

Declaration

I hereby declare that the work presented in this thesis titled '*Visible Light Driven Alkylation and Cascade Annulation Using N-(acyloxy)phthalimides and Aryl Diazo Esters*' submitted to the Indian Institute of Technology Jodhpur in partial fulfillment of the requirements for the award of the degree of Doctor of Philosophy is a bonafide record of the research work carried out under the supervision of Dr. Sandip Murarka. The contents of this thesis in full or in parts, have not been submitted to, and will not be submitted by me to, any other Institute or University in India or abroad for the award of any degree or diploma.

Sudhir Kumar Hota

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P19CY203

Date: 23-12-2024

Certificate

This is to certify that the thesis titled '*Visible Light Driven Alkylation and Cascade Annulation Using N-(acyloxy)phthalimides and Aryl Diazo Esters*' submitted by Sudhir Kumar Hota (P19CY203) to the Indian Institute of Technology Jodhpur for the award of the degree of Doctor of Philosophy, is a bonafide record of the research work done by him under my supervision. To the best of my knowledge, the contents of this report, in full or in parts, have not been submitted to any other Institute or University for the award of any degree or diploma.



Dr. Sandip Murarka
Ph. D. Thesis Supervisor
Date: 23-12-2024

N-heterocycles are fundamental architectures in medicinal chemistry and materials science and are the core structure of many drugs and biologically active compounds. The aim of this work was to develop green and sustainable strategies for preparing and tailoring *N*-heterocycles from alkylating agents, such as *N*-(acyloxy) phthalimides and aryl diazo esters. We describe a visible-light-mediated (4 + 2) cycloaddition reaction to construct fused tetrahydroquinolines using an electron donor-acceptor (EDA) complex. This metal and catalyst-free strategy employs alkyl *N*-(acyloxy)phthalimides and *N*-substituted maleimides to obtain products with outstanding regioselectivity, broad functional group compatibility, and excellent yields. Leveraging this success, we developed an unprecedented organophotoredox-catalyzed method for direct C–H alkylation of 3,4-dihydroquinoxaline-2-ones with NHPI esters. This strategy results in mild, high-yielding, and scalable access to sp³-enriched scaffolds, which is pivotal for pharmaceutical endeavors. We further developed a green and sustainable *N*-alkylation of azauracils using aryl diazo esters in our laboratory. This catalyst and additive-free protocol provided mild compatibility for imide alkylation with many substrates and functional groups. Notably, this useful transformation allows rare three-component reactions to occur in cyclic ethers and will thus likely facilitate the modification of biologically pertinent molecules and natural products. This study offers a new green approach to organic synthesis by employing sustainable synthetic methods. These methodologies take advantage of visible light to induce selective transformations with low-energy input, thus contributing to synthesizing complex molecules of interest in medicinal chemistry.

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"Even the greatest fool can accomplish a task if it were after his or her heart. But the intelligent ones are those who can convert every work into one that suits their taste."

- Swami Vivekananda

He had said- "I have often been asked how we can work if we do not have the passion we generally feel for work. I also thought in that way years ago, but as I grow older and gain more experience, I find it is not true. The less passion there is, the better we work. The calmer we are, the better for us and the more work we can do. When we let loose our feelings, we waste much energy, shatter our nerves, disturb our minds, and accomplish very little work. The energy that ought to have gone out as work is spent as mere feeling, which counts for nothing. It is only when the mind is calm and collected that all of its energy is spent doing good work." Thanks to Vivekananda for his teachings. It helps me a lot during my Ph.D. I am eternally grateful to the many wonderful individuals who have supported and guided me through this five-year journey. This achievement would not have been possible without their unwavering encouragement, motivation, and assistance in helping me reach my goals. I deeply appreciate all those who have touched my life, inspired me through their actions, and lifted me to achieve heights beyond my academic aspirations.

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When I first joined this lab, my knowledge of organic chemistry in a lab was negligible. However, with perseverance, repetition, and a problem-solving mindset—guided by my supervisor's advice—I gradually learned the intricacies of laboratory work. I made countless mistakes during the early days of my Ph.D., but my supervisor's patience and encouragement helped me grow. I am deeply grateful for your invaluable guidance and mentorship throughout this journey. I would also like to sincerely thank Sushanta, Raushan, and Sachin for their kindness and support when I started the lab.

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"Yesterday is history, tomorrow is a mystery, but today is a gift—that's why it's called the present."

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Sudhir Kumar Hota
Ph.D. Student

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List of Symbols

<i>Symbol</i>	<i>Description</i>
E	Energy
h	Planck's Constant
ν	Frequency
K_{EDA}	Rate Constant for EDA
K_{SET}	Rate Constant for SET
K_{BET}	Rate Constant for BET
K_P	Rate Constant for Product
K_f	Rate Constant for Forward Reaction
ω	Coulombic Interaction Term
S_0	Singlet Ground State
S_1	Singlet Excited State
ox	Oxidation
red	Reduction
τ_f	Life Time of Fluorescence
Φ_f	Quantum Yield of Fluorescence
Φ_{ISC}	Quantum Yield of Triplet Formation
τ_T	Life Time of Triplet Excited State
D	Donor
A	Acceptor
λ	Wavelength
h	Hour
δ	Chemical Shift
$^\circ$	Degree
%	Percentage

List of Abbreviations

<i>Abbreviation</i>	<i>Full form</i>
EDA	Electron Donor-Acceptor
CT	Charge Transfer
SET	Single Electron Transfer
CIP	Contact Ion Pair
IP	Ionisation Potential
EA	Electron Affinity
BET	Back Electron Transfer
PC	Photocatalyst
ISC	Inter System Crossing
MO	Molecular Orbital
MLCT	Metal-to-Ligand Charge Transfer
PET	Photoinduced Electron Transfer
TTET	Triplet-Triplet Energy Transfer
HOMO	Highest Occupied Molecular Orbital
LUMO	Lowest Unoccupied Molecular Orbital
LED	Light Emitting Diode
RCC	Radical Cross-Coupling
NHPI	N-(acyloxy)phthalimide
DAIRs	Diaryliodonium Salts
RAEs	Redox-Active Esters
RB	Rose Bengal
DFT	Density Functional Theory
TD-DFT	Time-dependent Density Functional Theory
IM	Intermediate
RNA	Ribonucleic Acid
p-QMs	para-Quinone Methides
HE	Hantzsch Ester
DIPEA	N,N-diisopropylethylamine
DABCO	1,4-Diazabicyclo[2.2.2]octane
DMAP	4-(Dimethylamino)pyridine
DMF	Dimethylformamide
DMSO	Dimethyl Sulfoxide
THF	Tetrahydrofuran
DCM	Dichloromethane
DCE	Dichloroethane
EtOAc	Ethyl Acetate
DDQ	2,3-Dichloro-5,6-dicyano-1,4-benzoquinone
DIBAL	Diisobutylaluminum Hydride
TEMPO	2,2,6,6-Tetramethyl-1-piperidinyloxy
BHT	Butylated Hydroxytoluene
DCC	N,N'-Dicyclohexylcarbodiimide
TLC	Thin-Layer Chromatography
UV	Ultraviolet
NMR	Nuclear Magnetic Resonance
HRMS	High-Resolution Mass Spectrometry
ppm	Parts Per Million
nm	Nanometer
MHz	Megahertz
ACS	American Chemical Society