In The Name of God

دانشگاه بوعلی سینا

Bu-Ali Sina University
Faculty of Chemistry

Submitted in Partial Fulfillment of the Requirements for

The Degree of Doctor of Philosophy (Ph.D.) in

ORGANIC CHEMISTRY

Title:

1- Synthesis of 1,4-dihydropyridines and their corresponding pyridines
2- Application of sodium perborate and silica sulfuric acid in organic functional groups transformation

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Bu-Ali Sina University
Faculty of Chemistry

Thesis

Submitted In Partial Fulfillment of the Requirements for the

Degree of Doctor of Philosophy (Ph.D.)

In the field of Organic Chemistry

Title

1. Synthesis of 1,4-dihydropyridines and their corresponding pyridines, and

2. Application of sodium perborate and silica sulfuric acid in the organic functional groups transformation

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Dedicated to:

My lovely mother and kind father

My patient husband

My sweet daughter (Atrin)

My honourable brothers

Professor D. Habibi

Professor M. A. Zolfigol

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Abstract

In this project, two different categories of research projects were carried out:

1. Application of sodium perborate and silica sulfuric acid in organic reactions, and
2. Synthesis of 1,4-dihydropyridines and their corresponding pyridines.

Sodium perborate is an inexpensive, safe and easily handle and capable to release the oxidizing species in organic medium which has made it a useful reagent in organic synthesis. In this respect sodium perborate has been successfully employed as a convenient substitute for the hazardous concentrated H_2O_2 in various oxidation reactions. Also, sodium perborate has been widely used in selective functional group transformations.

In a catalytic system $NaBO_3.4H_2O$/KBr/SSA, Br^- was converted into Br^+ and used as an oxidant in metal free oxidation of sulfides. In comparison with other catalytic systems, this method is cheap, safe and efficient. In this regard, sodium perborate in the presence of a catalytic amount of silica sulfuric acid was used for the oxidation of anilines to their corresponding nitro derivatives.

Silica sulfuric acid as a solid acid can be used as a reaction activator as well as a product purifier.

$Fe(NO_3)_3.9H_2O$ in the presence of silica sufuric acid generates NO_2^+ *in-situ* which can be used for the oxidation of alcohols under mild and heterogeneous conditions.

1,3-Dihalo-5,5-dimethylhydantoin was used for oxidation of urazoles and bis-urazoles for first time in this project and finally the produced triazolinedione was purified by silica sulfuric acid.

In the second part, the synthesis of some new dihydropyridines of some biological and medicinal importance carried out. These dihydropyridines containing a carbamate moiety at 4-position, were synthesized in two steps.

Phenyl isocyanate reacts with phenolic aldehyde to produce the intermediate (carbamate having an aldehyde functional group) which then reacts with ethyl acetoacetate and ammonium fluoride to give dihydropyridines.

Finally, in continuation of our studies on the chemistry of 4-phenyl- 1,2,3-triazole-3,5-dione, this compound was applied in oxidation of dihydropyridines. This method appears as simple, cheap and clean with easy workup

Abbreviations	
Abbreviates	**Name or formula**
BTF	α,α,α,-trifluorotoluene
CAN	Ceric ammonium nitrate
CDI	Carbonyldiimidazol
CTAB	Cetyltrimethylammonium bromide
DA	Diels-Alder reaction
DABCO	1,4-Diazabicyclo[2.2.2]octane
DDQ	3,4-Di-chloro-6,7-di-cyano-quinone
DPTBE	1,2-(Dipyridiniumditribromide) ethane
GC	Gas chromatogarphy
$H_3PW \cdot nH_2O$	Tungstophosphoric acid
HMTAB	Hexamethylenetetramine-bromine
IR	Infrared spectra
MTAD	4 -Methyl-1,2,4-triazoline-3,5-dione
NBS	*N*-Bromo succinimide
NMR	Nuclear magnetic resonance
PCC	Pyridinium chlorochromate
PIDA	Diacetoxy- iodobenzene
PTAD	4 –phenyl-1,2,4-triazoline-3,5-dione
PTC	Phase transfer catalyst
PVP-H_2O_2	Polyvinylpyrrolidone-supported hydrogen peroxide
SLE	Supported liquid extraction
SPB	Sodium perborate tetrahydrate
SPC	Sodium percarbonat
SSA	Silica sulfuric acid
TADs	4-Substituted-1,2,4-triazoline-3,5-diones
TBAI	tetra-*n*-butylammonium iodide
TBCA	Tribromoisocyanuric acid
TCCA	Trichloroisocyanuric acid
TCM	Trichloromelamine
TCT	2,4,6-trichloro[1,3,5]triazine (cyanuric chloride)
TLC	Thin-layer chromatography
TMGT	1,1,3,3-*N,N,N',N'*-tetra-methylguanidinum trifluoroacetate
TMS	Tetramethylsilane
TMSI	Iodotrimethylsilane
TPP	Tetraphenylporphyrine
UHP	Urea hydrogen peroxide

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Chapter One
Introduction
Part A

1.1. 1. Introduction

Development of new environmentally benign procedures and catalytic systems for the selective functional group transformation of organic compounds is an important goal in development of the modern methods for chemical synthesis. Therefore in recent years, the search for environmentally benign chemical processes or methodologies has received much attention by chemists, due to their necessity on the conservation of the global ecosystem. Also the development of heterogeneous catalysts for fine chemical synthesis has become a major research area, as the potential advantages of these materials (simplified recovery and reusability; the potential for incorporation in continuous reactors and micro reactors) over homogeneous systems can lead to novel environmentally benign chemical procedures both for academia and industry. In continuation of our investigations we found that sodium perborate was peroxygen compounds available at low price and extensively used in detergent industry as bleaching and antiseptic agent. Sodium perborate was successfully applied for some functional groups transportation instead of H_2O_2 to overcome disadvantageous of these concentrates reagent such as explosion, instability, hazardous and so on. For this purpose this reagent could be applied for oxidation of sulfides and anilines [1].

Silica sulfuric acid as a solid acid can be used as a reaction activator as well as a product purifier.

For the first purpose we used silica sulfuric acid (SSA) for oxidation of alcohols. In situ generation of NO_2^+ could take place when we used $[Fe(NO_3)_3.9H_2O]$ in presence of SSA [2].

For the second purpose when urazoles are oxidized with *N*-halo reagent, namely, 1,3-dihalo-5,5-dimethylhydantoin, triazole-3,5-diones that obtained can be purified with SSA.[3].