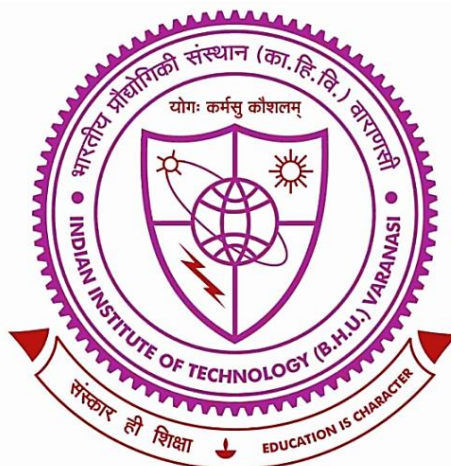


Synthesis and Applications of *N*-Nitrosamines and *N*-Nitrosamides in Different Organic Transformations



Thesis submitted in partial fulfilment for the

Award of Degree

Doctor of Philosophy

by

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Year of Submission
2023

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Dedicated to my loving

Parents...

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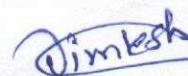
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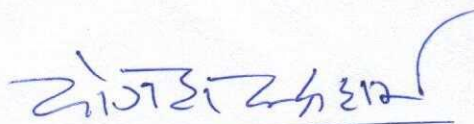
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Date: 01/02/2023



(Mr. Kanaujiya Vimlesh Kumar)

Research Scholar

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LIST OF NOTATIONS, SYMBOLS AND ABBREVIATIONS

Notations	Abbreviations
%	Percentage
<	Less than
>	More than
°	Degree
°C	Degree Celsius
©	Copyright
Å	Angstrom
1,10-Phen.	1, 10-phenanthroline
2,2-Bipy	2, 2-Bipyridine
Ac	Acetyl group
Ac ₂ O	Acetic anhydride
AIBN	Azobisisobutyronitrile
AcOH	Acetic acid
Aq.	Aqueous
atm.	Atmosphere
brs	Broad Singlet
Bn	Benzyl
Bz	Benzoyl group
Calc.	Calculated
calcd	Calculated
CHCl ₃	Chloroform
cm	Centimeter
CDCl ₃	Deuterated Chloroform
CD ₃ OD	Methanol-d ₄
c	Concentration
cc	Column chromatography
CSA	Camphorsulfonic acid
COSY	¹ H- ¹ H Correlation Spectroscopy
D ₂ O	Deuterated water
DCE	1,2-Dichloroethane
DMAP	4-Dimethylaminopyridine
DMF	Dimethylformamide
DCM	Dichloromethane
DEPT	Distortionless enhancement by polarization transfer
d	Doublet
dd	Doublet of doublet

ddd	Doublet of doublet of doublet
ddt	Doublet of doublet of triplet
dq	Doublet of quartet
dt	Doublet of triplet
DNA	Deoxyribonucleic acid
DABCO	1,4-Diazabicyclo[2.2.2]octane
Dppe	1,2-Bis(diphenylphosphino)ethane
EDG	Electron donating group
EWG	Electron withdrawing group
equiv.	Equivalent
EtOH	Ethanol
EtOAc	Ethyl acetate
Et ₃ N	Triethylamine
ESI	Electrospray ionization
g	Gram; Gravitational force
GC-MS	Gas Chromatography Mass Spectrometry
h	Hour
HRMS	High Resolution Mass Spectrometry
HPLC	High-performance liquid chromatography
Hz	Hertz
HSQC	Heteronuclear single quantum coherence spectroscopy
<i>i</i> -Pr	<i>Iso</i> -propyl
IR	Infra Red
<i>J</i>	Coupling constant
KI	Potassium iodide
KOH	Potassium hydroxide
LG	Leaving group
lit.	Literature
m	Multiplet
m/z	Mass to charge ratio
MeOH	Methanol
mg	Milligram
MHz	Megahertz
min	Minute
mL	Milliliter
mm	Millimeter
mmol	Milli Mole
μm	Micrometer
m.p.	Melting Point
MOM	Methoxymethyl
MS	Molecular sieve

MeOD	Duterated methanol
nm	Nanometer
NaCl	Sodium chloride
NMR	Nuclear Magnetic Resonance
<i>n</i> -BuLi	<i>n</i> -Butyllithium
NMP	N-Methyl-2-pyrrolidone
nr	Not reported
nd	Not determined
NBS	N-Bromosuccinimide
NIS	N-Iodosuccinimide
NCS	N-Chlorosuccinimide
NOESY	Nuclear Overhauser Effect Spectroscopy
Observed.	Observed
PDC	Pyridinium dichromate
PG	Protectin group
pH	Potential of hydrogen
ppm	Parts per million
Py	Pyridine
PTSA	<i>p</i> -Toluenesulfonic acid
Pd-C	Palladium on carbon
Quant.	Quantitative
RT	Room Temperature
RNA	Ribonucleic acid
<i>R_f</i>	Retardation Factor
s	Singlet
<i>t</i> -Bu	Tertiary butyl
TBN	<i>tert</i> -Butyl nitrite
THF	Tetrahydrofuran
TLC	Thin-Layer Chromatography
TMS	Tetramethylsilane
TMEDA	Tetramethylethylenediamine
TBAI	Tetran- <i>n</i> -Butyl Ammonium Iodide
TBAF	Tetran- <i>n</i> -Butyl Ammonium Fluoride
TBAB	Tetran- <i>n</i> -Butyl Ammonium Bromide
TBS	<i>tert</i> -Butyldimethylsilyl
TBDMS	<i>tert</i> -Butyldimethylsilyl
TBDPS	<i>tert</i> -Butyldiphenylsilyl
TEMPO	(2,2,6,6-Tetramethylpiperidin-1-yl)oxyl
TFA	Trifluoroacetic acid
TfOH	Trifluoromethanesulfonic acid
t	Triplet

TMSOTf	Trimethylsilyl trifluoromethanesulfonate
TsCl	4-Toluenesulfonyl chloride
UV	Ultraviolet
XRD	X-ray diffraction
α	Alpha
β	Beta
δ	Chemical shift
δ	Delta
[ox]	Oxidation
$[\alpha]$	Specific rotation
i.e.	that is
<i>o</i>	Ortho
<i>m</i>	Meta
<i>p</i>	Para

GENERAL EXPERIMENTAL CONSIDERATIONS

All the reactions were carried out in oven dried glasswares. Starting materials were prepared using modified literature procedures and modified procedures as described in the experimental sections. Solvents, Chemicals were purchased from commercial sources (Aldrich, Alfa Aesar, SD fine and Avra) and used without further purifications, unless otherwise stated. **Melting points** of products were measured Staurt SMP10 melting point apparatus using in open capillary tubes. **FT-IR** for the products were recorded on ALPHA BRUKER Eco-ATR fitted out on ZnSe ATR crystal in the range of 500-3000 cm^{-1} . **^1H NMR** and **^{13}C NMR** spectra were recorded on Bruker Avance 500 MHz NMR spectrometer using deuterated solvents. Chemical shifts are given in ppm, using tetramethylsilane (TMS) as an internal standard. **Mass spectra (HRMS)** were measured on water's Quattro Micro V 4.1. Electronic absorption spectra were recorded on Shimadzu UV-2450 spectrophotometer. **Optical rotation** was measured using JASCO-2000 polarimeter. **Thin layer chromatography (TLC)** was performed using pre-coated plates obtained from E. Merck (TLC silica gel 60 F254). The TLCs were visualized in UV Chamber with 254 nm wavelength lamp, then further analyzed by charring in stain solution (5% H_2SO_4 in MeOH) and also sometimes in iodine chamber. **Column chromatography** was performed on silica gel (60-120 or 100-200 mesh) using different eluents. Optical rotation for all compounds has been performed using Jasco P-2000 polarimeter. **IR spectra** of the new compounds have been recorded using PerkinElmer instrument. **HPLC analysis** was performed on Agilent LC/192168254.11. C-8 Reverse phase column was used for the analysis with solvent acetonitrile:water = 70:30. Flow rate was maintained 1mL/minute. 10 Micro litre sample was injected for each analysis. The details of other fine chemicals, reaction conditions, substrate preparation etc. are given in respective chapters.

PREFACE

N-Nitroso compounds and their derivatives occur in a wide range of foods, natural products, fluids, rubber additives, agricultural chemicals, tobacco, detergents, rust solvents, plastics, leather products, textiles, cosmetics, and drugs. They are occasionally used as solvents or synthetic intermediates in organic chemistry and act as a directing group for inert C-H bond activation to give *ortho*-functionalized aniline compounds. *N*-Nitrosamines undergo reduction, oxidation, cyclization, rearrangement, denitrosation, photochemical reaction, etc.

In this context, the thesis entitled “**Synthesis and Applications of *N*-Nitrosamines and *N*-Nitrosamides in Different Organic Transformations**” discuss about the synthesis and applications of *N*-Nitrosamines and *N*-Nitrosamides. **Chapter 1** provides a general introduction to different nitroso compounds and their synthetic applications. **Chapter 2** describes the synthesis of glycouronamides via transamidation approach using *N*-nitrosamide intermediates under mild conditions at room temperature. **Chapter 3** describes an efficient and practical method for the denitrosation of *N*-nitrosamines using ethanethiol with PTSA (*p*-toluenesulfonic acid) *via* trans-nitrosation strategy. **Chapter 4** describes the synthesis of *N*-nitroso sulfonamides from sulfonamides and tert-butyl nitrite (TBN) and their synthetic applications in nitroso transfer reactions under mild reaction conditions. **Chapter 5** describes the stereoselective synthesis of *O*-glycosides from 2-amino thioglycosides using *N*-nitroso group as directing group. The reaction was activated by using NIS/TfOH system in dichloromethane at -10 °C Finally, the **Chapter 6** Provides summarize and conclude the total thesis work.