Dedicated
To
My Beloved Parents,
Mayuri
&
Family Members

DECLARATION

I declare that the thesis entitled "**METHODOLOGICAL APPROACH ON CARBON-HETERO BOND FORMATION REACTION**", has been prepared by me under the guidance of Prof. Pranab Ghosh, Professor of Chemistry, University of North Bengal. No element of this thesis has formed the origin for the award of any degree or fellowship earlier.

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CERTIFICATE

I certify that **Mr. Suvodip Mukherjee** has prepared the thesis entitled **"METHODOLOGICAL APPROACH ON CARBON-HETERO BOND FORMATION REACTION"**, for the award of Ph.D. Degree of the University of North Bengal, under my guidance. He has carried out the research work at the Department of Chemistry, University of North Bengal. No part of this thesis has formed the basis for the award of any degree or fellowship previously.

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ACKNOWLEDGEMENT

This work would not have been possible without the help of many persons who were a constant source of inspiration and support. I would like to take this privilege to thank those persons.

First of all, I would like to express my sincere gratitude to my honorable supervisor Prof. Pranab Ghosh, Professor, University of North Bengal, Darjeeling, for his active guidance and supervision, valuable advice and constant encouragement and motivation following which this work has come to life.

I express my sincere gratitude Prof. B. Sinha, HOD, Department of Chemistry, NBU. I feel pride to have acquainted with all non-teaching staffs that always stood beside me for constant support and spent a lot of their valuable time to motivate me in my darker hours.

I would like to thank my past and present labmates, Bijeta di, Gyan da, Tandra di, Hridoy da, Rabindra da, Puja di, Bittu da, Debashis da, Manishita di, Kumaresh, Biswajit, Aminul, Sourav, Sharmistha, Subhankar,Koushik, Dina Bandhu da, Saikat and others for their active co–operation throughout my research period.

I would also like to convey my special thanks to Prasun da, Pranesh, da, Ananya di, Sudip, Soumik, Gautam for their constant help and support.

The story will remain incomplete if I fail to express my thanks to the Lab no.107, Dept. of Chemistry, NBU where I have done my research work with my laptop where I have made the draft of my thesis.

I am thankful to University of North Bengal for providing the infrastructural facilities.

Finally, this work would not have been possible without the blessings of my beloved parents Shri. Tapan Mukherjee and Smt. Chhandana Mukherjee and by very close friend smt. Mayuri Mukherjee who's always stood by my side and also my lovable dog DOGO.

I would also take this opportunity to express my sincere apologies for any mistake on my part or any word or behaviour of mine that may have hurt anyone working with me.

Finally, despite best of my efforts and sincerity I might have committed some unintentional errors and mistakes in my thesis. Suggestions and criticisms from learned professors will be thankfully accepted.

Thank you.

Suvodip Mukherjee

14.06.2022

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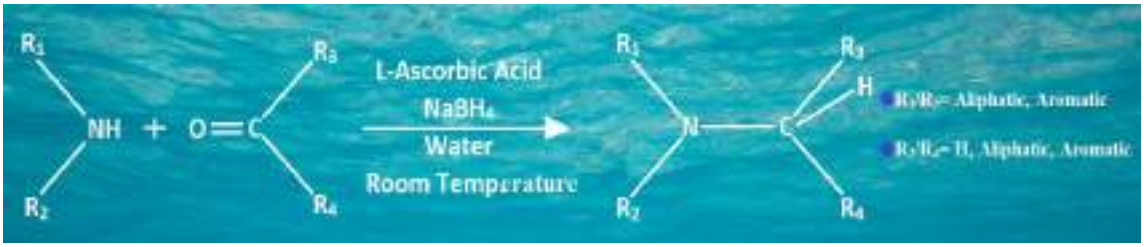
ABSTRACT

Beginning from the summer days of 2017, it took nearly five long years to finish the research work incorporated in this thesis entitled "**METHODOLOGICAL APPROACH ON CARBON-HETERO BOND FORMATION REACTION**". The work is mainly focused on development of efficient and environment benign methodologies for carbon-hereto bond formation reactions. The entire work depicted in this thesis has been divided into five chapters. In the beginning, **Chapter I** deals with a brief review on carbon-hetero bond formation reactions. Carbon-hetero bonder compounds has been extensively used in the designing of various pharmaceutically significant compounds. Apart from this, they are considered to be powerful starting materials for the construction of naturally occurring biological active compounds like amino acids, glycosides, naturally occurring heterocyclic compounds etc.

In **Chapter II** a novel, biomimetic concept for the direct reductive amination of aldehyde and ketones has been developed which uses largely available, low cost and harmless L- ascorbic acid as sustainable, versatile, non-toxic catalyst and $NaBH_4$ as a reductant. Described herein is a one-pot conversion of effortlessly accessible primary and secondary amines to biologically active higher degree amines in water at room temperature. The mild condition, environmentally benign by-products and broad scope of makes this transformation very useful.



In **Chapter III** an environmentally sustainable, green synthesis of thioamide through MCR (multi component reaction) of aldehyde, amine and sulfur catalyzed by humic acid in solvent-free condition at 100 °C. The key features of this protocol are use of humic acid, a greener, easily recyclable, easily available and almost unexplored catalyst and circumvention of noxious solvents that amplify the scope of the reaction. The proposed protocol also possess tolerance to aromatic as well as aliphatic aldehydes and amines comprising variety electron donating and withdrawing functional groups.

PREFACE

Carbon-hetero bond consisting group has been extensively used in the designing of various pharmaceutically significant compounds. These molecules also have their significant influence in the field of agrochemical industries as well. Apart from this, they are considered to be powerful starting materials for the construction of naturally occurring biological active compounds like amino acids, glycosides, naturally occurring heterocyclic compounds etc.

The present work describes methodologies for construction of various carbon-hetero bonds. The thesis starts with Chapter I, deals with a brief review on carbon-hetero bond formation reactions. Carbon-hetero functional group has been extensively used in the designing of various pharmaceutically significant compounds. Chapter II deals with a one pot conversion of effortlessly accessible primary and secondary amines to biologically active higher degree amines in water at room temperature. Chapter III describes green synthesis of thioamide through MCR (multi component reaction) of aldehyde, amine and sulfur catalyzed by Humic acid in solvent-free condition at100 ^{o}C. Chapter IV describes a facile one pot three component coupling of indoles, aldehydes and amines has been attained in a metal-free, economical and eco-friendly L-ascorbic acid in water medium and an alternate route has been also developed by using PEG-300 in a catalyst-free condition at 60 ^{o}C. Finally, at last Chapter V describes the synthesis of azobenzenes using Ethyl lactate as an efficient catalyst.

LIST OF TABLES

LIST OF SCHEMES

LIST OF FIGURES

LIST OF APPENDICES

APPENDIX A

List of Research Publications

1. "Room Temperature Direct Reductive Amination of Carbonyl compounds by L-ascorbic Acid – NaBH4 in Water." **Suvodip Mukherjee**, Gyan Chandra Pariyar, Bijeta Mitra, Pranab Ghosh*, Communicated to *Chemistry select* on April,**2022** with manuscript number: slct.202201022

2. "Humic acid catalyzed solvent-free green protocol for synthesis of thioamide." **Suvodip Mukherjee**, Gyan Chandra Pariyar, Bijeta Mitra, Pranab Ghosh*, Communicated to *Chemistry select* on June,**2022** with manuscript number: slct.202202168

3. "Greener One pot Synthesis of 3-Substituted Indoles using L-Ascorbic acid in water as green eco-friendly catalyst and alternatively using PEG-300 in catalyst -free condition". **Suvodip Mukherjee,** Gyan Chandra Pariyar, Pranab Ghosh*, (Communication under process.)

4. "Ethyl lactate mediated transition metal -free efficient synthesis of azobenzenes" Gyan Chandra Pariyar, Tandra Kundu, Bijeta Mitra, **Suvodip Mukherjee**, Pranab Ghosh*, *Chemistry Select*, **2020**, 5, 9781 –9786

5. "Organo-cu (ii) catalyst: an efficient synthesis of Substituted n-heterocycles via double Condensation/ tandem oxidationcyclization/elimination-cyclization reactions From easily accessible precursors", Bittu Saha, Bijeta Mitra, **Suvodip Mukherjee**, Raju Subba, Dhiraj Brahmin, Biswajit Sinha, Pranab Ghosh*, *RASAYAN J. Chem*., **2021**, 14, 2406-2412.

6. "Onion extract catalyzed novel synthesis of pyrazine." Hridoydip Ranjan Dasgupta, Suvodip Mukherjee, Pranab Ghosh*, *Asian journal of gren chemistry*, **2021**, 5, 235-247.

7. "Ascorbic Acid as an Efficient Organocatalyst for the Synthesis of 2-Substituted-2,3-dihydroquinazolin-4(1*H*) one and 2-Substituted Quinazolin-4(3H)-one in Water." Gyan Chandra Pariyar, Bijeta Mitra, **Suvodip Mukherjee**, Prof. Pranab Ghosh*, *Chemistry Select*, **2020,** 5, 104-108.

8. "A novel approach towards chemoselective reduction of nitro to amine." Hridoydip Ranjan Dasgupta, **Suvodip Mukherjee**, Pranab Ghosh*, *Tetrahedron Letters*, **2019**, 60, 151208.

9. "One pot three-component synthesis of 5-substituted 1*H*-tetrazole from aldehyde assisted by $(NH_4)_2Ce(SO_4)_4.2H_2O$, an efficient reusable catalyst." Bijeta Mitra, **Suvodip Mukherjee**, Gyan Chandra Pariyar, Pranab Ghosh*, *Tetrahedron Letters*, **2018**, 59, 1385-1389.

APPENDIX B

Poster Presentations

1. "**Novel protocol for one-pot three component synthesis of Dyhydroquinazolin-4(1*H*)-one**" by **Suvodip Mukherjee**, Gyan Chandra Pariyar, Pranab Ghosh* in the International Seminar on "Frontiers in Chemistry 2020" organized by DEPARTMENT OF CHEMISTRY, UNIVERSITY OF NORTH BENGAL, India, March, 2020.

2. "**A metal -free approach to Direct Reductive amination of Carbonyl Compounds in Water**", by **Suvodip Mukherjee** and Pranab Ghosh* in the International Seminar on "RECENT TRENDS IN CHEMISTRY (RTC-2019)" organized by DEPARTMENT OF CHEMISTRY, P.D WOMEN'S COLLEGE, JALPAIGURI, WEST BENGAL in association with INDIAN CHEMICAL SOCIETY, KOLKATA, January, 2019.

ABBREVIATION

Å	Angstrom
acac	Acetylacetonate
AcOH	Acetic acid
BDMS	Bromodimethylsulfonium bromide
BiNPs	Bismuth nanoparticles
br	Broad
cm	Centimeter
Cy	Cyclohexyl
d	Doublet
DCE	1,2-Dichloroethane
DMAP	4-Dimethylaminopyridine
DME	1,2–Dimethoxyethane
DMEDA	1,2-Dimethylethylenediamine
DMF	*N, N*–Dimethylformamide
DMSO	Dimethyl sulfoxide
Dppe	1,2-Bis(diphenylphosphino)ethane
Dppf	1,1′-Bis(diphenylphosphino)ferrocene
EQUIV	Equivalent
EtOH	Ethanol
FT-IR	Fourier-transform infrared spectroscopy
g	gram/grams
h	hour/hours
HRMS	High-resolution mass spectroscopy
IBS	4-(1-imidazolium)-butane sulfonate
LDA	Lithium diisopropylamide
m	Multiplet
MHz	Mega hertz
min	minute/minutes
mL	millilitre
mmol	millimole
mol%	mole percent

MS	Molecular sieve
MW	microwave
NCTS	*N*-Cyano-*N*-phenyl-p-toluenesulfonamide
NHPI	*N*-Hydrophthalimide
nm	Nanometer
NMR	Nuclear magnetic resonance
°C	Degree Celsius
PMA	Phosphomolybdic acid
PC	Phosphatidylcholine
PEG	Polyethylene glycol
Phen	Phenyl
PMHS	Polymethylhydrosiloxane
RT	Room temperature
s	Singlet
SPhos	Alkyl 2-(trimethylsilyl)ethyl sulfoxides
t	Triplet
TBAF	Tetra-n-butylammonium fluoride
TBAI	Tetrabutylammonium iodide
TBHP	*tert*-Butyl hydroperoxide
TBT	Tributyltin
t-BuOCl	*tert*-butyl hypochlorite
TCT	2,4,6-trichloro-1,3,5-triazine
TEMPO	(2,2,6,6-Tetramethylpiperidin-1-yl)oxyl
TfOH	Triflic acid
THF	Tetrahydrofuran
TLC	Thin-layer chromatography
TMEDA	*N,N,N',N'*-Tetramethylethylenediamine