments.

**Keywords:** Carbon-Chalcogen, B-(Nitroaryl)-Indole, Oxidative Cross Coupling, Synthesized Organochalcogen, Binedaline, Fluvastatin Drugs, Fragrance.

# Carbon-Chalcogen Coupling Reactions: Efforts toward the Synthesis of Diaryl Chalcogenides and Chalcogenyl Heterocycles

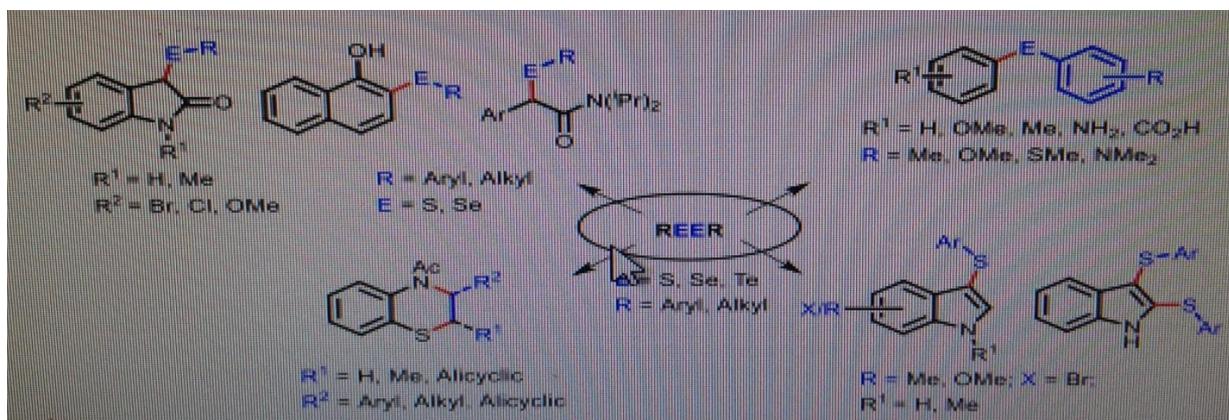
Ch. Durga Prasad

Supervisor: Dr. Sangit Kumar

Department of Chemistry

Accession No. T00057

This thesis reports the synthesis of diaryl chalcogenides and various chalcogenyl heterocycles using carbon-chalcogen coupling reactions. The formation of carbonchalcogen (S/Se/Te) bond is one of the fundamental reactions in synthetic chemistry of main group compounds and represents a key step for the construction of a broad range of organic molecules, which are of paramount importance in drugs, functional materials, and metal complexes. The construction of carbon-chalcogen bond by an atom-economical and environmentally benign conditions is always desirable. Unsymmetrical diaryl chalcogenides are ubiquitous structural motifs in numerous biologically active natural products, pharmaceuticals, and materials. Therefore, the synthesis of diaryl chalcogenides has attracted considerable interest. In this thesis, I have discussed a general method where dichalcogenides reacted with arenes to form respective diaryl chalcogenides. This method was remarkable in terms of synthesis of various monochalcogenides. It was extended with slight modifications, to synthesize 3-sulfenyl indole, a functionality that exists in a variety of natural products and synthetic drugs and plays a significant role in medicinal chemistry. Further, 2,3-bis sulfenyl indoles have also been obtained.



Synthesis of various chalcogenyl heterocycles from diaryl dichalcogenides Benzothiazine is considered as a promising unit in the field of pharmaceuticals and agrochemicals. A silver mediated two step methodology has been presented for the synthesis of benzothiazines from unactivated alkenes. Functionalized oxindoles have elicited significant synthetic interest because of their important applications in asymmetric synthesis, library design and drug discovery. A simple method has been demonstrated that involves direct sp<sup>3</sup> C-H functionalization to access diverse chalcogenyl heterocycles such as 3-sulfonyl oxindoles, sulfenyl and selenenyl heterocycles.

**Keywords:** Organochalcogens - C-S/Se coupling - Dichalcogenides – Heterocycles.

# **Transition Metal Catalyzed Regiodivergent C-H Functionalization of Nitrogen**

## **Heterocycles**

**Virendra Kumar Tiwari**

**Supervisor Dr. Manmohan Kapur**

**Department of Chemistry**

**Accession No. T00056**

Synthetic organic chemistry remains a dynamic and central area of chemistry. New compounds will always be required for evaluation as pharmaceuticals, agrochemicals, dyestuffs, organic materials, etc. Synthetic chemistry has many principles and strategies and many discoveries to make a more sustainable and beautiful world of organic materials, are yet to be made. Nitrogen heterocycles are important structural motifs found in numerous natural products and biologically active compounds. Therefore, development of more efficient and straight forward methods for the synthesis of nitrogen containing heterocyclic compounds using simple starting materials via direct C-H bond functionalization and transition metal catalyzed strategies is one of fastest developing fields in synthetic organic chemistry. Despite many advances of C-H functionalization of heteroaromatics, there remains a major, largely unmet challenge, namely of the control of selectivity for C-H activation in such molecules with multiple C-H bonds. To date, much of the focus has been on increasing selectivity at a ‘natural’ site of reactivity, but this has limitations, what if we want to functionalize at a different position or at more than one site in a predictable sequence? How do we go about ‘switching’ the site at will, in a predictable manner? The main objective of this dissertation to developed new methodologies, which allow the regiodivergent C-H functionalization in nitrogen heterocycles. In my doctoral studies I have chosen the goal of direct C-H functionalization of electron deficient heterocycles at their least reactive sites as well as of electron rich heterocycles and have shown the application of the developed methodology in the synthesis of biologically active molecules. I have also carried out mechanistic studies to understand the feasible pathway for the transformations. A heteroatom guided palladium catalyzed regioselective C-H bond functionalization/arylation of sp<sup>2</sup> C-H bond

of electron deficient nitrogen heterocycles was developed. The reaction was found to be general with variety of substrates. Heteroatom directed ruthenium catalyzed, regio- and chemo-selective sp<sub>2</sub> C-H bond functionalization/arylation was developed in electron deficient nitrogen heterocycles as well as electron rich heterocycles. The regioselectivity was successfully switched from one reactive site to another and the more reactive site to least reactive site by changing the C-H activation mechanism. A comprehensive investigation to elucidate the factors affecting the C-H functionalization/arylation by changing the transition metal catalyst was conducted.

**Keywords:** C-H Activation, Heteroatom-Controlled, Regiodivergent, C-H Functionalization, Transition metal catalysis.

**Lanthanide Based MOFs for Cryogenic Magnetocaloric Effect, Slow Magnetic Relaxation and Proton Conduction**

**Soumava Biswas**

**Supervisor: Dr. Sanjit Konar**

**Department of Chemistry**

**Accession No.: T00055**

**Chapter 1** describes the brief background to this presented work. All the general concepts behind those magnetic properties and proton conduction are discussed briefly. Also some relevant examples of lanthanide based metal organic framework (LnMOFs) are illustrated briefly with the proper comparison.

**Chapter 2** describes Mganetocalorc effect and slow magnetic relaxation behavior in a family of lanthanide baseddense metal-organic frameworks (MOFs). Complexes 1-5,  $[Gd_5(\mu_3-OH)_5(\mu_3-O)(CO_3)_2(HCO_2)_2(C_4O_4)(H_2O)_2]_n$  (1),  $[Dy_5(\mu_3-OH)_5(\mu_3-O)(CO_3)_2(HCO_2)_2(C_4O_4)(H_2O)_2]_n$  (2),  $[Gd(C_4O_4)(C_2O_4)0.5(H_2O)_2]_n$  (3),  $[Dy(C_4O_4)(C_2O_4)0.5(H_2O)_2]_n$  (4) were synthesized via solvothermal method and complex  $[Gd(C_4O_4)(OH)(H_2O)_4]_n$  (5) was synthesized through slow solvent diffusion. Single crystal analyses show that the presence of serendipitously self-assembled crown shaped building unit with the cubane based rectangular moiety that lead to a special array of metal centers in three-dimensional space in the complexes 1 and 2. Whereas for complexes 3 and 4, the three dimensional framework consists of extended cuboid nanoscopic cages. Complex 5 is a two dimensional layered coordination polymer. Magnetic investigations confirm that complex 1 exhibits one of the largest cryogenic magnetocaloric effects among the molecular magnetic refrigerant materials reported so far ( $-\Delta Sm = 64.0 \text{ J kg}^{-1} \text{ K}^{-1}$  for  $\Delta H = 9 \text{ T}$  at  $3 \text{ K}$ ). The cryogenic cooling effect (of 1) is also quite comparable with that of the commercially used magnetic refrigerant gadolinium–gallium garnet. For 2 and 3, the maximum magnetic entropy change ( $-\Delta Sm$ ) found to be  $44.0 \text{ J kg}^{-1} \text{ K}^{-1}$  (for  $\Delta H = 7 \text{ T}$  at  $3 \text{ K}$ ) and  $47.3 \text{ J kg}^{-1} \text{ K}^{-1}$  (for  $\Delta H = 9 \text{ T}$  at  $3 \text{ K}$ ) respectively. Complex 2 show slow magnetic relaxation whereas for complex 4, field induced single molecule magnetic behaviour was observed.

**Chapter 3** represents magnetic properties and selective adsorption behavior of two novel isostructural lanthanide based 3D Metal Organic Frameworks (MOFs),  $[Ln_2(pam)_3(DMF)_2(H_2O)_2]_n \cdot nDMF$  ( $Ln = Gd(1), Dy(2); H_2pam = 4,4'\text{-methylenebis}[3\text{- hydroxy-2-naphthalenecarboxylic acid}]$ ). Single crystal structure analysis shows that the 3D framework originates from the self-assembly of lanthanide metallo macro cycles made of dumble shaped basic secondary building units. In both the complexes, two eightcoordinated lanthanide centers are connected with six pamoate groups to give a paddlewheel type building block. The magnetic measurements show that complex 1 acts as a vii cryogenic magnetic refrigerant having magnetic entropy change,  $-\Delta Sm$  of  $17.25 \text{ Jkg}^{-1}\text{K}^{-1}$  ( $\Delta H = 7\text{T}$  at  $3\text{K}$ ) and complex 2 shows slow relaxation of magnetization. The adsorption studies reveals that complex 1 and 2 show selectivity towards CO<sub>2</sub> adsorption over other gases and exhibit high methanol vapor uptake ( $227 \text{ cm}^3 \text{ g}^{-1}$  for 1 and  $201 \text{ cm}^3 \text{ g}^{-1}$  for 2).

**Chapter 4** A is based on the studies of proton conductivity of three magnetic coordination Polymers (CPs),  $\{[Ln_2(L)_3(H_2O)_2]_n \cdot 2n(CH_3OH) \cdot 2n(H_2O)\}$  ( $Ln = Gd^{3+}$  (1),  $Tb^{3+}$  (2) and (3)  $Dy^{3+}$ ;  $H_2L =$  cyclobutane-1,1-dicarboxylic acid)". Single crystal structure analysis shows that in complexes 1-3, lanthanide centers are connected by  $\mu_3$  - bridging cyclobutane dicarboxylate ligands along the c-axis to form a rod-shaped infinite 1D coordination chain which is further linked with nearby chains by  $\mu_4$ -

connected cyclobutane dicarboxylate ligand to form 2D CPs along bc planes. Packing view of the complexes down the b axis reveals that the lattice methanol molecules are located in the interlayer space between the adjacent 2D layers and form H-bonding with lattice as well as coordinated water molecules to form 1D chains. Magnetic properties of complexes 1-3 are thoroughly investigated. Complex 1 exhibits dominant ferromagnetic interaction between two nearby gadolinium centers and also acts as a cryogenic magnetic refrigerant having significant magnetic entropy change ( $-\Delta S_m$ ) of 32.8 J kg<sup>-1</sup> K

-1 for  $\Delta H = 7$  T at 4 K (calculated from isothermal magnetization data). Complex 3 shows slow relaxation of magnetization below 10 K. The impedance analyses reveals that complexes show humidity dependent proton conductivity ( $\sigma = 1.5 \times 10^{-5}$  S cm<sup>-1</sup> for 1,  $\sigma = 2.07 \times 10^{-4}$  S cm<sup>-1</sup> for 2,  $\sigma = 1.1 \times 10^{-3}$  S cm<sup>-1</sup> for 3) at elevated temperatures ( $>75$  °C). Also, they retain the conductivity up to 10 h at high temperature and high humid condition. Furthermore, the proton conductivity results are correlated with the accumulation of the number of water molecules from the water vapor adsorption measurement.

**Chapter 5** describes two new lanthanide based three dimensional metal organic framework (MOFs),  $\{[Ln(L)(Ox)(H_2O)]_n \cdot x(H_2O)\}$  ( $Ln = Gd^{3+}$  (1),  $x=3$  and (2)  $Dy^{3+}$ ;  $x=1.5$  [ $H_2L$  = Mucic acid and  $OxH_2$  = Oxalic acid] show interesting magnetic properties and channel mediated proton conduction behaviour. Single crystal X-ray structure analysis shows that in complex 1, the overall framework originates from a gadolinium based fused rectangular metallocycles. These metallocycles are further connected through oxalate to form the overall three dimensional framework. The packing view reveals that the presence of (two types) hydrophilic 1D channel filled by the lattice water molecules which are strongly hydrogen bonded with coordinated water along a and b-axis. Whereas, for complex 2, the 3D framework originates from a carboxylate bridged dysprosium based criss-cross type secondary building block. Magnetic study reveals that 1 exhibits overall antiferromagnetic interaction and cryogenic magnetocaloric effect ( $-\Delta Sm = 30.6$  J kg<sup>-1</sup> K<sup>-1</sup>) for ( $-\Delta H = 7$  T at 3K). From the Complex 2 shows field induced single molecule magnetic behaviour. Impedance analysis shows that proton conductivity of both the complexes reaches up to the maximum value of  $4.7 \times 10^{-4}$  S cm<sup>-1</sup> for 1 and  $9.06 \times 10^{-5}$  S cm<sup>-1</sup> for 2 at high temperature ( $>75$  °C) and humidity (RH 95%). From the Monte Carlo simulation, the exact location of the adsorbed water molecules after humidification (RH 95%) in the framework (for complex 1) was confirmed.

# **Tetraphenylbenzene Appended Chromophores: Synthesis, Properties, and Applications**

**R. V. Ramana Reddy**

**Supervisor : Dr. J. Sankar**

**Department of Chemistry**

**Accession No.: T00053**

Chapter 1: Gives an introduction and brief literature survey of polyarylatedbenzenes (PABs) and their applications in photochemical/chemical molecular switches, selfassembly, and molecular fluorogenic recognition.

Chapter 2: This chapter describes details about reagents and solvents used to synthesize and characterize the compounds. Along with this, brief introduction of various instrumental techniques and methods required during the current work are included.

Chapter 3: This chapter demonstrates the synthesis and structural characterization of two novel tetraphenylbenzene appended BODIPYs and explored their photophysical properties which exhibit strong viscosity dependence, i.e. the fluorescence lifetime and intensity increases as a function of solution viscosity.

Chapter 4: This chapter reports the synthesis and characterization of close contact chromophores Porphyrin-(TPB) conjugates. Mesityl substituted A2B2 porphyrin exists in two isomers, cis and trans because of the restricted rotation around Cmeso-C bond of porphyrin and TPB. These isomers have reminiscent photophysical and electrochemical properties. The redox potentials of mesityl substituted porphyrins are cathodically shifted with respect to meso-free porphyrin. For the first time, cis and trans isomers are isolated and structurally confirmed.

Chapter 5: In this chapter, a new TPB-DAMN (Diaminomaleonitrile) scaffold has been designed and synthesized successfully. The intriguing electronic nature of the Schiff base is shown to exhibit solvent dependent reactivity with aqueous hypochlorite. Changing of the solvent from THF to DMSO resulted in shifting the reactivity from a -C=N chemodosimetry to proton transfer signaling, (PTS) between -NH<sub>2</sub> and OCl<sup>-</sup>. The PTS resulted in prompt signal transduction even at nano molar level.

Chapter 6: This chapter summarises the merits of the whole thesis.

# **Organocatalytic Enantioselective C-S and C-C Bond-Forming Reactions: Applications in Organic Synthesis**

**Rajshekhar Amrutrao Unhale**

**Supervisor Prof. Vinod K. Singh**

**Department of Chemistry**

**Accession No.: T00050**

This thesis is divided into three chapters. Chapter 1 deals with an introduction of asymmetric organocatalysis, a brief historical background, classification along with the concept of bifunctional organocatalysis, various literature approaches on organocatalysis and their application in an asymmetric synthesis. Chapter 2 deals with enantioselective organocatalytic Carbon–Sulfur bondforming reactions, which is subdivided into two parts.

Chapter 2 Part A describes thiourea catalyzed asymmetric protonation via conjugate thiol addition. Chiral tertiary carbon stereocenters are extremely common structural motifs in valuable biologically active natural products and pharmaceutical agents. Enantioselective protonation of a prosterogenic enolate derivative has been shown to be a convenient and practical method for the preparation of enantioenriched -tertiary carbon carbonyl compounds. In particular, such molecules containing sulfur element are an integral part of many drug molecules and synthetic intermediates. Therefore, a great deal of interest has been focused on preparing and manipulating chiral organosulfur species with chirality residing at sulfur, at carbon, or at both. This chapter deals with catalytic enantioselective transient enolate protonation in the conjugate addition of thioacetic acid to -substituted N acryloyloxazolidinones with bifunctional cinchona derived thiourea catalysts. Chapter 2 Part B describes Brønsted acid-catalyzed enantioselective thiol addition to ketimine. Due to the prevalence of C –S bonds in many biologically and pharmaceutically active compounds, considerable efforts have been given for the construction of new C–S bonds, mainly involving asymmetric 1,4-addition of sulfur nucleophiles to ,β-unsaturated compounds, 1,6-addition, addition to allenotes and desymmetrization of meso-aziridines, meso-epoxides. On the other hand, asymmetric methodologies for providing N,S-acetals and N,S-ketals which are important motifs present in a wide range of biologically active compounds, natural products and antibiotics are much less explored. This chapter describes the study of chiral Brønsted acid-catalyzed enantioselective 1,2-addition of thiols to in situ generated ketimines, derived from 3-hydroxyisoindolinones. The application of this methodology for the synthesis of non-nucleoside HIV-1 Reverse Transcriptase Inhibitor also described.

Chapter 3 deals with an organocatalytic enantioselective Mannich–lactamization cascade for the synthesis of enantioenriched isoindolinones. Optically active isoindolinones are found in many

naturally occurring alkaloids and pharmaceuticals. Because of their impressive biological activities, synthesis of enantioenriched isoindolinones has gained considerable interest in contemporary research. In this chapter, we have developed first organocatalytic (via enamine catalysis) enantioselective one-pot three component Mannich–lactamization sequence for the synthesis of syn- and antiselective isoindolinones. The synthetic viability of our methodology was shown by converting the isoindolinones into various synthetically useful intermediates.

**Keywords:** Asymmetric organocatalysis, Enantioselective protonation, Thiourea, N,S-Ketals and Mannich–lactamization, Isoindolinones.

# **Multi-metallic Modular Porphyrinoid Assemblies Syntheses, Structure and Properties**

**M Murugavel**

**Supervisor- Dr. Jeyaraman Sankar**

**Department of Chemistry**

**Accession No.: T00049**

Chapter 1: The effect of linkers on the photophysical properties of multi porphyrin arrays has been discussed. A meso-meso directly linked multiporphyrin array is a unique candidate favoring efficient energy and electron transfer processes because of the optimal center to center distance between porphyrin monomers. Corrole, a ring contracted porphyrinoid that stand out from the porphyrinoid family due to its unusual properties such as stabilizing metal ions in higher oxidation states, high fluorescence quantum yield, large stokes shift and lower oxidation potential. Multicorrole arrays can be quite interesting in terms of their coordination chemistry and applications. The existence of scarce reports on synthesis of corrole dimers and arrays has also been discussed. Multiporphyrin array could stabilize homonuclear or heteronuclear metal ions only in their bivalence. In the same manner, multicorrole array can stabilize metal ions only in their trivalence. We could envisage a multichromophoric platform stabilizing metal ions in multiple oxidation states. Corrole (trianionic)-porphyrin (dianionic) hybrid could be the possible candidate to achieve our goal.

Chapter 2: The detailed instrumentation and experimental methods have been explained.

Chapter 3A: Design, synthesis and photophysical properties of a new *meso-meso* directly linked corrole-porphyrin-corrole ( $C[1o] \bullet P[5,15] \bullet C[1o]$ ) hybrid have been explained. Fluorescence quantum yield of the hybrid is three times higher than that of porphyrin trimer. This  $C[1o] \bullet P[5,15] \bullet C[1o]$  hybrid could serve as a basic frame work to embed metal ions in multiple oxidation states.

Chapter 3B: Syntheses of three discrete heterometallic  $C[1o] \bullet P[5,15] \bullet C[1o]$  hybrids,  $C[10] \bullet ZnP[5,15] \bullet C[10]$ ,  $CuC[10] \bullet ZnP[5,15] \bullet CuC[10]$  and  $GaC[10] \bullet ZnP[5,15] \bullet GaC[10]$  has been detailed and their photophysical and electrochemical properties have been investigated. The  $GaC[10] \bullet ZnP[5,15] \bullet GaC[10]$  hybrid stands out from the crowd by exhibiting dual emission in visible region of the electromagnetic spectrum and five discrete oxidation potentials and two reduction potentials in electrochemical investigations. Eventually, the X-ray crystal structure of  $GaC[10] \bullet ZnP[5,15] \bullet GaC[10]$  hybrid has been revealed for the first time. Even though the versatility of the  $C[1o] \bullet P[5,15] \bullet C[1o]$  hybrid has proven by embedding metal ions in multiple oxidation states, there is a bottleneck for further functionalization due to lack of substituent-free meso-positions. Polymerization of corrole-porphyrin hybrids could be arrived only if it has substituent-free *meso-positions*. We have envisioned and achieved a transpose of  $C[1o]P[s, 15J \bullet Cr 10J]$  hybrid,  $P[stCrs, ls] \bullet P[sJ]$  hybrid with substituent free meso-positions at both terminals.

Chapter 4A: It deals with syntheses, structure, photophysical and electrochemical properties of P[stCrs,1stP[sJ hybrids with different metal, i9ns in a single molecular scaffold. Homotrinuclear (Ni) and heterotrinuclear (Ni-Cu-Ni) complexes of P[stC[s, 1stP[sJ hybrid has been designed and synthesized. The photophysical properties of P[sJ•Crs,1stP[sJ hybrids is more distinctive than C[loJ•P[s, 1sJ•CrwJ hybrids because of the lack of symmetry in its molecular entity.

Chapter 4B: The paramagnetic homotrinuclear (Cu) and heterotrinuclear (Cu-Ni-Cu) complexes of P[sJ•Crs,Is]•P[s] hybrid have been thoroughly investigated. The CuP[s]•CuCr5.1stCuP[5J hybrid has shown unprecedented observation in EPR studies. The half-field resonance signal ( $D.m = \pm 2$ ) was noticed at 1650 G, exactly half of the main signal ( $D.m = \pm 1$ ) due to the population of triplet state at room temperature. We were able to make use of this study to calculate the inter-spin distance between the copper metal and corrole rr-cationic radical. Our main objective of the present work is to achieve a narrow optical gap in such a way that could reach near-infra red region of the electromagnetic spectrum *via* extending the n-conjugation of P[sJ•Crs. 1stP[sJ hybrids. Bearing in mind, all meso-substituted NiP[stCuC[s,ls]•NiP[sJ hybrid has been synthesized and subjected to oxidative ring closure (ORC) reaction by screening various oxidizing agents.

Chapter 5: It explains the photophysical properties of fused P[stC[s, 15tP[sJ hybrid in comparison with singly linked P[sJ•Crs.ls]•P[sJ hybrid.

Chapter 6: It deals with the merits of the current work and hints at the future potential of C[lotP[s,!sJ•Crio] and P[sJ•Crs.ts]•P[s] hybrids.

**Keywords:** Multi Porphyrin Array, Corrole Trianionic, Porphyrin Dianionic, Multiporphyrin and Fluorescence Quantum.

# **Towards the Synthesis of Lariatin B: Synthesis of Macroyclic Framework and Side Chain**

**Aniket Ashok Mahapure**

**Supervisor: Dr. Manmohan Kapur**

**Department of Chemistry**

**Accession No.: T00048**

Macro cyclic peptides have recently attracted the attention of scientific community because of their promising biological activity profile and unexplored mechanism of action. Macro cyclic peptides are emerging class of therapeutics that can modify protein-protein interaction. However the field is challenging because of the difficulty in synthesizing cyclic peptides in solution phase. Lasso peptides are natural products that are found in bacterial domain and exhibit a versatile array of biological activities. Two antimycobacterial peptides with a lasso structure, named Lariatin A and B were isolated from the culture broth of Rhodococcus sp. K01-B01711. They showed growth inhibition against Mycobacterium smegmatis. These peptides consist of 18 and 20 amino acid residues in an internal linkage between the carboxyl group of glutamine and the alpha-amino group of glycine, and the tail passes through the macrocyclic ring region. During my graduate studies, I undertook a program towards the total synthesis of Lariatin B. First part of the thesis will be dedicated to the completion of synthesis of 28-membered macrocyclic portion of Lariatin. In particular the synthesis of linear precursor and macrolactamization using orthogonal protecting group strategy. This was made by the union of a hexapeptide and a dipeptide in order to get the linear macrocyclization precursor, and the attempts to construct the macrocyclic framework of Lariatin B. The second part of the thesis is focused on the synthesis of side chain framework of Lariatin B which consists of 12 amino acids. This part also describes the earlier failures and the successful strategy. This was made by a convergent union of the three quartapeptides to get the full linear precursor for the tail part of the Lariatin B. This forms a basis for our first approach towards the synthesis of this class of peptides. The thesis will explore on how the strategy for the chemical synthesis of Lasso peptides is evolved in time.

**Keywords:** Cyclic Peptides, Lasso Peptides, Macro cyclic Framework, Macro cyclization Precursor and Retrosynthesis.

**Organocatalytic Enantioselective Michael Addition Reactions to  $\alpha,\beta$ -Unsaturated Carbonyl Compounds**

**Nagaraju Molleti**

**Supervisor: Dr. Vinod K. Singh**

**Department of Chemistry**

**Accession No.: T00047**

This thesis is divided into three chapters. Chapter I describes chiral urea catalyzed enantioselective Michael addition of malononitrile to 2-enoylpyridines. Michael addition is one of the most fundamental and powerful tools for the formation of carbon-carbon bonds in synthetic organic chemistry. The asymmetric version of this reaction provides direct access to synthetically important enantioenriched products. In this regard, the enantioselective conjugate addition of malononitrile to -unsaturated carbonyls is an efficient route to access optically active -cyano carbonyl compounds, which are key intermediates in organic synthesis (Scheme 1). Scheme 1 In Chapter I, we demonstrated a cinchonine derived urea 1, catalyzed reaction of 2- enoylpyridines (2) and malononitrile (3) affording synthetically useful -cyano carbonyl compounds (4). This protocol offers several advantages such as operational simplicity, mild reaction conditions, low catalyst loading (10 mol %), and high enantioselectivities (up to 97% ee) and yields. Both the enantiomers have been synthesized with the same level of enantioselectivity by using two pseudo-enantiomeric catalysts. One of the enantioenriched products has been transformed to highly functionalized piperidone derivative 7 (Scheme 2). Scheme 2 Chapter II deals with enantioselective Michael addition of cyclic 1,3-dicarbonyl compounds to 2-enoylpyridines with bifunctional organocatalyst using 10 mol % cinchonine viii derived urea catalyst (1) in dichloromethane (Scheme 3). The corresponding Michael products were isolated as its acyl derivatives with excellent yield and enantioselectivities (up to 98% ee). The synthetic utility of our catalytic system was demonstrated by transforming some of the Michael adducts into 2,4-diaryl substituted 1,4-dihydropyridines as shown in Scheme 4. Scheme 3 Scheme 4 We then extended the catalytic system to enantioselective conjugate addition of 2-hydroxy-1,4-naphthoquinone to 2-enoylpyridines for the synthesis of naphthoquinone derivatives in high yields with excellent enantioselectivities (up to >99% ee) (Scheme 5). After extensive screening of different bifunctional organocatalysts, quinine derived bisquaramide 11, was found to be a most efficient catalyst for this reaction. Some of the Michael adducts have been successfully converted into various enantioenriched pyranonaphthoquinones derivatives (12) (Scheme 5). This protocol is further extended to the synthesis of various 4-hydroxy coumarin derivatives under mild reaction conditions. ix Scheme 5 Chapter III describes an organocatalytic

enantio- and diastereoselective synthesis of highly substituted -lactones via Michael-cyclization cascade. Chiral pyrrolidine catalyst 14, promoted the Michael-cyclization reaction between -unsaturated aldehydes (15) and pyrazoleamides (16) to yield highly substituted lactones (Scheme 6). Under optimized conditions, the reaction afforded corresponding -lactones (17) in good yields with excellent enantio- and diastereo selectivities (up to 97% ee and up to >20:1 dr respectively). Scheme 6 Further, we have shown the synthetic utility of these  $\delta$ -lactones by cleavage of pyrazole moiety from  $\delta$ -Lactone (18) and resulted in di-substituted lactone (19) with high enantioselectivity (92%) (Scheme 6). Furthermore,  $\delta$ -lactone (20) is transformed to benzazepine derivative (21) in a one-pot sequential process, in overall 50% yield with good enantioselectivity (92%) (Scheme 7). These benzazepine derivatives could serve as a key intermediate in the synthesis of 7-membered aza-heterocyclic aromatic chiral natural products and several pharmaceutically active compounds.

x Scheme 6

**Keywords:** Organocatalyst, 2-Enoylpyridines, Malononitrile, Dimedone, Pyrazoleamide and – $\delta$ -Lactones.

**Palladium-Catalyzed Regioselective  $\alpha$ -Arylation of Enones and its Applications in Organic  
Synthesis**

**Kale Ajit Prabhakar**

**Supervisor: Dr. Manmohan Kapur**

**Department of Chemistry**

**Accession No.: T00046**

Many organic compounds that possess interesting material and biological properties consist of the  $\alpha$ -aryl carbonyl moieties. Transition metal-catalyzed coupling reactions of substrates containing activated sp<sup>3</sup> hybridized C-H bonds and aryl halides or pseudohalides have been the subject of intense research over the past four decades. However, to the best of our knowledge, the  $\alpha$ -arylation of an enone is rarely reported and that too is very substrate specific. During my doctoral studies, we have investigated a novel strategy for  $\alpha$ -arylation of enones and explored its applications in organic synthesis. A new and efficient, highly regioselective approach for the synthesis of  $\alpha$ -aryl enones was developed. This result represents an important application of the Kuwajima-Urabe protocol for  $\alpha$ -arylation of ketones, by utilizing the silyl enol ethers as a synthetic equivalent of ketone, towards the synthesis of this simple albeit complex functional array. We also developed a novel method for the synthesis of 2-alkenylindoles and carbazoles, via palladium-catalyzed  $\alpha$ -arylation. In this approach, triethylsilylenol ethers of enones were utilized to direct the regioselectivity and offer a better alternative approach to the oxidative-Heck reaction of indoles. This methodology stands out because simple metalcatalyzed, base-mediated,  $\alpha$ -arylation reactions of o-haloanilines with enones do not result exclusively in 2 alkenylindoles. This is also true for the regioselective synthesis of substituted carbazoles which cannot be achieved by the base-mediated reaction. This approach was utilized in a short and quick assembly of 2-alkenyl-3-aryl indoles and its efficacy was demonstrated in the formal synthesis of the antilepimic agent Fluvastatin. The inspiration behind development of the palladium-catalyzed regioselective  $\alpha$ -arylation of enones was always the synthesis of biologically active and architecturally complex natural products such as resorcylic acid lactones (RALs). Therefore, the main purpose of this research was methodology development leading to its applications in organic synthesis. There are suitable targets such as resorcylic acid lactones Radicicol Monocillin I, Pochonins C and D or Neoeosmosin A, or biologically active molecules such as 7-Dcoxy-6,8-O-dimethylfusarcentin. where we could utilize our developed protocol, “Palladium-catalyzed regiosclective  $\alpha$ -arylation of enones” as a key step. In this context, our efforts towards the same have discussed.

**Keywords:**  $\alpha$ -Arylation, Palladium Catalysis, Silyl Enol Ethers Arylation and  $\alpha$ -Arylation.

# **Synthesis of Azides, Amines and Peroxides through Stabilized Carbenium Ions. Their Application in Organic Synthesis**

**Suman Pramanik**

**Supervisor: Dr. Prasanta Ghorai**

**Department of Chemistry**

**Accession No.: T00045**

$\alpha$ -Stabilized carbenium ions are important intermediates in many organic transformations and those have been trapped with nucleophiles to provide various organic compounds. Reactions through these stabilized carbenium ions offer the advantage of an easy access to structural variation and asymmetric synthesis. My doctoral studies involve the generation of carbenium ions from carbonyls and subsequent trapping by different nucleophiles to afford azides, homoallylic amines or  $\alpha$ -azidoperoxides through azidocarbenium *ion*, iminium ion or peroxycarbenium ion respectively.

Azides are important precursors for amines, nitrenes, isocyanates and several organic building blocks. Although the existence of azidocarbenium ion is known since middle half of twentieth century as the intermediate in Schmidt rearrangement, but they have never been trapped with any nucleophiles. The real obstacle to surmount in achieving trapping of the azidocarbenium ion is to stop the Schmidt and related rearrangements driven by the thermodynamically' favorable loss of molecular nitrogen (N<sub>2</sub>) gas from the azido group. This thesis highlights the trapping of these highly sensitive *azidocarbenium ion* intermediates for the synthesis of different azides. Further, the application of the synthesized benzylazides has been discussed for the base promoted generation of *N*-unsubstituted imines and subsequent synthesis of homoallylic amines.

Tertiary homoallylic amines have been synthesized directly from ketones *for the first time* using a three component reaction by *oxo-rhenium* catalysis.

Further, structurally challenging and biologically important  $\alpha$ -heteroatom substituted peroxide pharmacophore.  $\alpha$ -azidoperoxides have been synthesized from carbonyls through *peroxycarbenium ion*. The synthesized  $\alpha$ -azidoperoxides having a-H have been applied for the synthesis of *tert-butyl* esters using simple organic base through '*intramolecular*' rearrangement. Finally, an asymmetric kinetic resolution of  $\alpha$ -azido peroxides has been performed using cinchona derived chiral bases to prepare chiral  $\alpha$ -azido peroxides with high enantioselectivity.

**Keywords:** Carbenium Reactions, Decomposition to Imines, Homoallylic Amine, Iminium Ions, Azido-Peroxides and Tert-Butyl Ester.

**High Nuclearity Nanoscopic Magnetic Cages with 3d, 3d-4f and 4f Metal Ions Employing  
Polytopic Ligands**

**Javeed Ahmad Sheikh**

**Supervisor: Dr. Sanjit Konar**

**Department of Chemistry**

**Accession No.: T00044**

Chapter 1 In this chapter the broad background related to this work has been given in order to benefit the reader. This includes the basic concepts on molecular magnetism, synthetic strategies used to prepare the polynuclear complexes followed by few examples of high nuclearity cages based on phosphonate, polyalcohol and Schiff base ligands. Synthesis, structure and magnetic properties of each cage are illustrated here briefly.

Chapter 2 describes the synthesis, structural characterization and magnetic property studies of six new Co phosphonate cages employing phosphonate ligands. Complexes 1-3 are quasiisostructural and feature a dodecanuclear metal-oxo core. Complex 4 is also a dodecanuclear cobalt phosphonate cage. The only difference is that in this complex two 6-chloro-2- hydroxypyridine ligands replace two of the six monoprotonated carbonates present in complexes 1-3. Complexes 5 and 6 represent pentadecanuclear cobalt phosphonate cages. Structural investigation reveals some interesting geometrical features in the molecular cores. Magnetic property measurements of compounds 1-6 indicate the existence of antiferromagnetic interactions between magnetic centers for all the cages.

Chapter 3 (Part A) is based on the synthesis, characterization and magnetic properties of three new phosphonate-based Ni<sup>11</sup> cages isolated by using three different phosphonate ligands. Complex 1 is an octanuclear nickel phosphonate cage, having butterfly like core structure. Complexes 2 and 3 are quasi-isostructural and feature a dodecanuclear metal -oxo core. All the twelve metal centers are arranged at the vertices of a truncated tetrahedron in a manner similar to Keggin ion. Magnetic property measurements of compounds 1-3 indicate the coexistence of both antiferromagnetic and ferromagnetic interactions between magnetic centers for all cages.

Chapter 3 (Part B) is based on a novel octadecanuclear copper pyrazolate-phosphonate nanocage with a bowl-shaped arrangement of the copper (II) centers in the asymmetric unit. Characterization of intermediates in both solid and solution states helped to propose the mechanism of such a giant aggregation. Magnetic studies affirm the presence of antiferromagnetic interactions between the adjacent copper (II) centers. Extensive supramolecular interactions result in a framework structure.

Chapter 4 describes the synthesis, structure and magnetic studies of five polynuclear cages BVS calculations and bond lengths indicate the presence of mixed valent Co  $\{\text{Co}^{\text{II}}, \text{Co}^{\text{II}}\}$  centers in compounds 1, 2a and 2b and only Co111 centers in 3a, 3b as required for the charge balances and supported by the magnetic measurements. Structural investigation reveals irregular geometrical core for 1. Isostructural crab shaped complexes 2a and 2b feature distorted cubane cores that edge share to each other whereas the metallic core of 3a or 3b displays hemicubane like arrangement of metal centers and oxygen atoms. Magnetic studies reveal significant magnetic entropy changes for complexes 2a and 3a ( $-\Delta S_m = 21.57$  and  $19.39 \text{ J kg}^{-1} \text{ K}^{-1}$ ) and single molecular magnetic behaviors for 2b and 3b.

Chapter 5 is based on three new  $\text{Ln}^{3+}$  coordination compounds synthesized in one pot synthesis from 0-vanillin, diaminomaleonitrile (DAMN),  $\text{LnCl}_3 \cdot 6\text{H}_2\text{O}$  ( $\text{Ln} = \text{Gd}^{3+}, \text{Dy}^{3+}$ ) and sodium acetate for 3. Single crystal X-ray diffraction studies reveal that compounds 1 and 2 are quasi-isostructural exhibiting tetranuclear hemicubane like cores. For 3 the metal centers are arranged in a tetrahedral arrangement. Complexes 1-3 are formed *via in situ* ligand transformation. Magnetic' study reveals that compound 1 shows significant magnetocaloric effect ( $\Delta S_m = -27.2 \text{ J kg}^{-1} \text{ K}^{-1}$ ) at 3 K and 7 T. Magnetic properties of 2 and 3 are considerably different. Indeed, no out~of~phase alternating current (ac) signal is noticed for 2, whereas 3 shows slow relaxation of:magnetization. These considerable differences are most likely due to the different Dy-0-Dy angles observed for the respective cores.

**Keywords:** Polynuclear Complex, Molecular Cube, Magnetic Behavior, Octa-Dodecanuclear, Megnatic Refrigeration and Octadecanuclear.

**Design & Synthesis of New Class of Enaldiazo Compounds and Their Applications in  
Organic Synthesis**

**Dawande Sudam Ganpat**

**Supervisor: Dr. Sreenivas Katukojvala**

**Department of Chemistry**

**Accession No.: T00043**

This thesis reports the synthesis and applications of novel diazo compounds which consists of a four-carbon unit embedded with alkenyl and carbonyl moiety. These enaldiazo compounds include enaldiazo ketones, enaldiazo esters and alkenyl enaldiazo ketones which were prepared from known starting materials. In applications of these compounds in organic synthesis we disclosed first direct catalytic [4+2] benzannulation by unprecedented rhodium(II) enalcarbenoids onto pyrroles to obtain substituted indoles. The synthetic utility of the benzannulation was demonstrated by with the highly efficient one step synthesis of leiocarpone, as well as a short synthesis of a potent and selective adipocyte fatty-acid binding protein (A-F ABP) inhibitor. A synergistic rhodium(II) carboxylate and BINOL phosphoric acid catalyzed efficient multicomponent reaction of enaldiazo compounds, arylamines, and aryl aldehydes leading to the first transition-metalcatalyzed direct synthesis of valuable *a*-pyrrolyl benzylamines was established. Reaction proposed to involve a transient ammonium ylide of a new class of electrophilic rhodium enalcarbenoid, its regioselective Mannich reaction, and a cyclocondensation cascade. This was also applied in synthesis of N-Bocpyrroles and binaphthyl based chiral pyrroles. Similar methodology was extended in one pot synthesis of *a*-pyrrolylglycine esters using arylamines and glyoxalates. Rhodium(II) enalcarbenoids were also applied in efficient [ 4+2] pyridoannulation with 3 -substituted indoles to obtain pyrido( 1 ,2-a ]indoles. Pyrido[1,2-a]indoles were partially reduced to tetrahydropyrido(1,2-a]indoles which are structural cores of various alkaloids. This thesis also includes a novel atom economical Ag(I) catalyzed efficient domino reaction of ((2-alkynyl)aryl)cyclopropyl ketones leading to the densely functionalized fused 2,3-dihydronaphthofurans.

**Keywords:** Carbene, Carbenoid, Enaldiazo Compounds, *A*-Pyrrolylglycine, N-Bocpyrrole and Binaphthyl Based Chiral Pyrrole.

# **Investigation of Light Induced Changes in the Optical Properties of Binary GeSe and Ternary GeAsSe Family of Chalcogenide Glasses**

**Amiya Ranjan Barik**

**Supervisor: Dr. K.V. Adarsh**

**Department of Chemistry**

**Accession No.: T00042**

Chalcogenide glasses (ChG) are promising materials for various optical and optoelectronic applications because of their unique light-sensitivity depicted in terms of structural and optical changes when illuminated with bandgap light. A principal example of such phenomenon is photodarkening (PD), and can be effectively used to prepare intelligent materials possessing certain self control mechanisms which find many potential applications. It is believed that during bandgap light illumination, photogenerated carriers strongly couple to lattice through phonons and generate defect pairs, which accounts for many of the unusual light induced optical and electronic properties of ChG. However, the dynamics of light induced changes is not yet completely understood, in specific with respect to the interaction time of light (pulse width) with ChG, creation of defects in short time scales, and the dynamics of light induced changes from femtosecond (fs) to seconds in a-GeSe<sub>z</sub>, a-GexSe<sub>100-x</sub> and a-GexAs45-xSe55 thin films using time resolved pump-probe optical absorption spectroscopy.

fs and ns time resolved pump-probe optical absorption study demonstrate that ultrafast light induces broad time resolved optical absorption(TOA) in the forbidden gap of GeSe<sub>2</sub> thin film. TOA is attributed to creation and annihilation of light induced transient defects (LITD), which are short lived and form many states in the forbidden gap. Detailed global analysis of the kinetic data provides direct evidence of the multiple decay mechanisms of the LITD. Continuous wave (cw) pump-probe optical absorption study in a-GexAs45.xSe55 glasses (network rigidity is varied from 2.45 to 2.61) at ambient and liquid helium temperatures, demonstrate a dramatic influence of temperature and network rigidity on PD and its kinetics. The samples with low average coordination number show the strongest PD, however the kinetics are much slower. Similarly, PD effects are very much stronger and slower at low temperatures. The present results show that the PD can be easily controlled and tailored by manipulating the forward and recovery rate constants in the kinetics equations, which may find potential applications in designing photo sensitive/insensitive ChG. Another insightful results of PD, transition towards photostability and a slow crossover from PD to photobleaching is observed in a-GexSe<sub>100-x</sub> thin films, when composition of the chalcogenide glassy thin film changes from Ge deficient to rich (from  $x=5$  to 30). Subsequent Raman analysis on as-prepared and illuminated samples provide direct evidence of light induced structural rearrangement i.e, photo-crystallization of Se and removal of edge sharing GeSe<sub>2</sub> tetrahedra. Finally, nonlinear absorption of ultrashort laser pulses (100fs) On

as-prepared and photodarkened Ge<sub>16</sub>As<sub>29</sub>Se<sub>55</sub> thin films is measured by standard z-scan technique. A dramatic change in effective three-photon absorption coefficient of Ge<sub>16</sub>As<sub>29</sub>Se<sub>55</sub> thin films is observed, when its optical band gap decreases by 10 meV with 532 nm light illumination. This large change provides valuable information on the higher excited states, which are otherwise inaccessible via normal optical absorption. Thus, photodarkening in ChG can serve as an effective tool to tune the multiphoton absorption in a rather simple way.

**Keywords:** Chalcogenide glasses, Rigidity, Defects, Photodarkening, Photobleaching, and Spectroscopy.

# **High Valent Oxo - Rhenium Catalysts: Development and Application in Organic Transformations**

**Braja Gopal Das**

**Supervisor: Dr. Prasanta Ghorai**

**Department of Chemistry**

**Accession No.: T00041**

Development of mild and efficient catalytic systems is always a quest for synthetic organic chemist. In this regard, transition metal complexes play a very crucial role. However, as broadly as the low valent transition metal complexes are emphasized in catalysis, the high valent transition metal complexes are not. Nevertheless, high valent transition metal oxides are air and moisture stable compared to low valent transition metal complexes; and therefore, it will be much attractive catalyst for sustainable and industrial developments. However, those are mostly used for oxidation or oxygen transfer reactions as they are in high oxidation state. Recently a considerable attention has been paid to utilize the stable high valent oxo-metals in various organic transformations, other than oxidation reactions. In this context, high valent oxo-rhenium complexes have proven to be mild and non-toxic nature. During my doctoral studies, we have explored the catalytic activity of many high valent oxo-rhenium complexes in various organic transformations, other than oxidation reactions. We have developed an unprecedented direct reductive amination of carbonyls with useful protected amines such as Cbz-, Boc-, EtOCO-, Fmoc-, Bz-, ArSO<sub>2</sub>-, Ar<sub>2</sub>PO-, etc. for the first time. Various aromatic, aliphatic, heteroaromatic aldehydes were successfully examined in presence of 1.5 mol % Re<sub>20</sub>7 catalyst and silanes as stoichiometric hydride source. However, for ketone substrates 20 mol % of NaPF<sub>6</sub> was needed along with catalyst. The reaction undergoes very smoothly to give excellent chemo- and region-selective reductive amination products. 2-Alkyl cyclohexanone derivatives gave very good diastereoselectivity (upto >95:5). The methodology has been successfully applied for formal synthesis of perindopril drug. We have also applied oxorhenium catalyst for the direct substitution of *tert*-activated alcohols with different nucleophiles such as amines and active methylene groups under mild and open flask reaction conditions. The protocol successfully applied to allylic, benzylic and propargylic alcohols and to a variety of nucleophiles. Some of the compounds have an all carbon quaternary centre adjacent to tertiary centre. The mechanistic proof for the SN 1-type process has also been given. We have synthesised a chiral salicyloxazoline ligand based rhenium(V) -oxo complexes. The complexes are air-/moisture stable, crystalline, and storable, showed an excellent catalytic activity for asymmetric reduction of ketoimines. A broad substrate scope, high yields, and excellent enantioselectivities were

observed (up to 99%). further,. the synthesis of ~nantiopure  $\gamma$  and iS-substituted lactams has been exemplified from corresponding chiral amino esters.

**Keywords:** Oxo Rhenium Catalysts, Carbonyls, Hydroxyl, Air Moisture Stable and Organic Transformation.

# Multifunctional MOFs for Detection of Small Molecules and Proton Conduction

Sajal Khatua

Supervisor: Dr. Sanjit Konar

Department of Chemistry

Accession No.: T00040

The thesis entitled, "Multifunctional MOFs for Detection of Small Molecules and Proton Conduction" has been divided into three chapters.

**Chapter 1** In this chapter, the background related to the thesis work has been briefly described. This comprises the fundamental aspects of Metal-Organic Frameworks (MOFs), classifications, dynamic frameworks, and single-crystal to single-crystal (SC -SC) transformations. Dynamic structural transformation based on flexible frameworks is one of the most interesting phenomena of MOF materials. Construction of 3D MOFs with multifunctional molecular architecture can be of great significance as they are likely to afford new materials for potential applications in various fields with few examples are exemplified here briefly.

**Chapter 2** describes selective, reversible and visual colorimetric detection of small molecules (health hazardous and nitro-explosive materials) in vapor phase through a single crystal to single cryst-ftl transformation csc .. sc) without loss of structural integrity in a novel Cu(I)-based two-dimensional (2D, . 44net) metal-organic framework (MOF) [Cu(L)(I)hn·2nDMF·nMeCN (1); L = 4'(4-methoxyphenyl)-4,2':6',4"-terpyridine; DMF =.. - N,N-dimethylformamide, MeCN = acetonitrile). 1 has been synthesized under solvothermal technique. More over 1 selectivity encapsulates more polar molecules and shows excellent guest dependent luminescence behaviour through supramolecular interactions. In the presence of guest molecules, the MOF exhibits a blue shift in fluorescence emission spectra and the extent of the blue shift is appreciably high. It also displays high selectivity toward diethylamine (dea) among N-heterocycles, amine, and highly explosive trinitrophenol (TNP) ) among nitroaromatic explosives as revealed from concurrent luminescence quenching in solution.

**Chapter 3** of the thesis is divided in two parts. **Part A** illustrates by utilizing the breathing behavior of nanopores, helped to investigate the dependency of neutral guest-induced proton conductivity of an interpenetrated Cu<sup>1</sup>-MOF ([1]) on different class of guest molecules in a single framework. Proton conductivity over 10<sup>-3</sup> S/cm under humid conditions and moderate temperature is induced by a series of neutral guest-molecules. Detailed investigation on the neutral guest-incorporated complexes [1 $\supset$ H<sub>2</sub>O], [1 $\supset$ (H<sub>2</sub>O)(DMF)], [1 $\supset$ MeOH],

[1 $\supset$ DMSO], [1 $\supset$ dea], [1 $\supset$ DNB], [1 $\supset$ NB], [1 $\supset$ py] and [1 $\supset$ tz] (DMF = *N,N*-dimethylformamide, DMSO = dimethylsulfoxide, dea = diethylamine, DNB = 1,4-dinitrobenzene, NB = nitrobenzene, py = pyridine and tz = 1*H*-1,2,4-triazole) revealed that low-energy proton conduction occurs under humid conditions *via* Grotthuss mechanism in

[1 $\supset$ NB] and *via* vehicle mechanism in the rest of the complexes. Single point energy computations predicted considerable stabilization upon guest encapsulation. Moreover, all the complexes exhibit considerably high thermal stability and water-resistivity. This strategy possesses two prime potentials: one, facile synthesis of efficient proton-carrier-guest incorporated hybridized materials; and two, understanding of proton conductivity change upon changing the host-guest interactions in hybridized materials.

**Part B** of this chapter deals with the proton conductivity under both humidity and anhydrous conditions. In this regard, a pyrazine (pz) molecules-impregnated Cu<sup>I</sup>-MOF ([1 $\supset$ pz]) has been synthesized exclusively via single-crystal to single-crystal transformation starting from a porous Cu<sup>I</sup>-MOF ([1]), followed by post-synthetic modification with HCl vapor renders an interstitial-pyrazinium dihydrochloride salt-hybridized MOF [1 $\supset$ pz·6HCl] exhibiting superprotic conductivity over 10<sup>-2</sup> S/cm under both the conditions. Post-synthetic modification of [1 $\supset$ pz] with various volatile and non-volatile acids not only enhances the proton carrier concentration, but also confines the proton carriers more firmly in the 1D channels of the MOF. This accounts for such remarkable enhancement of proton conductivity. Moreover, [1 $\supset$ pz] and corresponding H<sub>2</sub>SO<sub>4</sub> or H<sub>3</sub>PO<sub>4</sub> impregnated analogue also exhibit superprotic conductivity over 10<sup>-2</sup> S/cm under humidity. Surprisingly, water-mediated proton conductivity of [1 $\supset$ pz] and corresponding HCl or H<sub>2</sub>SO<sub>4</sub> impregnated analogue is significantly high at room temperature and continuously increases with increasing temperature at least up to the measured maximum temperature 80 °C.

**Keywords:** Metal-Organic Frameworks, Visual Colorimetric Detection, Trinitrophenol, N-Heterocycle and Postsynthetic Modification.

**Total Syntheses of Benzo[c]phenanthridine and Pyrroloindoline Alkaloids via Transition Metal-Free C-C Bond-Forming Reactions**

**Subhadip De**

**Supervisor: Dr. Subhadip De**

**Department of Chemistry**

**Accession No.: T00038**

This thesis is divided into two parts viz. parts A and B. Part A of the thesis deals about the transition-metal-free biaryl-coupling approach to the total syntheses of benzo[c]phenanthridine alkaloids and subdivided into two chapters i.e. Chapters I and II. Chapter I of Part A entitled "Synthetic Approaches to the Benzo[c]phenanthridine Alkaloids: The Literature Overview" is a review on the synthetic approaches to the biological active benzo[c]phenanthridine alkaloids. Chapter II of Part A of the thesis entitled "Total Synthesis of Benzo[c]phenanthridine Alkaloids via Intramolecular Homolytic Aromatic Substitution (IHAS)" deals with the development of KOt Bu Promoted Intramolecular Homolytic Aromatic Substitution (IHAS) with the aid of a catalytic amount of bidentate organic ligands as shown in Scheme 1. Following exhaustive optimization, 40 mol% of organic ligands such as 1, 10-phenanthroline (condition A), 2, 2'-bipyridine (condition B), it was found that biaryl-coupling of 42a afforded desired biaryl-coupling product 43a in good yields (Scheme 1). Interestingly, it was observed that the method also works just in the presence of KOt Bu, without the use of organic molecule as ligand (condition C). The reaction follows a one-pot N-deprotection, organocatalytic biaryl-coupling in presence of KOt Bu followed by aerial oxidation. Above mentioned onepot strategy has been utilized for total syntheses of benzo[c]phenanthridine alkaloids viz. nornitidine (3a), norchelerythrine (3c) and other relatives alkaloids. A tentative mechanism has been proposed to understand the sense of biaryl-coupling reaction via IHAS process. Scheme 1: Synthetic approaches to the benzo[c]phenanthridine alkaloids via IHAS. Part B of the thesis has further subdivided into two chapters i.e. Chapters I and II. Chapter I of Part B entitled "Synthetic Approaches to the Dimeric Pyrroloindoline Alkaloids: The Literature Overview" is a review on the synthetic approaches to the pyrroloindoline alkaloids sharing bispyrrolidino[2,3-b]indoline structure. Pyrroloindoline alkaloids are biogenetically derived from L-tryptophan or tryptamine. Chapter II of Part B of the thesis entitled "Synthetic Approaches to the Dimeric Pyrroloindoline Alkaloids via Organocatalytic Aldol Reaction" deals with construction of all-carbon quaternary stereocenters via a bifunctional thio-urea (TU) catalyzed enantioselective aldol reaction and its application to the synthetic approaches to the 3a,3a'-bispyrrolidino[2,3- b]indoline alkaloids. Retrosynthetically, we envisioned that 3a,3a'-bispyrrolidino[2,3- b]indoline alkaloids can be synthesized from C2-symmetric advanced intermediate (R,R)- 37 (scheme 2), which can be

synthesized from enantioselective aldol reactions of ( $\pm$ )-and meso-67 via a dynamic kinetic asymmetric transformation (DYKAT). Scheme 2: Our working hypothesis utilizing a DYKAT concept. However, in practice, it was found that aldol reaction of 51a using paraformaldehyde in dichloromethane in the presence of TU catalyst provided only enantioenriched spiro-lactone compound 73a in 93% ee with 1:1 dr (Scheme 3). Later, a switching of diastereoselectivities has been shown using two pseudoenantiomeric ligands to accomplish optically active (+)-37a (91% ee with ~12:1 dr) and meso-37a (91% ee ~10:1 dr) (Scheme 3). We believe that these diol could be advanced intermediate for total synthesis of (+)-chimonanthine (ent-1b) and meso-chimonanthine (meso-1b). Scheme 3: Thio-urea-catalyzed aldol reaction and switching diastereoselectivities. Utilizing our organocatalytic aldol reaction, we have also completed the total syntheses of spiro-pyrroloindoline alkaloids, (+)-coerulescine (3a) and (+)-horsfiline (3b), pyrroloindoline alkaloids ( )-deoxyeseroline (2d) and ( )-esermethole (2c). Further, first enantioselective syntheses of prenylated pyrroloindole alkaloids, ( )-pseudophrynamines 272A (4b) and 270 (4c) have also been accomplished.

**Keywords:** Phenanthridine, Pyrroloindoline, organocatalytic, Metal free and Biaryl Coupling.

# Efficient Strategies for Total Syntheses of Ergot Alkaloids

Subhajit Bhunia

Supervisor: Dr. Alakesh Bisai

Department of Chemistry

Accession No.: T00037

This thesis entitled "Efficient Strategies for Total Syntheses of Ergot Alkaloids" is divided into four chapters *viz* chapters 1, 2, 3 and 4. Chapter 1 entitled "Synthetic Approaches to Ergot Alkaloids: The Literature Overview" is a review on the synthetic approaches to the tetracyclic ergot alkaloids sharing vicinal stereocenters (Figure 1). Some conceptual literature reports focussing on the total syntheses of naturally occurring and biologically active ergot alkaloids (Figure 1) have been discussed here. These alkaloids possess architecturally interesting tricyclic and tetracyclic motifs with vicinal stereocenters (in case of 1c) and also contain remote stereocenters (1a-h). In addition to their intriguing architecture, major congeners and synthetic analogue of this family exhibit interesting biological and physiological activity such as effects on blood circulation, neurotransmission, treatment for stopping postnatal bleeding and Parkinson's disease.

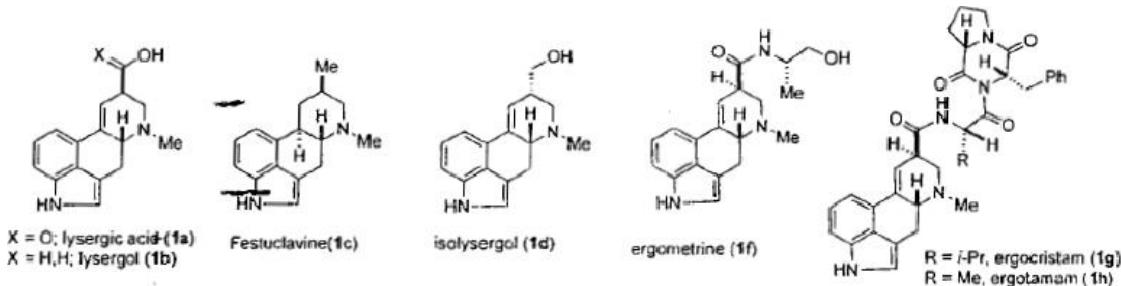
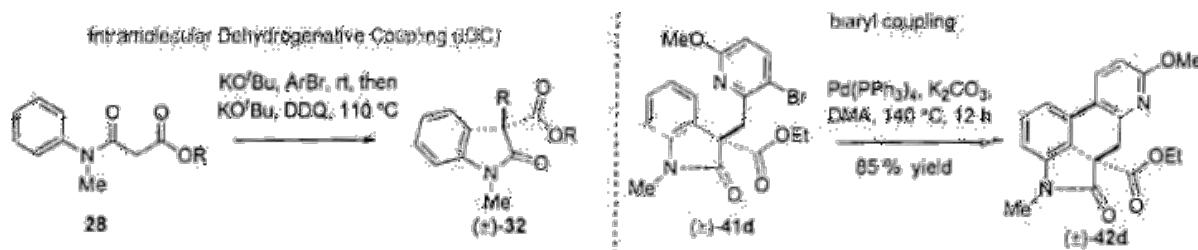


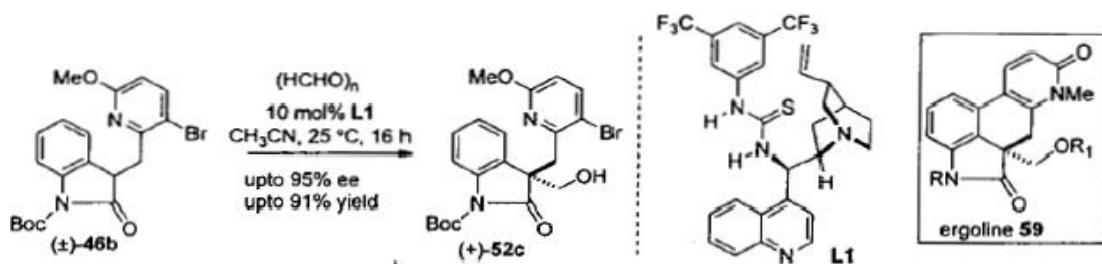
Figure 1: Representatives of ergot alkaloids.

Chapter 2 entitled "Synthesis of 2-Oxindoles Using Oxidative Coupling Strategy: Concise Synthesis of Ergoline" deals with the racemic approach to ergoline ( $\pm$ )-42d via key Intramolecular Dehydrogenative Coupling (IDC) strategy. Reterosynthetically, we would like to approach ( $\pm$ )-1a starting from ( $\pm$ )-42d via simple synthetic elaboration. In this chapter, development of a new synthetic route to synthesize ergoline ( $\pm$ )-42d following key Intramolecular Dehydrogenative Coupling (IDC) and intramolecular dehydrohalide coupling have been discussed (scheme 1).



Scheme 1: Construction of tetracyclic ergoline core via IDC and directed coupling.

Chapter 3 entitled "Thio-Urea Catalyzed Aldol Reactions Using Paraformaldehyde as Cl Unit: Concise Synthesis of Enantioenriched Ergoline" deals with the approach to enantioenriched ergoline 59 via key aldol reaction strategy. Reterosynthetically, we would like to approach (+)-la through simple synthetic elaboration starting from 59. Towards this, we have discussed here a thio-urea catalysed aldol reaction of ( $\pm$ )-46b to synthesize enantioenriched (+)-52c which was also applied to the synthesis of ergoline 59 (scheme 2).

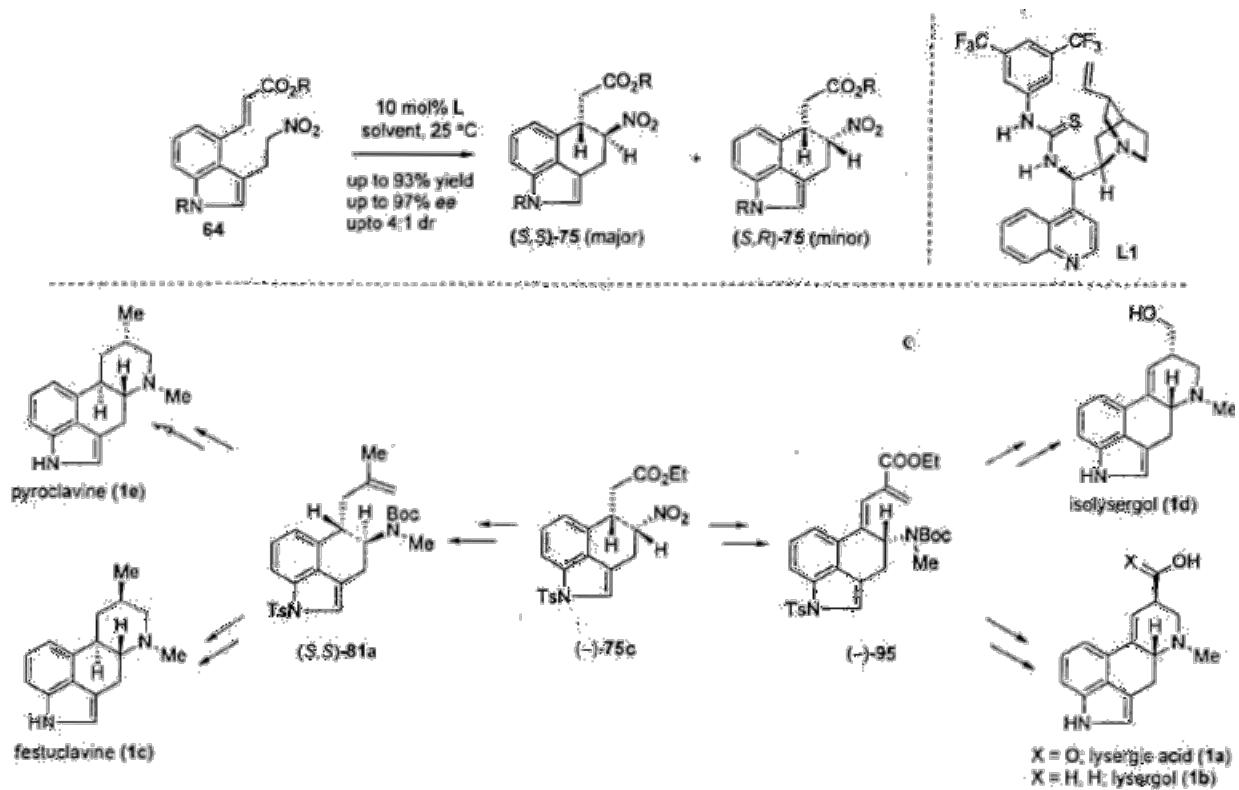


Scheme 2: Construction of enantioenriched ergoline 59 via enantioselective aldol reaction.

Chapter 4 entitled "Intramolecular Enantio- and Diastereoselective Michael Reaction Catalyzed by Thio-Urea: Total Syntheses of Lysergic Acid and Lysergol" deals with construction of vicinal stereocenters and its application in total syntheses of (+)-lysergic acid, (+)-lysergol and (+)-isolysergol and related ergot alkaloids. We hypothesized that (+)-la can be addressed through cyclization of 95 which can be synthesized from 75c via synthetic elaboration. Towards this, a thio-urea catalyzed Michael reaction has been developed in good yield (upto 93%) as well as excellent

enantioselectivity (up to 97% ee) and good ofdiastereoselectivity (up to 4:1) (Scheme 3).

Later on, various ergot congeners (la-e) of ergot alkaloid have been synthesized utilizing enantioenriched 75c shown in scheme 3.



Scheme 3: Total syntheses of ergot alkaloids via enantioenriched intermediate 75c.

**Keywords:** Ergot Alkaloid, 2-Oxindole, Oxidative Coupling Strategy, Enantioenriched Ergoline, Enantioselective Aldol Reaction, Intramolecular Enantio and Diastereoselective Michael Reaction.

**Unified Approach to the Total Syntheses of abeo- Abietane Diterpenoids, Abietane Diterpenoids, and Merosesquiterpenoids via Lewis Acid- Catalyzed C-C Bond-Forming Reactions**

**Badrinath N. Kakde**

**Supervisor: Dr. Alakesh Bisai**

**Department of Chemistry**

**Accession No.: T00034**

This thesis entitled "Unified Approach to the Total Syntheses of abeo-Abietane Diterpenoids, Abietane Diterpenoids, and Merosesquiterpenoids via Lewis Acid- Catalyzed C-C Bond-Forming Reactions" is divided into three chapters viz chapters I, II, and III. Chapter I is subdivided into two parts Parts A and B. Part A of Chapter I entitled "Literature Overview on the Synthetic Approaches to the abeo-Abietane Diterpenoids" is a review on the synthetic approaches to the abeo-abietane diterpenoids sharing [6,5,6]-carbotricyclic core. Part B of Chapter I entitled "Total Syntheses of abeo-Abietane Diterpenoids via Lewis Acid-Catalyzed Nazarov Type Cyclization and Hydroarylation Strategies" deals with the development of efficient Nazarov type cyclization and hydroarylation catalyzed by Lewis acid (Schemes 1 and 2). The first total synthesis of taiwaniaquinol F (2i) has been accomplished via an efficient Lewis acid catalyzed Nazarov type cyclization of arylvniylcarbinol 40e (Scheme 1), which essentially goes through a carbocationic intermediate 63e. Scheme 1: Lewis-acid catalyzed Nazarov type cyclization strategy to the abeo-abietane. In search for trans -fused abeo-abietane diterpenoids viz taiwaniaquinone G (2f), later hydroarylation strategy has been developed (Scheme 2). Under optimized conditions, it was found that this process affords a mixture of cis-fused and trans-fused (1.8:1 in favour of cis-fused) carbotricyclic cores. Utilizing this strategy, a concise total synthesis of taiwaniaquinone G (2f) has been accomplished. In addition, the aforementioned methodology also offers enough flexibility to accomplish total syntheses of several cisfused abeo-abietane diterpenoids viz taiwaniaquinol B (2g), dichroanone (2c) and taiwaniaquinone H (2d). Scheme 2: Lewis-acid catalyzed hydroarylation strategy to the abeo-abietane diterpenoids. Chapter II of this thesis also subdivided into two parts, Parts A and B, where first part entitled "Literature Overview on the Synthetic Approaches to the Abietane viii Diterpenoids" deals with the various synthetic approaches to abietane diterpenoids sharing [6,6,6]-carbotricyclic core. Part B of Chapter II entitled "Total Syntheses of Abietane Diterpenoids via Lewis Acid-Catalyzed Hydroarylation" centres around the development of efficient Lewis acid-catalyzed hydroarylation strategy (Scheme 3). It was found that compound of type 24d undergoes efficient Lewis acid-catalyzed hydroarylation process to afford [6,6,6]-carbotricyclic core sharing an all-carbon quaternary center 25d in excellent yields (Scheme 4). Utilizing aforementioned strategy first total syntheses of abietane diterpenoids, royleanone (1g) and inuroyleanol (1h) have been

achieved few steps (Scheme 4). Scheme 3: Lewis-acid catalyzed hydroarylation strategy to the abietane diterpenoids. Chapter III of this thesis is also subdivided into two parts, Parts A and B. Part A entitled "Literature Overview on the Synthetic Approaches to the Merosesquiterpenoids" is the discussion on synthetic approaches towards the total synthesis of [6,5,6,6] fused carbocyclic core of meroesquiterpenoids. Part B of Chapter III entitled "Approaches towards the Synthesis of Meroesquiterpenoids via Lewis Acid-Catalyzed Nazarov Type Cyclization" deals with the development of Lewis acid catalyzed diastereoselective Nazarov type cyclization of arylallylcarbinols 9e to synthesized enantioenriched advanced carbocyclic enantioenriched intermediate 10e (Scheme 4). One of the compounds (10e) has been synthetically elaborated to enantioenriched 1c, which can be utilized as advanced intermediate for synthesis of unnatural 9-*epi*-pelorol (see, *epi*-1c) and related unnatural meroesquiterpenoids. Scheme 4: Lewis -acid catalyzed Nazarov type cyclization strategy to the meroesquiterpenoids. In summary, this thesis describes expeditious approach to the total syntheses of abeo-abietane diterpenoids (Chapter I), abietane diterpenoids (Chapter II), and meroesquiterpenoids (Chapter III) via an efficient Lewis acid-catalyzed Nazarov type cyclization and hydroarylation strategies.

**Keywords:** Bietane Diterpenoids, Abietane Diterpenoids, Lewis-Acid Catalyzed and Meroesquiterpenoids.

**KOtBu-Mediated Synthesis of Substituted Dihydropyridinones, Pyridinones, and Synthesis  
and Structural Characterization of Mercury Selenolates**

**Abhimanyu Yadav**

**Supervisor: Dr. Sangit Kumar**

**Department of Chemistry**

**Accession No.: T00033**

This PhD thesis describes the synthesis of an important class of heterocyclic compounds known as dihydropyridinones, pyridinones, dihydropyridinethiones and synthesis, structural characterization of mercury selenolates. The analogues of dihydropyridinones have significant role in biological and medicinal science. These analogues are being used as hypertensive drugs for calcium channel blockages and for treatment of diabetes, obesity, and neuropeptide. The existing methods for the construction of dihydropyridinones require prefunctionalized substrates, such as  $\alpha,\beta$ -unsaturated acyl chlorides,  $\alpha,\beta$ -unsaturated ester, sodium cyanomethanide,  $\beta$ -aminonitrile etc. These substrates are either expensive or difficult to handle. Here, we have disclosed a potassium tert-butoxide base mediated coupling of aldehyde and acetonitrile for the synthesis of dihydropyridinones. We have also developed a simple and convenient approach for the synthesis of pyridinones from dihydropyridinones using KOTBu in DMSO solvent. The present methodology is highly practical for the synthesis of substituted dihydropyridinones and pyridinones with halogen functionalities such as fluoro, difluoro, chloro, bromo, diiodo, and electron donating substituents, such as -CH<sub>3</sub>, mono-, di-, and tri-OCH<sub>3</sub>, -SCH<sub>3</sub>, -N(CH<sub>3</sub>)<sub>2</sub> etc. shows good compatibility under optimized reaction condition. Again, when ferrocene aldehyde was subjected for coupling with acetonitrile, 4- ferrocene substituted pyridine was obtained in good yield instead of the expected ferrocenyl dihydropyridinones, which seems more exciting result. Synthesis and structural characterization of mercury selenolate complexes derived from 2-phenylbenzamide ligands and their isolation in monomeric form have been carried out for the first time. N,N-disubstituted Mercury(II) selenolate complexes were synthesized from diselenides benzamide ligands, on treatment with elemental mercury for several hours in methanol, whereas N-monosubstituted Mercury(II) selenolates were synthesized from isoselenazolone on treatment with HgCl<sub>2</sub>. The mercury complex derived from sterically bulky diisopropyl amide ligand shows strong intramolecular non-bonded Hg...O interaction, adopts linear geometry and exists as a monomer. Thermogravimetric analysis (TGA) of mercury selenolate complexes revealed the two-step decomposition, which leads to formation of HgSe.

**Keywords:** Dihydropyridinones, Pyridinones, Potassium Tert-Butoxide, C-C and C-N Coupling Reaction, Diselenides and Mercury Selenolates.

**“Synthesis of 2-Oxindoles Sharing All-Carbon Quaternary Centers: Synthetic Approaches to Benzofuro indoline and Pyrroloindoline Alkaloids”**

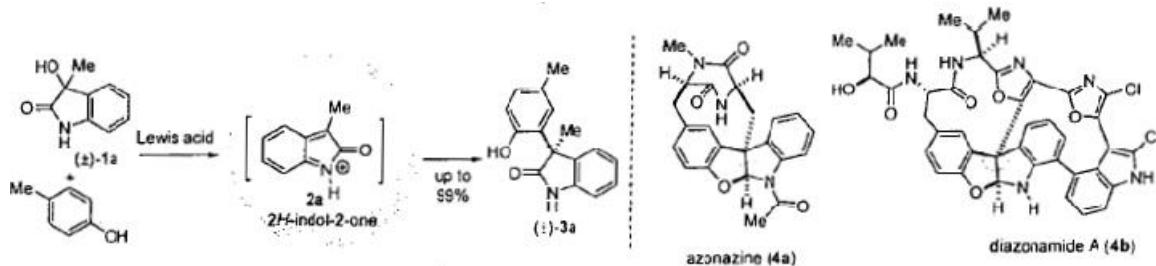
**Lakshmanakumar Kinthada**

**Supervisor: Dr. Alakesh Bisai**

**Department of Chemistry**

**Accession No.: T00031**

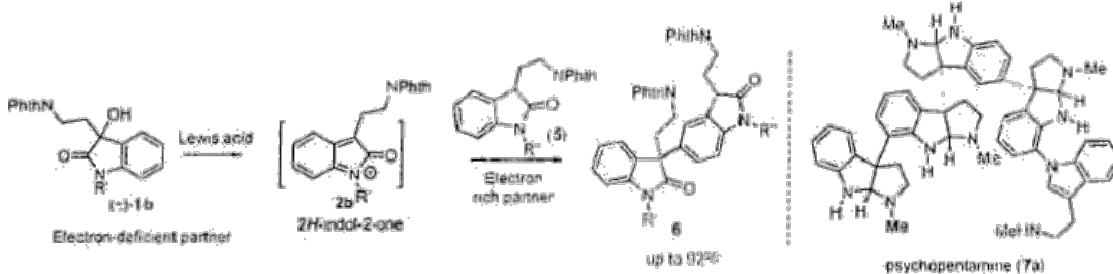
The thesis is divided into four chapters *viz* chapters 1, 2, 3 and 4. Chapter 1 entitled "Friedel-Crafts Alkylation of Electron-rich Aromatics with 3-Hydroxy-2-oxindoles: Approach to the "Synthesis of Benzofuro1naoline" ·describes the synthetic approaches to core structure of azonazine (4a).



Scheme 1: Azonazine (4a), diazonamide A (4b) and our Friedel-Crafts strategy.

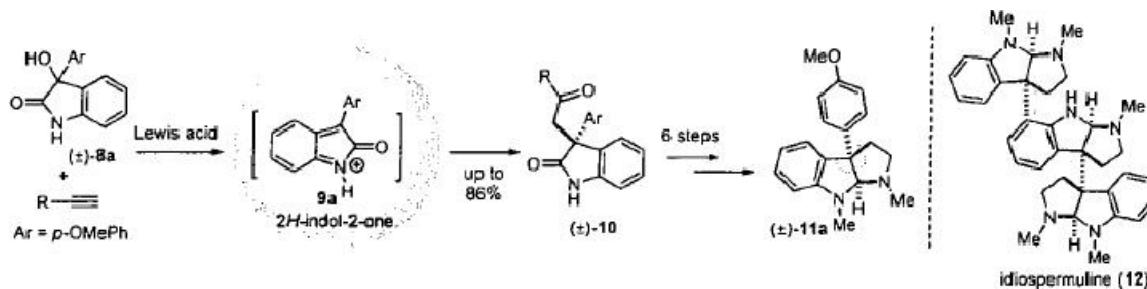
Azonazine (4a) is an architecturally interesting indole alkaloid isolated very recently, in 2010 from a Hawaiian marine sediment-derived fungus *Aspergillus insulicola*. It has a similar tetracyclic core as present in diazonamide A (4b), which was isolated earlier in 2004. Towards this, we have developed efficient Lewis acid-catalyzed Friedel-Crafts alkylations of 4-substituted phenols with 3-substituted 3-hydroxy-2-oxindoles [ $(\pm)$ -1a] to synthesize various 2-oxindoles [ $(\pm)$ -3] sharing an all-carbon quaternary stereocenter and we have utilized this methodology for the synthesis of core of azonazine (4a).

Chapter 2 entitled "Friedel-Crafts Alkylation of 2-oxindole with 3-Hydroxy- 2-oxindoles as Electron-deficient Partners" describes synthesis of 2-oxindoles (6) sharing an all-carbon quaternary stereocenter at the pseudobenzylic position. In 2004, cyclotryptamine alkaloid psychopentamine (7a), has been isolated from leaves of *Psychotria rostra* by Takayama and co-workers. Towards this, we have developed efficient Lewis-acid catalyzed F-C alkylations of 2-oxindoles with a variety of 3-hydroxy-2-oxindole as electron-deficient partners to construct dimeric 2-oxindoles with a C-3/C-5'linkage (Scheme 2).



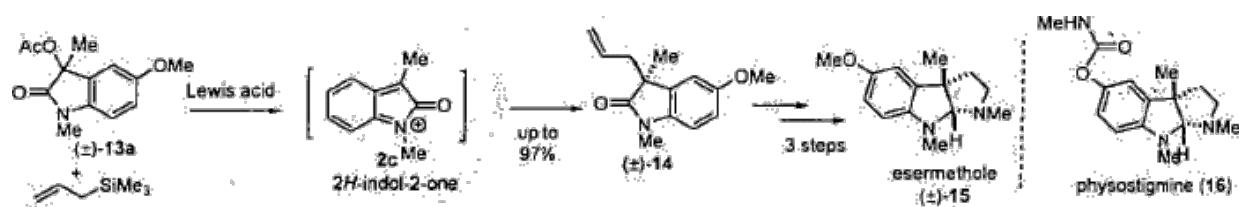
Scheme 2: Psychopentamine (7a) and our hypothesis of Friedel-Crafts alkylation.

Chapter 3 entitled "Reactions of 3-Hydroxy-2-oxindole with Terminal Alkynes: Applications in the syntheses of Pyrroloindoline Core" describes synthetic approaches to pyrroloindoline core structure of idiospermuline (12). 2-Oxindoles having all carbon quaternary stereocenter at the C-3(a)-position linked with aryl group is major core in many biologically active cyclotryptamine alkaloids such as idiospermuline (12) (Scheme 3). In this direction, we have developed efficient Lewis acid-catalyzed reaction of terminal alkynes with 3-aryl 3-hydroxy-2-oxindoles (8a) to synthesize various 2-oxindoles (10) (Scheme 3). Finally, we have utilized our methodology for the construction of cyclotryptamine core [(±)-8a] of idiospermuline (12) (Scheme 3).

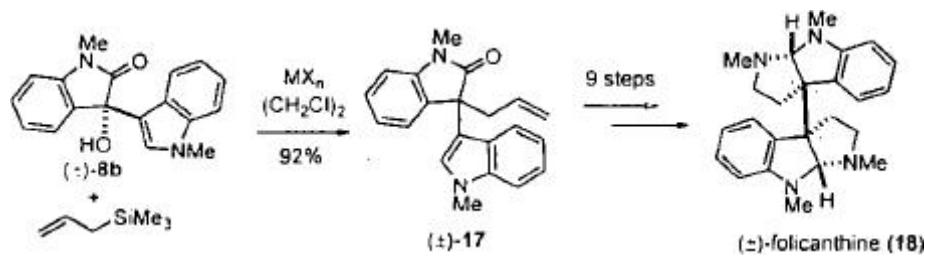


Scheme 3: Idiospermuline (12) and our strategy for the synthesis of cyclotryptamine core.

Chapter 4 in this thesis entitled "Reactions of 3-Hydroxy-2-oxindole with Allyltrimethylsilane: Formal Total Synthesis of (±)-Folicanthine" deals with development of efficient strategies for the synthesis of pyrroloindoline alkaloids such as physovenine, physostigmine (16) (Scheme 4). These alkaloids useful for the treatment of cholinergic disorders and myasthenia gravis. The dimeric pyrroloindoline alkaloids sharing vicinal all-carbon quaternary stereocentres, with a wide array of biological activities, remain one of the fascinating targets for synthetic interest.



Scheme 4: Cyclotryptamine (lOa-b), bis-cyclotryptamine alkaloids (11) and our strategy.



Scheme 5: Formal synthesis of bis-cyclotryptamine alkaloid, folicanthine (18).

Along this direction, we have developed efficient Lewis acid-catalyzed allylations of 3-methyl 3-acetoxy-2-oxindoles [( $\pm$ )-13a] and 3-aryl 3-hydroxyl 2-oxindoles (8b) with allyltrimethylsilane to synthesize various 2-oxindoles [such as ( $\pm$ )-14], ( $\pm$ )-17] sharing an allcarbon quaternary stereocenter (Scheme 5). We have utilized the strategy in the formal synthesis of esermethole (16) and folicanthine (18).

**Keywords:** Bis-Cyclotryptamine Alkaloids, Ldiospermiline, Fricdcl-Crafts Alkylation, Diazonamide A (4b) and Carbon Quaternary.

**Multifunctional Behavior in 3d and 4f Metal Based Magnetically Imperative Coordination Complexes**

**Soumyabrata Goswami**

**Supervisor: Dr. Sanjit Konar**

**Department of Chemistry**

**Accession No.: T00030**

This thesis work describes the synthesis, detail characterizations and multifunctional behavior of magnetically important 3d and 4f metal based coordination complexes. Chapter 1 is an introduction to the basic concepts on different types of functional behaviors exhibited by the complexes. At first, discussions on molecular magnetism including different terminologies like magnetic exchange interactions, single molecular magnetism, magnetocaloric effect and spin crossover have been done. This is followed by discussion on other functional properties such as heterogeneous catalysis, proton conduction and photoluminescence. Thorough literature review on each of the discussed functional behaviors has also been included here. Chapter 2 describes the synthesis and characterization of a new FeII based Metal Organic Framework (MOF),  $[Fe_3(OH)_3(C_4O_4)(C_4O_4)0.5]_n$  (1), using a short bridging ligand dilithium squarate. Interesting structural feature is that the 3D framework is made up of nanoscopic cuboctahedral cages extending in three dimensions. The framework also contains two types of voids, larger ones are hydrophobic and the smaller ones are hydrophilic in nature. Variable temperature magnetic study shows spin-canted antiferromagnetic behavior and long-range magnetic ordering in the low temperature region. In addition, the complex shows excellent heterogeneous catalytic activity for the transformation of tetrazines to oxadiazole derivatives at room temperature ( $25\text{ }^{\circ}\text{C}$ ). The synergism of these two important functional properties makes the 3D framework an excellent multifunctional material. Chapter 3 Part A discusses about two new 1D coordination polymers with general formula  $\{[M_3(HL)_3(H_2O)_6]_n \cdot 13n(H_2O)\}$ , synthesized using oxonate ( $L^{3-}$ ) as the ligand [ $M = Fe^{II}$  (1) and  $Co^{II}$  (2)]. Single crystal X-ray diffraction analysis shows that the complexes are isostructural in nature. Interesting structural features are the zig-zag arrangement formed by repeating  $[M(H\text{-oxonato})(H_2O)_2]$  units and continuous H-bonded water channels running between two adjacent chains. Complex 1 shows spin-canted antiferromagnetic behavior and long range ordering at lower temperature region while complex 2 shows dominant antiferromagnetic behavior. In addition, the complexes reveal good proton conduction ability which is comparable to other reported magnetic MOFs, at high temperature and high humidity conditions. The reported complexes are rare examples to show the co-existence of interesting magnetic and proton conduction behaviors. Part B describes the synthesis and

characterization of three new lanthanide based 1D coordination polymers with general formulae  $[LnNa(C_5O_5)_2(H_2O)_7]_n$ , using croconate as the ligand [ $H_2C_5O_5$  = croconic acid;  $Ln = Gd^{III}$  (1),  $Nd^{III}$  (2) and  $Dy^{III}$  (3)]. Structural characterization showed that the complexes are isostructural in nature and consist of alternately arranged  $Ln^{III}$  and  $Na^+$  ions bridged by croconate ligand. Magnetic characterization revealed that  $Gd$  (1) and  $Nd$  (2) analogues exhibit magnetocaloric effect (MCE) while the  $Dy$  analogue (3) shows single chain magnetic (SCM) behavior. Chapter 4 discusses about two new classes of complexes [Class 1 (Sphenocorona coordination geometry around  $Ln$  center):  $\{Ln(ntbi)(NO_3)_3\}_2 \cdot 3CH_3OH$ ;  $Ln = Dy$  (1),  $Ho$  (3) and Class 2 (Cubic coordination geometry):  $\{Ln(ntbi)_2\}_5 \cdot 15Cl \cdot xH_2O$ ;  $Ln = Dy$ ,  $x = 18$  (2) and  $Ln = Tb$ ,  $x = 27$  (4)] synthesized using a fluorophoric tripodal ligand ntbi [tris(benzimidazole-2-ylmethyl)amine]. Structural analysis shows that complexes 1 and 3 exhibit sphenocorona coordination geometry around the  $Ln^{III}$  centers whereas 2 and 4 show cubic geometries. AC magnetic susceptibility measurements display significant difference in slow magnetic relaxation behaviors in terms of energy barriers that discloses the effect of small changes in coordination environment around the  $Ln^{III}$  centers on relaxation dynamics. Solid state photoluminescence studies showed prominent difference in intensities of 1 and 2 confirming the effect of the coordination environments on the luminescence behaviors. Chapter 5 describes two  $Fe^{II}$  based mononuclear complexes,  $[Fe(L1)_3(ClO_4)_2 \cdot 3H_2O]$  ( $1 \cdot 3H_2O$ ) and  $[Fe(L2)_3(ClO_4)_2 \cdot 2CH_3CN]$  ( $2 \cdot 2CH_3CN$ ) that have been synthesized using the ligands 4,4'-dimethyl-2,2'-bipyridine ( $L1$ ) and 4,4'-ditertiarybutyl-2,2'-bipyridine ( $L2$ ). Single crystal X-ray diffraction, DC magnetic susceptibility and variable temperature EPR studies show that the complexes exist in low-spin (LS) state in the solvated forms, but show spin-crossover (SCO) behavior in desolvated forms [ $1 \{Fe(L1)_3(ClO_4)_2\}$  and  $2 \{Fe(L2)_3(ClO_4)_2\}$ ]. The strategic introduction of substituents viz. methyl (Me) and tertiary butyl (tBu) with different electron donating effects at the 4-position of the 2,2'-bipyridine ligand affect the electronic nature of the  $Fe^{II}$  centers and therefore the desolvated complexes exhibit different SCO behaviors with different transition temperatures. Overall, the dual roles of solvents and substituents on thermal SCO behavior in  $Fe^{II}$  based mononuclear complexes have been investigated.

**Keywords:** Heterogeneous Catalysis, Spectroscopic, Thermogravimetric Characterization, Spin-Canted Antiferromagnetic and Thermal Spin-Crossover.

**Luminescent Metal Nanoclusters and Nanoparticle: Synthesis, Spectroscopic Investigations and Applications**

**Subhadip Ghosh**

**Supervisor: Dr. Saptarshi Mukherjee**

**Department of Chemistry**

**Accession No.: T00027**

This thesis reports the synthesis of metal nanoclusters (NCs) and nanoparticles (NPs) exhibiting highly interesting luminescent properties which were exploited to demonstrate these nanomaterials as probes in several unique and promising applications. We have synthesized Human Serum Albumin (HSA) templated highly luminescent Silver (Ag) NCs, with blue ( $\text{Ag}_9@\text{HSA}$  NCs) and red ( $\text{Ag}_{14}@\text{HSA}$  NCs) emission possessing unusual property of interconversion from one NCs to the other based on simple redox chemistry with the retention of their photo-physical properties. These Ag NCs were found to be highly efficient sensors for metal ions namely Co(II), Zn(II) and Hg(II) ions which have important biological roles as well as toxic effects. The level of detection of these metal ions by the Ag NCs was fairly noteworthy in real water samples collected from different sources. Further the  $\text{Ag}_9@\text{HSA}$  NCs exhibited the phenomenon of photo-switch whereby the luminescence quenching observed in the presence of Co(II) ions was completely restored in the presence of Zn(II) ions. We have also tried to investigate the effect of the proteolysis of HSA on the luminescence of the Ag NCs by subjecting the  $\text{Ag}@\text{HSA}$  NCs to trypsin digestion. The tryptic cleavage of HSA resulted in the destabilization of the  $\text{Ag}_9@\text{HSA}$  NCs with the loss in luminescence. The loss was subsequently accompanied by the gradual evolution of enhanced luminescence due to the formation of highly stable meta AgTp NCs by the coalition of the smaller Ag NCs along with protein fragments. For the first time, we have revealed the growth kinetics of NCs using Fluorescence Correlation Spectroscopy based on the intrinsic luminescence of the Ag NCs. We have also synthesized Copper (Cu) NCs with fairly good luminescence and photo-stability and demonstrated their capability to act as FRET probes. Further the unique temperature detection ability of these luminescent and biocompatible Cu NCs enlightens their prospects as a non invasive nano-thermometer in biological studies. Besides NCs, Ag NPs were synthesized solely based on the drug Ciprofloxacin, which were found to be exhibiting unusual luminescence due to the drug coverage. It was also observed and confirmed by various spectroscopic analysis that the drug binding as well as its release from the surface of the Ag NPs was time dependent and took place close to the physiological conditions, thus illustrating the efficiency of these nano-hybrids in drug delivery applications.

**Keywords:** Nanoclusters, Nanoparticle: Synthesis, Spectroscopic Investigations, luminescence and Drug Design.

**Synthesis of Cinnamyl Derivatives from Cinnamyl Alcohols and Their Application in  
Heterocycle Synthesis: A Facile Synthesis of 2-Benzyl Indoles and 2-Benzyl Furans**

**Rajender Nallagonda**

**Supervisor: Dr. Prasanta Ghorai**

**Department of Chemistry**

**Accession No.: T00025**

The cinnamyl derivatives are important precursors in organic synthesis with several possibilities for further functionalization of double bond. Anilines with  $\pi$ -activated alkyl substitution represent recurring structural motifs in bioactive molecules with pharmaceutical relevance and also the precursors of many heterocycles. In this regard, Friedel-Crafts reactions are amongst the most efficient carbon-carbon bond forming processes by which the incorporation of alkyl substituents onto aromatic rings occurs. Despite the tremendous progress of Friedel-Crafts alkylations, very rare success has been documented where anilines are directly been used with respect to arene counterpart. Therefore, direct C -alkylation of anilines attracted more attention in recent years. During my doctoral studies, we have developed a new strategy for the direct Friedel-Craft reaction of anilines with  $\pi$ -activated alcohols via Hofmann-Martius rearrangement of N-alkylated product. And further applied it in the synthesis of substituted 2-benzyl indoles via palladium catalysed aerobic oxidative-cycloisomerization pathway. In this protocol we have also demonstrated a one-pot sequential synthesis of ocinnamylanilines, starting from the corresponding anilines and substituted cinnamyl alcohols followed by oxidative cycloannulation. We have also utilized this strategy for the synthesis of substituted 2-benzyl furans from 2-cinnamyl-1,3-dicarbonyls which in turn were prepared from 1,3-dicarbonyls and substituted cinnamyl alcohols. Finally, an oxidation of  $\alpha$ - cinnamyl- $\beta$ -ketonitrile is also discussed under the similar catalytic reaction conditions.

**Keywords:** Friedel-Crafts Reaction, Cinnamyl Derivative, Silylated Nucleophiles, Catalytic Reaction and Catalysed Aerobic Oxidative-Cycloisomerization.

**Catalytic Asymmetric Mukaiyama-Michael and Direct Vinylogous Michael Addition Reactions**

**Subhrajit Rout**

**Supervisor: Prof. Vinod K. Singh**

**Department of Chemistry**

**Accession No.: T00023**

This thesis is divided into two chapters. Chapter I describes a chiral pyridine-2,6- bis(5',5'-diphenyloxazoline)- Zn(II) catalyzed enantioselective Mukaiyama-Michael reaction of acyclic silyl enol ethers with 2-enoylpyridine N-oxides in an external additive free condition at ambient temperature. Although considerable efforts have already been put forth towards asymmetric Mukaiyama-Michael reactions, but it is still difficult and challenging task to carry out the reaction without catalyst activation or in an external additive free conditions to afford the corresponding product in synthetically useful level. Moreover, most of the strategies require prolonged reaction time. Most of the metal catalyzed asymmetric version of Mukaiyama-Michael reactions known till date need some alcohol as additive and lower temperatures to achieve good chemical yields and enantioselectivitie. However, the asymmetric version of Mukaiyama-Michael reaction at ambient temperature is unexplored and therefore, there is the need of development of catalytic system. In this context, an additive free, and efficient catalytic asymmetric pathway to synthesize enantioenriched functionalized 1,5-dicarbonyls utilizing 2-enoyl pyridine N-oxide 2 as template for Mukaiyama-Michael reaction with acyclic silyl enol ether 3 as nucleophile at ambient temperature catalyzed by chiral PYBOX-DIPH-Zn(OTf)<sub>2</sub> complexes has been reported (Scheme 1). Scheme 1 This protocol is operationally simple and affords a variety of Michael adduct in excellent level of yields and enantioselectivities (up to 96% ee). To show the versatility of methodology, one of the products was converted to carboxylic acid under saponification conditions, which was then transformed to synthetically useful 3, 4-dihydro- $\alpha$ -pyrone. Further, in order to explain the stereochemical outcome of the Michael adduct, a transition state model has been proposed. Chapter II deals with the asymmetric direct vinylogous Michael reaction of  $\alpha,\alpha$ - dicyanoalkenes to 2-enoylpyridine N-oxides with cinchona derived bifunctional thio(urea) as organocatalyst. Among various synthetic protocols of the asymmetric direct vinylogous Michael reaction, addition of  $\alpha,\alpha$ -dicyanoalkenes to different electrophilic partners provides enantioenriched  $\gamma$  carbon functionalized exocyclic or acyclic activated alkenes. Scheme 2 It is noteworthy to mention that 2-enoylpyridine N-oxide has appeared as an efficient and privileged substrate for various asymmetric transformations in the presence of catalytic chiral metal-complexes. However, no report has been disclosed utilizing 2-enoylpyridine Noxide as a substrate under asymmetric organocatalysis, to the best of knowledge. In order to show the scope of the 2-enoylpyridine N-oxide towards organocatalysis, the first

catalytic asymmetric and direct vinylogous Michael reaction of  $\alpha,\alpha$ -dicyanoalkenes to 2-enoylpyridine N-oxides with cinchona derived bifunctional thio(urea) as organocatalyst has been reported (Scheme 2). This process is operationally simple and afforded a variety of vinylogous Michael products in exclusive  $\gamma$  selectivity with excellent diastereo- and enantioselectivities (up to 99% ee). The scope of the methodology is extended towards asymmetric desymmetric strategy using 4-substituted cyclohexanone derived achiral  $\alpha,\alpha$ -dicyanoalkene to afford highly functionalized enantioenriched activated methylenecyclohexane derivatives with three chiral centers. The synthetic utility of the reaction was shown by reduction of vinylogous Michael adduct to access hydrofuran fused hexahydrocyclopenta[c]chromane with two contiguous stereogenic quaternary carbons adjacent to two contiguous stereogenic tertiary carbons.

**Keywords:** Catalyzed Enantioselective Mukaiyama-Michael Reaction, Vinylogous Michael Reaction and Hexahydrocyclopenta.

**Metal- Organic Frameworks for Sorption, Proton Conduction  
and Sensing Applications**

**Suresh Sanda**

**Supervisor: Dr. Sanjit Konar**

**Department of Chemistry**

**Accession No.: T00020**

Chapter 1 in this chapter the broad background related to the thesis work has been given in order to benefit the readers. This includes the basic concepts of Metal-Organic Frameworks (MOFs), brief history and classifications. In addition, synthetic strategies and synthetic methods used to prepare the MOF materials followed by important applications with few examples are illustrated here briefly.

Chapter 2 describes the synthesis, structural characterization, adsorption and proton conduction properties in a family of flexible MOFs, namely,  $\{[\text{Zn}(\text{pyromellitate})0.5(\text{aldrithiol})]\cdot 5\text{H}_2\text{O}\}\text{n}$  (1),  $[\text{Co}(\text{aldrithiol})(\text{pyromellitate})0.5(\text{H}_2\text{O})_2]\text{n}$  (2),  $[\text{Cu}(\text{aldrithiol})_2(\text{pyromellitate})]\text{n}\cdot 2\text{n}(\text{H}_2\text{O})$  (3),  $[\text{Ni}_2(\text{aldrithiol})_2(\text{pyromellitate})(\text{H}_2\text{O})_2]\text{n}\cdot 2\text{n}(\text{C}_2\text{H}_5\text{OH})\cdot 11\text{n}(\text{H}_2\text{O})$  (4) ( $\{[\text{Zn}(\text{pyromellitate})0.5(\text{aldrithiol})]\cdot 2\text{H}_2\text{O}\}\text{n}$ ) (5). Compounds 1-4, were synthesized through slow diffusion technique and compound 5 was synthesized under hydrothermal conditions. SC-XRD studies show that compounds 1-3 have 2D layered architectures, compound 4 adopts a 3D framework and 5 is a 1D co-ordination polymer. Adsorption studies reveal that, compound 1 shows unique selective, stepwise, reversible, and hysteretic adsorption behaviour towards CO<sub>2</sub> gas and H<sub>2</sub>O, MeOH, and CH<sub>3</sub>CN vapours. Compounds 2 and 3 show high MeOH uptake whereas compound 4 shows a decent amount of H<sub>2</sub>O adsorption. In addition, the proton conduction properties of compounds 1 and 5 show high conductivity values of  $2.55 \times 10^{-7}$  and  $4.39 \times 10^{-4}$  S cm<sup>-1</sup> at 80°C and 95% RH.

Chapter 3 presents the synthesis, structural characterisation, adsorption and luminescence properties of three new 2D/3D MOFs having formula of  $\{[\text{Zn}(1,3-\text{adaa})(\text{bpmh})]\text{n}$  (1),  $\{[\text{Cd}(1,3-\text{adaa})(\text{bpmh})]\text{n}$  (2),  $\{[\text{Zn}(1,4-\text{pdAA})(\text{bpmh})]\text{n}$  (3) (bpmh = N,N-bis-pyridin-4-ylmethylene-hydrazine, 1,3-adaa = 1,3-adamantane diacetic acid, 1,4-pdAA = 1,4-phenylene diacetic acid). All the compounds were synthesized through slow diffusion technique. Structural determination reveals that compounds 1 and 2 have 2D layered architectures with similar framework topology, whereas 3 is a 3D framework. In compounds 1-3, the used dicarboxylic acids act as pillars between the metal bpmh layers. Solid-state photoluminescence properties of compounds 1-3 show ligand ( $n \rightarrow \pi^*$  and  $\pi \rightarrow \pi^*$ ) based florescence.

Chapter 4 is based on dual sensing property of a Zn(II) based luminescent MOF ( $\{[\text{Zn}(\text{tcpb})0.5(\text{bpeb})0.5]\cdot [0.5(\text{bpeb})\cdot 2\text{H}_2\text{O}]\text{n}$ ) (1). The compound was synthesized by using a highly conjugated, rigid bpeb linker (bpeb = 1,4-bis[2-(4 pyridyl) ethenyl] benzene) in combination with a  $\pi$ -electron-rich tetra-topic carboxylate ligand (H<sub>4</sub>tcpb = 1,2,4,5-tetrakis(4-carboxyphenyl)benzene) and

$\text{Zn}(\text{NO}_3)_2 \cdot 6\text{H}_2\text{O}$ . Fluorescence sensing studies reveal that, compound 1 shows rapid and convenient visual detection towards Picric Acid (PA) with the exceptional selectivity (94%) and it could detect  $\text{Pd}^{2+}$  in the concentrations of as low as 0.03 ppm and can serve as a dual functional fluorescent sensor. Additionally, the compound shows highly selective and sensitive detection of PA and  $\text{Pd}^{2+}$  in the concurrent presence of other competing nitroanalytes and metal ions. Chapter 5 describes the multifunctional behaviour in a series of 2D/3D MOFs, namely,  $\{[\text{Zn}(2,6\text{nDC})(\text{aldrithiol})] \cdot 3(\text{H}_2\text{O})\}_n$  (1),  $\{[\text{Co}(2,6\text{nDC})(\text{aldrithiol})(\text{H}_2\text{O})_2] \cdot 2(\text{H}_2\text{O})\}_n$  (2),  $\{[\text{Cd}_2(2,6\text{nDC})_2(\text{aldrithiol})_2(\text{H}_2\text{O})_2] \cdot (\text{aldrithiol})(\text{EtOH})_3(\text{H}_2\text{O})\}_n$  (3), ( $2,6\text{-nDC}$  = 2,6-naphthalene dicarboxylic acid; aldrithiol = 4,4'-dipyridyl disulphide). Single crystal analysis reveal that, compounds 1 and 2 have 2D layered architectures with similar framework topology whereas 3 is a 2-fold interwoven three dimensional framework. Sorption studies reveal that compounds 1-3 selectively adsorbs  $\text{CO}_2$  over other gases and  $\text{H}_2\text{O}$  over other solvents. Proton conductivity study of compounds 1 and 2 show highest values of  $6.73 \times 10^{-7} \text{ S cm}^{-1}$ ,  $1.96 \times 10^{-5} \text{ S cm}^{-1}$  at 318 K and 95% RH and these values are humidity dependent. Photoluminescent properties of compounds 1 and 3 show metal perturbed ( $\pi^*-\pi$  and  $\pi^*-n$ ) intra ligand charge transfer transitions. Additionally, Compound 3 also displays reversible adsorption of molecular iodine.

**Keywords:** Metal Organic, Metal Perturbed, Crystal Analysis and Dicarboxylic Acids.

**Catalytic Enantioselective Construction of Vicinal all-Carbon Quaternary Stereogenic Centers:  
Total Synthesis of Dimeric Cyclotryptamine Alkaloids (+) - and (-) – Folicanthine**

**Santanu Ghosh**

**Supervisor: Dr. Alakesh Bisai**

**Department of Chemistry**

**Accession No.: T00019**

This thesis is divided into three chapters viz chapters I, II, and III. Chapter I "Synthetic Approaches to the Dimeric Cyclotryptamine Alkaloids: The Literature Overview" is a review on asymmetric construction of vicinal all-carbon quaternary stereogenic centers and its importance in the syntheses of the dimeric cyclotryptamine alkaloids. Chapter II entitled "Catalytic Enantioselective Decarboxylative Allylation via a Dynamic Kinetic Asymmetric Transformation (DYKAT)" deals with the asymmetric synthetic approaches to (+)- and (-)-folicanthine 1a via a key enantioselective Pd-catalyzed decarboxylative allylation strategy. We envisioned that, total synthesis of folicanthine (-)-1a can be achieved starting from C2-symmetric (S,S)-2a, which in turn can be synthesized from (R)-3a via synthetic elaboration. We envisioned that (R)-3a can be synthesized from an enantioselective decarboxylative allylation of allylester type ( $\pm$ )-4 involving a DYKAT. Compound ( $\pm$ )-4 can be obtained from oxidative coupling of ( $\pm$ )-7. Towards this, we have also developed oxidative coupling strategy to synthesize various 2-oxindoles of type ( $\pm$ )-4 starting from ( $\pm$ )-7 and 8 or, alternatively, a one-pot alkylation of 9 followed by oxidative coupling. In addition, the compound of the type (R)-3a can also be obtained from allylcarbonate 5 via a DYKAT as shown in scheme 1. Scheme 1: First generation retrosynthetic analysis of (-)-folicantine via a proposed DYKAT. Utilizing a strategy shown in Scheme 1, we have synthesized enantioenriched product of type (R)-3 in up to 98% ee with excellent yields. Finally, (R)-3a was converted to (S,S)-2a following synthetic elaboration via a key diastereoselective allylation using allylbromide and a base, which is the advanced intermediate for total synthesis of (-)-folicanthine 1a. Chapter III entitled "Catalytic Enantioselective Construction of Vicinal All-Carbon Quaternary Stereocenters: Total Synthesis of (+)- and (-)-Folicanthine" deals with sequential construction of vicinal all-carbon quaternary stereocenters and its application in total synthesis of (+)- and (-)-folicanthine 1a. We envisioned that racemic and meso-diastereomers of bisesters 12 of any dr could effectively undergo Pd-catalyzed enantioselective double decarboxylative allylations to afford a major (S,S)-2a over meso-2a (Scheme 2) in the presence of (S,S)-L-Pd(0). The major obstacles in realizing this transformation include the presence of pre-existing stereocentres in the substrates that may interfere with inherent catalyst selectivity and the potential for developing mismatched catalyst–substrate interactions that can negatively

impact the chemical yield. This situation is even much more complex than a DYKAT discussed in chapter II. Scheme 2: Second generation retrosynthetic analysis of ( )-folicantine. We have synthesized C2-symmetric products (S,S)-2a over the meso-2a with exceptional levels of diastereo- (up to 17:1 dr) and enantioselectivities (up to 99% ee) as per Scheme 2. Interestingly, the double enantioselective decarboxylative allylation of a 1:1 mixture of bisesters 12 and ester-carbonate ( $\pm$ )-13 also proceeds with similar efficiencies. Utilizing aforementioned strategy, we have completed total synthesis of ( )-folicanthine (1a). Later, we also completed total synthesis of ( )-folicanthine (ent-1a) from (R, R)-2a.

**Keywords:** Catalytic Enantioselective, Dimeric Cyclotryptamine Alkaloids, Asymmetric Construction and Carbon Quaternary Stereogenic.

**Application of Snar in the Synthesis of Unsymmetrical Diaryl Chalcogenides and Novel  
Nitro-Biaryl-Ols: Transformation of Nitro-Biaryl-Ols into Indoles, Carbazoles and  
Dibenzofurans**

**Amit Kumar**

**Supervisor: Dr. Sangit Kumar**

**Department of Chemistry**

**Accession No.: T00017**

This thesis reports the synthesis of one of the important class of organochalcogen compounds known as “diphenyl chalcogenides” and synthesis of nitro-biaryl-ols by direct formation of carbon-carbon bonds. This class of chalcogenide compounds have significant role in organic synthesis, biological, polymer and material science. Existing methods for the synthesis of diphenyl chalcogenides suffer from moderate yield and narrow substrate scope. Here we have disclosed the potassium tert-butoxide mediated synthesis of unsymmetrical diphenylsulphides and unsymmetrical diphenylselenides by the reaction of diphenyldisulphide/selenide with bromoarenes. Optimized reaction conditions applied for the synthesis of unsymmetrical diphenyl ethers also. We have also developed a simple and convenient approach for the synthesis of unsymmetrical diaryl chalcogenides (Te, Se and S) by copper catalyzed cross-coupling reaction of organoboronic acid with diaryl dichalcogenide in ethanol using NaBH<sub>4</sub> in air or oxygen. The present methodology is highly practical for the synthesis of unsymmetrical diaryl tellurides with various functionalities such as -NO<sub>2</sub>, -F, -Br and -COOH that have been obtained in good to excellent yields. Methodology is also effective for the synthesis of unsymmetrical diaryl selenides and sulfides. Moreover, symmetrical diaryl selenides have also been obtained from arylboronic acids using elemental selenium powder under optimized reaction conditions. Phenols are common and important structural motifs in natural products, pharmaceuticals and agrochemicals. Therefore, direct arylation of phenol attracts more attention. In this light a series of electron withdrawing or donating substituted phenols were chemoselectively arylated with variously substituted bromo nitroarenes using KOtBu at room temperature via SNAr pathway. Synthesis of natural alkaloids (carbazoles), dibenzofurans, and biarylindole has been achieved from synthesized nitrobiarylols. We have also developed an alternative approach to 4-nitration of dibenzofuran: sodium nitrite mediated synthesis of 4-nitrodibenzofurans from amino-biaryl-ols. Further functionalization of the obtained 4-nitro-dibenzofurans has been carried to obtain 3-nitro-terphenyl-2-ol, novel benzofuro-indoles, and amino-dibenzofurans. The mechanistic understanding on double functionalization of 2'-amino-biphenyl-2-ols suggests that reaction proceeds by a combination of nitration of phenol ring and Sandmeyer reaction for dibenzofuran ring formation.

**Keywords:** Organo-Chalcogenides, Organo-Boronic Acid, Cu-Catalyst, Carbon-Carboncoupling Reaction, Nitro-Biaryl-Ols and 4-Nitro-Dibenzofurans.

**Molecular Recognition of Environmental Analytes by Modulating the Electron Deficiency  
of Receptors**

**Masood Ayoub Kaloo**

**Supervisor: Dr. Jeyaraman Sankar**

**Department of Chemistry**

**Accession No.: T00016**

Chapter 1: In this chapter, an introduction and brief literature survey of various molecular receptor strategies is presented. The need for the exploration and development of new receptor approaches to characterize analytes in the environment, including CO<sub>2</sub>, HCO<sub>3</sub><sup>-</sup> and NH<sub>3</sub> is highlighted. Chapter 2: This chapter describes details about chemical, reagents and solvents used to synthesize and characterize the receptors, including their recognition properties. Along with this, brief introduction of various instrumental techniques and methods required during the whole work are included. Chapter 3: This chapter reports a new anion receptor design from pi-donor-acceptor ( $\pi$ - DA) charge transfer system, DAMN. Herein, schiff-base derivatives of this amine were synthesized and explored for anion recognition properties. The strategy turned out to be a first receptor approach with polarized N-H bonds in a free NH<sub>2</sub> group, unlike the common amide functionalized system. Structural-tuning of the receptor design was done to fully assess the recognition trends. After establishing the mechanistic aspects, a promising naked-eye detection of ambient CO<sub>2</sub> was demonstrated using this receptor. CO<sub>2</sub> recognition in solution was probed with HCO<sub>3</sub><sup>-</sup> anion formation in presence of fluoride. Interaction of HCO<sub>3</sub><sup>-</sup> with fluoride-activated receptor was found suitable to display signal readout even under ambient conditions. Chapter 4: This chapter demonstrates the DAMN-receptor approach towards the recognition of anions of sodium/potassium salts as a novel attempt to real-time applications in environmental media. A few DAMN derivatives were synthesized and for the first-time a receptor motivated analysis of water soluble HCO<sub>3</sub><sup>-</sup>/CO<sub>3</sub><sup>2-</sup> anion in water, was obtained. Most importantly, an “in-situ” estimation and multi-modal(emission, panchromatic UV-Vis-NIR) read-out signal transduction was obtained by tuning of receptor framework. The anion-receptor exploration was further extended to test its applicability for various water samples from several environmental water bodies across India. In addition, upon selective modulation of design for HCO<sub>3</sub><sup>-</sup>/CO<sub>3</sub><sup>2-</sup>, a novel address towards agricultural soil alkaline-sodicity has been demonstrated. This method provides a tool to assess sodicity hazard in irrigation supplies and/or agricultural soils. Chapter 5: In this chapter, heterogeneous detection of ammonia in both aqueous and vapour phases has been presented. Pentafluoro-BODIPY dye was explored as a receptor with a strong potential for bimodal ammonia monitoring at ppb levels. The highly sensitive and specific chemodosimetric strategy by aromatic nucleophilic substitution reaction of BODIPY core at 3- and 5- positions

was tailored by fine-tuning of electronic nature of the aryl groups at meso-position. For the first-time, a dual-channel and visible (chromogenic and fluorogenic) signal transduction for ammonia monitoring at the source has been presented. Owing to the solid-phase recognition behaviour, a portable dualchannel test-strip based platform for “in-situ” detection was developed and demonstrated for NH<sub>3</sub> detection. In addition to the chemodosimetric strategy, strongly polarized N-H bond in the dinitrophenyl-DAMN receptor was utilized for selective colorimetric ammonia vapour detection in both solution and solid phase of the receptor via proton transfer signalling mechanism. Chapter 6: This chapter is based on recognition and discrimination of anions by two advanced receptor approaches. In the first approach, ammonia-driven chemodosimetric product (BODIPY-NH<sub>2</sub>) was synthesized. Structural investigations showed existence of intramolecular hydrogen bonding between free -NH<sub>2</sub> moiety and BF<sub>2</sub>. This became a new basis for highly sensitive and selective distinction of F<sup>-</sup> and CN<sup>-</sup> via solvent tuning. In the second approach, sensitive anion recognition was obtained for the first time, through selective modulation of electron-deficient perylenebisimides. A fascinating signal transduction across whole spectral region (UV-Vis-NIR) was observed through single electron transfer from anion to the PBI. Incorporation of electron-rich silyl-acetylene moiety in direct electronic communication with PBI core offered a dual-channel binding. This observation suggested a SET process between F<sup>-</sup>/CN<sup>-</sup> and PBI core, and Si-F bond based chemodosimetry for fluoride anion. These results demonstrate a highly promising fluoride and cyanide discrimination. Chapter 7: This chapter summarizes the salient features of the whole thesis. It also briefly highlights some of the applications, other than environmental perspectives.

**Keywords:** Electron Deficiency, Molecular Receptor, Ammonia-Driven Chemodosimetric, Fluoride Anion and DAMN-Receptor.

**Design and Synthesis of Novel Enaldiazo Esters: Cyclopropanation and Benzannulations  
via Enalcarbenoids**

**Kuldeep Singh Rathore**

**Supervisor: Dr. Sreenivas Katukojvala**

**Department of Chemistry**

**Accession No.: T00015**

Despite the incredible growth in diazo chemistry, there is still an opportunity to broaden the horizon for diazo compounds due to their synthetic utility in various reaction such as cyclopropanations, annulations, insertions, etc. This thesis involves the design, synthesis and study of new reactivity of novel enaldiazo esters. In the first chapter, a novel class of enaldiazo esters synthesis was contemplated. These diacceptor enaldiazo compounds hold an electron withdrawing group (-COOR) together with a four carbon moiety embedded with an olefinic and aldehyde functionality. In the second chapter, these new diazo compounds were successfully utilized in an efficient Rh(II) carbozoles. The reaction proceeds through a regioselective C-3 functionalization of indole with rhodium enalcarbenoids followed by a Bronsted acid assisted cyclo-dehydration. The reaction was extended to a two-fold benzannulation of NH-pyrroles to 4,8-disubstituted carbazoles. With this methodology, analogs of hepatitis C virus replication inhibitor and secreted phospholipases A2 (sPLA2) inhibitor were synthesized. The third Chapter involves, an efficient Rh(II) acetate catalyzed highly diastereoselective cyclopropanation of styrenes with enaldiazo esters (up to > 95:5 dr). The reaction is proposed to involve di acceptor electrophilic rhodium enalcarbenoids and offers the direct synthesis of enal-cyclopropanes with an all carbon  $\gamma$ -quaternary stereocenter. In the fourth chapter, a novel Rh(II) carboxylate and Bronsted acid catalyzed tandem reaction of enaldiazo carbonyl compounds with oxindoles was developed. The reaction allowed direct regioselective synthesis of valuable 1-hydroxy-carbazole-2-carboxylates and 1-hydroxy-2aroyl-carbazoles. Based on the mechanistic studies, the tandem reaction is proposed to involve insertion of rhodium enalcarbenoid into oxindole sp<sup>2</sup> c-o bond; an unprecedented intermolecular carbonyl conjugate addition to enals by a semipinacol rearrangement of thus obtained  $\gamma$ -hydroxy enals and concomitant benzannulation. The methodology extended to the synthesis of chiral menthyl 1-hydroxycarbazole 2-carboxylates. Chapter five (appendix) involves synthesis of benzo-fused oxepine like derivatives from 2-(cyclopropenyl) ethanols via trimethylenemethane (TMM) rearrangement upon oxidation with Dess-Martin-Periodinane (DMP).

**Keywords:** Cyclopropanations, Annulations, Insertions, Enaldiazo and Enal Cyclopropanes.

# **Lewis-Basic Heteroatoms in Transition Metal Catalyzed C-H Functionalizations**

**Pawar Govind Goroba**

**Supervisor: Dr. ManmohanKapur**

**Department of Chemistry**

**Accession No.: T00012**

Although chemists have shown that almost any molecule can be synthesized, provided the appropriate amount of recourse are at hand, there is yet a considerable amount of innovation to be made in terms of synthetic efficacy. Today, the development of new methods and synthetic strategies in which C-H bonds can be activated and used as the most fundamental functional group, represents one of the most exciting and promising areas of research in the field of synthetic organic chemistry. For this purpose, during my doctoral studies, we have been interested in developing transition metal- catalyzed regioselective C-H functionalization protocols to make diverse C-C and C-X bonds, in this context, during my doctoral studies, we have developed new regioselective Lewis – basic heteroatom guided and directed, transition metal catalyzed C-H functionalizations. This thesis highlights the new advances in this area, Chapter 1. The Significance of C-H functionalization in organic synthesis and a brief history of C-H activation are presented. The importance of Lewis-basic heteroatoms in C-H activation and relevant achievement in the field are presented as well. Chapter 2. Presented herein is the study of Lewis-basic heteroatom directed C-H nitration of anilines. The literature examples for directed sp<sup>2</sup> C-H functionalization are discussed in detail along with the significance of our work. Chapter 3. This chapter provides the detailed mechanistic studies in the heteroatom guided palladium-catalyzed C-H functionalization of electron- rich cyclic alkenes and their application in natural product synthesis.

**Keywords:** Metal Catalyzed, Heteroatom, Metal Catalyzed and C-H nitration.

**Experimental and Theoretical Investigation of Intermolecular Interactions  
in Molecular Crystals**

**Piyush Panini**

**Supervisor: Dr. Deepak Chopra**

**Department of Chemistry**

**Accession No.: T00010**

This thesis reports the detailed crystallographic and theoretical investigation on the nature and role of different intermolecular interactions which is responsible for assembly of the molecules in the solid state. This includes ion-ion, ion-dipole, dipole-dipole, ion/dipole-induced dipole and instantaneous dipole-induced dipole interactions. These interactions have been explored and studied in the formation of polymorphs in case of an organic salt, namely the derivatives of crystalline dihydropyrimidinium hydrochlorides. In the realm of intermolecular interactions, strong H-bonds, namely N/O-H $\cdots$ N/O have been well understood. On the contrary, intermolecular interactions involving organic fluorine (the “C-F group”), namely C-H $\cdots$ F, C-F $\cdots$ F-C and C-F(l.p) $\cdots$  $\pi$  have always been questioned and its existence is still a subject of debate. Hence investigation of the ability of organic fluorine in the participation of different intermolecular interactions is a prime focus in the crystal chemistry of such compounds. In this regard, a large library of molecule containing the organic fluorine group have been synthesized, crystallized and investigated for polymorphism and a systematic exploration of the participation of the fluorine atom in the formation of different supramolecular motifs have been studied experimentally and theoretically. These interactions are explored both in the presence and absence of a strong hydrogen bond. It is a significant discovery that we have observed the presence of various short contacts with organic fluorine (of the C-H $\cdots$ F type) in the presence of conventional H-bonds in crystals. These are not a consequence of crystal packing and have implications in the generation of polymorphs in the solid state. Analysis from PIXEL method and QTAIM approach, it is now unequivocally established that such short contacts to organic fluorine are “true” hydrogen bonds. Organic fluorine was observed to form different “reoccurring” structural motifs (or supramolecular synthons) like chains, dimer, chain of dimer etc in the crystal packing utilizing interactions involving C(sp<sub>2</sub>)/(sp<sub>3</sub>)-F group. It was observed that the highest stabilized molecular motifs primarily consist of C(sp<sub>2</sub>)-H $\cdots$ F-C(sp<sub>2</sub>) H bond in preference to C(sp<sub>2</sub>)-H $\cdots$ F-C(sp<sub>3</sub>) H bond in the crystal. The C(sp<sub>2</sub>)/(sp<sub>3</sub>)-F $\cdots$ F-C(sp<sub>2</sub>)/(sp<sub>3</sub>) interactions were observed to exhibit closed shell nature for the entire F $\cdots$ F bond path length and provide local stabilization (indicates formation of bond) similar to the case of weak hydrogen bonds in crystals.

**Keywords:** Crystallographic, Intermolecular, Interactions and Solids.

**Synthesis, Characterization & Formulation of Polyaspartamide Based Soft Nanomaterials  
for Biomedical Applications**

**Aashish Sharma**

**Supervisor: Dr. Aasheesh Srivastava**

**Department of Chemistry**

**Accession No.: T00009**

This Thesis reports the synthesis, characterization and formulations of soft nanomaterials for biomedical applications utilizing one of the important class of biocompatible polymers known as “Polyaspartamides”. Polyaspartamides are synthetic polyamides and are amenable to structural variability to result into materials of desired properties with synthetic ease and cost-effectiveness. We wanted to undertake structure tenability of polyaspartamides for in vivo applications. Here we have synthesized the thiolated counter polyelectrolytes (PEs) which upon mixing as aqueous solutions in specific ration produced nanosized polyelectrolyte complexes (PECs) that underwent spontaneous crosslinking through reagent less bio-reducible disulphide formation under ambient conditions. These PECs are stable to variations of pH and electrolyte concentration and proteolytic enzymes and utilized for cytosolic peptide delivery. These thiolated counter PEs were also used in higher concentration to formulate underwater, self curing, and optically transparent adhesives. These adhesives were explored for adhering broken bones and were studied by UTM, rheology, AFM and SEM. These adhesives were found to be biodegradable and remained transparent. Subsequently, we synthesized a series of novel amphiphilic randompolyaspartamides by attachment of 1- propylimidazole pendants and dimethylpropylammonium pendants to introduced well-defined, reversible thermosensitivity at and around physiological conditions ( at 370C and pH = 7.4)in phosphate buffer. The cloud Points (CP) could easily be modulated by varying the ratios of the two pendants. We found that the thermoresponse of these polymers could be readily modulated by multiple stimuli viz. pH and metal-ions, anions, as well as solvent isotope. Thus Prepared cationic amphilic copolymers were utilized as synthetic antimicrobial polypeptides (SAMPs) . The antimicrobial activity of these prepared SAMPs was evaluated against M. smegmatis and E.coli while biocompatibility (cytotoxicity to mammalian cells) was studied against lung cancer cell line (A549) and RBCs by MTT assay and haemolytic assay respectively. These studies exhibited that prepared SAMPs exhibit highly selective and potent inhibition of Mycobacterium (MIC<20ug/ml) over E. coli or mammalian cells. Growth curve studies of Mycobacterium in presence suggested that SAMPs can reduce the high bacterial load within ~4 h. These SAMPs are selectively internalized by Mycobacterium and mammalian cells (celllipopolysaccharide layer) over E. coli as

investigated by confocal microscopy. The antimycobacterial activity of the SAMPs against *Mycobacterium* is ascribed to their interaction with the unprotected genomic DNA of bacteria as confirmed by gel retardation assay. Finally we prepared thiolated SAMP possessing antimycobacterial activity and obtained nanogels by simply heating the solution of thiolated SAMP in phosphate buffer (1M,pH 7.4) at ~40 0 C.

**Keywords:** Synthesis, Characterization, Antimycobacterial, Coliormammalian Cell, Polyaspartamide and Polyelectrolyte.

**Self-assembling derivatives of L-alanine and L-phenylalanine for biomedical Applications**

**Amarendar Reddy M**

**Supervisor: Dr. Aasheesh Srivastava**

**Department of Chemistry**

**Accession No.: T00008**

This thesis reports the design and applications of molecularly concise self assembling amino acid derivatives based on an l-alanine and Lphenylalanine. A key feature of derivatives prepared in this thesis is the utilization of rotationally- flexible aromatic residues such as naphthyl, phenyl and carboxybenzyl as the N-protecting groups for alanine and phenylalanine . We hypothesized that the rotational flexibility inherent in these molecules will allow formation of versatile gelators. This hypothesis is tesyed through preparation of different derivatives. The results obtained from these investigation have been divided in to five chapters. The First Chapter gives a brief review on the self assembly of peptides which includes (i) different definitions and classification of gels (ii) short introduction to low molecular weight peptide hydrogels (iii) N-terminally conjugated (Naphthyl, Fmoc, pyrenyl) dipeptide hydrogelators (iv) N-terminally conjugated (Naphthyl, Fmoc, pyrenyl) single amino acid hydrogelators (v) bolaform peptide gelators (vi) peptide metallhydrogels (vii) enzyme triggered hydrogelation of small peptides (viii) biomedical applications of peptide hydrogels. The second chapter part A describes preparation of different bolaform homodiamides of N- protected alanines that exhibit efficient gelation of a broad variety of solvents by thermal process as well as by simplebath sonication. Phase-selective gelation, even in the presence of salts in the aqueous layer, could be observed- both by thermal processing as well as by bath-sonication at room temperature. The ability to achieve phase-selective gelation by sonication at ambient conditions opens new avenues for spill-control applications. Entrapment of tetracylinc and its papin-assosted relase was demonstrated to exemplify the potential utility of these gels in durg-delivery applications.....

**Keywords:** Amino Acid, Bolaform Homodiamide, Lphenylalanine, Naphthyl, Phenyl, Carboxybenzyl and Drug Delivery.

**Self- assembled Polynuclear Cages Derived from Polytopic Dihydrazide Ligands:  
Syantheses, Structures and Magnetic Properties**

**Amit Adhikary**

**Supervisor: Dr. Sanjit Konar**

**Department of Chemistry**

**Accession No.: T00007**

Polynuclear cages draw a special attention of recent research because of their diverse application particularly in the area of molecular magnetism. Molecular self -assembly is a powerful synthetic tool for polynuclear cages. Polymetallic cages having specific geometrical shape is symmetry-related subunits and can be developed when designed ligands are considered to metal ions according to their coordination requirement. Various factors are considered to be critical to self-assembly including reaction pH, metal ion identity, mole ratio and counter anions. As the number of coordination sites and thereby number of coordinating metal centers increase, the self-assembly strategies of pre-mediated polynuclear structural arrays become exponentially complied because of chemical as well as thermodynamical reasons. Chapter 1 describes brief introduction of the thesis including concepts on molecular magnetism, description on the design of ditopic, tetratopic hydrazide based ligands for molecular self-assembly of various grid and helicates. Literature study on different types of grid and helicate complexes, their synthesis, structures, mechanism of their formation, and magnetic properties are illustrated here. Chapter 2 describes the formation of different copper cages complexes by varying pH. The designed ligand bis[(2-pyridyl)methylene] pyridine, 2,6 dicarbohydrazone ( $H_2L$ ) on reaction with cupric perchlorate in  $cH_3CN/MeOH$  (1:1) at different pH generates three complexes having molecular formulae  $\{[Cu_6L_2(ClO_4)_4(\mu-ClO_4)_2(H_2O)_9](ClO_4)_2.8H_2O\}_n$  (1),  $[Cu_6L_2Cl_6(\mu_2-Cl)_2(H_2O)_2].3H_2O$  (2) and  $[Cu_9L_6](ClO_4)_6.6H_2O.2CH_3CN.CH_3OH$  (3) by self-assembly process. Their transformation from one cage to another has also been studied at mild reaction conditions. Magnetic study of complex 1 shows weak antiferromagnetic interaction at low temperature whereas complexes 2 and 3 show ferromagnetic and antiferromagnetic interactions. In addition, magneto structural correlations have been established.....

**Keywords:** Syanthesis, Crystal Structure, Magneto Structural, Antiferromagnetic Interaction and Polynuclear Cage.

**Copper Catalyzed Synthesis of Benzoisothia-zolones, Selenophenols and KOtBu Mediated  
Synthesis of Phenanthridinones, Biaryls and Isoindolinones**

**Bhagat Singh Bhakuni**

**Supervisor: Dr. Sangit Kumar**

**Department of Chemistry**

**Accession No.: T00004**

The Present Thesis describes developments of novel methodologis towards the synthesis of pharmacologically and naturally important organochalcogen comounds and KOtBu mediated C-C coupling for the contruction of phenanthridinone, Isoindolinones and biphenyls. Synthesis of various benzoisothiazolone and selenophenols compounds (Bhakuni et.al TL 2012, 53, 1354, ) is organo sulphur compounds found as core in many drugs like ziprasidone ( Pfizer drug) and also found in artificial sweetener like properties (Bhakuni et.al.2014 under communication) Itami et.al. in 2008 initiated a novel application KOtBu in C-C coupling reaction in intermolecular reaction. In 2010 Shi and Kwong independently report C-C coupling of benzene with aryl benzene using phenathroline and DMEDA respectively as catalyst. These literature reports inspired me to explore the field of C-H functionalization through base mediated approach. Phenanthridinone are the core molecule found in various naturally occurring alkaloids. Palladium catalysed synthetic hydrogen. Methodology ( Bhakuni et al., Ol. 2012, 14, 2838, and Bhakuni et.al.,Org Syn,2013 90, 164,) explored different electron donating and electron withdrawing rection gave seven member dibenzazepinones regioselectively. EPR studies had been done to characterise the involvement of radical. This project was followed up by AMVN initiated synthesis of biphenyls and heterobiphenyls (Bhakuni et al., NJC, 2014, 38,827). After completion of biphenyl synthesis, KOtBu- Mediated synthesis of Dimethylisoindolin-1-ones and Dimethyl-5-phenylisoindolin-1-ones (Bhakuni et al., JOC, 201, 79, 2944) which coupled selectively shows tert-sp<sup>3</sup> C-H over primary sp<sup>3</sup> C-H. Substrate like ferrocene also works fine under this reaction condition. Isoindolinones are found as core in most of natural products and pharmaceutical drugs. Working on the organic synthesis and developing new efficient synthetic strategies that can be utilized to synthesize compounds that have biological activity and can be used as drugs to cure fatal disease. Further, better understanding of organic chemistry can enable us to synthesize compounds having novel function like biomolecules for pharmaceutical applications.

**Keywords:** Drug Design, Phenanthridinone, Isoindolinones and Biphenyls.

**Synthetic Studies towards Organoselenium Heterocyclic Compounds: Isoselenazolones. Their Catalytic Applications in Bromination Reaction and as GPx Mimics**

**Shah Jaimin Balkrishna**

**Supervisor: Dr. Sangit Kumar**

**Department of Chemistry**

**Accession No.: T00003**

This thesis reports the synthesis and applications of one of the important class of organoselenium heterocyclic compounds known as “Isoselenazolones”. This class of heterocyclic compounds contain intramolecular Se-N bond. Ebselen (PZ 51, 2-phenyl-1,2- benzoisoselenazol-3-(2H)-one) is one such compound with promising antioxidant activity and biological non-toxicity (LD<sub>50</sub> = 6.8 g/kg). It is in the final phase of clinical trials for the treatment against stroke. Existing methods for the synthesis of isoselenazolones suffer from moderate yield and narrow substrate scope. Here we have disclosed the first catalytic route for the synthesis of wide range of isoselenazolones from corresponding 2- halobenzamides. Application of synthesized isoselenazolones is studied as catalyst for the activation of bromine to accomplish bromolactonization of alkenoic acids, bromoesterification of alkenes and oxidation of alcohols. Detailed mechanistic investigation on the isoselenazolone-catalyzed bromination reaction is carried out by <sup>77</sup>Se NMR spectroscopic and ES-MS studies and it suggests that oxidative addition of bromine to the isoselenazolone gives the isoselenazolone (IV) dibromide, which is responsible for the activation of bromine under mild conditions. Also, we could synthesize diversely substituted chiral isoselenazolones and employed them as catalysts for the enantioselective bromolactonization reaction. We could also study the reaction of benzamide ringsubstituted isoselenazolones with PhSH by <sup>77</sup>Se NMR. Ortho-Methyl isoselenazolone with quinine moiety reacted with PhSH to yield a selenol which mimics the selenoenzyme glutathione peroxidase (GPx), as it also contains selenol functionality in its active site. <sup>77</sup>Se NMR and DFT studies suggest that the presence of an ortho-methyl group together with the presence of a tert-N atom is crucial for the generation of selenol. Due to facile formation of selenol, this quinine derived isoselenazolone showed a high rate of oxidation of PhSH with H<sub>2</sub>O<sub>2</sub> ( $0.33 \pm 0.002 \times 103 \mu\text{M}.\text{min}^{-1}$ ) which is ~103-folds more than the ebselen drug. Also, this isoselenazolone is less toxic than ebselen with respect to the growth of yeast cells. Also we could develop two organochalcogen colorimetric probes which possess high specificity for thiophenols, cysteine and glutathione in aqueous medium. One of isoselenazolone probe could behave in a reversible manner for more than 10 cycles. Reasons behind the characteristic color change in the presence of thiol have been investigated. We have also developed simple and economical copper catalyzed method for the synthesis of 2-hydroxybenzamides from corresponding 2-halobenzamides in water. It is important to note that this is the first report of hydroxylation in neat water.

**Keywords:** Organoselenium Heterocyclic, Isoselenazolone, Heterocyclic and Thiophenols.

# **Noval Mono-bay Substituted Perylene Bisimides: Synthesis, Structure and Properties**

**Ruchika Mishra**

**Supervisor: Dr. J. Shankar**

**Department of Chemistry**

**Accession No.: T00002**

This thesis describes the development of a new class of chromophores known as mono-bay substituted perylenebisimides and their structure-property correlation has been investigated. Perylenebisimide (PBI) derivatives containing various phenylalkynyl substituents at a single bay position have been synthesized by Sonogashira coupling. All the dyads undergo two reversible reductions thus demonstrating their structural and electrochemical rigidity. The most interesting spectral signatures were exhibited by a PBI having a strong electron donor 4-Ethynyl-N,Ndimethylaniline moiety. Twisted intramolecular charge transfer process that is related to the rotational motion is also demonstrated. The first solid state structure of the phenyl derivative is found to have a flat PBI core, without any noticeable steric constraints from the substituents, as predicted. An exciting and unprecedented formation of a new class of dyes named azepinoperylenebisimides by a simple and metal-free approach is disclosed in this work. Counterintuitive nucleophilic participation of DBU in addition to alkyne cyclization was observed to form the seven-membered hetero-cyclic residue in the sterically crowded bay area of PBI. Their absorption signatures cover whole visible range and demonstrate an interesting panchromatic absorption. This new member of core-expanded PBI family has been unambiguously characterized by single crystal x-ray diffraction. The delocalization within the azepine ring shows a weakened anti-aromatic contribution. A D- $\pi$ -A dyad containing a metallated porphyrin (D) and perylenebisimide (A) linked via an alkynyl bridge for effective conjugation was synthesized in moderate yield. The interesting photophysical properties revealed an excellent coupling of both the chromophores displaying absorption from visible to NIR region. An imidazole derivative of mono-bay substituted PBI has been demonstrated to specifically bind the epidermal cells of third instar larvae of *Drosophila Melanogaster*.

**Keywords:** Chromophore, Metallated Porphyrin, Perylenebisimide and Ndimethylaniline.

**Study of Conformational Dynamics and Molecular Interactions of Self- Organized Systems  
Using Spectroscopic Approaches**

**Uttam Anand**

**Supervisor: Dr. Saptarshi Mukherjee**

**Department of Chemistry**

**Accession No.: T00001**

This Thesis reports the conformational dynamics of Proteins when subjected to several chemical denaturants and the counter effects of temperature and urea on the microviscosities and microheterogeneity of a Pluronic micelle, F127. For this purpose we have used several spectroscopic approaches mainly based on steady state, picosecond time-resolved and Circular Dichroism (CD) techniques. The Addition of an anionic surfactant , sodium dodecyl sulphate (SDS) to the circulatory protein, Human Serum Albumin (HSA) was shown to occur via a sequential manner; the binding of SDS to HSA proceeds via three distinct stages followed by a saturation phase. The behaviour of SDS towards the native and reduced states of HSA were found to be different and also upon reduction by Dithiothreitol (DTT), the reduced state was not molyen-globule like. the binding of the antibiotic drug, Tetracycline (TC) to three proteins HSA, its homologue Bovine Serum Albumin (BSA) and Lysozyme quenches the intrinsic fluorescence (from the tryptophan amino acid residue (S) of the Proteins and the mechanism of quenching was proved to be mainly static in nature. The thermodynamic parameters as estimated from the Stern-Volmer and modified Stern- Volmer plots suggest that the binding of TC to the Proteins is rather Enthalpy and not Entropy driven. PH induced conformational changes of BSA in the presence of another drug, Ciprofloxacin (CpH) established that the binding of the drug to the protein and also the mechanism of quenching was a function of pH. CD and Dynamic Light Scattering (DLS) data confirm that CpH is causing structural changes at all the three pH values. The protein BSA when subjected to unfolding by the chaotrope, Guanidine Hydrochloride and the surfactant, SDS loses a significant portion of its secondary structure. However, the protein regains almost all its native- like conformation when subjected to manifold dilution and treatment with the cyclic macromolecule  $\beta$ -Cyclodextrin. Finally, the three regions of the Pluronic micelle, F127 were investigated using three different fluorophores (depending on their relative polarities ) by Red Edge Excitation Shift (REES) and monitored using different concentrations of urea at varying temperatures. It was substantiated that for F127, the effect of urea and temperature exhibited counter effects in terms of microviscosity and microheterogeneity.

**Keywords:** Conformational Dynamics,  $\beta$ -Cyclodextrin, Molecular, Microviscosity and Microheterogeneity.

**Department of Physics**

# **Role of electron correlation and cation arrangements in perovskite derived transition metal oxides**

**Baddipalli Harinathreddy**

**Supervisor: Dr. Ravi Shankar Singh**

**DEPARTMENT OF PHYSICS**

**Accession No.: T00147**

## **Abstract**

Transition metal oxides are known for their broad spectrum of unusual physical properties that originate from the collective motion of valence electrons of the constituent transition metal ions. Studying the interplay of the two types of transition metal ions with different degrees of electron correlation could be an attractive way to explore several unusual ground state properties. The effects of electron correlation are extremely important in materials with open d and f electron shells, where electrons are confined in narrow orbitals. Electronic structures of these narrow orbital systems are difficult to describe due to the simultaneous presence of strong electron correlation ( $U$ ) strength and sizable hopping interaction strength ( $t$ ), while large  $U$  leads to the formation of local magnetic moments and sizable  $t$  leads to the formation of delocalized bands. Thus, the simultaneous presence of these two opposing tendencies gives rise to the wide and often exotic spectrum of physical and chemical properties.

The perovskite derived A-site ordered quadruple perovskite and B-site ordered/disordered double perovskites offer such a possibility. The interplay between spin-orbit coupling (SOC), electron correlation ( $U$ ) and crystal field ( $\Delta$ ) effects in 4d and 5d transition metal oxides (TMOs) has been focused due to the most fascinating challenges in modern solid-state physics, such as heavy fermionic state in quadruple perovskites, novel  $J_{\text{eff}} = \frac{1}{2}$  states in iridates and narrow bandgap semiconducting to metallic behaviour in alkaline earth ternary palladates. The role of electron correlation and cation arrangements in perovskite derived TMOs and how this affects the physical properties and the electronic structure, are studied using photoemission spectroscopy. In 4d and 5d TMOs, traditional viewpoint suggests that the larger spread of atomic wavefunctions leads to a smaller local repulsion and a larger overlap between neighbouring atomic orbitals, which cooperate to suppress strong correlation effects. Indeed, simple oxides like  $\text{RuO}_2$ ,  $\text{IrO}_2$  are good metals. This traditional picture has been challenged by recent work on iridium-based complex oxides, which shows that the large SOC in Ir can split the  $t_{2g}$  crystal field levels, yielding a reduced bandwidth for effective  $J_{\text{eff}} = 1/2$  electrons and the re-emergence of strong electron correlation.

# **Terahertz Electrodynamics of Correlated Electrons in Transition Metal Oxides**

**K. Santhosh Kumar**

**Supervisor: Prof. Dhanvir Singh Rana**

**DEPARTMENT OF PHYSICS**

**Accession No.: T00146**

## **Abstract**

In strongly correlated electron materials, the electron-electron Coulomb repulsion, spin-orbit coupling and kinetic energies are of the typically same order and competition between these energetics determines the physical properties of the materials. Study of these materials has been continuously inspiring the researchers by emergence of new quantum phases that revolutionizing the condensed matter physics. The fundamental physics of these materials is governed by the combined influence of electron-electron interaction and spin-orbit coupling which are the two central areas in quantum material research. In 3d TMOs, localized nature of the orbitals leads to strong electron correlation effects which drive the metal-insulator (M-I) transition, superconductivity and unusual magnetism. However, in 5d TMOs, the extended nature of 5d orbitals reduces the electron-electron interaction but simultaneously spin-orbit coupling increases and the various topological semi metallic phases arise due to competition between these two interactions.

In the past three decades, terahertz time domain spectroscopy (THz-TDS) has played an indispensable role in probing these quantum phases in condensed matter systems in the energy range of ~1-12 meV. THz-TDS has explores the physics of free carrier dynamics, charge/spin density waves, superconducting gap, optical phonons, polarons, polariton, Josephson plasmons, magnons, magnetic monopoles, and electromagnons, *etc* adequately. This thesis mainly focus on the carrier dynamics of M-I transition in nickelates and in hole-doped orthoferrites probed using THz-TDS. The present study on M-I transition has addressed two open questions in the  $\text{RNiO}_3$  family, 1) how the interactions evolve to drive the M-I transition and what is the signature of M-I transition, 2) the conductive dynamics of electrons in the phase separated state of nickelates. Also, the characteristics of the complex valance skipping charge order transition in hole-doped orthoferrite  $\text{La}_{0.33}\text{Sr}_{0.67}\text{FeO}_3$  is discussed based on the THz optical conductivity dynamics. In addition, the thesis work includes the study of topological semi metallic state in iridates using THz-TDS. In this context, the topological semi metallic phase that arises due to the synergistic influence of spin-orbit coupling and electron-electron interactions which is protected by

the crystalline symmetries in perovskite iridates is discussed. The THz optical response of SrIrO<sub>3</sub> thin films indicate the existence of the high mobility Dirac electrons. This work suggests a procedure to uniquely determine the electronic ground state of topological phases using THz-TDS in terms of conductivity dynamics.

# **Exchange Bias Effect in Complex Magnetic Oxide Systems**

**Prachi Mohanty**

**Supervisor: Dr. R. P. Singh**

**DEPARTMENT OF PHYSICS**

**Accession No.: T00139**

## **Abstract**

The intriguing fundamental and technological aspects of the exchange bias (EB) effect have garnered great interest since the discovery by Meiklejohn and Bean. Exchange bias refers to a unidirectional shift in the magnetic hysteresis loop due to the anisotropy induced across the exchange-coupled ferromagnetic (FM) and antiferro-magnetic (AFM) interfaces after being cooled in an externally applied field ( $H_{FC}$ ). Recent developments on the EB have highlighted its usefulness in several technological applications such as in magnetic recording read heads, thermally assisted magnetic random-access memories, and other spintronic devices. The complex oxide systems are the chemical compounds that contain oxygen and at least two other elements (or oxygen and just one other element with at least two oxidation states). The recent research interest in complex oxide materials are notable for their wide range of magnetic and electronic properties, such as ferromagnetism, ferroelectricity, and high-temperature superconductivity arising from the strongly correlated electrons in d or f orbitals. The possible role of sample-specific disorder, such as oxygen vacancies, roughness, and dislocations arises major challenges in complex oxide systems.

Recently, Dzyaloshinskii-Moriya (D-M) interactions system based on structural inversion asymmetry properties, have been proposed as a possible mechanism responsible to explain the EB in a spin compensated system. In this regard, we report the EB effect in  $Sr_2LnRuO_6$  ( $Ln = Dy, Ho$ , and  $Er$ ) and  $Ba_2ScRuO_6$  compounds. This ruthenium-based double perovskite compounds exhibited the EB effect below their AFM ordering temperatures when they cooled in the presence of a magnetic field. Detailed magnetization measurements indicate that the EB properties may associate with the D-M interactions originated due to the low crystallographic symmetry in these system types.

For the feasibility of room temperature application, it would be worth to study the nearly compensated ferrimagnetic materials having transitions higher than the room temperature to explore the EB (such as in  $Mn_{3-x}Pt_{3-x}Ga$ ). A small lack of compensation, which is formed as a consequence of intrinsic antisite disorder originates the giant EB effects in these systems and indeed provides a novel approach to design new materials with a large EB. In this context, the nearly compensated "314-type" ferrimagnetic systems ( $Sr_3YCo_4O_{10.5}$ ) with ferrimagnetic transition above room temperature are interesting

material systems to search for a magnetically compensated material to observe the EB. The coexistence of nearly compensated and ferrimagnetic regions in the layered structure originate the EB in these samples, especially near room temperature when the samples are cooled in the presence of a magnetic field.

Thirdly, an interesting magnetic and magneto-transport properties are presented for the mixed iron and cobalt  $\text{Sr}_4\text{Fe}_3\text{CoO}_{11}$  material. The magnetic structure involves G-type antiferromagnetic ordering of  $\text{Fe}^{4+}/\text{Fe}^{3+}$  ions associated with the appearance of interesting temperature induced magnetization reversal. The magnetization reversal can be elucidated considering the competition between the weak ferromagnetic (WFM) component due to the canting of  $\text{Fe}^{3+}$  spins and the paramagnetic (PM) behavior of substantial amount of doped  $\text{Co}^{3+}$  ions under the influence of negative internal field due to the AFM interaction. Large EB effect also commences near the Neel temperature ( $T_N$ ) and reaches a maximum value when the sample is cooled in the presence of a magnetic field. This indicates that the antiferromagnetically ordered  $\text{Fe}^{4+}(2)$  moments and the exchange coupling to ferromagnetically ordered spins are somehow involved in the manifestations of the exchange anisotropy.

Lastly, we report the appearance of a significant EB effect for the highly frustrated spinel material  $\text{CoAl}_2\text{O}_4$  and  $\text{CoFeRhO}_4$ . A long-collinear ferrimagnetic order with AFM inter-sublattice exchange interactions appears below the Curie temperature ( $T_C$ ) for  $\text{CoFeRhO}_4$ . The substitution of non-magnetic  $\text{Rh}^{3+}$  ( $4d^6$ ) cations in  $\text{CoFeRhO}_4$  completely dilutes the long-range FM ordering below the magnetic ordering temperatures which possibly has a great influence on the observed exchange anisotropy.  $\text{CoAl}_2\text{O}_4$  shows a large value of frustration parameter as observed from the dc susceptibility measurements. It exhibits the EB effect below  $T_N$  when it is cooled in the presence of a magnetic field. Detailed magnetization measurements indicate that the EB properties in this compound are associated with the frustration present in this material.

# **Designing multifunctional heterostructure for nonlinesr optical response**

**Rajesh Kumar Yadav**

**Supervisor: Dr. K.V. Adarsh**

**DEPARTMENT OF PHYSICS**

**Accession No.: T00137**

## **Abstract**

The advancement of nonlinear optical materials has gained much research interest in recent days due to its extensive applications in laser technology, light generation, quantum photonics, photonic nanodevices, and optical switching. However, the nonlinear optical response of the conventional materials is very weak due to the perturbative nature of light-matter interaction. Therefore, realizing strong nonlinear optical response is a long-standing goal of both fundamental and technological significance because the magnitude of this quantity (nonlinear absorption coefficient) determines the device performance, for example, optical limiting and pulse shaping. The ideal materials for optical limiting applications must have high transmission at low ambient intensity, reduced transmission at high intensity and a large dynamic range at which the device damages (irreversibly) to the limiting input. The primary nonlinear absorption processes that used for optical limiting are multi-photon and excited state absorptions. In this thesis, we report the charge transfer between donor and acceptor materials as a new method to get an unprecedented enhancement of the nonlinear optical response towards the realization of high-performing optical limiters. We implemented this strategy in the various type of heterostructure (HS) such as metalsemiconductor, metal-metal, and semiconductor- semiconductor. The wet chemical technique is employed for the synthesize of three types of HS namely AuNP-reduced graphene oxide/graphene oxide, Sb<sub>2</sub>Se<sub>3</sub>-Au core-shell, and graphene oxide -Sb<sub>2</sub>Se<sub>3</sub> nanowire. Nonlinear absorption (NLA) measurements performed on these HS shows giant enhancement in the NLA in contrast to the week NLA of constituent materials. We have verified our proposed mechanism in both femtosecond and nanosecond pulse width. This mechanism confirmed by ultrafast pump-probe spectroscopy as well as density

functional theory (DFT). Further, this work quantitatively establishes the charge transfer mechanism between donor and acceptor materials for the strong nonlinear absorption. For this, we have developed a five-level/ three-level rate equation model based on the idea of charge transfer and numerically simulated the results. It precisely reproduces the experimental outcome. All previously published five level/three

level models are based on a single molecular species, and the charge transfer occurs between the singlet and triplet states. We have modified our rate equations and introduced intermolecular charge transfer, which reproduces the experimental results. The primary goal of the present thesis is to provide concrete experimental and theoretical calculation on the mechanism of enhancement in nonlinear absorption. The new insights uncovered in our work enable fresh approaches for the development of next-generation optical limiters based on charge transfer induced excited state absorption. The broad applicability of this work is that it provided critical visions on the theoretical modelling and experimental measurement of nonlinear optical effect. For instance, our new mechanism can be even used for other organic and inorganic materials that show only saturable absorption to get strong NLA. At this point, we envision that our current work represents a significant advance in nonlinear optics and opens up new avenues, ranging from fundamental investigations to technology applications. For example, our studies reveal that the charge transfer occurs from AuNP to GO at higher ligand concentration, and the situation gets reversed at low ligand concentration. The excellent agreement between experimental and theoretical results in our work, provide test beds for design guidelines to make HS for enhancing, tuning and modulating the nonlinear optical response. With this idea, we have fabricated liquid cell-based high-performance absorptive optical limiter with important device parameters better than that of the benchmark optical limiters. We have summarized the major outcomes of the thesis in the following section.

**Supervisor: Dr. Dhanvir Singh Rana**

**DEPARTMENT OF PHYSICS**

**Accession No.: T00118**

**Abstract**

The research on the correlated transition metal oxides has gained a huge attention in recent years as they exhibit a wide variety of electronic and magnetic phases based on their tunable complex ground states. In these systems, the correlated electron dynamics on verge of simultaneously active and competitive charge, spin, lattice, and orbital degree of freedom offer a platform where the physical properties of these systems can be modified by the external perturbations such as electric field, magnetic field, pressure, temperature,epitaxial strain,etc. All the exotic properties shown by these materials are mainly controlled by their structural symmetry and, consequently, the disorder and defect also play a crucial role in defining the ground states. The d-orbital physics in presence of defects and/or disorder, therefore, can lead to several anomalous conducting phases and the co-existence of such multiple phases in microscopic scale derives for more complex charge dynamics in a system. Such elusive phases can be explored using terahertz (THz) time-domain spectroscopy.

In this thesis, we have unveiled the exquisite role of quenched disorder, a key control to obtain novel phases and functionalities and effect of which has been elusive so far the complex phase diagram of  $RNiO_3$  ( $R$  = rare-earth ion)perovskites. Here two different nickelates, namely,  $(La_{0.5}Eu_{0.5})NiO_3$  (LENO) and  $NdNiO_3$  (NNO), having same average R-cation size, were investigated. The LENO is the mixture of two very different nickelates ( $LaNiO_3$  and  $EuNiO_3$ ) and contains substantial amount of quenched disorder while NNO lacks such disorder.Comparing the physical properties of these two systems *i.e.*, LENO and NNO, we discovered that the cation-disorder can dramatically evolve new ground states of nickelate thin films, thus driving the system toward the quantum critical limit.This study also depicts the ease with ease with which a variety of electronic phases can be tuned in disordered nickelates and emphasize the need to incorporate quenched disorder as a key control in the phase diagram of nickelates. In next part of thesis, we continued our investigation in another disordered system, *i.e.*,  $(La_{0.5}Eu_{0.5})NiO_3$  (LENO) in which we observed that the complex entanglement between bi-axial epitaxial strain and quenched disorder induces a unique type of anisotropic carrier modulations.The THz time domain spectroscopic investigations on PENO thin films showed a rare co-existence of charge-density-wave (CDW) type excitations and Drude-smith free carries response in same orthorhombic phase but along two orthogonal in-plane axes. This study unveiled a unique dependency of CDW excitations on preferential crystallographic orientation which opens up promising technological aspects of the nickelate thin films.

In remaining part of the thesis, we investigated the control of ionic defects (including oxygen defects) over the charge-ordered ground state of another nickelate member, *i.e.*,  $\text{SmNiO}_3$  (SNO) which lacks any finite cation-disorder. With the help of detailed structural and d.c.electrical transport measurements we found that the tensile strained  $\text{SmNiO}_3$  thin films show unique control of oxygen defect ( oxygen vacancy) formation with variation of film thickness. The THz spectroscopic measurements of these SNO thin films exhibit the two resonance absorption peaks of ‘pinned’ and ‘bound’ CDW modes in THz optical conductivity spectra. Moreover, we have observed a unique dependency of CDW instability upon variation of film thickness which is directly interconnected with the defect density This study provide understanding of the complex evolution of CDW type instability in charge-ordered nickelates. In final section of the thesis, we explored the novel effects of cation-diorder in ruthenate thin films via introducing aliovalent chemical disorder in Ce-doped  $\text{Ca}_{1-x}\text{Ce}_x\text{RuO}_3$  ( $0 \leq x \leq 0.1$ ) thin films. The de transport, Hall effect, and THz spectroscopic measurements suggest that the doping modulated physical properties of these films entirely depend on Ce-Content.These new phases highlight the novel subtleties abd versatility of the systems lying near the quantum critical point.

**Keywords:** Transition metal oxides, Rare-earth nickelates, Insulator-metal transition, Quenched disorder, Oxygen defects, Charge density wave, Terahertz time domain spectroscopy

**Supervisor: Dr. Ravi Prakash Singh**

**DEPARTMENT OF PHYSICS**

**Accession No.: T00103**

**Abstract**

Recently, there has been a great deal of interest in noncentrosymmetric superconductors (NCSs) due to the complex nature of their superconducting properties . The lack of inversion symmetry in these materials induces an antisymmetric spin-orbit coupling (ASOC), which causes mixed spin-singlet and spin-triplet superconducting ground state. This mixed pairing can lead NCSs to display significantly different properties from conventional superconducting systems. Despite intense theoretical and experimental efforts, the superconducting properties of NCS remain uncertain, as most of the reported noncentrosymmetric compounds show conventional behaviour except few where unconventional superconducting properties observed. Theoretical work on NCSs suggests that the ASOC play an essential role in the mixing of pair states. However, the experimental work does not fully comprehend the predictions.

Along with magnetization, transport and heat capacity measurements, muon spin relaxation, rotation ( $\mu$ SR) used to confirm the presence of an unconventional superconducting state. The  $\mu$ SR technique is the implantation of 100% spin-polarized muons in the matter. As the muon probes the flux line lattice directly, it gives direct information about the symmetry of the superconducting gap.  $\mu$ SR can also be used to establish the onset of time -reversal symmetry breaking (TRSB) in superconductors unambiguously. The magnetic moments associated with the Cooper pairs are nonzero in superconductors having TRSB and local alignment of these moments produces spontaneous, but tiny small internal magnetic fields.  $\mu$ SR is especially sensitive to small changes in internal fields and can easily measure fields of  $\sim 10 \mu$  Tesla which correspond to moments that are just a few hundredths of a  $\mu_B$ .

In this these , we have systematically studied compounds having two different non-centrosymmetric crystal structure cubic  $\alpha$ - Mn:  $Re_6 X$ [X= Hf, Ti], OsX[X=Nb,Ta] and hexagonal:  $La_7Rh_3$  to understand the role of SOC and crystal structure on the pairing mechanism of NCS. Both the families contain heavy elements, in which SOC is usually expected to be strong, which in turn can enhance the parity mixing ratio. We have found  $Re_6[Hf/Ti]$ , and  $La_7Rh_3$  shows TRSB. At the same time, TRSB is preserved in OsX[X= Nb, Ta].

**Terahertz charge dynamic in the proximity of quantum critical point in the phase diagram of rare earth nickelates**

**V ESWARA PHANINDRA**

**Supervisor: Dr. Dhanvir Singh Rana**

**DEPARTMENT OF PHYSICS**

**Accession No.: T00088**

The intertwined and competing energy scales of various interactions arising from spin, orbital and lattice inter-relations in rare-earth nickelates  $RNiO_3$  ( $R = La$  to  $Lu$ ) hold potential for wide range of exotic ground states. The first two compounds in these series are known to exhibit the most contrasting behavior; the  $LaNiO_3$  (LNO) lacks any phase transition, thus, seems to lie near the quantum critical point, while the second compound  $PrNiO_3$  (PNO) exhibits concomitant insulator-metal (I-M) and magnetic transition around 130 K. The origin of this contrasting behavior realized upon a very small change in cation size is far from understood. To understand this, we studied the novel electronic phase crossovers in structurally modified PNO and LNO thin films, which lies in the proximity of quantum critical point (QCP) in the phase diagram of nickelates.

The present thesis is divided into two parts. In the first part, the low-energy charge dynamics in structurally modulated PNO thin films were probed by terahertz time domain spectroscopy (THz-TDS) to unravel the complexity of the ground state across I-M transition. We observed that the THz conductivity of compressive films lack any I-M transition and follow the Drude model of conductivity. The THz conductivity of the tensile strained PNO films, however, deviate from pure Drude model but follow a disorder modified Drude-Smith (D-S) phenomenological model. Such distinct THz spectral features evolving as a function of type of strain are accompanied by novel electronic phase crossovers such as transition from non-Fermi liquid (implying proximity to a QCP) to Fermi liquid behavior as one traverse from compressive to tensile PNO films. Such structure-property relationship is a novel facet of the PNO system which lies on the vicinity of QCP. We further demonstrated that the I-M transition of these perovskite nickelates has the potential to design efficient THz modulators, thus, suggesting new pathways towards their employability as temperature driven THz transmittance modulators.

In the second part of the thesis, with LNO as a model system, we observed epitaxial strain driven crossover of THz conductivity features (i.e., Drude to D-S type disordered behavior), albeit both type of strained films displaying qualitatively similar dc conductivities. This i) brings out the potential of THz technology in distinguishing between similar dc electronic phases and ii) suggests that LNO under compressive strain is a better candidate for applications as bottom electrode in

**Engineering Multiferroic Properties in Double Perovskite Oxides and Metal-Organic Frameworks:  
A First-Principles Approach**

**Paresh Chandra Rout**

**Supervisor : Dr. Varadharajan Srinivasan**

**Department of Physics**

**Accession No.: T00079**

A material is said to exhibit multiferroicity if it displays more than one ferroic order such as ferromagnetism, ferroelectricity, ferroelasticity, etc. Physical principles governing these phenomena often preclude the simultaneous existence of ferromagnetism and ferroelectricity within the same phase rendering large classes of naturally occurring materials unsuitable for multiferroicity. As a result, very few multiferroics exist in nature or have been synthesized in the laboratory so far. First-principles electronic structure calculations based on density-functional theory (DFT) have been very successful not only in understanding and predicting properties of the multiferroic materials in existence but also designing novel candidates. In the present thesis, we have employed DFT-based techniques to explore the potential of materials with the double-perovskite structure ( $ABB^0O_3$ ) as multiferroics. In particular, we have focused on Bi-based double-perovskite oxides and a more recent alternative to double-perovskite oxides -multiferroic metal-organic frameworks (MOFs).

Considering the experimentally relevant thin-film geometry, we have investigated the influence of epitaxial strain on the ferroic properties of these oxides. In the case of  $Bi_2FeCrO_6$  (BFCO), our work has been successful in explaining the experimentally observed lowered magnetic moments in thin-films of the material. By performing structural optimization incorporating various basic magnetic and different B-site cation orderings, we have shown that the thin-films of BFCO prefer to adopt a cation disordered structure. We also found that, the thin-films are characterized by C-type antiferromagnetic (AFM) order, which was in contrast to its

bulk form (G-type AFM) and the main cause of lowered magnetic moments observed in these samples. The finite temperature magnetic moment obtained from the MC simulation is consistent with the experimental result. Building on this result, we have proposed two possible routes -A-site doping, B-site doping- to encode multiferroic properties and mitigate the observed problems in BFCO thin-films.

In A-site doping approach, we substituted a divalent Sr atom in place of Bi atoms at different stoichiometries. We have successfully stabilized the cation ordered structure while making the ground state robustly ferromagnetic (7 b/f.u.) under epitaxial strain. We found a non-polar-to-polar phase transition driven insulator-to-metal transition in the thin-films. We have also discovered a novel half-metallic polar phase in tensile strain region at both 50% and 25% Sr doping. In B-site cation doping, we have computationally designed two 3d-5d thin films -  $\text{Bi}_2\text{FeReO}_6$  and  $\text{Bi}_2\text{FeIrO}_6$ . The  $\text{Bi}_2\text{FeReO}_6$  thin-films adopt C-type AFM magnetic ordering leading to zero magnetic moment. However, they undergo a monoclinic C-type AFM to monoclinic G-type AFM transition at higher compressive strain. The  $\text{Bi}_2\text{FeIrO}_6$  thin-films show a ferromagnetic ground state with a magnetic moment of 5 b/f.u. under all epitaxial strain. We have also shown a cor-relation driven ferrimagnetic metal to ferromagnetic insulator transition in  $\text{Bi}_2\text{FeIrO}_6$  thin-films.

As an alternative to double-perovskite oxides, we have studied multiferroic double-perovskite metal-organic frameworks (MOFs). In this work, we have shown a giant enhancement of ferromagnetic moment and ferroelectric polarization in a weakly ferromagnetic multiferroic MOF ( $[\text{C}(\text{NH}_2)_3]\text{Cu}[(\text{HCOO})_3]$ ), through a mixed metal strategy. In particular, we have computationally designed a mixed metal perovskite MOF - $[\text{C}(\text{NH}_2)_3][(\text{Cu}_{0.5}\text{Mn}_{0.5})(\text{HCOO})_3]$  that is predicted to have magnetization two orders of magnitude larger than its parent ( $[\text{C}(\text{NH}_2)_3][\text{Cu}(\text{HCOO})_3]$ ) (from 0.02 b/cell to 8 b/cell), a significantly larger polarization (9.9  $\text{C}/\text{cm}^2$ ) and an enhanced  $T_c$  up to 56 K, unprecedented in perovskite MOFs. This work represents a first step towards rational design of multiferroic perovskite MOFs through the largely unexplored mixed metal approach.

# **Late Time Cosmology of f(R) Theory of Modified Gravity**

**Patel Avani Vikrambhai**

**Supervisor : Dr. Sukanta Panda**

**Department of Physics**

**Accession No.: T00073**

**ABSTRACT** This thesis is about the investigation of viabilities of f(R) theories of modified gravity and its cosmological implications. Looking at its wide popularity as an effective theory of gravity permitting late-time universe to expand acceleratingly, our domain of study is late-time Cosmology provided by the theory. We first examine the viabilities of f(R) models recently proposed by Miranda et al. 2009 and Kruglov 2014. Our prime aim is to inquire that whether a given model satisfies local gravity constraints as well as becomes free from curvature singularity for a set of parameter values. Later, in the thesis, we build a new f(R) model which evades local gravity tests.

The recent time accelerating expansion of our universe is in the forefront of research topics in Cosmology. Even after more than one and half decade, the physical cause of the late-time acceleration is not fully resolved. In literature, there exist several theories and many cosmological models which strive to explain the accelerating expansion. Among them, Dark Energy models and modified gravity theories are two major alternative paths. The cosmological constant is believed to be the best candidate for the Dark Energy which is the essential component of the popular Lambda Cold Dark Matter( $\Lambda$ CDM) model. There also exist evolving Dark Energy models whose equation of state varies with time. The alternative to Dark Energy is modifying General Relativity in such a way that no exotic component like Dark energy is needed to fuel the universe to expand with acceleration. This approach, commonly known as Modified Gravity, has also earned serious attention in recent time. The f(R) theory is the simplest extension to General Relativity. The Ricci scalar R is replaced by an arbitrary function of f(R) in the gravitational Lagrangian.

Since General Relativity correctly describes gravitational physics at solar system scale, any valid f(R) model also should give same results at solar system scale. In other words, f(R) models should satisfy all local gravity constraints allowed by experiments. The f(R) theory gives the extra dynamical scalar field in addition to usual spin-2 field. This socalled fifth force can change the dynamics on the local gravity scales, and therefore it is vii viii important to constrain the models. The curvature singularity is another serious problem in f(R) models. Due to the nonlinear motion of the scalar field, the oscillations around the potential minimum can make the field displaced to the singular point. In this thesis, we consider a model proposed by Miranda which reduces to famous Starobinsky model, HuSawicki model and Appleby-Battye model in different limits. We carry out investigations to check whether this model satisfies fifth-force constraints and becomes free from curvature singularity for the same parameter values or not. We also test the viabilities of the arctan model given by Kruglov and find that it violates the fifth-force constraints.

In the later stage of the thesis, a new f(R) model is constructed which evades local gravity tests. The

cosmological evolution for this  $f(R)$  gravity model is also analyzed in the Friedmann Robertson Walker(FRW) background. To understand observational significance of the model, cosmological parameters are obtained numerically and compared with those of  $\Lambda$ CDM model. We also scrutinize the model with supernova data. We apply Om diagnostic given by Sahni et al. 2008 to the model. Using this diagnostic, we detect the distinction between cosmic evolution caused by the  $f(R)$  model and  $\Lambda$ CDM. We find best-fit parameter values of the model using Baryon Acoustic Oscillations data.

**The dynamics of chemo-mechanically active polymer: Loop formation, Self-propulsion and spontaneous oscillation**

**Debarati Sarkar**

**Supervisor: Dr. Snigdha Thakur**

**Department of Physics**

**Accession No.: T00070**

**KEYWORDS:** Active polymer, self-propulsion, loop-formation, spontaneous oscillation, coarse grained model, hydrodynamics, molecular dynamics, multi particle collision dynamics. Self-propulsion by conversion of chemical energy to mechanical work is ubiquitous in nature. Bacteria, molecular, self-propelled vesicles, cilia etc. are the most common biological examples of such self-propelled particles. Apart from these naturally occurring auto-motile particles, significant work has been done on synthetic self-propelled objects like bimetallic rods, self – propelled janus spheres, polymeric nano-rockets, etc. All the above said examples of active particles are observed in nano/micron-scale and are dealt with non-equilibrium statistics. Motivated by the examples as mentioned above, this with non-equilibrium statistics. Motivated by the examples as mentioned above, this thesis work deals towards the better understanding of the various dynamical properties executed by the chemically active polymers by using the methods of statistical and computational tools. In particular, we try to explore some insight into the dynamics of the self-propulsion, loop formation, spontaneous and synchronous oscillation.

The thesis begins with in-silico building of the chemically active polymer that can successfully address the phenomena discussed above. The loop forming active polymer has been designed by attaching two active sites, catalytic (C) and non- catalytic ( N ) to the different parts of the polymer. To model a self –propelled active polymer, few chemically active dimmers ( consists of C and N ) are inserted along the length of the polymer in a regular interval that gives rise to the tangential forces on the polymer. This self-propelled polymer exhibits interesting spontaneous beating upon clamping. In this work, the dynamics of the models are studied in the presence of the hybrid MD-MPCD technique where the time evaluation of the polymer beads are carried out by using the molecular dynamics (MD), and the solvent dynamics is considered through the multiparticle collision dynamics ( MPCD ).

Next part of the thesis discusses the dynamics of the end-to-end and end-to-internal loop formation of the active polymer. Here we observe that the two active sites of the polymer come close to each other by forming the loop to the diffusiophoresis mechanism as opposed to the diffusion limited loop formation. It is fascinating to note that the presence of the activity( presence of C and N ) alters the loop formation dynamics drastically. We notice that the active polymer executes much ring closure in comparison

To the inactive case. The stiffness of the polymer also plays an important role and slows down the loop formation process. The loop formation dynamics in the presence of the crowded environment has also been studied here, and it is observed that due to the steric effect of the crowder, loop formation dynamics slow down.

Our next study involves the analysis of the self-propulsion properties of the active polymer. Here we observe that the polymer displays different kinds of trajectories namely, "Snaking", "Rotation" and " Translation " To quantify such trajectories, an order parameter has been defined that tells us various modes of propulsion. For our model, the hydrodynamics interaction ( HI ) plays a crucial role in the self-propulsion , and that is shown by the mapping of the flow profile in the near vicinity of the automobile polymer. Further, we analyse the non- Gaussian properties of the self-propelled polymer by calculating

the excess-kurtosis, and the probability distribution of the displacement vector of the active polymer. We have also calculated the efficiency of our polymeric model.

Last part of the thesis deals with the spontaneous cilia-like oscillation executed by the active polymer. The active dimmers situated along the active polymer length play the similar role as motor proteins play inside the cilia. We observe that the dynamics are purely governed by the interplay between the active and elastic forces. It is observed that such oscillation is only noticed for the semi-flexible polymer beyond a critical value of the active force. It is very important to be noted that the HI interaction has immense importance for the spontaneous oscillation of the polymer. The important of the HI effect has been shown by the mapping of the flow profile in the near vicinity of the active polymer in the straight and bent configurations. The synchronous oscillation by the pair of the polymer is also analysed in the last chapter of this thesis work. We observe that the synchronous oscillation depends upon the intermediate distance between the pair of polymers. This effect is due to the hydrodynamic couplings, mediated through the HI interaction between the polymers. Further analysis shows that the polymers beat synchronously with a constant phase difference in between them.

# **Ultrafast exciton dynamics in 2-dimensional and amorphous chalcogenides**

**Rituraj Sharma**

**Supervisor: Dr K. V. Adarsh**

**Department of Physics**

**Accession No: T00065**

The optical response of 2-dimentional (2D) and amorphous chalcogenides (materials containing S, Se or Te as one of the major constituents) is governed by excitons, the Coulomb bound electron–hole pairs. The excitonic quasi-particles have a pronounced role in the absorption and emission spectra of these materials. Therefore, understanding the properties of excitons and their dynamics is of crucial importance since they significantly affect the optoelectronic properties. Interestingly, the exciton dynamics are strongly influenced by the materials' electronic structure, amorphous or crystalline nature, presence of trap states, etc. Nonetheless, many questions remain to be answered, and many opportunities remain to be explored. The primary aim of this thesis is to address sequentially the role of disorder on the exciton dynamics in two class of chalcogenide systems: 1) 2D crystalline transition metal dichalcogenides (TMDCs) and 2) amorphous chalcogenide glass (ChG) thin films. We employ ultrafast pump-probe transient absorption spectroscopy to study the exciton dynamics.

In the first part of this thesis we address the detrimental role of trap states below the optical bandgap in exciton interactions of indirect bandgap of few layer (FL) MoS<sub>2</sub>. Our ultrafast pump-probe transient absorption measurements of FL-MoS<sub>2</sub>, reveal the blueshift and broadening of A and B exciton resonances due to band renormalization and exciton interactions respectively. Subsequently, the excitons are quickly captured by the trap states.

At lower fluences, a simple three-level rate equation accurately models the bleaching dynamics and allows us to extract lifetimes at different levels. At extremely high carrier densities (beyond Mott density), the recombination kinetics follows a bimolecular law. Further, we move on to show that the excitonic transitions are completely quenched, when we form a complex few-layer MoSe<sub>2</sub>/graphene oxide (GO) heterostructure with strong interlayer coupling. Spectroscopic evidence of our study indicates that the optical signatures of isolated MoSe<sub>2</sub> and GO domains are significantly modified in the heterostructure, displaying a direct coupling of both domains. Furthermore, our first-principles calculations indicate that strong interlayer coupling between the layers dramatically suppresses the MoSe<sub>2</sub> excitonic bands. We also demonstrate a giant enhancement of two-photon absorption that is in stark contrast to the reverse saturable absorption of a weakly coupled MoSe<sub>2</sub>/GO heterostructure and saturable absorption of isolated MoSe<sub>2</sub>. In amorphous chalcogenides, on the other hand, the lattice is not stable and the excited carriers are trapped in their own lattice deformation. In the second part of the thesis, we experimentally and theoretically demonstrate the excited state relaxation dynamics through TDs in a-Se thin films when illuminated with 120 fs laser pulses. The TD dynamics induce an unusually broad and fully reversible absorption spectra in the interband and subbandgap region. The induced absorption (IA) shows a strong and fast decaying IA in the sub-bandgap and weak and slow decaying IA in the interband regions. Our experiments provide a direct experimental evidence of self-trapping of excitons in amorphous lattice. Subsequently, we have demonstrated that the plasmon-exciton interaction at the ultrafast time scale in an amorphous Ge<sub>24</sub>Se<sub>76</sub>/AuNP heterostructure. Interestingly, the coupling can be controlled by varying the plasmon wavelength. Our studies show that the strong coupling in these heterostructures leads to dramatic suppression of exciton and plasmon absorptions. Further, exciton quenching is found to be most efficient when the SPR wavelength matches the optical bandgap. The results are explained by assuming the transfer of photo excited electrons from a-Ge<sub>24</sub>Se<sub>76</sub> to AuNP, which then leads to the mixing of the electronic wave function and the formation of interfacial trap states.

The thesis also addresses an independent problem: engineering the optical response of a-Se by employing morphological disorder. Till now, all the previous studies have reported PD in a-Se, with no indication of photobleaching (PB) i.e. shift of optical absorption edge towards shorter wavelength. We demonstrate for the first time that PB can be induced in a-Se by engineering the surface morphology.

**Keywords:** Chalcogenides, 2-dimensional, ultrafast exciton, PhD Thesis

**Tailoring between network rigidity and lightinduced effects in a-GexAs35-xSe65 thin films**

**Pritam Khan**

**Supervisor: Dr. K. V. Adarsh**

**Department of Physics**

**Accession No.: T00036**

Chalcogenide glasses (ChG) are based on the chalcogen element S, Se and Te in combination with group IV or V elements of the periodical table. One of the unique and striking properties of ChG is the exhibition of a wide variety of lightinduced effects. Such effects have various applications ranging from holographic recording, waveguide designing, making diffraction elements and fabricating nano-antenna. Lightinduced effects in ChG are instigated from the photo-generation of electron-hole pairs which lead to the formation of exciton by the mutual Columbic interaction. The excitons are highly unstable and consequently interact with the deformable lattice of ChG and become self-trapped. The exciton self-trapping is associated with the structural rearrangement in the lattice that accounts for the various lightinduced optical properties in ChG. The lightinduced effects depend strongly on ChG structure, i.e. rigidity of the network because the extent of selftrapping will be different in floppy and rigid network. Till date, there is no direct relationship between the lightinduced effects and the rigidity of ChG network. The primary aim of the present thesis is to study the tailoring between network rigidity and lightinduced effects in a-GexAs35-xSe65 ( $0 \leq x \leq 25$ ) thin films in a time domain that extends from nanoseconds (ns) to seconds. The thesis addresses another independent problem: kinetics of Ag photo-dissolution and photo-diffusion in As<sub>2</sub>S<sub>3</sub> matrix as a function of the thickness of Ag and As<sub>2</sub>S<sub>3</sub> layer. We have used time resolved pump-probe optical absorption spectroscopy to study the lightinduced effects. Continuous wave (cw) pump-probe optical absorption study in a-GexAs35-xSe65 thin films reveals that metastable lightinduced effects do not exhibit a regular trend with network rigidity, rather Ge:As ratio plays the major role in determining the lightinduced response. Composition dependent light-induced responses of these samples indicate that there exist two parallel competing mechanisms of instantaneous photodarkening (PD) and slower photobleaching (PB). Subsequent Raman analysis on as-prepared and illuminated sample provides the direct evidence of structural rearrangements. For example, lightinduced enhancement in AsSe<sub>3</sub>/2 pyramidal unit gives rise to PD, whereas photooxidation of Ge together with decrease in edge sharing GeSe<sub>4</sub>/2 tetrahedra leads to PB. In a stark contrast, nanosecond (ns) laser induced transient absorption (TA) decreases dramatically from floppy to rigid system in consistent with network rigidity theory. Our viii results provide the direct experimental evidence of a self-trapped exciton recombination mechanism. Light-

induced transient bonding rearrangement via self-trapped exciton recombination mechanism accounts for the large TA in the floppy network. On the other hand, rigid systems are unable to undergo any such bond rearrangements and consequently show weaker effects. In another independent project, we demonstrate the combined effect of photodoping and photoinduced-surface deposition in a bilayer of As<sub>2</sub>S<sub>3</sub> and Ag as an alternative method to optically synthesize Ag nanoparticles (AgNP) on the surface of ChG. Pump-probe optical transmission measurements indicate that photo-dissolution becomes faster for thinner Ag samples, whereas the thickness of As<sub>2</sub>S<sub>3</sub> matrix plays little to no role in controlling such process. We foresee that the formation of AgNP on As<sub>2</sub>S<sub>3</sub> would have potential to be used as a substrate for surface-enhanced Raman scattering (SERS).

**Keywords:** Chalcogenide Glasses, Lightinduced Effects, Network Rigidity, Raman Spectroscopy, Self-Trapped Exciton.

## **Anisotropic Cosmology**

**Manabendra Sharma S**

**Supervisor: Dr. Sukanta Panda**

**Department of Physics**

**Accession No.: T00029**

This thesis can be broadly divided into two parts. While the first part studies an extension of an FRW universe to an anisotropic spacetime induced by anisotropic sources, the second part involves analysis of models of bouncing scenario. The common thread between two is the focus on anisotropic spacetime. In particular, a large portion of this thesis is devoted to studying a homogeneous but anisotropic spacetime, Bianchi I, with a residual symmetry. The first part involves studying an anisotropic universe with anisotropic sources and finding the plausibility of the kind considered from observation. The anisotropic sources examined here are cosmic strings, domain walls, Lorentz violation generated magnetic field(LVMF) and magnetic field. We begin with analysing the state space of a Bianchi-I universe with each of the aforesaid anisotropic energy-momentum densities. The extended state space includes null geodesic equations along with Einstein field equations in this background. The evolution equations of all the state observables are derived. Fixed point analysis is carried out using a dynamical system approach, where asymptotic stable fixed points are obtained for all dynamical variables. We show the numerical evolution of the variables both in cosmic time and expansion normalized time. The above analysis is followed by a repetition of the same with a more realistic scenario. In order to construct such a scenario, we add an isotropic (dust like dark) matter and a cosmological constant (dark energy) to our anisotropic sources and study their co-evolution. The universe now approaches a de Sitter space asymptotically dominated by the cosmological constant at late times. The cosmic microwave background anisotropy maps due to shear are also generated in this scenario having anisotropic matter along with the usual (dark) matter and the vacuum (dark) energy since decoupling. We find that they contribute dominantly to the CMB quadrupole. We also constrain the current level of anisotropy and also search for any cosmic preferred axis present in the data. We use the Union 2 Supernovae data to this extent and find an anisotropy axis close to the mirror symmetry axis seen in the cosmic microwave background data from Planck probe. We also study the fate of an anisotropically contracting universe dominated by each of the anisotropic sources considered. This study has its usefulness also in the later half of the thesis when we discuss bouncing scenario. The behaviour of the Raychaudhuri Equation and investigation of whether a congruence of timelike geodesics focuses to a point has been carried out, in a universe with Bianchi I background dictated by the anisotropic sources considered. Thus,

Focusing theorem has been checked for initially contracting or diverging universe with each of these anisotropic sources. In this way, this piece of work acts as a bridge between the first and second half of this thesis. The second half of the thesis is devoted to studying bouncing scenario. Using dynamical system analysis, we investigate a toy model consisting of a Lagrangian with a noncanonical kinetic term and an additional matter in FRW closed, open and Bianchi I background. A fixed point analysis is carried out in terms of dynamical variable suitable for studying bouncing solutions. Following this, solutions satisfying nonsingular bouncing conditions are shown, numerically, to exist for some choice of parameters in all the three cases. The finitude, at the bounce, of curvature parameter in the case of closed and open universe and shear parameter in Bianchi I universe is also noted.

**Keywords:** Anisotropic Universe, Anisotropic Source, Null Geodesic, Bouncing Scenario and Cosmic Anisotropy.

**Novel Hetero - Interface Phases and Low Energy Dynamics in Correlated Systems Parul**

**Pandey**

**Supervisor: Dr.D.S.Rana**

**Department of Physics**

**Accession No.: T00018**

Complex oxides exhibit strong correlations among spin, charge, lattice and orbital degrees of freedom. This results in the exotic physical phenomenon, such as insulator-metal transition, colossal magnetoresistance, high-temperature superconductivity, multiferroicity, etc. The interaction among these degrees of freedom at the artificial engineered interfaces is particularly intriguing, as it may lead to exotic and unexpected states of matter. In this context, exploration of exchange bias effect in correlated oxides is highly relevant as it has direct implications for magnetic memory devices. A new paradigm in this area is the realization of the exchange bias interface properties, in oxide heterostructures with disordered magnetic phases. The unconventional combination of paramagnetic-antiferromagnetic perovskite oxides presents the unique opportunity to understand new facets of the exchange bias effect in disordered-ordered magnetic phases. In the first part of this thesis, the novel exchange bias characteristics, an anomalous magnetic moment, large exchange bias fields, vertical magnetization shift, of paramagnetic CaRuO<sub>3</sub> and antiferromagnetic Eu<sub>0.42</sub>Sr<sub>0.58</sub>MnO<sub>3</sub> have been explored. For the first time, a remarkable and unusual electronic (non-magnetic) control of these interface magnetic properties is presented. Also, the exchange bias properties of antiferromagnetic- paramagnetic Eu<sub>0.42</sub>Sr<sub>0.58</sub>MnO<sub>3</sub>-CaRuO<sub>3</sub> heterostructure were compared with that of the conventional magnetically ordered antiferromagnetic-ferromagnetic Eu<sub>0.42</sub>Sr<sub>0.58</sub>MnO<sub>3</sub>- SrRuO<sub>3</sub> system. It was shown that the exchange bias properties, originating from the former, are predominantly stronger than that induced in the latter. Further, this thesis also explores the heterostructures of NdNiO<sub>3</sub>-La<sub>0.7</sub>Sr<sub>0.3</sub>MnO<sub>3</sub> films, in which properties of the constituent NdNiO<sub>3</sub> can be vastly improved by suitably optimizing the multilayer structure. Specifically, improved electrical properties of NdNiO<sub>3</sub> were generated by intercalating thin La<sub>0.7</sub>Sr<sub>0.3</sub>MnO<sub>3</sub> layers. A large conductivity and better hysteretic behaviour were obtained by retaining its insulator-metal characteristics. The entanglement of various degrees of freedom in 3d-transition metal oxides also results in some exotic low-energy phenomena. In this context, the observations of charge-density wave (CDW) excitations in perovskite oxides have given a new insight into the area of charge dynamics and their correlations with the lattice. In the last part of this thesis, the CDW excitations in the charge-ordered Eu<sub>0.5</sub>Sr<sub>0.5</sub>MnO<sub>3</sub> and Eu<sub>0.42</sub>Sr<sub>0.58</sub>MnO<sub>3</sub> correlated oxides are investigated using Terahertz time-domain spectroscopy. The impact of intrinsic disorder/pinning on the low-energy collective excitations

of CDW in Eu<sub>1-x</sub>Sr<sub>x</sub>MnO<sub>3</sub> ( $x = 0.50, 0.58$ ) manganites were explored. In this system, the short range and long range charge-ordering in Eu<sub>0.5</sub>Sr<sub>0.5</sub>MnO<sub>3</sub> and Eu<sub>0.42</sub>Sr<sub>0.58</sub>MnO<sub>3</sub>, respectively, have a direct correlation with the collective excitations such as the CDW condensate. It was shown that range of charge-ordering influences the CDW mode formation and this seems to be a generic feature of the charge-ordering in manganites.

**Keywords:** Exchange Bias, Interfacial Phenomenon, Charge Density Wave and Terahertz Time Domain Spectroscopy.

**Terahertz Excitations of Charge Density Waves and Generation of  
Exchange Bias Fields in Complex Oxide Thin Films**

**Rakesh Rana**

**Supervisor: Dr. D. S. Rana**

**Department of Physics**

**Accession No.: T00011**

Correlated materials are known for their exotic physical properties which are markedly different from those of the conventional band insulators. One such promising class of materials belongs to 3d-transition metal oxides in which the spin, charge, orbital and lattice degrees of freedom result in colossal magnetoresistance, superconductivity, insulator-metal transition and some low energy phenomena. In this context, the observation of charge density wave (CDW) excitations in perovskite oxides has given a new insight into the area of charge dynamics and their correlations with the lattice. The present thesis is divided into two parts. In the first part, the CDW excitations in the charge-ordered Pr<sub>0.5</sub>Sr<sub>0.5</sub>MnO<sub>3</sub>, Nd<sub>0.5</sub>Sr<sub>0.5</sub>MnO<sub>3</sub> and NdNiO<sub>3</sub> correlated oxides are investigated using Terahertz time domain spectroscopy. The patterned phases in these systems exhibit a rich diversity, such as the charge-order in A-type antiferromagnetic Pr<sub>0.5</sub>Sr<sub>0.5</sub>MnO<sub>3</sub> is stripe type and anisotropic in nature, the charge-order in CE-type antiferromagnetic Nd<sub>0.5</sub>Sr<sub>0.5</sub>MnO<sub>3</sub> is isotropic in nature and the charge-order in the NdNiO<sub>3</sub> depends on the off-centering of the spin density wave state. Present studies reveal that the CDW is a generic feature of the charge-order in these manganites and nickelates. The implications of the dilution of charge-order on the manifestation of CDW and the structural control of the CDW are also studied. Various correlated oxide combinations can be utilized to obtain exotic spintronic functionalities via spin, charge, orbital reconstructions at the interface of heterostructures. The ‘exchange-bias’ is an interface effect of magnetic origin which has important applications in the magnetic storage devices. The choice of suitable perovskite oxide combinations presents the unique opportunity to understand various attributes of the exchange-bias effect. In the second part of the thesis, the novel exchange-bias properties in the epitaxial bilayers of the ferromagnet SrRuO<sub>3</sub> and the antiferromagnetic La<sub>0.3</sub>Sr<sub>0.7</sub>FeO<sub>3</sub> is shown. In these investigations, an uncharacteristic low-field positive exchange bias, a cooling-field driven reversal of positive to

negative exchange -bias and vertical magnetization shift which are all novel facets of exchange bias effect are realized for the first time in magnetic perovskite oxides. The vertical magnetization shift and exchange bias fields have also been tuned by varying the thicknesses of ferromagnetic and antiferromagnetic constituent layers.

**Keywords:** Charge Density Waves, Terahertz Time Domin Spectroscopy and Exchange Bias Effect.

**Department of  
Earth and Environmental Sciences**

**Neoproterozoic tectonism at the Eastern Ghats Belt-Baster Craton interface, Eastern India: constraints from geochemical, metamorphic and geochronological investigations**

**Dicton Saikia**

**Supervisor: Dr. Pritam Nasipuri**

**Department of Earth and Environmental Sciences**

**Accession No.: T00127**

**Abstract**

This doctoral dissertation represents results of lithological mapping, chemical analyses of bulk rocks and minerals, equilibrium  $P$ - $T$  estimations including phase diagram constructions and monazite geochronology of around Koraput Anorthosite pluton, Eastern Ghats Belt (EGB) and adjacent metasedimentary rocks from Bastar craton (BC) to model Neoproterozoic tectonism at the EGB-BC interface.

Lithological mapping in and around Koraput implies the occurrence of an anorthosite pluton, that is elliptical with long axis running in NE-SW direction for about 3 kilometers. In the Koraput pluton, gabbro-anorthosite dominate in the western part, that gradually change to norite-diorite in the eastern part via anorthosite *sensu stricto* in the central part. Silica undersaturated ferrodiorite occur in the western part of the pluton. The western part of the pluton is least deformed where magmatic plagioclase crystals are embedded into a fine-grained recrystallized matrix of plagioclase and pyroxene. Towards the east, the intensity of deformation increases, and an outward dipping margin parallel foliation is perceptible. Tens of centimeter thick metasedimentary bands alternating with volcanic tuffs are observed as scattered outcrops for more than two kilometers at the south-eastern margin of Bastar craton, adjacent to BC-EGB

boundary near Koraput Anorthosite pluton. In the outcrops, metasedimentary rocks are extremely fine-grained splintery and exhibit razor-sharp edges when hit with a hammer.

Plagioclase feldspar, clinopyroxene, orthopyroxene, ilmenite, biotite, amphibole, and garnet are the major constituent minerals in anorthosite. The sequence of metamorphic minerals preserved in Koraput Anorthosite pluton suggests an initial phase of hydration leading to the formation of biotite and amphibole by consuming orthopyroxene and clinopyroxene respectively, followed by dehydration and granulite facies metamorphism leading to the formation of garnet destabilizing biotite and amphibole. Carpholite, chlorite, mica, and biotite are the constituent minerals in the metasedimentary rocks. Detailed petrographic and phase equilibria analysis implies reaction textures preserved in metasedimentary rocks are related to stabilization of low-temperature - low-pressure mineral assemblages (chlorite-mica<sub>I</sub>) by consuming low temperature-high pressure mineral phase, carpholite. A second-generation (Mica<sub>II</sub>) and biotite overgrow the low-temperature chlorite-micaI assemblages due to magma underplating and subsequent heating.

Around 200-500  $\mu\text{m}$  monazite grains occur as inclusions within orthopyroxene and plagioclase in Koraput Anorthosite pluton. Most of the monazite grains exhibit complex chemical zonation. Mean age of  $939 \pm 5$  Ma is obtained from monazites with a low-ThO<sub>2</sub> core surrounded by high ThO<sub>2</sub> rims. The younger low ThO<sub>2</sub> monazites surrounding the relict high ThO<sub>2</sub> core are characterized with mean ages  $877 \pm 5$  Ma and  $749 \pm 18$  Ma. The youngest age population, i.e., mean  $574 \pm 19$  Ma is obtained from the peripheral monazite rims and monazite veins. In the metasedimentary rocks, monazite grains also exhibit complex chemical zonation. The oldest age population with a mean age of  $2162 \pm 42$  Ma is obtained from a group of monazite grains with an angular shape and transgranular fractures. The low ThO<sub>2</sub> core monazite grains

yield ages spanning between 1600-1700 Ma. Younger age with a distinct peak at  $1528 \pm 10$  Ma obtained from high ThO<sub>2</sub> rims surrounding the low ThO<sub>2</sub> core. The youngest ages with a mean value at  $528 \pm 20$  Ma are obtained from monazite grains in the quartz-alkali feldspar (K-feldspar)-kaolinitic matrix.

The oldest age ( $2162 \pm 42$  Ma) obtained from the metasedimentary rock is related to basin subsidence in Bastar craton. The  $1616 \pm 10$  Ma aged monazites are correlated with the presence of a subduction zone below Bastar craton leading to 1700-1600 Ma rhyolite magmatism. The continued subduction leads to the final amalgamation of Antarctica with BC at  $\sim 1500$  Ma. In the EGB, monazite growth at  $939 \pm 45$  Ma is related to anorthosite emplacement. The magmatic activities leading to emplacement of Koraput Alkaline complex promote another set of monazite growth in Koraput Anorthosite pluton between  $877 \pm 5$  Ma -  $749 \pm 18$  Ma. An younger set of monazite growth in Koraput Anorthosite pluton, and in metasedimentary rock, Bastar craton at  $\sim 574 \pm 19$  Ma and  $558 \pm 2$  Ma respectively, marked the final moments of crustal amalgamation. The geochronological evidence imply EGB coherently evolved with Antarctica at 1000-900 Ma and welded with Bastar craton at 500 Ma overlapping with the final assembly of Gondwanaland.

**Keywords:** Koraput Anorthosite pluton; Gondwanaland; Rodinia; Bastar; Monazite;

**Source Apportionment of Fine particles over a National Park in Central India**

**Samresh Kumar**

**Supervisor: Dr. Ramya Sunder Raman**

**Department of Earth and Environmental Sciences**

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**Abstract**

Atmospheric fine particulate matter ( $PM_{2.5}$ ) across locations in the world, is a cause of concern due to its role in detrimental health effects (Giannadaki et al., 2016), visibility degradation and alteration of Earth's radiation budget. In India, National Ambient Air Quality Standards (NAAQS) 2009 included  $PM_{2.5}$  as a regulated species. In response to the revised NAAQS and the need to better understand the nature of  $PM_{2.5}$  over data-deficient Central India, a monitoring station was set-up at Van Vihar National Park, Bhopal to measure fine aerosol ( $PM_{2.5}$ ) and apportion its sources. The study objectives were to better understand:

- = The mass, chemical composition and optical properties of  $PM_{2.5}$  over Van Vihar National Park, (VVNP) in Bhopal, Central India
- = The temporal variability of these species and their relationships with meteorology
- = Potential sources and their mass contributions to  $PM_{2.5}$ , including an identification of their geographical locations

$PM_{2.5}$  mass, its chemical constituents, and optical properties were measured for two years, between January 2012 and December 2013. 12 hour integrated samples were collected every-other-day, alternating between day (06:00 to 18:00) and night (18:00 to 06:00, the following day), on multiple filter substrates using co-located air samplers. In addition to determining  $PM_{2.5}$  mass, the filter samples were subjected to a variety of chemical analyses. Concentrations of organic, pyrolytic, and elemental carbon, eleven water-soluble inorganic ions, and over twenty six trace elements concentrations, were thus obtained. Additionally, optical properties including fine PM scattering co-efficient at 550 nm and attenuation at 370

and 880 nm were measured. These measurements in conjunction with on-site meteorological data were used to understand the temporal behaviour and the sources of fine PM measured at VVNP, Bhopal. Some the key results of this thesis are as follow:

N The mean  $\text{PM}_{2.5}$  concentration for the entire sampling period was  $44 \mu\text{g m}^{-3}$ ; however; the mean  $\text{PM}_{2.5}$  concentration for 2012 and 2013 were  $40 \mu\text{g m}^{-3}$  and  $48 \mu\text{g m}^{-3}$  for 2012 and 2013, respectively. Also, there was no statistical difference in the diurnal  $\text{PM}_{2.5}$  mass concentration.

O The  $\text{PM}_{2.5}$  dry scattering coefficient at 550 nm, often used as surrogate for  $\text{PM}_{2.5}$  mass, was found to correlate well with fine PM mass only during the post-monsoon season. During the post-monsoon season, the mass scattering efficiency was  $1.44 \text{ m}^2 \text{ g}^{-1}$ , a value at the lower end of the range of scattering efficiencies reported in literature, for various locations in the world.

ϕ WSIIIs were accounted for 31.5% of  $\text{PM}_{2.5}$  load.  $\text{NH}_4^+$  was found to be major neutralizing species for acidic anions like  $\text{NO}_3^-$ ,  $\text{SO}_4^{2-}$  in fine particles at the sampling site, contrary to results reported for  $\text{PM}_{10}$  and total suspended particles (TSP) over other locations in India, where mineral aerosol species (specifically  $\text{Ca}^{2+}$ ) played an important role in neutralizing acidic species (Chapter-4).

γ Trace elements except reconstructed soil, S and K contributed around 0.7% to mean  $\text{PM}_{2.5}$  mass concentration where reconstructed soil accounted for about 16.4% of the mean  $\text{PM}_{2.5}$  mass concentration.

ηη Carbonaceous fraction is composed of organic matter (1.5\*organic carbon) and elemental carbon and contributed 58% to the mean  $\text{PM}_{2.5}$  mass concentration.

Finally, an advanced factor analytic model, Positive Matrix Factorization (PMF5, USEPA version) was applied to the concentrations of  $\text{PM}_{2.5}$  mass and its chemical species. The model resolved seven factors that accounted for  $\text{PM}_{2.5}$  mass over the study site (Kumar and Sunder Raman, 2019). A combination of source profiles, temporal evolution and potential source locations were used to identify these factors as secondary sulfate, combustion aerosol, re-suspended crustal dust, pyrolysis carbon-rich aerosol, biomass burning aerosol, secondary nitrate, and sea salt with mean contributions of 24.8%, 23.6%, 17.3%, 15.7%, 11%, 4.1%, 0.8% respectively, and remaining 2.6% of total  $\text{PM}_{2.5}$  mass was not apportioned by PMF5.