

**PHOTOINDUCED REGIOSELECTIVE C-C BOND
FORMATION AND TRANSITION METAL CATALYZED
C-H ACTIVATION**

KRISHNA NAND TRIPATHI



**DEPARTMENT OF CHEMISTRY
INDIAN INSTITUTE OF TECHNOLOGY DELHI**

July 2020

© Indian Institute of Technology Delhi (IITD), New Delhi, 2020

**PHOTOINDUCED REGIOSELECTIVE C-C BOND
FORMATION AND TRANSITION METAL CATALYZED
C-H ACTIVATION**

by

KRISHNA NAND TRIPATHI

Department of Chemistry

Submitted

In fulfillment of requirements of degree of Doctor of Philosophy

to the



Indian Institute of Technology Delhi

July 2020

Dedicated to my beloved Parents

CERTIFICATE

This is to certify that the thesis entitled, “**Photoinduced Regioselective C–C Bond Formation and Transition Metal Catalyzed C-H Activation**”, being submitted by **Mr. Krishna Nand Tripathi** to the Indian Institute of Technology Delhi for the award of the degree of **Doctor of Philosophy** in Chemistry is a record of bonafide research work carried out by him. Mr. Krishna Nand Tripathi worked under my guidance and supervision and has fulfilled the requirements for the submission of this thesis, which to my knowledge has reached the requisite standard.

The results contained in this dissertation have not been submitted in part or full to any other University or Institute for the award of any degree or diploma.

(Dr. Ravi P. Singh)

Associate Professor

Department of Chemistry

Indian Institute of Technology Delhi

New Delhi-110016

ACKNOWLEDGEMENTS

Completion of this doctoral dissertation was possible with the support of several people. I would like to express my sincere gratitude to all of them. First and foremost, I want to thank my advisor **Dr. Ravi P. Singh**. Without his enthusiasm, encouragement, support and continuous optimism this thesis would hardly have been completed. I am also very grateful to him for his scientific advice and knowledge and many insightful discussions and suggestions. He showed me different ways to approach a research problem and the need to be persistent to accomplish any goal. His advice on both research as well as on my career have been invaluable. I also must thank the members of my SRC committee, Prof. N. G. Ramesh, Prof. Anil J. Elias, and Prof. Anurag S. Rathore for their helpful suggestions and advice in general. I also thank all the past and the present Head of the Department of Chemistry, for the academic support and the facilities provided to carry out my research work. I would also like thank Prof. J. D. Singh (Chairman, DRC) for streamlining curricular formalities. I would especially like express my gratitude towards Dr. S. L. Gholap, for his timely encouragement and support. I gratefully acknowledge all the faculty members and staff for providing the necessary facilities to pursue my research activities. I would also like to thank Dr. Neetu Singh, for her kind and generous nature, constant support and encouragement. I would like to thank CSIR, India, for providing the research fellowship which allowed me to undertake this research program.

A healthy environment and a support system are crucial for staying and surviving in a working place. I am blessed to be a part of what we like to call as “CCSL Group”. The foundation stone of this group was laid down by my senior lab mates Dr. Amol, Dr. Bhaskara Rao and Dr. Devalina. They created a cordial working environment in the lab. I would also like to thank Dr. Belal, Dr. Abhijeet, and Krishna Kumar for timely guidance and countless support in completing my research projects. I feel very lucky to have such seniors in my life and I express my special thank of gratitude to them.

I am forever thankful to my colleagues in the lab for their friendship and support. Their presence was very important in a process that is often felt as tremendously solitaire. I heartily thank my lab mate Dr. Vijay with whom I had pleased to work and impeccable blending. He is having nicest persona who always helped and supported me throughout my tenure. His companionship has imprinted unforgettable moments. A good support system is important to

surviving and staying sane in grad school. I was lucky to be a part of what we like to call as “CCSL Group”. I am forever thankful to my colleagues in the lab for their friendship and support and for creating a cordial working environment. Their presence was very important in a process that is often felt as tremendously solitaire formed the core of my research time and we have been there for one another throughout this journey. I would like to thank all my colleagues (past and present), Pradeep, Arup, Amjad, Manish, Soumyadip, Sanjay, Ravneet, Debashis, Bhuvnesh, Manju, Harish, Khushboo, Sonu, Shrikesh, Neha, Pooja, Richa, Ashima, Shweta, Deepak, Aarti, Satish, Priyankar, Rajesh, Jitendra Saini, and Shivam. I also recognize the support and contributions from Shashank not only with the projects but in many ways. I would like to thank all my friends at Allahabad University including Ankush, Sachchidanand, Vishal, Dhananjay and Amit for their personal and scholarly interactions with me. It is a pleasure to thank my friends at IIT Delhi including, Dr. Rituraj, Dr. Ashish, Dr. Lakhbeer, Dr. Jagriti, Deepa, Kapil, Samim, Tripti, Vipin, Bhawana, Pritam. I am also greatly indebted to many teachers in the past including Prof. LDS Yadav, Prof. J. D. Singh. Prof. Santosh Singh, and Dr. V. P. Srivastava for creating my interest in the chemistry research field. Words cannot express how grateful I am to my family: my parents, Pt. Saty Nath Tripathi and Hirawati Devi for educating me the best possible way, for unconditional support, blessings, constant love and encouragement to pursue my interests. I express my deepest gratitude to my sisters, brother Sachchida Nand and sister-in-law Renu for believing in me and selflessly encouraging me to explore new directions in life and seek my own destiny. Credit to smiles on my face goes to my all niece and my nephew specially Amit, Shivangi, Swati, Shashwat and Swara who has been the light of our life and has given me the extra strength and motivation to get things done. Finally, and most importantly, I would like to thank my wife Jyoti. Her support, encouragement, quiet patience and unwavering love were undeniably the basis upon which the past three years of my life have been built.,

Last, but not the least, I would like to thank the almighty God for showers of blessings and for providing me strength and courage to face the challenges laid out before me.

Krishna Nand Tripathi

ABSTRACT

The thesis entitled “Photoinduced regioselective C–C bond formation and transition metal-catalyzed C–H activation” deals with the development of chemical reactions for the synthesis of heterocyclic molecules *via* a relatively greener approach. Visible light catalyzed selective construction of carbon–carbon bond has started to garner huge attention from chemists recently. The attractiveness of such selective photoreactions is attributed to the synthetic utility for the development of new reactions. We have developed regioselective C–C bond formation in heterocyclic compounds, which leads to the construction of analogues to biologically active molecules.

This dissertation comprises of five chapters. In the **first chapter**, the importance of photoredox catalysis, photophysical and electrochemical process and types of photocatalysts with emphasis on photoredox catalysis has been described. In the second part of the introduction chapter, discussions on various types of oxidative coupling reactions employed in C–C bond formation with the main emphasis on the dehydrogenative coupling of aromatic compounds is presented.

Chapter two describes a metal-free and mild, photoinduced decarboxylative alkylation of coumarins at C4-position. Photoinduced single electron transfer has been initiated by utilizing the visible-light absorptivity of Eosin Y for a reductive generation of alkyl radicals from *N*-(acyloxy)-phthalimide esters. Depending on the nature of *N*-(acyloxy)-phthalimide esters (primary, secondary, and tertiary carboxylic acid derived), several saturated and unsaturated C4-alkylated coumarins were synthesized. To showcase the utility of the transformation for diversifying carboxylic acids containing natural-products and drugs, also have been used for the synthesis of coumarins derivative.

In **chapter three** development of Eosin Y catalyzed, photoinduced deaminative C4-position alkylation of coumarins *via* C–N bond activation has been reported. We have attempted to explore the reactivity of the radical intermediates generated by photocatalytic deaminative alkylpyridinium salts with 3-substituted coumarins and its analogues. Various secondary and benzylic amines derived pyridinium salts provided several exclusive unsaturated C-4 alkylated coumarins. Further, control experiments studies supported a radical based mechanism for the selective deaminative alkylation.

Chapter four deals with visible light-mediated regioselective functionalization of coumarins. This methodology offered selective functionalization of the benzo ring rather than a heterocyclic ring of coumarins. Several tertiary carboxylic acids derived *N*-(acyloxy)phthalimide (NHPI) afforded exclusive C7-alkylated coumarins. Other carboxylic acid-containing drug derivative NHPI also provided corresponding coumarin products. All synthesized coumarin derivatives in this chapter are analogous to biological and pharmaceutical molecules.

In the **fifth chapter**, a transition metal-catalyzed regioselective, intramolecular, dehydrogenative cross-coupling reactions at the C5 and C2 position of pyrrole derivatives have been described for the synthesis of polyheterocyclic arenes, which is further divided into three subchapters.

In **chapter 5a**, we have disclosed a Cu-catalyzed, intramolecular dehydrogenative cross-coupling in 3-substituted and 3',4'-disubstituted pyrrole-azole systems. The site-selective C2-H activation of unsymmetrically substituted pyrroles in presence of C5 position has been successfully achieved in moderate to good yields for direct access to six- and seven-membered annulated pyrroles, which is an important scaffold, considering the wide biological activity of nitrogen-containing heterocycles.

Chapter 5b described the synthesis of polycyclic pyrrole-azole structures possessing fused six-membered and seven-membered rings *via* ligand-enabled, Pd-catalyzed, site-selective, intramolecular cross-couplings of *N*-substituted pyrrole-azoles. C5-H activation in the presence of a reactive C2-H remains a challenge that needs to be addressed and this was targeted to be resolved through the present approach by specifically generating the cyclized products with high selectivity. The featured methodology provides a novel disconnection for the synthesis of pyrrole containing alkaloids and medicinal compounds.

Chapter 5c deals a highly efficient and regioselective palladium-catalyzed annulation protocol for a series of linear and terminally substituted 1,2 and 1,3-diheteroaryl alkanes to corresponding polyheterocyclic arenes. Intramolecular oxidative coupling involving double C(sp²)-H bond functionalization provides feasible access to a bi-heteroaryl system annulated into a six-membered ring. The methodology is not only restricted to six-membered annulations but also extended to the synthesis of the seven-membered ring with bi-heteroaryl core.

सार

थिसिस "फोटोइंड्यूज्ड रिजियोसेलेक्टिव सी-सी बॉन्ड गठन और संक्रमण धातु-उत्प्रेरित सी-एच सक्रियण" नामक एक अपेक्षाकृत हरियाली दृष्टिकोण के माध्यम से हेटेरोसायक्लिक अणुओं के संश्लेषण के लिए रासायनिक प्रतिक्रियाओं के विकास से संबंधित है। कार्बन-कार्बन बॉन्ड के दर्शनीय प्रकाश उत्प्रेरित चयनात्मक निर्माण ने हाल ही में केमिस्टों से भारी ध्यान आकर्षित करना शुरू कर दिया है। इस तरह के चयनात्मक फोटोरिएक्शन के आकर्षण को नई प्रतिक्रियाओं के विकास के लिए सिंथेटिक उपयोगिता के लिए जिम्मेदार ठहराया जाता है। हमने हेट्रोसाइक्लिक यौगिकों में रिजियोसेलेक्टिव सी-सी बॉन्ड गठन विकसित किया है, जो जैविक रूप से सक्रिय अणुओं के लिए एनालॉग्स के निर्माण की ओर जाता है।

इस शोध प्रबंध में पाँच अध्याय शामिल हैं। पहले अध्याय में, फोटोरिडॉक्स कैटेलिसिस के आधार पर, फोटोरिडॉक्स कैटेलिसिस, फोटोफिजिकल और इलेक्ट्रोकेमिकल प्रक्रिया और फोटोकैटलिस्ट्स के प्रकारों के महत्व का वर्णन किया गया है। परिचय अध्याय के दूसरे भाग में, सुगंधित यौगिकों के निर्जलीकरणीय युग्मन पर मुख्य जोर देने के साथ सी-सी बंध गठन में कार्यरत विभिन्न प्रकार के ऑक्सीडेटिव युग्मन प्रतिक्रियाओं पर चर्चा प्रस्तुत की गई है।

अध्याय दो में सी ४-स्थित क्यूमेरिन के एक धातु-मुक्त और सौम्य, फोटोइंड्यूज्ड डीकार्बाक्सिलेटिव एल्काइलेशन का वर्णन किया गया है। एन-(एसाइक्लोक्सी)-थैलिडामाइड एस्टर से एल्काइल रेडिकल की एक रिडक्टिव जेनरेशन के लिए इओसिन वाई के दृश्य-प्रकाश अवशोषण का उपयोग करके फोटोइंडिटेड सिंगल इलेक्ट्रॉन ट्रांसफर किया गया है। एन-(एसाइक्लोक्सी)-थैलिडामाइड एस्टर (प्राथमिक, द्वितीयक, और तृतीयक कार्बोक्जिलिक एसिड व्युत्पन्न) की प्रकृति के आधार पर, कई संतृप्त और असंतृप्त सी ४-अल्केलाइज्ड क्यूमेरिन को संश्लेषित किया गया है। प्राकृतिक-उत्पादों और दवाओं से युक्त कार्बोक्जिलिक एसिड में विविधता लाने के लिए परिवर्तन की उपयोगिता को दर्शाने के लिए, क्यूमेरिन व्युत्पन्न के संश्लेषण के लिए भी उपयोग किया गया है।

अध्याय तीन में इओसिन वाई उत्प्रेरित, सी-एन बांड सक्रियण के माध्यम से फोटोइंड्यूज्ड डीएमिनेटिव क्यूमेरिन के सी ४-स्थिति अल्काइलेशन की सूचना दी गई है। हमने ३-स्थानापन्न युग्मकों और इसके एनालॉग्स के साथ फोटोकैटलिटिक डीएमिनेटिव अल्काइलीपीरिडिनियम लवण

द्वारा उत्पन्न मध्यवर्ती की प्रतिक्रिया का पता लगाने का प्रयास किया है। विभिन्न माध्यमिक और बेन्ज़ाइल एमीन व्युत्पन्न पिरिडिनियम लवण कई विशिष्ट असंतृप्त सी-४ अल्काइलेटेड क्यूमेरिन प्रदान करते हैं। इसके अलावा, नियंत्रण प्रयोगों के अध्ययन ने चयनात्मक डीएमिनेटिव अल्काइलेशन के लिए एक रेडिकल आधारित तंत्र का समर्थन किया।

अध्याय चार में क्यूमेरिन के दृश्य प्रकाश की मध्यस्थता वाले प्रतिगामी कार्यात्मककरण के बारे में बताया गया है। इस पद्धति ने युग्मकों के विषमकोणीय वलय के बजाय बेन्जो वलय के चयनात्मक क्रियाकलाप की पेशकश की। कई तृतीयक कार्बोक्जिलिक एसिड व्युत्पन्न एन-(एसाइक्लोक्सी)-थैलिडामाइड (एनएचपीआई) अनन्य सी७-अल्काइलेटेड क्यूमेरिन प्रदान करते हैं। अन्य कार्बोक्जिलिक एसिड युक्त दवा व्युत्पन्न एनएचपीआई भी इसी प्रकार के क्यूमेरिन उत्पादों को प्रदान करता है। इस अध्याय में सभी संश्लेषित क्यूमेरिन यौगिक जैविक और दवा के अणुओं के अनुरूप हैं।

पांचवें अध्याय में, एक संक्रमण धातु-उत्प्रेरित प्रतिगामी, इंट्रामोलीक्युलर, पायरोल डेरिवेटिव के सी५ और सी२ की स्थिति पर निर्जलीकरण संबंधी क्रॉस-कपलिंग प्रतिक्रियाओं से पॉलीहेट्रोसाइक्लिक एरीनो के संश्लेषण को वर्णित किया गया है, जिसे आगे तीन उपचारों में विभाजित किया गया है।

अध्याय ५अ में, हमने ३-प्रतिस्थापित और ३', ४'- द्विप्रतिस्थापित पायरोल-एज़ोल सिस्टम में एक कापर -उत्प्रेरित, इंट्रामोलीक्युलर डिहाइड्रोजनेटिव क्रॉस-कपलिंग का खुलासा किया है। सी-५ की उपस्थिति में साइट-चयनात्मक सी२-एच सक्रियण असममित पायरोल में अच्छी पैदावार के साथ सफलतापूर्वक प्राप्त किया गया है जो कि सीधा ६ और सात-सदस्यीय पायरोल चक्र युक्त पिरामिड प्रदान करता है, और व्यापक जैविक गतिविधि को देखते हुए एक नाइट्रोजन युक्त हेट्रोसायकल की महत्वपूर्ण पाइ है।

अध्याय 5 बी में पॉलीसाइक्लिक पिरामिड-एज़ोल संरचनाओं के संश्लेषण का वर्णन किया गया है जिसमें लिगैंड-सक्षम, पैलेडियम-उत्प्रेरित, साइट-चयनात्मक, एन-प्रतिस्थापित पाइरोल-एज़ोल्स की इंट्रामोलीक्युलर क्रॉस-कपलिंग के माध्यम से छह-सदस्यीय और सात-सदस्यीय छल्ले प्राप्त होते हैं। प्रतिक्रियाशील सी२-एच की उपस्थिति में सी५-एच सक्रियण एक चुनौती है जिसे संबोधित करने की आवश्यकता है और इसे विशेष रूप से उच्च चयनात्मकता के साथ चक्रीय

उत्पादों को उत्पन्न करके वर्तमान दृष्टिकोण के माध्यम से हल करने का लक्ष्य रखा गया था। चित्रित कार्यप्रणाली अल्कलॉइड और औषधीय यौगिकों वाले पिरामिड के संश्लेषण के लिए यह एक नवीन वियोग प्रदान करता है।

अध्याय ५सी में रेखिक और अन्तिम छोर रूप से प्रतिस्थापित १,२ और १,३-डायथेरोयेरल अल्केन्स की एक श्रृंखला के लिए एक अत्यधिक कुशल और प्रतिगामी पैलेडियम-उत्प्रेरित कुंडलीकरण प्रोटोकॉल संबंधित पालीहेट्रोसायक्लिक एरीन्स को प्रदान करता है। इंट्रामोल्युलर ऑक्सीडेटिव युग्मन जिसमें डबल सी (एसपी^२)-एच बॉन्ड कार्यतरुव्यवस्था शामिल है, एक छह-सदस्यीय रिंग में घोषित द्विहेट्रोएरिल सिस्टम के लिए संभव पहुंच प्रदान करता है। कार्यप्रणाली केवल छह-सदस्यीय घोषणाओं तक ही सीमित नहीं है, बल्कि द्विहेट्रोसायक्लिक कोर के साथ सात-सदस्यीय चक्र के संश्लेषण तक विस्तारित है।

CONTENTS

Certificate	i
Acknowledgements	ii
Abstract	iv
Contents	ix
List of Figures	xii
List of Tables	xiv
List of Schemes	xv
List of Abbreviations	xix
CHAPTER 1. Introduction	
1.1 Prologue	2
1.2 Photoredox catalysis	3
1.2.1 Why photochemistry?	3
1.2.2 Why visible light?	3
1.3 Photophysical and electrochemical considerations	4
1.3.1 Photophysical properties of photoredox catalysis	5
1.3.2 Electrochemical consideration	6
1.4 Mechanisms of Photocatalysis:	8
1.4.1 Single electron transfer (SET)	9
1.4.2 Electron donor-acceptor (EDA) Complexes	10
1.4.3 Hydrogen atom transfer (HAT)	11
1.5 Photocatalyst	11
1.5.1 Transition metal photoredox catalysts	12
1.5.2 Organophotoredox Catalysts	13
1.6 Cross-dehydrogenative coupling (CDC) reactions	18
1.6.1 CDC <i>via</i> Heck type mechanism	19
1.6.2 Direct arylation	20
1.6.3 CDC <i>via</i> ionic intermediate	21
1.6.4 CDC <i>via</i> radical intermediate	21
1.7 Overview of the Thesis	26
1.7.1 Organo photoinduced decarboxylative alkylation of coumarins	26
1.7.2 Photoinduced deaminative C4-alkylation of coumarins	27
1.7.3 Regioselective C7-alkylation of coumarins	27
1.7.4 Transition metal-catalyzed regioselective C-H activation	28
1.7.4.1 Synthesis of pyrrole annulated heterocycles <i>via</i> a copper catalyzed site-selective dehydrogenative cross coupling	28
1.7.4.2 Pd-catalyzed regioselective intramolecular dehydrogenative C-5 cross-coupling in an <i>N</i> -substituted pyrrole- Azole System	28
1.7.4.3 Palladium-Catalyzed Oxidative Annulation of Pyrrolyl-alkyl-1 <i>H</i> -azoles: Towards the Synthesis of Polyheterocyclic Arenes	29

1.8 References	30
CHAPTER 2: Organo Photoinduced Decarboxylative Alkylation of Coumarins	
2.1 Introduction	34
2.2 Objectives	41
2.3 Results and Discussion	42
2.4 Conclusions	47
2.5 Experimental Section	48
2.5.1 General information	48
2.5.2 Preparation of starting materials	48
2.5.3 General Methods for decarboxylative alkylation of coumarins	51
2.5.4 Mechanistic investigation	52
2.6 Crystallographic data	63
2.7 ¹H and ¹³C spectra of compounds	64
2.8 References	98
CHAPTER 3. Photoinduced Deaminative C4-Alkylation of Coumarins	
3.1 Introduction	102
3.2 Objectives	107
3.3 Results and Discussion	107
3.4 Conclusions	112
3.5 Experimental Section	113
3.5.1 General information	113
3.5.2 Preparation of starting materials	113
3.5.3 General methods of deaminative alkylation reaction	115
3.6 Crystallographic data	119
3.7 ¹H and ¹³C spectra of compounds	120
3.8 References	134
CHAPTER 4. Regioselective C7-Alkylation of Coumarins	
4.1 Introduction	137
4.2 Objectives	141
4.3 Results and Discussion	144
4.4 Conclusions	148
4.5 Experimental Section	149
4.5.1 General Information	149
4.5.2 Preparation of starting materials	149
4.5.3 General procedure of the C7-alkylation coumarins	151
4.6 Crystallographic data	156
4.7 ¹H and ¹³C spectra of compounds	157
4.8 References	174
CHAPTER 5a. Synthesis of pyrrole annulated heterocycles <i>via</i> a copper catalyzed site-selective dehydrogenative cross coupling	

5a.1 Introduction	177
5a.2 Objectives	182
5a.3 Results and Discussion	183
5a.4 Conclusions	188
5a.5 Experimental Section	189
5a.5.1 General information	189
5a.5.2 Preparation of starting materials	189
5a.5.3 General procedure for dehydrogenative cross coupling of <i>N</i> -alkylated 3-pyrrolicarboxaldehyde	196
5a.6 ¹H and ¹³C spectra of compounds	202
5a.7 References	233
5b. Pd-Catalyzed Regioselective Intramolecular Dehydrogenative C-5 Cross Coupling in an <i>N</i>-substituted Pyrrole-Azole System	
5b.1 Introduction	237
5b.2 Objective	240
5b.3 Results and Discussion	241
5b.4 Conclusions	247
5b.5 Experimental Section	248
5b.5.1. General Information	248
5b.5.2 Preparation of starting materials	248
5b.5.4 General procedure for dehydrogenative cross coupling of <i>N</i> -alkylated pyrrole-3-carboxaldehydes	259
5b.6 Crystallographic data	268
5b.7 ¹H and ¹³C spectra of compounds	269
5b.8 References	322
5c. Palladium-Catalyzed Oxidative Annulation of Pyrrolyl-alkyl-1<i>H</i>-azoles: Towards the Synthesis of Polyheterocyclic Arenes	
5c.1 Introduction	326
5c.2 Objectives	329
5c.3 Results and Discussion	330
5c.4 Conclusions	334
5c.5 Experimental Section	335
5c.5.1. General information	335
5c.5.2 Preparation of starting materials	335
5c.5.3 General procedure for intramolecular dehydrogenative cross coupling of Pyrrolyl-alkyl-1 <i>H</i> -azoles	340
5c.6 ¹H and ¹³C spectra of compounds	345
5c.7 References	375
Bio-data	378

List of Figures

Figure No.	Figure Caption	Page No.
1.2.1	Wavelength of light - visible spectrum	3
1.2.2	Papers published per year in the field of organic photoredox catalysis	4
1.3.1	Energy levels of a typical organic molecule and the photophysical processes	5
1.4.1.1	General example of an oxidative quenching catalytic cycle	9
1.4.1.2	General example of a reductive quenching catalytic	10
1.5.1	Simplified molecular orbital depiction of Ru(bpy) ₃ ²⁺ photochemistry	12
1.5.2	Simplified molecular orbital depiction of Ir(ppy) ₃ photochemistry	13
1.5.2.1	Common organic photoredox catalysts	14
1.6.1	General scheme for cross-dehydrogenative coupling	18
1.6.2	Transition metal-based coupling	19
1.6.3	General mechanism for Pd-catalyzed cross-dehydrogenative coupling <i>via</i> Heck-type pathway	19
1.6.4	General mechanism for cross-dehydrogenative coupling involving direct arylation	20
2.1.1	Some examples of biologically active coumarin derivatives	38
2.5.4.1	Fluorescence spectra of EY (100 μM) in DCM	52
2.5.4.2	Fluorescence spectra collected by using 520 nm excitation wavelengths at different interval of time	52
2.5.4.3	Cyclic voltammogram of 3-cyanocoumarin (146a) in CH ₃ CN under argon	53
2.6.1	ORTEP diagram of compound 148a . Thermal ellipsoids are drawn at the 50% probability level	63
2.6.2	ORTEP diagram of compound 149a . Thermal ellipsoids are drawn at the 50% probability level	63
3.6.1.1	Single crystal X-ray structure of compound 183c	119
4.1.1	Few biological active compounds containing 7-substituted coumarins	140
4.2.1	Active sites in coumarins	142
4.6.1.1	Single Crystal X-ray Structure of Compound 221e	156
5a.1.1	Few pyrrole containing biological active compounds	177
5a.2.1	Selectivity issues associated with cross dehydrogenative coupling (CDC) of pyrrole-azole system	182
5a.3.1	Mechanistic approach of dehydrogenative cross coupling	187
5a.3.2	Single Crystal X-ray Structure of 264d	188
5b.3.1	Proposed mechanism for regioselective cyclization	245

5b.3.2	Single Crystal X-ray Structure of 299	246
5b.6.1	Molecular structure of compound 299q	268
5c.1.1	Representative bioactive compounds of imidazo-pyrrole, imidazo-pyrrolo-pyridine and other synthetically evolved polyheterocycles	326
5c.3.1	Proposed mechanism for intramolecular dehydrogenative coupling	334
5c.3.2	Single Crystal X-ray Structure of 327a	334

List of Tables

Table No.	Table Caption	Page No.
2.3.1	Selected optimization reaction condition results	43
2.3.2	Scope of decarboxylative 4-position alkylation of coumarins with various secondary and tertiary carboxylic acid derived NHPI esters	44
2.3.3	Scope of decarboxylative 4-position alkylation of coumarins with various primary carboxylic acid derived NHPI esters	45
3.3.1	Selected optimization reaction condition results	108
3.3.2	Scope of deaminative 4-Position alkylation of coumarins with various Secondary and benzylic amine derived alkylpyridinium salts	109
4.3.1	Selected optimization reaction condition results	145
4.3.2	Scope of decarboxylative 7-position alkylation of coumarins with various tertiary carboxylic acid derived NHPI esters	146
5a.3.1	Optimization of reaction conditions	184
5a.3.2	Substrate scope for dehydrogenative cross-coupling	186
5b.3.1	Optimization of cross-coupling reaction	242
5b.3.2	Substrate scope for intra-molecular cross-coupling reaction	243
5c.3.1	Optimization of the reaction conditions	331
5c.3.2	Substrate scope for cross coupling reaction	332

List of Schemes

Scheme No.	Scheme Caption	Page No.
1.5.2.1	DCN catalyzed oxidative α -arylation of ketones	15
1.5.2.2	Radical conjugate addition reaction	15
1.5.2.3	DDQ promoted Hydroxylation of Benzene	15
1.5.2.4	Pyrylium-catalyzed Diels-Alder reaction	16
1.5.2.5	Aerobic C–H oxidation of cyclic hydrocarbons	17
1.5.2.6	Redox potentials of eosin Y	18
1.6.1	Pd-catalyzed oxidative ortho-alkenylation of anilides	20
1.6.2	Pd-catalyzed oxidative 2-arylation of heterocycles	21
1.6.3	Iron-catalyzed cross-dehydrogenative coupling of ethers and <i>N</i> -nucleophiles <i>via</i> Ionic Intermediates pathway	21
1.6.4	Cu-catalyzed cross-coupling of tetrahydroisoquinolines with aryl	22
1.6.5	Pd(II)-catalyzed oxidative coupling of heteroarenes with terminal alkynes	22
1.6.6	Palladium-catalyzed oxidative coupling of thiophene with terminal alkynes	23
1.6.7	Cu(II)-catalyzed oxidative alkynylation of trimethylamine <i>N</i> -oxides	23
1.6.8	Cu-catalyzed asymmetric oxidative cross-coupling	24
1.6.9	Cu-catalyzed oxidative arylation of isochromanes	24
1.6.10	Fe(II)-catalyzed oxidative coupling of indoles with diphenylmethanes	24
1.6.11	Pd-catalyzed oxidative cross-coupling of <i>N</i> -methoxybenzamides with aryl ring	25
1.6.12	Pd-catalyzed oxidative cross-coupling of polyfluoroarenes with arene	25
1.6.13	Oxidative coupling of cyclic benzylic ethers with methyl ketones	25
1.6.14	Oxidative coupling of benzylic alcohols and acetonitrile	26
2.1.1	Radical generation from <i>N</i> -(acyloxy)-phthalimide esters and acids	34
2.1.2	Alkylation of styrene from <i>N</i> -(acyloxy)-phthalimide esters	35
2.1.3	Oxyalkylation of styrene with <i>N</i> -(acyloxy)-phthalimide esters	35
2.1.4	Decarboxylative Heck-type coupling of carboxylic acids with alkenes	35
2.1.5	Photoinduced Michael addition of glyoxylic acid acetals	36
2.1.6	Organophotoinduced decarboxylative 1,4-addition of aliphatic carboxylic acids	36
2.1.7	Asymmetric decarboxylation arylation of amino acids	36
2.1.8	Decarboxylative fluorination of carboxylic acids with Selectfluor	37
2.1.9	Photoinduced vinylation of carboxylic acids	37
2.1.10	Intramolecular decarboxylative allylation of allyl esters	37
2.1.11	Decarboxylative ynonylation of ketoacids	38

2.1.12	Heck coupling of coumarins with acrylates	39
2.1.13	Dehydrogenative arylation of coumarins	39
2.1.14	Cu(OTf) ₂ catalyzed alkylation of coumarins	40
2.1.15	Oxidative cross-coupling of coumarins	40
2.1.16	Cu(OAc) ₂ catalyzed benzylation of coumarins	40
2.1.17	C-3 alkylation of coumarins with aliphatic acids	40
2.1.18	Metal free C-4 alkylation of coumarins	41
2.1.19	Di-functionalization of coumarins	41
2.2.1	Decarboxylative 4-position alkylation of coumarins	42
2.3.1	Plausible mechanism of alkylation	46
2.3.2	Control Experiment	46
3.1.1	Reduction of alkylpyridinium salt through SET	103
3.1.2	Suzuki cross-coupling of Katritzky salts	103
3.1.3	Negishi cross-coupling of alkylzinc halides and Katritzky salts	104
3.1.4	Reductive cross-coupling using of alkylpyridinium salts	104
3.1.5	Deaminative alkylation of heteroarenes	105
3.1.6	Desulfonative alkynylation with Katritzky salts	105
3.1.7	Allylation of pyridinium salts	105
3.1.8	Heck type reaction of Katritzky salts	106
3.1.9	C4 alkylation of coumarin with diazoalkanes	106
3.1.10	Alkylation of coumarins <i>via</i> Negishi cross coupling	106
3.1.11	Alkylation of coumarins with boronic acid	107
3.2.1	Photoinduced deaminative alkylation of coumarins	107
3.3.1	Control studies for mechanistic insight	110
3.3.2	Plausible mechanism of deaminative alkylation	111
4.1.1	Ni(0)–Al(III) catalyzed <i>para</i> -alkenylation of pyridine	138
4.1.2	<i>para</i> -functionalization of unprotected phenols	138
4.1.3	Template assisted <i>para</i> -functionalization of toluene derivatives	138
4.1.4	Cobalt-catalyzed C4 alkylation of quinolines	139
4.1.5	Ruthenium-catalyzed C5-selective tosylation of quinolines	139
4.1.6	Regioselective direct C-4 functionalization of indoles	140
4.1.7	Old strategy for synthesis of coumarins	141
4.2.1	Ir-catalyzed asymmetric vinylogous allylic alkylation	142
4.2.2	Enantioselective vinylogous allylic alkylation	142
4.2.3	Asymmetric ring-opening reaction of coumarin with oxabicyclo	143
4.2.4	Vinylogous decarboxylative Michael reaction with 3-cyano-4-methylcoumarins	143
4.2.4	Regioselective C7-alkylation of coumarins	144
4.3.1	Radical trapping experiment	147
4.3.2	Plausible mechanism of alkylation	147
5a.1.1	Copper-catalyzed dehydrogenative arylation of thiophene	177

5a.1.2	Copper-catalyzed <i>meta</i> -arylation of α -arylketones	178
5a.1.4	Catalyst-controlled regioselective C4/C8 arylation of isoquinolones	178
5a.1.5	Remote C-H activation of arenes	178
5a.1.6	Regioselective synthesis of biaryl heteroaromatics	179
5a.1.7	Palladium-catalyzed C-2 arylation of chromones	179
5a.1.8	Dehydrogenative cross-coupling of heteroarenes	180
5a.1.9	Regioselective coupling of azoles with 2-phenyl pyridines	180
5a.1.10	Dehydrogenative-coupling of benzothiazoles with thiazoles	180
5a.1.11	Decarboxylative direct arylation of azoles	180
5a.1.12	Cu-promoted intermolecular direct biaryl coupling	181
5a.1.13	C2-benzylation of Indoles with alkylarenes	181
5a.2.1	Solvent controlled regioselective arylation	182
5a.2.2	Copper catalyzed site-selective dehydrogenative cross-coupling reaction	183
5a.5.1	Coupling of 1-(2- or 3-haloalkyl)-1 <i>H</i> -azole derivatives with 3-substituted and 3,4-disubstituted pyrroles	190
5a.5.2	Coupling of 1-(2-chloroethyl)-1 <i>H</i> -pyrrole derivatives with substituted azoles	191
5a.5.3	Dehydrogenative cross-coupling of heteroaromatics	196
5b.1.1	Palladium-catalyzed regioselective C3 arylation of <i>N</i> -acetylindoles	237
5b.1.2	Regioselectivity in oxidative arene cross-coupling	238
5b.1.3	Palladium-catalyzed cross-coupling of aromatics	238
5b.1.4	Aerobic heterocoupling of arenes	238
5b.1.5	Intramolecular oxidative coupling of indole and benzimidazole	239
5b.1.6	Palladium-catalyzed solvent controlled regioselective alkenylation of indole	239
5b.1.7	Ligand controlled regioselective arylation of thiophene	240
5b.1.9	Regioselective alkenylation of pyrrole	240
5b.2.1	Regioselectivity in dehydrogenative intramolecular cross-coupling reaction	241
5b.3.1	Regioselective cyclization in the presence of TEMPO or other coupling partners	245
5b.5.1	Coupling of 1-(2-haloalkyl)-1 <i>H</i> -azole derivatives with 3-substituted and 3,4-disubstituted pyrroles	249
5b.5.2	Coupling of 1-(2-chloroethyl)-1 <i>H</i> -pyrrole derivatives with substituted azoles	250
5b.5.3	Dehydrogenativecross coupling of heteroaromatics	259
5c.1.1	Palladium-catalyzed endo ring closure of acyclic alkenes	327
5c.1.2	Palladium-catalyzed dehydrogenative arylation of triazole	327
5c.1.3	Intramolecular oxidative-coupling of pyrrole with an unactivated methyl group	328
5c.1.4	Phosphoric acid catalyzed intramolecular aza-Friedel–Crafts reaction	328
5c.1.5	Palladium-catalyzed regioselective cyclization of <i>N</i> -allyl-pyrrolo-2-carboxamides	328

5c.1.6	Gold-catalyzed synthesis of pyrazolo-pyrrolo-pyrazine	329
5c.1.7	Synthesis of pyrrolo[1,2- <i>a</i>]pyrazines from <i>N</i> -propargyl(pyrrolyl) enaminones	329
5c.2.1	Oxidative annulation of pyrrolyl-alkyl-1 <i>H</i> -azoles for the Synthesis of polyheterocyclic arenes	329
5c.3.1	Cyclization in presence of TEMPO and other controlled condition	333
5c.5.1	Coupling of 2-(1 <i>H</i> -pyrrol-1-yl) alkyl 4-methylbenzenesulfonate with substituted azoles	336

List of Abbreviations

Abbreviation	Full form
Ar	Aryl
AcOLi	Lithium acetate
ACN	Acetonitrile
AgOAc	Silver acetate
BF ₃ .OEt ₂	Boron trifluoride etherate
Bn	Benzyl
Boc	<i>tert</i> -butyloxycarbonyl
^t Bu	<i>tert</i> -Butyl
BuLi	n-Butyllithium
Bu ₃ SnH	Tributyltin hydride
CDCl ₃	Deuterated chloroform
CHCl ₂ CHCl ₂	Tetrachloroethane
cm ⁻¹	Wavenumbers
°C	Degrees Celsius
Cu(OAc) ₂	Copper acetate
Cs ₂ CO ₃	Cesium carbonate
CH ₃ ONa	Sodium methoxide
CsF	Cesium fluoride
DCM	Dichloromethane
DIPEA	<i>N,N</i> -diisopropylethylamine
DMA	Dimethylacetamide
DMAP	<i>N, N</i> -Dimethylpyridin-4-amine
DMF	Dimethylformamide
DABCO	1,4-diazabicyclo[2.2.2]octane
DBU	1,8-Diazabicyclo[5.4.0]undec-7-ene
d	Doublet
dd	Doublet of doublets

d ₆ -DMSO	Deuterated dimethyl sulfoxide
δ	Chemical shift
<i>ee</i>	Enantiomeric excess
ESI-TOF	Electrospray ionization - Time-of-flight
EtOAc	Ethyl acetate
EtOH	Ethanol
FTIR	Fourier transform infrared
H ₂ O	Water
HMPA	Hexamethylphosphoramide
h	Hour
In	Indium
In(OTf) ₃	Indium trifluoromethanesulfonate
<i>J</i>	Coupling constant
λ	Wavelength
K ₂ CO ₃	Potassium carbonate
KF	Potassium fluoride
KOH	Potassium hydroxide
KO ^{<i>t</i>} Bu	Potassium <i>tert</i> -butoxide
KOAc	Potassium acetate
La(O ^{<i>i</i>} Pr) ₃	Lanthanum isopropoxide
LDA	Lithium diisopropylamide
LED	Light-emitting diode
LiCl	Lithium chloride
LiHMDS	Lithium bis(trimethylsilyl)amide
min	Minute
MTBE	Methyl <i>tert</i> -butyl ether
m	Multiplet
MBH	Morita-Baylis-Hillman
MHz	Megahertz
mL	Millilitre
μ L	Microlitre

NaOMe	Sodium methoxide
NaOAc	Sodium acetate
PC	Photocatalyst
PhONa	Sodium phenoxide
<i>p</i> -TsOH	<i>para</i> -Toluenesulfonic acid
s	Singlet
Sc(OTf) ₃	Scandium trifluoromethanesulfonate
Na ₂ CO ₃	Sodium carbonate
rt	Room temprature
NaO ^t Bu	Sodium <i>tert</i> -butoxide
TBHP	<i>tert</i> -butyl hydroperoxide
TBAF	Tetra- <i>N</i> -butylammonium floride
TFA	Trifluoroacetoc acid
TFFA	Trifluoroacetic anhydride
TBS	<i>tert</i> -butyldimethylsilyl
TBPB	<i>tert</i> -butylperoxybenzoate
TIPS	Triisopropylsilyl
^t BuOH	<i>tert</i> -Butyl alcohol
THF	Tetrahydrofuran
TMS	Tetramethylsilane
TMSOTf	Trimethylsilyl trifluoromethanesulfonate
TMSAN	Trimethylsilyl acetonirile
Tr	Trityl or triphenylmethyl
UV	Ultraviolet
Yb(OTf) ₃	Ytterbium trifluoromethanesulfonate
Zn	Zinc