Multicomponent Synthesis of N-Containing Heterocyclic Compounds

THESIS SUBMITTED IN PARTIAL FULFILLMENT FOR THE AWARD OF DEGREE

DOCTOR OF PHILOSOPHY

By

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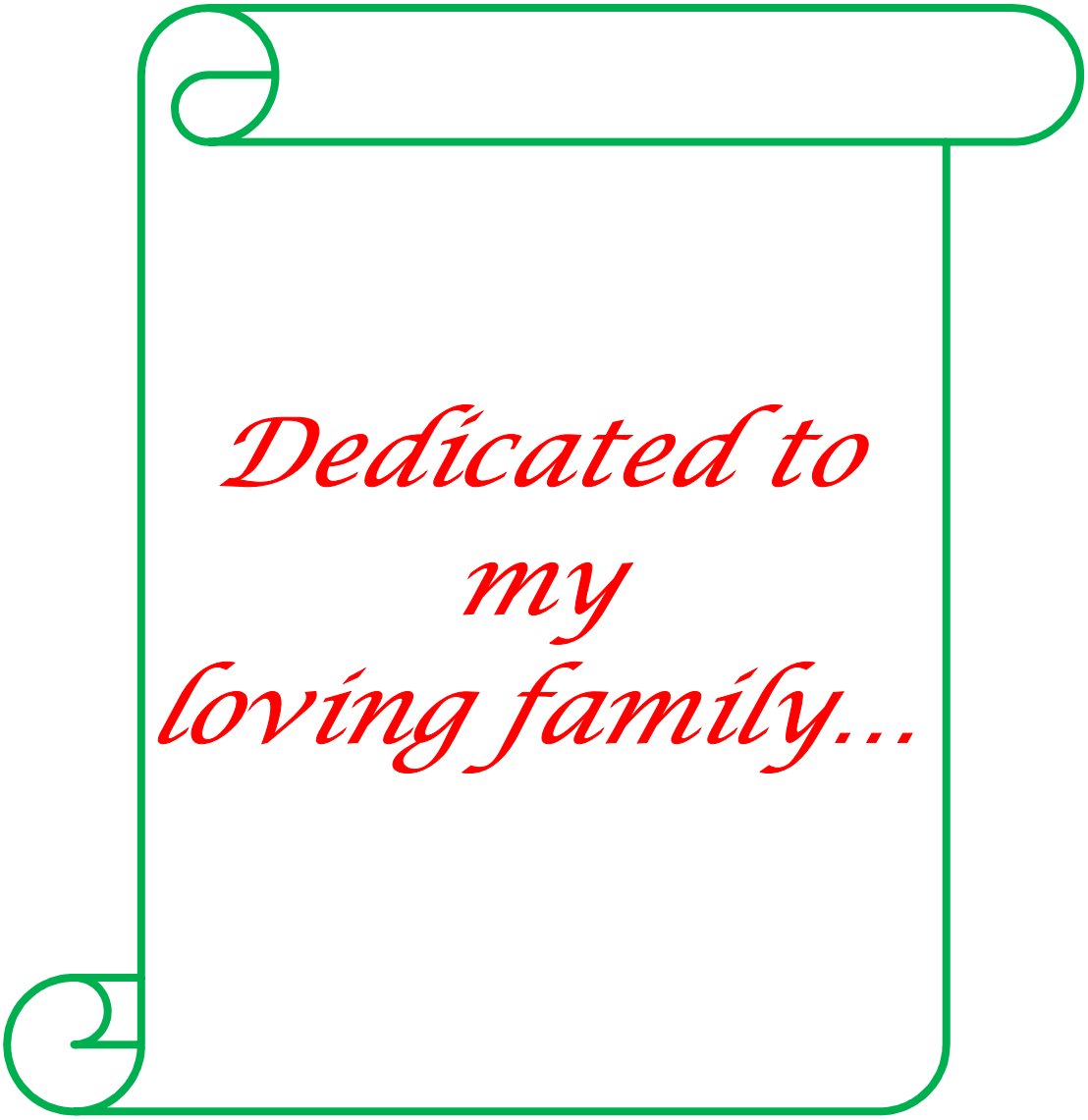
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I, ***" Himanshu Kumar Singh"*** certify that the work embodied in this thesis is my own bonafide work and carried out by me under the joint supervision of ***"Dr. (Mrs.) Sundaram Singh" and "Prof. Vandana Srivastava"*** from ***"July 2017"*** to ***"June 2023"*** at the ***"Department of Chemistry,"*** Indian Institute of Technology, Banaras Hindu University, Varanasi. The matter embodied in this thesis has not been submitted for the award of any other degree/diploma. I declare that I have faithfully acknowledged and given credits to the research workers wherever their works have been cited in this thesis. I further declare that I have not willfully copied any other's work, paragraphs, text, data, results, etc., reported in journals, books, magazines, reports, dissertations, theses, etc., or available at websites and have not included them in this thesis and have not cited as my own work.

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ACKNOWLEDGEMENTS

I give honor to God, the creator, and sustainer of life, for blessing me to be able to pursue and complete this milestone. I thank God for giving me much knowledge, wisdom, and health to complete this work on time.

Foremost, I **"Mr. Himanshu Kumar Singh"** would like to thank my Research Supervisor **"Dr. (Mrs.) Sundaram Singh"** Department of Chemistry, Indian Institute of Technology (Banaras Hindu University), Varanasi, for her wide experience, unrivaled knowledge of chemistry, learned guidance, stimulating discussion, and unstinting moral support which helped me immensely in completing this work in time. I thank her for putting up with my shortcomings and helping me to improve and overcome the same. Particularly, in the final stages, she has sustained me with her paternal care and thoughtful advice. I am beholden to my Co-Supervisor **Prof. Vandana Srivastava** who had been a constant source of support and encouragement.

I am thankful to **Prof. Yogesh Chandra Sharma** Head of the Department and **Prof. Rashmi Bala Rastogi,** and **Prof. Dhanesh Tiwary,** former Head of the Department of Chemistry, Indian Institute of Technology (Banaras Hindu University), for providing necessary lab facilities and a congenial working atmosphere in the Department.

I would also like to thank my RPEC members, **Prof. Vandana Srivastava**, Department of Chemistry, Indian Institute of Technology (Banaras Hindu University), **Dr. Jeyakumar Kandasamy** (former Internal subject expert), **Dr. Manisha Malviya** (Internal subject expert) Department of Chemistry, Indian Institute of Technology (Banaras Hindu University), and **Dr. Abha Mishra** (External subject expert), Department of Biochemical

Engineering, Indian Institute of Technology (Banaras Hindu University), for their valuable suggestions throughout this work.

I'm highly indebted to CIFC, Indian Institute of Technology (BHU) for providing NMR Spectroscopy facility, Department of Chemistry, Banaras Hindu University (BHU) for Mass Spectrometry.

I also wish to thank all the non-teaching staff of the Department of Chemistry, Indian Institute of Technology (BHU) for their cooperation and timely help.

I am thankful to all lab members Dr. Savita Kumari, Dr. Dhirendra Kumar, Dr. Arsala Kamal, Dr. Suresh Kumar Maury, Ambuj Kumar Kushwaha, and Shikha Pandey for their kind cooperation and friendly environment during the entire period of my research.

I would like to express my deepest affection to my father "Mr. Vijay Bahadur Singh", my mother, "Mrs. Prem Lata Singh", younger brother "Shubhanshu Singh", and other family members for their unconditional love, concern, continuous moral support, and encouragement which enabled me to perform my liabilities. I also would like to thank my friends Alok Kumar Singh, Nivedita Shukla, Dr. Suresh Kumar Pandey, Sushant Singh, and Vishal Singh for their affection, prayer, and support as well as hard scolds to focus on my aim.

At the last but not least, I thank to all my well-wishers whose names I may have failed to mention here unintentionally.

Himanshu Kumar Singh

Research Scholar

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Notations	Abbreviations
%	Percentage
<	Less than
>	More than
°	Degree
Å	Angstrom
Ac	Acetyl
Ac_2O	Acetic anhydride
AcOH	Acetic acid
Bn	Benzyl
Bz	Benzoyl group
Boc	Di-*tert*-butyl dicarbonate
brs	Broad singlet
Obser.	Observed
Calc.	Calculated
©	Copyright
$CHCl_3$	Chloroform
CD_3OD	Methanol-d4
$CDCl_3$	Deuterated chloroform
cm	Centimeter
J	Coupling constant
DMF	Dimethylformamide
DMSO-d_6	Deuterated dimethyl sulfoxide
D_2O	Deuterated water
ºC	Degree Celsius
d	Doublet
DMAP	4-Dimethylaminopyridine
DCE	Dichloroethane
DCM	Dichloromethane

dd	Doublet of doublet
ddd	Doublet of doublet of doublet
ddt	Doublet of doublet of triplet
DMSO	Dimethyl sulfoxide
dq	Doublet of quartet
dt	Doublet of triplet
DBU	1,8-Diazabicyclo[5.4.0]undec-7-ene
DABCO	1,4-Diazabicyclo[2.2.2]octane
equiv.	Equivalent
EtOH	Ethanol
EtOAc	Ethyl acetate
EDG	Electron donating group
EWG	Electron withdrawing group
EY	Eosin Y
equiv.	Equivalent
g	Gram; Gravitational force
BAs	Barbituric acids
h	Hour
$Sc(OTf)_3$	Scandium (III) Trifluoromethanesulfonate
H_2DEBA	Diethylbarbituric acid
Hz	Hertz
IR	Infra-Red
LDA	Lithium diisopropylamide
m	Multiplet
H_3BA	Barbituric acid
MeOH	Methanol
mg	Milligram
MHz	Megahertz
min	Minute
mL	Milliliter
mm	Millimeter
mmol	Millimole
µm	Micrometer

M.p.	Melting point
nm	Nanometer
NMR	Nuclear Magnetic Resonance
n-BuLi	*n*-Butyllithium
KOH	Potassium hydroxide
pH	Potential of hydrogen
ppm	Parts per million
RT	Room temperature
NaCl	Sodium chloride
s	Singlet
NMP	N-Methyl-2-pyrrolidone
t-Bu	Tertiary butyl
THF	Tetrahydrofuran
TLC	Thin-Layer Chromatography
TMS	Tetramethylsilane
CF_3COOH	Trifluoroacetic acid
UV	Ultraviolet
XRD	X-ray Diffraction
α	Alpha
β	Beta
γ	Gamma
δ	Chemical shift
[ox]	Oxidation
R_f	Refractive Index
i.e.	that is
o	Ortho
m	Meta
p	Para
H_2O_2	Hydrogen peroxide
H_2SO_4	Sulfuric acid
Et_3N	Triethylamine
$Cu(OTf)_2$	Copper (II) trifluoromethanesulfonate
$Yb(OTf)_3$	Ytterbium (III) trifluoromethanesulfonate

TBHP	*tert*–Butylhydroperoxide
BHT	Butylatedhydroxytoluene
Ag_2O	Silver(I) oxide
$LiAlH_4$	Lithium aluminium hydride
$ZnCl_2$	Zinc chloride
$Ni(OTf)_2$	Nickel (II) trifluoromethanesulfonate
$KMnO_4$	Potassium permanganate
$K_2S_2O_8$	Potassium persulfate
TEMPO	(2,2,6,6-Tetramethylpiperidin-1-yl)oxidanyl
ZnO	Zinc oxide
CH_3COOH	Acetic acid
p-TSA	*p*-Toluenesulfonic acid
TiO_2	Titanium dioxide
CuCl	Copper (I) chloride
$AlCl_3$	Aluminium chloride
$NaBH_4$	Sodium borohydride
DTBP	Di-*tert*-butyl peroxide
et al.	et alia, Latin for “and others”
i.e.	that is
e.g.	Example
equiv.	Equivalents

General Experimental Considerations

All the chemicals were procured from Aldrich, USA, and E. Merck, Germany, and were used as received. The solvents were purchased from Merck, India, and Ranbaxy, India, and were purified before their use. The preparation and particulars of the substrates employed for the work undertaken are given in their respective chapters. **Melting points** were measured using Stuart Melting point apparatus SPM10 in open capillary tubes and are uncorrected. **UV-visible spectroscopy** of the reaction solution was recorded on a SHIMADZU UV-3600 UV-visible spectrophotometer. **Infrared (IR)** spectra were recorded on the Perkin-Elmer FT-IR-5300 spectrophotometer (ν_{max} expressed in cm^{-1}). The **^{1}H** (500 MHz) and **^{13}C** (126 MHz) **NMR ^{19}F** (126 MHz) **NMR** spectra were run on a Bruker Advance 500 MHz FT-NMR at 500 MHz spectrometers. Chemical shifts are given in δ ppm, using tetramethylsilane (TMS) as an internal standard **HRMS (m/z) and** were recorded in an electron ionization or electrospray ionization (ESI) mode on Waters-Q-TOF Premier-HAB213 and Sciex X500R QTOF instruments. The **elemental microanalyses** were performed on Exeter Analytical Inc Model, CE-440 elemental analyzer.

Thin-layer Chromatography (TLC) was performed on glass plates (7.5 × 2.5 and 7.5 × 5.0 cm) coated with Merck silica gel GF 254 using various combinations of ethyl acetate and n-hexane as an eluent. Visualization of spots was accomplished either in an iodine chamber or by exposure to UV light. Merck silica gel (100-200 mesh) was used for column chromatography (approximately 15-20 g per 1 g of the crude product).

Preface

The fundamental goal of this thesis is to create novel synthetic methodologies for the synthesis of N-Containing heterocyclic Compounds.

The effective green synthesis of Nitrogen-containing heterocyclic compounds is embodied in the thesis titled **"Multicomponent Synthesis of N-Containing Heterocyclic Compounds"**. **Chapter 1** provides a detailed explanation of multicomponent synthesis and its significance in organic synthesis, N-Containing heterocycles and its importance, and different methods for the synthesis of Nitrogen Containing Compounds.

Chapter 2 will describe the Eosin Y-Catalyzed Synthesis of 3-Aminoimidazo[1,2-*a*]Pyridines via the HAT Process under Visible Light through Formation of the C-N Bond. **Chapter 3** will disclose Visible-Light-Promoted Synthesis of Fused Imidazoheterocycle by Eosin Y under Metal-Free and Solvent-Free Conditions. **Chapter 4** will highlight a Green Synthesis of Pyrimido[4,5-b]Quinolines and Pyrido [2,3-d] Pyrimidines via mechanochemical approach. **Chapter 5** will present Transition metal-free Synthesis of Pyrido[2,3-d]pyrimidines via Csp^3/Csp^2-H functionalization using $K_2S_2O_8$ as Oxidant finally, **Chapter 6** will summarize and conclude the total thesis work.