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

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DEDICATED TO MY LOVING FATHER & FAMILY MEMBERS.....

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It is certified that the work contained in the thesis titled "**Tert-butyl hydroperoxide(TBHP) Mediated Development of Some New C-C & C-N Bond Formation**" by ***"Dhirendra Kumar"*** has been carried out under my supervision and that this work has not been submitted elsewhere for a degree.

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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
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
equiv.	Equivalent
g	Gram; Gravitational force
BAs	Barbituric acids
h	Hour
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
$FeCl_2$	Feffous chloride
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
TBHP	*tert*–Butylhydroperoxide
BHT	Butylatedhydroxytoluene
Ag_2O	Silver(I) oxide
$LiAIH_4$	Lithium aluminium hydride
$ZnCl_2$	Zinc chloride
$KMnO_4$	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 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 (ν_{max} expressed in cm^{-1}). The **^{1}H** (500 MHz) and **^{13}C** (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. 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 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

*t*ert-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_3N catalyzed oxidative coupling of methyl arenes with malononitrile using TBHP as an oxidant at 100ºC 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 80ºC. **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_2 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.