5410
DUT

T346

# STUDIES OF REACTION INTERMEDIATES TOWARDS THE SYNTHESIS OF XANTHENE DERIVATIVES AND DEVELOPMENT OF SAFER CATALYTIC SYSTEMS FOR PROTECTION OF CARBONYL GROUP

**A THESIS**

**SUBMITTED IN PARTIAL FULFILLMENT OF THE REQUIREMENTS**

**FOR THE DEGREE OF**

**DOCTOR OF PHILOSOPHY**

By

**PAPIA DUTTA**

**Registration No. 039 of 2010**


**School of Sciences**

**Department of Chemical Sciences**

**Tezpur University**

**Napaam, Tezpur-784028**

**Assam, India**

**December, 2014**

*To My Parents and Teachers...*

## Abstract

The content of this thesis consists of two types of research works. First part of the work covers the characterization of reaction intermediates in the direction of synthesis of xanthene derivatives which have diverse applications in medicinal chemistry and material science. It has been observed that xanthene moieties constitute the biologically active structural unit of a large number of natural products such as secalonic acid A, the eumitrin pigments, the beticolin toxins and the antibiotic xanthoquinodin A1. We have utilized heterogeneous and homogeneous catalytic systems for the preparation of 14-alkyl or aryl-14*H*-dibenzoxanthenes and the corresponding precursor intermediates, aryl-*bis*(2-hydroxy-1-naphthyl) methane (bisnaphthol) and its keto tautomers. For the first time, use of microwave radiation under solvent-free medium showed product selectivity against the different amount of solid acids for the preparation of dibenzoxanthenes and bisnaphthol derivatives. We also identified the existence of keto-enol tautomer for the first time towards the synthesis of dibenzoxanthene derivatives from the acid catalyzed two component reaction of 2-naphthol and aromatic aldehydes under reflux in methanol. The unstable keto isomers were fully characterized which gave a direct support for the proposed mechanism of dibenzoxanthene preparation. The bisnaphthol derivatives were also prepared in solution using homogenous catalyst at room temperature in less time. Another class of xanthene compounds, 1,8-dioxo-octahydroxanthene derivatives was prepared in neat condition using mechanochemical energy in presence of heterogeneous catalysts.

The second part includes the development of safer catalytic systems for the protection of carbonyl groups in the context of green chemistry. The protection of this group becomes a necessity in a multifunctional compound where the nucleophilic reaction is to be carried out at a different site other than the carbonyl group. The carbonyl group can be protected by converting it into different types of derivatives. We have utilized polymer supported Brønsted acid as reusable catalyst for the chemoselective preparation of 1,1-diacetate (acylal) from aldehyde group and deprotection of acylals to the carbonyl group in different condition. Similarly we have employed polyethylene glycol (PEG) as reusable catalyst and medium for

the efficient conversion of carbonyl compounds to oxime derivatives using microwave energy without addition of any acid or base catalyst. After that we have made a conversion of the 1,8-dioxo-octahydroxanthene compound, synthesized in the first part, to the corresponding oxime under microwave irradiation using PEG-600 as reusable reaction medium.

**The content of the thesis is divided into five chapters.**

## Chapter 1: Review of Literature

This chapter illustrates about the oxygen containing heterocyclic xanthene derivatives which exhibit various medicinal as well as industrial applications. Two xanthene derivatives namely dibenzoxanthenes and xanthenediones have been extensively studied during the course of this work. Dibenzoxanthenes form the basic structural unit of various pharmaceutics and are used in photodynamic therapy and as antagonists for the paralyzing action of zoxazolamine. These compounds have also found applications in the industrial field as leuco-dye and in laser technologies and pH sensitive fluorescence materials for visualization of biomolecules. The second xanthene derivative of our interest, the xanthenediones has also been extensively examined by chemists because of their presence as structural moiety in numerous compounds having both medicinal and industrial value. Moreover the reaction intermediate leading to dibenzoxanthenes namely the aryl-bis(2-hydroxy-1-naphthyl) methane, often termed as bisnaphthols in short have been reported to possess non-steroidal pharmaceutical properties of anticancer, anti-inflammatory and anti-analgesic activity with large gastric tolerance. Some of them are also utilized as non-linear optical materials, enzyme mimetics, ion-selective electrodes or sensors, chiral ligands in organometallic chemistry, synthetic precursors for the formation of spirans and sometimes, as high-performance liquid chromatography stationary phases with some modifications. The detailed literature survey of the synthetic methodologies leading to dibenzoxanthenes and xanthenediones along with those of bisnaphthols were primarily emphasized.

The review also discusses the importance of carbonyl group protection in multistep reactions. Out of several carbonyl protecting groups, we were interested

to transform into 1,1-diacetates and oxime derivatives by considering the green chemistry approach. The stability of the acylals in neutral as well as basic media has made them an attractive alternative to the acetals. Acylals have varied industrial applications as cross-linking reagents for cellulose in cotton and activators in the composition of bleaching mixture used for the treatment of wine-stained fabrics. They are also utilized for the synthesis of 1-acetoxydienes and dihalovinyl acetates in Diels-Alder reactions, mainly the ones derived from α,β-unsaturated aldehydes. The oxime compounds are found to be potent intermediates for the synthesis of various nitrogen containing compounds and some heterocyclic moeities. Some oxime compounds possess medicinal properties as antimicrobial agents, pesticides, antioxidants, vasodilators, and inhibitors of P450. This chapter highlights the reported methods for synthesis of acylals using polymer supported solid acid catalysts and also the formation of oximes under solvent-microwave irradiation.

Furthermore, this chapter briefly presents about the general techniques wherein solid acid catalysts, polyethylene glycol and solvent-less organic reactions using microwave and mechanical energies were used during our work. In modern day research, solid acid catalysts have been extensively used as heterogeneous catalysts which have been the choice of interest in many research fields because of the reusability and eco-friendly factors. This property is very appreciating when the reactions are carried out at large scales basically in industries where disposal of the catalysts once the processes are over is a matter of environmental issue. Moreover, this brings down the cost of the entire system. Polyethylene glycols have also being exhibiting dual behavior both as reaction media and as phase transfer catalyst. The tunable property of this class of polymers upon adjustment of physical properties such as pressure, temperature has aided them to be easily recovered from the reaction mixture where they are used once the reaction is over. Merely decreasing the temperature leads to the precipitation of PEGs from the reaction mixture. PEGs have found enormous applications in varied fields of research. Solvent-free organic syntheses have become the interest of researchers and industrial workers because of the disposal issues of the toxic solvents used during bulk synthesis. Solvent-free mechanochemical grinding displays several advantages such as reduced pollution, minimization of energy consumption and

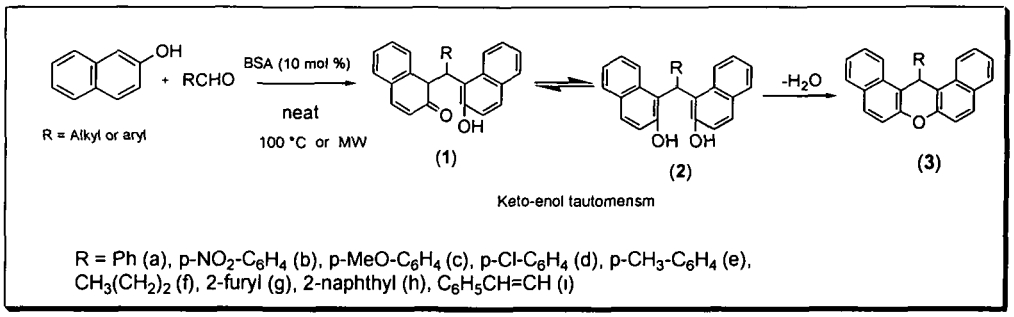
cost reduction. The replacement of the unnecessary and wasteful heating by microwave heating is considered to be quite effective for such syntheses as these leads to the uniform and homogeneous nature of the energy consumption by the reactants.

## Chapter 2: Synthesis and characterization of Aryl-*bis*(2-Hydroxy-1-Naphthyl) Methane and 14-Alkyl or Aryl-14*H*-Dibenzoxanthenes

This chapter is divided into two sections namely **Section 2A** and **Section 2B**.

### Section 2A: Boron Sulfonic Acid (BSA) Catalyzed Selective Synthesis of Aryl-*bis*(2-Hydroxy-1-Naphthyl) Methane and 14-Alkyl or Aryl-14*H*-Dibenzoxanthenes under Solvent-free Condition

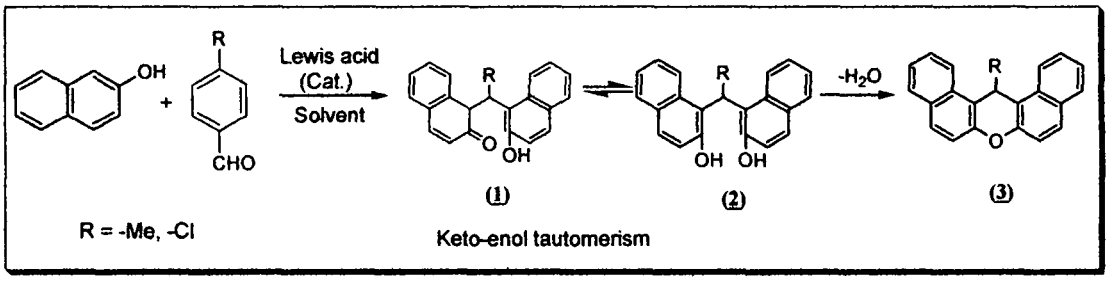
This section of the chapter mainly contains the detailed synthesis of dibenzoxanthenes (3) and its precursor intermediate, the bisnaphthols (2) using boron sulfonic acid (BSA) as the reusable solid acid catalyst in solvent-free condition (**Scheme-1**). The reactions have been carried out both via thermal as well as microwave heating of the reactants. The selectivity of the formation of products largely depends on the reaction condition. Thermal treatment in general leads to dibenzoxanthenes whereas microwave irradiation seems to yield selectively the bisnaphthols. The reusability of the catalyst was tested and the activity was found to remain intact for four cycles giving almost the same yield. Moreover avoidance of solvents and the use of heterogeneous catalyst make the processes environment friendly and cost effective. The combination of the catalyst boron sulfonic acid and the process used make the reaction quite feasible. Monitoring of the progress of the reaction was done by thin layer chromatography.




**Scheme-1**

**Section 2B: Investigation of Keto-enolTautomers during the Synthesis of Aryl-bis(2-hydroxy-1-naphthyl)Methanes**

In this section three Lewis acid catalysts, two heterogeneous, i.e., $FeSO_4.7H_2O$ and $CuSO_4.5H_2O$ and the homogeneous $BF_3.OEt_2$have been studied for the synthesis of bisnaphthols (**2**). However, it was observed that $FeSO_4.7H_2O$ was not that effective for the synthesis as $CuSO_4.5H_2O$ in methanol under reflux condition. Moreover, $BF_3.OEt_2$alone was not sufficient for the formation of bisnaphthols. The reactions seem to give satisfactory result only when acetic acid was used as promoter along with the $BF_3.OEt_2$ at room temperature in dichloromethane. Moreover for the first time, the isolation of the keto tautomer (**1**) of aryl-bis (2-hydroxy-1-naphthyl)methanes (**2**) was possible from the reactions of 2-naphthol and 4-chlorobenzaldehyde or 4-methylbenzaldehyde under reflux in methanol using $CuSO_4.5H_2O$ as heterogeneous catalyst. These two keto isomers distinctly confirm the plausible mechanism for the dibenzoxanthene synthesis from aldehydes and 2-naphthol through the formation of keto-enoltautomerism (**Scheme-2**).

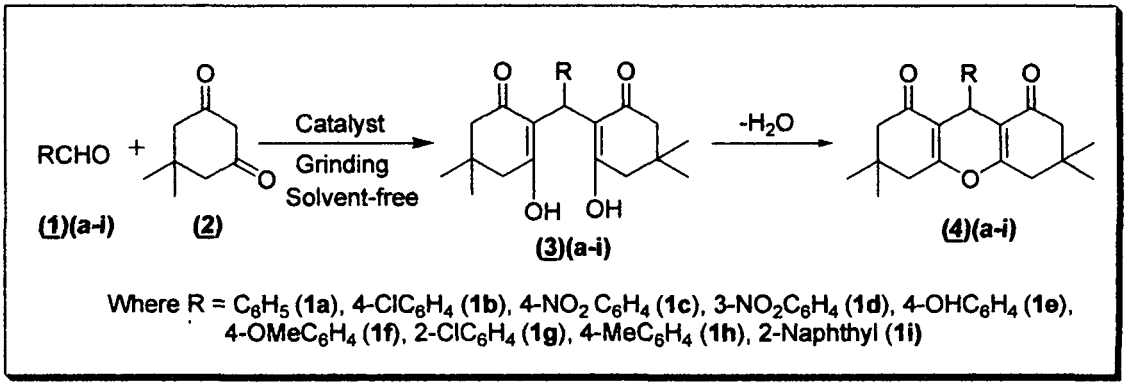



**Scheme-2**

In both the sections, all known and unknown products were characterized by melting points, $^1H$ and $^{13}C$ NMR, FT-IR, and elemental analysis techniques after purification via thin layer chromatography. The keto compounds (**1**) were identified with the help of DEPT, COSY along with the existing analysis.

## Chapter 3: Mechanochemical Synthesis of 1,8-Dioxo-Octahydroxanthene Derivatives under Solvent Free Condition using Heterogenized Acid Catalysts

In this chapter, the synthesis of xanthenediones was investigated via mechanochemical grinding of aldehydes and 5,5-dimethyl-1,3-cyclohexanedione (dimedone) using polyaniline (PANI) supported Brønsted and Lewis acid catalysts (**Scheme-3**). Comparison between the unsupported catalysts, i.e*p*-toluenesulfonic acid (*p*-TSA) and $FeCl_3$ with the supported ones over PANI was done for the synthesis. The supported catalysts were found to be better both in terms of time and yield. The selective formation of xanthenediones (**4**) was observed unlike in case of the unsupported ones. However, another catalyst, ferric nitrate nonahydrate was found to lose its activity when it was supported on montmorillonite K-10 as clayfen. The reaction was also carried out in different solvents taking *p*-chlorobenzaldehyde as the substrate in the model reaction. However, solvent-free condition was found to be the most effective. The change in the state of the reaction mixture during the progress of the reaction was distinctly visible. The reusability was also studied for the three supported catalysts. The activity almost remains unchanged for three consecutive cycles.



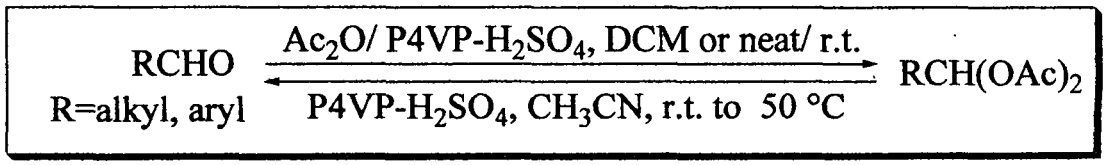

**Scheme-3**

## Chapter 4: Protection of carbonyl group using safer catalytic systems

The work in this chapter is divided in **Section 4A** and **Section 4B**.

**Section 4A: Polymer-supported Brønsted Acid Catalyzed Chemoselective Protection of aldehydes to 1, 1-Diacetates and Deprotection to Carbonyl Group**

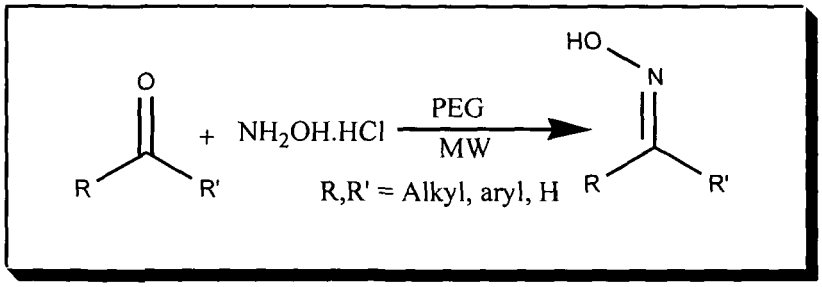
This section basically deals with the chemoselective protection of aldehydes by converting them into 1,1-diacetates (acylals) at room temperature and deprotection to carbonyl group under reflux using poly(4-vinyl)pyridine supported sulfuric acid as catalyst in organic solvents (**Scheme-4**). The chemoselective nature of the catalyst along with reusability property makes this catalyst quite attractive to researchers and in industries. Moreover, acylals themselves are quite stable and have several practical utility. The reaction was studied both in dichloromethane and neat condition at room temperature. However, solvent-free media was found to be inferior as compared to the reactions in dichloromethane. In this case also, the catalyst was found to be reusable.




**Scheme-4**

**Section 4B: Dual Nature of Polyethylene Glycol under Microwave Irradiation for the Clean Synthesis of Oximes**

In this section, polyethylene glycols have been studied for oxime synthesis from the reaction of equal molar amounts of carbonyl compound and hydroxylamine hydrochloride under microwave irradiation without addition of any acid or base catalyst (**Scheme-5**). However it was observed that among the three PEGs studied, i.e. 200, 400 and 600, the best result was obtained in 600. PEGs have been found to possess dual behavior, one as reaction media and the other as catalyst. PEGs have tunable property, which means that their property mainly depends on external factors like pressure, temperature and composition.




**Scheme-5**

## Chapter 5: Summary of the Present Work

This chapter summarizes the entire work described in this thesis.

**TEZPUR UNIVERSITY**
**(A CENTRAL UNIVERSITY)**
***Napaam, Tezpur -784028***

---

# DECLARATION

This is my solemn assertion that the research findings embodied in this thesis entitled "***Studies of reaction intermediates towards the synthesis of xanthene derivatives and development of safer catalytic systems for protection of carbonyl group***" is the outcome of the work carried out completely by me during the period of Ph.D. research undertaken under the guidance of Dr. Ruli Borah, Associate Professor in the Department of Chemical Sciences, Tezpur University, India. Due suggestions from others have also been included.

As per the general ethics of reporting scientific observations, the original sources of the information included have been adequately cited along with proper references and acknowledgements. I also declare that no misrepresentation or falsification of any idea/data has been done. I understand that any violation of the above will be taken for disciplinary action by the Institute.

Papia Dutta

Date: 01-04-2015 **Papia Dutta**

Tezpur University

**Dr. Ruli Borah**
Department of Chemical Sciences
Tezpur University, Napaam
Tezpur - 784028, Assam, INDIA
E-mail: ruli@tezu.ernet.in
Mobile: +91 94353 80377

## Certificate of the Supervisor

This is to certify that the thesis entitled "***Studies of reaction intermediates towards the synthesis of xanthene derivatives and development of safer catalytic systems for protection of carbonyl group***" submitted to the School of Sciences, Tezpur University in partial fulfillment of the requirements for the award of the degree of Doctor of Philosophy in ***Chemical Sciences*** is a record of research work carried out by Ms. Papia Dutta under my supervision and guidance since January, 2010 in the Department of Chemical Sciences, School of Sciences, Tezpur University. She has been duly registered (Registration No. 039 of 2010) and has fulfilled all the requirements specified in the regulations of Tezpur University including course work.

All help received by her from various sources have been duly acknowledged.

The thesis is the result of her own investigations on the subject. No part of this thesis has been submitted elsewhere for award of any other degree or diploma by this or any other university/institution.

Place: Tezpur University

R. Borah
Associate Professor
Dept. of Chemical Sciences
Tezpur University- 784028

**(Dr. Ruli Borah)**
Associate Professor
School of Sciences
Department of Chemical Sciences
Tezpur University
Napaam, 784 028, India

Date: 01.04.2015

तेजपुर विश्वविद्यालय
(केंद्रीय विश्वविद्यालय)
नपाम, तेजपुर - 784 028, असम, भारत

TEZPUR UNIVERSITY
( A Central University)
Napaam, Tezpur - 784 028, Assam, India

## CERTIFICATE OF THE EXTERNAL EXAMINER AND ODEC

This is to certify that the thesis entitled "***Studies of reaction intermediates towards the synthesis of xanthene derivatives and development of safer catalytic systems for protection of carbonyl group***" submitted by ***Ms. Papia Dutta*** to Tezpur University in the Department of Chemical Sciences under the School of Sciences, in partial fulfillment for the award of the Degree of Doctor of Philosophy in Chemical Sciences, has been examined by us on ..... and found to be satisfactory.

The committee recommends for the award of the Degree of Doctor of Philosophy.

Signature of

Principal Supervisor

Date:

External Examiner

Date:



फोन / Phone : 03712-267007 - 9 (3 lines) • फेक्स / Fax : 03712-267005, 267006 • ई-मेल / e-mail : admn@tezu.ernet.in

# Acknowledgements

First of all, I would like to take the opportunity to express my heartfelt and sincere gratitude to my teacher and supervisor, Dr. Ruli Borah for the constant support and motivation she has lent me throughout the entire phase of my research work. This work would never have been able to see the light of this day without her being beside me and the tremendous enthusiasm and moral support bestowed by her upon me.

I thank the Head of the Department of Chemical Sciences and my doctoral committee members, Prof. Ramesh C. Deka and Dr. Ashim J. Thakur for the valuable suggestion that I received from them whenever I was in true need. I will always remain thankful to all the faculties and technical staffs of the department for all the help they extended during the needful moments of my research period.

I would like to thank the Vice Chancellor of Tezpur University for allowing me to do research in this University and providing me the institutional fellowship for the same. For the later part of the fellowship, I thank UGC for the BSR fellowship. I greatly acknowledge the Sophisticated Analytical Instrumentation Centre, Tezpur University for the analysis of the different samples. I am also thankful to the administrative staff for their help.

The role of my undergraduate teacher, Dr. Diganta Choudhury of B. Borooah College, in motivating and inspiring me to pursue a career in chemistry is far beyond worth to express in words. Mere words cannot define his influence upon me.

I am very fortunate indeed and thankful to the Almighty to have a friend like Subhi who has always supported and helped me in every possible manner. Her friendship is a precious treasure for a lifetime.

I am thankful to my seniors, Dr. Kalyan Jyoti Borah, Dr. Dhrubajyoti Talukdar Dr. Siva Prasad Das, Dr. Jeena Jyoti Baruah, Dr. Bidyut Deka for their help

during my research phase. I am very gratified to all my lab juniors, Parishmita, Arup, Pinky and Susmita who were always ready to help me at any problem.

Certain people have always helped me and I can count on to them at any time who I would like to thank specially. They are Tridib Da, Aradhana Ba, Gaurango, Apurba, Hemanta, Rasna ba, Nibedita Ba, Shaswat, Pratisha, Julee, Pranav, Monoj, Kundan, Jyotish, Ujjal.

I would like to thank Hriday, Hirak, Iftikar and Priyakshi for solving the computer- related technical problems whenever I encountered.

I would like to mention that some people have contributed immensely towards my being independent by turning down to help me. I thank these people who unknowingly and indirectly have made me strong enough to face this challenging world and overcome any crisis confidently. I might miss out someone, but would like to thank everyone who has helped me in any manner, no matter how minute it is, during my Ph.D period.

Being a hostel boarder, I cannot ignore the care I got from the hostel menials, "mahis" especially during the days of my ill health. Far away from home, they made me feel at home.

Last but not the least, I would like to thank my parents and my sister for supporting me through every thick and thin and for the constant moral support. They were the targets of all my bad moods and frustrations, but they always understood and stood strong beside me. This day is an answer to all the prayers and blessings of my family, relatives and well wishers.

**Papia Dutta**

## Table of Contents

# LIST OF TABLES

## Abbreviations/Symbols Used

| | |
|---|---|
| $^{13}C$ | Carbon-13 isotope |
| BSA | Boron Sulfonic acid |
| Brs | Broad singlet (in NMR) |
| cat. | Catalyst |
| $CDCl_3$ | Deuterated chloroform (used as NMR solvent) |
| CHN | Carbon Hydrogen Nitrogen |
| Cm | Centimetre |
| Conc. | Concentrated |
| Corp. | Corporation |
| COSY | Correlation Spectroscopy |
| CTMS | Chlorotrimethylsilane |
| d | Doublet (in NMR) |
| DBSA | 4-dodecylbenzenesulfonic acid |
| DCM | Dichloromethane |
| DEPT | Distortionless Enhancement Polarization Transfer |
| DMF | Dimethyl formamide |
| eq. | Equivalent |
| FT-IR | Fourier Transform-Infrared |
| g | Gram |
| GC-MS | Gas Chromatography-Mass Spectrometry |
| h | Hour |
| HPA | Heteropoly acid |
| Hz | Hertz |
| $IC_{50}$ | Half maximal inhibitory concentration |

| | |
|---|---|
| i.e. | That is |
| IR | Infrared |
| *J* | Coupling constant (in NMR) |
| kHz | Kilo Hertz |
| m | Multiplet (in NMR) |
| *m* | Meta |
| MAO-A | Monoamine oxidase-A |
| Me | Methyl |
| MeOH | Methanol |
| Mg | Milligram |
| MHz | Mega Hertz |
| Min | Minutes |
| mL | Milli litre |
| mmol | Milli mole |
| mol | Mole |
| M.p. | Melting point |
| m.p. | Melting point |
| MPA-DAZY | Dealuminated zeolite-Y with 12-molybdophosphoric acid |
| MW | Microwave |
| MWI | Microwave irradiation |
| NMR | Nuclear Magnetic Resonance |
| No. | Number |
| NSPVPC | N-sulfonic acid poly(4-vinylpyridinium) chloride |
| *o* | Ortho |
| *p* | Para |
| PANI | Polyaniline |

| | |
|---|---|
| PEDOT | poly-(3,4-ethylenedioxythiophene) |
| PEG | Polyethylene Glycol |
| P4VP | Poly(4-Vinylpyridine) |
| ppm | Parts per million (in NMR) |
| PPY | Polypyrrole |
| *p*-TSA | Para toluene sulfonic acid |
| r.t. | Room temperature |
| s | Singlet (in NMR) |
| t | Triplet (in NMR) |
| Ter | Tertiary |
| TfOH | trifluoromethanesulfonic acid |
| THF | Tetrahydrofuran |
| TLC | Thin Layer Chromatography |
| TMEDA | N,N,N′,N′-tetramethylethylenediamine |
| TMS | Tetramethylsilane |
| TOF | Turnover Frequency |
| TPPMS | Sodium triphenylphosphine-m-sulfonate |
| UV | Ultra Violet |
| VOC | Volatile Organic Compound |
| W | Watt |
| °C | Degree Celsius |
| < | Greater or smaller than |
| % | Percentage |
| Å | Angstrom |
| δ | chemical shift (in NMR) |

# Chapter 1

## Review of Literature

## 1.1. General Introduction

The content of this thesis includes two types of studies based on the synthesis of xanthene derivatives and protection of carbonyl group for multistep synthesis of target molecules.

### 1.1.1. Xanthene Derivatives as Heterocyclic Compounds

Heterocyclic compounds are widely distributed in nature in the form of alkaloids, essential amino acids, vitamins, hemoglobin, hormones and plant pigments and many of them are of fundamental importance for life processes. The particular interest of heterocyclic compounds in medicinal chemistry has catalyzed the discovery and development of much heterocyclic chemistry and methods. Among the numerous heterocyclic compounds, oxygen containing xanthenes occupy a very pivotal position being the biologically active structural unit of a large number of natural products and in medicinal chemistry (**Fig. 1**) [1-4]. Particularly, the study [3] of xanthone in *Hypericum* species is interesting from the pharmacological point of view such as strong and selective inhibition of MAO-A, in vitro toxicity, in vivo antitumor activity along with other antiviral and antibacterial activities. Dibenzoxanthenes have displayed their diverse utility as various medicaments such as antibacterial [5], antivirals [6] and anti-inflammatory agents [7] as well as efficiency in photodynamic therapy [8-9] and antagonists for the paralyzing action of zoxazolamine [10-11]. These compounds are also utilized as leuco-dye, in laser technologies and in pH sensitive fluorescence materials for visualization of biomolecules [12-15]. Another derivative, xanthenediones are considered as valuable synthons because of the inherent reactivity of pyran ring [16]. The reduced form of xanthone unit (3,4,4a,9-tetrahydro-2*H*-xanthen-9-one) in secalonic acid (**Fig. 1**) is typical example of natural product. The tetrahydroxanthone moiety is also observed in the lactone ergochrisin, the eumitrin pigments, the beticolin toxins and the antibiotic xanthoquinodin A1 [17].

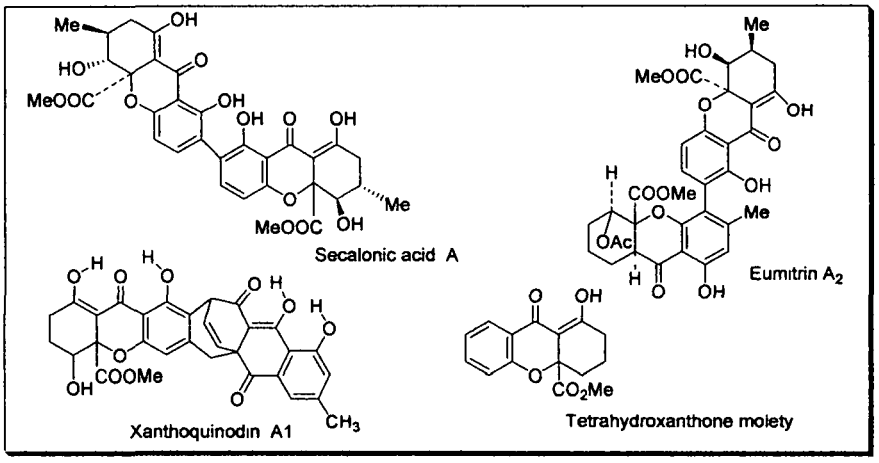
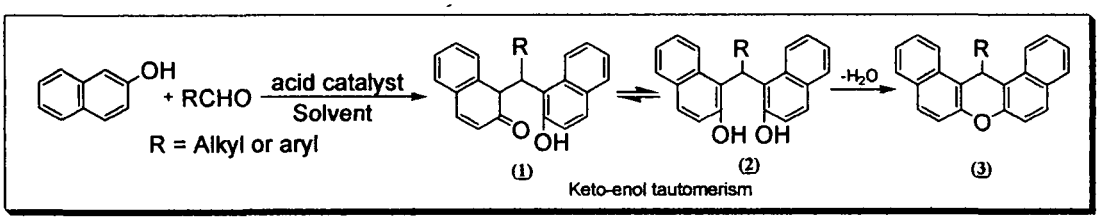



**Fig. 1**

Various synthetic strategies have been reported in literature for the preparation of xanthene compounds [18]. The acid catalyzed cyclocondensation of 2-naphthol with aldehydes is the common method for the synthesis of dibenzoxanthene derivatives (3) via the formation of tautomeric mixture of intermediates, aryl-bis(2-hydroxy-1-naphthyl) methane (2) and its keto isomer (1) (**Scheme-1**). The intermediate aryl-bis(2-hydroxy-1-naphthyl) methane (2) also known as bisnaphthol constitutes a non-steroidal class of medicaments with anticancer, anti-inflammatory and anti-analgesic activity with large gastric tolerance [19-20]. Some of these compounds are effective against alzheimer disease with very good $IC_{50}$ values [21]. These compounds are also utilized as non-linear optical materials, enzyme mimetics, selective membranes, ion-selective electrodes or sensors, chiral ligands in organometallic chemistry, synthetic precursors for the formation of spirans and sometimes, as high-performance liquid chromatography stationary phases with some modifications [22-23]. This chapter contains a section about the review of various developed methodologies for the synthesis of 14-alkyl or aryl-14*H*-dibenzo[a,j]xanthenes and 1,8-dioxo-octahydroxanthenes in addition to the precursor intermediate aryl-bis(2-hydroxy-1-naphthyl) methane (2).




**Scheme-1**

## 1.1.2. Chemistry of Carbonyl Protecting Groups

Multistep synthesis of complex organic molecules usually needs to deal with a major problem, i.e. functional group incompatibility since the birth of organic chemistry. Fisher *et al.* first introduced the idea of temporarily blocking of reactive functional group in a multifunctional molecule when a chemical reaction is to be carried out selectively at one reactive site that could then later be removed [24]. A protecting group must fulfill certain requirements such as inertness of the protecting group to the projected reactions, easy separation from side products, minimum additional functionality to avoid further site of reactions and simple regeneration of original functional groups [25]. Many protecting groups have been, and are being, developed to synthesize more complicated organic moieties through multistep synthesis [25]. The presence of highly electronegative oxygen atom with lone pairs of electrons in the carbonyl group makes it more prone to nucleophilic attack in comparison to other reactive functionality in a synthetic sequence. Thus protection of this group becomes a necessity in a multifunctional compound where the nucleophilic reaction is to be carried out at a different site other than the carbonyl group. The carbonyl group can be protected by converting it into different types of derivatives. Some of them are (**Fig. 2**) acyclic acetals and ketals (**4**), cyclic 1,3-dioxanes (**5**), salicylate acetals (**6**), 1,3-dioxolanes (**7**), acylals (**8**), acyclic dithioacetals and ketals (**9**), cyclic 1,3-dithiane (**10**), 1,3-dithiolane (**11**), oximes (**12**), etc.

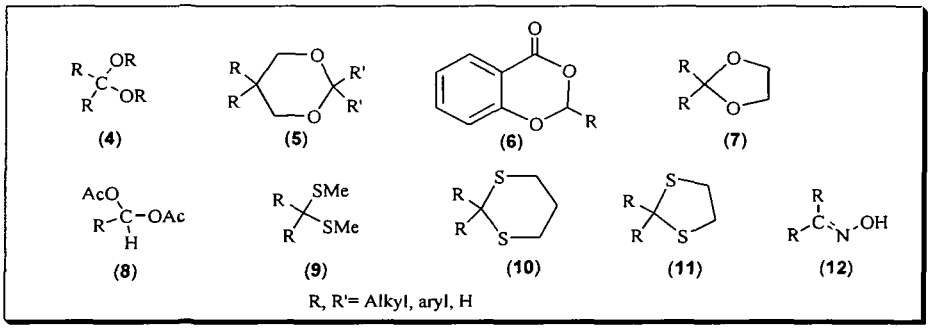



**Fig. 2**

Out of these several protecting groups, we were interested to develop some safer procedures for the transformation of carbonyl group to acylal derivatives using solid acid catalysts and microwave assisted synthesis of oxime in polyethylene glycol without use of any acid or basic catalyst. Both protecting groups have found varied applications in different fields. The acylals of α,β-unsaturated aldehydes have been

utilized for the synthesis of 1-acetoxydienes and dihalovinyl acetates in Diels-Alder reactions [26-30], as cross-linking reagents [31] for cellulose in cotton and activators in the composition of bleaching mixture used for the treatment of wine-stained fabrics [32]. The oxime compounds are potent intermediates for the synthesis of amides [33], nitriles [34], nitro compounds [35], nitrones [36], amines [37], hydroxylamines [38], and some heterocyclic compounds [39]. Some oxime compounds have medicinal properties as antimicrobial agents [40], pesticides [41-42], antioxidants [43], vasodilators [44], and inhibitors of P450 [45]. This review also covers a part of the up to date literatures of acylal synthesis using heterogeneous catalysts and use of microwave energy in oxime preparations.

## 1.2. Review of Literature on General Techniques

### 1.2.1. Solid Acid Catalysts

Catalysis has been playing a central role in academic research as well as in industrial fields being the core of innumerous chemical protocols [46]. The growing awareness regarding environmental pollution and its hazardous impact over mankind and nature has restricted the use of non eco-friendly chemicals as catalysts which will disrupt the global ecosystem, basically in large scale industries. Thus the necessity for this conservation has compelled the chemists of the recent era to search and develop environmentally benign chemical processes, methodologies and catalysts. The efficient use of safe, non-corrosive and selective solid acid catalysts represents an important area in organic synthesis. One way to convert strong Brønsted or Lewis acids into environment friendly catalyst is to heterogenize these acids by supporting on high surface area solids such as graphite, alumina, silica, zeolites, clays etc. or various kinds of polymers. The type of material used as support frequently plays a crucial role in the performance of the resulting supported catalyst. Basically, the support has to be thermally and chemically stable during the reaction process and has to provide accessibility and a good dispersion of the active sites [47]. The multifaceted advantages of solid acid catalysts such as simple and rapid experimental procedures, easy separation from reaction mixture by filtration, recyclable, environmental compatibility, safety in handling, chemo selectivity and cost effective have proved them to be an alternative to the conventional inorganic and organic acids [48]. Polymer supported solid catalysts have been developed by immobilization of

active sites of catalysts via chemical bonding or weaker interactions such as H-bonds or donor acceptor interactions [49]. Literature survey indicates that polymers have been extensively used as a suitable choice for the support in solid acid catalysts due to their advantageous properties which allow them to expand the range of applicable solvents. Some of the common insoluble polymer supports are polystyrene, poly(4-vinylpyridine), polyaniline, polyacrylate, etc. (**Fig. 3**) [49].

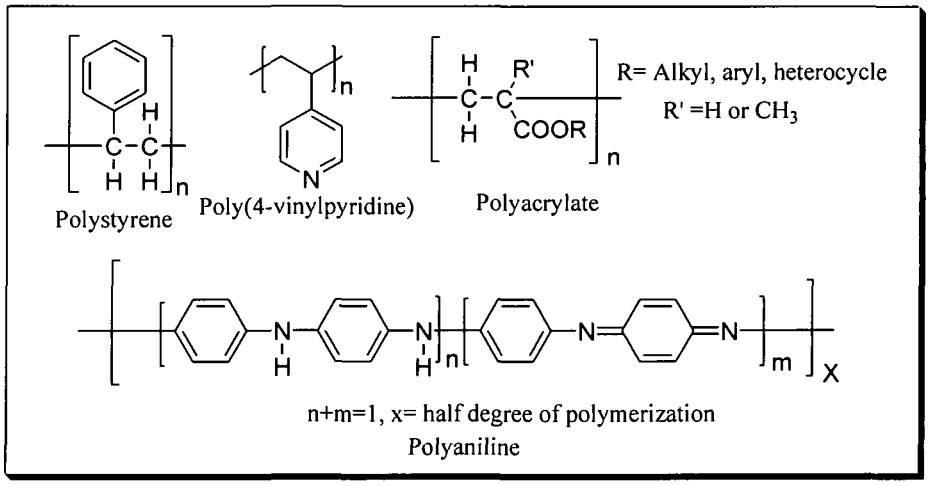



**Fig. 3**

## 1.2.2. Polyethylene Glycol (PEG) as Greener Media

Polyethylene glycol (PEG) is the linear polymer formed from the polymerization of ethylene oxide as monomer unit. It covers wide range of molecular weights starting from right 200 to tens of thousands and is known to be inexpensive, thermally stable, recoverable, biologically compatible and non-toxic [50-54]. Furthermore, PEG and its mono methyl ethers have lower vapour pressure, nonflammable, present simple work-up procedures and can be recycled. When its molecular weight is < 600, it remains as hygroscopic, water miscible, colorless and viscous liquid at room temperature, but as the molecular weight exceeds 800; it turns into a white waxy, water soluble solid [55]. Lower molecular weight PEG can be used as solvents in organic reactions with or without addition of water. PEG has been reported to be stable towards acidic, basic and high temperature reactions [56-59]. Additionally, the inactiveness of PEG for common oxidation and reduction reactions makes it more suitable to be an environmentally benign alternative to volatile organic solvents and a highly practical medium for organic reactions. Noted applications of PEG was seen in the fields of biotechnology and medicine [60-61], in PEG-metal ion coordination chemistry, in

PEG and PEG-supported catalysis, as phase transfer catalyst and solvent [62-67]. PEG is a hydrophilic polymer, easily soluble in water and many organic solvents including DMF, dichloromethane, toluene, acetonitrile and acetone, but it is not soluble in aliphatic hydrocarbons such as hexane, cyclohexane, diethyl ether, t-butyl methyl ether, isopropyl alcohol and cold ethanol [55]. As a reaction medium or catalyst, PEG may be recovered from the aqueous solution of reactions by extraction with a suitable solvent or by direct distillation of water or solvent [68]. PEG has the ability to serve as a phase transfer catalyst in aqueous biphasic medium, since the polyethylene oxide chains can form complexes with metal cations, similar to crown ethers [69]. The high solubility of some metal salts in low molecular weight PEG had increased the use of this medium in some homogenous oxidation and substitution reactions resulting in high yields [68]. Several review of literature on PEG had briefly explored the possibility of PEG as tunable solvent systems in organic synthesis [70]. Tunable solvent systems combine homogeneous catalytic reactions to heterogeneous separations, consequently combining multiple unit operations into a single step and ensuing reducing waste generation and production cost. The homogeneous polar medium of PEG (or aqueous solution) can be split into two relatively immiscible phases with the addition of suitable non-polar aprotic solvents. The non-polar phase contains the hydrophobic product, and the aqueous PEG phase contains the hydrophilic catalyst. Variation of temperature and pressure on the homogeneous solution of PEG can also facilitate the convenient separation of PEG. Careful cooling of PEG solutions in suitable solvents precipitate out the PEG as solid form and subsequent filtration with ether can facilitate the separation of the products and left starting materials [71]. The dual behavior of low molecular weight PEG as catalyst and reaction medium has opened up the greater suitability of this medium as alternative benign solvent in organic synthesis.

### 1.2.3. Solvent-less Organic Reactions using Microwave and Mechanical Energies

The development of cleaner methodologies for organic synthesis has become a major thrust area both in chemical industry and academia by replacement of these obnoxious solvents with environmentally benign and safe alternatives. Solvent-free techniques are highly encouraged to a large extent in industries wherein the disposal of the harmful solvents used in large scale processes is a matter of environmental safety

[72]. The inherent advantageous qualities of solvent-free reactions are product selectivity, faster rate as compared to reactions in organic solution, economic viability and simplicity in handling. Rothenberg *et al.* (2001) clearly explained the differences of solvent-free reactions from solid-phase reactions and solid-solid or solid–state synthesis [73]. In absence of solvent, some organic reactions occur more efficiently and selectively than does its solution counterparts, since molecules in a crystal are arranged tightly and regularly. Literature studies indicate the utilization of mechanical, thermal, microwave, ultrasound and photochemical energies to precede various types of solvent-free organic reactions [74-79]. These solvent-free reactions can be easily monitored by measurement of IR and UV spectra in the solid state or in neat condition [80]. This review also covers the detail uses of solvent-less methods towards the synthesis of xanthene derivatives and carbonyl protecting groups.

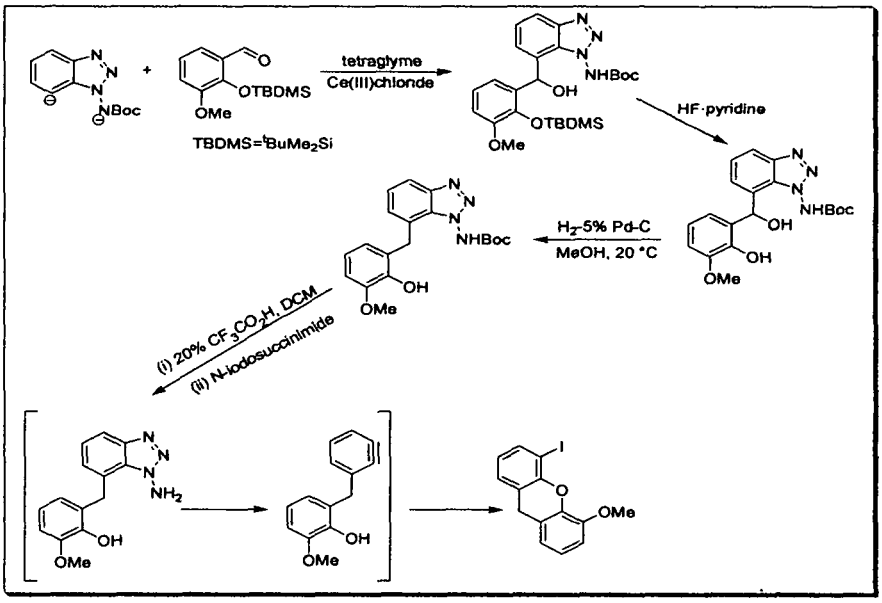
The applications of microwave energy in organic synthesis was started in the mid of 1980s with domestic microwave oven [81-82]. The development of safe commercial microwave reactor had considerable increase in the use of this technology since the mid-1990s [83]. The notable advantages like shorter reaction times, cleaner reaction, expanded reaction rates; higher yields have made it attractive in organic synthesis as well as in industries to implement their processes [83]. In thermal method, energy is transferred to the reaction vessel by conduction process from a preheated source. Hence, the heating in this process is not always uniform and homogeneous as compared to microwave heating method. The microwave dielectric heating depends on the ability of a solvent or matrix to absorb microwave energy and to convert it into heat [84]. Molecules absorb radiations via two mechanisms: dipole polarization and conduction. Under the oscillating applied fields, the dipole of molecules attempts to realign itself with the alternating electric field and subsequently reduction in heat energy through molecular friction and dielectric loss. The strength of the matrix to align itself with the applied electric field determines the amount of heat generation. This process generates intense internal heating within the core molecules. Compounds with higher dielectric constants tend to absorb microwave energy than compounds with no net dipole moment which are said to be microwave inactive. Mono mode and multimode are two reactors utilized for the microwave assisted organic reactions. Several review of literature on this technique has collected the up to date utilization of microwave energy in different types of organic synthesis [85].

Toda and his coworkers first revealed the application of mechanochemical energy to activate molecules in solvent-less mediums for chemical change in organic reactions [86]. This process includes simply grinding reactants manually, using mortar and pestle as well as the more effort-free use of ball mills [87]. The use of solvent-free medium with this method includes several additional greener components such as reduced pollution, low cost, simple procedure and more importantly eliminating excessive and wasteful heating. The application of ball milling can easily scale up the mechanochemical techniques in the paint industry, material science, and pharmaceutical industry [88]. Later, the grinding technique was redefined as 'Grindstone Chemistry' by Bose *et al.* which includes grinding of all types of reagent pairs that may be solid/solid, solid/liquid, or even liquid/liquid at room temperature [88]. The flexibility in choice of reagent pairs in grindstone chemistry recognizes it as suitable solvent less synthesis. During grinding, thermal energy is transferred through friction which initiates the reaction. It has been observed that majority of these reactions are exothermic in nature [89]. The rate of reaction can be accelerated by the use of friction enhancing components such as sand and $MgSO_4.7H_2O$ [88]. The kinetic energy involved during the grinding of solid reagents may effect in several factors including heating, decrease in particle size (with concomitant increase in surface area and the generation of fresh surfaces), and formation of surface defects [90]. Grinding also provides a sort of 'stirring' and can prevent exothermic reactions forming hot spots, which would lead to decomposition.

## 1.3. Review of Literature for the Synthesis of Xanthene Derivatives and their Precursors

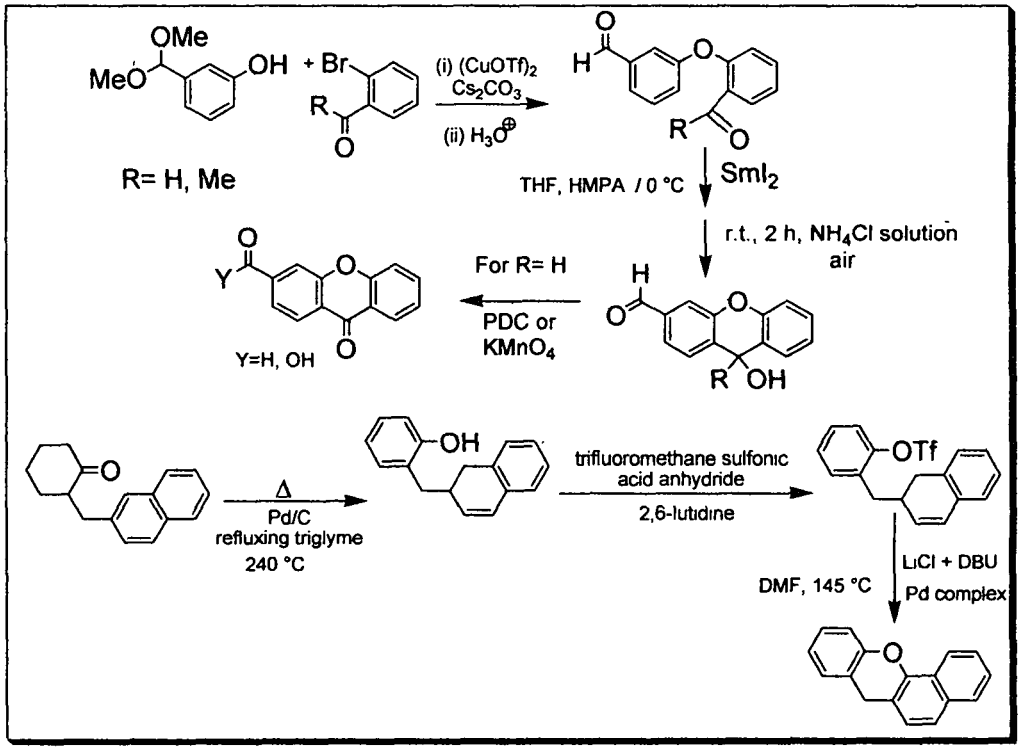
### 1.3.1. Synthesis of Dibenzoxanthene using Solid Acid Catalysts

The preparation of xanthene derivatives were initially achieved by the reaction of 2-naphthol with formamide [91], 2-naphthol-1-methanol [92] and carbon monoxide [93]. The other methods include dehydration of bis(2-hydroxy-1-naphthyl) methane using $POCl_3$ or by boiling acetic acid diester of bis(2-hydroxy-1-naphthyl) methane [94-95]. Later on various modified methodologies have been investigated for the construction of xanthenes and dibenzoxanthene derivatives. Knight *et al.* (2001) described an efficient multistep approach for the synthesis of iodoxanthenes involving intramolecular trapping of benzynes by phenols (**Scheme-2**) [96].



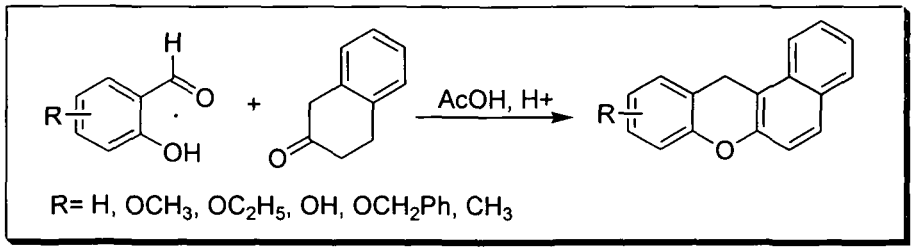

**Scheme-2**

Kuo *et al.* (2001) prepared xanthene derivatives from the reaction of benzaldehyde with acetophenone according to **Scheme-3** [97]. The palladium catalyzed cyclization of polycyclic aryltriflate esters was also investigated by Wang *et al.* (2002) to get xanthenes (**Scheme-3**) [98].

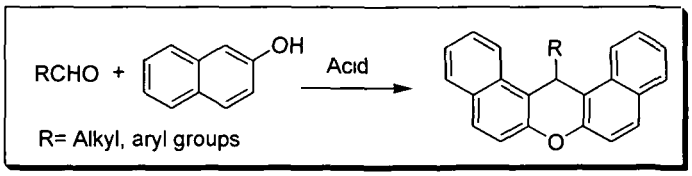



**Scheme-3**

Again, Jha *et al.* (2004) described a convenient synthesis of 12*H*-benzo[a]xanthenes from 2-tetralone and substituted 2-hydroxyaryl aldehydes at 0 °C in glacial acetic acid in presence of conc. HCl acid during 16 hours reaction **(Scheme-4)** [99].




**Scheme-4**

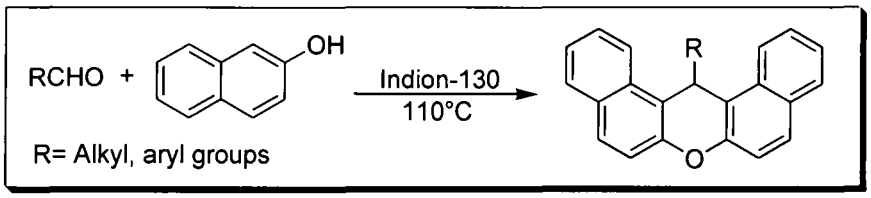



**Scheme-5**

The most general synthesis of aryl-14*H*-dibenzoxanthenes involves the condensation of 2-naphthol with aldehydes (**Scheme-5**) using traditional Brønsted or Lewis acid catalysts such as HCl [100], $H_3PO_4$ [101], $H_2SO_4$ [102], $I_2$ [103-104], sulfamic acid [105], *p*-TSA [106] etc. All of these methods have many disadvantages such as low yields, longer reaction times, and use of toxic non-recyclable catalysts, formation of side products, excess reagents/catalysts and drastic reaction conditions. In literature several modified procedures and new catalytic systems have been developed to overcome the limitations of these classical routes by the use of heterogeneous catalysts [107], acidic ionic liquids [108], solvent-free thermal treatment [109], microwave irradiation [110] and ultrasonication [111]. Presently, the use of solid phase-catalysts/reagents plays a prominent role in organic synthesis because of their ease of handling, enhanced reaction rates, greater selectivity, simple work up and recoverability of catalysts [112]. For acid catalyzed reactions of 2-naphthol with aldehydes various heterogeneous catalysts are reported in the form of metal salts, heteropoly acids and supported solid acids using silica, alumina, polymer and zeolite etc. as inert supports [113]. It has been found that many of these heterogeneous catalysts require longer reaction time and high temperature under reflux condition as well as in solvent-free thermal reactions. Few catalysts utilized microwave irradiation for reducing the reaction time as compared to thermal methods. Although most of

them offered lots of eco-friendly nature to the above cyclocondensation reaction, these routes still keep opportunities to search for new solid catalysts in terms of milder reaction condition and shorter reaction time with excellent yields of required product.

In 2006, Patil *et al.* successfully employed Indion-130, as recyclable cation-exchange resin to prepare 14-alkyl/aryl-14*H*-dibenzo[a,j]xanthenes in good yields within 12 min to 1 h at 110 °C in solvent-free medium (**Scheme-6**) [107].




**Scheme-6**

The above reaction was observed with aromatic aldehydes by Ko *et al.* (2006) in neat condition at 125 °C during 20 min to 2 hours reaction period using Amberlyst-15 as solid acid [48]. It needed 2-4 h to give good yield of products under reflux in 1,2-dichloroethane solution [114].

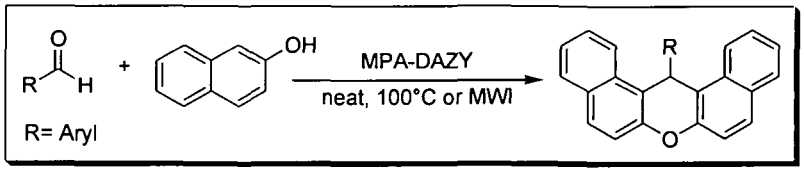
In 1,2-dichloromethane solvent, Naik *et al.* (2010) observed that the reaction time increases up to 24 h at 85°C in presence of sulfonic acid functionalized mesoporous SBA-15 catalyst (SBA-15/$SO_3H$) [115].

Activated montmorillonite K-10 catalyzed the synthesis of 14-aryl-14*H*-dibenzo[a,j]xanthene in solvent-less medium at lower temperature (80 °C) for a prolonged reaction time (24 h) while it required only 4-6 mins under microwave irradiation [116].

The substitution of harmful liquid acids by solid reusable HPAs as catalyst was also studied by Heravi *et al.* (2007) [117] and other groups [118-119] for the synthesis of 14-substituted-14*H*-dibenzo[a,j]xanthenes from 2-naphthol and aromatic aldehydes. These compounds possess unique properties, such as well-defined structure, Brønsted acidity, possibility to modify their acid–base and redox properties by changing their chemical composition (substituted HPAs), ability to accept and release electrons, high proton mobility, etc [120]. The three types of heteropoly acids $H_{14}[NaP_5W_{30}O_{110}]$ [117], silicotunsgtic acid $H_4[SiW_{12}O_{40}]$ [118] and

$H_5PW_{10}V_2O_{40}$/MCM-48 [119] showed their higher catalytic activity in neat condition around 90-110°C .

An encapsulated dealuminated zeolite-Y with 12-molybdophosphoric acid catalyst (MPA-DAZY) was prepared by Moghadam *et al.* (2011) and examined the catalytic activity for one step preparation of xanthene derivatives of aromatic aldehydes in solvent-less condition at 100 °C and microwave irradiation at 800 W (**Scheme-7**) [121].

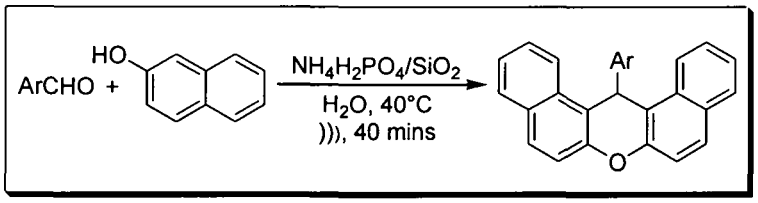



**Scheme-7**

Nagarapu *et al.* (2007) observed the synthesis of dibenzoxanthene derivatives at 125 °C in absence of solvent using HPA potassium dodecatungstocobaltate trihydrate ($K_5CoW_{12}O_{40}\cdot 3H_2O$) within 1-2 h reaction [122]. The microwave assisted reactions required only 2 min to produce 71-91% yields of product under 300 W microwave power. In 2013, two more sandwich-type polyoxometalates, $K_{12}[As_2W_{18}Cu_3O_{68}]\cdot 30H_2O$ and $K_{12}[As_2W_{18}U_3O_{74}]\cdot 21H_2O$ were used by Shabnam [123] in neat condition at 125 °C as well as under microwave irradiation at 900 W.

Shaterian and his co-workers [124-128] exploited the applications of several metal hydrogen sulfates such as $Fe(HSO_4)_3$, $NaHSO_4$, $Al(HSO_4)_3$, $[Mg(HSO_4)_2]$ and silica-sulfuric acid as heterogeneous catalysts in neat at 125 °C to generate aryl-14*H*-dibenzo[a,j]xanthene derivatives. They also synthesized the same moiety via microwave irradiation using sodium hydrogen sulfate. Hashemi *et al.* (2008) again investigated the synthesis of dibenzoxanthene at 90 °C in absence of solvent with sodium hydrogen sulfate [129]. Hunnur *et al.* (2008) also [130] observed the efficiency of silica sulfuric acid under reflux condition in 1,2-dichloroethane and solvent-free method at 120 °C. The reactivity of $Fe(HSO_4)_3$ was further studied by Eshghi *et al.* (2008) [131] under reflux condition in 1,2-dichloroethane and in solvent-free medium for $Mg(HSO_4)_2$ at lower temperature (60 °C) by Mirjalili *et al.* in 2011 [132]. In both cases it requires longer reaction time. They also used ultrasonication under reflux condition in DCM for the same synthesis.

The modified procedures with silica supported sodium hydrogen sulfates were reported by various groups in solvent-free thermal condition or in solution under reflux [114, 133-134]. The silica supported heterogeneous catalysts of Brønsted acids or metal salts include the applications of $HBF_4$-$SiO_2$, $NH_4H_2PO_4/SiO_2$, polyphosphoric acid/$SiO_2$, $Fe(HSO_4)_3/SiO_2$, $HClO_4$-$SiO_2$ for the synthesis of 14-aryl or alkyl-14*H*-dibenzo[a,j]xanthenes under solvent–free thermal methods at high temperature [135-139]. For $HClO_4$-$SiO_2$ catalyst [140] the solution method needed 7-15 h reaction time to give above 85-95% yields as compared to solvent-less condition (8-20 min). Mahdavinia *et al.* (2009) carried out the same synthesis under ultrasonic irradiation in water at 40 °C using $NH_4H_2PO_4/SiO_2$ catalyst (**Scheme-8**) [141].




**Scheme-8**

Hashemi *et al.* (2013) utilized silica supported 4-dodecylbenzenesulfonic acid (DBSA) as reusable catalyst in solvent-free condition at 85 °C to produce 14-aryl- and 14-alkyl-14*H*-dibenzo[a,j]xanthenes [142].

The first alumina supported PPA was employed by Norouzi *et al.* in 2011 under solvent-free medium at 120 °C to prepare 14-Aryl-14*H*-dibenzo[a,j]xanthenes [143].

Zarei and his colleagues (2010) also added $P_2O_5/Al_2O_3$ to a mixture of 2-naphthol and aldehydes and subjected the entire mixture for 10-15 min to microwave irradiation to yield dibenzoxanthenes [110].

Nagarapu *et al.* (2007) described another supported solid acid catalyst 5% $WO_3/ZrO_2$ for the same reactions in neat condition at elevated temperature with more reaction time (2-8 h) [134].

The utility of polymer-supported catalysts is now well recognized because of their ease of workup and separation of products and catalysts, from the economical point of view, and in application to industrial processes, recyclability, easier handling, greater selectivity, enhanced stability, non-toxicity, and non-corrosiveness [144-146].

The catalysts are immobilized on polymers via coordinate or covalent bonds. Its hydrophobic nature protects water-sensitive Lewis acids from hydrolysis by atmospheric moisture until it is suspended in an appropriate solvent where it can be used in a chemical reaction [147-149]. The 20 mol% crossed-linked polystyrene supported $AlCl_3$ was utilized by Rahmatpour *et al.* (2011) in acetonitrile under reflux for the one-pot synthesis of 14-aryl or alkyl-14*H*-dibenzo[a,j]xanthenes [150].

Khaligh in 2012 studied the application of poly(4-vinylpyridinium)hydrogen sulfate, a solid acid catalyst both by heating the mixture of 2-naphthol and aryl aldehydes at 100 °C and ultrasonication with a frequency of 35 kHz in ethanol at 40 °C [151]. Mokhtary *et al.* (2013) synthesized 14-aryl-14*H*-dibenzo[a,j] xanthenes in neat condition at 120 °C using poly-vinyl-polypyrrolidone-supported boron trifluoride (PVPP-$BF_3$) catalyst [152]. Madhav *et al.* (2009) successfully employed cellulose silica sulfuric acid as biodegradable and recyclable solid acid catalyst with substituted aryl aldehydes within 1-3 h at 110-115 °C without any solvent [153]. In 2011, Quan *et al.* used polystyrene-poly(ethylene glycol) resin-supported sulfonic acid catalyst (PS-PEG-$OSO_3H$) for the condensation of 2-naphthol with aryl aldehydes in glycerol at 120 °C for 12 h to get good yield of xanthenes [154].

Recently, the usage of nano materials as heterogeneous catalyst has gained significant role in organic synthesis due to simple work-up procedure, environmentally benign nature, product selectivity, reusability, low cost, and ease of isolation [155]. The reactivity of catalytic nanoparticles is largely determined by the energy of surface atoms, which can be easily gauged by the number of neighboring atoms by the bonding modes and accompanying energies of small molecules to be transformed on the nanoparticles surface [156]. The applications of AgI and ZnO nanoparticles (NPs) were observed by Safaei-Ghomi *et al.* (2012) [157] and Rao *et al.* (2012) [158] respectively in solvent-free medium at 120-140°C. Mirjalili *et al.* (2012) reported an efficient solvent-free method at lower temperature (90 °C) for the synthesis of 14-Aryl-or 14-alkyl-14*H*-dibenzo[a,j]xanthenes using nano-$SnCl_4 \cdot SiO_2$ at 90 °C [159]. Highly sulfonated single walled carbon nanotubes (SWCNTs-$SO_3H$) also catalyzed the reaction of 2-naphthol with aromatic aldehydes in neat condition at 70 °C [160]. In 2013, nanorods of vanadate sulfuric acid (VSA NRs) and nano silica phosphoric acids were employed by Masoud *et al.* (2013) [161] and Bamoniri *et al.*

(2013) [162] in solvent-free thermal method and under microwave irradiation respectively.

Two efficient sulfonic group functionalized acids include carbon-based sulfonated acid and sulfonic acid functionalized silica ($SiO_2$-Pr-$SO_3H$) for the synthesis of 14-Aryl-14*H*-dibenzo[a,j]xanthenes under solvent-free medium within 1 h with excellent yields [163-164]. The carbon based sulfonated acid was also used in 1,2-dichloroethane at 85 °C during 9-30 h reaction period.

In 2011, Mohammadpoor-Baltork *et al.* for the first time reduced the reaction time to 2-5 min in solvent-free method at 120 °C using [$ZrO(OTf)_2$] as reusable solid Lewis acid catalyst [165].

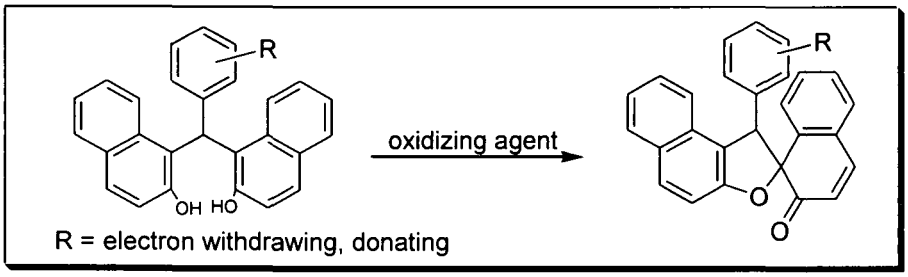
Recently, Huo *et al.* (2014) used a solid complex formed from sodium triphenylphosphine-m-sulfonate (TPPMS) and carbon tetrabromide, TPPMS/$CBr_4$ as a recoverable catalyst system to synthesize dibenzoxanthenes from aldehydes and 2-naphthol under solvent-free condition at 110 °C within 15-60 min [78].

From the above mentioned literatures it was distinctly clear that most of the synthesis of 14-aryl or alkyl-14*H*-dibenzo[a,j]xanthenes were carried out in solvent-free/solution in the temperature range of 80-125 °C with longer reaction time. Only a few methods described the completion of reactions within half an hour at high temperature (80-125°C). Therefore, it is very necessary to develop some efficient catalytic system which will complete the title reaction within less time at mild conditions in an efficient manner.

## 1.3.2. Preparation of Aryldi-(2-Hydroxy-1-Naphthyl)Methane

Aryldi-(2-hydroxy-1-naphthyl)methanes (**2**) represent a class of bisnaphthols which contain two naphthol units connecting through $\alpha$-position with a methylene (-CHR-) group. They have synthetic, medicinal and industrial value besides their applications as the precursors of dibenzoxanthene derivatives. They are structural units of calixarenes, and have applications as enzyme mimetics, ion selective electrodes or sensors, selective membranes, nonlinear optical materials and sometimes, with some modifications, as high-performance liquid chromatography stationary phases [22-23, 166]. The oxidative cyclization of bisnaphthols to spirans {arylnaphtho[2,1-b]furan-2(1*H*)-spiro-1'(2'*H*)-naphthalen-2'-one}(**Scheme-9**) is an important reaction in

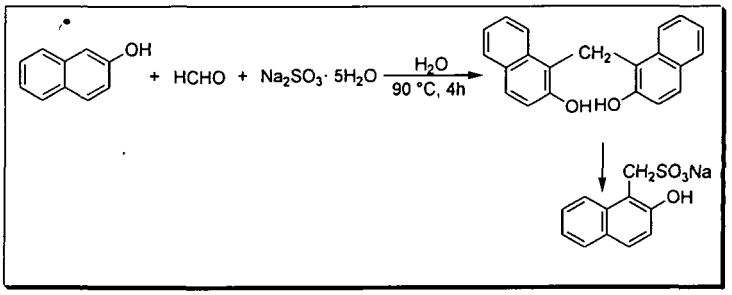
biosynthesis of certain plant products [167-169]. Various oxidizing agents have been utilized to control the stereochemistry of spirans [170].




**Scheme-9**

Literature studies revealed that aryldi-(2-hydroxy-1-naphthyl)methanes (2) have been synthesized by the acid catalysed reaction of aldehydes with 2-naphthol which is one of the precursors of aryl dibenzoxanthene synthesis from the same mixture under reflux or in neat conditions [171-172]. Most of the procedures reported the selective formation of aryl dibenzoxanthenes without the intermediary of aryldi-(2-hydroxy-1-naphthyl)methanes under the above mentioned acidic condition [173]. The literature survey shows that there are few reports on the synthesis of aryldi-(2-hydroxy-1-naphthyl)methanes from aldehydes and 2-naphthol.

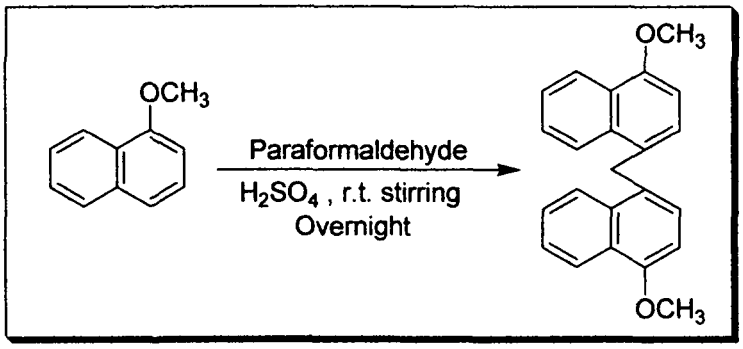
Shearing *et al.* (1937) isolated bis(2-hydroxy-1-naphthyl) methane as an intermediate during the sulfomethylation of 2-naphthol with 40% HCHO solution and sodium sulfite in water at 100 °C for 10 mins [174]. Later on, the mechanism of sulphomethylation of 2-naphthol was extensively studied by Ogata and his coworkers through the formation of bis(2-hydroxy-1-naphthyl) methane from the mixture of 2-naphthol, 37% HCHO solution and sodium hydroxide in water at 100 °C for 1 h stirring followed by acidification [175]. The above product was again identified as reaction intermediate for the synthesis of 2-hydroxy-1-naphthylmethanesulphonate according to the **Scheme-10**.




**Scheme 10**

In 1936, Kharasch and his coworkers prepared various derivatives of 1,1'-aryl bis-2-naphthol (2) from aromatic aldehydes and 2-naphthol in glacial acetic acid at 5 °C for 48 h using conc. HCl as catalyst [171].

The synthesis of bis(4-methoxy-1-naphthyl) methane was reported by Schreiber and Kennedy (1956) from sulfuric acid catalyzed reaction of paraformaldehyde with 1-methoxynaphthalene (**Scheme-11**) [176]. The employment of their reaction condition with 1-naphthol did not produce bis(4-hydroxy-1-naphthyl) methane (**Fig.4**) and yielded only an intractable resinous product (**Fig.4**) [166].




**Scheme-11**

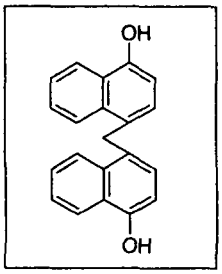



**Fig. 4**

Bennett *et al.* (1980) synthesized benzylidene-1,1'-bis-2-naphthol (2) by the reaction of 2-naphthol with aromatic aldehydes in acetic acid medium using conc. HCl as catalyst for 50 h at 0 °C and studied the oxidative cyclisation of (2) to the stereoisomer of (13) and (14) of phenyl-naphthol[2,1-b] furan-2(1H)-spiro-1'(2'H)-naphthalene-2'-one (**Fig. 5**) [172].

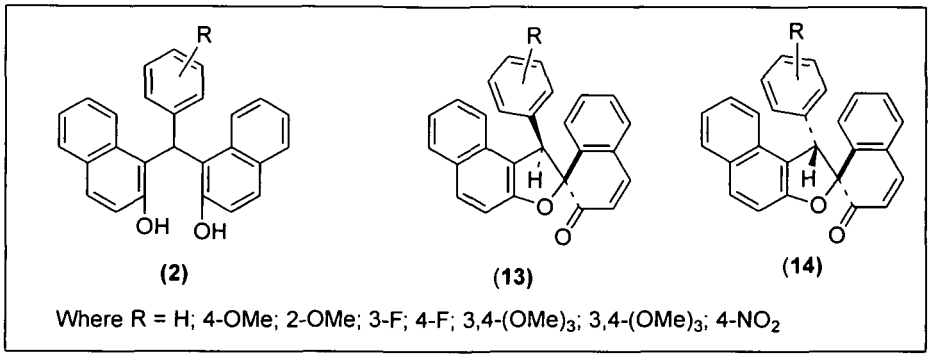
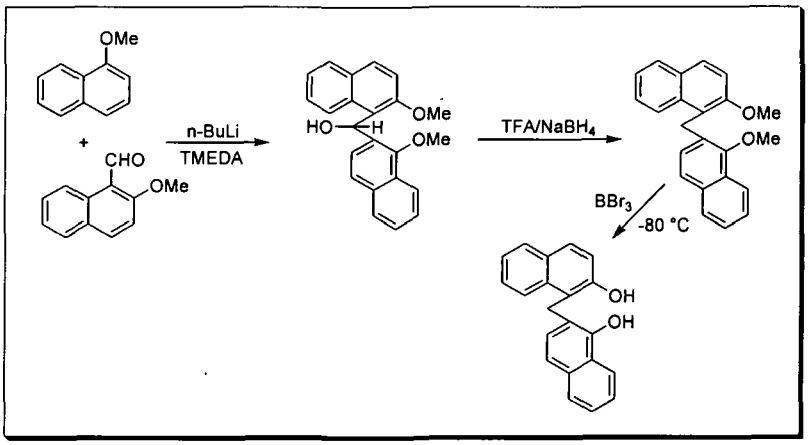


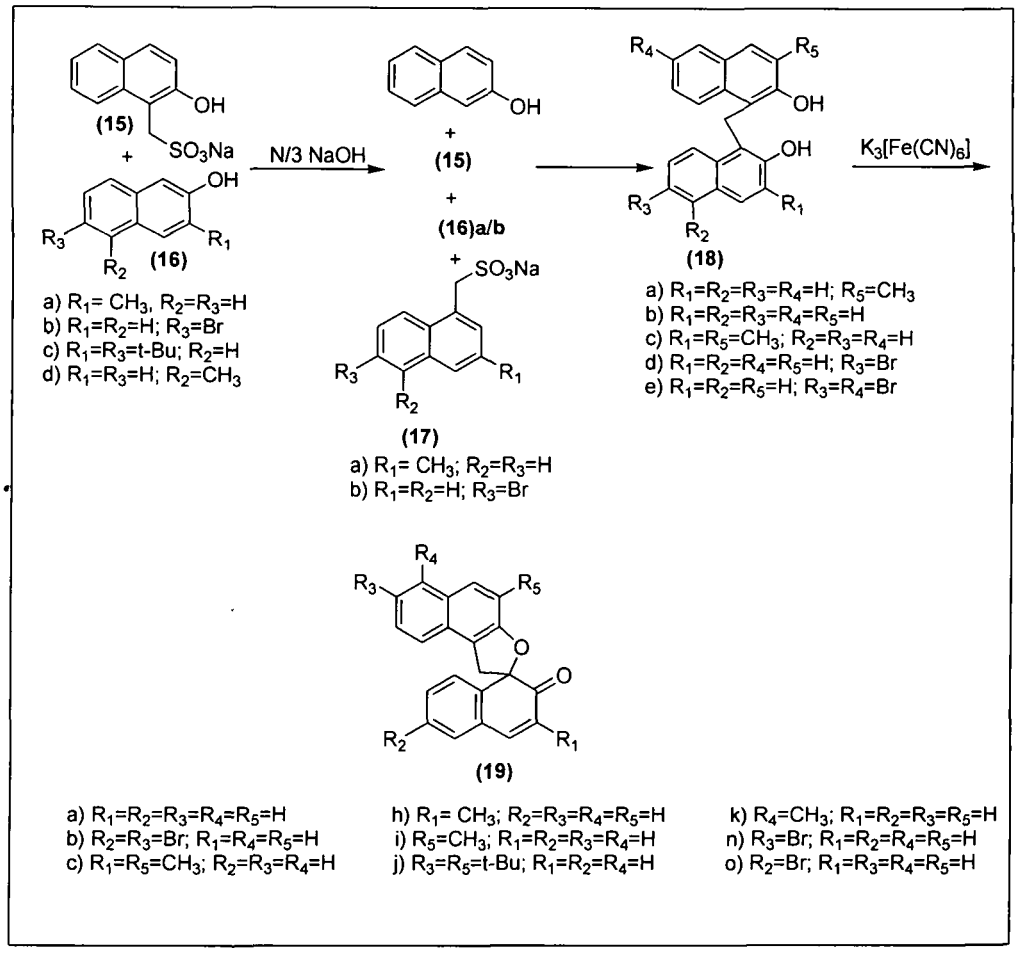

**Fig. 5**

Kasturi *et al.* (1995) also prepared 2-hydroxy-1-naphthyl-1'-hydroxy-2'-naphthylmethane (bisnaphthol) from the multistep reactions of 1-methoxynaphthalene with 1-formylnaphthalene in presence of n-BuLi/TMEDA followed by deoxygenation and demethylation (**Scheme-12**) [177].



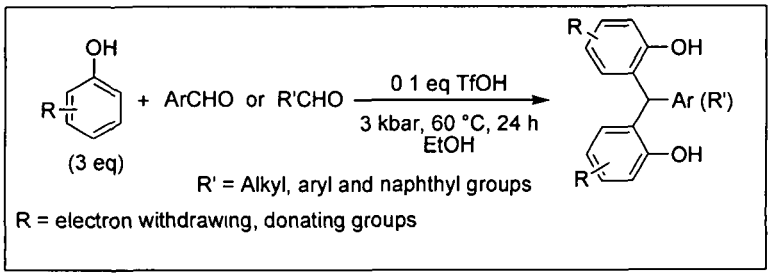

**Scheme-12**

In 1993, they also prepared a variety of bisnaphthols [178] adopting the two step procedure of Shearing and Smiles [174] according to the **Scheme-13** for subsequent oxidation with $K_3[Fe(CN)_6]$




**Scheme-13**

Kotsuki and his colleagues in 2001, synthesized bisnaphthol derivatives from phenols and aldehydes in about 24 hours at 3 kbar pressure using a catalytic amount of trifluoromethanesulfonic acid (TfOH) in ethanol at 60 °C. Using propanal as an aliphatic aldehydes the reaction with 2-naphthol produced lower yield of bisnaphthol (10%) accompanied by major amount of dibenzoxanthene compound (31%) (**Scheme-14**) [179]. However, for some typical substrates, the products were formed only after prolonged period of time.




**Scheme-14**

In 2007, Ranjbar *et al.* used concentrated hydrochloric acid in acetic acid to generate 1-[(2-hydroxy-1-naphthyl)(phenyl)methyl]-2-naphthol solvated with ethanol (I) (**Fig. 6**) as crystalline compound by refrigerating the mixture of 2-naphthol and benzaldehyde for 50 hour [180].

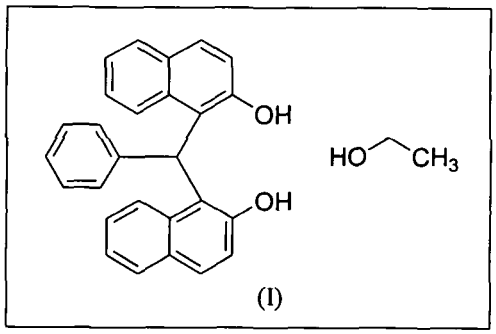


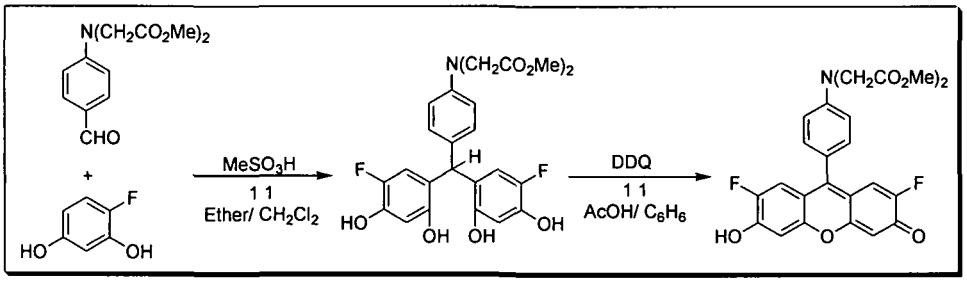

**Fig. 6**

In 2010, Alizadeh *et al.* prepared aryldi-(2-hydroxy-1-naphthyl)methanes by the reaction of a series of aryl aldehydes and 2-naphthol in the presence of $H_3[P(Mo_3O_{10})_4].nH_2O$ (HPA) as catalyst in refluxing dichloromethane within 40 min reaction time [181].

### 1.3.3. Synthesis of 1,8-Dioxo-Octahydroxanthene using Solid Acid Catalysts

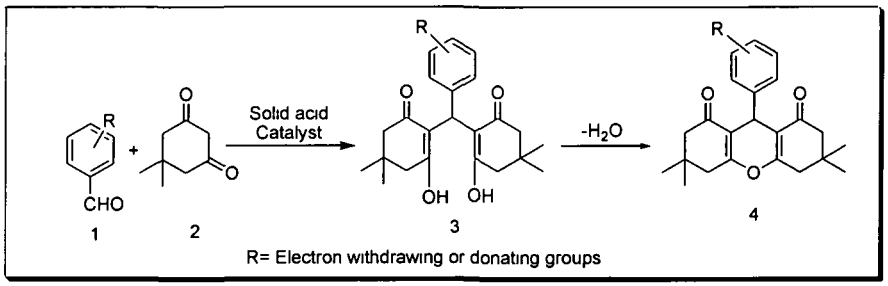
Several natural products constituted with parent xanthenedione moieties have potent biological and pharmaceutical activities which may be possible only for inherent reactivity of inbuilt pyran rings [182-186, 16]. The first synthesis of xanthenediones observed in 1946 from the condensation of appropriate active methylene carbonyl compounds with aldehydes catalyzed by sulfuric acid or hydrochloric acid [187]. In 1996, Singh *et al.* [188] reported the preparation of xanthenediones through carbon transfer reactions of 1,3-oxazinanes and oxazolidines with carbon nucleophiles. A two-step synthesis of 9-aryl-6-hydroxy-3H-xanthen-3-one fluorophores was also described by Bacci *et al.* (2005), from the condensation of aryl aldehydes and fluororesorcinol (**Scheme-15**) [189]. Regarding the availability and the economic viability of starting materials, the initial method is far superior to the other methods. After that several acids investigated as non-recyclable catalysts for the condensation of active methylene carbonyl compound and aldehydes to prepare xanthenediones in organic solvents under reflux condition with various limitations such as high

temperature reaction, use of organic solvents, longer reaction time and complicated in work-up procedures [190-191].




**Scheme-15**

For elimination of various problems of known methods, a number of modified procedures have been reported by different groups involving ionic liquids [192], heterogeneous catalysts [193], solvent-free reactions under thermal and microwave energies in addition to mechanochemical methods [194] to generate chemical synthesis with less waste and more facile isolation of products perhaps with reuse of the catalysts as well. This section includes the review of literature of solid acid catalyzed synthesis of xanthenedione derivatives through cyclocondensation of active methylene carbonyl compound with aldehydes in presence of thermal, mechanical and microwave energies (**Scheme-16**). In organic synthesis, heterogeneous catalysts have received tremendous applications due to economic and environmental considerations in combination with the above sources of energies.




**Scheme-16**

Das *et al.* (2006) first utilized Amberlyst-15 ion exchange resin, as efficient solid acid catalyst to complete the synthesis of 1,8-dioxo-octahydroxanthenes by refluxing aromatic aldehydes and 5,5-dimethyl-1,3-cyclohexanedione in $CH_3CN$ for 5 h with excellent yields [193]. Similarly Dowex-50W ion exchange also acted as eco-friendly reusable catalyst for the above reactions under solvent-free conditions at 100 °C in 2-5 hours [195]. Bazgir and his group (2008) employed Montmorillonite K10 as solid

acid catalyst for the condensation of dimedone and aromatic aldehydes in neat condition at 100°C within 1-2 h time to give 75-90% yields of product [196]. In ethanol solution at 100 °C Song *et al.* (2007) observed 84-96% of xanthenediones during 6 h reaction time using $Fe^{3+}$-montmorillonite catalyst [197]. Another method involved with the use of heteropolyacid ($H_3PW_{12}O_{40}$) supported MCM-41 as reusable solid acid catalyst in ethanol under reflux for 5 h to give good results [198].

The use of clay catalyst, Envirocat EPZ-10 in water was exploited by Pore *et al.* (2010) at 70 °C to generate moderate to excellent yields of xanthenediones from aldehydes and dimedone/cyclohexane-1,3-dione in 2-3 hours [199].

The direct use of metal salts as heterogeneous acids was studied in presence of $Fe(HSO_4)_3$ [200], $NaHSO_4$ [201] and $ZrOCl_2 \cdot 8H_2O$ [202] in neat condition under thermal treatment. In both cases the reactions produced excellent yields within 10-30 min in the temperature range of 80-120 °C. With $Fe(HSO_4)_3$ catalyst, additional investigations were observed using solvent-free microwave irradiation and in water solution under reflux. The solution phase reaction required longer reaction time (1.5-15 h) as compared to solvent-free medium.

Several reports discussed the efficient applications of silica or alumina supported solid acids for the preparation of xanthenedione derivatives from the reaction of dimedone and aromatic aldehydes in solution and neat conditions. Some of the examples of silica supported metal salts are $NaHSO_4 \cdot SiO_2$ [203], $SbCl_3/SiO_2$ [204] and $FeCl_3$-$SiO_2$ [205]. Das *et al.* (2007) also observed $NaHSO_4 \cdot SiO_2$ as solid acid in refluxing acetonitrile for the formation of 1,8-dioxo-octahydroxanthenes during 6-6.5 h reaction [203]. The other two supported metal salts produced good yields of product at 120 °C in solvent-less media within one hour reaction. Shaterian *et al.* (2008) also investigated the catalytic activity of $FeCl_3$-$SiO_2$ catalyst under solvent-free microwave irradiation at 450 W for 4-17 min [205]. Kanteveri *et al.* (2007) catalysed the cyclodehydration of dimedone with various aromatic aldehydes in refluxing acetonitrile and solvent free conditions at 140 °C using PPA-$SiO_2$ [206]. The neat method produced excellent yields within half an hour as compared to poor results in acetonitrile during 12 h reaction to give 1,8-dioxo-octahydroxanthenes.

The anchoring of $-SO_3H$ group on solid material generate many efficient solid acid catalysts and they were found to be very useful heterogeneous acids for the

synthesis of xanthenedione moieties. In 2009, Bigdeli and his co-workers [207] exploited the application of covalently anchored sulfonic acid on silica gel ($SiO_2$-R-$SO_3H$) as reusable catalyst under neat condition at 80 °C with all types of aromatic aldehydes in 3.5-5 h reaction period. Seyyedhamzeh *et al.* (2008) used silica sulphuric acid as reusable catalyst under solvent-free conditions at 80 °C during 1- 2.5 h reaction [208]. Heravi and co-workers in 2010 used cellulose sulfonic acid under solvent-free condition at 110 °C to synthesize 1,8-dioxo-octahydroxanthenes from aromatic aldehydes and dimedone in 5-6 h [209]. Alumina sulfuric acid also successfully applied as solid acid by Pramanik *et al.* (2012) for the generation of xanthenediones from aldehydes and cyclic 1,3-diketones in 3-5 h under reflux condition in ethanol [210].

Like silica and alumina supports, polymer supported solid acids were also studied for the preparation of xanthene units. Palaniappan and his group examined the catalytic activity of polyaniline supported p-toluenesulfonate in refluxing water for the preparation of xanthenedione derivatives for 6 h to give 73-84% yields [211]. Mokhtary *et al.* (2014) used poly(vinyl)poly (pyrrolidone)-supported boron trifluoride (PVPP-$BF_3$) as heterogeneous catalyst in $CH_3CN$ at room temperature in 3-4.5 h reaction time to form the required xanthenedione derivatives [212]. The formation of 1,8-dioxo-octahydroxanthenes was observed with poly(4-vinylpyridine) supported copper iodide nanoparticle catalyzed reaction in neat environment at 80 °C in 7-36 mins from aldehydes and dimedone [213].

Mishra and co-workers (2013) reported the application of sulfate-grafted iron stabilized zirconia nanoparticles ($SO_4^{2-}$/xFe-Zr-O) as heterogeneous catalyst for the synthesis of xanthenediones by exposing the mixture of dimedone and aromatic aldehydes to microwave radiation under solvent-free condition for 11-18 min [214].

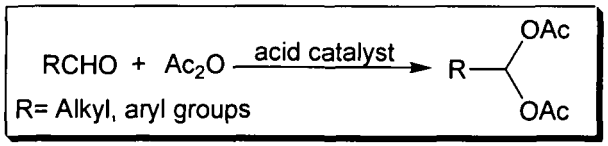
In 2005, Jin *et al.* first applied the mechanochemical energy for the preparation of xanthenedione derivatives at mild condition under solvent-free grinding method in presence of $TiO_2/SO_4^{2-}$ solid super acid catalyst during 24 h reaction time with excellent yields [215].

The literature survey of xanthenedione synthesis prompted us to investigate the reactions in solvent-free grinding method at mild condition using polymer/zeolite supported solid acid as reusable catalysts.

## 1.4. Review of Literature for the Protection of Carbonyl Group using Safer Catalytic Systems

### 1.4.1 Protection of Carbonyl Group as 1,1-Diacetates using Polymer Supported Solid Acid Catalysts

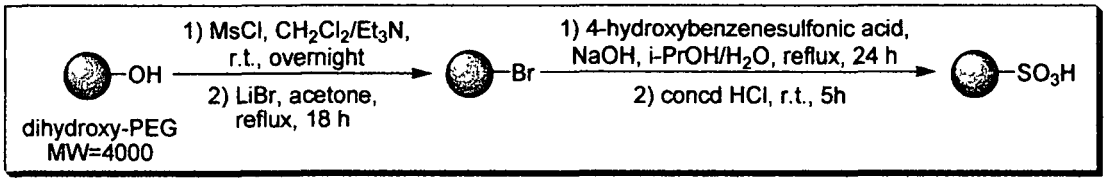
The selective protection and deprotection of carbonyl groups are essential steps in modern organic chemistry [25]. 1,1-Diacetates (acylals) are useful carbonyl-protecting group because of their stability in neutral, basic and acidic conditions [216]. Moreover, the acylal functionality can be converted into other functional groups by reaction with appropriate nucleophiles [217-218] and used as carbonyl surrogates for asymmetric synthesis [219]. α,β-Unsaturated diacetates are important starting materials for Diels-Alder reactions [31]. They have been applied as cross-linking reagents in cellulose and cotton [31] industries and as stain-bleaching agents [32]. As synthons, they have been utilized in well-known reactions of organic chemistry [217, 220-222] such as nitrile synthesis, Grignard reactions, Prins reactions, and condensation reactions such as Knoevenagel and Benzoin.




**Scheme-17**

Acylals are prepared from the acid catalyzed reaction of aldehydes and acetic anhydride (**Scheme-17**). Some common examples of acidic catalysts include $H_2SO_4$ [223] phosphoric [224], methanesulfonic [30], $HClO_4$ [225], $I_2$ [226], CTMS/NaI [227], $ZnCl_2$ [228], $FeCl_3$ [216, 222], $FeSO_4$ [229], $PCl_3$ [230], $InCl_3$ [231], $InBr_3$ [232], $Zr(HSO_4)_4$ [233], $VSO_4$ [234], cyanuric chloride [235], $Sc(OTf)_3$ [236], $Cu(OTf)_2$ [237], $Bi(OTf)_3$ [238], LiOTf [239] and $In(OTf)_3$ [240]. Many of these catalysts are toxic, corrosive, non-recyclable, non-chemoselective and require longer reaction time in organic solvents. The utilization of heterogeneous solid acidic material is an efficient approach to reduce the above mentioned limitations of acylal synthesis [241]. The impregnation of non-recyclable Brønsted/Lewis acids on inert supports (such as charcoal, alumina, silica, zeolite, clay and polymers etc.) make them heterogeneous which improve the availability of active sites of catalyst for the synthesis of small molecules under especially simple, mild and more environmentally

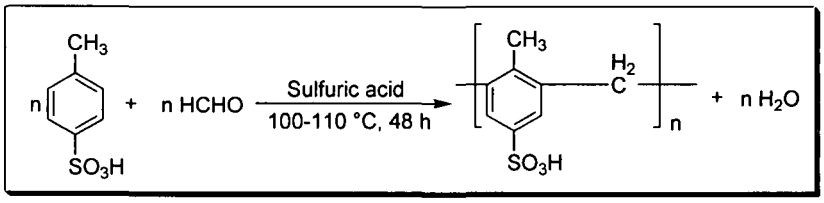
benign conditions [242]. The recycling capability of such catalyst simplifies the purification steps, avoiding wastes and gives potential for utilization in large-scale operations [243]. Some heterogeneous catalysts of the acylal preparations are claimed to give both protection and deprotection of carbonyl functionality [244]. Deprotection of 1,1-diacetates to their parent aldehydes is also of practical importance and several methods have been reported in the literature for this purpose [25, 216, 245]. In this part of the thesis, we have included the up to date literature of polymer supported solid acidic catalysts/reagents for the protection and deprotection of carbonyl groups as 1,1-diacetates by following the reaction in **Scheme-17** in different reaction conditions. Among the various supports, polymer has particular importance because of its range of applicable solvents, provide convenience of work-up and product purification, lower the environmental hazards, and in most case provide for recovery and reuse of polymer supported reagent. Li *et al.* (2000) poly(vinylchloride) supported $FeCl_3$ (PVC-$FeCl_3$) as reusable solid acid catalyst for the synthesis of acylals in excess $Ac_2O$ from a variety of aldehydes within 5-20 min at room temperature in excellent yields. They also successfully completed the reaction with unsaturated aldehydes [246]. Wang *et al.* (2007) synthesized solid polyethylene glycol (PEG-4000) supported sulfonic acid catalyst according to **Scheme-18** for the 1,1-diacetate formation in solvent-free medium at room temperature in 25-50 min from aldehydes [247].




**Scheme-18**

Wang *et al.* (2009) immobilized zinc chloride on chloroacetylated polystyrene to generate a polymer-supported reusable Lewis acid catalyst for Scheme-17 in neat media at ambient temperature [248]. Boroujeni (2011) also utilized cross-linked polystyrene-supported $Al(OTf)_3$ [Ps-$Al(OTf)_3$] as noncorrosive, nontoxic and highly efficient chemoselective Lewis acid catalyst in dichloromethane at mild condition for 1-2.2 h [249]. It can be recovered simply and reused efficiently at least five times without any noticeable loss of catalytic activity. Another chemoselective polymer catalyst was prepared by Fan *et al.* (2010) for the title reaction through sulfuric acid catalyzed copolymerization of *p*-TSA and paraformaldehyde (**Scheme-19**) which

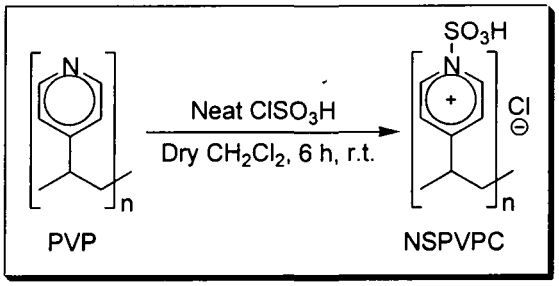
displays extremely high activities at 25°C with 0.5 mol%, affording average yields over 90% within several minutes [250].




**Scheme-19**

A comparative study on the catalytic activity of conducting polyaniline (PANI), polypyrrole (PPY), and poly-(3,4-ethylenedioxythiophene) (PEDOT) salts as solid acid catalysts for the synthesis of 1,1-diacetates was studied by Nabid *et al.* (2011) and his group under solvent-free conditions in 2011 [251]. Excellent results were obtained in 10-45 min with polyaniline sulfate salts in solvent-free medium from various aldehydes at room temperature among the three types of conjugate polymer supported acids.

Khaligh *et al.* (2011) also prepared poly(4-vinylpyridinium) hydrogen sulfate salts by the treatment of [poly(4-vinylpyridine)] cross-linked with 2% DVB-60 mesh, (molecular weight: 60,000) in dry methanol with $H_2SO_4$ for 8 hour at room temperature. After filtration, the solid powder was dried under vacuum at 65 °C for 48 h to afford P(4-VPH)$HSO_4$ (0.5 mmol $g^{-1}$) as a pale yellow powder. It acted as efficient catalyst for protection of aldehydes in neat and deprotection of acylal in methanol solvent at ambient conditions within short period in excellent yields [252]. The catalyst can be reused and recovered but they were observed to be less active. They also studied the catalytic performance of P(4-VP)$HSO_4$ salt under ultrasonic irradiation for the same protection-deprotection reaction at room temperature [253]. The same group reported the preparation of N-sulfonic acid poly(4-vinylpyridinium) chloride (NSPVPC) by the reaction of poly(4-vinylpyridine) with neat chlorosulfonic acid **(Scheme-20)** for the title protection-deprotection reaction in neat and methanol solvent respectively [254].



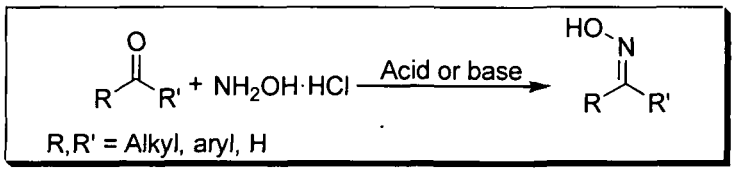

**Scheme-20**

In 1982, Olah *et al.* synthesized 1,1 diacetates from aldehydes using Nafion-H as solid super acid catalyst [255].

The literature studies indicate that polymer supported Brønsted or Lewis acids generate stable, chemo selective and efficient heterogeneous catalytic system for the protection-deprotection reactions under mild conditions in solvent-less media or in organic solvents during short time to produce satisfactory yields of 1,1-diacetates from aromatic aldehydes. Most of the reported catalysts had easily fulfilled the advantageous properties of heterogeneous catalysts like recyclable and easy separations from the reaction mixture. By observing all these properties we are interested to study the application of poly(4-vinylpyridine) supported sulfuric acid as reusable catalyst for the synthesis of 1,1-diacetates from carbonyl compounds as a continuation of our works on polymer supported catalysts [256].

## 1.4.2. Microwave Assisted Solvent-free Synthesis of Oximes

Oximes are extensively used as preferred and readily prepared derivatives for purification and characterization of carbonyl compounds which are usually prepared by the reaction of carbonyl compounds with hydroxylamine hydrochloride (**Scheme-21**) in acidic or basic conditions [25]. Further, oximes of aldehydes and ketones served as protecting [257], selective α-activating [258] groups and intermediates for many reactions such as the preparation of amides by Beckmann rearrangement [259]. Also, their synthesis from non-carbonyl compounds, such as by nitrosation of an active methylene group [260] and condensation of a nitroalkene with an aldehyde [261] provides a valid alternative pathway to carbonyl compounds.




**Scheme-21**

A variety of acidic and basic catalysts have been documented for the classical synthesis of oximes (**Scheme-21**), such as formic acid [262], pyridine/ chloroform [263], ethanol/pyridine [264] and sulfuric acid [265]. They all have their own merits and shortcomings. Some methods are not very satisfactory due to drawbacks such as low yields, high temperature reaction, use of reagent amount of acidic or basic compounds, long reaction time, volatile organic solvent as reaction medium, complicated in product isolation and effluent pollution. Some patents relating to the

formation of cyclohexanone oxime was produced by liquid-phase ammoximation of cyclohexanone using ammonia hydrogen peroxide as the oxidizing agent and titanium silicalite as the catalyst [266]. This method was also effective for other several oximes [267]. Allied Chemical Corp. patented the process of a heterogeneously catalyzed gas-phase route employing ammonia with molecular oxygen as the oxidant, but the yields were relatively low [268].

The modified new techniques for the classical oxime preparation include the applications of microwave irradiation [269], solvent free thermal and mechanochemical energies [270-271], ultrasonication [272] and ionic liquids [273]. Besides, nitrosation at a carbon bearing an active hydrogen [260] addition of NOCl to olefins [274], addition of Grignard reagents to conjugate bases of nitro compounds [275] photolysis of nitrites [276] oxidation of primary amines [277] and reduction of nitro compounds [278] also have been reported in literature as methods for oxime formation. In this section we are discussing the modified solvent-free synthesis of oximes of various carbonyl compounds with hydroxylamine hydrochlorides under thermal and microwave energies in acidic or basic catalysts or reagents.

Hajipour *et al.* (1999) prepared oximes under microwave irradiation of a mixture of carbonyl compounds and hydroxylamine hydrochloride in dry media using silica gel as catalyst within 2-8 min [269]. Sharjhi *et al.* (2000) utilized CaO as reagents for the preparation of oximes from carbonyl compounds and hydroxylamine hydrochloride at 130 °C in 1 min except benzophenone which took 2 h to give above 90% yield. Though the yields were high but the tedious workup made this process unsuitable [279].

Bandgar *et al.* (2001) reported the microwave assisted chemoselective preparation of oximes from aromatic aldehydes and hydroxylamine hydrochloride with a few drops of methanol within 0.5-4 mins [280].

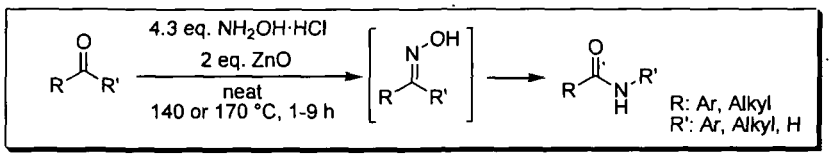
The use of reusable solid superacid $TiO_2/SO_4^{2-}$ required 1-2 min reaction time to form 85-96% yields of aromatic oximes from aryl substituted carbonyl compounds at 130 °C in neat condition. This catalyst also needed longer reaction time (2 h) to yield 75% of oxime from benzophenone [270].The oxime preparation was also observed by Kad *et al.* (2001) in excellent yields within less time from aromatic aldehydes and ketones under MWI in solvent-free medium in presence of wet basic

alumina as reagents [281]. The same group also reported another solvent-less grinding procedure using 4A molecular sieves as reagents at mild condition.

Osadchenko *et al.* (2002) utilized perfluorinated higher carboxylic acids as phase-transfer catalyst in aqueous NaOH solution to generate oximes at 65-70 °C in several hours [282].

Heravi and his colleagues (2002) synthesized oximes in 80-98% yields by grinding a mixture of carbonyl compounds and hydroxylamine hydrochloride and powdered 3Å molecular sieves at ambient temperature for 10 min whereas benzophenone produced only 30% under the optimized condition [283].

Sharghi and his co-workers (2002) studied ZnO mediated in situ Beckmann rearrangement of oximes from several carbonyl compounds and hydroxylamine hydrochloride at 140-170 °C within 1-9 h (**Scheme-22**). They also optimized the reaction conditions for oxime preparation at 80 °C in neat condition during 5-15 min time [284].




**Scheme-22**

Damljanović *et al.* (2006) developed the solvent-free grinding method with sodium hydroxide for the synthesis of oximes of alicyclic and aliphatic carbonyl compounds as well as aromatic aldehydes in neat condition at room temperature during 30-40 min reaction time. However, this procedure was unsuccessful in the case of aromatic ketones. In this case it was necessary to add silica gel as catalyst [271]. Hoelz *et al.* (2010) reported the solvent-free synthesis of oximes via microwave irradiation of a grounded mixture of aromatic aldehydes bearing an electron withdrawing group and hydroxylamine hydrochloride using $TiO_2$ while electron donating group containing aromatic aldehydes gave nitrile through Beckmann rearrangement [285].

Saikia *et al.* (2011) prepared oximes by grinding a mixture of carbonyl compounds and hydroxylamine hydrochloride with $Bi_2O_3$ as catalyst using mortar and pestle at room temperature within 1.5-20 min [286].

After the literature survey has been completed, the following objectives have been set.

**OBJECTIVES**

- Development of efficient methodology for the selective formation of 14-alkyl or aryl-14*H*-dibenzoxanthenes and their precursors intermediate, bisnaphthols under solvent-free thermal and microwave energies using reusable solid acid catalysts.
- Identification and characterization of the keto-enol tautomers as precursor intermediates towards the synthesis of 14-alkyl or aryl-14*H*-dibenzoxanthenes from the reaction of 2-naphthol and aldehydes using homogeneous or heterogeneous acid catalysts.
- Investigation of efficient catalytic systems for the synthesis of 1,8-dioxo-octahydroxanthene derivatives under solvent-free mechanochemical methods at mild condition in presence of supported solid acid catalysts.
- Observation of polymer supported Brønsted acid as reusable catalyst for the protection of carbonyl group as 1,1-diacetates (acylal) and its applications for deprotection to carbonyl group.
- Exploration of the dual nature of polyethylene glycol as reaction medium and catalyst for the protection of carbonyl group as oximes using thermal and microwave irradiations.
- Characterization of all the known and unknown products by melting point determination and different spectroscopic tools like FT-IR, $^{1}H$ NMR, $^{13}C$ NMR, CHN analysis, etc.

# References


[1] El-Brashy, A. M., et al. *II Farmaco* **59** (10), 809--817, 2004.

[2] Chibale, K., et al. T*etrahedron* **59** (13), 2289--2296, 2003.

[3] Demirkiran, O. Xanthones in *Hypericum*: Synthesis and Biological Activities, in *Bioactive Heterocycles III*, M.T.H. Khan, ed., Springer-Verlag Berlin Heidelberg, New York, 2007, 139-178.

[4] Kinjo, J., et al. *Tetrahedron Lett.* **36** (31), 5599--5602, 1995.

[5] Hideu, T. *[1]Benzopyrano[2,3-b]xanthene derivatives*, **Jpn. Tokkyo Koho No. JP 56005480,** June 27, 1979.

[6] Lambert, R. W., Martin, J. A., Merrett, J. H, Parkes, K. E. B. and Thomas, G. J. *Pyrimidine nucleosides*, **PCT Int. Appl. No. WO1997006178 A1**, February 20, 1997.

[7] Poupelin, J. P., et al. *Eur. J. Med. Chem.* **13**, 381--385, 1978.

[8] Ion, R-M. *Prog. Catal.* **2**, 55--76, 1997.

[9] Ion, R-M., et al. *Acta Biochim. Pol.* **45** (3), 833--845, 1998.

[10] Saint-Ruf, G., et al. *Naturwissenschaften* **62** (12), 584--585, 1975.

[11] Saint-Ruf, G., et al. *Bull. Chim. Ther.* **7**, 83--86, 1972.

[12] Menchen, S. M., Benson, S. C., Lam, J. Y. L., Zhen, W., Sun, D., Rosenblum, B. B., Khan, S. H. and Taing, M. *Sulfonated diarylrhodamine dyes*, **US Patent No. 6583168 B1**, June 24, 2003.

[13] Banerjee, A., & Mukherjee, A. K. *Stain Technol.* **56** (2), 83--85, 1981.

[14] Reynolds, G. A., Tuccio, S. A., Peterson, O. G. and Specht, D. P. *Laseranordnung zum erzeugen stabilisierter impulse*, **German Patent No. DE2109040 A1**, September 16, 1971.

[15] Bhowmik, B. B. & Ganguly, P. *Spectrochim. Acta, Part A* **61A** (9), 1997--2003, 2005.

[16] O' Callaghan, C. N., & McMurry, T. B. H. *J. Chem. Res., Synop.* 214--218, 1995.

[17] Gabbutt, C. D., et al. *J. Chem. Soc., Perkin Trans. 1* (12), 1819--1824, 1997.

[18] Karami, B., et al. *Catal. Sci. Technol.* **2** (2), 331--338, 2012.

[19] Lacroix, R., et al. *Ann. Pharm. Fr.* **43** (5), 479-489, 1985.

[20] Poupelin, J. P. *Anti-inflammatory and analgesic medicaments*, **US Patent No. 4147806**, April 3, 1979.

[21] Colombo, L., et al. *Arch. Virol.* **154** (9), 1539--1544, 2009.

[22] Vries, J. G. D. & Lefort, L. *Chem. Eur. J.* **12** (18), 4722--4734, 2006.

[23] Handique, J. G. & Barauh, J. B. *React. Funct. Polym.* **52** (3), 163--188, 2002.

[24] Kocieński, P. J. *Protecting Groups*, Thieme Medical Publishers Inc, New York, 2000.

[25] Greene, T. W. and Wuts, P. G. M. *Protective Groups in Organic Synthesis*, 3rd ed., Wiley-Interscience Publication John Wiley & Sons, Inc., New York, 1999.

[26] Kumar, P., et al. *Tetrahedron Lett.* **36** (4), 601--602, 1995 and references cited therein.

[27] Snider, B. B. & Amin, S. G. *Synth. Commun.* **8** (2), 117--125, 1978.

[28] Held, H., Rengstl, A. & Mayer, D. Acetic Anhydride and Mixed Fatty Acid Anhydrides, in *Ullman's Encyclopedia of Industrial Chemistry*, W. Gerhartz, ed., 5th Ed., Wiley-VCH, New York, 2000, 68.

[29] Banks, R. E., et al. *J. Chem. Soc., Perkin Trans. 1* 1096--1102, 1981.

[30] Freeman, F. & Karchefski, E. M. *J. Chem. Eng. Data* **22** (3), 355--357, 1977.

[31] Frick, J. G. & Harper, R. J. *J. Appl. Polym. Sci.* **29** (4), 1433--1447, 1984.

[32] Sanderson, W. R. *Peroxygen compounds*, **Eur. Pat. Appl. EP 0 125 781 A1**, November 21, 1984.

[33] Furuya, Y., et al. *J. Am. Chem. Soc.* **127** (32), 11240--11241, 2005.

[34] Dewan, S. K., et al. *Arkivoc* (2), 41--44, 2006.

[35] Dave, P. R. & Forohar, F. *J. Org. Chem.* **61** (25), 8897--8903, 1996.

[36] Smith, P. A. S., & Gloyer, S. E. *J. Org. Chem.* **40** (17), 2508--2512, 1975.

[37] Negi. S., et al. *Synthesis* (8), 991--996, 1996.

[38] Das, M. K. & Bhaumik, A. *Indian J. Chem., Sect B* **36** (11), 1020--1024, 1997.

[39] Narasaka, K. *Pure Appl. Chem.* **75** (1), 19--28, 2003.

[40] Attia, A. & Michael, M. *Pharmazie* **37** (8), 551--553, 1982.

[41] Nakayama, A., et al. *J. Agric. Food Chem.* **33** (6), 1034--1041, 1985.

[42] Song, B-A., et al. *Chin. J. Org. Chem.* **25** (5), 507--525, 2005.

[43] Ley, J. P. & Bertram, H-J. *Eur. J. Lipid Sci. Technol.* **104** (6), 319--323, 2002.

[44] Kato, M., et al. *Bioorg. Med. Chem. Lett.* **6** (1), 33--38, 1996.

[45] Hartmann, R. W., et al. *J. Med. Chem.* **43** (22), 4266--4277, 2000.

[46] Nasseri, M. A., et al. *J. Chem. Sci.* **125** (1), 109--116, 2013.

[47] Price, P. M., et al. *J. Chem. Soc., Dalton Trans.* (2), 101--110, 2000.

[48] Ko, S. & Yao, C-F. *Tetrahedron Lett.* **47** (50), 8827--8829, 2006.

[49] Benaglia, M., et al. *Chem. Rev.* **103** (9), 3401--3429, 2003.

[50] Chen, J., et al. *Green Chem.* 7 (2), 64--82, 2005.

[51] Heldebrant, D. J. & Jessop, P. G. *J. Am. Chem. Soc.* **125** (19), 5600--5601, 2003.

[52] Hesis, L. & Gais, H. J. *Tetrahedron Lett.* **36** (22), 3833--3836, 1995.

[53] Haimov, A. & Neumann, R. *Chem. Commun.* (8), 876--877, 2002.

[54] Chandrasekhar, S., et al. *Chem. Commun.* (14), 1716--1717, 2003.

[55] Bailey Jr., F. E. & Koleske, J. V. *Poly(EthyleneOxide)*, Academic Press, New York, 1976.

[56] Guo, Z., et al. *Ind. Eng. Chem. Res.* **41** (10), 2535--2542, 2002.

[57] Chen, J., et al. *Ind. Eng. Chem. Res.* **43** (17), 5358--5364, 2004.

[58] Chen, J., et al. *J. Chromatogr., B: Biomed. Appl.* **807** (1), 145--149, 2004.

[59] Naik, S. D. & Doraiswamy, L. K. *AIChE J.* **44** (3), 612--646, 1998.

[60] Harris, J. M. *Poly(ethyleneglycol) Chemistry: Biotechnical and Biomedical Applications*, Plenum Press, New York, 1992.

[61] Harris, J. M. & Zalipsky, S. *Poly (ethyleneglycol) Chemistry and Biological Applications*, American Chemical Society, Washington, DC, 1997.

[62] Rogers, R. D., et al. *J. Coord. Chem.* **29** (4), 187--207, 1993.

[63] Rogers, R. D., et al. *J. Am. Chem. Soc.* **114** (8), 2967--2977, 1992.

[64] Rogers, R. D., et al. *Inorg. Chem.* **35** (24), 6964--6973, 1996.

[65] Rogers, R. D., et al. *J. Alloys Compd.* **249** (1-2), 41--48, 1997.

[66] Rogers, R. D., et al. *J. Coord. Chem.* **26** (4), 299--311, 1992.

[67] Rogers, R. D., et al. *Inorg. Chem.* **33** (25), 5682--5692, 1994.

[68] Santaniello, E., et al. *Tetrahedron Lett.* **20** (47), 4581--4582, 1979.

[69] Totten, G. E., et al. *J. Macromol. Sci. Rev. Macromol. Chem. Phys.* **C38**, 77--142, 1998.

[70] Blasucci, V. M., et al. *J. Phys. Chem. A* **114** (11), 3932--3938, 2010.

[71] Pollet, P., et al. *Acc. Chem. Res.* **43** (9), 1237--1245, 2010.

[72] Tundo, P. & Anastas, P. T. *Green Chemistry: Challenging Perspectives*, Oxford University Press, Oxford, 1999.

[73] Rothenberg, G., et al. *J. Am. Chem. Soc.* **123** (36), 8701--8708, 2001.

[74] Hernández, J. G., Avila-Ortiz, C. G. and Juaristi, E. Useful Chemical Activation Alternatives in Solvent-Free Organic Reactions, in *Reference Module in Chemistry, Molecular Sciences and Chemical Engineering Comprehensive Organic Synthesis II*, 2nd ed., Elsevier, Amsterdam, 2014, 287-314.

[75] Naeimi, H. & Nazifi, Z. S. *C. R. Chimie* **17** (1), 41--48, 2014.

[76] Prousis, K. C., et al. *Ultrason. Sonochem.* **21** (3), 937--942, 2014.

[77] Kamalraja, J. & Perumal, P. T. *Tetrahedron Lett.* **55** (25), 3561--3564, 2014.

[78] Huo, C-D., et al. *Chin. Chem. Lett.* **25** (5), 699--701, 2014.

[79] Griesbeck, A. G. & Bartoschek, A. *Chem. Commun.* (15), 1594--1595, 2002.

[80] Marvaniya, H. M., et al. *Int. J. Drug Dev. & Res.* **3** (2), 34--43, 2011.

[81] Gedye, R., et al. *Tetrahedron Lett.* **27** (3), 279--282, 1986.

[82] Giguere, R. J., et al. *Tetrahedron Lett.* **27** (41), 4945--4948, 1986.

[83] Lidström, P., et al. *Tetrahedron* **57** (45), 9225--9283, 2001.

[84] Kappe, C. O. & Stadler, A. *Microwaves in Organic and Medicinal Chemistry*, Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim, 2005.

[85] Mason, B. P., et al. *Chem. Rev.* **107** (6), 2300--2318, 2007.

[86] Toda, F., et al. *J.Chem. Soc., Chem. Commun.* (4), 279--280, 1987.

[87] Tanaka, K. & Toda, F. *Chem. Rev.***100** (3), 1025--1074, 2000.

[88] Bose, A. K., et al. *Tetrahedron Lett.* **45** (45), 8351--8353, 2004.

[89] Tanaka, K. *Solvent-free Organic Synthesis*, Wiley-VCH, Weinheim, 2003.

[90] Garay, A. L., et al. *Chem. Soc. Rev.* **36** (6), 846--855, 2007.

[91] Papini, P. & Cimmarusti, R. *Gazz. Chim. Ital.* 77, 142--143, 1947.

[92] Sen, R. N. & Sarkar, N. N. *J. Am. Chem. Soc.* **47** (4), 1079--1091, 1925.

[93] Ota, K. & Kito, T. *Bull. Chem. Soc. Jpn.* **49** (4), 1167--1168, 1976.

[94] Wolff, W. *Chem. Ber.* **26** (1), 83--86, 1893.

[95] Rosebush, I. K. *Das Leder.* **6**, 58, 1955.

[96] Knight, D. W. & Little, P. B. *J. Chem. Soc., Perkin Trans. 1* (15), 1771--1777, 2001.

[97] Kuo, C-W. & Fang, J-M. *Synth. Commun.* **31** (6), 877--892, 2001.

[98] Wang, J-Q. & Harvey, R. G. *Tetrahedron* **58** (29), 5927--5931, 2002.

[99] Jha, A. & Beal, J. *Tetrahedron Lett.* **45** (49), 8999--9001, 2004.

[100] Sirkecioglu, O., et al. *J. Chem. Res. Synop.* 502--506, 1995.

[101] Khoramabadi-zad, A., et al. *J. Kor. Chem. Soc.* **46** (6), 541--544, 2002.

[102] Sarma, R. J. & Baruah, J. B. *Dyes Pigm.* **64** (1), 91--92, 2005.

[103] Pasha, M. A. & Jayashankara, V. P. *Bioorg. Med. Chem. Lett.* **17** (3), 621--623, 2007.

[104] Fei-Qing, D., et al. *Chin. J. Chem.* **25** (5), 645--648, 2007.

[105] Rajitha, B., et al. *Tetrahedron Lett.* **46** (50), 8691--8693, 2005

[106] Khosropour, A. R., et al. *Synlett* (6), 955--958, 2005.

[107] Patil, S. B., et al. *Synth. Commun.* **36** (15), 2163--2168, 2006.

[108] Kumari, P., et al. *Synth. Commun.* **38** (4), 637--648, 2008.

[109] Kumar, P. S., et al. *Arkivoc* (12), 46--50, 2006.

[110] Zarei, A., et al. *Dyes Pigm.* **85** (3), 133--138, 2010.

[111] Puri, S., et al. *Heterocycl. Lett.* **1** (3), 269--274, 2011.

[112] Itsuno, S., et al. *J. Org. Chem.* **55** (1), 304--310, 1990.

[113] Tayebee, R. & Tizabi, S. *Chin. J.Catal.* **33** (6), 962--969, 2012.

[114] Kumar, C. N. S. S. P., et al. *J. Heterocycl. Chem.* **46** (5), 997--999, 2009.

[115] Naik, M. A., et al. *Catal. Commun.* **11** (14), 1148--1153, 2010.

[116] Sharifi, A., et al. *Synth. Commun.* **38** (17), 2958--2966, 2008.

[117] Heravi, M. M., et al. *J. Mol. Catal. A: Chem.* **273** (1-2), 99--101, 2007.

[118] Allameh, S., et al. *Chin. Chem. Lett.* **23** (1), 17--20, 2012.

[119] Tayebee, R. & Maleki, B. *J. Chem. Sci.* **125** (2), 335--344, 2013.

[120] Briand, L. E., et al. *Appl. Catal. A: Gen.* **256** (1-2), 37--50, 2003.

[121] Moghadam, M., et al. *C. R. Chimie* **14** (5), 489--495, 2011.

[122] Nagarapu, L., et al. *Catal. Commun.* **8** (8), 1173--1177, 2007.

[123] Sheshmani, S. *J. Chem. Sci.* **125** (2), 345--351, 2013.

[124] Shaterian, H. R. & Ghashang, M. J. *J. Braz. Chem. Soc.* **19** (5), 1053--1058, 2008.

[125] Shaterian, H. R., et al. *Chin. J. Chem.* **26** (2), 338--342, 2008.

[126] Shaterian, H. R., et al. *Arkivoc* (15), 1--10, 2007.

[127] Shaterian, H. R., et al. *Phosphorus, Sulfur Silicon Relat. Elem.* **185** (1), 171--180, 2010.

[128] Shaterian, H. R., et al. *Dyes Pigm.* **76** (2), 564--568, 2008.

[129] Hashemi, M. M. & Karimi-Jaberi, Z. *Monatsh Chem.* **139** (6), 605--608, 2008.

[130] Hunnur, R. K., et al. *Chem. Heterocycl. Compd.* **44** (2), 143--147, 2008.

[131] Eshghi, H., et al. *Chin. Chem. Lett.* **19** (12), 1423--1426, 2008.

[132] Mirjalili, B. B. F., et al. *Chin. Chem. Lett.* **22** (1), 45--48, 2011.

[133] Rostamizadeh, S., et al. *Chin. Chem. Lett.* **19** (10), 1151--1155, 2008.

[134] Nagarapu, L., et al. *Synth. Commun.* **37** (15), 2519--2525, 2007.

[135] Liu, Y-H., et al. *Synth. Commun.* **39** (4), 580--589, 2009.

[136] Rostamizadeh, S., et al. *Chin. Chem. Lett.* **20** (7), 779--783, 2009.

[137] Khojastehnezhad, A., et al. *Chin. J. Chem.* **29** (2), 297--302, 2011.

[138] Eshghi, H., et al. *Org. Prep. Proced. Int.* **43** (3), 302--307, 2011.

[139] Das, B., et al. *Helv. Chim. Acta* **90** (7), 1330--1334, 2007.

[140] Bigdeli, M. A., et al. *J. Mol. Catal. A: Chem.* **275** (1-2), 25--29, 2007.

[141] Mahdavinia, G. H., et al. *Ultrason. Sonochem.* **16** (1), 7--10, 2009.

[142] Hashemi, H. & Sardarian, A. R. *Iran. J. Sci. Technol. A* **37** (1), 75--82, 2013.

[143] Norouzi, H., et al. *Bull. Korean Chem. Soc.* **32** (7), 2311--2315, 2011.

[144] Bailey, D. C. & Langer, S. H. *Chem. Rev.* **81** (2), 109--148, 1981.

[145] Akelah, A. & Sherrington, D. C. *Chem. Rev.* **81** (6), 557--587, 1981.

[146] Ley, S. V., et al. *J. Chem. Soc., Perkin Trans. 1* (23), 3815--4195, 2000.

[147] Santelli, M. & Pons, J.-M. *Lewis Acids and Selectivity in Organic Synthesis*, CRC Press, Boca Raton, FL, 1995.

[148] Ran, R., et al. *J. Polym. Sci. Part A: Polym. Chem.* **31** (12), 2915--2921, 1993.

[149] Drago, R. S. & Getty, E. E. *J. Am. Chem. Soc.* **110** (10), 3311--3312, 1988.

[150] Rahmatpour, A. & Aalaie, J. *Heteroat. Chem.* **22** (1), 51--54, 2011.

[151] Khaligh, N. G. *Ultrason. Sonochem.* **19** (4), 736--739, 2012.

[152] Mokhtary, M. & Refahati, S. *Dyes Pigm.* **99** (2), 378--381, 2013.

[153] Madhav, J. V., et al. *J. Mol. Catal. A: Chem.* **304** (1-2), 85--87, 2009.

[154] Quan, Z-J., et al. *Synth. Commun.* **41** (20), 3106--3116, 2011.

[155] Astruc, D. *Nanoparticles and Catalysis*, Wiley-VCH Verlag GmbH, Weinheim, 2008.

[156] Min, Y., et al. *Nat. Mater.*7 (7), 527--538, 2008.

[157] Safaei-Ghomi, J. & Ghasemzadeh, M.A. *Journal of. Saudi Chemical Society*, in press.

[158] Rao, G. B. D., et al. *Tetrahedron Lett.* **53** (22), 2741--2744, 2012.

[159] Mirjalili, B. F., et al. *Chem. Heterocycl. Compd.* **48** (6), 856--860, 2012.

[160] Fareghi-Alamdari, R., et al. *C. R. Chimie* **16** (10), 878--887, 2013.

[161] Nasr-Esfahani, M. & Abdizadeh, T. *Rev. Roum. Chim.* **58** (1), 27--35, 2013.

[162] Bamoniri, A., et al. *Curr. Chem. Lett.* **2** (1), 27--34, 2013.

[163] Mirkhani, V., et al. *Synth. Commun.* **39** (24), 4328--4340, 2009.

[164] Ziarani, G. M., et al. *Sci. Iran., Trans. C* **18** (3), 453--457, 2011.

[165] Mohammadpoor-Baltork, I., et al. *Chin. Chem. Lett.* **22** (1), 9--12, 2011.

[166] Georghiou, P. E., et al. *J. Org. Chem.* **60** (22), 7284--7289, 1995.

[167] Day, A. C., et al. *J. Chem. Soc.* 4067--4074, 1961.

[168] Hassall, C. H. & Lewis, J. R. *J. Chem. Soc.* 2312--2315, 1961.

[169] Davidson, T. A. & Scott, A. I. *J. Chem. Soc.* 4075--4078, 1961.

[170] Kasturi, T. R., et al. *Tetrahedron* **49** (1), 125--134, 1993.

[171] Kharasch, M. S. & Porsche, J. *J. Org. Chem.* **1** (3), 265--274, 1936.

[172] Bennett, D. J., et al. *J. Chem. Soc., Perkin Trans. 1.* 1978--1985, 1980.

[173] Naidu, K. R. M., et al. *Molecules* **17** (6), 7543--7555, 2012 and references cited therein.

[174] Shearing, E. A. & Smiles, S. *J. Chem. Soc.* 1348--1351, 1937.

[175] Ogata, Y., et al. *Tetrahedron* **25** (13), 2589--2602, 1969.

[176] Schreiber, K. C. & Kennedy, M. C. *J. Org. Chem.* **21** (11), 1310--1311, 1956.

[177] Kasturi, T. R., et al. *Tetrahedron* **51** (10), 3051--3060, 1995.

[178] Kasturi, T. R., et al. *Tetrahedron* **49** (1), 113--124, 1993.

[179] Ohishi, T., et al. *Tetrahedron Lett.* **42** (13), 2493--2496, 2001.

[180] Ranjbar, P. R., et al. *Acta Cryst. E* **63** (5), o2093--o2094, 2007.

[181] Alizadeh, A., et al. *J. Iran.Chem. Soc.*7 (2), 351--358, 2010.

[182] Robak, J. & Gryglewski, R. J. *Pol. J. Pharmacol.* **48** (6), 555--564, 1996.

[183] Wang, H. K., et al. *Med. Res. Rev.* **17** (4), 367--425, 1997.

[184] Griffith, O. H. *Tetrahedron Lett.* **39** (37), 6637--6640, 1998.

[185] Hatakeyama, S., et al. *J. Chem. Soc., Chem. Commun.* (17), 1202--1204, 1988.

[186] Cingolani, G. M., et al. *J. Med. Chem.* **12** (3), 531--532, 1969.

[187] Horning, E. C. & Horning, M. G. *J. Org. Chem.* **11** (1), 95--99, 1946.

[188] Singh, K., et al. *Tetrahedron* **52** (45), 14273--14280, 1996.

[189] Bacci, J. P., et al. *J. Org. Chem.***70** (22), 9051--9053, 2005.

[190] Shi, D., et al. *Synth. Commun.* **30** (4), 713--726, 2000.

[191] Jin, T-S., et al. *Synlett* (5), 866--870, 2004.

[192] Dabiri, M., et al. *Catal. Commun.* **9** (5), 939--942, 2008.

[193] Das, B., et al. *J. Mol. Catal. A: Chem.* **247** (1-2), 233--239, 2006.

[194] Sivaguru, P. & Lalitha, A. *Chin. Chem. Lett.* **25** (2), 321--323, 2014.

[195] Shakibaei, G. I., et al. *Appl. Catal. A: Gen.* **325** (1), 188--192, 2007.

[196] Dabiri, M., et al. *Chem. Pap.* **62** (5), 522--526, 2008.

[197] Song, G., et al. *Catal. Commun.* **8** (4), 673--676, 2007.

[198] Karthikeyan, G. & Pandurangan, A. *J. Mol. Catal. A: Chem.* **311** (1-2), 36--45, 2009.

[199] Pore, D. M., et al. *Synth. Commun.* **40** (15), 2215--2219, 2010.

[200] Shaterian, H. R., et al. *Turk. J. Chem.* **33** (2), 233--240, 2009.

[201] Ma, J-J., et al. *Chin. J. Org. Chem.* **27** (5), 640--642, 2007.

[202] Mosaddegh, E., et al. *Arab. J. Chem.* **5** (1), 77--80, 2012.

[203] Das, B., et al. *Catal. Commun.* **8** (3), 535--538, 2007.

[204] Zhang, Z-H. & Liu, Y-H. *Catal. Commun.* **9** (8), 1715--1719, 2008.

[205] Shaterian, H. R, et al. *Phosphorus, Sulfur Silicon Relat. Elem.* **183** (12), 3136--3144, 2008.

[206] Kantevari, S., et al. *J. Mol. Catal. A: Chem.* **269** (1-2), 53--57, 2007.

[207] Mahdavinia, G. H., et al. *Chin. Chem. Lett.* **20** (5), 539--541, 2009.

[208] Seyyedhamzeh, M., et al. *Dyes Pigm.***76** (3), 836--839, 2008.

[209] Oskooie, H. A., et al. *E-J. Chem.* 7 (3), 717--720, 2010.

[210] Pramanik, A. & Bhar, S. *Catal. Commun.* **20**, 17--24, 2012.

[211] John, A., et al. *J. Mol. Catal. A: Chem.* **248** (1-2), 121--125, 2006.

[212] Mokhtary, M. & Langroudi, S. A. M. *Monatsh. Chem.* **145** (9), 1489--1494, 2014.

[213] Albadi, J., et al. *J. Chem. Sci.* **125** (2), 295--298, 2013.

[214] Samantaray, S., et al. *Ind. Eng. Chem. Res.* **52** (17), 5862--5870, 2013.

[215] Jin, T.-S., et al. *Synth. Commun.* **35** (17), 2339--2345, 2005.

[216] Kochhar, K. S., et al. *J. Org. Chem.* **48** (10), 1765--1767, 1983.

[217] Sandberg, M. & Sydnes, L. K. *Tetrahedron Lett.* **39** (35), 6361--6364, 1998.

[218] Yadav, J. S., et al. *Synlett* (5), 673--675, 2001.

[219] Trost, B. M. & Lee, C. *J. Am. Chem. Soc.* **123** (49), 12191--12201, 2001.

[220] Sydnes, L. K. & Sandberg, M. *Tetrahedron* **53** (37), 12679--12690, 1997.

[221] Trost, B. M. & Vercauteran, J. *Tetrahedron Lett.* **26** (2), 131--134, 1985.

[222] Trost, B. M., et al. *J. Am. Chem. Soc.* **117** (27), 7247--7248, 1995.

[223] Tomita, M., et al. *Chem. Pharm. Bull.* **11** (12), 1484--1490, 1963.

[224] Davey, W. & Gwilt, J. R. *J. Chem. Soc.* 1008--1014, 1957.

[225] Marshall, J. A. & Wuts, P. G. M. *J. Org. Chem.* **42** (10), 1794--1798, 1977.

[226] Deka, N., et al. *J. Org. Chem.* **62** (5), 1563--1564, 1997.

[227] Deka, N., et al. *J. Chem. Res., Synop.* (2), 94--95, 1998.

[228] Seriabine, I. *Bull. Chem. Soc. Fr.* 1194--1198, 1961.

[229] Jin, T.-S., et al. *Indian J. Chem., Sect B* **37**, 939--940, 1998.

[230] Michie, J. K. & Miller, J. A. *Synthesis* (10), 824, 1981.

[231] Yadav, J. S., et al. *Synth. Commun.* **32** (14), 2169--2174, 2002.

[232] Yin, L., et al. *Synlett* (10), 1727--1730, 2004.

[233] Mirjalili, B. F., et al. *J. Chin. Chem. Soc.* **53** (4), 955--959, 2006.

[234] Heravi, M. M., et al. *J. Chin. Chem. Soc.* **54** (2), 273--275, 2007.

[235] Bandgar, B. P., et al. *J. Chin. Chem. Soc.* **54** (2), 489--492, 2007.

[236] Aggarwal, V. K., et al. *Synlett* (8), 849--850, 1998.

[237] Chandra, K. L., et al. *Synlett* (3), 359--360, 2000.

[238] Carrigan, M. D., et al. *Tetrahedron Lett.* **42** (46), 8133--8135, 2001.

[239] Karimi, B. & Maleki, J. *J. Org. Chem.* **68** (12), 4951--4954, 2003.

[240] Ghosh, R., et al. *J. Mol. Catal. A: Chem.* **215** (1-2), 49--53, 2004.

[241] Dehghani, F., et al. *Chinese Chemical Letters*, in press and references cited therein.

[242] Seneci, P. *Solid-Phase Synthesis and Combinatorial Technologies*, John Wiley and Sons, Canada, 2000.

[243] Clark, J. H. *Acc. Chem. Res.* **35** (9), 791--797, 2002.

[244] Shirini, F., et al. *Catal. Commun.* **36**, 31--37, 2013.

[245] Ghorbani-Vaghei, R., et al. *Mendeleev Commun.* **16** (1), 55--56, 2006 and references cited therein.

[246] Li, Y-Q. *Synth. Commun.* **30** (21), 3913--3917, 2000.

[247] Wang, Q-Y., et al. *Synth. Commun.* **37** (6), 1019--1026, 2007.

[248] Wang, L. & Cai, C. *J. Appl. Polym. Sci.* **112** (4), 2087--2093, 2009.

[249] Boroujeni, K. P. *Synth. Commun.* **41** (2), 277--284, 2011.

[250] Fan, D-H., et al. *Molecules* **15** (9), 6493--6501, 2010.

[251] Nabid, M. R., et al. *Synth. Commun.* **41** (2), 191--199, 2011.

[252] Khaligh, N. G. & Shirini, F. *J. Mol. Catal. A: Chem.* **348** (1-2), 20--29, 2011.

[253] Khaligh, N. G. & Shirini, F. *Ultrason. Sonochem.* **20** (1), 19--25, 2013.

[254] Shirini, F. & Jolodar, O. G. *J. Mol. Catal. A: Chem.* **356**, 61--69, 2012.

[255] Olah, G. A. & Mehrotra, A. K. *Synthesis* (11), 962--963, 1982.

[256] Borah, K. J. & Borah, R. *Monatsh. Chem.* **142** (12), 1253--1257, 2011.

[257] Cornelis, A. & Laszlo, P. *Synthesis* (10), 849--850, 1980.

[258] Whitesell, J. K. & Whitesell, M. A. *Synthesis* (7), 517--536, 1983.

[259] Bosch, A. I., et al. *Synlett* (12), 1259--1260, 1995.

[260] Williams, F. J. *Nitrosation*, Cambridge University Press, Cambridge, 1988.

[261] Katritzky, A. R., Meth-Cohn, O. & Rees, C. W. *Comprehensive Organic Functional Group Transformations*, Pergamon, New York, 1995.

[262] Olah, G. A. & Keumi, T. *Synthesis* (2), 112--113, 1979.

[263] Sosnovsky, G., et al. *Synthesis* (9), 722--724, 1979.

[264] Miller, C. P. & Kaufman, D. H. *Synlett* (8), 1169--1171, 2000.

[265] Weissermel, K. & Arpe, H.-J. *Industrial Organic Chemistry*, 3rd ed., VCH, Germany & New York, 1978.

[266] Roffia, P., Padovan, M., Leofanti, G., Mantagazza, M. A., Allberti, G. D. and Tauszik, G. R. *Catalytic process for the manufacture of oximes*, **US Patent No. 4794198**, December 27, 1988.

[267] Bars, J. L., et al. *Appl. Catal., A* **136** (1), 69--80, 1996 and references cited therein.

[268] Armor, J. N. *Direct oximation of ketones*, **US Patent No. 4163756**, August 7, 1979.

[269] Hajipour, A. R., et al. *J. Chem. Res., Synop.* (3), 228-229, 1999.

[270] Guo, J-J., et al. *Green Chem.* **3** (4), 193--195, 2001.

[271] Damljanović, I., et al. *Monatsh. Chem.* **137** (3), 301--305, 2006.

[272] Li, J-T., et al. *Ultrason. Sonochem.* **13** (3), 200--202, 2006.

[273] Zang, H., et al. *Ultrason. Sonochem.* **16** (3), 301--303, 2009.

[274] Kadzyauskas, P. P. & Zefirov, N. S. *Russ. Chem. Rev.* **37** (7), 543--550, 1968.

[275] Richey, Jr., H. G., et al. *Tetrahedron Lett.* **17** (4), 233--234, 1976.

[276] Nickon, A., et al. *J. Am. Chem. Soc.* **99** (13), 4518--4520, 1977.

[277] Kahr, K. & Bether, C. *Chem. Ber.* **93**, 132, 1960.

[278] Kabalka, G. W., et al. *Synth Commun.* **20** (16), 2453--2458, 1990.

[279] Sharjhi, H. & Sarvari, M. H. *J. Chem. Res., Synop.* (1), 24--25, 2000.

[280] Bandgar, B. P., et al. *Monatsh. Chem.* **132** (3), 403--406, 2001.

[281] Kad, G. L., et al. *Green Chem.* **3** (6), 275--277, 2001

[282] Osadchenko, I. M. & Tomilov, A. P. *Russ. J. Appl. Chem.* **75** (3), 511--512, 2002.

[283] Bigdeli, M. A., et al. *J. Chem. Res., Synop.* (1), 20--21, 2002.

[284] Sharghi, H. & Hosseini, M. *Synthesis* (8), 1057--1059, 2002.

[285] Hoelz, L. V-B., et al. *Molecules* **15** (1), 94--99, 2010.

[286] Saikia, L., et al. *Org. Med. Chem. Lett.* **1** (1), 12--17, 2011.

# Chapter 2

# Synthesis and Characterization of Aryl-*bis*(2-Hydroxy-1-Naphthyl) Methane and 14-Alkyl or Aryl-14*H*-Dibenzoxanthenes

Published and communicated with small modifications:

**Dutta, P.** & Borah, R. Boron sulfonic acid (BSA) catalyzed selective synthesis of aryl-*bis*(2-hydroxy-1-naphthyl) methane and 14-alkyl or aryl-14*H*-dibenzoxanthenes under solvent-free condition, 2014 (communicated).

**Dutta, P.**, Saikia, M. K., Das, R. J., Borah, R. Investigation of keto-enol tautomers during the synthesis of aryl-*bis*(2-hydroxy-1-naphthyl) methanes, *Journal of Chemical Sciences* 2014 (accepted).

# Section 2A

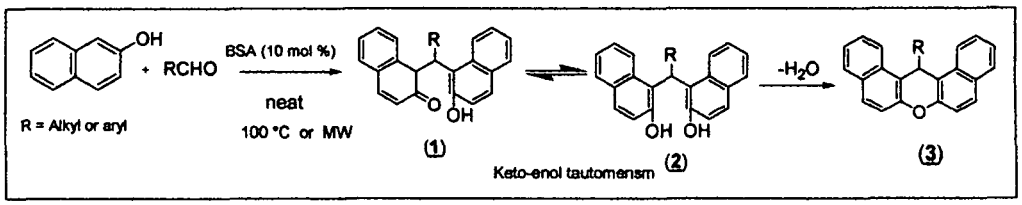
## Boron Sulfonic Acid (BSA) Catalyzed Selective Synthesis of Aryl-*bis*(2-Hydroxy-1-Naphthyl) Methane and 14-Alkyl or Aryl-14*H*-Dibenzoxanthenes under Solvent-free Condition

---

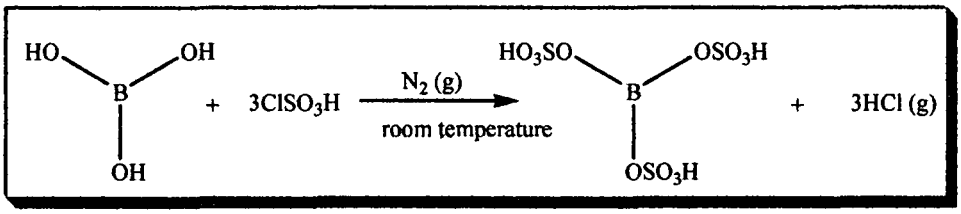
## 2A.1. Introduction

The realm of this work started with the development of efficient methodologies for the selective synthesis of dibenzoxanthene (3) and its precursor bisnaphthol (2) via keto isomer (1) under solvent-less medium using reusable solid acid catalysts (**Scheme-1.2A**). Both types of compounds have wide range of applications in medicinal chemistry and material science as already mentioned in the first chapter of this thesis. A large number of acid catalysts have been reported in literature for the synthesis of dibenzoxanthenes which include traditional Brönsted/Lewis acids along with reusable heterogeneous acids [1]. Some of the examples of solid acids are Amberlyst-15 [2], silica sulfuric acid [3], $HClO_4/SiO_2$ [4], heteropoly acid [5], $Yb(OTf)_3$ [6], montmorillonite K-10 [7], and cellulose sulfuric acid [8]. Most of the acid catalysed synthesis of dibenzoxanthene (**Scheme-1.2A**) described the selective formation of the required product without the intermediary of aryldi-(2-hydroxy-1-naphthyl)methanes (2) under solvent-free thermal treatment or microwave irradiation as already cited in Chapter 1. The literature survey shows few reports on the synthesis of aryldi-(2-hydroxy-1-naphthyl) methane from aldehydes and 2-naphthol [9-11]. The preparation of bisnaphthols was described as lower yields from the mixture of 2-naphthol and benzaldehyde in AcOH using conc. HClas catalyst for 50 h in a refrigerator [9]. Alizadeh *et al.* (2010) introduced $H_3[P(Mo_3O_{10})_4].nH_2O$ as reusable heteropolyacid catalyst in refluxing dichloromethane [10]. Similarly the condensation of phenols with aromatic aldehydes in ethanol utilized 3 kbar pressures in 24 hours at 60 °C in presence of TfOH catalyst to produce good to excellent yields of bisnaphthols [11]. All these studies reveal that there is a scope to examine the selective synthesis of both

compounds (2) and (3) with different energy sources in solution or in neat condition using recyclable reactive solid acid catalyst like boron sulfonic acid. Boron sulfonic acid (BSA) is a versatile solid acid which was first introduced by Kiasat *et al.* (2008) that makes reaction processes convenient, more economic and environmentally benign (**Scheme-2.2A**) [12]. Owing to the numerous advantages associated with this cheap and non-hazardous reagent, BSA has been explored as a powerful catalyst for various organic transformations under mild conditions [13]. Here, we have the opportunity to explore the catalytic activity of BSA for the selective generation of 14-alkyl or aryl-14*H*-dibenzoxanthenes and its precursor aryl or alkyl-*bis*(2-hydroxy-1-naphthyl) methane from the acid catalysed reaction of 2-naphthol with aldehydes (**Scheme-1.2A**) under thermal method and microwave irradiation respectively.




**Scheme-1.2A**




**Scheme-2.2A**

It is well established that the uses of microwave energy with solvent-less medium reduces the reaction time and thus make the reaction path cleaner by single product formation [14].

## 2A.2. Results and Discussion

Initially, we optimized the amount of BSA catalyst with the model reaction of benzaldehyde (1 mmol) and 2-naphthol (2 mmol) (**table 1.2A**) in solvent-less medium under thermal as well as microwave energies to study the appropriate

conditions for the selective synthesis of aryl-bis(2-hydroxy-1-naphthyl) methane (2a) and dibenzoxanthene derivatives (3a).

**Table 1.2A**: Standardization of the amount of BSA catalyst

| Entry | Catalyst( mol%) | Time[a] (mins) A | B | MW Power(W) | Product Yields (%) (2a) (A/B) | (3a) (A/B) |
|---|---|---|---|---|---|---|
| 1 | 1 | 1 h | 5 | 500 | 10/10 | 50/10 |
| 2 | 5 | 15 | 5 | 500 | 10/25 | 68/10 |
| 3 | 10 | 15 | 5 | 500 | -/80 | 96/15 |
| 4 | 10 | - | 5 | 625 | -/- | -/95 |
| 5 | 25 | 10 | 5 | 250 | -/- | 97/96 |

[a]Methods A: solvent-free thermal method at 100°C; B: microwave irradiation in neat condition

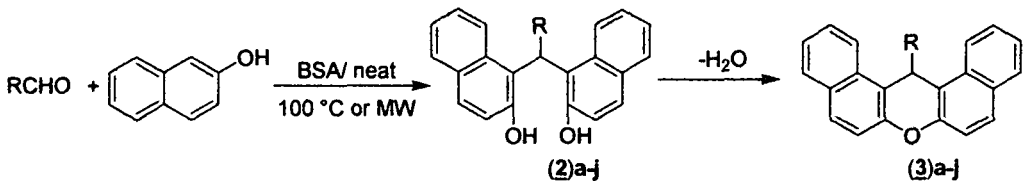
These studies clearly identified two optimized conditions for selective formation of (2a) and (3a) under microwave and thermal energies with 10 mol% of BSA catalyst (table1.2A, entry 3). The thermal treatment needed 100 °C to give 96% yield of dibenzoxanthene (3a) during 15 min reaction time (table 1.2A, entry 3) whereas it was 80% yield of bisnaphthol (2a) within 5 min with 500 W microwave power irradiation (table 1.2A, entry 3). The reaction mixture was found with unreacted 2-naphthol at 80 °C in neat condition. The dehydration of bisnaphthol to dibenzoxanthene became faster upon increasing the MW power to 25% with 10 mol% of BSA for 5 min irradiation (table 1.2A, entry 4). The use of 25 mol% of BSA produced dibenzoxanthene (3a) as sole product in both methods within 10 min at 100 °C in thermal treatment and at 50% lower microwave power than the power of bisnaphthol (2a) synthesis under optimized condition (table 1.2A, entry 5). We also examined the effect of various polar and non-polar solvents for the synthesis of dibenzoxanthene (3a) under reflux conditions using 10 mol% of BSA as catalyst (table 2.2A). The model reaction was not efficient to produce good yields of products in water, dichloromethane, chloroform, acetonitrile and ethanol under reflux in solution as compared to neat environment (table 2.2A, entry 6).

**Table 2.2A**: Solvent optimization of (3a) under conventional heating

| Entry | Solvent | Time (h) | (3a) Yield (%) |
|---|---|---|---|
| 1 | $H_2O$ | 1 | 10 |
| 2 | $CH_2Cl_2$ | 1 | 45 |
| 3 | $CHCl_3$ | 1 | 50 |
| 4 | EtOH | 1 | 65 |
| 5 | $CH_3CN$ | 1 | 40 |
| 6 | Neat | 15min | 96 |

By examining the above optimization results, we extended the synthesis of alkyl or aryl-bis(2-hydroxy-1-naphthyl)methane (2) and their dehydration product dibenzoxanthene(3) with different aldehydes in solvent-free medium using both thermal as well as microwave energies with 10 mol% and 25 mol% of BSA catalysts. All these observations were included in table 3.2A.

**Table 3.2A**: Formation of (2) and (3)with different aldehydes using BSA catalyst in solvent-free methods




(2)a-j (3)a-j

R = Ph (a); p-$NO_2$-$C_6H_4$ (b); p-MeO-$C_6H_4$ (c); p-Cl-$C_6H_4$ (d); p-$CH_3$-$C_6H_4$ (e); $CH_3(CH_2)_2$ (f); 2-furyl (g); 2-naphthyl (h); $C_6H_5CH$=CH (i)

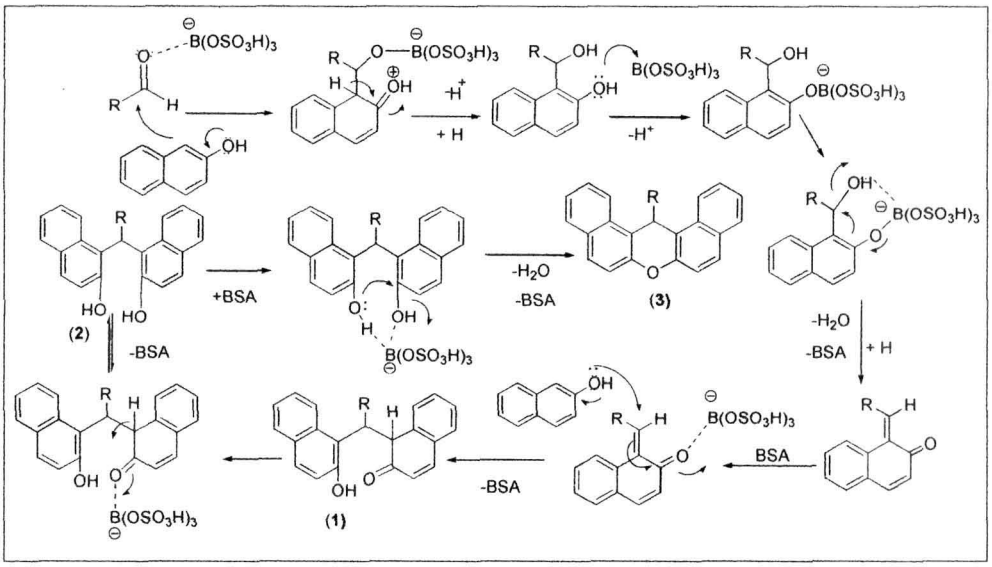
| Entry | Aldehydes R- | MWPower(W) | Catalyst(mol%) | Time(mins)A/B | Yield(%)(2)A/B | Yield(%)(3)A/B | M.p. (°C) Found (Reported) (2) | M.p. (°C) Found (Reported) (3) |
|---|---|---|---|---|---|---|---|---|
| 1 | Ph- | 500 | 10 | 15/5 | -/80 | 96/5 | 203-205(200)[11] (2a) | 182.9 (183-184)[15] (3a) |
| | | 625 | 10 | -/5 | -/- | -/87 | | |
| | | 250 | 25 | 10/5 | - | 97/92 | | |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| 2 | p-$NO_2$-$C_6H_4$- | 625<br>625 | 10<br>25 | 15/3<br>60/5 | 95/96<br>72/75 | -<br>24/15 | 303-305 (>300)[39] (2b) | 310.5 (308-309) [15] (3b) |
| 3 | p-MeO-$C_6H_4$- | 250<br>500 | 10<br>25 | 45/5<br>-/5 | -/75<br>-/ 65 | 70/-<br>-/25 | 201- 202.5 (202) [11] (2c) | 203.8 (204-205) [15] (3c) |
| 4 | p-Cl-$C_6H_4$- | 625<br>750 | 10<br>25 | 15/3<br>-/ 3 | -/92<br>-/70 | 90/-<br>-/22 | 184.9-187.1 (187.5-188) [11] (2d) | 291 (289-290)[38] (3d) |
| 5 | p-Me-$C_6H_4$- | 375<br>625 | 10<br>25 | 30/5<br>-/ 2 | -<br>- | 80/85<br>-/96 | - | 229.1 (228-230) [15] (3e) |
| 6 | $CH_3(CH_2)_2$- | 250 | 10 | 40/5 | - | 75/10 | - | 155.2 (152-154) [4] (3f) |
| 7 | 2-Furyl- | 500 | 10 | 15/5 | Polymer-ic product | - | - | - |
| 8 | 2-Naphthyl- | 500<br>625 | 10<br>25 | 40/5<br>60/3 | 30/85<br>-/60 | 65/-<br>85/30 | 153.8 (152.5-154) [11] (2h) | 216.5 (217) [16] (3h) |
| 9 | $C_6H_5CH$=CH- | 250 | 10 | 15/5 | - | 95/90 | - | 176.9 (178-180) [17] (3i) |

[a]Methods A: solvent-free thermal method at 100°C; B: microwave irradiation in neat condition; [b]Isolated products; [c]All the isolated compounds are characterized by FT-IR, $^1$H NMR, $^{13}$C NMR and elemental analysis.

The results in table 3.2A showed selective behavior of BSA catalyst for the formation of dibenzoxanthene (3) at 100 °C with 10 mol% of catalyst from aliphatic or aromatic aldehydes except 4-nitrobenzaldehyde (table 3.2A, entry 2). The same amount of catalyst generated bisnaphthol (3) as major product from aromatic aldehydes (75-96%) under microwave in short time excluding *p*-tolualdehyde (table 3.2A, entry 5). Cinnamaldehyde produced dibenzoxanthene (3i) as single product under microwave and thermal energies (table 3.2A, entry 9). Butanal formed dibenzoxanthene as major product in thermal method at 90 °C with 10 mol% of BSA (table 3.2A, entry 6). The BSA catalyst lost its selectivity with 25 mol% under microwave irradiation for the formation of bisnaphthol derivatives while benzaldehyde and *p*-tolualdehyde yielded dibenzoxanthene as major product (table 3.2A, entries 1, 5). Ultimately, using the same model reaction of benzaldehyde and 2-naphthol, the recyclability of the BSA catalyst was tested for the formation of dibenzoxanthene (3a). Taking 10 mol% of the catalyst, the

reaction was carried out under thermal treatment at 100 °C. The property of the catalyst remained intact for four cycles with almost the same yield. Pictorial graph is depicted in **Fig. 1.2A** as given below. The plausible mechanism of BSA catalyzed selective synthesis of dibenzoxanthene (**3**) and bisnaphthol (**2**) from the reaction of 2-naphthol and aldehyde is expressed by the **Scheme-3.2A** in neat condition.




**Scheme-3.2A**: Plausible mechanism of BSA catalyzed reactions

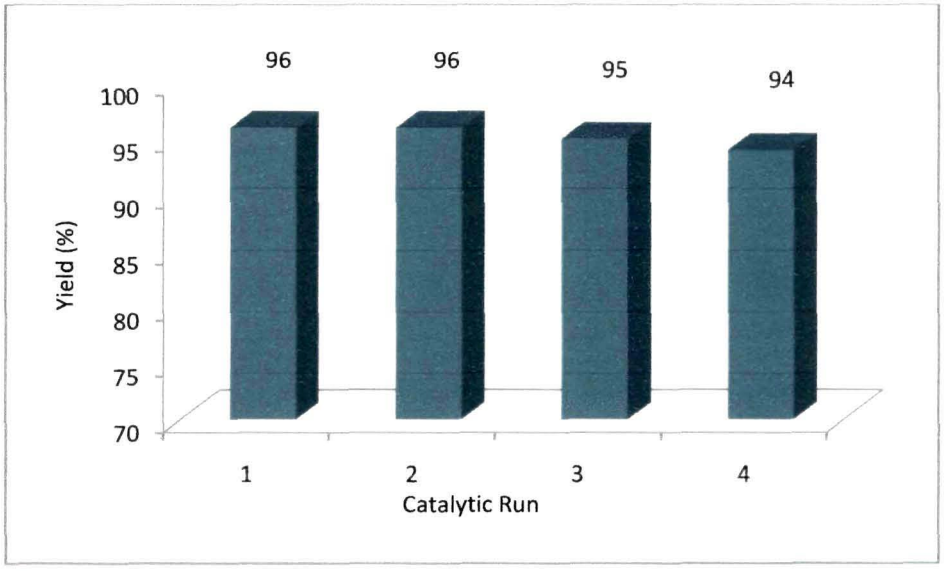



**Fig 1.2A**: Recycling of BSA catalyst for the preparation of (**3a**) at 100 °C

## 2A.3. Conclusion

This section explores the catalytic activities of boron sulfonic acid as reusable solid acid in neat conditions for the selective preparation of dibenzoxanthene and its precursor intermediate bisnaphthol under thermal and microwave energies in an efficient way. We observed different selectivity of BSA catalyst towards the synthesis of dibenzoxanthene in thermal and microwave conditions with variation of the amount of catalysts under optimized conditions. The catalyst was found to be recyclable for four runs for the synthesis of dibenzoxanthene in neat under thermal method and thus making it quite attractive in terms of green chemistry. Moreover, this is the first method for the selective synthesis of aryl-bis(2-hydroxy-1-naphthyl) methane under microwave irradiation in presence of heterogeneous catalyst with excellent yields of product. In both conditions the selective syntheses of both compounds were possible within short time.

## 2A.4. Experimental Section

### 2A.4.1. General Information

All chemicals were purchased from chemical supplier and were used without purification. $^{1}H$ and $^{13}C$ NMR spectra were recorded on a JEOL JNM ECS-400 MHz FT-NMR spectrometer in $CDCl_3$ solution using TMS as internal standard. *J*-values were given in Hertz. IR spectra were recorded on a Nicolet Impact-410 spectrometer. The products were identified by comparison of their FT-IR, $^{1}H$ NMR and $^{13}C$ NMR spectroscopic data with those of authentic compounds and literature reported data [4, 11, 15-17, 38-39]. The elemental analysis were performed on Perkin Elmer 20-analyzer. Melting points were recorded in a Buchi B-540 melting point apparatus and were uncorrected.

### 2A.4.2. Preparation of boron sulfonic acid catalyst

The boron sulfonic acid (BSA) catalyst was prepared via the reaction of boric acid with chlorosulfonic acid by following the procedure reported by Kiasat *et al.* in 2008 [12]. A 50 mL suction flask fitted with a constant pressure dropping funnel

was connected to a vacuum system through water and an alkali trap. To the flask, 12 mmol (0.742 g) of boric acid was introduced and after that, 36 mmol (2.4 mL) of chlorosulfonic acid was added drop wise over a period of an hour at ambient temperature with the help of pressure dropping funnel. The immediately evolved HCl generated was trapped by the water and alkali solutions through suction. Once the addition was completed, the resulting mixture was shaken for an hour. The solid residue was washed with diethyl ether to remove the unreacted chlorosulfonic acid. Finally, the product was collected as grey solid with 94% (7.1 g) yield.

### 2A.4.3. Typical procedure for the preparation of 14-alkyl or aryl-14*H*-dibenzoxanthenes (3) under solvent-free conventional heating

A mixture of aldehyde (1 mmol) and β-naphthol (2 mmol) along with BSA (10 mol%) was grounded in mortar into a fine powder and was introduced in a 50 mL round bottomed flask fitted with a reflux condenser to a preheated oil bath at 100 °C for the specified time. After completion of the reaction, the mixture was diluted with ethyl acetate (5 mL) and filtered to isolate the solid catalyst for recycling. The crude filtrate was washed with dilute aqueous solution of sodium hydroxide to remove the unreacted 2-naphthol. The organic extract was dried over anhydrous $Na_2SO_4$ and distilled under reduced pressure to furnish the crude product. The crude product was further purified by preparative thin layer chromatography with ethyl acetate and hexane as solvent system to get analytically pure product.

### 2A.4.4. Typical procedure for the preparation of aryl-bis(2-hydroxy-1-naphthyl) methanes (2) and 14-alkyl or aryl-14*H*-dibenzoxanthenes (3) under microwave energy

A mixture of finely grounded aldehyde (1 mmol), 2-naphthol (2 mmol) and BSA (10 mol% or 25 mol%) was irradiated at different power level in a microwave reactor (Catalyst System) for the specified time as mentioned in the table 3.2A. After completion of the reaction, as indicated by TLC, the reaction mixture was cooled to room temperature and ethyl acetate was added in order to recover the insoluble catalyst by filtration. The filtrate was washed with dilute aqueous solution of sodium hydroxide to remove the unreacted 2-naphthol. The organic

extract was dried over anhydrous $Na_2SO_4$ and distilled under reduced pressure to furnish the crude product. The product was purified by preparative chromatography using ethyl acetate and hexane as solvent system to get analytically pure product.

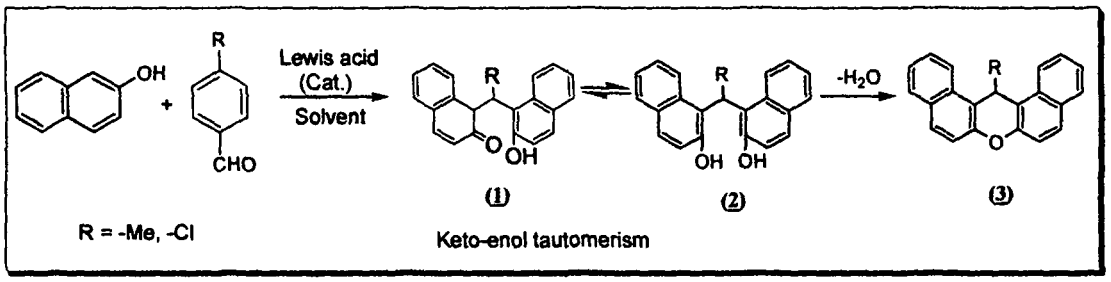
# Section 2B

## Investigation of Keto-enol Tautomers during the Synthesis of Aryl-bis(2-Hydroxy-1-Naphthyl) Methanes

## 2B.1. Introduction

The acid catalyzed mechanism of dibenzoxanthene (3) synthesis from 2-naphthol and aldehydes proposes the existence of tautomeric mixture of intermediates, aryl-bis(2-hydroxy-1-naphthyl) methane (2) and its keto isomer (1) (**Scheme-1.2A and Scheme-3.2A**) in first section (part-A) of this chapter. Only few reports described the synthesis of aryl-bis(2-hydroxy-1-naphthyl) methane (2) according to **Scheme-1.2A** with concentrated hydrochloric acid, $H_3[P(Mo_3O_{10})_4].nH_2O$ (HPA) and TfOH as homogeneous and heterogeneous catalysts [9-11]. All these methods have their own limitations, such as use of high pressure, longer reaction time, low yield and less product selectivity. The literature survey didn't find any method for the isolation of keto isomer (1) which indirectly supported the less stability of keto (1) tautomer as compared to enol form (2) under the reaction conditions during the synthesis of dibenzoxanthene derivatives (3). Thus, these aspects have led us to search new methodologies in mild condition with cheap and easily available heterogeneous or homogeneous acid catalysts for the synthesis of aryl-bis(2-hydroxy-1-naphthyl) methane (2) and its keto isomer (1). In this section, we examined the existence of keto-enol tautomerism by isolation of aryl-bis(2-hydroxy-1-naphthyl) methane (2) and its keto-isomer (1) from the reaction of 2-naphthol and alkyl or aryl aldehydes with three different catalysts $CuSO_4\,5H_2O$, $FeSO_4\,7H_2O$ and $BF_3\,OEt_2$ at different temperature. The Lewis acid property of transition metal salt has made them to be rigorously explored in organic reactions as heterogeneous catalyst to a considerable extent. The acidity of the metal-aqua complexes is affected by the charge and size of the metal ions which together make the charge density. A small, higher charged ion has a greater polarizing power to make an aqueous solution more acidic through hydrolysis of hydrated metal salt which releases more $H^+$ to the solution. Ferrous sulfate heptahydrate ($FeSO_4 \cdot 7H_2O$) [18] and copper sulphate pentahydrate ($CuSO_4 \cdot 5H_2O$) [19-27] have been used as reusable solid catalysts by many research

groups for organic transformations mainly due to their inexpensive, available and eco-friendly nature. Tian *et al.* (2007) used $FeSO_4 \cdot 7H_2O$ as an efficient catalyst to produce protected homoallylic amines via a multi component reaction [18]. Khan *et al.* (2004) investigated the application of $CuSO_4 \cdot 5H_2O$ in tetrahydropyranylation/depyranylation of alcohols and phenols [20]. Another interesting homogeneous Lewis acid is the boron trifluoride which is commercially available in convenient combination with diethyl ether as $BF_3 \cdot OEt_2$. Several organic syntheses have already been documented in literatures which are catalyzed by it providing a homogeneous catalytic system [28-29]. The inconvenience related to reusability arising from this catalytic system was overcome by many groups wherein they explored the ability of $BF_3 \cdot OEt_2$ supported on organic and inorganic supports [30-33]. During our observation, we identified the keto-enol tautomers for the first time from the reactions of 2-naphthol with *p*-tolualdehyde and 4-chlorobenzaldehyde in methanol using $CuSO_4.5H_2O$ as heterogeneous Lewis acid catalyst under reflux condition (**Scheme-1.2B**). The exclusive formation of aryl-bis(2-hydroxy-1-naphthyl) methanes were observed in dichloromethane at room temperature in presence of $BF_3.OEt_2$ /AcOH as homogeneous catalyst.




**Scheme-1.2B**

## 2B.2. Results and Discussion

Initially, we screened the catalytic activity of three Lewis acids $FeSO_4.7H_2O$, $CuSO_4.5H_2O$ and $BF_3.OEt_2$ (Table 1.2B) in solution (or solvent-free) at different temperature with the model reaction of benzaldehyde (1 mmol) and 2-naphthol (2 mmol) for the synthesis of aryl-bis(2-hydroxy-1-naphthyl) methane (**2a**).

**Table 1.2B**: Optimization of the reaction condition using homogeneous and heterogeneous acid catalysts

| Entry | Catalyst (Promoter) | Catalyst (mol%)[b] | Solvent | Temp (°C) | Time (h) | (%) Yield (2a) |
|---|---|---|---|---|---|---|
| 1 | $FeSO_4.7H_2O/CuSO_4.5H_2O$ | 10 | - | 120 | 4 | 40/50 |
| 2 | $FeSO_4.7H_2O$ /$CuSO_4.5H_2O$ | 10 | MeOH | 65 | 7 | 38/95 |
| 3 | $CuSO_4.5H_2O$ | 5/10/25 | EtOH | 78 | 7 | 50/70/72 |
| 4 | $CuSO_4.5H_2O$ | 10 | THF/ MeCN/ Acetone | 66/82/57 | 4 | NR/20/NR |
| 5 | $CuSO_4.5H_2O$ | 10 | $H_2O$/ EtOH : $H_2O$ (1:1) / $C(Me)_3OH$ | 100/100/83 | 7 | 45/18/NR |
| 6 | $BF_3.OEt_2$ | 28 | $CH_2Cl_2$ | r.t.[c] | 4 | 50 |
| 7 | $BF_3.OEt_2$ (AcOH)[a] | 28 | $CH_2Cl_2$ | r.t. / 65 | 1/2.2 | 85/60 |
| 8 | $BF_3.OEt_2$ (AcOH) | 10 | $CH_2Cl_2$ | r.t. | 1 | 40 |
| 9 | $BF_3.OEt_2$ (AcOH) | 28 | EtOH/MeOH/ $H_2O$/THF/ $CH_3CN$ | r.t. | 2 | 10/15/NR/NR/NR |
| 10 | $BF_3.OEt_2$ | 28 | AcOH | r.t. | 2 | 80 |
| 11 | AcOH (2 drops) | --- | $CH_2Cl_2$ | '' | 12 | NR |
| 12 | $BF_3$-$SiO_2$ | 28 | $CH_2Cl_2$ | '' | 12 h | NR |
| 13 | $BF_3$-$SiO_2$ (2 drops) | 28 | $CH_2Cl_2$ | '' | 12 h | 20 |

[a] *Using 2-drops of AcOH as promoter,* [b] *Reactions were carried out with 2 mmol of 2-naphthol and 1 mmol of aldehydes,* [c] *Room temperature*

We observed better result with 10 mol% of $CuSO_4.5H_2O$ in methanol under reflux condition (table 1.2B, entry 2). The weak acid-base interaction of smaller size methanol and $CuSO_4.5H_2O$ may activate some solvent molecules to form H-bonds with the carbonyl group of aldehyde molecule for nucleophilic attack of 2-naphthol. Such types of activation will be less effective using bulkier size alcohol as reaction medium like ter-butanol (table 1.2B, entry 5). The use of $BF_3.OEt_2$ catalyst alone gave poor result (table 1.2B, entry 6) as compared to its combination with AcOH as promoter (table 1.2B, entry 7). The optimized condition utilized 0.28 mmol of $BF_3.OEt_2$ and 2 drops of AcOH in dichloromethane at room temperature for 1 h time (table 1.2B, entry 7). Use of acetic acid as reaction medium completed the reaction within 2 h with good yield of product using 0.28 mmol of $BF_3.OEt_2$ (table 1.2B, entry 10). No reaction occurred up to 12 h reaction time with 2 drops of AcOH in dichloromethane at room temperature stirring (table 1.2B, entry 11). This observation indirectly supported the role of AcOH as promoter for the synthesis of bisnaphthol

derivatives. In 1931 Bowlus and his co-worker [34] also prepared a strong fuming liquid acid $(CH_3OOH)_2BF_3$ by passing one mole of $BF_3$ gas into two moles of acetic acid. The high electron deficient nature of boron in $BF_3$ makes easy complexation with protic oxygenated compounds such as alcohols, acetic acid, and ether to generate strong Brønsted acid systems [35-37]. We also tried to synthesize bisnaphthol (**2a**) in solution with $BF_3.SiO_2$ as heterogeneous catalyst (table 1.2B, entry 12) [38]. The combination of acetic acid and $BF_3$-silica produced only 20% of (**2a**) under optimized condition during 12 h (table 1.2B, entry 13).

The efficiency and applicability of the present methods for the synthesis of (**2a**) and (**3a**) have been compared with some of the previously known methods in table 2.2B.

**Table 2.2B**: Comparison of the results obtained for the preparation of (**2a**) and (**3a**) using other catalysts

| Entry | Catalyst | Conditions | Time (h) | Yields (%) | | References |
|---|---|---|---|---|---|---|
| | | | | (**2a**) | (**3a**) | |
| 1 | $BF_3.SiO_2$ | Solvent-free/ 60 °C | 0.25 | - | 96 | Ref.[38] |
| 2 | $BF_3.SiO_2$ | Chloroform/ r.t. | 24 | - | - | Ref.[38] |
| 3 | $BF_3.SiO_2$ | Sonication/ reflux in $CHCl_3$ | 6 min | - | 95 | Ref.[38] |
| 4 | $BF_3.SiO_2$ /AcOH | $CH_2Cl_2$ / r.t. | 12 | 20 | - | Present method |
| 5 | $BF_3.OEt_2$ /AcOH | $CH_2Cl_2$ / r.t. | 1 | 85 | - | " |
| 6 | $H_3[P(Mo_3O_{10})_4].nH_2O$ | $CH_2Cl_2$/ 40 °C | 1 | 51 | - | Ref.[10] |
| 7 | Conc. HCl in AcOH | 0 °C | 50 | 64 | - | Ref.[9] |
| 8 | TfOH | EtOH/ 3kbar, 60 °C | 24 | 89 | - | Ref.[11] |

After standardizing the reaction conditions, we extended these studies with different aromatic and aliphatic aldehydes to synthesize aryl-bis(2-hydroxy-1-naphthyl) methanes (**2**) and its keto isomers (**1**). All these results are tabulated in table 3.2B.

**Table 3.2B**: Reactions of various aldehydes with 2-naphthol using $CuSO_4.5H_2O$ and $BF_3.OEt_2$ /AcOH as acid catalysts

| Entry | Aldehyde | Time (h) [Method][a] | Found m.p. °C (Reported) | | | (%) Yield [b,c] products | | |
|---|---|---|---|---|---|---|---|---|
| | | | (1) | (2) | (3) | (1) | (2) | (3) |
| 1 | Benzaldehyde | 6[A]/1[B] | - | 203-205 (200)[11] | - | - | 95/85 (**2a**) | - |
| 2 | 2-nitrobenzaldehyde | 7[A]/2.5[B] | - | 206.7-209 (206-208)[10] | - | - | 10/82 (**2j**) | - |
| 3 | 3-nitrobenzaldehyde | 7[A]/2.3[B] | - | 192.8-194.2 (189-190)[10] | - | - | 12/83 (**2k**) | - |
| 4 | 4-nitrobenzaldehyde | 7[A]/2[B] | - | 303-305 ( >300)[39] | 310.5 (308-309)[15] | - | 50/85 (**2b**) | 20/-(**3b**) |
| 5 | 4-chlorobenzaldehyde | 7[A]/2[B] | 243-245 | 184.9-187.1 (187.5-188)[11] | 291 (289-290)[38] | 20/-(**1d**) | 20/81 (**2d**) | 10/-(**3d**) |
| 6 | 4-tolualdehyde | 8[A]/4[B] | 204-208 | 164.5 (165)[10] | 229.1 (228-230)[15] | 15/20 (**1e**) | 20/40 (**2e**) | 15/-(**3e**) |
| 7 | 4- methoxybenzaldehyde | 7[A]/3.5[B] | - | 201-202.5 (202)[11] | - | - | NR/86 (**2c**) | - |
| 8 | 2-naphthaldehyde | 7[A]/3[B] | - | 153.8 (152.5-154)[11] | - | - | NR/70 (**2h**) | - |
| 9 | 2-furaldehyde | 4[A]/0.5[B] | - | - | - | - | NR/polymer | - |
| 10 | n-pentanal | 7[A]/3[B] | - | - | - | - | NR | - |
| 11 | Cinnamaldehyde | 8[A]/1[B] | - | - | - | - | NR/more product | - |

[a]Method A: $CuSO_4.5H_2O$ in refluxing methanol; Method B: $BF_3.OEt_2$-AcOH in $CH_2Cl_2$ at room temperature, [b]Isolated products; [c]All the isolated compounds are characterized by FT-IR, $^1H$ NMR, $^{13}C$ NMR and elemental analysis.

The observations in table 3.2B clearly expressed the non-selective behavior of $CuSO_4.5H_2O$ catalyst with aromatic aldehydes under reflux condition in methanol except benzaldehyde molecule (table 3.2B, entry 1) which gave bisnaphthol (**2a**) as single product. With *p*-nitrobenzaldehyde we got diol (**2b**) as major and dibenzoxanthene (**3b**) as minor products (table 3.2B, entry 4) while *o*- and *m*-nitrobenzaldehydes selectively yielded diols (**2j**, **2k**) as minor products (table 3.2B, entries 2-3). For the first time, it was possible to isolate the keto intermediates (**1d**, **1e**) from the reaction mixtures of 4-chlorobenzaldehyde and *p*-tolualdehyde along with diol (**2**) and dibenzoxanthene derivatives (**3**) using $CuSO_4.5H_2O$ as catalyst (table 3.2B, entries 5-6). The $BF_3.OEt_2$-AcOH catalyst produced diol (**2**) selectively from aromatic aldehydes in dichloromethane at ambient temperature with excellent yields in short time (table 3.2B, entries 1-5, 7) except *p*-tolualdehyde (table 3.2B, entry 6). The reaction of *p*-tolualdehyde showed the equilibrium mixture of keto and enol forms in solution (table 3.2B, entry 6). 2-Naphthaldehyde yielded only 70% of diol in 3 h with $BF_3.OEt_2$-AcOH catalyst (table 3.2B, entry 8). Pentanal was inactive in both cases during 3-7 h reaction times (table 3.2B, entry 10). Under the reaction conditions of $BF_3.OEt_2$-AcOH, 2-Furaldehyde polymerized and cinamaldehyde produced more side products (table 3.2B, entries 9, 11). The reaction of 1-naphthol and benzaldehyde also generated many products with $BF_3.OEt_2$-AcOH catalyst.

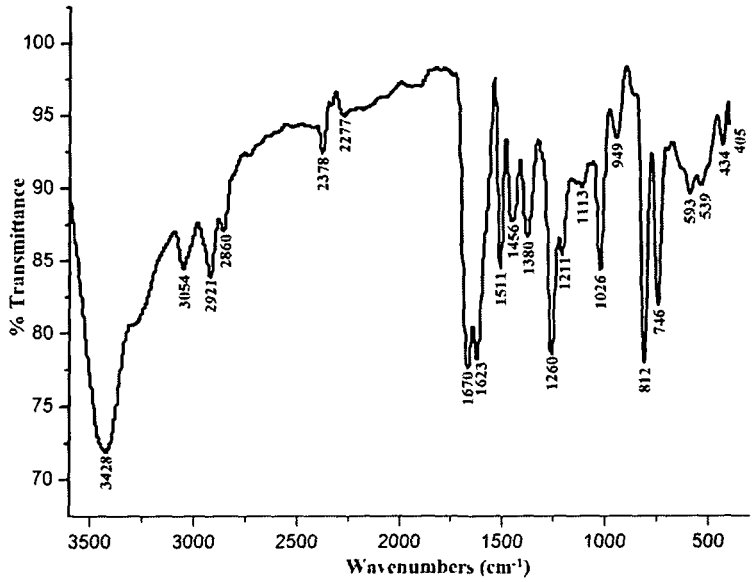



**Fig. 1.2B** FT-IR spectra of the product mixture of (**1d**-**2d**)

During isolation of the keto intermediate (**1d**, **1e**) by preparative TLC technique we obtained single product in dichloromethane at 25 °C. But after distillation at 50 °C in vacuum, it decomposed to diol (**2d**, **2e**) almost in equal proportion. The FT-IR spectra of the product mixture of (**1d**-**2d**) indicated characteristic -OH absorption in the range of 3400-3428 $cm^{-1}$, and strong carbonyl absorption at 1657-1670 $cm^{-1}$ which clearly expressed the existence of keto-enol tautomers at high temperature (**Fig. 1.2B**). We isolated the keto product in pure form after removal of the organic solvent under reduced pressure at room temperature. With increasing temperature, the keto intermediate slowly converted to the diol through keto-enol equilibrium (**Scheme-1.2B**) for the reaction of 4-chlorobenzaldehyde and *p*-toluadehyde. The simultaneous acid-base complexation of $CuSO_4.5H_2O$ catalyst (**Fig. 2.2B**) with the carbonyl and –OH groups of the keto-isomer (**1**) may stabilize this intermediate as compared to $BF_3.OEt_2$/acetic acid according to the plausible mechanism of $BF_3.OEt_2$/acetic acid (**Scheme-2.2B**).

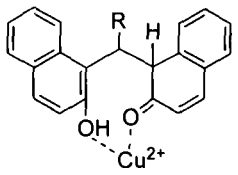
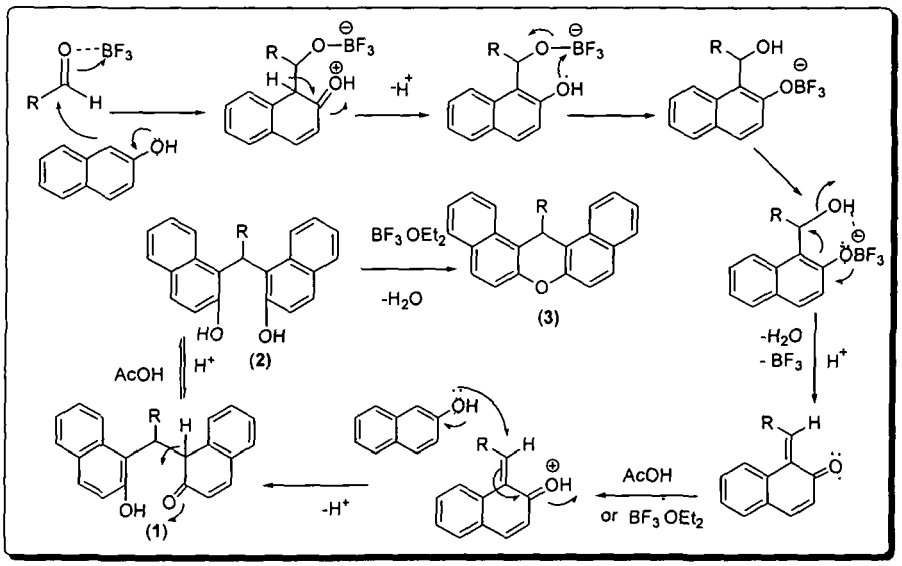



**Figure 2.2B**: Plausible complexation of $Cu^{2+}$ with the keto-isomer (**1**)




**Scheme-2.2B.** Plausible mechanism of $BF_3.OEt_2$ /AcOH catalyzed synthesis of (**2**) and (**3**)

The COSY spectra of keto compounds (**1d**, **1e**) have no cross-peak for the two tertiary 1,2-protons in the chemical shift range of δ 5.12-5.16 (s) and 5.55 (d) ppm which confirm the *anti*-orientation of these protons in (**1**) (**Fig. 3.2B**). But the proton with doublet at 5.55 ppm for the tertiary carbon has one cross peak with the aromatic region by long range coupling with coupling constant $J$ = 10.1 Hz of the *o*-proton of 4-chloro phenyl ring.

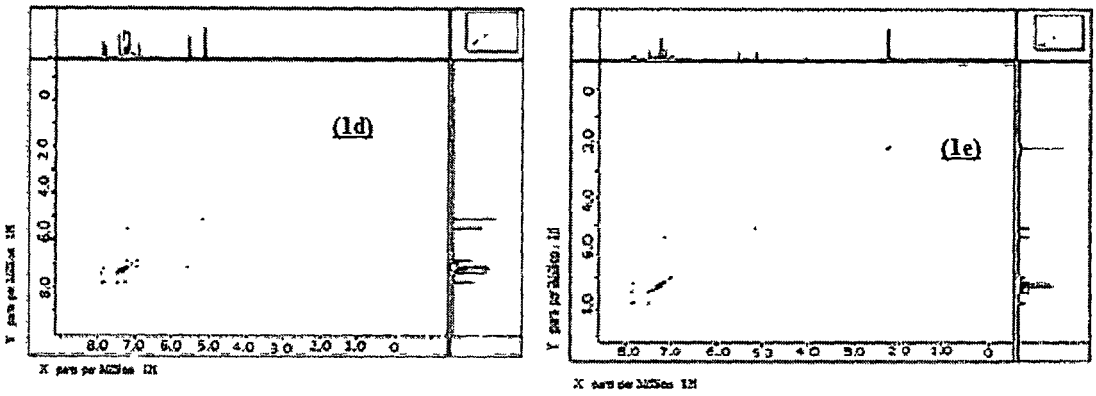



**Figure 3.2B**: COSY spectra of (**1d**) and (**1e**)

The DEPT-45 spectra (**Fig. 4.2B**) have all the methine (-CH-) and methyl carbons except the quaternary carbons. In DEPT-90 spectra, all –CH- signals are present in normal positions. The DEPT-135 spectra of the keto isomers are identical with the DEPT-45 spectra which confirm the exact structure of the keto intermediate.

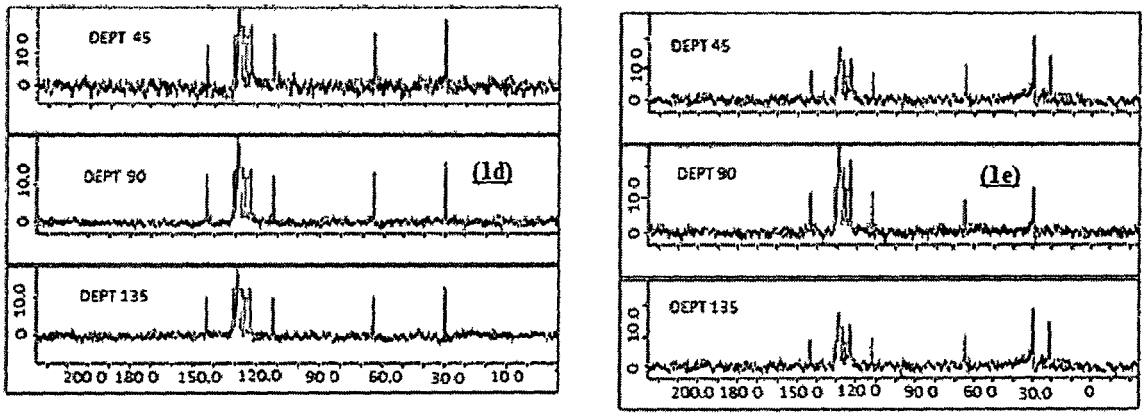



**Figure 4.2B**: DEPT spectra of (**1d**) and (**1e**)

## 2B.3. Conclusion

In summary, the existence of keto-enol mechanism was fully supported by the isolation of two reactive keto intermediates towards the synthesis of aryl-bis(2-hydroxy-1-naphthyl) methane (2) and its cyclization product dibenzoxanthenes (3) for the first time. Furthermore, this study developed a new catalytic system for the selective synthesis of bisnaphthol derivatives under mild condition using $BF_3.OEt_2$-AcOH as homogeneous catalyst. The silica supported $BF_3$ was almost inactive under the reaction condition using AcOH as promoter.

## 2B.4. Experimental Section

### 2B.4.1. General Information

The products were identified by comparison of their FT-IR, $^1H$ NMR and $^{13}C$ NMR spectroscopic data with those of authentic compounds and literature reported data [10-11, 15, 38-39].

### 2B.4.2. Typical procedure for the preparation of aryl-bis(2-hydroxy-1-naphthyl) methanes (2) and its keto isomers (1)

In a 50 mL round bottomed flask, 2-naphthol (2 mmol) and aldehydes (1 mmol) were added in presence of catalysts $CuSO_4.5H_2O$ (10 mol%) or $BF_3.OEt_2$ (28 mol%) and acetic acid (2 drops). The entire mixture was then treated thermally at different temperature in organic solvent (3mL) for the specified reaction period. The progress of the reactions was monitored by observing TLC at certain intervals of time. After completion of the reaction, the mixture was diluted with ethyl acetate (5 mL) and filtered to remove the solid catalyst ($CuSO_4.5H_2O$) which was not applicable for the $BF_3.OEt_2$ catalyzed reaction. The organic extract was dried over anhydrous $Na_2SO_4$ and distilled under reduced pressure to furnish the crude product. Further purification by preparative TLC yielded the pure product, which was analyzed by different spectroscopic techniques.

# References


[1] Olyaei, A., et al. *Open J. Org. Chem.* **1** (2), 22--26, 2013.

[2] Ko, S. & Yao, C-F. *Tetrahedron Lett.* **47** (50), 8827--8829, 2006.

[3] Hunnur, R. K., et al. *Chem. Heterocycl. Compd.* **44** (2), 143--147, 2008.

[4] Bigdeli, M. A., et al. *J. Mol. Catal. A: Chem.* **275** (1-2), 25--29, 2007.

[5] Heravi, M. M., et al. *J. Mol. Catal. A: Chem.* **273** (1-2), 99--101, 2007.

[6] Wang, L-M., et al. *Chin. J. Chem.* **26** (6), 1105--1108, 2008.

[7] Sharifi, A., et al. *Synth. Commun.* **38** (17), 2958--2966, 2008.

[8] Madhav, J. V., et al. *J. Mol. Catal. A: Chem.* **304** (1-2), 85--87, 2009.

[9] Ranjbar, P. R., et al. *Acta Cryst. E* **63** (5), o2093--o2094, 2007.

[10] Alizadeh, A., et al. *J. Iran. Chem. Soc.* 7 (2), 351--358, 2010.

[11] Ohishi, T., et al. *Tetrahedron Lett.* **42** (13), 2493--2496, 2001.

[12] Kiasat, A. R. & Fallah-Mehrjardi, M. *J. Braz. Chem. Soc.* **19** (8), 1595--1599, 2008.

[13] Sajjadifar, S., et al. *Am. J. Org. Chem.* **2** (2), 1--6, 2012.

[14] Bamoniri, A., et al. *Curr. Chem. Lett.* **2** (1), 27--34, 2013.

[15] Naeimi, H. & Nazifi, Z. S. *C. R. Chimie* **17** (1), 41--48, 2014 and references cited therein.

[16] Soleimani, E., et al. *Chin. Chem. Lett.* **22** (8), 927--930, 2011.

[17] Kumar, R., et al. *Tetrahedron Lett.* **51** (2), 442--445, 2010.

[18] Tian, S-K., et al. *J. Org. Chem.* **72** (14), 5407--5410, 2007.

[19] Ferrett, R. R., et al. *Tetrahedron Lett.* **44** (12), 2573--2576, 2003.

[20] Khan, A. T., et al. *Tetrahedron Lett.* **45** (42), 7891--7894, 2004.

[21] Sandhu, J. S., et al. *Synlett* (2), 235--238, 2004.

[22] Akhlaghinia, B. & Tavakoli, S. *Synthesis* (11), 1775--1778, 2005.

[23] Heravi, M. M., et al. *Monatsh. Chem.* **137** (8), 1075--1078, 2006.

[24] Heravi, M. M., et al. *J. Braz. Chem. Soc.* **17** (5), 1045--1047, 2006.

[25] Liao, M. & Wang, J. *Tetrahedron Lett.* **47** (50), 8859--8861, 2006.

[26] Kidwai, M. & Priya. *Indian J. Chem.* **48B**, 1045--1048, 2009.

[27] Ganguly, N. C., et al. *Tetrahedron Lett.* **53** (11), 1413--1416, 2012.

[28] Nair, V., et al. *Tetrahedron Lett.* **37** (46), 8271--8272, 1996.

[29] Chang, M-Y., et al. *Org. Lett.* **12** (6), 1176--1179, 2010.

[30] Chung, T. C., et al. *Polym. Bull.* **30** (4), 385--391, 1993.

[31] Wilson, K. & Clark, J. H. *Chem. Commun.* (19), 2135--2136, 1998.

[32] Mirjalili, B. F., et al. *J. Iran. Chem. Soc.* **5** (4), 694--698, 2008.

[33] Mokhtary, M. & Refahati, S. *Dyes Pigm.* **99** (2), 378--381, 2013.

[34] Bowlus, H. & Nieuwland, *J. Am. Chem. Soc.* **53** (10), 3835--3840, 1931.

[35] Hennion, G. F., et al. *J. Am. Chem. Soc.* **55** (7), 2857--2860, 1933.

[36] Sowa, F. J. & Nieuwland, J.A. *J. Am. Chem. Soc.* **55** (12), 5052--5053, 1933.

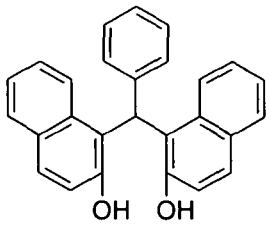
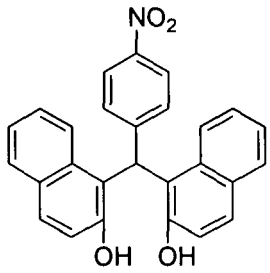
[37] Dorris, T. B., et al. *J. Am. Chem. Soc.* **56** (12), 2689--2690, 1934.

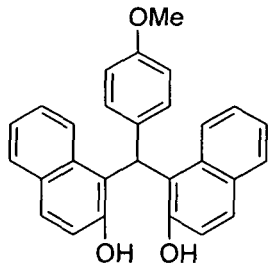
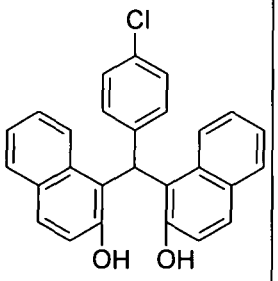
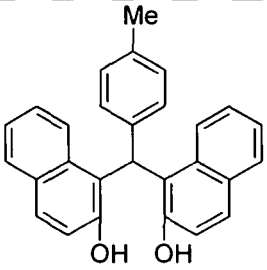
[38] Mirjalili, B. B. F., et al. *Tetrahedron. Lett.* **49** (45), 6454--6456, 2008.

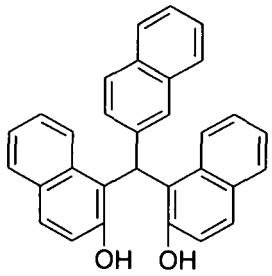
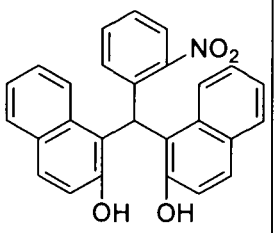
[39] Kasturi, T. R., et al. *Tetrahedron* **49** (1), 125--134, 1993 and references cited therein.

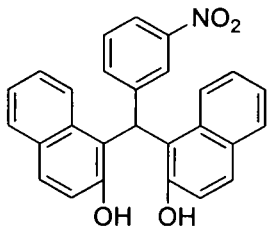
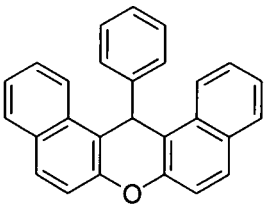
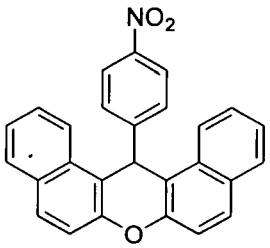
# Section 2C

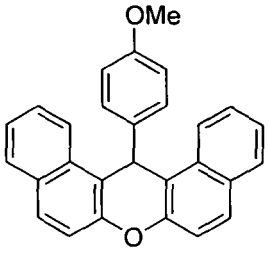
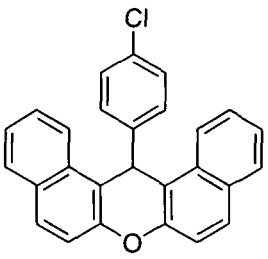
## Spectral Analysis of Section 2A and Section 2B Products

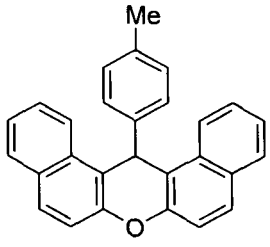
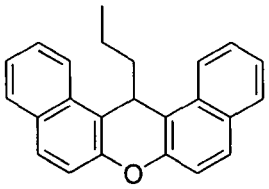
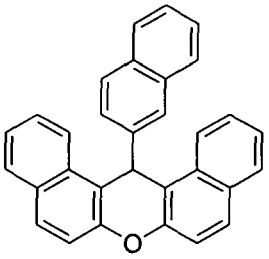
| | |
|---|---|
|  | **Phenyl-bis(2-hydroxy-1-naphthyl) methane (2a) (Table 3.2A, Entry 1) (Table 3.2B, Entry 1)**<br><br>White solid, m.p. 203-205 °C; $^1$H NMR (400 MHz, $CDCl_3$) δ ppm: 6.3 (s, 1H), 7.01 (d, $J$ = 8.7 Hz, 2H), 7.20-7.39 (m, 9H), 7.7 (d, $J$ = 9.1 Hz, 2H), 7.8 (d, $J$ = 8.2 Hz, 2H), 7.91 (d, $J$ = 8.2 Hz, 2H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ ppm: 42.7, 118.6, 119.9, 122.6, 123.6, 127.5, 128.4, 129, 129.7, 129.9, 130.1, 133.6, 140.6, 152.9; FT-IR (KBr): 3422, 2926, 2378, 1953, 1618, 1505, 1436, 1358, 1257, 1210, 1146, 1031, 957, 813, 749, 699 cm$^{-1}$; CHN analysis: Calculated for $C_{27}H_{20}O_2$ (%): C 86.17, H 5.31, Found: C 86.21, H 5.35. |
|  | **4-Nitrophenyl-bis(2-hydroxy-1-naphthyl) methane (2b) (Table 3.2A, Entry 2) (Table 3.2B, Entry 4)**<br><br>Yellow solid, m.p. 303-305 °C; $^1$H NMR (400 MHz, $CDCl_3$) δ ppm: 6.98 (m, 2H), 7.24-7.42 (m, 7H), 7.68 (d, $J$ = 8.2 Hz, 2H), 7.81 (d, $J$ = 7.3 Hz, 2H), 7.92 (d, $J$ = 8.2 Hz, 2H), 8.06 (d, $J$ = 6.9 Hz, 2H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ ppm: 42.2, 118.1, 119.3, 122.2, 123.7, 123.9, 127.7, 128.6, 129.3, 130.3, 135, 146.5, 150.4, 152.2; FT-IR (KBr): 3394, 2927, 2858, 2379, 2285, 1603, 1511, 1342, 1257, 1209, 1147, 954, 811, 743 cm$^{-1}$; CHN analysis: Calculated for $C_{27}H_{19}O_4N$ (%): C 76.95, H 4.51, N 3.32, Found: C 77.10, H 4.55, N 3.36. |

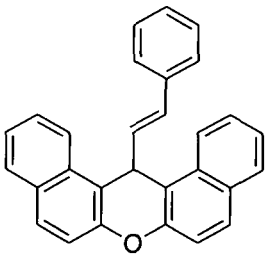
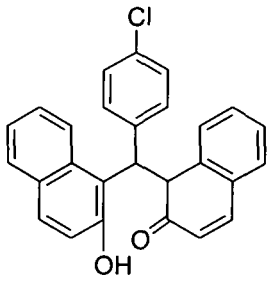
| | |
|---|---|
|  | **4-Methoxyphenyl-bis(2-hydroxy-1-naphthyl) methane (2c) (Table 3.2A, Entry 3) (Table 3.2B, Entry 7)**<br><br>White solid, m.p. 201-202.5 °C; $^1$H NMR (400 MHz, $CDCl_3$) δ ppm: 3.87 (s, 3H), 6.86 (d, $J$ = 8.7 Hz, 2H), 6.99-7.06 (m, 3H), 7.18 (d, $J$ = 8.7 Hz, 2H), 7.23-7.34 (m, 4H), 7.7 (d, $J$ = 8.7 Hz, 2H), 7.78 (d, $J$ = 7.8 Hz, 2H), 7.84 (d, $J$ = 7.4 Hz, 1H), 7.94 (d, $J$ = 8.2 Hz, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ ppm: 42.2, 55.3, 119.8, 120.1, 122.6, 123.5, 127.4, 128.9, 129, 129.1, 129.7, 129.9, 130.1, 131, 134.2, 153.2, 153.3, 159.2; FT-IR (KBr): 3278, 3052, 2929, 2832, 2379, 2284, 1611, 1508, 1451, 1398, 1357, 1255, 1207, 1030, 957, 811, 747 cm$^{-1}$; CHN analysis: Calculated for $C_{28}H_{22}O_3$ (%): C 82.75, H 5.42, Found: C 82.78, H 5.47. |
|  | **4-Chlorophenyl-bis(2-hydroxy-1-naphthyl) methane (2d) (Table 3.2A, Entry 4) (Table 3.2B, Entry 5)**<br><br>White solid, m.p. 184.9-187.1 °C; $^1$H NMR (400 MHz, $CDCl_3$) δ ppm: 6.45 (s, 1H), 6.95 (d, $J$ = 8.6 Hz, 2H), 7.11 (d, $J$ = 8.2 Hz, 2H), 7.21 (d, $J$ = 7.8 Hz, 2H), 7.30-7.45 (m, 4H), 7.65 (d, $J$ = 9.1 Hz, 2H), 7.77 (d, $J$ = 8.5 Hz, 2H), 7.92 (d, $J$ = 8.7 Hz, 2H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ ppm: 41.7, 118.2, 119.5, 122.3, 123.5, 127.4, 129, 129.1, 129.4, 129.7, 129.9, 134.1, 139.8, 143.4, 148.7, 152.4; FT-IR (KBr): 3385, 3054, 2970, 1895, 1802, 1618, 1486, 1442, 1395, 1249, 1086, 1042, 956, 878, 812, 743, 699 cm$^{-1}$; CHN analysis: Calculated for $C_{27}H_{19}ClO_2$ (%): C 78.92, H 4.62, Found: C 78.97, H 4.66. |
|  | **4-Methylphenyl-bis(2-hydroxy-1-naphthyl) methane (2e) (Table 3.2B, Entry 6)**<br><br>White solid, m.p. 164.5 °C; $^1$H NMR (400 MHz, $CDCl_3$) δ ppm: 2.4 (s, 3H), 6.30 (s, 1H), 6.82 (d, $J$ = 7.6 Hz, 2H), 7.16-7.22 (m, 6H), 7.20 (t, $J$ = 7.2 Hz, 1H), 7.29 (t, $J$ = 7.4 Hz, 1H), 7.38 (d, $J$ = 7.7 Hz, 3H), 7.70-7.73 (m, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$) |

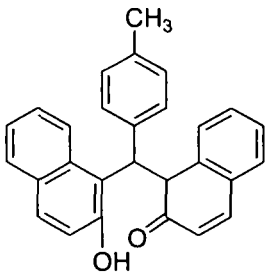
| | |
|---|---|
| | δ ppm: 28.8, 118.6, 120.2, 123.1, 125.7, 126.6, 127.1, 127.2, 127.7, 128.3, 129, 129.2, 135.3, 137.2, 152.7, 153; FT-IR (KBr): 3365, 3063, 2920, 1630, 1595, 1513, 1464, 1435, 1405, 1248, 1122, 1086, 968, 880 $cm^{-1}$; CHN analysis: Calculated for $C_{28}H_{22}O_2$ (%): C 86.15, H 5.64, Found: C 87.87, H 4.57. |
|  | **2-naphthyl-bis(2-hydroxy-1-naphthyl) methane (2h) (Table 3.2A, Entry 8) (Table 3.2B, Entry 8)**<br><br>Shiny white solid, m.p. 153.8 °C; $^1H$ NMR (400 MHz, $CDCl_3$) δ ppm: 6.65 (s, 1H), 7.28 (t, *J* = 8.2 Hz, 1H), 7.35-7.37 (m, 4H), 7.49-7.60 (m, 7H), 7.78-7.81 (m, 5H), 8.04 (s, 1H), 8.49 (d, *J* = 8.2 Hz, 2H); $^{13}C$ NMR (100 MHz, $CDCl_3$) δ ppm: 38.4, 117, 118.1, 122.7, 124.3, 125.6, 127.9, 128.9, 129.1, 131, 131.4, 132, 142.2, 148.7; FT-IR (KBr): 3510, 2369, 1593, 1512, 1402, 1248, 1153, 1074, 962, 811, 742 $cm^{-1}$; CHN analysis: Calculated for $C_{31}H_{22}O_2$ (%): C 87.32, H 5.16, Found: C 87.37, H 5.21. |
|  | **2-Nitrophenyl-bis(2-hydroxy-1-naphthyl) methane (2i) (Table 3.2B, Entry 2)**<br><br>Faint yellow solid, m.p. 206.7-209 °C; $^1H$ NMR (400 MHz, $CDCl_3$) δ ppm: 6.74 (d, *J* = 8.7 Hz, 1H), 7.03 (d, *J* = 8.7 Hz, 1H), 7.17 (d, *J* = 7.8 Hz, 1H), 7.22-7.25 (m, 2H), 7.31-7.35 (m, 2H), 7.43 (t, *J* = 8.7 Hz, 1H), 7.53 (d, *J* = 9.2 Hz, 1H), 7.62-7.66 (m, 2H), 7.72-7.76 (m, 3H), 7.88 (d, *J* = 8.2 Hz, 2H), 8.30 (d, *J* = 8.7 Hz, 1H); $^{13}C$ NMR (100 MHz, $CDCl_3$) δ ppm: 38.02, 116, 118.1, 119.9, 121.1, 122.5, 124.8, 127.4, 127.7, 127.9, 128.8, 129.4, 130.3, 130.4, 132.7, 134.1, 136, 149.8, 150.5, 153.9; FT-IR (KBr): 3440, 2380, 2282, 1619, 1517, 1436, 1356, 1251, 1210, 1151, 1034, 955, 856, 812, 742, 650 $cm^{-1}$; CHN analysis: Calculated for $C_{27}H_{19}NO_4$ (%): C 76.95, H 4.51, N 3.32, Found: C 76.97, H 4.57, N 3.36. |

| | |
|---|---|
|  | **3-Nitrophenyl-bis(2-hydroxy-1-naphthyl) methane (2k) (Table 3.2B, Entry 3)**<br><br>White solid, m.p. 192.8-194.2 °C; $^1$H NMR (400 MHz, $CDCl_3$) δ ppm: 6.6 (s, 1H), 7.25-7.30 (m, 1H), 7.44 (t, $J$ = 6.9 Hz, 2H), 7.52 (d, $J$ = 8 Hz, 2H), 7.61 (m, 2H), 7.82-7.86 (m, 6H), 8.31 (d, $J$ = 8.2 Hz, 2H), 8.42 (s, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ ppm: 37.8, 116, 118.2, 121.8, 122.1, 122.7, 124.6, 127.3, 129.1, 129.6, 131.0, 134.4, 146.9, 148.2, 148.8; FT-IR (KBr) 3283, 3071, 2927, 2861, 2379, 2284, 1902, 1803, 1706, 1617, 1524, 1469, 1399, 1347, 1254, 1210, 1150, 1088, 960, 811, 749 cm$^{-1}$; CHN analysis: Calculated for $C_{27}H_{19}NO_4$ (%): C 76.95, H 4.51, N 3.32, Found: C 76.98, H 4.57, N 3.26. |
|  | **14-(Phenyl)-14*H*-dibenzo[a.j]xanthene (3a) (Table 3.2A, Entry 1)**<br><br>Pale yellow solid, m.p. 182.9 °C; $^1$H NMR (400 MHz, $CDCl_3$) δ ppm: 6.46 (s, 1H), 6.94-6.98 (t, $J$ = 7.7 Hz, 1H), 7.10-7.14 (t, $J$ = 7.7 Hz, 2H), 7.38-7.40 (t, $J$ = 7.4 Hz, 2H), 7.45-7.47 (m, 4H), 7.49-7.55 (t, $J$ = 7.3 Hz, 2H), 7.75-7.77 (d, $J$ = 8.7 Hz, 2H), 7.79-7.80 (d, $J$ = 8.0 Hz, 2H), 8.36-8.38 (d, $J$ = 8.8 Hz, 2H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ ppm: 38.1, 118.0, 118.5, 122.7, 124.3, 126.8, 128.3, 128.6, 128.8, 128.9, 131.1, 131.5, 145.0, 148.7; FT-IR (KBr): 3061, 3020, 1624, 1592, 1513, 1458, 1409, 1249, 1078, 962, 805, 743 cm$^{-1}$; CHN analysis: Calculated for $C_{27}H_{18}O$ (%): C 90.50, H 5.02, Found: C 88.90, H 6.81. |
|  | **14-(4-Nitrophenyl)-14*H*-dibenzo[a.j]xanthene (3b) (Table 3.2A, Entry 2) (Table 3.2B, Entry 4)**<br><br>Light yellow solid, m.p. 310.5 °C; $^1$H NMR (400 MHz, $CDCl_3$) δ ppm: 6.95 (s, 1H), 7.40-7.44 (m, 2H), 7.50 (d, $J$ = 9.2 Hz, 2H), 7.58 (t, $J$ = 7.8 Hz, 2H), 7.65 (d, $J$ = 8.3 Hz, 2H), 7.81-7.85 (m, 4H), 7.99 (d, $J$ = 8.2 Hz, 2H), 8.28 (d, $J$ = 8.2 Hz, 2H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ ppm: 37.9, 116, 118.1, 122.1, 123.9, |

| | |
|---|---|
| | 124.7, 127.3, 129, 129.1, 129.7, 131.1, 146.4, 148.9, 152; FT-IR (KBr): 3418, 2924, 2853, 2372, 2188, 1719, 1591, 1509, 1397, 1335, 1240, 1099, 952, 810, 741 $cm^{-1}$; CHN analysis: Calculated for $C_{27}H_{17}O_3N$ (%): C 80.39, H 4.21, N 3.47, Found C 80.43, H 4.24, N 3.51. |
|  | **14-(4-Methoxyphenyl)-14*H*-dibenzo[a.j]xanthene (3c) (Table 3.2A, Entry 3)**<br><br>White solid, m.p. 203.8 °C; $^1H$ NMR (400 MHz, $CDCl_3$) δ ppm: 3.57 (s, 3H), 6.46 (s, 1H), 6.63-6.68 (d, *J* = 8.2 Hz, 2H), 7.36-7.40 (m, 4H), 7.44-7.46 (d, *J* = 8.6 Hz, 2H), 7.52-7.57 (t, *J* = 7.6 Hz, 2H), 7.75-7.78 (d, *J* = 8.7 Hz, 2H), 7.82-7.84 (d, *J* = 8.3 Hz, 2H), 8.34-8.36 (d, *J* = 8.2 Hz, 2H); $^{13}C$ NMR (100 MHz, $CDCl_3$) δ ppm: 37.4, 55.6, 113.9, 117.6, 118.2, 122.8, 123.6, 124.3, 126.4, 126.8, 128.8, 129.0, 129.2, 131.1, 131.5, 137.4, 148.7, 157.9; FT-IR (KBr): 3058, 1592, 1511, 1460, 1397, 1250, 963, 817, 746 $cm^{-1}$; CHN analysis: Calculated for $C_{28}H_{20}O_2$ (%): C 86.59, H 5.15, Found: C 86.65, H 5.17. |
|  | **14-(4-Chlorophenyl)-14*H*-dibenzo[a.j]xanthene (3d) (Table 3.2A, Entry 4) (Table 3.2B, Entry 5)**<br><br>White solid, m.p. 291 °C; $^1H$ NMR (400 MHz, $CDCl_3$) δ ppm: 6.44 (s, 1H), 7.09 (d, *J* = 8.7 Hz, 2H), 7.37-7.43 (m, 5H), 7.47 (d, *J* = 8.7 Hz, 1H), 7.56 (t, *J* = 6.9 Hz, 2H), 7.78 (d, *J* = 8.7 Hz, 2H), 7.82 (d, *J* = 7.8 Hz, 2H), 8.3 (d, *J* = 8.2 Hz, 2H); $^{13}C$ NMR (100 MHz, $CDCl_3$) δ ppm: 37.4, 116.8, 117.9, 122.4, 124.4, 126.9, 128.6, 128.8, 129, 129.5, 131, 131.3, 143.4, 148.7; FT-IR (KBr): 2925, 1590, 1484, 1242, 1083, 807 $cm^{-1}$; CHN analysis: Calculated for $C_{27}H_{17}OCl$ (%): C 82.54, H 4.33, Found C 82.58, H 4.37. |

| | |
|---|---|
|   | **14-(4-Methylphenyl)-14*H*-dibenzo[a.j]xanthene (3e) (Table 3.2A, Entry 5) (Table 3.2B, Entry 6)**<br><br>Yellow solid, m.p. 229.1 °C; $^{1}$H NMR (400 MHz, $CDCl_3$) δ ppm: 2.3 (s, 3H), 6.14 (s, 1H), 6.77 (d, *J* = 7.8 Hz, 2H), 6.91 (t, *J* = 7.3 Hz, 1H), 7.13-7.16 (m, 6H), 7.27 (t, *J* = 6.9 Hz, 1H), 7.36 (d, *J* = 7.8 Hz, 3H), 7.69-7.78 (m, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ ppm: 21.1, 62.7, 111.8, 116.5, 121.4, 122.8, 126.8, 127.9, 128.9, 129.1, 129.4, 129.9, 130, 138.4, 146.5, 156, 199.9; FT-IR (KBr): 3068, 2917, 1626, 1597, 1515, 1466, 1437, 1404, 1258, 1125, 1087, 967, 840, 815, 785, 745 $cm^{-1}$; CHN analysis: Calculated for $C_{28}H_{20}O$ (%): C 90.32, H 5.37, Found C 90.37, H 5.40. |
|   | **14-Propyl-14*H*-dibenzo[a.j]xanthene (3f) (Table 3.2A, Entry 6)**<br><br>White solid, m.p. 155.2 °C; $^{1}$H NMR (400 MHz, $CDCl_3$) δ ppm: 0.55 (t, *J* = 7.3 Hz, 3H), 0.88 (m, 2H), 2.03 (m, 2H), 5.55 (t, *J* = 4.2 Hz, 1H), 7.34 (d, *J* = 9.1 Hz, 2H), 7.45 (t, *J* = 7.3 Hz, 2H), 7.62 (m, 2H), 7.75 (d, *J* = 8.7 Hz, 2H), 7.85 (d, *J* = 8.2 Hz, 2H), 8.22 (d, *J* = 8.6 Hz, 2H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ ppm: 14.7, 20.1, 42.0, 43.2, 115.3, 118.7, 122.5, 123.5, 126.3, 128.2, 128.5, 128.9, 133.7, 150.2; FT-IR (KBr): 3062, 2952, 2866, 1622, 1591, 1516, 1468, 1397, 1242, 1140, 1075, 1048, 959, 813 $cm^{-1}$; CHN analysis: Calculated for $C_{24}H_{20}O$ (%): C 88.88, H 6.17, Found: C 86.98, H 7.67. |
|   | **14-(2-naphthyl)-14*H*-dibenzo[a.j]xanthene (3h) (Table 3.2A, Entry 8)**<br><br>White solid, m.p. 216.5 °C; $^{1}$H NMR (400 MHz, $CDCl_3$) δ ppm: 6.67 (s, 1H), 7.26 (t, *J* = 8.2 Hz, 1H), 7.33-7.36 (m, 3H), 7.45-7.57 (m, 7H), 7.75-7.80 (m, 5H), 7.98 (s, 1H), 8.43 (d, *J* = 8.5 Hz, 2H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ ppm: 47.6, 117.5, 118.3, 123.7, 124.5, 126.3, 126.6, 128.5, 129.0, 130.2, 131.3, |

| | |
|---|---|
| | 132.4, 133.2, 136.5, 156.8; FT-IR (KBr): 3056, 1666, 1597, 1514, 1405, 1255, 1138, 1083, 968, 817 $cm^{-1}$; CHN analysis: Calculated for $C_{31}H_{20}O$ (%): C 91.17, H 4.90, Found: C 90.01, H 5.84. |
|  | **14-(cinnamyl)-14*H*-dibenzo[a.j]xanthene (3i) (Table 3.2A, Entry 9)**<br><br>White solid, m.p. 176.9 °C; $^1H$ NMR (400 MHz, $CDCl_3$) δ ppm: 5.32 (d, $J$ = 5.1 Hz, 1H), 6.43-6.55 (m, 2H), 6.87 (d, $J$ = 8.2 Hz, 2H), 7.24-7.27 (m, 5H), 7.33-7.40 (m, 4H), 7.45-7.47 (d, $J$ = 8.7 Hz, 2H), 7.76-7.80 (d, $J$ = 8.8 Hz, 2H), 8.32-8.35 (d, $J$ = 8.3 Hz, 2H); $^{13}C$ NMR (100 MHz, $CDCl_3$) δ ppm: 40.1, 119.8, 122.8, 123.7, 123.9, 126.3, 127.1, 127.7, 128.0, 128.4, 129.9, 131.7, 134.2, 148.3, 155.7; FT-IR (KBr): 2930, 1639, 1582, 1516, 1500, 1420, 1203, 1107, 956 $cm^{-1}$; CHN analysis: Calculated for $C_{29}H_{20}O$ (%): C 90.62, H 5.20, Found: C 89.68, H 5.27. |
|  | **4-chlorophenyl-(2-hydroxy-1-naphthyl)(Benzocyclohex-3-en-2-one)methane (New) (1d) (Table 3.2B, Entry 5)**<br><br>Red solid, m.p. 243-245 °C; $^1H$ NMR (400 MHz, $CDCl_3$) δ ppm: 5.12 (s, 1H), 5.55 (d, $J$ = 10.1 Hz, 1H), 6.91 (d, $J$ = 7.8 Hz, 1H), 7.15-7.44 (m, 13H), 7.82 (d, $J$ = 8.3 Hz, 1H), 7.87 (d, $J$ = 8.7 Hz, 1H); $^{13}C$ NMR (100 MHz, $CDCl_3$) δ ppm: 29.8, 64.0, 112.0, 117.2, 122.7, 123.4, 125.1, 125.5, 127.0, 128.9, 129.1, 129.6, 130.4, 130.5, 130.9, 131.3, 133.9, 136.7, 143.7, 143.8, 158.7, 198.7; FT- IR (KBr): 3425, 2917, 3050, 2851, 1677, 1624, 1465, 1383, 1256, 1205, 1089, 1024, 939, 813, 747 $cm^{-1}$; CHN analysis: Calculated for $C_{27}H_{19}O_2Cl$ (%): C 78.92, H 4.62, Found: C 79.10, H 4.68.<br><br>The COSY and DEPT spectra are included in Fig. 3.2B and Fig. 4.2B. |




**4-methylphenyl-(2-hydroxy-1-naphthyl)(Benzocyclohex-3-en-2-one)methane (New) (1e) (Table 3.2B, Entry 6)**

Red solid, m.p. 204-208 °C; $^{1}$H NMR (400 MHz, $CDCl_3$) δ ppm: 2.25 (s, 3H), 5.16 (s, 1H), 5.55 (d, $J$ = 10.1 Hz, 1H), 6.92 (d, $J$ = 7.7 Hz, 1H), 7.14-7.47 (m, 13H), 7.83 (d, $J$ = 7.8 Hz, 1H), 7.88 (d, $J$ = 8.7 Hz, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ ppm: 21.2, 29.7, 64.5, 112.0, 117.9, 122.9, 123.2, 124.9, 125.6, 126.7, 128.6, 129.0, 129.4, 130.3, 130.9, 135.1, 137.6, 143.3, 144.0, 158.6, 198.6; FT IR (KBr): 3408, 3049, 2919, 2853, 1683, 1623, 1511, 1457, 1380, 1256, 1112, 1024, 946, 810, 746 $cm^{-1}$; CHN analysis: Calculated for $C_{28}H_{22}O_2$ (%): C 86.15, H 5.64, Found: C 86.21, H 5.68.

The COSY and DEPT spectra are included in Fig. 3.2B and Fig. 4.2B.

# Chapter3

---

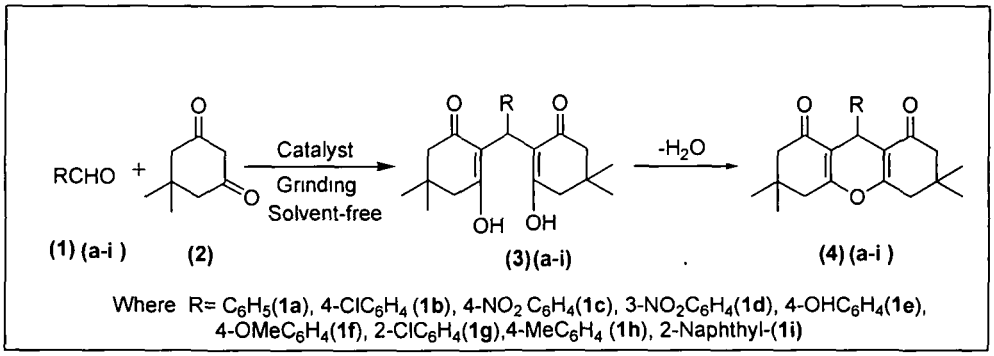
# Mechanochemical Synthesis of 1,8-Dioxo-Octahydroxanthene Derivatives under Solvent Free Condition using Heterogenized Acid Catalysts

Published with small modifications:

**Dutta, P.**, Sarma, P., Borah, R. Investigation of efficient synthesis of 1,8-dioxo-octahydroxanthene derivatives under solvent-free grinding method, *Current Chemistry Letters***2** (4),159--166, 2013.

## 3.1. Introduction

The natural abundances of xanthenedione as core unit in several natural products encouraged researchers to develop modified approaches [1-2] for 1,8-dioxo-octahydroxanthene (**4**) synthesis involving acid or base catalyzed condensation of aldehydes and 5,5-dimethyl-1,3-cyclohexanedione (**Scheme-1.3**) in ionic liquid and aqueous medium, under solvent-free microwave, thermal and mechanical energies. Some of these methods require longer reaction time and high temperature (80-120 °C) to generate good to excellent yield of products. As results, there is a scope to study the reaction with efficient recyclable solid acid catalyst at mild condition, with less time and simple work-up procedure for isolation of product. The use of reusable supported solid acid catalysts [3-4] in organic synthesis make reaction methods more convenient, economic and environmentally benign, since the product purification becomes simple by filtration of insoluble support from the solution of crude product mixture [5-6]. The solid acid catalyzed preparation of xanthenedione (**4**) under mechanochemical method using mechanical energy reduce pollution and cost, simplify the work-up steps, and eliminate excessive and wasteful heating [7]. The flexibility in choice of all types of reagent pairs at room temperature is an important aspect of mechanochemical processes. Jin *et al.* (2005) first reported the synthesis of xanthenedione derivatives (**4**) under solvent-free grinding for 30 min using $TiO_2/SO_4^{2-}$ solid super acid catalyst and kept at room temperature for 24 h [2].




**Scheme-1.3**: Synthesis of xanthenedione derivatives (**4**)

Polyaniline-supported (PANI) acid salts have been utilized as efficient reusable solid acid in various organic syntheses because of easy preparation, good

thermal stability, and excellent activity with fewer amounts of catalysts [8] **(Fig. 1.3).** Gangadasu *et al.* (2006) prepared some of the acid salts of polyaniline (PANI) such as polyaniline-hydrochloride, polyaniline-sulfate and polyaniline-nitrate by oxidation of aniline using ammonium persulfate as oxidizing agents and applied these salts as efficient heterogeneous catalysts for Biginelli reaction under reflux in methanol [9]. In 2011, Borah *et al.* also utilized the PANI salt of TsOH and $FeCl_3$ as reusable catalysts for the formation of 2,4-disubstituted tetrahydropyran ether and 1,3-dioxane derivatives in dichloromethane at 65 °C via Prins reactions [10]. Furthermore, polyaniline-supported metals (Pd, Pt, etc.) and polyaniline-doped heteropoly acids (12-tungstosilicic acid, 12-molybdophosphoric acid) also exhibited high catalytic activity in organic synthesis [11].

It is well known that Lewis acids are good electron acceptors like oxidizing agents with partial transfer of a pair of electron via Lewis acid-base complex while oxidant involves complete transfer of one or several electron facilitating redox reactions. Thus, oxidizing agents provide high probability of fulfilling the requirement of acid catalyst for the synthesis of 1,8-dioxo-octahydroxanthene derivatives. Ferric nitrate nonahydrate is a such type of reagent which successfully catalyzed the Biginelli (or like) reaction for the preparation of 3,4-dihydropyrimidinone derivatives under solvent-less mechanochemical method [12]. It has been observed that Clayfen is an efficient supported form of $Fe(NO_3)_3.9H_2O$ in presence of Montmorillonite K-10 clay [18].

In view of the activities of both polyaniline salts and ferric nitrate nonahydrate in organic reactions, we were interested to study the preparation of 1,8-dioxo-octahydroxanthene derivatives (**4**) from aromatic aldehydes and 5,5-dimethyl-1,3-cyclohexanedione (**Scheme-1.3**) in mild conditions using PANI-TsOH, PANI-$FeCl_3$ and Clayfen as heterogeneous acids.

## 3.2. Results and Discussions

The catalysts PANI-TsOH and PANI-$FeCl_3$ were prepared by following the three steps procedure reported in literature [9]. Similarly, the Clayfen catalyst was synthesized by immobilization of $Fe(NO_3)_3.9H_2O$ on Montmorillonite K-

10 clay [18]. The FT-IR spectra of two PANI supported catalysts were observed to be similar with the spectra of PANI-Salt and PANI-Base in **Fig. 2.3.** The FT-IR spectra of Clayfen catalyst was also compared with the spectra of ferric nitrate nonahydrate and Montmorillonite K-10 clay in **Fig. 6.3.**

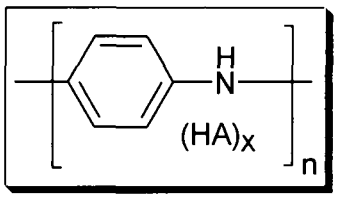



**Fig. 1.3**: Simple structure of polyaniline salt

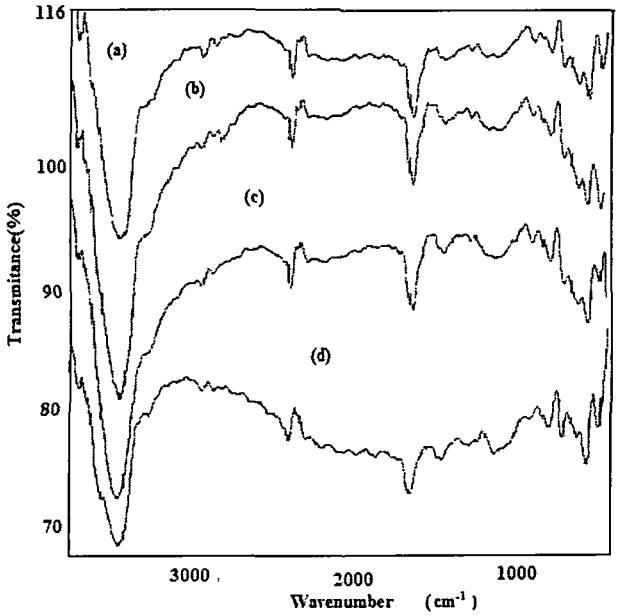
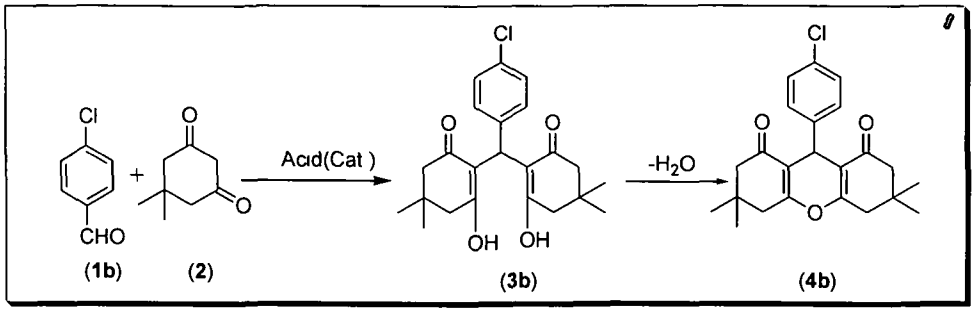



**Fig. 2.3**: FT-IR Spectra of (a) PANI-Salt, (b) PANI-Base, (c) PANI-PTSA, (d) PANI-$FeCl_3$

After that, we examined the catalytic activity of three unsupported acids (TsOH, $FeCl_3$, $Fe(NO_3)_3.9H_2O$) and their supported forms (PANI-TsOH, PANI-$FeCl_3$, Clayfen) for the synthesis of xanthenedione derivatives (**4b**) from *p*-chlorobenzaldehyde and 5,5-dimethyl-1,3-cyclohexanedione in chloroform

under reflux and solvent-free grinding method at ambient temperature. The results are shown in **Table 1.3**.

**Table 1.3**: Optimization of the amount of catalysts for the synthesis of (**3b**) and (**4b**)




| Entry | Catalysts | Amount (mol%) | Time (min) | Method[a] | Product yields (%) | | Total conversion (%) |
|---|---|---|---|---|---|---|---|
| | | | | | Diol (**3b**) | Dione (**4b**) | |
| 1 | $TsOH/FeCl_3/Fe(NO_3)_2.9H_2O$ | 10 | 3h/3h/30 | A | 20/25/58 | -/-/42 | 20/25/100 |
| 2 | PANI-TsOH/PANI-$FeCl_3$/Clayfen | 10 | 45/45/20 | A | 54/60/65 | 46/40/35 | 100/100/100 |
| 3 | $TsOH /FeCl_3/ Fe(NO_3)_2.9H_2O$ | 10 | 55/20/10 | B | 30/28/10 | 70/72/ 90 | 100/100/100 |
| 4 | PANI-TsOH /PANI-$FeCl_3$/Clayfen | 10 | 25/15/60 | B | 15/10/43 | 85/90/57 | 100/100/100 |
| 5 | $TsOH /FeCl_3/ Fe(NO_3)_2.9H_2O$ | 5 | 90/ 70/15 | B | 10/10/5 | 45/53/70 | 55/63/75 |
| 6 | $Fe(NO_3)_2.9H_2O$ | 20 | 10 | B | 8 | 92 | 100 |
| 7 | -- | -- | 40 | B | 90 [2] | -- | 90 |

[a] Method A: Using 3 mL of chloroform under reflux condition; Method B: Solvent-free grinding method at room temperature

The table 1.3 expressed the selective formation of (**4b**) with all catalysts in solvent-free grinding method (table 1.3, entries 3-4) as compared to reactions in chloroform (table 1.3, entries 1,2). The above reaction was also studied in other polar (ethanol, acetone) and non-polar solvents (dichloromethane, toluene) with optimized amount of catalysts (table 2.3). The solvent studies showed similar trends of catalytic activity for supported form of TsOH, $FeCl_3$ and ferric nitrate nonahydrate. The catalysts TsOH and $FeCl_3$ become more reactive and selective in supported form with polyaniline support (table 1.3, entry 4) under solvent-free medium for the formation of product (**4b**) as compared to Clayfen (Clay-supported ferric nitrate), catalyst. It is found that ferric nitrate nonahydrate lost its activity and selectivity in the form of Clayfen catalyst. The optimum amount of catalyst was found to be 10 mol% for polyaniline supported catalyst and ferric nitrate nonahydrate against 1 mmol of 4-chlorobenzaldehyde and 2 mmol of 5,5-dimethyl-1,3-cyclohexanedione. We observed incompletion of the reactions with 5 mol% of unsupported TsOH, $FeCl_3$ and $Fe(NO_3)_3.9H_2O$ catalysts (table 1.3, entry 5).

**Table 2.3**: Synthesis of (**3b**) and (**4b**) in various solvents under reflux using optimized amount of catalysts

| Entry | Solvent | Time (min)[a] | | | Product Yields (%) | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | i | | ii | | iii | |
| | | i | ii | iii | (**3b**) | (**4b**) | (**3b**) | (**4b**) | (**3b**) | (**4b**) |
| 1 | $CHCl_3$ | 45 | 45 | 30 | 54 | 46 | 60 | 40 | 58 | 42 |
| 2 | EtOH | 75 | 75 | 60 | 35 | 40 | 33 | 43 | 36 | 39 |
| 3 | Acetone | 75 | 75 | 60 | 35 | 37 | 30 | 44 | 34 | 42 |
| 4 | $CH_2Cl_2$ | 45 | 45 | 30 | 52 | 48 | 45 | 55 | 56 | 44 |
| 5 | Toluene | 45 | 45 | 60 | 44 | 42 | 47 | 40 | 53 | 35 |
| 6 | Neat | 25 | 15 | 10 | 15 | 85 | 10 | 90 | 10 | 90 |

[a]Catalysts: (i) PANI-TsOH; (ii) PANI-$FeCl_3$; (iii) $Fe(NO_3)_3.9H_2O$

To see the feasibility of the reaction under solvent-free method we had extended the above standard reaction condition with other aromatic aldehydes containing both electron withdrawing and donating groups using supported acid (PANI-TsOH, PANI-$FeCl_3$) and unsupported acid (TsOH, $FeCl_3$, $Fe(NO_3)_3.9H_2O$) catalysts. All these results are summarized in **Table 3.3.**

**Table3.3**: Synthesis of 1,8-dioxo-octahydroxanthene derivatives (4) under optimized conditions with acid catalysts by mechanochemical mixing under solvent-free condition

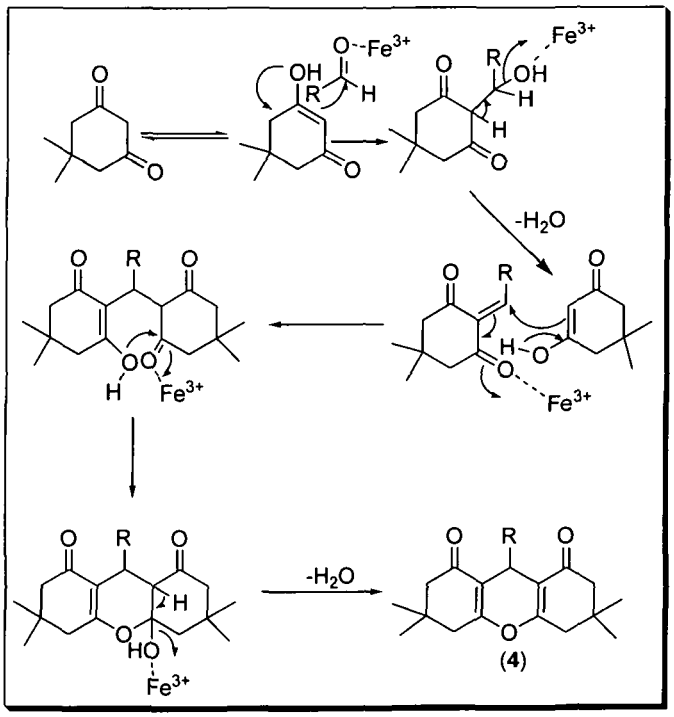
| Entry | Catalysts[a] | R- | Time (min) | Product yields (%)[b]M.p. °C (reported)[2,13-15] | |
|---|---|---|---|---|---|
| | | | | Diol (3)(a-i) | Dione (4)(a-i) |
| 1 | C/D/E/F/G | $C_6H_5$- | 45/25/25/15/10 | 55/20/52/17/15; 195(193-195) | 45/80/48/83/85; 204(205) |
| 2 | C/D/E/F/G/H | 4-$ClC_6H_4$- | 55/20/20/15/10/60 | 30/15/28/16/10/43;141(140-142) | 70/85/72/84/90/57;231 (228-230) |
| 3 | C/D/E/F/G | 4-$NO_2C_6H_4$- | 40/30/60/30/12 | 47/8/32/13/14; 187 (188-190) | 53/92/68/87/86; 219 (216-218) |
| 4 | C/D/E/F/G | 3-$NO_2C_6H_4$- | 60/25/30/15/10 | 27/12/46/9/11; 196 (198-199) | 73/88/54/91/89; 171 (170-173) |
| 5 | C/D/E/F/G | 4-$OHC_6H_4$- | 45/60/60/55/60 | 25/12/17/9/18; 191 (190-192) | 75/89/83/91/82; 250 (249-251) |
| 6 | C/D/E/F/G | 4-$OMeC_6H_4$- | 10/10/15/10/10 | ------ | 94/96/95/97/98; 243 (241-243) |
| 7 | C/D/E/F/G | 2-$ClC_6H_4$- | 20/15/20/10/15 | 46/16/7/- /-; 203 ( 203-204) | 54/84/93/97/95;229 (229-230) |
| 8 | C/D/E/F/G | 4-$MeC_6H_4$- | 35/15/30/15/10 | 25/8/35/-/-; 127 (126-127) | 75/92/65/95/96; 213 (212-214) |
| 9 | C/D/E/F/G | 2-Naphthyl- | 40/25/45/25/15 | 60/15/55/13/16; 207 (207-209) | 40/85/45/87/84; 195 (194-195) |

[a]Where C/D/E/F/G/H indicate TsOH/PANI-TsOH/$FeCl_3$/PANI-$FeCl_3$/$Fe(NO_3)_2.9H_2O$/Clayfen catalysts.

[b]Isolated yields. All products were characterized by $^1$HNMR and also their TLC comparison with authentic sample prepared by reported method.

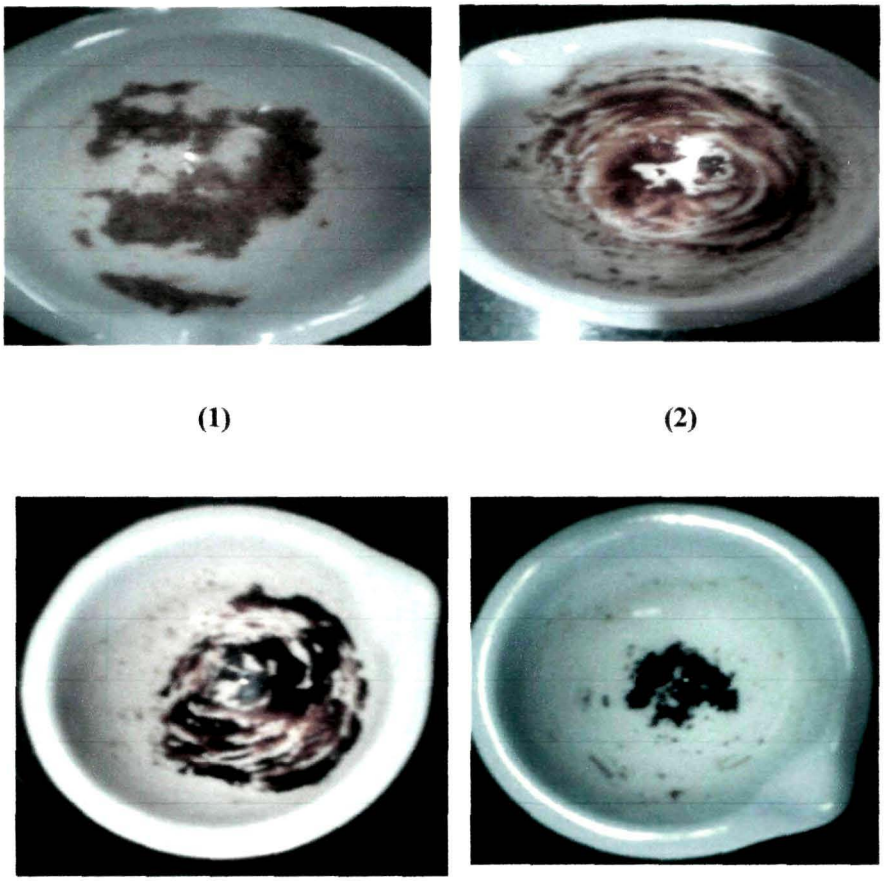
The results in table 3.3 clearly indicated that PANI supported TsOH and $FeCl_3$ catalysts are superior regarding the time of reaction and better selectivity of product formation with all aromatic aldehydes. The presence of strong electron withdrawing groups in *p*-nitrobenzaldehyde and *p*-hydroxybenzaldehyde slightly decreases the reaction rate (table 3.3, entries 3, 5). *p*-Anisaldehyde selectively formed the product (**4**) within short time in presence of electron donating -OMe group (table 3.3, entry 6). 2-Naphthaldehyde selectively produced xanthenedione derivative with the two supported catalysts and ferric nitrate nonahydrate (table-3.3, entry 9). The –NH group on the polyaniline support tightly binds the Lewis or Brønsted acid catalysts through donation of lone pair of electrons on the nitrogen atom. The strong binding interaction of ferric ion on the support may effect on the catalytic activity of Clayfen (table 3.3, entry 2). The three supported catalysts were found to be inactive with aliphatic aldehyde pentanal. Furaldehyde forms polymeric product with these catalysts.

The plausible mechanism of ferric nitrate nonahydrate catalyzed reaction can be explained with the **Scheme-2.3**.




**Scheme-2.3**: Plausible mechanism of $Fe(NO_3)_2.9H_2O$ catalyzed synthesis of (**4**)

During grinding the reaction mixture of 4-nitrobenzaldehyde and 5,5-dimethyl-1,3-cyclohexanedione transformed into a viscous liquid (melt) in presence of ferric nitrate nonahydrate catalyst which eventually solidifies on reaction completion which is clearly visible in the photographs at different time intervals **Fig. 3.3**. The pictures given below show that at initial time the reaction mixture is in solid state (picture '1') which with time turns into a semi-solid state (picture '2'). This semi-solid form then turns into a sticky mass (picture '3') which ultimately forms a powdery solid (picture '4')



**(1)** **(2)**

**(2)** **(4)**

**Fig. 3.3**: Photograph showing the change of phase of reaction mixture at different time; (1) taken at the initial time; (2) after 5 min of grinding; (3) after 7 min of grinding; (4) on reaction completion.

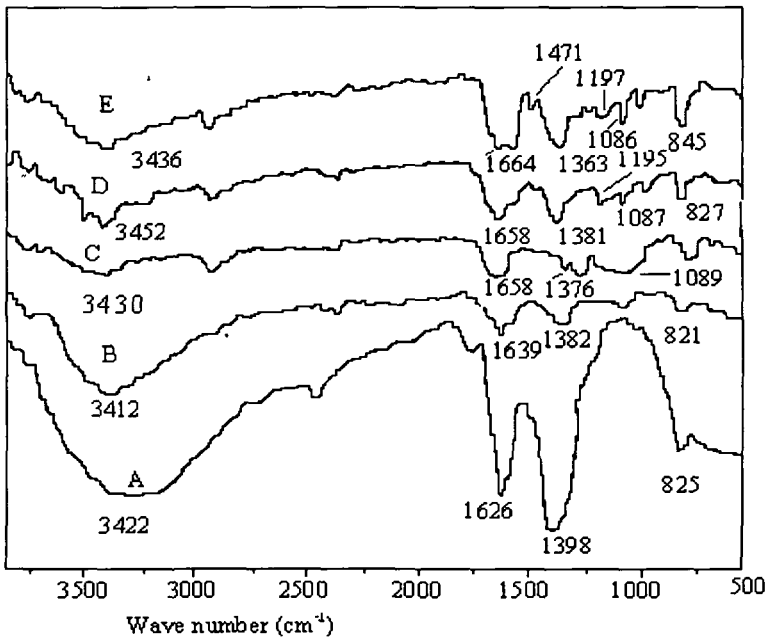



**Fig. 4.3**: FT-IR monitoring on the progress of reaction; A: Spectra of $Fe(NO_3)_3.9H_2O$ catalyst; B: Initial reaction mixture without grinding; C: Reaction mixture after 5 min of grinding; D: Reaction mixture after 10 min of grinding; E: Spectra of pure product.

The various reaction mixture collected at different time intervals were utilized to monitor the progress of the reaction in solid phase with FT-IR studies. The spectra were included in the **Fig. 4.3** at initial time (B), 5 min (C) and 10 min (D) along with the spectra of $Fe(NO_3)_3.9H_2O$ (A) catalyst and pure product (**4b**) (E). The spectra B-D in **Fig. 4.3** did not show any prominent signal for the catalyst $Fe(NO_3)_3.9H_2O$ during the course of reaction, which may be due to the lower concentration of catalyst and its interaction with the reaction mixture.

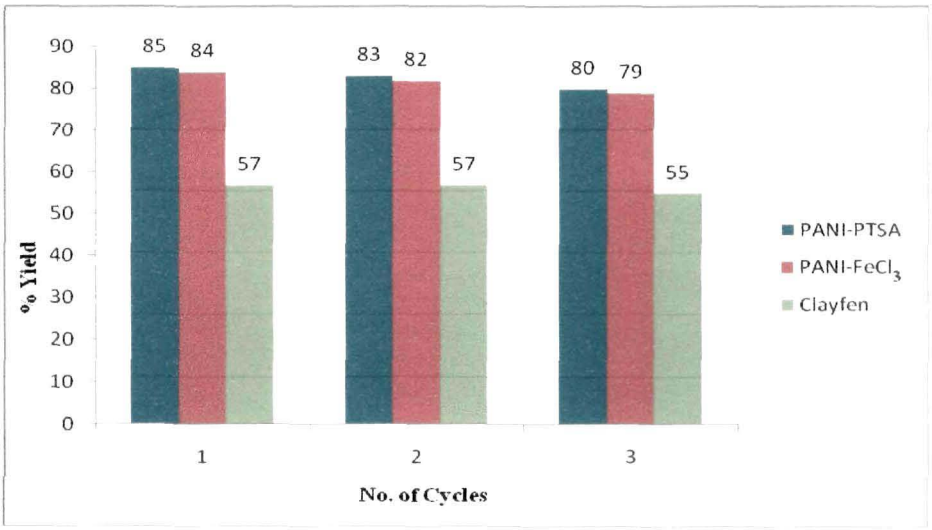



**Fig. 5.3**: Histogram of reusability of supported catalysts

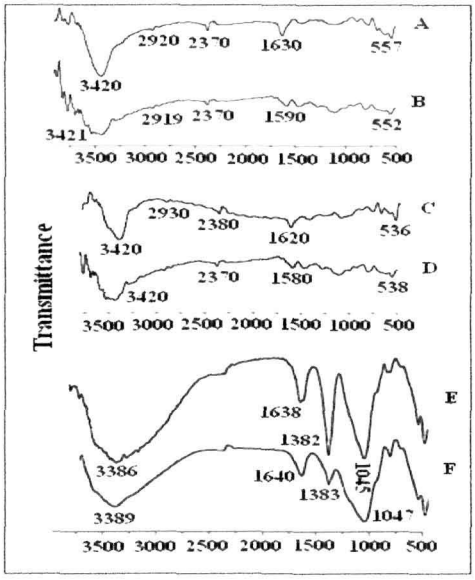



**Fig. 6.3**: FT-IR spectra of fresh and 3rd recyclable catalyst. A: PANI-TsOH (fresh); B: PANI-TsOH (3rd); C: PANI- $FeCl_3$ (fresh); D: PANI-$FeCl_3$ (3rd); E: Clayfen (fresh); F: Clayfen (3rd)

The reusability of the three supported catalysts (PANI-TsOH, PANI-$FeCl_3$, Clayfen) were investigated for the same model reaction of *p*-chlorobenzaldehyde and dimedone for three times (**Fig 5.3**) in solvent-free methods which were further supported by FT-IR spectra of reused catalyst up to 3rd cycles (**Fig 6.3**). The reusability of $Fe(NO_3)_3.9H_2O$ catalyst in organic solvents was again observed by dissolving the reaction mixtures after completion in chloroform, dichloromethane, ethanol, ethyl

acetate and diethyl ether. The hygroscopic nature of the catalyst changes its state from solid to liquid and makes very difficult to filter as solid from the reaction solution.

## 3.3. Conclusion

In these studies, we had observed polyaniline (PANI) supported *p*-toluene sulfonic acid (TsOH) and $FeCl_3$ (PANI-TsOH, PANI-$FeCl_3$) as excellent reusable solid acid catalysts for the synthesis of 1,8-dioxo-octahydroxanthene derivatives (**4**) under solvent-free grinding method at mild conditions. Additionally, in the same optimized condition ferric nitrate nonahydrate also acted as (non-reusable) very reactive selective inexpensive Lewis acid catalyst. The ferric nitrate nonahydrate lost its activity in the form of Clayfen. The advantage of this protocol lies in the avoidance of organic solvent as medium, high yield, energy efficiency, variation of substrates, and use of inexpensive reusable catalyst.

## 3.4. Experimental Section

### 3.4.1. General Information

All chemicals were purchased and were used without further purification. The products were identified by FT-IR, $^1$H NMR, $^{13}$C NMR and CHN analysis data and also compared the melting point with those of literature reported data [1-2,13-17]. The polyaniline supported acids and Clayfen catalysts were prepared using already reported method [9,18].

### 3.4.2. Methods for the preparation of supported solid acids

#### (A) Preparation of polyaniline supported acid catalysts

Three steps were involved for the synthesis of PANI supported TsOH and $FeCl_3$ catalysts.

(i) Preparation of polyaniline salt

A solution of 15 mL of sulphuric acid in 350 mL of water was prepared in a 500 mL round bottom flask with stirring. To the stirring solution, 5 mL of aniline was added at 5–10 °C and allowed to continue for stirring in presence of 130 mL aqueous solution of sodium persulfate (12 g) for 4 h at the same temperature. The polyaniline powder

was precipitated, filtered and washed with distilled water followed by acetone. The polyaniline salt powder was dried at 100 °C till a constant weight (3.5g).

(ii) Synthesis of polyaniline base

In this step, 3.5 g of polyaniline salt powder was kept in a 500 mL round bottom flask and stirred in 300 mL aqueous sodium hydroxide solution (1.0 M) for 8 h at ambient temperature. Polyaniline base was precipitated, filtered and washed with water and then with acetone. The base was dried at 100 °C till a constant weight.

(iii) Redoped polyaniline salt

Firstly, 50 mL of 1.0 M two standard solution of TsOH and $FeCl_3$ in acetone were prepared separately. To each of the above solutions, 0.5 g of polyaniline base was added and kept under constant stirring at ambient temperature for 4 h. The supported catalyst was isolated through filtration, washed with acetone and dried at 100 °C till a constant weight. Amount of acid group present in the polymeric chain was calculated based on the weight of redoped polyaniline salt obtained and the weight of polyaniline base used. Amount of dopant present in PANI-TsOH and PANI- $FeCl_3$ were found to be 40.2% and 27.1% respectively.

**(B) Preparation of clayfen catalyst**

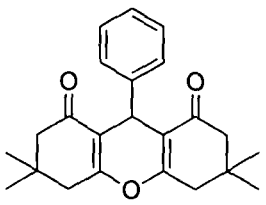
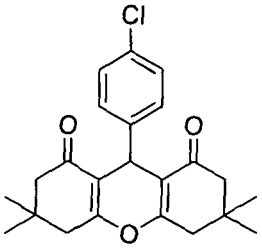
In a 100 mL round bottom flask, $Fe(NO_3)_3.9H_2O$ (500 mg) was added to acetone (8.3 mL) and stirred vigorously for 5 min, until complete dissolution of the crystals. Montmorillonite K-10 clay (667 mg) was added in small portions and stirred again for 5 min. The solvent was evaporated under reduced pressure on rotary evaporator at 50 °C. Yellow color powder of $Fe(NO_3)_3.9H_2O$ supported on Montmorillonite K-10 clay (clayfen) was obtained which was further dried under the same condition for 30 mins. Freshly prepared clayfen was used in every reaction.

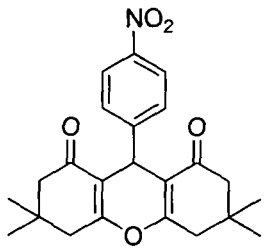
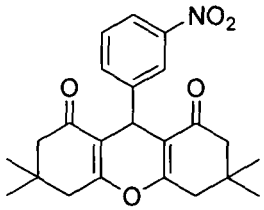
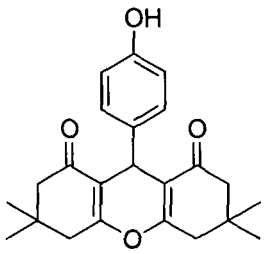
### 3.4.3. General procedure for the synthesis of 1,8-dioxo-octahydroxanthene derivatives (4) in organic solvent and mechanochemical mixing under solvent-free condition

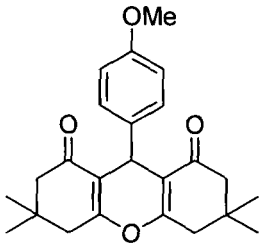
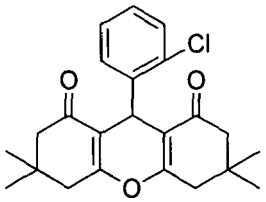
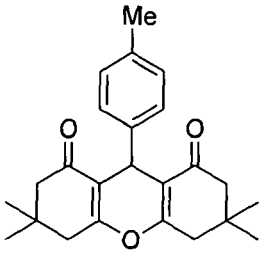
A mixture of 0.5 mmol of 4-chlorobenzaldehyde and 1 mmol of 5,5-dimethyl-1,3-cyclohexanedione in organic solvent (3 mL) is taken in a 25 mL round bottom flask

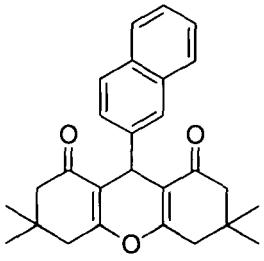
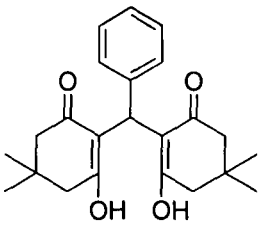
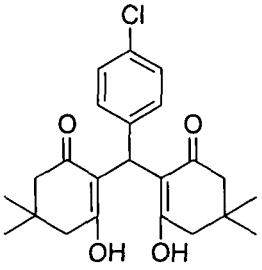
containing 10 mol% of acid catalyst. For solvent-free method, the above mixture is grinded continuously with the help of mortar and pestle. The progress of the reaction in both conditions is monitored with the help of TLC technique. After completion, the reaction mixture is diluted with ethyl acetate and filtered to get the catalysts as residue. During the work-up step, the filtrate is diluted with aqueous sodium bicarbonate ($NaHCO_3$) solution and the organic part is extracted with ethyl acetate. The organic extract is dried over anhydrous sodium sulfate. The solvent ethyl acetate is distilled under reduced pressure to get the crude product. Recrystallization of crude product from ethanol yielded the pure product. The used catalyst is dried at 100 °C and made ready for reuse.

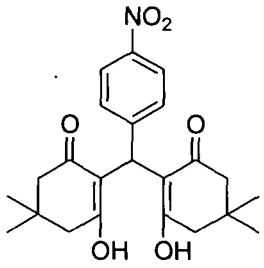
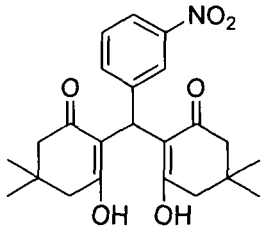
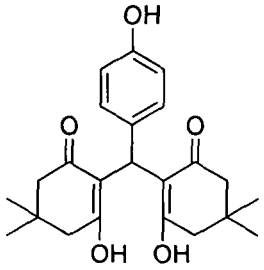
### 3.4.4. Spectral data of 1,8-dioxo-octahydroxanthene derivatives (4) and their diols (3)

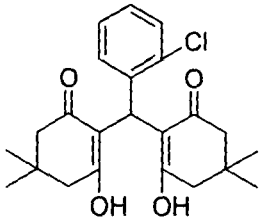
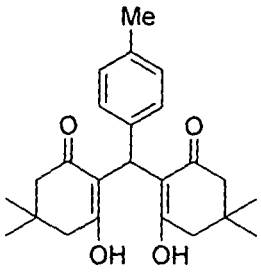
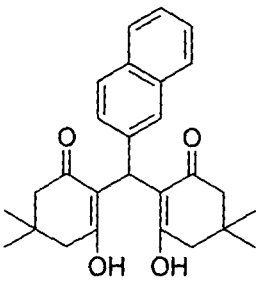
| | |
|---|---|
|  | **9-Phenyl-3,3,6,6-tetramethyl-1,8-dioxo-octahydroxanthene (4a) (Table 3.3, Entry 1)**<br>White solid, m.p. 204° C; $^1$H NMR (400 MHz, $CDCl_3$) δ ppm: 0.95 (s, 6H), 1.06 (s, 6H), 2.15-2.26 (m, 4H), 2.43 (s, 4H), 4.71 (s, 1H), 7.06-7.24 (m, 5H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ ppm: 27.4, 28.0, 29.3, 31.8, 32.2, 41.1, 50.8, 52.9, 115.7, 126.4, 128.1, 128.4, 144.1, 162.1, 196.4; FT-IR (KBr): 3439, 2954, 1663, 1458, 1362, 1198, 1146, 1004, 697 cm$^{-1}$; CHN analysis: Calculated for $C_{23}H_{26}O_3$ (%): C 78.83, H 7.47, Found: C 78.94, H 7.52. |
|  | **9-(4'-Chlorophenyl)-3,3,6,6-tetramethyl-1,8-dioxo-octahydroxanthene (4b) (Table 3.3, Entry 2)**<br>White solid, m.p. 231 °C; $^1$H NMR (400 MHz, $CDCl_3$) δ ppm: 0.97 (s, 6H), 1.13 (s, 6H), 2.20 (s, 8H), 4.73 (s, 1H), 7.24 (d, $J$ = 8.6 Hz, 2H), 7.29 (d, $J$ = 8.6 Hz, 2H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ ppm: 27.2, 29.3, 31.5, 32.3, 41.0, 50,8, 115.5, 128.4, 129.7, 132.1, 142.8, 162.5, 196.2; FT-IR (KBr): 3436, 2954, 2877, 2376, 1664, 1471, 1363, 1197, 1152, 1008, 845 cm$^{-1}$; CHN analysis: Calculated for $C_{23}H_{25}ClO_3$ (%): C 71.78, H 6.50, Found: C 71.76, H 6.49. |

| | |
|---|---|
|  | **9-(4'-nitrophenyl)-3,3,6,6-tetramethyl-1,8-dioxo-octahydroxanthene (4c) (Table 3.3, Entry 3)**<br>White solid, m.p. 219 °C; $^{1}$H NMR (400 MHz, $CDCl_3$) δ ppm: 1.00 (s, 6H), 1.13 (s, 6H), 2.16-2.29 (m, 4H), 2.51 (s, 4H), 4.84 (s, 1H), 7.48 (d, $J$ = 8.2 Hz, 2H), 8.10 (d, $J$ = 8.7, 2H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ ppm: 27.8, 29.1, 29.6, 32.5, 32.7, 41.7, 50.6, 110.7, 123.7, 123.8, 127.3, 129.4, 141.4, 145.8, 147.9, 148.7, 169.8, 195.8; FT-IR (KBr): 3431, 2956, 1660, 1515, 1355, 1199, 1138, 1005, 869, 828 cm$^{-1}$; CHN Analysis: Calculated for $C_{23}H_{25}NO_5$ (%): C 69.87, H 6.32, N 3.54, Found: C 69.85, H 6.31, N 3.53. |
|  | **9-(3'-Nitrophenyl)-3,3,6,6,-tetramethyl-1,8-dioxo-octahydroxanthene (4d) (Table 3.3, Entry 4)**<br>White solid, m.p. 171 °C; $^{1}$H NMR (400 MHz, $CDCl_3$) δ ppm: 1.11 (s, 6H), 1.3 (s, 6H), 2.35-2.47 (m, 8H), 5.53 (s, 1H), 8.22-8.71 (m, 4H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ ppm: 27.5, 29.2, 29.7, 32.4, 32.8, 41.5, 50.2, 110.4, 123.5, 123.7, 127.1, 129.2, 141.3, 145.7, 148, 148.5, 169.7, 196.0; FT-IR (KBr): 3475, 2958, 2872, 2380, 1595, 1528, 1458, 1372, 1250, 1155, 888, 805 cm$^{-1}$; CHN analysis: Calculated for $C_{23}H_{25}NO_5$ (%): C 69.87, H 6.32, N 3.54, Found: C 69.86, H 6.33, N 3.52. |
|  | **9-(4'-Hydroxyphenyl)-3,3,6,6,-tetramethyl-1,8-dioxo-octahydroxanthene (4e) (Table 3.3, Entry 5)**<br>White solid, m.p. 250 °C; $^{1}$H NMR (400 MHz, $CDCl_3$) δ ppm: 0.96 (s, 6H), 1.15 (s, 6H), 2.12-2.27 (m, 8H), 5.4 (s, 1H), 7.20 (d, $J$ = 8.4 Hz, 2H), 7.73 ( d, $J$ = 8.3 Hz, 2H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ ppm: 27.7, 29.1, 30.9, 32.2, 40.7, 50.9, 111.2, 115.4, 129.1, 133.1, 154.5, 168.2, 196.9; FT-IR (KBr): 3429, 2962, 2858, 2377, 2284, 1654, 1604, 1514, 1366, 1262, 1096, 1025, 804 cm$^{-1}$; CHN analysis: Calculated for $C_{23}H_{26}O_4$ (%): C 75.38, H 7.15, Found: C 75.43, H 7.20. |

| | |
|---|---|
|  | **9-(4'-Methoxyphenyl)-3,3,6,6,-tetramethyl-1,8-dioxo-octahydroxanthene (4f) (Table 3.3, Entry 6)**<br>White solid, m.p. 243 °C; $^1$H NMR (400 MHz, $CDCl_3$) δ ppm: 0.99 (s, 6H), 1.13 (s, 6H), 2.17-2.25 (m, 4H), 2.47 (s, 4H), 3.74 (s, 3H), 4.73 (s, 1H), 6.76 (d, $J$ = 8.7 Hz, 2H), 7.23 (d, $J$ = 8.6 Hz, 2H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ ppm: 27.2, 29.1, 31.0, 32.3, 41.0, 51.0, 55.2, 113.4, 115.7, 129.2, 136.4, 157.8, 162.2, 195.3; FT-IR (KBr): 3004, 2957, 2858, 2374, 1736, 1666, 1513, 1363, 1262, 1092, 1023, 801 cm$^{-1}$; CHN analysis: Calculated for $C_{24}H_{28}O_4$ (%): C 75.78, H 7.36, Found: C 75.76, H 7.34. |
|  | **9-(2'-Chlorophenyl)-3,3,6,6-tetramethyl-1,8-dioxo-octahydroxanthene (4g) (Table 3.3, Entry 7)**<br>White solid, m.p. 229 °C; $^1$H NMR (400MHz, $CDCl_3$) δ ppm: 1.02 (s, 6H), 1.12 (s, 6H), 2.19-2.25 (m, 4H), 2.46 (s, 4H), 5.05 (s, 1H), 7.10-7.47 (m, 4H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ ppm: 27.8, 29.5, 32.0, 32.3, 41.2, 51.2, 114.1, 126.8, 128.1, 130.5, 132.1, 132.6, 140.3, 165.1, 196.7; FT-IR (KBr): 3294, 3064, 2957, 1720, 1643, 1461, 1383, 1239, 1150, 1047, 748 cm$^{-1}$; CHN analysis: Calculated for $C_{23}H_{25}ClO_3$ (%): C 71.78, H 6.50, Found: C 71.77, H 6.48. |
|  | **9-(4'-Methylphenyl)-3,3,6,6-tetramethyl-1,8-dioxo-octahydroxanthene (4h) (Table 3.3, Entry 8)**<br>White solid, m.p. 213 °C; $^1$H NMR (400 MHz, $CDCl_3$) δ ppm: 1.02 (s, 6H), 1.09 (s, 6H), 2.18 (m, 4H), 2.30 (s, 3H), 2.52 (s, 4H), 4.93 (s, 1H), 6.86 (d, $J$ = 8.2 Hz, 2H), 7.13 (d, $J$ = 8.3 Hz, 2H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ ppm: 21.3, 27.2, 29.3, 32.0, 32.3, 42.1, 50.1, 112.3, 125.1, 129.3, 135.3, 141.5, 162.7, 195.7; FT-IR (KBr): 3134, 2956, 1722, 1593, 1377, 1191, 1083, 850, 840 cm$^{-1}$; CHN analysis: Calculated for $C_{24}H_{28}O_3$ (%): C 79.12, H 7.69, Found: C 79.11, H 7.68. |

| | |
|---|---|
|  | **9-(2'-Naphthyl)-3,3,6,6-tetramethyl-1,8-dioxo-octahydroxanthene (4i) (Table 3.3, Entry 9)**<br>White solid, m.p. 195 °C; $^{1}$H NMR (400 MHz, $CDCl_3$) δ ppm: 0.98 (s,6H), 1.10 (s, 6H), 2.10-2.47 (m, 8H), 5.10 (s, 1H), 7.33-7.49 (m, 3H), 7.68-7.80 (m, 4H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ ppm: 27.2, 29.3, 29.7, 32.0, 32.2, 40.9, 50.8, 115.4, 125.3, 125.6, 126.7, 127.3, 127.5, 127.7, 127.9, 132.4, 133.3, 141.6, 162.4, 196.4; FT-IR (KBr): 3058, 2958, 1663, 1627, 1460, 1361, 1192, 1162, 1137, 1001, 913, 784 $cm^{-1}$; CHN analysis: Calculated for $C_{27}H_{28}O_3$ (%): C 81.0, H 7.0, Found: C 79.95, H 6.98. |
|  | **2,2'-Phenylmethylenebis(3-hydroxy-5,5-dimethyl-2-cyclohexen-1-one) (3a) (Table 3.3, Entry 1)**<br>White solid, m.p. 195 °C; $^{1}$H NMR (400 MHz, $CDCl_3$) δ ppm: 1.09 (s, 6H), 1.23 (s, 6H), 2.33-2.43 (m, 8H), 5.54 (s, 1H), 7.09-7.26 (m, 5H), 11.9 (s, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ ppm: 27.4, 28.0, 29.6, 31.4, 32.8, 46.5, 47.1, 115.6, 125.8, 126.8, 128.0, 128.2, 128.4, 138.1, 160.4, 162.2, 189.3, 190.4; FT-IR (KBr): 2960, 2875, 2375, 1591, 1449, 1371, 1298, 1248, 1158, 1044, 848, 778 $cm^{-1}$; CHN analysis: Calculated for $C_{23}H_{28}O_4$ (%): C 75.0, H 7.60, Found: C 74.2, H 7.55. |
|  | **2,2'-(4-Chlorophenyl)methylenebis(3-hydroxy-5,5-dimethyl-2-cyclohexen-1-one) (3b) (Table 3.3, Entry 2)**<br>White solid, m.p. 141 °C; $^{1}$H NMR (400 MHz, $CDCl_3$) δ ppm: 1.10 (s, 6H), 1.26 (s, 6H), 2.33-2.44 (m, 8H), 5.47 (s, 1H), 7.0 (d, $J$ = 8.4 Hz, 2H), 7.23 (d, $J$ = 8.2 Hz, 2H), 11.9 (s, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ ppm: 27.5, 29.6, 31.5, 32.5, 46.5, 47.1, 115.4, 128.3, 128.4, 131.6, 136.8, 189.5, 190.7; FT-IR (KBr): 2927, 2866, 2635, 1588, 1462, 1372, 1302, 1251, 1156, 1090, 1014, 880 $cm^{-1}$; CHN analysis: Calculated for $C_{23}H_{27}ClO_4$ (%): C 68.65, H 6.71, Found: C 68.63, H 6.68. |

| | |
|---|---|
|  | **2,2'-(4-Nitrophenyl)methylenebis(3-hydroxy-5,5-dimethyl-2-cyclohexen-1-one) (3c) (Table 3.3, Entry 3)**<br>Yellow solid, m.p. 187 °C; $^1$H NMR (400 MHz, $CDCl_3$) δ ppm: 1.07 (s, 6H), 1.23 (s, 6H), 2.29-2.47 (m, 8H), 5.54 (s, 1H), 7.23 (d, *J* = 8.8 Hz, 2H), 8.11 (d, *J* = 8.8 Hz, 2H), 11.8 (s, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ ppm: 27.5, 28.0, 29.5, 31.6, 33.3, 41.5, 46.5, 47.0, 114.9, 123.6, 124.4, 127.7, 130.5, 146.2, 146.6, 189.6, 190.9; FT-IR (KBr): 2954, 2874, 1589, 1511, 1459, 1369, 1302, 1247, 1157, 1044, 851 cm$^{-1}$; CHN analysis: Calculated for $C_{23}H_{27}NO_6$ (%): C 66.82, H 6.53, N 3.38, Found: C 65.49, H 6.50, N 3.35. |
|  | **2,2'-(3-Nitrophenyl)methylenebis(3-hydroxy-5,5-dimethyl-2-cyclohexen-1-one) (3d) (Table 3.3, Entry 4)**<br>White solid, m.p. 196 °C; $^1$H NMR (400 MHz, $CDCl_3$) δ ppm: 1.03 (s, 6H), 1.16 (s, 6H), 2.22-2.47 (m, 8H), 5.45 (s, 1H), 7.28-7.95 (m, 4H), 11.81 (s, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ ppm: 27.6, 28.2, 29.4, 31.3, 33.2, 41.5, 46.4, 47.2, 115.0, 123.7, 124.6, 127.8, 130.2, 146.3, 147.0, 189.5, 191; FT-IR (KBr): 3268, 2955, 1719, 1616, 1523, 1385, 1291, 1231, 1146, 1070, 985, 839 cm$^{-1}$; CHN analysis: Calculated for $C_{23}H_{27}NO_6$ (%): C 66.82, H 6.53, N 3.38, Found: C 66.79, H 6.51, N 3.37. |
|  | **2,2'-(4-Hydroxyphenyl)methylenebis(3-hydroxy-5,5-dimethyl-2-cyclohexen-1-one) (3e) (Table 3.3, Entry 5)**<br>Red solid, m.p. 191 °C; $^1$H NMR (400 MHz, $CDCl_3$) δ ppm: 1.02 (s, 6H), 1.15 (s, 6H), 2.13-2.38 (m, 8H), 5.47 (s, 1H), 6.67 (d, *J* = 8.8 Hz, 2H), 6.97 (d, *J* = 8.8 Hz, 2H), 11.8 (s, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ ppm: 27.4, 29.2, 31.0, 32.3, 40.6, 50.5, 115.1, 128.7, 129.1, 136.8, 189.2, 191.2; FT- IR (KBr): 3418, 3025, 2550, 2958, 2870, 1625, 1514, 1368, 1252, 1208, 1169, 1036, 837 cm$^{-1}$; CHN analysis: Calculated for $C_{23}H_{28}O_5$ (%): C 71.87, H 7.29, Found: C 71.79, H 7.27. |

| | |
|---|---|
|  | **2,2'-(2-Chlorophenyl)methylenebis(3-hydroxy-5,5-dimethyl-2-cyclohexen-1-one) (3g) (Table 3.3, Entry 7)**<br>White solid, m.p. 203 °C; $^{1}$H NMR (400 MHz, $CDCl_3$) δ ppm: 1.05 (s, 6H), 1.14 (s, 6H), 2.24-2.47 (m, 8H), 5.63 (s, 1H), 7.15-7.39 (m, 4H), 11.9 (s, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ ppm: 27.4, 29.2, 32.1, 40.5, 50.6, 114.0, 126.2, 128.2, 131.1, 133.6, 188.9, 190.2; FT-IR (KBr): 2928, 2862, 2633, 1583, 1460, 1367, 1298, 1248, 1152, 1087, 1012, 877 $cm^{-1}$; CHN analysis: Calculated for $C_{23}H_{27}ClO_4$ (%): C 68.65, H 6.71, Found: C 68.64, H 6.70. |
|  | **2,2'-(4-Methylphenyl)methylenebis(3-hydroxy-5,5-dimethyl-2-cyclohexen-1-one) (3h) (Table 3.3, Entry 8)**<br>Yellow solid, m.p. 127 °C; $^{1}$H NMR (400 MHz, $CDCl_3$) δ ppm: 0.99 (s, 6H), 1.09 (s, 6H), 2.17 (m, 4H), 2.29 (s, 3H), 2.45 (s, 4H), 5.49 (s, 1H), 7.01 (d, $J$ = 8.6 Hz, 2H), 7.16 (d, $J$ = 8.6 Hz, 2H), 11.8 (s, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ ppm: 21.1, 27.2, 29.1, 32.0, 32.2, 42.3, 50.4, 112.4, 125.4, 129.6, 136.3, 188.6, 190.5; FT- IR (KBr): 3428, 2956, 2875, 2378, 1664, 1595, 1513, 1460, 1362, 1311, 1194, 1142, 1001, 917 $cm^{-1}$; CHN analysis: Calculated for $C_{24}H_{30}O_4$ (%): C 75.39, H 7.85, Found: C 74.42, H 7.82. |
|  | **Naphthalen-2-yl-2,2'-methylenebis(3-hydroxy-5,5-dimethyl-2-cyclohexene-1-one) (3i) (Table 3.3, Entry 9)**<br>White solid, m.p. 207 °C; $^{1}$H NMR (400 MHz, $CDCl_3$) δ ppm: 1.11 (s, 6H), 1.29 (s, 6H), 2.22-2.48 (m, 8H), 5.68 (s, 1H), 7.25 (m, 1H), 7.39-7.41 (m, 2H), 7.51 (s, 1H), 7.72-7.74 (m, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ ppm: 27.5, 28.1, 29.7, 31.6, 33.1, 41.5, 46.6, 47.2, 52.9, 115.7, 125.4, 125.5, 125.9, 127.8, 127.9, 131.9, 135.7, 160.5, 189.5, 190.5; FT-IR (KBr): 3428, 3059, 2958, 2876, 1653, 1591, 1457, 1370, 1308, 1255, 1154, 1060, 926, 814 $cm^{-1}$; CHN analysis: Calculated for $C_{27}H_{30}O_4$ (%): C 77.51, H 7.17, Found: C 76.99, H 7.14. |

# References


1. Venkatesan, K., et al. *Ultrason. Sonochem.* **15** (4), 548--553, 2008.

2. Jin, T-S., et al. *Synth. Commun.* **35** (17), 2339--2345, 2005.

3. Delmas, M. & Gaset, A. *Synthesis* (11), 871--872, 1980.

4. Karthikeyan, G. & Pandurangan, A. *J. Mol. Catal. A: Chem.* **311** (1-2), 36--45, 2009.

5. Blaz, E. & Pielichowski, J. *Molecules* **11** (1), 115--120, 2006.

6. Hunnur, R.K., et al. *Chem. Heterocycl. Compd.* **44** (2), 143--147, 2008.

7. Bose, A.K., et al. *Tetrahedron Lett.* **45** (45), 8351--8353, 2004.

8. Palaniappan, S. & Sairam, M. *J. Appl. Polym. Sci.* **96** (5), 1584--1590, 2005.

9. Gangadasu, B., et al. *J. Appl. Polym. Sci.* **102** (2), 1741--1745, 2006.

10. Borah, K.J. & Borah, R. *J. Chem. Sci.* **123** (5), 623--630, 2011.

11. Lapkowski, M., et al. *Synth. Met.* **69** (1-3), 127--128, 1995.

12. Phukan, M., et al. *Green Chem. Lett. Rev.* **3** (4), 329--334, 2010.

13. Fan, X., et al. *Can. J. Chem.* **83** (1), 16--20, 2005.

14. Jung, D.H., et al. *Bull. Korean. Chem. Soc.* **30** (9), 1989--1995, 2009.

15. Song, G., et al. *Catal. Commun.* **8** (4), 673--676, 2007.

16. Jin, T-S., et al. *Synlett* (5), 866--870, 2004.

17. Das, B., et al. *Catal. Commun.* **8** (3), 535--538, 2007.

18. Badathala, V. *Synlett* (2), 388--389, 2004.

19. Hu, X.Y., et al. *Chin. Chem. Lett.* **16** (3), 293--295, 2005.

20. Jin, T-S., et al. *Chin.. J. Org. Chem.* **25** (3), 335--338, 2005.

# Chapter 4

# Protection of Carbonyl Group using Safer Catalytic Systems

Published with small modifications:

**Dutta, P.**, Sarma, P., Borah, R. P4VP-$H_2SO_4$ Catalyzed Chemoselective Protection of Aldehydes to Acylal along with Deprotection Reactions, *Synthetic Communications* **43** (10), 1378--1386, 2013.

**Dutta, P.**, Dutta, A. K., Sarma, P., Borah, R. Dual nature of polyethylene glycol under microwave irradiation for the clean synthesis of oximes, *Monatshefte für Chemie* **145** (3), 505--508, 2014.

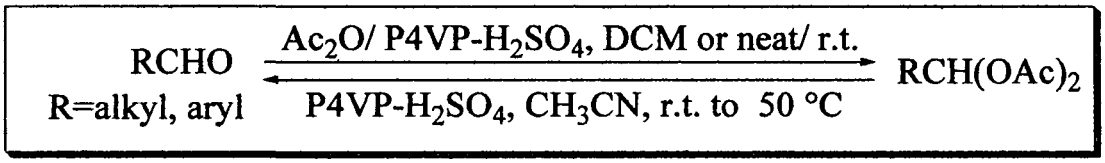
# Section 4A

## Polymer-supported Brønsted Acid Catalyzed Chemoselective Protection of Aldehydes to 1,1-Diacetates and Deprotection to Carbonyl Group

### 4A.1. Introduction

Heterogeneous acids in the form of polymer supported catalysts display several positive aspects which make them a suitable alternative choice in organic transformations. The idea of converting liquid homogeneous acids into heterogeneous ones by impregnating them upon polymer surfaces led to whole new concept of catalysis. Advantages such as reusability, thermal and chemical stability, cost effective and safety to human and society are quite attractive for large scale industries. These supports are to be chosen in such a manner that they provide accessibility and a good dispersion of the active sites [1] along with a wide range of applicable solvents.Various types of polymers such as polystyrene, poly(4-vinylpyridine), polyaniline, polyacrylate, etc. have been extensively utilized as insoluble and inert supports by different research groups to successfully carry out their works [2]. The lone pair of electron on nitrogen of poly(4-vinylpyridine) acts as a basic site to which the Brønsted acids can bind actively making them convenient and useful solid Brønsted acid catalysts. Borah and group (2011) described the synthesis, characterization and applications of poly(4-vinylpyridine) supported Brønsted acids ($H_2SO_4$, HCl, and $H_3PO_4$) as reusable catalyst for acetylation reaction at room temperature. They observed higher catalytic activity of P4VP-$H_2SO_4$ catalyst for the preparation of acetates from different alcohol and phenolic compounds in solution [3]. Furthermore P4VP has also been utilized as surface modifier for immobilization of metal triflates, ruthenates and nanoparticles [4-6]. By observing such catalytic activity of P4VP supported solid acid we thought to extent the use of sulfuric acid supported catalyst in protection-deprotection chemistry of carbonyl group (**Scheme-1.4A**). The protection of carbonyl group as 1,1-diacetates is an important strategy in organic synthesis [7] because of their stability in neutral as well as basic media [8-9]. The review chapter discussed the applications of acylals in organic synthesis and other fields. Similarly, deprotection of acylals in presence of acid catalyst is also a

necessary step in multistep synthesis of complex organic molecules via protection of carbonyl group. In this section we also examined the deprotection of acylals to carbonyl compounds in presence of P4VP-$H_2SO_4$ catalyst in different temperatures and solvents (**Fig 1.4A**).




**Scheme-1.4A**

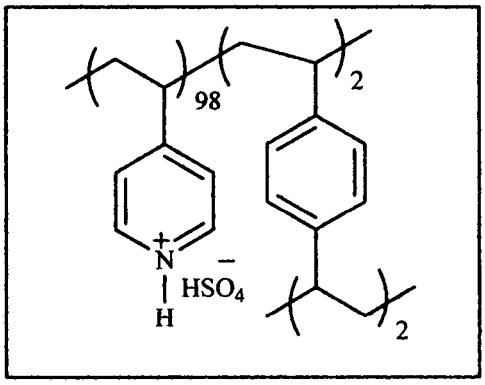



**Fig.1.4A**: Structure of P4VP-$H_2SO_4$ catalyst

## 4A.2. Results and Discussion

The catalyst P4VP-$H_2SO_4$ was prepared by simple wet impregnation method according to the literature procedure [3]. It is relatively nontoxic, safe to handle and reusable after reactivation which makes the process more economical and benign. The amount of dopant present in poly(4-vinylpyridine) sulfuric acid (P4VP-$H_2SO_4$) was found to be 0.652 mol%. Our first approach started with the optimization of carbonyl protection reaction by stirring a mixture of benzaldehyde (1 mmol) and acetic anhydride (3 mmol) using different amount of catalyst in solution and solvent-less medium at ambient temperature (**table 1.4A**).

**Table 1.4A**: Optimization of reaction conditions for the preparation of 1,1-diacetates from benzaldehyde at room temperature

| Entry | Catalyst (mol%) | Solvent | Time (min.) | Product Yield (%) |
|---|---|---|---|---|
| 1 | 0.00652 | $CH_2Cl_2$ | 1 h | 30 |
| 2 | 0.0163 | $CH_2Cl_2$ | 1 h | 70 |
| 3 | 0.0326 | $CH_2Cl_2$ | 15 | 100 |
| 4 | 0.0652 | $CH_2Cl_2$ | 6 | 100 |
| 5 | 0.0326 | $CH_2Cl_2$ | 2 h[a] | 75 |
| 6 | 0.0326 | $CH_3CN$ | 30 | 60 |
| 7 | 0.0326 | Acetone | 30 | 55 |
| 8 | 0.0326 | THF | 30 | 45 |
| 9 | 0.0326 | neat | 5 | 98 |

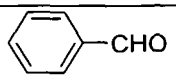
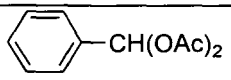
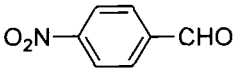
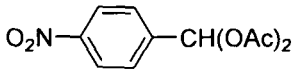
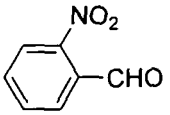
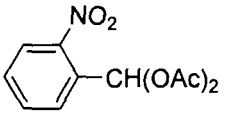
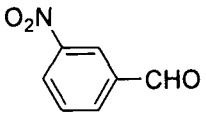
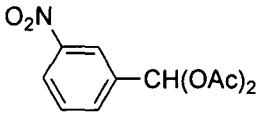
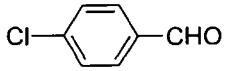
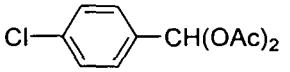
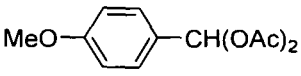
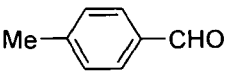
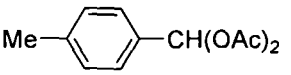
[a] Using 1·2 ratio of benzaldehyde and acetic anhydride

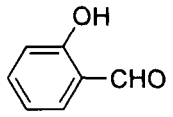
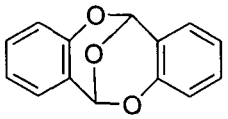
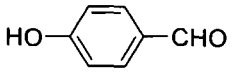
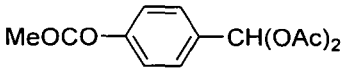
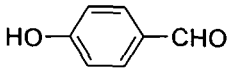
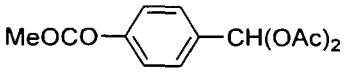
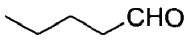
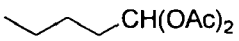
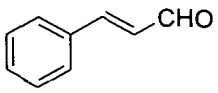
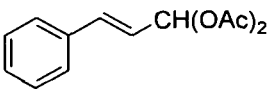
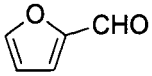
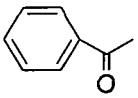
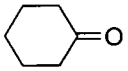
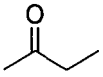
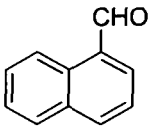
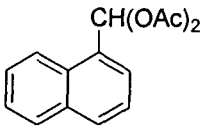
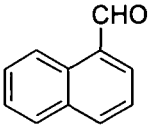
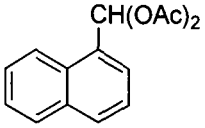
The results compiled in the above table infer that the optimized amount of catalyst necessary for the reaction to go to completion is 0.0326 mol% (table 1.4A, entry 3), as lesser amounts could not complete the reaction and afford the expected yield within satisfactory time (table 1.4A, entries 1,2). The doubling of catalyst amount decreased the reaction time to 6 min (table 1.4A, entry 4). The reaction was also tested in various organic solvents, but the results were not as satisfactory as in dichloromethane (table 1.4A, entries 6, 7, 8). The presence of small amount of miscible water with these polar solvents may hydrolyze the acetic anhydride to acetic acid or reverse the equilibrium of acylal to carbonyl compound. When, the ratio of benzaldehyde to acetic anhydride was decreased from 1:3 to 1:2, it took 2 h to give 75% yield of acylal using 0.0326 mol% of catalyst (table 1.4A, entry 5), thus confirming that 1:3 is the optimized ratio of benzaldehyde and acetic anhydride. The reaction was also observed in solvent-free grinding method with 0.0326 mol% of catalyst and 3 mmol of acetic anhydride. The reaction showed excellent results in terms of reducing reaction time as compared to solution phase reaction (table 1.4A, entry 9).

To generalize the feasibility of the reaction, we examined different aldehydes (table 2.4A) including aromatic and aliphatic, bearing electron withdrawing as well as

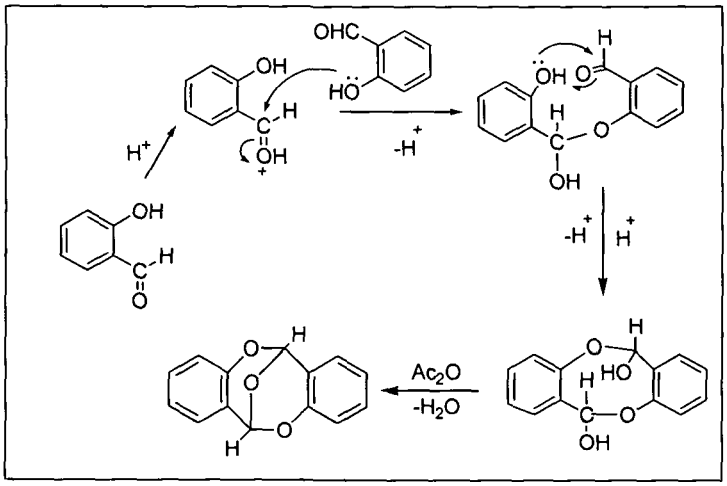
electron donating substituents, heteroatoms and α,β-unsaturated ones. We observed best catalytic activity in table 2.4A with both aromatic and aliphatic aldehydes (table 2.4A, *entry 11) to afford the corresponding 1,1-diacetates in good to excellent yields* within less time. Salicylaldehyde produced 85% yield (table 2.4A, entry 8) of anhydro dimer of o-hydroxybenzaldehyde (**Scheme-2.4A**) and minor amount of starting compound whereas sulfuric acid catalyzed method provides only 65% of the dimer [10-11]. The keto group of acetophenone and other aliphatic ketones such as cyclohexanone, acetone and butanone remained unreactive under the experimental condition (table 2.4A, entries 14-17) within 12 h, which showed the chemoselective nature of P4VP-$H_2SO_4$ catalyst for the protection of aldehyde to acylal group. The reaction of cinnamaldehyde formed (table 2.4A, entry 12) only 10% acylal product during 24 h. Furaldehyde, under the described (table 2.4A, entry 13) experimental conditions formed an unidentified polymer. The reaction of 1-naphthaldehyde showed 60% conversion (table 2.4A, entry 18) with 1:3 molar ratios of aldehyde and acetic anhydride in 2h. The increasing amount of acetic anhydride completed the reaction (table 2.4A, entry 19) within 30 min.

**Table 2.4A**: P4VP-$H_2SO_4$ catalyzed acylal formation of different aldehydes with acetic anhydride

| Entry | Substrate | Product | Time (min) | Yield[a] (%) | M.p. Reported (°C) | M.p. Found (°C) |
|---|---|---|---|---|---|---|
| 1 |  |  | 15 | 100 | 44-46[9] | 46 |
| 2 |  |  | 10 | 100 | 125[12] | 125 |
| 3 |  |  | 5 | 100 | 85.5-86.5[13] | 86 |
| 4 |  |  | 5 | 100 | 64-66[9] | 65 |
| 5 |  |  | 5 | 100 | 79-80[13] | 80 |
| 6 |  |  | 20 | 50 | 64-65[13] | 65 |
| 7 |  |  | 30 | 80 | 68-70[9] | 70 |

| | | | | | | |
|---|---|---|---|---|---|---|
| 8 |  |  | 5 | 85 | 130[11] | 128 |
| 9 |  |  | 19 h | 50 | 57[14] | 57 |
| 10 |  |  | 25 | 100[b] | 57 | 57 |
| 11 |  |  | 30 | 100 | Oil[15] | Oil |
| 12 |  |  | 24 h | 10 | 84-87[9] | 86 |
| 13 |  | - | 5 | Polymer | - | - |
| 14 |  | - | 12 h | NR | - | - |
| 15 |  | - | 12 h | NR | - | - |
| 16 |  | - | 12 h | NR | - | - |
| 17 |  | - | 12 h | NR | - | - |
| 18 |  |  | 2 h | 60 | 110[16] | 110 |
| 19 |  |  | 30 | 80[c] | 110 | 110 |

[a]All products were characterized by $^{1}H$ NMR, $^{13}C$ NMR, FT-IR and also their TLC comparison with authentic sample prepared by reported method.
[b]The reaction was carried out using 1:6 ratio of substrate and acetic anhydride.
[c]The reaction was carried out using 1:4 ratio of substrate and acetic anhydride.




**Scheme-2.4A** Mechanism of anhydro dimer formation from o-hydroxybenzaldehyde

Since the optimization studies identified another suitable condition for the synthesis of acylals in solvent-less medium under grinding method (table 1.4A, entry 9), therefore, we extended our investigation for different types of aldehydes in neat environment using mechanochemical energy by mortar and pestle with the optimized amount of catalyst. The results are summarized in **table 3.4A**.

**Table 3.4A**: Synthesis of acylals using solvent-less mechanochemical method

| Entry | Substrate | Time (min) | Product Yield[a] (%) |
|---|---|---|---|
| 1 | Benzaldehyde | 5 | 98 |
| 2 | 4-Nitrobenzaldehyde | 5 | 99 |
| 3 | 4-Chlorobenzaldehyde | 2 | 98 |
| 4 | 4-Methoxybenzaldehyde | 10 | 80 |
| 5 | 4-Hydroxybenzaldehyde | 15 | 95 |
| 6 | Pentanal | 10 | 97 |
| 7 | 1-Naphthaldehyde | 20[b] | 85 |
| 8 | Acetophenone | 2 h | NR |

[a]Isolated Yield, [b]1:4 ratio of aldehyde to $Ac_2O$

The data given in table 3.4A expressed higher activity of the catalyst in neat as compared to solution phase reaction at ambient temperature in terms of decreasing reaction time.

After completion of the reactions, the catalyst was recovered by filtration and reused for four times with minimal difference in yield (98-100%) in each cycle within five min for the reaction of m-nitrobenzaldehyde and acetic anhydride in dichloromethane (**Fig. 2.4A**). The FT-IR spectra of the used catalyst indicated similar absorption patterns with original IR spectra of P4VP-$H_2SO_4$ acid (**Fig-3.4A**).

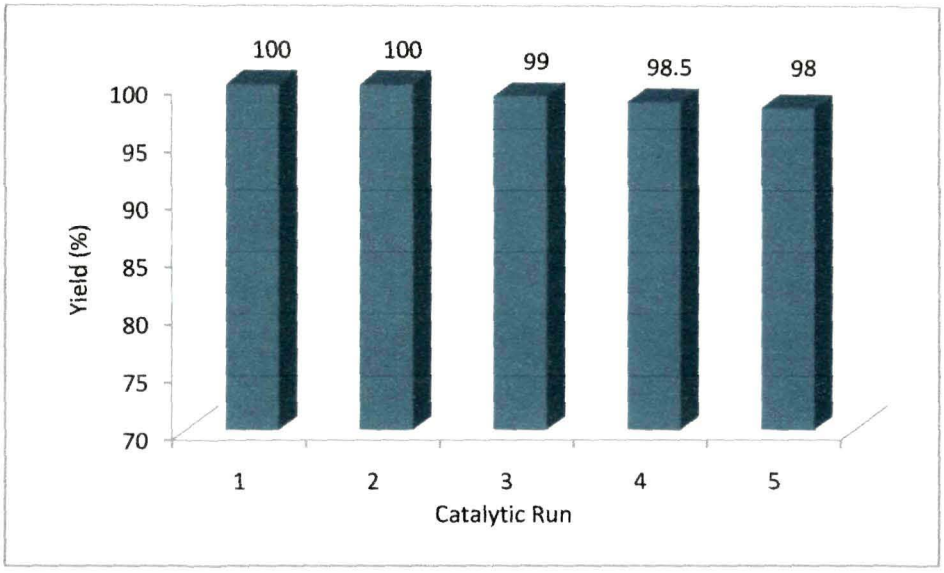



**Fig. 2.4A:** Reusability of P4VP-$H_2SO_4$ catalyst within 5 mins

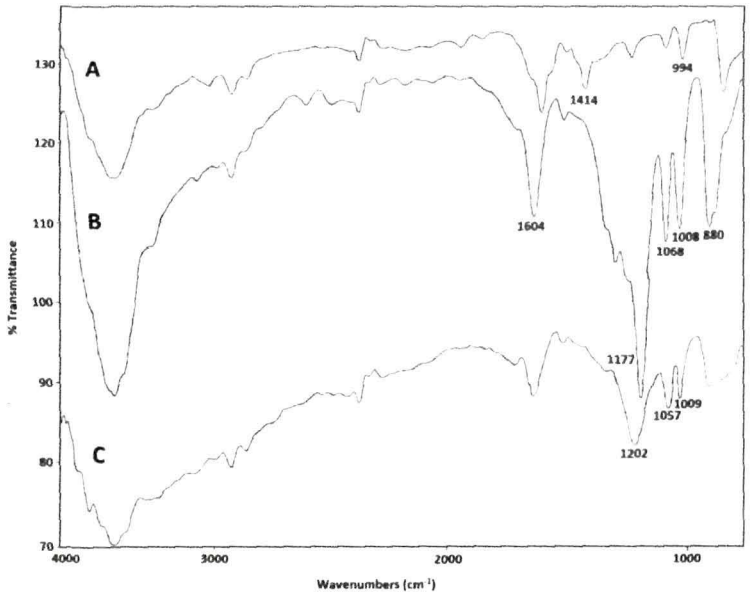
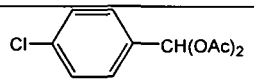
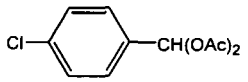
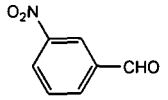
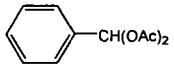
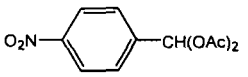
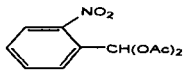
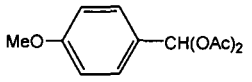
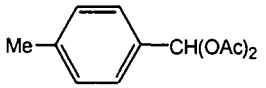
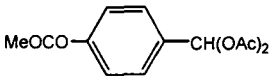
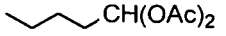
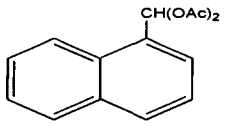



**Fig 3.4A**: FT-IR spectrum of P4VP (A), P4VP-$H_2SO_4$ (B) and reused P4VP-$H_2SO_4$ (C)

The catalyst was again tested for the deprotection of acylals to aldehydes. Table 4.4A shows the results of the deprotection of acylals to the corresponding aldehydes using catalytic amounts of P4VP-$H_2SO_4$ in acetonitrile at different temperatures. It was

observed that at room temperature the reaction takes more time (table 4.4A, entries 1, 4, 7, 8 and 10) to complete the conversion.

**Table 4.4A**: Deprotection of 1,1-diacetates to aldehydes in acetonitrile

| Entry | Substrate | Temp (°C) | Time (h) | Product | Product Yield (%)[a] |
|---|---|---|---|---|---|
| 1 |  | r.t. | 12 | 4-Chlorobenzaldehyde | 80 |
| 2 |  | 50 | 45 min | '' | 100 |
| 3 |  | 50 | 1 | m-Nitrobenzaldehyde | 100 |
| 4 |  | r.t. | 12 | Benzaldehyde | 85 |
| 5 |  | 50 | 1 | p- Nitrobenzaldehyde | 100 |
| 6 |  | 50 | 1 | o- Nitrobenzaldehyde | 100 |
| 7 |  | r.t. | 2.5 | p- Anisaldehyde | 80 |
| 8 |  | r.t. | 4 | p-Tolualdehyde | 85 |
| 9 |  | 50 | 45 min | p- Hydroxybenzaldehyde | 96 |
| 10 |  | r.t. | 1.5 | Pentanal | 100 |
| 11 |  | 50 | 1 | 1-Naphthaldehyde | 95 |

[a] Isolated yield.

## 4A.3. Conclusion

In this section, we have successfully demonstrated the catalytic activity of P4VP-$H_2SO_4$ and its use as a simple, eco-friendly, reusable and efficient heterogeneous acid catalyst for the chemoselective synthesis of 1,1-diacetates from aldehydes in dichloromethane at room temperature and in neat condition under mechanochemical treatment within few minutes. The protection of salicylaldehyde generated anhydro-dimer as single product under similar reaction condition. The catalyst is equally applicable for the deprotection of acylal in acetonitrile.

## 4A.4.Experimental Section

### 4A.4.1. General Information

All chemicals were purchased and used without further purification. The products were identified by comparison of their FT-IR, $^1H$ NMR spectroscopic data with those of authentic compounds (prepared by known method) and literature reported data [9, 11-16].

### 4A.4.2 Preparation of P4VP-$H_2SO_4$ catalyst

The solid acid catalyst, poly(4-vinylpyridine)-supported sulfuric acid (P4VP-$H_2SO_4$) was prepared by wet impregnation technique as already reported in literature [3]. 0.6 mL of $H_2SO_4$ was added to 500 mg of the polymer, i.e. poly(4-vinylpyridine). The entire mixture was then stirred in 5 mL of diethyl ether at room temperature for 15 minutes. After the complete formation of the catalyst, it was filtered and washed with diethyl ether for three times. Finally, drying at 70 °C for 2 h yielded the catalyst which can be stored in vacuum desiccator for further use. Characterization of the catalyst was done by Fourier transform–infrared (FT-IR) analysis.

### 4A.4.3 General procedure for the synthesis of 1,1-diacetates from aldehydes in solution:

The polymer supported catalyst 0.0326 mol% was added to a stirred solution of aldehyde (1 mmol), acetic anhydride (3 mmol) and dichloromethane (2 mL) in a 50 mL round bottom flask at room temperature. The progress of the reaction was monitored by thin layer chromatography (TLC). After completion, the mixture was

diluted with dichloromethane and filtered to recover the catalyst. The organic solution was washed with $NaHCO_3$ solution and dried over anhydrous sodium sulfate. The dichloromethane solution was evaporated under reduced pressure and the crude product was found to be almost pure product. All the compounds were characterized by taking $^1H$ NMR, $^{13}C$ NMR and FT-IR.

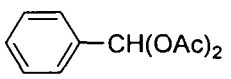
### 4A.4.4. General procedure for the preparation of acylals via mechanochemical method under solvent-free condition.

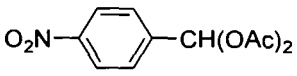
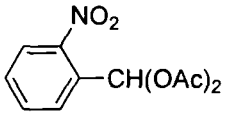
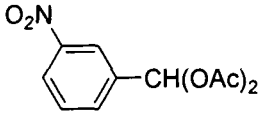
A mixture of 1 mmol of aldehyde and 3 mmol of acetic anhydride was grinded in a mortar and pestle in presence of 0.0326 mol% of P4VP-$H_2SO_4$ catalyst for the specified time. Thin layer chromatography (TLC) was observed to monitor the progress of the reaction. Once the completion of the reaction was confirmed, dichloromethane was added to the mixture and filtered to remove the catalyst. The organic solution was then thoroughly washed with $NaHCO_3$ solution and dried over anhydrous sodium sulfate. The organic layer was evaporated under reduced pressure, wherein the crude product was found in almost pure form. All the products were characterized using the same technique used for the previous procedure.

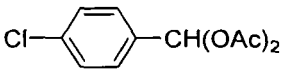
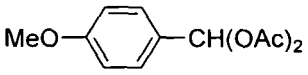
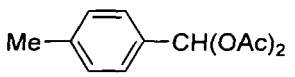
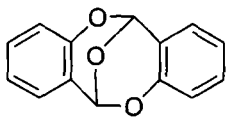
### 4A.4.5. General procedure for the deprotection of 1,1-diacetate to aldehydes.

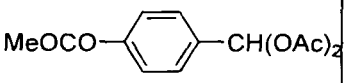
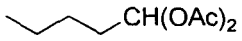
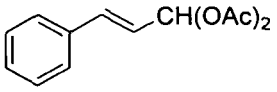
The polymer-supported catalyst (0.0326 mol%) was added to a stirred solution of 1,1-diacetate (1 mmol) in acetonitrile (4 mL) (at room temperature or 50 °C) in a 50-mL round-bottom flask with a reflux condenser. The progress of the reaction was monitored by TLC. After completion of the reaction, the catalyst was recovered by filtration, and the filtrate was extracted with dichloromethane and dried over anhydrous sodium sulfate. The dichloromethane solution was then evaporated under reduced pressure to give the corresponding aldehydes in pure form.

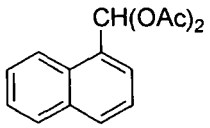
### 4A.4.6. Spectral data of 1,1-diacetate compounds

| | |
|---|---|
|   | **1,1-Diacetate-1-(phenyl)methane (Table 2.4A, Entry 1)**<br><br>White solid, m.p. 46 °C; $^1H$ NMR (400 MHz, $CDCl_3$) δ ppm: 2.12 (s, 6H), 7.38-7.43 (m, 3H), 7.50-7.53 (m, |

| | |
|---|---|
| | 2H), 7.68 (s, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ ppm: 20.9, 89.8, 126.7, 128.7, 129.6, 135.5, 168.7; FT-IR (KBr): 3041, 2928, 1758, 1596, 1439, 1368, 1244, 1202, 1054, 1003, 760 cm$^{-1}$. |
|  | **1,1-Diacetate-1-(4-nitrophenyl)methane (Table 2.4A, Entry 2)**<br>Faint yellow solid, m.p. 125 °C; $^1$H NMR (400 MHz, $CDCl_3$) δ ppm: 2.16 (s, 6H), 7.70 (s, 1H), 7.73 (d, $J$ = 9.1 Hz, 2H), 8.26 (d, $J$ = 9.1 Hz, 2H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ ppm: 20.8, 88.3, 123.9, 127.9, 141.9, 148.6, 168.6; FT-IR (KBr): 1761, 1530, 1356, 1204, 1059, 1012, 813 cm$^{-1}$. |
|  | **1,1-Diacetate-1-(2-nitrophenyl)methane (Table 2.4A, Entry 3)**<br>Faint yellow solid, m.p. 86 °C; $^1$H NMR (400 MHz, $CDCl_3$) δ ppm: 2.13 (s, 6H), 7.57-7.70 (m, 3H), 8.03-8.05 (m, 1H), 8.19 (s,1H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ ppm: 20.2, 85.7, 124.8, 127.6, 130.2, 133.3, 168; FT-IR (KBr): 2936, 2872, 1757, 1527, 1364, 1202, 1016, 970 cm$^{-1}$. |
|  | **1,1-Diacetate-1-(3-nitrophenyl)methane (Table 2.4A, Entry 4)**<br>Faint yellow solid, m.p. 65 °C; $^1$H NMR (400 MHz, $CDCl_3$) δ ppm: 2.14 (s, 6H), 7.57-7.61 (t, $J$ = 8 Hz, 1H), 7.72 (s, 1H), 7.83 (d, $J$ = 7.7 Hz, 1H), 8.24-8.28 (dd, $J$ = 8.2, 1.2 Hz, 1H), 8.39 (s, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ ppm: 20.9, 88.4, 122.0, 124.7, 129.8, 133.0, 137.6, 148.4, 168.7; FT-IR (KBr): 2963, 1760, 1533, 1358, 1255, 1203, 1091, 1016, 809, 685 cm$^{-1}$. |

| | |
|---|---|
|  | **1,1-Diacetate-1-(4-chlorophenyl)methane (Table 2.4A, Entry 5)**<br><br>White solid, m.p. 80 °C; $^{1}$H NMR (400 MHz, $CDCl_3$) δ ppm: 2.16 (s, 6H), 7.39 (d, $J$ = 8.2 Hz, 2H), 7.47 (d, $J$ = 8.2 Hz, 2H), 7.63 (s, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ ppm: 20.8, 89.07, 128.1, 128.8, 133.9, 135.7, 168.7; FT-IR (KBr): 1755, 1599, 1491, 1371, 1213, 1013, 821 $cm^{-1}$. |
|  | **1,1-Diacetate-1-(4-methoxyphenyl)methane (Table 2.4A, Entry 6)**<br><br>White solid, m.p. 65 °C; $^{1}$H NMR (400 MHz, $CDCl_3$) δ ppm: 2.13 (s, 6H), 3.83 (s, 3H), 6.90 (d, $J$ = 8.7 Hz, 2H), 7.45 (d, $J$ = 8.7 Hz, 2H), 7.60 (s, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ ppm: 19.8, 63.5, 107.2, 114.9, 129.6, 142.7, 163.2, 169.0; FT-IR (KBr): 3012, 2936, 1748, 1617, 1380, 1243, 1204, 1020, 937 $cm^{-1}$. |
|  | **1,1-Diacetate-1-(4-methylphenyl)methane (Table 2.4A, Entry 7)**<br><br>White solid, m.p. 70 °C; $^{1}$H NMR (400 MHz, $CDCl_3$) δ ppm: 2.11 (s, 6H), 2.43 (s, 3H), 7.25 (d, $J$ = 8.2 Hz, 2H), 7.35 (d, $J$ = 8.2 Hz, 2H), 7.64 (s, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ ppm: 19.9, 27.8, 89.6, 127.0, 130.6, 135.3, 143.1, 169.4; FT-IR (KBr): 2953, 1765, 1742, 1513, 1396, 1250, 1010, 957 $cm^{-1}$. |
|  | **6,12-Epoxydibenzo-6*H*,12*H*-dibenzo[b,f][1,5] dioxocin (Table 2.4A, Entry 8)**<br><br>White solid, m.p. 128 °C; $^{1}$H NMR (400 MHz, $CDCl_3$) δ ppm: 6.32 (s, 2H), 6.86 (d, $J$ = 8.2 Hz, 2H), 6.94 (ddd, $J$ = 0.92, 7.8, 8.2 Hz, 2H), 7.20-7.24 (m, 2H), 7.28 (dd, $J$ = 1.36, 7.3 Hz, 2H); $^{13}$C NMR (100 MHz, |

| | |
|---|---|
| | $CDCl_3$) δ ppm: 89.1, 115.6, 118.9, 120.5, 126.5, 129.9, 149.5; FT-IR (KBr): 3441, 2922, 1592, 1484, 1325, 1219, 1108, 951, 752 $cm^{-1}$. |
|  | **1,1-Diacetate-1-(4-acetoxyphenyl)methane (Table 2.4A, Entry 9)**<br><br>Faint yellow solid, m.p. 57 °C; $^1H$ NMR (400 MHz, $CDCl_3$) δ ppm: 2.1 (s, 6H), 2.19 (s, 3H), 7.16 (d, $J$ = 8.1 Hz, 2H), 7.42 (d, $J$ = 8.1 Hz, 2H), 7.56 (s, 1H); $^{13}C$ NMR (100 MHz, $CDCl_3$) δ ppm: 19.7, 20.0, 88.2, 120.7, 127.1, 133.0, 150.6, 167.7, 168.2; FT-IR (KBr): 2942, 2838, 1762, 1703, 1596, 1369, 1203, 1060, 1004, 915 $cm^{-1}$. |
|  | **1,1-Diacetoxy Pentane (Table 2.4A, Entry 11)**<br><br>Colourless oil, $^1H$ NMR (400 MHz, $CDCl_3$) δ ppm: 0.91 (t, $J$ = 6.9 Hz, 3H), 1.35-1.37 (m, 4H), 1.75-1.78 (m, 2H), 2.08 (s, 6H), 6.78 (t, $J$ = 5.5 Hz, 1H); $^{13}C$ NMR (100 MHz, $CDCl_3$) δ ppm: 13.9, 20.8, 22.3, 25.8, 32.9, 90.6, 169; FT-IR (KBr): 2953, 2870, 2381, 1759, 1441, 1371, 1247, 1208, 1114, 1004 $cm^{-1}$. |
|  | **1,1-Diacetoxy-3-phenylprop-2-ene (Table 2.4A, Entry 12)**<br><br>White solid, m.p. 86 °C; $^1H$ NMR (400 MHz, $CDCl_3$) δ ppm: 2.06 (s, 6H), 6.67-6.72 (m, 2H), 7.26 (s, 1H), 7.40-7.42 (m, 5H); $^{13}C$ NMR (100 MHz, $CDCl_3$) δ ppm: 21.0, 89.6, 121.5, 127.1, 128.7, 128.9, 135.1, 135.5, 168.9; FT-IR (KBr): 3080, 3036, 2988, 2931, 1759,1375, 1241, 1198, 1138, 1063, 993 $cm^{-1}$. |

| | |
|---|---|
|   | **1,1-Diacetate-1-(naphthyl)methane(Table 2.4A, Entry 18 )**<br><br>White solid, m.p. 110 °C; $^{1}$H NMR (400 MHz, $CDCl_3$) δ ppm: 2.10 (s, 6H), 7.46-7.58 (m, 3H), 7.72-7.74 (m, 1H), 7.87-7.90 (m, 2H), 8.18-8.20 (m, 1H), 8.22 (s, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ ppm: 21.9, 105.8, 120.7, 124.6, 125.9, 126.6, 128.1, 128.7, 129.2, 132.0, 134.6, 138.5, 168.8; FT-IR (KBr): 2928, 1764, 1740, 1514, 1370, 1237, 1203, 940, 738 $cm^{-1}$. |

## References


1. Price, P. M., et al. *J. Chem. Soc., Dalton Trans.* (2), 101--110, 2000.

2. Benaglia, M., et al. *Chem. Rev.* **103** (9), 3401--3429, 2003.

3. Borah, K. J., et al. *Bull. Korean Chem. Soc.* **32** (1), 225--228, 2011.

4. Lee, B. S., et al. *Tetrahedron* **61** (12), 3081--3086, 2005.

5. Friedrich, H. B. & Singh, N. *Cat. Lett.* **110** (1-2), 61--70, 2006.

6. Malynych, S., et al. *J. Phys. Chem. B* **106** (6), 1280--1285, 2002.

7. Greene, T. W. & Wuts, P. G. M. *Protective Groups in Organic Synthesis*, 3rd ed., Wiley Interscience, New York, USA, 1999, 306.

8. Gregory, M. J. *J. Chem. Soc. B* 1201--1207, 1970.

9. Kochhar, K. S., et al. *J. Org. Chem.* **48** (10), 1765--1767, 1983.

10. Kulkarni, V. S. & Hosangadi, B. D. *Synth. Commun.* **16** (2), 191--193, 1986.

11. Palacios-Grijalva, L. N., et al. *Molecules* **14** (10), 4065--4078, 2009.

12. Deka, N., et al. *J. Org. Chem.* **62** (5), 1563--1564, 1997.

13. Li, Y. Q. & Cheng, L. H. *Chin. Chem. Lett.* **12** (7), 565--568, 2001.

14. Khan, A. T., et al. *J. Mol. Catal. A: Chem.* **255** (1-2), 230--235, 2006.

15. Fan, D-H., et al. *Molecules* **15** (9), 6493--6501, 2010.

16. Jermy, B. R. & Pandurangan, A. *Catal. Commun.* **9** (5), 577--583, 2008.

# Section 4B

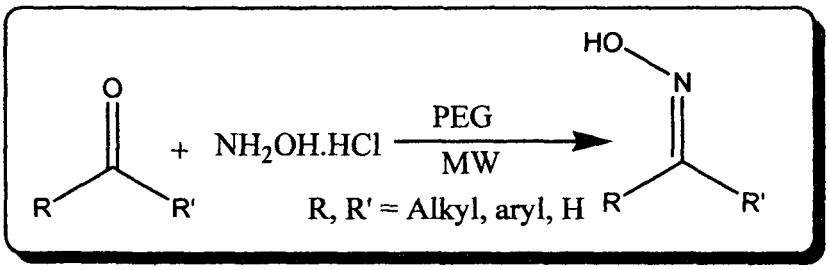
## Dual Nature of Polyethylene Glycol under Microwave Irradiation for the Clean Synthesis of Oximes

### 4B.1. Introduction

The wide use of microwave energies in organic synthesis simplifies the complicated purification steps through the formation of selective product and thus eliminating laborious chromatographic separation with organic solvents. This method provides excellent yields in lesser time as compared to thermal treatment which was already mentioned in the review chapter [1]. We also discussed the applications of polyethylene glycols and their solutions as alternative reaction media to volatile organic solvents (VOCs) in organic synthesis in the first chapter. Development of a synthetic protocol for organic transformation with alternative reaction media of VOCs remains an ever-challenging objective [2-3]. The unique solvent properties, higher solubilizing power and cation coordination ability of polyethylene glycol (PEGs) solutions make them extensively useful as green solvents and phase transfer catalysts in organic synthesis [4]. Polyethylene glycols are inexpensive, non-ionic, thermally stable, non-toxic, and recoverable media by phase separation method. Unlike volatile organic compounds, low molecular weight liquid PEGs are non volatile, low flammability, and biodegradable. PEG has been found to be stable to acid, base and high temperature [5-6]. Both liquid and solid PEGs are highly soluble in water. Lower PEGs can be used as solvents in their own right with or without addition of water. PEGs exhibit different solubility in organic solvents which help them to induce precipitation of PEGs from reaction mixture in organic solvent for purification. The combined use of microwaves (MW) with PEGs as reaction media can accelerate organic reactions by the selective absorption of microwave energy by polar molecules. The short reaction time and selective product formation offered by microwave assisted synthesis are suited to meet the increased demands in environmentally benign protocols.

The synthesis of oximes from aldehydes and ketones is a valuable organic transformation, because of their higher thermal stability to use as protecting groups [7] and also as reaction intermediate for the synthesis of amides [8], nitriles [9], nitro

compounds [10] and amines [11]. A large number of methods [12-16] with different limitations have been reported in the literature for the preparation of oximes catalyzed by both acids and bases. By observing the advantageous positions of PEG as reaction medium or catalyst in organic synthesis under microwave irradiation, we decided to study the synthesis of oxime in PEG-400 and PEG-600 as recyclable homogeneous reaction medium / catalyst (**Scheme-1.4B**) from aldehydes and ketones with hydroxylamine hydrochloride under microwave irradiation and thermal treatment without use of acid and base catalysts.




**Scheme-1.4B**

## 4B.2. Results and Discussion

Our efforts began with the synthesis of benzophenone oxime from benzophenone (3 mmol) and hydroxylamine hydrochloride (3 mmol) in PEG-200, 400 and 600 (**table 1.4B**) respectively as reaction media under microwave irradiation. From these results, PEG-600 was found to be the best medium (**Fig.1.4B**) for the oxime synthesis.

**Table 1.4B**: Optimization of the reaction condition with PEGs for the synthesis of benzophenone oxime under microwave irradiation within 5 min at different temperatures

| Entry | MW power (W) | Amount of PEG (mL) | Temp. (°C) | [a,b] Product yield (%) | | |
|---|---|---|---|---|---|---|
| | | | | PEG-200 | PEG-400 | PEG-600 |
| 1 | 280 | 1 | 64 | 25 | 30 | 65 |
| | | 0.5 | | | 29 | 65 |
| 2 | 350 | 1 | 67 | 30 | 40 | 94 |
| | | 0.5 | | | 40 | 94 |
| 3 | 420 | 1 | 70 | 40 | 55 | 95 |
| | | 0.5 | | | 54 | 94 |
| 4 | 490 | 1 | 75 | 45 | 75 | 95 |

| | | | | | | |
|---|---|---|---|---|---|---|
| | | 0.5 | | | 74 | 95 |
| 5 | 560 | 1 | 79 | 50 | 85 | 95 |
| | | 0.5 | | | 84 | 94 |
| 6 | 560 | 0 | 66 | - | - | - |

[a] Isolated yield, [b] Using 3 mmol of benzophenone and 3 mmol of hydroxylamine hydrochloride in PEGs.

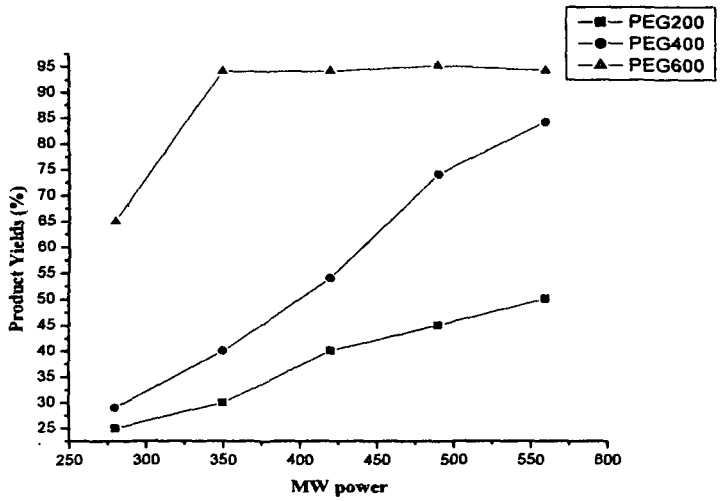



**Fig. 1.4B**: Comparison of the yields of benzophenone oxime against microwave powers in 0.5 mL of PEGs

The catalytic activity of polyethylene glycol for this reaction was again investigated using 0.5 and 1 mL of PEGs at different power levels of microwave energy. With increasing microwave energies, we observed increase yields of the product (table 1.4B) within the temperature range of 64-79°C which were found to be the same in both 0.5 and 1 mL of PEG (table 1.4B, entries 1-5). Increasing microwave power causes more collisions of substrate molecules in PEGs by dipolar ionization mechanism which are expressed as rise in the reaction temperature. Without PEG, no product formation also observed at higher power level (table 1.4B, entry 6). All observations indicate that the hydrophilic nature of PEGs is the driving force for this reaction under microwave energy to behave PEGs as medium and catalyst.

**Table 2.4B**: Synthesis of oximes in PEG-600 under microwave energy and conventional heating

| Entry | Ketone | MW (W) | Temp. (°C) | Product m.p./°C (lit)[a] | Time (mins) | | Product Yields[b] (%) | | |
|---|---|---|---|---|---|---|---|---|---|
| | | | | | A | B | A TOF[c] (% Conversion)[d] | B | B TOF[c] (% Conversion)[d] |
| 1 | Cyclohexanone | 280 | 60 | 87 (91) | 2 | 30 | 90 | 165.2(45.9) | 65 | 6.5(1.8) |
| 2 | Acetophenone | 280 | 60 | 58 (59) | 5 | 50 | 91 | 42.1(11.7) | 50 | 0 |
| 3 | Acetone | 280 | 42 | 59 (60) | 2 | 20 | 88 | 159.4(44.3) | 65 | 9.7(2.7) |
| 4 | Benzophenone | 350 | 67 | 143 (144) | 5 | 2h | 94 | 54(15) | 70 | 0 |
| 5 | Cyclopentanone | 280 | 70 | 54 (55) | 3 | 50 | 95 | 106.5(29.6) | 60 | 3.96(1.1) |
| 6 | Ethyl methyl ketone | 280 | 44 | Liq. (-30) | 3 | 30 | 85 | 102.6(28.5) | 50 | 5.4(1.5) |
| 7 | Benzophenone | - | 25 | - | - | 24h | - | - | NR | - |
| 8 | Acetophenone[e] | 280 | 61 | - | 5 | - | NR | - | - | - |

A: MW method, B: Thermal method; [a]Literature data [17-20]; [b]Isolated yields;

[c]Turnover frequency = (mmol of product/amount of PEG in mL) $h^{-1}$; [d]Conversion calculated with GC analysis during the first 1 minute; [e]No addition of PEG.

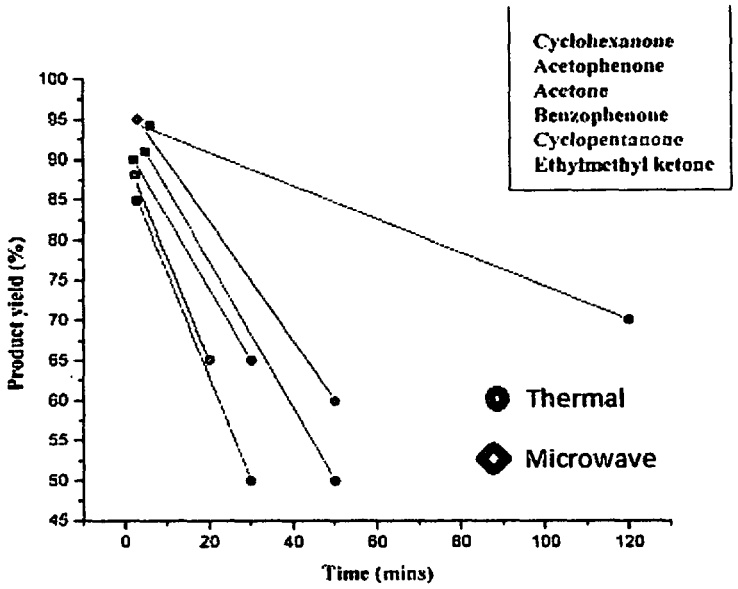
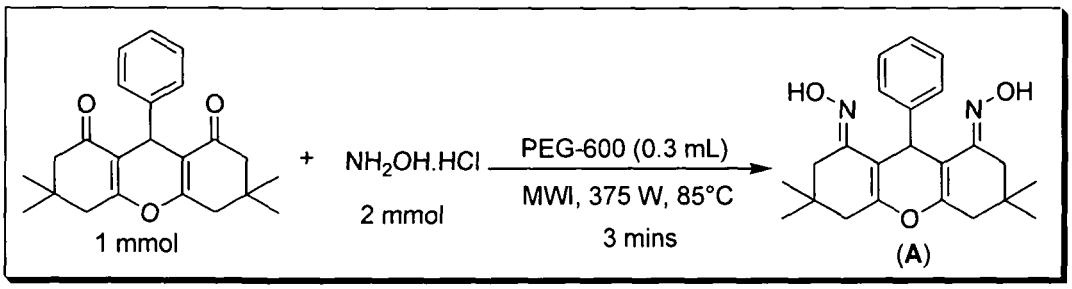



**Fig. 2.4B**: Graphical representation of thermal and microwave assisted reactions in PEG-600 for the synthesis of oximes with different keto compounds

After optimization of the reaction condition with 3 mmol of ketone, 3 mmol of hydroxylamine hydrochloride and 0.5 mL of PEG-600, we extended the above synthesis to different aliphatic and aromatic keto compounds using both thermal and microwave energies (**table 2.4B**) for comparative studies. The graphical presentation (**Fig. 2.4B**) of product yields against reaction times for both methods shows that thermal treatment consumes more time as compared to MWI for the synthesis of oximes. However no product was obtained if the reaction carried out at room temperature (table 2.4B, entry 7) stirring. The reaction of acetophenone did not give any product in absence of 0.5 mL of PEG under microwave irradiation (280 W) for 5 minutes (table 2.4B, entry 8). The turnover frequencies (TOF) were determined by knowing the percentage conversion from GC analysis at the initial time for all reactions. The thermal condition gave lower TOF and less yields of product at the same temperature with microwave irradiation (**table 2.4B**). We observed higher TOF for all aliphatic keto compounds (table 2.4B, entries 1, 3, 5, 6) as compared to aromatic keto compounds (table 2.4B, entries 2, 4) under microwave energies. All keto compounds yielded excellent results within 2-5 min reaction time (table 2.4B). The results for the synthesis of aldoximes from aliphatic and aromatic aldehydes using standard condition are included in **table 3.4B**. In presence of strong electron donating groups, the aldehyde molecules were found to be inactive (table 3.4B, entries 8-9) at higher microwave energies. All other aldehyde molecules yielded good

to better results within 2-6 min at different microwave energies (**table 3.4B**). The turnover frequencies also increased in case of 4-nitrobenzaldehyde and 4-chlorobenzaldehyde respectively with increase of the microwave power from 280W to 350 W (table 3.4B, entries 4,7).

As the above optimized reaction condition was successful for the oximation of cycloalkanones (table 2.4B, entries 1, 4), so we were interested to carry out the same reaction for the synthesis of oxime of 1, 8-dioxo-octahydroxanthene derivative in PEG-600 under microwave irradiation (**Scheme-2.4B**).




**Scheme-2.4B: Synthesis of oxime of 9-phenyl-3,3,6,6-tetramethyl-1, 8-dioxo-octahydroxanthene**

The substrate 9-phenyl-3, 3, 6, 6-tetramethyl-1,8-dioxo-octahydroxanthene was already synthesized in chapter 3. The reaction produced 82% yield of oxime (A) at 375 W (85 °C) within 3 min which was again purified by preparative thin layer chromatography for spectroscopic analysis.

The used PEG is recovered from the aqueous solution by evaporation of water under reduced pressure and again used for next cycle of reaction without loss of activity. The same recovered PEG is utilized for five cycles of reactions for the preparation of benzophenone oxime (**Fig. 3.4B**).

**Table 3.4B**: Synthesis of aldoximes in PEG-600 under microwave energies

| Entry | Aldehydes | MW (W) | Temp. (°C) | Time (min) | Product m.p.(°C) (lit)[a] | Product Yields[b] (%) | TOF[c] (% Conversion)[d] |
|---|---|---|---|---|---|---|---|
| 1 | Benzaldehyde | 280 | 60 | 2 | liq.(-35) | 90 | 158.7 (44.1) |
| 2 | 2-Nitrobenzaldehyde | 350 | 70 | 3 | 97(98) | 98 | 123.2(34.2) |
| 3 | 4-Nitrobenzaldehyde | 280 | 70 | 5 | 132(133) | 98 | 70.2(19.5) |
| 4 | 4-Nitrobenzaldehyde | 350 | 75 | 2 | 132(133) | 97 | 177.1 (49.2) |
| 5 | 3-Nitrobenzaldehyde | 560 | 65 | 5 | 121(122) | 70 | 268(74.5) |
| 6 | 4-Chlorobenzaldehyde | 280 | 62 | 6 | 105(107) | 80 | 48.6(13.5) |
| 7 | 4-Chlorobenzaldehyde | 350 | 66 | 2 | 105(107) | 96 | 332.2(92.3) |
| 8 | 4-Hydroxybenzaldehyde | 560 | 60 | 5 | - | NR | 0 |
| 9 | 4-Methoxybenzaldehyde | 560 | 56 | 5 | - | NR | 0 |
| 10 | 4-Methylbenzaldehyde | 490 | 65 | 5 | 78(80) | 75 | 77.4(21.5) |
| 11 | Furaldehyde | 490 | 75 | 2 | 71(72) | 97 | 243.3(67.6) |
| 12 | Cinnamaldehyde | 490 | 76 | 2 | 137(139) | 85 | 153(42.5) |
| 13 | Butanal | 350 | 78 | 2 | -(29) | 94 | 169.2(47) |
| 14 | Pentanal | 350 | 80 | 2 | -(52) | 96 | 173.5(48.2) |
| 15 | D-Glucose | 280 | 65 | 2 | - | Decom-posed | - |
| 16 | Acrolein | 280 | 50 | 2 | - | Polymeric product | - |
| 17 | 2,2-Dimethyl 1,3-dioxolane 4-carbaldehyde | 350 | 70 | 3 | - | trace | - |

[a]Literature data [17-20]; [b]Isolated yields; [c]Turnover frequency = (mmol of product/amount of PEG in mL) $h^{-1}$ ; [d]Conversion calculated with GC analysis during the first 1 minute.

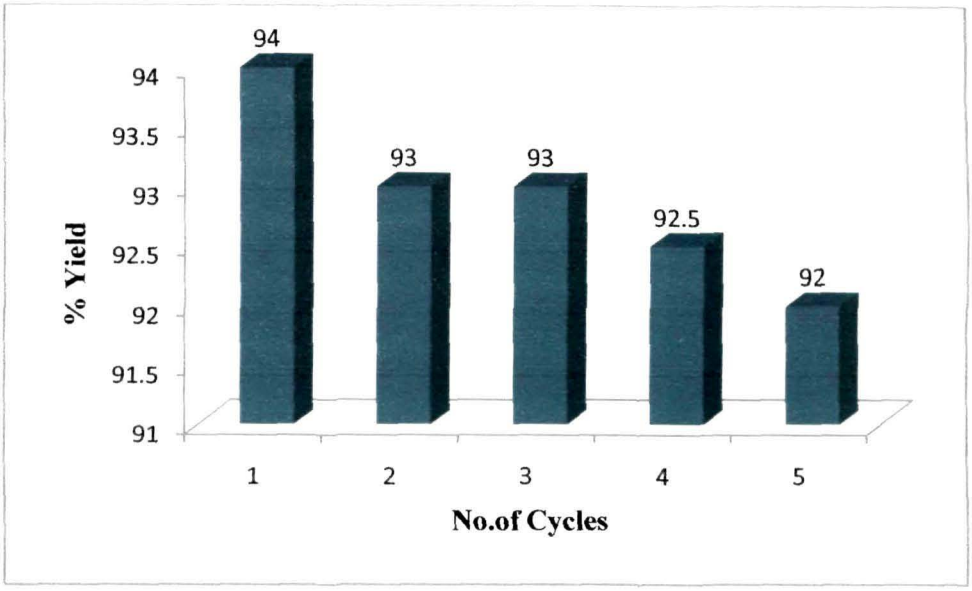



**Fig. 3.4B**: Reusability chart of PEG for the preparation of benzophenone oxime.

## 4B.3. Conclusion

The work focuses on the use of dual nature of PEGs as efficient, inexpensive and recyclable homogeneous medium and catalyst under microwave irradiation for the synthesis of oximes from carbonyl compounds and hydroxylamine hydrochloride. This method offers a rapid and clean alternative and reduces reaction times which fulfill several aspects of green chemistry.

## 4B.4. Experimental Section

### 4B.4.1. General Information

The same analytical instruments already mentioned in the **Section-4A** were also utilized for taking NMR, FT-IR and melting point of various products. The GC-MS spectra and percentage conversion for TOF in the initial time were recorded in the apparatus from Perkin Elmer Clarus 600.

### 4B.4.2. General procedure for the synthesis of oximes under microwave irradiation / conventional heating:

A finely powdered mixture of 3 mmol of aldehyde or ketone and 3 mmol of hydroxylamine hydrochloride in 0.5 mL of PEG-600 was placed in an open glass tube (or heated classically in oil bath) in a mono mode microwave reactor (Catalyst

System) and irradiated at various power levels with the monitoring (digital) of specified temperature. The progress of the reaction was observed using thin layer chromatography. After completion, the reaction mixture was diluted with 5 mL of distilled water and extracted the product from the aqueous solution with diethyl ether (3 x 4 mL) or any other organic solvent (which one is applicable). The ether extract was dried over anhydrous $Na_2SO_4$ and evaporated under reduced pressure. For spectroscopic analysis, the product is further purified by TLC techniques using hexane and ethyl acetate as mobile phases. The recovered PEG retained its activity for several cycles. All synthesized products reported in literature [17-20] and are fully characterized by spectral analysis.

## 4B.4.3. Spectraldata ofoximes:

**Cyclohexanone oxime (Table 2.4B, Entry1)**

Gray crystal, m.p. 87 °C; $^1$H NMR (400 MHz, $CDCl_3$) δ ppm: 1.61-1.69 (m, 6H), 2.24 (t, 2H, *J*= 5.4, 6.8 Hz), 2.53 (t, 2H, *J*= 5.4, 6.8 Hz); $^{13}$C NMR (100 MHz, $CDCl_3$) δ ppm: 24.5, 25.7, 25.9, 27.0, 29.8, 32.2, 160.8; FT-IR (KBr): 3394, 2924, 1718, 1640, 1456, 1353, 1100, 946 $cm^{-1}$.

**Acetophenone oxime (Table 2.4B, Entry 2)**

Brown solid, m.p. 58 °C; $^1$H NMR (400 MHz, $CDCl_3$) δ ppm: 2.3 (s, 3H), 7.36-7.39 (m, 3H), 7.60-7.63 (m, 2H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ ppm: 12.4, 126.1, 128.6, 129.3, 136.6, 156.1; FT-IR (KBr): 3461, 2927, 2367, 1642, 1448, 1371, 1296, 1004, 920,759 $cm^{-1}$.

**Acetone oxime (Table 2.4B, Entry 3)**

White crystal, m.p. 59 °C; $^1$H NMR (400 MHz, $CDCl_3$) δ ppm: 1.9 (s, 6H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ ppm: 15.0, 21.8, 155.6; FT-IR (KBr): 3456, 2920, 2377, 1637, 1436, 1367, 1262, 1065, 978, 924, 804 $cm^{-1}$.

**Benzophenone oxime (Table 2.4B, Entry 4)**

White solid, m.p. 143 °C; $^1$H NMR (400 MHz, $CDCl_3$) δ ppm: 1.67 (br, 1H), 7.34-7.48 (m, 6H), 7.80-7.82 (m, 4H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ ppm: 127.9, 128.3,

128.4, 128.43, 129.3, 130.2, 136.6, 158.1; FT-IR (KBr): 3240, 2920, 2375, 1630, 1441, 1322, 1161, 995, 920, 766, 695 $cm^{-1}$.

**Cyclopentanone oxime (Table 2.4B, Entry 5)**

Faint brown solid, m.p. 54 °C; $^1H$ NMR (400 MHz, $CDCl_3$) δ ppm: 1.70-1.76 (m, 4H), 2.36-2.38 (m, 2H), 2.44-2.46 (m, 2H); $^{13}C$ NMR (100 MHz, $CDCl_3$) δ ppm: 24.6, 25.2, 27.2, 31.9, 160.2; FT-IR (KBr): 3392, 2897, 1685, 1474, 1289, 1210, 1152, 936, 787 $cm^{-1}$.

**Butan-2-one oxime (Table 2.4B, Entry 6)**

Colourless liquid, $^1H$ NMR (400 MHz, $CDCl_3$) δ ppm: 1.04 (t, $J$ = 7.2 Hz, 3H), 1.41 (q, $J$ = 7.1 Hz, 2H), 1.9 (s, 3H); $^{13}C$ NMR (100 MHz, $CDCl_3$) δ ppm: 8.7, 18.4, 31.7, 159.2; FT-IR (KBr): 3426, 3289, 2917, 1629, 1512, 1461, 1356, 1241, 1104, 946, 833, 761 $cm^{-1}$.

**Benzaldehyde oxime (Table 3.4B, Entry 1)**

Pale yellow liquid, $^1H$ NMR (400 MHz, $CDCl_3$) δ ppm: 7.35-7.42 (m, 3H), 7.52-7.54 (m, 2H), 8.3 (s, 1H), 9.16 (brs, 1H); $^{13}C$ NMR (100 MHz, $CDCl_3$) δ ppm: 126.4, 128.2, 130.1, 131.2, 150.2; FT-IR (KBr): 3300, 3059, 1450, 1305, 1213, 948, 872, 754 $cm^{-1}$.

**2-Nitrobenzaldehyde oxime (Table 3.4B, Entry 2)**

Brown solid, m.p. 97 °C; $^1H$ NMR (400 MHz, $CDCl_3$) δ ppm: 7.62 (t, $J$ = 8.1 Hz, 1H), 7.66 (t, $J$ = 7.8 Hz, 1H), 7.90 (d, $J$ = 7.8 Hz, 1H), 7.95 (d, $J$ = 8.1 Hz, 1H), 8.35 (s, 1H), 9.18 (brs, 1H); $^{13}C$ NMR (100 MHz, $CDCl_3$) δ ppm: 123.1, 126.7, 131.5, 132.6, 135.6, 149.0, 149.7; FT-IR (KBr): 3328, 3085, 1603, 1530, 1425, 1355, 1270, 1183, 1079, 1040, 970, 959, 830, 752 $cm^{-1}$.

**4-Nitrobenzaldehyde oxime (Table 3.4B, Entry 3)**

Pale orange solid, m.p. 132 °C; $^1H$ NMR (400 MHz, $CDCl_3$) δ ppm: 7.95 (d, $J$ = 8.8 Hz, 2H), 8.17 (s, 1H), 8.40 (d, $J$ = 8.7 Hz, 2H), 9.95 (s, 1H); $^{13}C$ NMR (100 MHz, $CDCl_3$) δ ppm: 120.8, 121.2, 129.8, 130.4, 140.5, 148.8, 151.6; FT-IR (KBr): 3334, 3078, 2937, 1925, 1802, 1600, 1534, 1348, 1211, 1102, 967, 843, 745 $cm^{-1}$.

**3-Nitrobenzaldehyde oxime (Table 3.4B, Entry 5)**

Light brown solid, m.p. 121 °C; $^1$H NMR (400 MHz, $CDCl_3$) δ ppm: 7.71 (d, $J$ = 8.2 Hz, 1H), 7.93 (d, $J$ = 8.3 Hz, 1H), 8.16 (s, 1H), 8.27-8.34 (m, 2H), 9.87 (s, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ ppm: 123.8, 124.3, 130.5, 135.2, 136.0, 148.7, 149.5; FT-IR (KBr): 3305, 3097, 1605, 1527, 1458, 1384, 1302, 1290, 1191, 1074, 1053, 976, 955, 924, 883, 824 $cm^{-1}$.

**4-Chlorobenzaldehyde oxime (Table 3.4B, Entry 6)**

Pale yellow solid, m.p. 105 °C; $^1$H NMR (400 MHz, $CDCl_3$) δ ppm: 7.45 (d, $J$ = 8.6 Hz, 2H), 7.56 (d, $J$ = 8.7 Hz, 2H), 8.20 (s, 1H), 8.97 (brs, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ ppm: 128.3, 129.0, 130.6, 135.9, 149.4; FT-IR (KBr): 3309, 2922, 1496, 1090, 974, 877, 830, 699 $cm^1$.

**4-Methylbenzaldehyde oxime (Table 3.4B, Entry 10)**

White solid, m.p. 78 °C; $^1$H NMR (400 MHz, $CDCl_3$) δ ppm: 2.37 (s, 3H), 7.24 (d, $J$ = 7.6 Hz, 2H), 7.49 (d, $J$ = 7.7 Hz, 2H), 8.16 (s, 1H), 8.88 (brs, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ ppm: 21.5, 127.0, 129.3, 130.2, 140.5, 151.2; FT-IR (KBr): 3285, 2927, 1452, 1209, 1110, 957, 820 $cm^{-1}$.

**2-Furaldehyde oxime (Table 3.4B, Entry 11)**

Brown solid, m.p. 71 °C; $^1$H NMR (400 MHz, $CDCl_3$) δ ppm: 6.48-6.52 (m, 1H), 7.32-7.36 (m, 1H), 7.52(m, 1H), 8.02 (s, 1H), 9.88 (brs. 1H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ ppm: 111.5, 135.0, 145.1, 150.2; FT-IR (KBr): 3309, 2910, 1615, 1499, 1212, 1020, 901, 840 $cm^{-1}$.

**Cinnamaldehyde oxime (Table 3.4B, Entry 12)**

Pale orange solid, m.p. 137 °C; $^1$H NMR (400 MHz, $CDCl_3$) δ ppm: 6.85-7.40 (m, 2H), 7.50-7.58 (m, 5H), 7.95-8.03 (m, 1H), 10.2 (s, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ ppm: 126.7, 127.2, 128.4, 128.5, 129.1, 129.6, 135.7, 143.2, 151.6; FT-IR (KBr): 3388, 3057, 2877, 2218, 1671, 1619, 1491, 1448, 1298, 1204, 1124, 972, 750, 692 $cm^{-1}$.

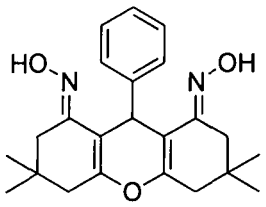
**Butanal oxime (Table 3.4B, Entry 13)**

Colourless semi solid, $^1$H NMR (400 MHz, $CDCl_3$) δ ppm: 0.98 (t, $J$ = 7.3 Hz, 3H), 1.35 (m, 2H), 1.58 (m, 2H), 7.37 ( m, 1H), 8.86 (brs,1H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ ppm: 14.9, 19.2, 32.7, 153.1; FT-IR (KBr): 3391, 2956, 2874, 1648, 1458, 1355, 1295, 1252, 1107, 947 cm$^{-1}$.

**Pentanal oxime (Table 3.4B, Entry 14)**

Light brown liquid,$^1$H NMR (400 MHz, $CDCl_3$) δ ppm: 1.21 (t, $J$ = 7.2 Hz, 3H), 1.32-1.35 (m, 4H), 1.55-1.57 (m, 2H), 7.42 (m, 1H), 9.20 (brs, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ ppm: 14.5, 24.3, 28.5, 31.3, 153.2; FT-IR (KBr): 3424, 2951, 2871, 1640, 1458, 1353, 1251, 1106, 950, 847 cm$^{-1}$.

**9-Phenyl-3, 3, 6, 6-tetramethyl-1,8-dioxo-octahydroxanthene oxime (A)**




Yellowish brown viscous liquid, $^1$H NMR (400 MHz, $CDCl_3$) δ ppm: 1.3 (s, 12H), 2.1 (s, 4H), 2.2 (s, 4H), 3.64 (d, $J$ = 16.5 Hz, 1H), 7.20-7.26 (m, 5H), 7.82 (br, 1H), 8.37 (br, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ ppm: 29.3, 29.4, 29.7, 31.9, 37.4, 40.9, 50.7, 104.8, 126.0, 128.1, 128.4, 146.5, 155.2, 156.4; FT-IR (KBr): 3425, 3230, 2926, 2860, 2375, 2279, 1638, 1422, 1265, 1168, 1077, 993, 803 cm$^{-1}$; CHN analysis: Calculated for $C_{23}H_{28}N_2O_3$ (%): C 72.63, H 7.36, N 7.36, Found: C 71.91, H 7.68, N 6.86.

# References


1. Lidström, P., et al. *Tetrahedron* **57** (45), 9225--9283, 2001.
2. Anastas, P. T. & Warner, J. C. *Green Chemistry, Theory and Practice*, Oxford University Press, Oxford, 1998.
3. Clark, J. H. & Macquarrie, D. J. *Handbook of Green Chemistry & Technology*, Wiley-Blackwell, New York, 2002.
4. Chen, J., et al. *Green Chem.* **7** (2), 64--82, 2005.
5. Chen, J., et al. *Ind. Eng. Chem. Res.* **43** (17), 5358--5364, 2004.
6. Guo, Z., et al. *Ind. Eng. Chem. Res.* **41** (10), 2535--2542, 2002.
7. Greene, T. W. and Wuts, P. G. M. *Protective Groups in Organic Synthesis*, 3rd ed., Wiley-Interscience Publication John Wiley & Sons, Inc., New York, 1999.
8. Park, S., et al. *Chem. Commun.* (15) 1936--1937, 2003.
9. Dewan, S. K., et al. *Arkivoc* (2), 41--44, 2006.
10. Ballistreri, F. P., et al. *Synlett* (11), 1093--1094, 1996.
11. Negi, S., et al. *Synthesis* (8), 991--996, 1996.
12. Olah, G. A. & Keumi, T. *Synthesis* (2), 112--113, 1979.
13. Sosnovsky, G., et al. *Synthesis* (9), 722--724, 1979.
14. Miller, C. P. & Kaufman, D. H. *Synlett* (8), 1169--1171, 2000.
15. Weissermel, K. & Arpe, H.-J. *Industrial Organic Chemistry*, 3rd ed., VCH, Germany & New York, 1978.
16. Ramon, R. S., et al. *J. Org. Chem.* **75** (4), 1197--1202, 2010.
17. Furniss, B. S., Hannaford, A. J., Smith, P. W. G. & Tatchell, A. R. *Vogel's textbook of practical organic chemistry*, 5th ed., Pearson Education, India, 2008.
18. Guo, J-J., et al. *Green Chem.* **3** (4), 193--195, 2001.
19. Saikia, L., et al. *Org. Med. Chem. Lett.* **1** (1), 12--17, 2011.
20. Buckingham, J. & Macdonald, F. *Dictionary of organic compounds*, 6th ed., Chapman and Hall/CRC, New York, 1995.

# Chapter 5

## Summary of the Present Work

In **Section 2A** of **Chapter 2**, the selective synthesis of dibenzoxanthene and its precursor intermediate bisnaphthol have been documented using boron sulfonic acid (BSA) as reusable solid acid catalyst in neat condition under microwave and thermal energies within less time. The catalyst BSA showed selective nature with these two conditions against the variation of the catalyst amounts towards the synthesis of dibenzoxanthene and bisnaphthol intermediate. The selective synthesis of aryl-bis(2-hydroxy-1-naphthyl) methane under microwave irradiation becomes the first method using solid acid catalyst in solvent-free medium. The reusability of the catalyst was tested and it was found to be recyclable for four runs for the synthesis of dibenzoxanthene in neat under thermal method without any change in its catalytic properties to a very large extent. Thus, this makes it quite attractive in the context of green chemistry.

The **Section 2B** of **Chapter 2** successfully supported the existence of keto-enol mechanism during the synthesis of dibenzoxanthene in acid catalyzed two component reactions of 2-naphthol and aromatic aldehydes. We have isolated the two reactive keto intermediate from the reactions of 2-naphthol and 4-chlorobenzaldehyde/4-tolualdehyde using copper sulfate pentahydrate as heterogeneous catalyst in methanol under reflux condition. The two keto products were characterized by various analytical techniques such as $^{1}$HNMR, $^{13}$CNMR, FT-IR, DEPT, COSY and elemental analyses. Furthermore, a new catalytic system for the selective synthesis of bisnaphthol derivatives under mild condition using $BF_3.OEt_2$-AcOH as a homogeneous catalyst was developed efficiently during the course of the reaction. It was also seen that conversion of the homogeneous catalyst to the heterogeneous counterpart by supporting it upon silica gel was almost inactive under the reaction condition using AcOH as promoter and was thus not a feasible catalytic system.

**Chapter 3** illustrates our observation that the polyaniline (PANI) supported *p*-toluene sulfonic acid (TsOH) and $FeCl_3$ (PANI-TsOH, PANI-$FeCl_3$) can be used as excellent reusable solid acid catalysts for the synthesis of 1,8-dioxo-octahydroxanthene derivatives under solvent-free grinding method at mild condition. This study also reveals the inability of the supported ferric nitrate

nonahydrate upon Montmorillonite K-10, i.e. clayfen to successfully carry out the synthesis of 1,8-dioxo-octahydroxanthene. Ferric nitrate nonahydrate itself without conversion to the supported heterogeneous catalyst acted as very reactive selective inexpensive Lewis acid catalyst. However the reusability of the catalyst was lost in this process. There are several positive aspects in this work. Mention may be made that this protocol utilizes solvent-less medium and room temperature condition to form the required product using simple grinding apparatus mortar and pestle. The use of mechanochemical process enhances the energy efficiency and safety of this technique. Moreover, the liberty for variation of substrates and use of inexpensive reusable catalyst add to the advantageous facet.

In **Section 4A** of **Chapter 4,** the chemoselective behaviour of P4VP-$H_2SO_4$ catalyst has been demonstrated in the formation of 1,1-diacetates from aldehydes in dichloromethane at room temperature and in neat condition under mechanochemical treatment within few minutes. The reaction procedure is very simple and environment friendly. In addition, the catalyst seems to be highly reusable without any loss of its catalytic property. Under the same optimized reaction condition, the protection of salicylaldehyde however, did not yield the expected acylal product; instead it yielded the anhydro-dimer as single product. The catalyst is equally applicable for the deprotection of acylal in acetonitrile with satisfactory regeneration of the aldehydes.

The experimental findings in **Section 4B** of **Chapter 4** highlight upon the utility of dual property of polyethylene glycols (PEGs) both as efficient, inexpensive and recyclable homogeneous medium and catalyst under microwave irradiation for the synthesis of oximes from carbonyl compounds and hydroxylamine hydrochloride. This method describes a simple method of oxime synthesis under microwave energy without release of any waste material to the environment. The application of microwave heating techniques in this method reduces the laborious efforts of reaction procedures involved with continuous conventional heating. The heating in this case is uniform leading to rapid and clean alternative. Several aspects of green chemistry have been fulfilled along with considerably high yield, while using this

method. We also applied this method for the synthesis of di-oxime of 1,8-dioxo-octahydroxanthene derivative

# Appendices

# Appendices

## List of Publications

1. **Dutta, P.** & Borah, R. Boron sulfonic acid (BSA) catalyzed selective synthesis of aryl-*bis*(2-hydroxy-1-naphthyl) methane and 14-alkyl or aryl-14*H*-dibenzoxanthenes under solvent-free condition, (communicated).

2. **Dutta, P.**, Saikia, M. K., Das, R. J., Borah, R. Investigation of keto-enol tautomers during the synthesis of aryl-*bis*(2-hydroxy-1-naphthyl) methanes, *Journal of Chemical Sciences* 2014 (accepted).

3. **Dutta, P.**, Dutta, A. K., Sarma, P., Borah, R. Dual nature of polyethylene glycol under microwave irradiation for the clean synthesis of oximes, *Monatshefte fur Chemie* **145** (3), 505--508, 2014.

4. **Dutta, P.**, Sarma, P., Borah, R. Investigation of efficient synthesis of 1,8-dioxo-octahydroxanthene derivatives under solvent-free grinding method, *Current Chemistry Letters* **2** (4),159--166, 2013.

5. **Dutta, P.**, Sarma, P., Borah, R. P4VP-$H_2SO_4$ Catalyzed Chemoselective Protection of Aldehydes to Acylal along with Deprotection Reactions, *Synthetic Communications* **43** (10), 1378--1386, 2013.

6. Borah, K. J., **Dutta, P.**, Borah , R. Synthesis, Characterization and Application of Poly(4-vinylpyridine)-Supported Brønsted Acid as Reusable Catalyst for Acetylation Reaction, B*ulletin of the Korean Chemical Society* **32** (1), 225--228, 2011.

## Papers/ Posters presented in conferences

1. **P. Dutta**, M. Saikia, R. Das, R. Borah "Characterization of keto-enol tautomers towards the synthesis of dibenzoxanthene derivatives via NMR techniques'' Presented as poster in "20$^{th}$ National Magnetic Resonance Society Symposium Cum Annual Meeting", 2-5$^{th}$ Feb, 2014, Dept. of Chemical Sciences, Tezpur University. Tezpur.
2. **P. Dutta**, P. Sarma, R. Borah "Investigation of One Pot Synthesis of Dibenzoxanthene Derivatives" Presented as poster in "International Symposium on Chemistry and Complexity", 6-8$^{th}$ Dec, 2011, IACS, Kolkata.

3. **P. Dutta**, P. Sarma, R. Borah "Polymer supported acid as reusable catalyst for chemo-selective protection of aldehydes to acylals along with deprotection reactions" Presented as poster in "National Conference on Chemistry, Chemical Technology and Society", 11-12$^{th}$ November, 2011, Dept. of Chemical Sciences, Tezpur University. Tezpur.
4. P. Sarma, **P. Dutta**, R. Borah "Solvent-less Synthesis β-Amino Carbonyl Compounds" Presented as poster in "National Conference on Chemistry, Chemical Technology and Society", 11-12$^{th}$ November, 2011, Dept. of Chemical Sciences, Tezpur University. Tezpur.
5. **P. Dutta** and R. Borah "Synthesis of Xanthenedione Derivatives under Solvent Free Condition, using Polymer Supported Catalysts" Presented as poster in "20$^{th}$ National Symposium on Catalysis, Energy Conservation and Conservation of Environment", 19-22$^{nd}$ December, 2010, National Centre for Catalysis Research, IIT-Madras.