LIGHT-INDUCED ORGANIC TRANSFORMATIONS USING HOMOGENEOUS PHOTOCATALYSIS

RITU

DEPARTMENT OF CHEMISTRY

INDIAN INSTITUTE OF TECHNOLOGY DELHI

June 2023

LIGHT-INDUCED ORGANIC TRANSFORMATIONS USING HOMOGENEOUS PHOTOCATALYSIS

by

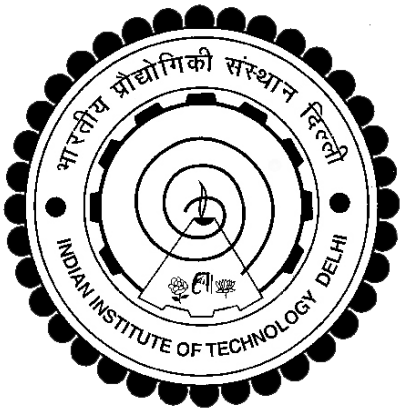
RITU

Department of Chemistry

Submitted

In fulfillment of requirements of degree of Doctor of Philosophy

to the



Indian Institute of Technology Delhi

June 2023

Dedicated to my beloved Parents

CERTIFICATE

This is to certify that the thesis entitled, **"Light-Induced Organic Transformations Using Homogeneous Photocatalysis"** being submitted by **Ms. Ritu** 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 her. **Ms. Ritu** has 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 award of any degree or diploma.

Dr. Nidhi Jain
Professor
Department of Chemistry
Indian Institute of Technology Delhi
New Delhi - 110016

ACKNOWLEDGEMENTS

First and foremost, I am extremely grateful to my supervisor, Prof. Nidhi Jain for her invaluable advice, continuous support, and patience during my PhD study. Her immense knowledge and plentiful experience have encouraged me in all the time of my academic research and daily life. I am grateful to her for providing me with the chance to gain research experience in Germany during my PhD studies. I am also grateful to Prof. Dr. Burkhard König for giving me the opportunity to do some part of my PhD thesis in his working group. I thank him for his guidance, constant support, insightful discussions, and valuable suggestions. I thank both of you for allowing me to visit different places to present my results there. Furthermore, I would also like to thank them for their help and the additional input in writing scientific manuscripts. Their advice on both research as well as on my career has been invaluable. I also must thank the members of my SRC committee, Prof. Ravi Shankar, Prof. Shivajirao L Gholap, and Prof. Sreedevi Upadhyayula for their helpful suggestions and advice in general. I also thank all the past and the present Head of the Department of Chemistry, IITD for the academic support and the facilities provided to carry out my research work. I also thank all the permanent staff members of Prof. Burkhard König's group for their constant help. I would like to thank DST-inspire, and DAAD for providing the research fellowship which allowed me to undertake this research program. I also like to thank my seniors from both labs (Dr. Sharvan Kumar, Dr. Parul Chauhan, Dr. Arun Sharma, Dr. Poonam Sharma, Dr. Preeti Jha, Dr. Raman Kaur, Dr. Alankrita Garia, Dr. Saikat Das, and Dr. Yaming Tian) for their guidance, valuable suggestions and meaningful discussions; my juniors (Vikas Dixit, Rajat Joshi, Charu Sharma, Mansi Sharma, Jatin Grover, Riya Halder, Shruti Rajput, Rohit Kumar, and Anirban) for their help, cooperation and friendly environment in the lab. A special gratitude to Dr. Shravan Kumar for timely guidance and countless support in completing my

research projects. I feel very lucky to have such a senior in my life. A hearty thanks to Mr. Vikas Dixit for his kind support in many ways throughout my PhD. I am also thankful to the other doctoral students of the chemistry department for their friendly acquaintance and cooperation. I would like to thank my colleagues from AK König's Group specially Daniel Kolb, Tobias Karl, Michela Marcon, Florence Babawale, and Rok Narobe for their help and friendly atmosphere in the group. I want to extend my heartfelt thanks to my dear friends from IIT Delhi - Shivani Goyal, Aanchal Jaisingh, Ravneet Kaur, and Rekha Agarwal. Their unwavering motivation, compassionate care, invaluable assistance, and unwavering emotional support have been an immense source of comfort and strength throughout my entire PhD journey. I am thankful for the continuous love and well wishes from my college friends Ritu Yadav, Jonu Yadav, and Nidhi Deswal throughout my life. I am grateful to my parents, Mr. Maha Singh Chahal and Mrs. Savitri Devi, for their unwavering love, encouragement, and blessings. They have provided me with the best education possible and have offered unconditional support throughout my life. I am grateful to both of you for empowering me to aim for the stars and pursue my aspirations. My siblings (Kavita Chahal, and Sandeep Chahal) and my sister-in-law Sunita deserve my wholehearted thanks as well. I must express my deepest gratitude to my elder sister Kavita Chahal for believing in me and selflessly encouraging me to explore new directions in life. Most importantly, I want to express my heartfelt gratitude to my dear friend, Mr. Mohit Singh Maan, for his unending encouragement, emotional support, and unwavering care since the very beginning. Your constant presence and support have made it all possible, and I couldn't have done it without you. Thank you for being there for me during tough times. Finally, thank you, God, for the gift of life and for the countless opportunities and experiences that have shaped me into who I am today.

Ritu

ABSTRACT

The thesis entitled “Light induced organic transformations using homogeneous catalysis” deals with the development of organic transformations for the synthesis of heterocyclic and acyclic molecules in a relatively greener and environmentally friendly way. In recent years, visible light has turned into an ideal tool to achieve chemical reactions. It enables access to highly active intermediates which can form *in situ* without the use of stoichiometric reagents. We have designed ring opening, C-H activation, and desaturation reactions in heterocyclic and acyclic molecules, which leads to the formation of analogous to biologically relevant active compounds.

This dissertation comprises five chapters. Chapter 1 delves into the significance of photochemistry and electrochemical processes, the categorization of photocatalysts, a detailed explanation of the processes involved in photocatalysis, and a precise discussion of some homogeneous photocatalysts utilized in our projects.

In **Chapter 2** a tandem cleavage of carbon–carbon and carbon–nitrogen bonds in imidazo[1,2-*a*] pyridines and imidazo[1,2-*a*] quinolines is reported in the presence of eosin Y and visible light. The ring opening occurs under ambient conditions through singlet oxygen insertion, bond cleavage and CO_2 elimination, and produces *N*-(pyridin-2-yl) amides and *N*-(quinolin-2-yl) amides in high yields. The reaction shows good versatility and does not require strong external oxidants and additives.

Further in continuation to our efforts to develop new strategies in visible light, in **Chapter 3** an efficient C-3 halogenation of quinolin-4-ones is reported with halogenated fluorescein dyes which serve both as a halogen source and photocatalyst. This reaction shows broad substrate scope and gives good to excellent yields of C-3 brominated/iodinated quinolones with eosin Y/rose bengal in green light under ambient conditions. The mechanistic investigations suggest a radical pathway involving the oxidative dehalogenation of the dye in the presence of air.

In **Chapter 4** we report the iridium−nickel dual photocatalytic acceptorless and redox neutral dehydrogenation of aliphatic heterocycles yielding cyclic alkenes without overoxidation at room temperature. Excitation of the iridium photocatalyst initiates the formation of a nickel hydride intermediate that yields alkenes and H_2 via β-hydride elimination. The reaction proceeds regioselectively and the scope was demonstrated by the synthesis of 12 biologically relevant

molecules and drugs. In addition, commercially and easily available N-heterocyclic alkane starting materials were converted into functionalized alkenes of high synthetic and commercial value using the method.

In **Chapter 5** we adapted a previously reported system involving tetrabutylammonium decatungstate (TBADT) as hydrogen atom transfer (HAT) agent and a cobaloxime co-catalyst for dihydrogen evolution for the dehydrogenative preparation of linear enamides and enecarbamates from saturated precursors. The substrate scope includes several natural products and drug derivatives. The reaction does not require noble metal catalysts, exhibits short reaction times compared to previous methods and is suitable for the late-stage functionalization of drug derivatives.

सार

थीसिस शीर्षक "सजातीय कटैलिसीस का उपयोग करके फोटो प्रेरित कार्बनिक परिवर्तन" एक अपेक्षाकृत हरित और पर्यावरण के अनुकूल तरीकों से हेटरोसाइक्लिक और एसाइक्लिक अणुओं के संश्लेषण के लिए कार्बनिक परिवर्तनों के विकास से संबंधित है। हाल के वर्षों में, रासायनिक प्रतिक्रियाओं को प्राप्त करने के लिए दृश्यमान प्रकाश एक आदर्श उपकरण बन गया है। यह अत्यधिक सक्रिय मध्यवर्ती तक पहुंच को सक्षम बनाता है जो स्टोइकोमीट्रिक अभिकर्मकों के उपयोग के बिना सीटू में बना सकते हैं। हमने हेट्रोसायक्लिक और एसाइक्लिक अणुओं में रिंग ओपनिंग, सी-एच एक्टिवेशन और डीसैचुरेशन रिएक्शन तैयार किए हैं, जो जैविक रूप से प्रासंगिक सक्रिय यौगिकों के अनुरूप बनते हैं।

इस शोध प्रबंध में पाँच अध्याय शामिल हैं। पहले अध्याय में फोटोकैमिस्ट्री, इलेक्ट्रोकेमिकल प्रक्रिया, फोटोकैटलिस्ट्स का वर्गीकरण, प्रक्रियाओं की विस्तृत चर्चा में फोटोकैटलिसिस और कुछ सजातीय फोटोकैटलिस्ट्स की सटीक चर्चा शामिल है, जिनका हमने अपनी परियोजनाओं में उपयोग किया था।

अध्याय 2 में इमिडाज़ो [1,2-ए] पाइरिडाइन्स और इमिडाज़ो [1,2-ए] क्विनोलिनों में कार्बन-कार्बन और कार्बन-नाइट्रोजन बांडों के एक अग्रानुक्रम दरार को ईओसिन वाई और दृश्य प्रकाश की उपस्थिति में रिपोर्ट किया गया है। सिंगलेट ऑक्सीजन सम्मिलन, बॉन्ड क्लीवेज और CO_2 उन्मूलन के माध्यम से परिवेशी परिस्थितियों में रिंग ओपनिंग होता है, और उच्च पैदावार में *N*-(पाइरिडिन-2-वाईएल) एमाइड्स और एन-(क्विनोलिन-2-वाईएल) एमाइड्स का उत्पादन करता है। प्रतिक्रिया अच्छी बहुमुखी प्रतिभा दिखाती है और इसके लिए मजबूत बाहरी ऑक्सीडेंट और एडिटिव्स की आवश्यकता नहीं होती है।

इसके अलावा दृश्य प्रकाश में नई रणनीतियों को विकसित करने के हमारे प्रयासों को जारी रखते हुए, अध्याय 3 में क्विनोलिन-4-वनों के एक कुशल सी-3 हलोजनेशन को हलोजनयुक्त फ्लोरेसीन रंगों के साथ रिपोर्ट किया गया है जो हलोजन स्रोत और फोटोकैटलिस्ट दोनों के रूप में सेवा करें। यह प्रतिक्रिया व्यापक सब्सट्रेट गुंजाइश दिखाती है और परिवेशी परिस्थितियों में हरे रंग की रोशनी में ईओसिन वाई/रोज बंगाल के साथ सी-3 ब्रोमिनेटेड/आयोडीनेटेड क्विनोलोन की उत्कृष्ट पैदावार देती है। मशीनी जांच हवा की उपस्थिति में डाई के ऑक्सीडेटिव डिहैलोजनेशन को शामिल करते हुए एक कट्टरपंथी मार्ग का सुझाव देती है।

अध्याय 4 में हम इरिडियम-निकल डुअल फोटोकैटलिटिक एक्सेप्टरलेस और रिडॉक्स न्यूट्रल डिहाइड्रोजनेशन ऑफ एलिफैटिक हेटरोसायकल्स की रिपोर्ट करते हैं, जो कमरे के तापमान पर ओवरऑक्सीडेशन के बिना चक्रीय अल्केन्स का उत्पादन करते हैं। इरिडियम फोटोकैटलिस्ट का उत्तेजना

निकल हाइड्राइड इंटरमीडिएट के गठन की शुरुआत करता है जो एलिकेंस और एच 2 को β-हाइड्राइड उन्मूलन के माध्यम से उत्पन्न करता है। प्रतिक्रिया प्रतिगामी रूप से आगे बढ़ती है और 12 जैविक रूप से प्रासंगिक अणुओं और दवाओं के संश्लेषण द्वारा गुंजाइश का प्रदर्शन किया गया था। इसके अलावा, व्यावसायिक रूप से और आसानी से उपलब्ध एन-हेटेरोसाइक्लिक एल्केन शुरुआती सामग्री को विधि का उपयोग करके उच्च सिंथेटिक और वाणिज्यिक मूल्य के क्रियाशील अल्केन्स में परिवर्तित किया गया।

अध्याय 5 में हमने टेट्राब्यूटाइलमोनियम डेकाटंगस्टेट (TBADT) को हाइड्रोजन परमाणु हस्तांतरण (HAT) एजेंट के रूप में और डायहाइड्रोजन विकास के लिए एक कोबालोक्सिम सह-उत्प्रेरक के रूप में लीनियर एनामाइड्स की डीहाइड्रोजेनेटिव तैयारी के लिए और संतृप्त अग्रदूतों से एनकार्बामेट्स को शामिल करते हुए पहले से रिपोर्ट की गई प्रणाली को अनुकूलित किया। सब्सट्रेट दायरे में कई प्राकृतिक उत्पाद और ड्रग डेरिवेटिव शामिल हैं। प्रतिक्रिया के लिए महान धातु उत्प्रेरक की आवश्यकता नहीं होती है, पिछले तरीकों की तुलना में कम प्रतिक्रिया समय प्रदर्शित करता है और दवा डेरिवेटिव के देर से चरण के कार्यात्मककरण के लिए उपयुक्त है।

TABLE OF CONTENTS

Chapter 3: Photoredox halogenation of quinolones: the dual role of halo-fluorescein dyes.

Chapter 4: Photocatalyzed dehydrogenation of aliphatic *N*-heterocycles releasing dihydrogen.

LIST OF FIGURES

Chapter 1

Chapter 2

Chapter 3

Chapter 4

Chapter 5

LIST OF TABLES

Chapter 2

Chapter 3

Chapter 4

Chapter 5

LIST OF SCHEMES

Chapter 1

Chapter 2

Chapter 3

Chapter 4

Chapter 5

GLOSSARY OF SYMBOLS AND ABBREVIATIONS

Ac	Acetyl
ACN	Acetonitrile
AcOH	Acetic acid
Ar	Aryl
$BF_3.Et_2O$	Borontrifluoride etherate
BNAH	1-Benzyl-1,4-dihydronicotinamide
Boc	*Tert*-butyloxycarbonyl
Br_2	Bromine
Bz	Benzyl
Calcd.	Calculated
CCDC	Cambridge crystallographic data entre
Cat.	Catalyst
CsF	Caesium fluoride
$CDCl_3$	Deuterated chloroform
CH_2Cl_2	Dichloromethane
CT	Charge transfer
$Cu(OTf)_2$	Copper triflate
CuI	Copper iodide

Cu	Copper
CV	Cyclic voltammeter
DABCO	1,4-diazabicyclo[2.2.2]octane
DMA	Dimethylacetamide
DPV	Differential pulse voltammetry
D_2O	Deuterium oxide
DCE	Dichloroethane
DG	Directing group
DMF	Dimethylformamide
DIPEA	Diisopropylethylamine
DMAP	4-Dimethylaminopyridine
DMSO	Dimethylsulfoxide
DABCO	1,4-diazabicyclo[2.2.2]octane
$dmgH_2$	Dimethylglyoxime
DCM	Dichloromethane
DIPEA	*N*, *N*-Diisopropylethylamine
DTBP	Di-*tert*-butyl peroxide
EtOH	Ethanol
EI-MS	Electron ionization mass spectrometry
Et	Ethyl
EtOAc	Ethyl acetate
ESI	Electron spray ionization
EDG	Electron withdrawing group
Equiv.	Equivalent

ET	Energy transfer
EDA	Electron donor-acceptor
EPR	Electron paramagnetic resonance
FCC	Flash column chromatography
FIPA	Phenyliodine bis(trifluoroacetate)
FLP	Frustrated lewis pairs
FID	Flame ionization detector
GC-MS	Gas chromatography–mass spectrometry
Ir	iridium
h	Hour
Hz	Hertz
HOMO	Highest occupied molecular orbital
HPLC	High performance liquid chromatography
HATU	Hexafluorophosphate azabenzotriazole tetramethyl uronium
HRMS	High resolution mass spectroscopy
HCl	Hydrochloric acid
HAT	Hydrogen atom transfer
I_2	Iodine
ISC	Inter-system crossing
LEDs	Light emitting diodes
K_2CO_3	Potassium carbonate
$K_2S_2O_8$	Potassium persulfate
K_2HPO_4	Potassium hydrogen phosphate
KIE	Kinetic isotope effect
LiHMDS	Lithium bis(trimethylsilyl)amide

LRMS	Low resolution mass spectrometry
Mpg-CN	Graphitic carbon nitride
MeOH	Methanol
mL	Mililitre
Mg	Milligram
$MgSO_4$	Magnesium sulphate
mm	Milimetre
Max.	Maximum
Min.	Minimum
min.	Minutes
MLCT	Metal to ligand charge transfer
Me	Methyl
MHz	Megahertz
m/z	Mass by charge ratio
Na_2SO_4	Sodium sulphate
$Na_2S_2O_3$	Sodium thiosulphate
NBS	*N*-Bromosuccinimide
NaOH	Sodium hydroxide
NIS	*N*-Iodosuccinimide
NaI	Sodium iodide
NaBr	Sodium bromide
NMR	Nuclear magnetic resonance
NEt_3	Triethylamine
NH_4Cl	Ammonium chloride
Nu	Nucleophile

OAc	Acetoxy
ORTEP	Oak Ridge Thermal Ellipsoid Plot
OTf	Trifluoromethanesulphonate
PET	Photoinduced electron transfer
$Pd(OAc)_2$	Palladium acetate
POMs	polyoxometalates
PCET	Proton-coupled electron transfer
$POCl_3$	Phosphorus oxychloride
^{i}Pr	Isopropyl
Ph	Phenyl
ppm	Parts per million
p-tolyl	Para-toluene
PXRD	Powder x-Ray crystallography
Ru	Ruthenium
Rf	Retention factor
RT	Room temperature
SET	Single electron ttransfer
S_0	Singlet ground state
S_1	Singlet excited state
SCE	Standard calomel electrode
SOMO	Singly occupied molecular orbital
TBADT	Tetra-n-butylammonium decatungstate
TBAX	tetrabutylammonium halide
TEA	Triethylamine
TEMPO	(2,2,6,6-tetramethylpiperidin-1-yl) oxidanyl

TFA	Trifluoroacetic acid
THF	Tetrahydrofuran
TM	Transition metal
TMEDA	Tetramethylethylenediamine
TFAA	Trifluoroacetic anhydride
T_1	Triplet energy state
TBHP	*tert*-butyl hydroperoxide
Temp.	Temperature
TLC	Thin layer chromatography
Ts	*para*-tolunesulfonyl
TOF	Time of flight
^{t}Bu	*tert*-butyl
TMS	Tetramethylsilane
$TMSCF_3$	Trimethyl(trifluoromethyl)silane
UV	Ultra-violet