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ABSTRACT

Nitrogen-containing heterocycles represent vast and significant potential in the multidisciplinary fields of chemistry. The work mentioned in this thesis entitled “**Catalytic Approach Towards the Synthesis of Indole based Heterocycles**” presents the one-pot synthesis of five/six-membered indole-based nitrogen heterocycles. This work is mainly based on the organocatalytic direct Mannich reaction between various imines with succinaldehyde, and glutaraldehyde for [3+2], and [4+2] annulation to access five/six-membered ring systems. Besides, the synthesis of 2,2-disubstituted indolin-3-ones, a critical indole-based unit, was synthesized using metal-catalyzed dimerization of 2-arylindoles, and cross addition of indoles with various 2-substituted indoles.

The first chapter of the thesis depicts a concise discussion about the organocatalysis approach and its utility for several reactions, amine-catalyzed direct Mannich reactions, its mechanism, and exploration of synthetic strategy in the development of the synthesis of complex scaffolds. This chapter also provides an overview of the importance of N-heterocycles. A report on the utilization of linear dialdehydes such as; succinaldehyde and glutaraldehyde for the synthesis of five and six-membered nitrogen heterocycles via aminocatalytic cascade transformations has been presented.

The second chapter of the thesis deals with the proline-catalyzed multicomponent direct Mannich reaction between imines, *in situ* generated from Ar/HetAr/Indole-aldehydes and amines, and succinaldehyde, followed by cyclization-IBX mediated oxidative aromatization to indolyl-pyrrole-3-carbaldehydes with good to high yields in one-pot operation.

The third chapter deals with the one-pot organocatalytic synthesis of indolyl-3-piperidines in asymmetric fashion through [4+2] annulation between glutaraldehyde and indolyl-imines. This reaction proceeds through proline-catalyzed direct Mannich reaction, followed by NaBH₄-mediated reductive-cyclization in good yields with high stereoselectivity (up to >25:1 dr, up to >99:1 er). The Anti-HIV activities were tested with the synthesized compounds.

The fourth chapter explains a general approach for the direct synthesis of 2,2-disubstituted indolin-3-ones through mild Cu(II)-catalysis conditions. Under the developed conditions, self-dimerization of 2-aryl-indoles and cross-addition of indole with 2-arylindoles was achieved. A series of 2,2-disubstituted indolin-3-ones, decorated with C2-quaternary center, were synthesized in good to high yields.

The fifth chapter summarizes the overall outcome of the research work and future scope of the work.

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LIST OF ABBREVIATIONS / SYMBOLS

Abbreviation/Symbol	Description
α	Alpha
$[\alpha]$	specific rotation
β	Beta
γ	Gamma
δ	Chemical shift
Å	Angstrom
Ac	Acetyl
Aqu	Aqueous
Ar	Aryl
Bn	Benzyle
Boc	Butoxycarbonyl
Bu	Butyl
<i>t</i> -BuOK	Potassium <i>tert</i> -butoxide
Bz	Benzoyl
Calcd.	Calculated
°C	Degree centigrade
¹³ CNMR	Carbon-13 nuclear magnetic resonance
Cat.	Catalyst
CDCl ₃	Deuterated chloroform
Conc	Concentration
COSY	Correlation Spectroscopy (NMR)
d	Doublet
dd	Doublet of doublet
DDQ	2,3-Dichloro-5,6-Dicyanobenzoquinone
DMSO	Dimethylsulphoxide
DCM	Dichloromethane
DMF	<i>N,N</i> -Dimethylformamide
ESI	Electron Spray Ionization (MS)
Equiv	Equivalent

LIST OF ABBREVIATIONS / SYMBOLS

g	Gram
h	Hours
HRMS	High Resolution Mass Spectra
IBX	2-Iodoxybenzoic acid
IR	Infrared
Hz	Hertz
hr	Hour
<i>i</i>	<i>Iso</i>
K ₂ CO ₃	Potassium carbonate
<i>J</i>	Coupling constant
Lit.	Literature
MCR	Multi component reaction
m-CPBA	Meta-chloroperbenzoic acid
Me	Methyl
MS	Mass spectrometry
M.P	Melting point
m	Multiplet
mg	Milligram
MHz	Mega hertz
min	Minutes
mL	Milliliter
mmol	Millimole
Nu	Nucleophile
PEG	Polyethylene glycol
Ph	Phenyl
ppm	Parts per million
%	Percentage
psi	<i>Per square inch</i>
<i>p</i> -TsOH	<i>p</i> -Toluenesulfonic acid
PMP	<i>p</i> -methoxyphenyl

LIST OF ABBREVIATIONS / SYMBOLS

Py	Pyridine
rt	Room temperature
s	Singlet
t	Triplet
<i>t</i>	Tertiary
TBHP	<i>tert</i> -butylhydrogen peroxide
Ts	Tosyl
<i>Tert</i> -	Tertiary
TFA	Trifluoroacetic acid
THF	Tetrahydrofuran
TLC	Thin layer chromatography
TMS	Tetramethylsilane
σ	Sigma
*	Chiral



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