

# *tert*-Butyl Hydroperoxide Mediated Development of Some New C-C And C-N Bond Formation



Thesis submitted in partial fulfillment for the  
award of degree

**Doctor of Philosophy**

Submitted by

*Mr. Dharendra Kumar*

Supervisor

*Dr. (Mrs.) Sundaram Singh*

Co-Supervisor

*Prof. Vandana Srivastava*

DEPARTMENT OF CHEMISTRY  
INDIAN INSTITUTE OF TECHNOLOGY  
(BANARAS HINDU UNIVERSITY)  
VARANASI - 221005  
INDIA

Roll No. 15051501

2022

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It is further certified that the student has fulfilled all the requirements of Comprehensive, Candidacy and SOTA for the award of PhD degree.

  
Supervisor

**Dr. (Mrs.) Sundaram Singh**

**Department of Chemistry**

**IIT (BHU), Varanasi-221005**

**(Mrs.) Sundaram Singh**  
Associate Professor  
Department of Chemistry  
Indian Institute of Technology,  
Varanasi-221005

  
Co-Supervisor

**Prof. Vandana Srivastava**

**Department of Chemistry**

**IIT (BHU), Varanasi-221005**

*Dr. Vandana Srivastava*  
Professor  
Department of Chemistry  
Indian Institute of Technology (BHU)  
Varanasi-221005

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Place : Varanasi



(Dhirendra Kumar)

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It is certified that the above statement made by the student is correct to the best of my knowledge.



Supervisor

(Department of Chemistry)  
Dr. (Mrs.) Sundaram Singh  
Associate Professor  
Department of Chemistry  
Indian Institute of Technology  
Banaras Hindu University Varanasi-221005



Co-Supervisor

(Department of Chemistry)  
Dr. Vandana Srivastava  
Professor  
Department of Chemistry  
Indian Institute of Technology (BHU)  
Varanasi-221005

Signature of Head of Department

"SEAL OF THE DEPARTMENT"

विभागाध्यक्ष/HEAD

रसायन विज्ञान विभाग

Department of Chemistry  
भारतीय प्रौद्योगिकी संस्थान (का.हि.वि.वि.)  
Indian Institute of Technology (B.H.U.)  
वाराणसी-२२१००५/Varanasi-221005

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## ACKNOWLEDGEMENTS

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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 would like to thank my Research Supervisor **Dr. (Mrs.) Sundaram Singh**, 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. Y.C Sharma**, Head of the Department and **Prof. Dhanesh Tiwary**, **Prof. Rashmi Bala Rastogi**, 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** (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 Department of Chemistry for IR and CIFC, Indian Institute of Technology (BHU) for providing NMR Spectroscopy facility.

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 would also like to thank my friends **Dr.Om Prakash, Dr. Nikhil Singh, Dr. Sonam Soni, Dr. Vinay pandey** and **Varsha Tiwari** for their affection, prayer and support in my research work.

My warm sense of gratitude is due to my lab members, **Dr. Savita Kumari, Arsala Kamal, Suresh Kumar Maury, Himanshu Kumar Singh, Ambuj Kumar Kushwaha Kavita** and **Sikha Pandey** for their help and cooperation at every step of the research work.

I take this opportunity to register my sincere thanks to Department of Chemistry, Indian Institute of Technology (BHU) for a Research Fellowship and valuable pecuniary support.

At the last but not the least, I thank to all my well-wishers whose names I may have failed to mention here unintentionally. Thanks to all of you for being there for me when times were the toughest.

**Date:**

**Dhirendra Kumar**  
Research Scholar

# CONTENTS

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	<b>Page No.</b>
<b>Acknowledgements</b>	<b>vi</b>
<b>List of Titles</b>	<b>viii</b>
<b>List of Schemes</b>	<b>xiv</b>
<b>List of Figures</b>	<b>xv</b>
<b>List of Tables</b>	<b>xvi</b>
<b>List of Notations, Symbols and Abbreviations</b>	<b>xviii</b>
<b>General Experimental Considerations</b>	<b>xxii</b>
<b>Preface</b>	<b>xxiii</b>

## LIST OF TITLES

<b>Titles</b>	<b>CHAPTER-1</b>	<b>Page No.</b>
	<b>Introduction</b>	
1.1	Brief Introduction of tert-Butyl hydroperoxide (TBHP)	1
1.2	Application of TBHP	4
1.2.1	TBHP Mediated C-C Bond Formation:	4
1.2.1.1	Synthesis of [6,6,5] tricyclic frameworks	5
1.2.1.2	Synthesis of 1H-indole derivatives	5
1.2.1.3	Synthesis of indole derivatives via cross-dehydrogenativecoupling	6
1.2.1.4	Oxidative Coupling of $\beta$ -ketoesters with carboxylic acids	6
1.2.1.5	Coupling of azoles with $\alpha$ -C(sp <sup>3</sup> )-H of ethers and thioethers	6
1.2.1.6	sp <sup>3</sup> C-H bond functionalizationof toluene derivatives	7
1.2.1.7	Synthesis of isoxazoline-functionalized phenanthridines	

1.2.1.8	Domino synthesis of 3-aryloindoles via two sp <sup>3</sup> C–H activation.	8
1.2.1.9	C-2-Alkylation of azoles	9
1.2.1.10	Preparation of double bond	9
1.2.1.11	Oxidative coupling of benzothiazoles with aldehydes	10
1.2.1.12	1,3-Dipolar cycloaddition/ oxidation/ aromatization cascade reaction	10
1.2.1.13	Tandem Michael addition/oxidative annulations	10
1.2.1.14	Regioselective synthesis of C-3 dicarbonyl indole derivatives	
1.2.2	TBHP Mediated C-N Bond formation	11
1.2.2.1	Oxidative imidation of ketones	12
1.2.2.2	Oxidative amidation of aldehyde	12
1.2.2.3	Coupling reaction between isocyanide and aryl methanes	13
1.2.2.4	Amination of benzylic C–H bonds	13
1.2.2.5	Amination of benzoxazoles with amines	14
1.2.2.6	Amide bond formation from aldehydes and aromatic tertiary amines	14
1.2.2.7	Alkylation of aryl tetrazoles	15
1.2.2.8	Synthesis of $\alpha$ -ketoamides from aryl methyl ketones	15
1.2.2.9	Synthesis of amides from alcohols and N,N-disubstituted formamides	16
1.2.2.10	Synthesis of tertiary amides from tertiary amines and anhydrides	16
1.2.2.11	Oxidative amidation of aldehydes using amine HCl salts	17
1.2.2.12	Oxidative aminations of benzoxazole	17

1.2.2.13	Amide bond formation from benzyl alcohols/aldehydes	18
1.2.2.14	Synthesis of N-sulfonyl formamide	19
1.2.2.15	Imidation of the C(sp <sup>3</sup> )-H bond	19
1.2.2.16	Synthesis of amide from methyl arenes and the HCl salt of amines	20
1.2.2.17	Cross-dehydrogenative amination	21
1.2.2.18	Intramolecular dehydrogenative cyclization of N-acyl dipeptide esters	22
1.2.2.19	The Synthesis of 4,3-fused 1,2,4-triazoles	22
1.2.2.20	N-Amidoalkylation of purine	22
1.2.2.21	The stereoselective Synthesis of trans-disubstituted aziridines	23
1.2.2.22	The Synthesis of [1,2,4]triazolo[3,4-c]quinoxaline scaffolds	23
1.2.3.1	Synthesis of $\alpha$ -ketoamides	24
1.2.3.2	Synthesis of $\beta$ -acylated enaminones	25
1.2.3.3	TBHP-Initiated Transamidation of secondary amides	25
1.2.3.4	Aqueous Domino synthesis of quinazolinones and quinoxalines	26
1.2.3.5	C-3 Functionalization of quinoxalin-2(1H)ones	26
1.2.3.6	Four component synthesis of enaminones	26
1.2.3.7	Synthesis of achiral axial 3, 3'-biindole-2, 2'-dibenzene sulfonothioate	27
1.2.3.8	Synthesis of 3,5-disubstituted-1,2,4-triazoles	27
1.2.3.9	Transition-metal-free synthesis of 3-sulfonylated thioflavones	28
1.2.3.10	One-pot synthesis of 2-amino-1,3,4-oxadiazoles	28

1.3	References	30
-----	------------	----

## CHAPTER-2

### **TBHP Mediated Solvent-Free Cascade Csp<sup>3</sup>-H Bond Functionalization of Methyl Arene with Active Methylene Compounds using Et<sub>3</sub>N- as a Catalyst**

2.1	Introduction	41
2.2	Results and Discussion	43
2.3	Control experiment	49
2.4	Mechanism of C-H functionalization	51
2.5	Conclusion	52
2.6	Experimental Section	52
2.6.1.	General experimental procedure	52
2.6.2	Physical and spectral data of representative compounds	52
2.6.3	Spectral Data of Product 2 Benzylidenemalononitrile 2a	56
2.6.4	Spectral Data of Product (Z)-Ethyl 3-(4-chlorophenyl)-2-cyanoacrylate 3n	58
2.7	References	60

## CHAPTER-3

### **TBHP initiated C-N Bond Formation via Oxidative Coupling of Benzyl Bromides with Amine using TBAI as a Catalyst**

3.1	Introduction	66
3.2	Results and Discussion	68
3.3	Control experiment	73
3.4	Mechanism of amide formation	74
3.5	Conclusion	76
3.6	Experimental Section	78
3.6.1	General experimental procedure for the synthesis of amide	78
3.6.2	Characterization data of synthesized compounds 3(a-r)	78
3.6.3	Spectral Data of Product N-phenylbenzamide (3a)	82
3.6.4	Spectral Data of Product N-Butyl-N-methylbenzamide (3n)	84

3.6.5 Spectral Data of Product phenyl(pyrrolidin-1-yl)methanone (3p)	86
3.7 References	88

#### CHAPTER-4

##### **NaI/TBHP-Promoted C-N Bond Formation Via Oxidative Coupling of Benzyl Mercaptan with Amine: A Facile Approach for The Synthesis of Amides**

4.1 Introduction	93
4.2 Results and Discussion	94
4.3 Control experiments to establish mechanism of the reaction	101
4.4 Mechanism of C-N Bond Formation Via Oxidative Coupling	103
4.5 Gram-scale synthesis of Benzamide with Benzylmercaptan & Aniline	104
4.6 Conclusion	105
4.7 Experimental Section	105
4.7.1 General experimental procedure for the synthesis of compound 3	105
4.7.2 Characterization data of synthesized compounds and 3(a-t)	106
4.7.3 Spectral Data of Product N-Phenylbenzamide 3a	110
4.7.4 Spectral Data of Product 1-(2 Naphthalenecarbonyl)piperidine(3m)	113
4.7.5 Spectral Data of Product piperidin-1-yl(pyridin-4-yl)methanone(3t)	115
4.8 References	117

#### CHAPTER-5

##### **I<sub>2</sub>/TBHP Mediated Oxidative Coupling of Indole with Active methylene Compounds Via C-C and C-O bond formation**

5.1 Introduction	121
5.2 Results and Discussion	122
5.3 Control Experiment	129
5.4 Mechanism for coupling of indole with active methylene groups	130
5.5 Conclusion	132
5.6 Experimental Section	132

5.6.1	General experimental procedure for the synthesis of the compound of 3a	132
5.6.2	Characterization data of the compounds	132
5.6.3	Spectrul data of Product 2-(2-oxoindolin-3-ylidene) malononitrile 4a	138
5.6.4	Spectrul data of Product Ethyl-2-cyano-2-(2-oxoindolin-3-ylidene) acetate 4g	140
5.6.5	Spectrul data of Product 5, 5-Dimethyl-2-(2-oxoindolin-3-ylidene) cyclohexane-1, 3-dione 4m	142
5.7	References	144

### **Summary and Conclusions**

### **List of Research Publications**

## LIST OF SCHEMES

---

---

Scheme	LIST OF SCHEMES	Page No.
1.1	Bu <sub>4</sub> NI-catalyzed intramolecular cyclization of the $\alpha$ -cyano-TMS/aryl-capped alkynyl aryl alkyl ketones.	5
1.2	Bu <sub>4</sub> NI-catalyzed intramolecular oxidative coupling of N-arylenamines	5
1.3	TBAI/TBHP-Mediated indole synthesis	6
1.4	TBAI-Catalyzed synthesis of $\alpha$ -carboxylic- $\beta$ -ketoesters	6
1.5	TBAI/TBHP-catalyzed synthesis of <i>N</i> -substituted azoles	7
1.6	TBAI- catalyzed synthesis of allylbenzene derivatives.	7
1.7	TBHP-mediated synthesis of isoxazoline-functionalized phenanthridines.	8
1.8	TBHP mediated synthesis of 3-aryloindole	8
1.9	Direct C-2-alkylation of azoles via dehydrogenative cross-coupling	9
1.10	TBAI/TBHP catalyzed the formation of a new C-C bond	9
1.11	Oxidative Coupling of benzothiazoles with aldehydes	10
1.12	1,3-Dipolar cycloaddition/oxidation/aromatization	10
1.13	Synthesis of polysubstituted furan	11
1.14	Synthesis of C-3 dicarbonyl indole derivatives	11
1.15	TBAI-catalyzed oxidative imidation of ketones with imides	12
1.16	TBHP initiated oxidative amidation of aldehyde	13
1.17	TBAI-catalyzed reaction of methylarene with isocyanide	13
1.18	TBAI/TBHP-mediated amination of toluenes	13
1.19	TBAI-catalyzed synthesis of 2-amino-benzoxazoles	14
1.20	TBAI/TBHP-mediated synthesis of amides from tertiary amines	14
1.21	TBAI/TBHP-mediated synthesis of amides from tertiary amines	15

1.22	Synthesis of benzylated and alkylated aryl tetrazoles	15
1.23	TBAI/TBHP-mediated synthesis of $\alpha$ -ketoamides	16
1.24	TBAI/TBHP-Mediated synthesis of amides from alcohols.	16
1.25	Synthesis of tertiary amides from tertiary amines and anhydrides	17
1.26	Synthesis of tertiary amides	17
1.27	Oxidative amination of benzoxazole	18
1.28	Metal-free direct amination of benzoxazoles	18
1.29	Synthesis of substituted spirofuropyrimidines	19
1.30	Synthesis of N-sulfonyl formamidine	19
1.31	Synthesis of N-sulfonyl formamidine	20
1.32	Imidation of the C(sp <sup>3</sup> )-H bond	20
1.33	Synthesis of amide	21
1.34	Cross-dehydrogenative amination	21
1.35	Cyclization of N-acyl dipeptide esters	22
1.36	Synthesis of 4,3-fused 1,2,4-triazoles	22
1.37	Synthesis of N-amidoalkylation of purine	23
1.38	Synthesis of <i>trans</i> -disubstituted aziridines	23
1.39	Synthesis of [1,2,4]triazolo[3,4-c]quinoxaline scaffolds	24
1.40	Synthesis of $\alpha$ -ketoamides	24
1.41	Synthesis of $\beta$ -acylated enaminones	25
1.42	Transamidation of secondary amides	25
1.43	Synthesis of quinazolinones and quinoxalines	26
1.44	C-3 Functionalization of quinoxalin-2(1H)-ones	26
1.45	Four component synthesis of enaminones	27
1.46	Synthesis of achiral axial 3, 3'-biindole-2, 2' dibenzenesulfonylthioate	27
1.47	Synthesis of 3,5-disubstituted-1,2,4-triazoles	27

1.48	Transition-metal-free synthesis of 3-sulfonylated thioflavones	28
1.49	One-pot synthesis of 2-amino-1,3,4-oxadiazoles	28
2.1	Et <sub>3</sub> N catalyzed C-H functionalization of methylarene with malononitrile/ ethyl cyanoacetate under solvent-free condition.	43
2.2	Control experiments using radical trapping agents	50
2.3	Mechanism of C-H functionalization of methyl arene with malononitrile /ethyl cyanoacetate under solvent-free condition	51
3.1	Synthesis of an amide from benzyl bromide and amine	67
3.2	Control experiments to establish mechanism of the reaction	75
3.3	Plausible reaction mechanism	76
4.1	NaI/TBHP-Promoted C-N Bond Formation Via Oxidative Coupling of Benzyl Mercaptan with Amine	94
4.2	Control experiments to establish mechanism of the reaction	102
4.3	Plausible mechanism of amide bond formation	104
4.4	Gram-scale synthesis of Benzamide(3a)	104
5.1	Oxidative coupling of indole and active methylene compound	123
5.2	Control experiments to establish mechanism of the reaction	130
5.3	Plausible mechanism for the synthesis of 2-(2-Oxoindolin-3-ylidene) malononitrile	132

## LIST OF FIGURES

---

Figure	List of Figures	Page No.
1.1	Structure of TBHP	3
1.2	Importance of TBHP as an oxidant	4
2.1	$^1\text{H}$ NMR of product 2a	57
2.2	$^{13}\text{C}$ NMR of product 2a	58
2.3	$^1\text{H}$ NMR of product 3n	59
2.4	$^{13}\text{C}$ NMR of product 3n	60
3.1	$^1\text{H}$ NMR of product 3a	82
3.2	$^{13}\text{C}$ NMR of product 3a	83
3.3	$^1\text{H}$ NMR of product 3n	84
3.4	$^{13}\text{C}$ NMR of product 3n	85
3.5	$^1\text{H}$ NMR of product 3n	86
3.6	$^{13}\text{C}$ NMR of product 3n	87
4.1	$^1\text{H}$ NMR of product 3a	111
4.2	$^{13}\text{C}$ NMR of product 3a	112
4.3	$^1\text{H}$ NMR of product 3m	113
4.4	$^{13}\text{C}$ NMR of product 3m	114
4.5	$^1\text{H}$ NMR of product 3t	115
4.6	$^{13}\text{C}$ NMR of product 3t	116
5.1	$^1\text{H}$ NMR of product 4a	138
5.2	$^{13}\text{C}$ NMR of product 4a	139
5.3	$^1\text{H}$ NMR of product 4g	140
5.4	$^{13}\text{C}$ NMR of product 4g	141
5.5	$^1\text{H}$ NMR of product 4m	142
5.6	$^{13}\text{C}$ NMR of product 4m	143

## LIST OF TABLES

---

---

<b>Table</b>	<b>List of Tables</b>	<b>Page No.</b>
2.1	Optimization of reaction conditions for the synthesis of 3a	44
2.2	Effect of molar ratio on condensation of Toluene with Malononitrile on yield of product.	46
2.3	C-H functionalization of methyl arene with an active methylene compound	47
3.1	Optimization of reaction conditions for the synthesis of 3a	69
3.2	Screening of substrates for the synthesis of Amide	70
4.1	Optimized reaction condition for the model reaction 3a	96
4.2	Screening of substrates for the synthesis of Amide	98
5.1	Optimization of reaction conditions for the synthesis of 3a	124
5.2	Screening of substrates for the synthesis of 2-(2-Oxoindolin-3-ylidene) malononitrile	125

## **LIST OF NOTATIONS, SYMBOLS AND ABBREVIATIONS**

<b>Notations</b>	<b>Abbreviations</b>
%	Percentage
<	Less than
>	More than
°	Degree
Å	Angstrom
Ac	Acetyl
Ac <sub>2</sub> O	Acetic anhydride
AcOH	Acetic acid
Bn	Benzyl
Bz	Benzoyl group
brs	Broad singlet
Obser.	Observed
Calc.	Calculated
©	Copyright
CHCl <sub>3</sub>	Chloroform
CD <sub>3</sub> OD	Methanol-d <sub>4</sub>
CDCl <sub>3</sub>	Deuterated chloroform
cm	Centimeter
<i>J</i>	Coupling constant
DMF	Dimethylformamide
DMSO- <i>d</i> <sub>6</sub>	Deuterated dimethyl sulfoxide
D <sub>2</sub> O	Deuterated water
°C	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
equiv.	Equivalent
g	Gram; Gravitational force
BAs	Barbituric acids
h	Hour
H <sub>2</sub> DEBA	Diethylbarbituric acid
Hz	Hertz
IR	Infra-Red
LDA	Lithium diisopropylamide
m	Multiplet
H <sub>3</sub> BA	Barbituric acid
MeOH	Methanol
mg	Milligram
MHz	Megahertz
min	Minute
mL	Milliliter
mm	Millimeter

mmol	Millimole
$\mu\text{m}$	Micrometer
M.p.	Melting point
nm	Nanometer
NMR	Nuclear Magnetic Resonance
<i>n</i> -BuLi	<i>n</i> -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
<i>t</i> -Bu	Tertiary butyl
THF	Tetrahydrofuran
TLC	Thin-Layer Chromatography
TMS	Tetramethylsilane
CF <sub>3</sub> COOH	Trifluoroacetic acid
UV	Ultraviolet
FeCl <sub>2</sub>	Iron(II) chloride
$\alpha$	Alpha
$\beta$	Beta
$\gamma$	Gamma
$\delta$	Chemical shift
[ox]	Oxidation
R <sub>f</sub>	Refractive Index
i.e.	that is
<i>o</i>	Ortho
<i>m</i>	Meta
<i>p</i>	Para

H <sub>2</sub> O <sub>2</sub>	Hydrogen peroxide
H <sub>2</sub> SO <sub>4</sub>	Sulfuric acid
Et <sub>3</sub> N	Triethylamine
TBHP	<i>tert</i> -Butylhydroperoxide
BHT	Butylatedhydroxytoluene
Ag <sub>2</sub> O	Silver(I) oxide
LiAlH <sub>4</sub>	Lithium aluminium hydride
ZnCl <sub>2</sub>	Zinc chloride
KMnO <sub>4</sub>	Potassium permanganate
K <sub>2</sub> S <sub>2</sub> O <sub>8</sub>	Potassium persulfate
TEMPO	(2,2,6,6-Tetramethylpiperidin-1-yl)oxidanyl
ZnO	Zinc oxide
CH <sub>3</sub> COOH	Acetic acid
<i>p</i> -TSA	<i>p</i> -Toluenesulfonic acid
TiO <sub>2</sub>	Titanium dioxide
CuCl	Copper (I) chloride
AlCl <sub>3</sub>	Aluminium chloride
NaBH <sub>4</sub>	Sodium borohydride
DTBP	Di- <i>tert</i> -butyl peroxide
et al.	et alia, Latin for “and others”
i.e.	that is
e.g.	Example
equiv.	Equivalentents

## **GENERAL EXPERIMENTAL CONSIDERATIONS**

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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 its 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. **Infrared (IR)** spectra were recorded on Perkin-Elmer FT-IR-5300 spectrophotometer ( $\nu_{\max}$  expressed in  $\text{cm}^{-1}$ ). The  $^1\text{H}$  (500 MHz) and  $^{13}\text{C}$  (126 MHz) **NMR** spectra were run on a Bruker Advance 500 MHz FT-NMR at 500 MHz spectrometers. Chemical shifts are given in  $\delta$  ppm, using tetramethylsilane (TMS) as an internal standard. The **elemental microanalyses** were performed on Exeter Analytical Inc Model, CE-440 elemental analyzer.

**Thin-layer Chromatography (TLC)** was performed on glass plates ( $7.5 \times 2.5$  and  $7.5 \times 5.0$  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 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

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*tert*-Butylhydroperoxide (TBHP) is a colorless, clear liquid found in 70–90% aqueous solutions and as anhydrous in hydrocarbon solvents. To obtain anhydrous TBHP, a phase separation method can be employed to dry aqueous solutions, followed by azeotropic distillation to remove any leftover water. By oxidizing a variety of substrates, the reagent yields epoxides, 1–3 ketones, aldehydes, allylic alcohols, and nitro or imine compounds. The reagent has been carefully investigated, as have its metal complexes. This thesis looks at how it's been used to solve organic synthesis problems. Because the hydroxyl group in tertiary alcohols is labile, liquid hydrogen peroxide in a nonaqueous solution was suspected early on of reversibly reacting with *tert*-butyl alcohol to produce *tert*-butylhydroperoxide (TBHP). In this context, the thesis entitled "***tert*-butyl hydroperoxide mediated development of some new C-C and C-N bond formation**" will introduce the various aspect of the TBHP mediated synthesis of C-C and C-N bond formation in organic synthesis.

**Chapter 1** will provide a general introduction and literature review of TBHP mediated C-C and C-N bond formation in organic synthesis. **Chapter 2** will describe an Et<sub>3</sub>N catalyzed oxidative coupling of methyl arenes with malononitrile using TBHP as an oxidant at 100°C under solvent-free conditions. **Chapter 3** will provide a new, metal-free, and TBAI catalyzed synthesis of amide in excellent yield (85-90% ) via oxidative coupling of benzyl halide with various amines in the presence of TBHP at 80°C. **Chapter 4** will explore a facile, transition metal-free approach for the direct amidation of benzyl mercaptan through oxidative coupling with an amine using TBHP as an oxidant and NaI as a catalyst. **Chapter 5** will provide a metal-free I<sub>2</sub> catalyzed oxidative

coupling of indole and active methylene compounds into the corresponding 3-ylidene oxindole through C-C and C-O bond formation using TBHP under mild reaction conditions.