

**DESIGN AND DEVELOPMENT OF IMMOBILIZED, RECYCLABLE
CATALYSTS FOR C-C, C-N, S-N BOND FORMATION AND SELECTIVE
HYDROGENATION REACTIONS**

The thesis deals with the design, development and application of immobilized catalysts for various C-C, C-N, S-N bond formation reaction and selective hydrogenation reactions. Immobilized catalysts are particularly attractive for the synthesis of fine chemicals as they allow the production and ready separation of large quantities of products with the use of a small amount of catalyst. Further, in the recent years, the stringent environmental legislations and increasing awareness for human health have put more emphasis on cleaner and greener technologies which helps in reducing the amounts of toxic wastes and effluents. Immobilized and recyclable catalysts are immensely helpful in this context.

The thesis is divided into five chapters. Chapter I highlights the importance of cleaner catalytic technologies for the synthesis of fine chemicals and pharmaceuticals. Further, this chapter focuses on the properties and applications of inorganic solid supports, ionic liquids and soluble polymers for various organic transformations. Chapter II deals with the preparation and application of nanocrystalline magnesium oxide supported palladium(0) for C-C bond formation reactions and reduction of nitro compounds and alkenes using molecular hydrogen as a reducing agent. Chapter III describes in detail, the synthesis, characterization and application of magnesium oxide supported on mesoporous carbon for the synthesis of sulfinamides. Chapter IV deals with the synthesis and application of mesoporous aluminosilicates and ionic liquids in the ring opening of epoxides with amines and nitrogen heterocycles. Chapter V details the

synthesis, characterization and application of Poly (N-vinyl-2-pyrrolidone)-Cu(OAc)₂ in the sulfimidation reaction using PhI=NTs [(N-(p-tolylsulfonyl)imino]phenyliodinane) as nitrene donor.

Chapter I. Introduction

This chapter describes the various catalysts/process options available for an industrial chemist to effect different organic transformations. It includes a brief introduction of homogeneous, heterogeneous and heterogenized homogeneous catalysis. The design and development of environmentally cleaner catalytic methodologies is highlighted in this chapter.

Different supports for the immobilization of catalysts are also detailed. The structures, properties and applications of nanocrystalline metal oxides, mesoporous materials, ionic liquids, and soluble polymers are discussed in this chapter.

Chapter II. Synthesis of Dibenzyls, Alkyl Phenyl Esters and Reduction of Nitro Compounds by Molecular Hydrogen using Nanocrystalline Magnesium Oxide Stabilized Palladium(0)

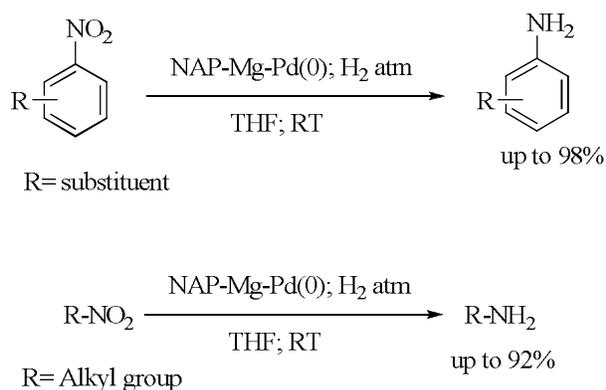
This chapter describes the synthesis and catalytic application of nanocrystalline magnesium oxide supported palladium catalyst [NAP-Mg-Pd(0)]. The catalyst was synthesized by counter ion stabilization of PdCl₄²⁻ on to the high surface area aerogel prepared nanocrystalline magnesium oxide followed by reduction with hydrazine hydrate. [NAP-Mg-Pd(0)] was then employed in the synthesis of dibenzyls, alkyl phenyl esters and the reduction of nitro compounds using molecular hydrogen as the reducing agent.

This chapter is divided into two sections:

Section A. Selective Reduction of Nitro Compounds using Nanocrystalline Magnesium Oxide-Stabilized Palladium(0)

Organic amines are important starting materials for the manufacture of a variety of chemicals such as dyestuffs, pharmaceuticals, agrochemicals, surfactants, pesticides and polymers etc. Further, amino groups can easily be replaced by other groups (H, F, Cl, Br, I, OH etc.) *via* the corresponding diazonium salts.

This section describes the reduction of a variety of aromatic and aliphatic nitro compounds to the corresponding amines at ambient temperature in good to excellent yields by using ligand-free nanocrystalline magnesium oxide-stabilized palladium(0) catalyst with molecular hydrogen as the reductant (Scheme 1).



Scheme 1

The catalyst was successfully applied to the synthesis of aromatic and aliphatic amines from a diverse range of aromatic and aliphatic nitro compounds. This method is highly selective and a large number of sensitive functional groups in the aromatic ring such as aldehydes and ketones are well tolerated. No dehalogenated products were detected in case of the halogen substituted nitroaromatics.

Section B. One-pot Synthesis of Dibenzyls and Alkyl Phenyl Esters *via* a Sequential Heck Coupling and Hydrogenation using Nanocrystalline Magnesium Oxide stabilized Palladium (0)

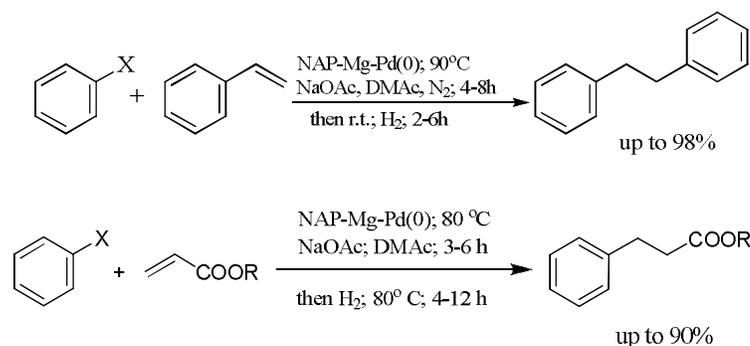
Substituted dibenzyls are found to form the backbones of several compounds such as Lunularic acid, an antifungal agent and Bifluranol, an anti-androgen agent.

Alkyl phenyl esters on the other hand are useful compounds in fragrances and fine chemical industries.

These compounds are generally synthesized by multistep synthetic processes. One of the major challenges faced by the fine chemicals industry in recent times is the synthesis of target molecules by a large number of different reaction steps involving elaborate work up and refining procedures. The recently introduced one-pot synthetic approach not only helps to improve atom economy, but also reduces the number of steps in isolation and purification of the intermediate compounds in a multistep synthesis.

In the recent years, the versatility of palladium catalysts is well established in a variety of organic transformations. Therefore, supported palladium catalysts became the best choice to be applied to the multistep catalytic syntheses under mild reaction conditions and under ambient pressure.

This section describes a practical and atom economic synthesis of dibenzyls and alkyl phenyl esters by a sequential Heck coupling of haloarenes (chloro, bromo and iodo) and styrenes or alkyl acrylates followed by hydrogenation employing molecular hydrogen under atmospheric pressure (Scheme 2) using nanocrystalline magnesium oxide stabilized palladium [NAP-Mg-Pd(0)] catalyst.



Scheme 2

A diverse range of haloarenes underwent the reaction smoothly to afford the corresponding dibenzyls and alkyl phenyl propionates in good to excellent yields *via* a Heck coupling followed by hydrogenation of the alkenyl double bond. The catalyst [NAP-Mg-Pd(0)] was recovered by simple filtration, and reused for several cycles with consistent activity.

Chapter III. Design, Synthesis and Characterization of Magnesium Oxide Modified Mesoporous Carbon and its Application in the Synthesis of Sulfenamides

Sulfenamides play a very vital role in modern organic chemistry. These are useful compounds and can be transformed to a number of other important functional groups such as sulfonimidoyl chlorides and cyclic sulfonimidates, which are valuable starting materials in the synthesis of various oxa- and aza-heterocyclic compounds.

The conventional syntheses of these compounds refer to the treatment of sulfinyl chlorides with secondary amines or with Grignard reagents. But low yields of the desired products due to unstable precursor formation and concomitant side reactions are the major drawbacks of these methods. Moreover, they are sensitive to hydrolysis and require the use of highly toxic reagents as thionyl chloride. Therefore, mild and easier process for the synthesis of sulfenamides is desired.

- A simple method for the synthesis of sulfinamides using easily available reagents.
- Easy separation of the catalyst by simple filtration.
- The catalyst is easy to handle and is reusable for several cycles with consistent activity.

Chapter IV. Ring Opening of Epoxides using Three-Dimensional Cage Type Aluminosilicates and Ionic Liquids

Epoxides are well known carbon electrophiles capable of reacting with a variety of nucleophiles (*viz.* aromatic and aliphatic amines resulting in the formation of a C-N bond and carbon nucleophiles resulting in a C-C bond formation) and their ability to undergo regioselective ring opening reactions contribute largely to their synthetic value.

These reactions are mostly catalyzed by Lewis acidic or Lewis basic catalysts. In the recent years the shifting of focus towards green chemistry have paved the way for the development of recyclable catalysts for these reactions which in its turn forms lesser quantities of environmentally toxic wastes.

In this chapter, the development of immobilized, recyclable catalysts for efficiently catalyzing the ring opening reactions of epoxides has been described.

This chapter is divided into two sections.

Section A. Ring Opening of Epoxides with Aromatic and Aliphatic Amines using Three-Dimensional Cage Type Aluminosilicates

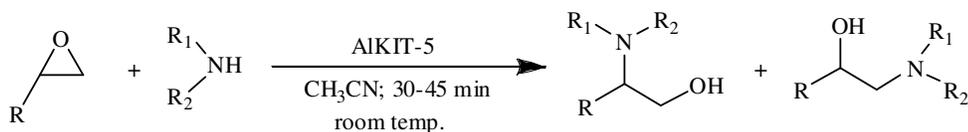
Vicinal amino alcohol moiety is a common structural component in a vast group of naturally occurring and synthetic molecules. The common name for this group varies, from vicinal amino alcohol to β -amino alcohol or 1,2-amino alcohol. Either the amine or the alcohol can be acylated, alkylated or contained within rings. The presence of this

moiety and the relative (as well as absolute) stereochemistry are generally important for the biological activity of molecules containing a vicinal amino alcohol.

The classical approach for the synthesis of β -amino alcohols involves the ring opening of epoxides with amines. However, these reactions are generally carried out with large excess of amines at elevated temperatures and are accompanied by poor regioselectivity. To overcome these problems, several metal amides, metal triflates, metal halides and other transition metal based Lewis acids were reported for this reaction. Among the heterogeneous catalysts, zirconium sulfophenyl phosphonate, aluminum oxide and silica gel were earlier employed for the reaction.

Ordered mesoporous materials with tunable pore size in the range of 2–50 nm owing to their unique structures with organized porosity, high specific surface area and large specific pore volume have been recently receiving much attention in the field of catalysis.

In the present study, mesoporous solid super acid AIKIT-5 with different Al contents has been synthesized and applied to the synthesis of β -amino alcohols *via* the ring opening of epoxides with aromatic and aliphatic amines (Scheme 5).



Scheme 5

Aryl amines on reaction with styrene oxide gave the corresponding β -amino alcohols in a regioselective manner with preferential nucleophilic attack at benzylic position. Aliphatic amines on reaction with styrene oxide gave the product with opposite

regiochemistry. The catalyst was recovered by simple filtration and reused for several cycles with consistent activity.

Section B. Ring Opening of Epoxides by Nitrogen Heterocycles using Recyclable Catalytic Systems

Indoles form the key structural motif in many biologically active natural products. The vinca alkaloids, which are potent anti-cancer agents, consist of alkyl indoles as its central moiety.

Pathologically important antibiotic indolemycin contains alkyl indoles as its central structure. This exhibits an antibacterial activity that provides a cure to various pathogenic species like *Pasteurella*, *Haemophilus* and *Mycoplasma* which are responsible for many of the respiratory diseases.

On the other hand, several bioactive alkaloids are composed of five-membered nitrogen containing heterocyclic pyrrole ring fused to five-, six-, or seven membered ring or an alkyl chain attached to its 2- or 3- position. Pyrrole nucleus finds expression as the central structure of several natural products like the pyrrole alkaloid funebrine and in CC-1065, a potent antitumor agent.

The general method of synthesis of these alkylated nitrogen heterocycles are by acid or base catalyzed Friedel-Crafts' alkylation. In the absence of catalysts, the reaction is extremely sluggish resulting in trace yield of the corresponding products.

Recently, several Lewis acids have been reported as effective mild catalysts for the Friedel-Crafts' alkylation reaction of the nitrogen heterocycles. But these catalysts suffer from some severe drawbacks such as moisture sensitivity and environmental

toxicity. Therefore there is a need for the development of efficient reusable catalysts for this reaction.

In this section, ring opening of epoxides by nitrogen heterocycles using recyclable catalytic systems have been described.

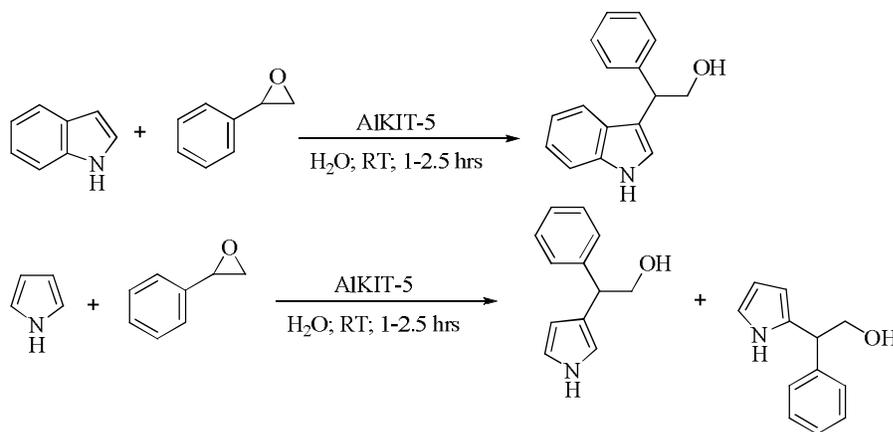
This section comprises of two topics:

Topic 1 deals with the ring opening of epoxides by nitrogen heterocycles using three dimensional cage type aluminosilicates.

Topic 2 deals with the ring opening of epoxides by nitrogen heterocycles using ionic liquids as a catalyst and also as reaction medium.

Topic 1. Ring Opening of Epoxides by Nitrogen Heterocycles using Three Dimensional Cage type Aluminosilicates in Water.

In the present study, Friedel-Crafts' alkylation of nitrogen heterocycles with epoxides in water under ambient conditions to afford the corresponding alkylated derivatives of indoles and pyrroles in good yields (Scheme 6) has been described.



Scheme 6

Different substituted indoles and pyrroles underwent reaction with styrene oxide as well as other epoxides to afford the corresponding products in good yields. The

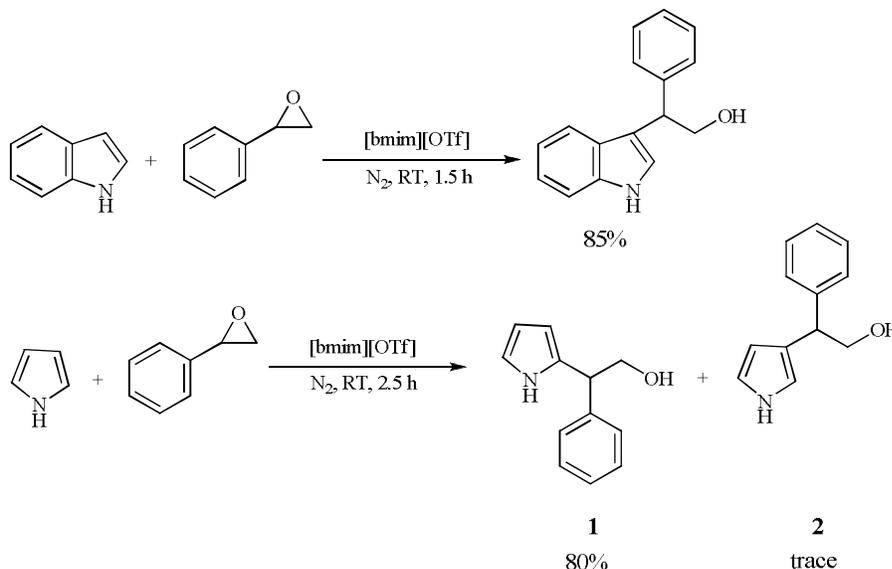
reaction occurred in aqueous media and required only a catalytic amount of ALKIT-5 catalyst. No other promoters or additives were required for obtaining good yield of the product. The catalyst ALKIT-5 dispersed in water forms a robust and recyclable catalytic system, which can be reused several times without any regeneration, thus reducing the amount of waste considerably.

Topic 2. Ring Opening of Epoxides by Nitrogen Heterocycles using Ionic Liquid as a Catalyst and Reaction Medium.

Room temperature ionic liquids (RTILs) also have emerged as one of the most attractive eco-benevolent alternatives to volatile organic solvents and also as effective catalysts in many reactions. The uniqueness of ionic liquids as potential solvents lies in their interesting physical properties such as low vapor pressure, wide liquid range and high thermal stability. Moreover they are good solvents for a wide range of both organic and inorganic materials, and unusual combination of reagents can be brought into the same phase. They are often composed of poorly co-ordinating ions, so they have the potential to be highly polar yet non-coordinating solvents. They are immiscible with a number of organic solvents and provide nonaqueous, polar alternative for two-phase systems. The development of various ionic liquids which are air and moisture stable has indeed added a new dimension to the research area of alternative solvents. In addition to these features, the ionic liquids can be recycled easily without any significant loss of activity.

In the present study, Friedel-Crafts' alkylation of nitrogen heterocycles *viz.* indoles and pyrroles under ambient conditions in ionic liquids have been described. This

procedure allows a facile reaction, followed by a simple work up procedure to give the corresponding products in moderate to good yields (Scheme 7).



Scheme 7

A diverse range of indoles and pyrroles underwent facile alkylation with several epoxides of varied character affording the corresponding products in good yields. This occurs at ambient temperature, *via* ring opening of aromatic epoxides using ionic liquid [bmim][OTf] as an efficient catalyst and reaction medium. The notable features of this novel procedure are mild reaction conditions, high regio- and chemo- selectivity and simplicity in operation.

Chapter V. Poly (N-vinyl-2-pyrrolidone)-Cu(OAc)₂: An Efficient and Reusable Catalyst for Sulfimidation.

Sulfoxides, sulfimides and sulfonium ylides are very useful reagents in organic synthesis. Several successful methods have been developed for the synthesis of sulfoxides. But sulfimides, the nitrogen analogues of sulfoxides although have been widely used as important auxiliaries for chiral ligands and structural units in

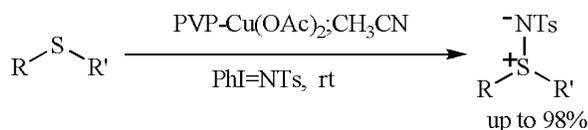
pseudopeptides, are less investigated due to scarcity of appropriate nitrogen sources, as opposed to oxidants that are available in wide variety and forms.

In view of this, development of efficient methods for selective imidation of sulfides to sulfimides has been desired for many years. In the recent years a few methods of transforming sulfides into sulfimides have been reported using various nitrene sources such as chloramine-T and PhI=NTs [(N-(p-tolylsulfonyl)imino]phenyliodinane).

However, some of these methods suffer from one or more limitations including the use of stoichiometric amount of transition metal complexes, slow rate of reactions and moderate yields.

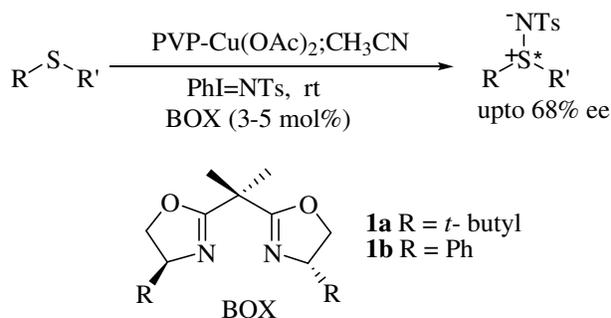
A new efficient catalyst for sulfimidation was developed with high selectivity, high atom efficiency and reusability.

In the present study, poly(vinylpyrrolidone) supported cupric acetate was prepared and characterized FT-IR, X-ray photoelectron spectroscopy (XPS), ESR, TGA-MS and UV-Vis DRS techniques. The catalyst was evaluated for sulfimidation reaction using PhI=NTs as a nitrene donor in acetonitrile solvent at room temperature to afford sulfimides in good to excellent yields (Scheme 8).



Scheme 8

The activity of the catalyst was further tested for enantioselective sulfimidation using bisoxazoline ligands under the same reaction conditions (Scheme 9).



Scheme 9

The catalyst was applied for the sulfimidation of a wide range of sulfides such as aryl, alkyl and allylic sulfides. Aryl and alkyl sulfides underwent the reaction smoothly to afford the corresponding sulfimides in good to excellent yields. Allylic sulfides underwent a [2,3] sigmatropic rearrangement with the formation of sulfonamide through a sulfimide intermediate. In the presence of chiral bis(oxazoline) ligand, asymmetric induction occurs to afford chiral sulfimides with moderate enantioselectivities.

The distinctive features of the present work are:

- A simple method for sulfimidation at room temperature in shorter reaction times.
- Easy separation of the catalyst by simple removal of the solvent and extracting the product with suitable solvent.
- The catalyst is easy to handle and is reusable for several cycles with consistent activity.