ABSTRACT

The thesis entitled "**DEVELOPMENT OF ENVIRONMENTALLY BENIGN METHODOLOGIES FOR THE SYNTHESIS OF INDOLE AND PYRIDINE DERIVATIVES**" is divided into seven chapters. We have reported the synthetic strategies for the preparation of 3-arylmethyl/diarylmethyl indole derivatives, 2-arylamino-3-cyanopyridine derivatives, 2-arylamino-3-cyano-6-aryl pyridine derivatives and 4-oxo-4, 5, 6, 7-tetrahydroindole derivatives.

Chapter 1:

This chapter provides brief introduction about indole, indole derivatives and their biological importance, Pyridine, pyridine derivatives and their biological importance, Multicomponent reactions and their importance.

Chapter 2:

This chapter describes literature survey about C3-alkyl/aryl substituted indole derivatives, *N*-substituted 2-amino-3-cyanopyridine derivatives, *N*-substituted 2-amino-3-cyano-6-arylpyridine derivatives and 4-oxo-4, 5, 6, 7-tetrahydroindole derivatives.

Chapter 3:

This chapter deals with development of a simple, efficient and multicomponent synthesis of 3-arylmethyl/diarylmethyl indoles by a greener aza-Friedel-Crafts reaction catalyzed by PMA-SiO_2 in PEG-400, leading to 3-arylmethyl/diarylmethyl indole derivatives.

Chapter 4:

This chapter provides an efficient synthesis of 2-arylamino-3-cyanopyridine derivatives by a four-component reaction catalyzed by $SnCl_2.2H_2O$ in water.

Chapter 5:

This chapter describes an efficient and ultrasound assisted synthesis of 2-arylamino-3-cyano-6-arylpyridine derivatives by four component reaction catalyzed by FeF_3 in PEG-400.

Chapter 6:

This chapter explains a highly efficient and simple strategy for the synthesis of 4-oxo-4, 5, 6, 7-tetrahydroindole derivatives promoted by Wang resin supported sulfonic acid in water.

Chapter 7:

This chapter includes overall summary, conclusion and recommendations of the present research work.

Chapter 1

This chapter provides brief introduction about indole, indole derivatives and their biological importance, Pyridine, pyridine derivatives and their biological importance, Multicomponent reactions and their importance.

1.1. Introduction.

Synthetic organic chemistry progress is associated with searching and synthesis of new organic compounds with desired properties. The great challenge for the pharmaceutical industry is to proceed to innovate, to provide clinically discriminated medicines and really make a significant change in patient's livelihood. For every 5,000-10,000 organic compounds that enter the research and development pipeline (R&D), eventually only one could be able to receive the approval and clinical development takes about 10-12 years.

In order to find new drugs and to explore their biological activity, generally organic or medicinal chemists perform the literature search for commercially feasible combinatorial libraries. The large numbers of heterocyclic building blocks were identified for their varied applications in drug discovery and pharmaceutical research. A majority of heterocyclic organic compounds containing nitrogen have been confirmed to have better biological activity than heterocyclic organic compounds without nitrogen. So in this regard, nitrogen containing indole and pyridine derivatives are chosen as vital building blocks for drug discovery.

Indole ring system was found in many natural products, alkaloids, amino acids, hormones and etc.,

Pyridine ring is considered as one of the most important heterocyclic aromatic compound. Pyridine ring system is found in many naturally occurring important organic compounds such as vitamins and alkaloids. In pharma industry, more than 7000 existing drugs having the pyridine ring system.

1.2. Multicomponent reactions:

In a chemical reaction three or more than three chemical components are made to react in one pot and produce desired final compound or product known as Multicomponent reaction (MCR). Multicomponent reactions have more advantages than conventional reactions in many aspects, such as; a) reduces cost and reaction time b) It can be prepared by using easily available raw materials c) Resource effective d) Easy to operate e) Multiple bond forming efficiency f) Atom economy g) Environmentally benign

So, here we wish to present our research work on the novel synthesis of below mentioned indole derivatives and pyridine derivatives by means of new multicomponent and environmentally benign approach.

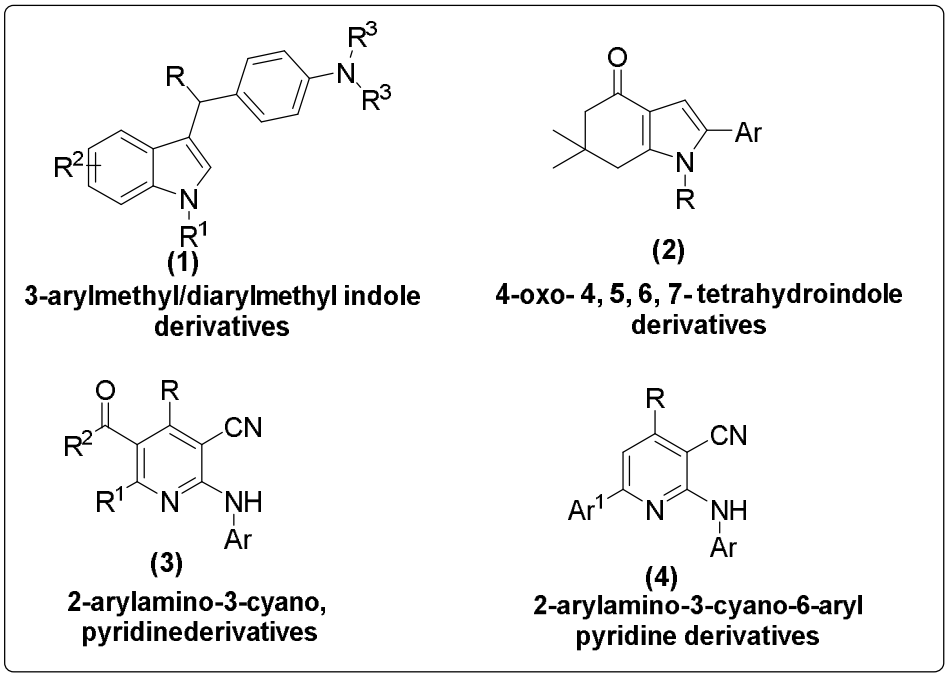


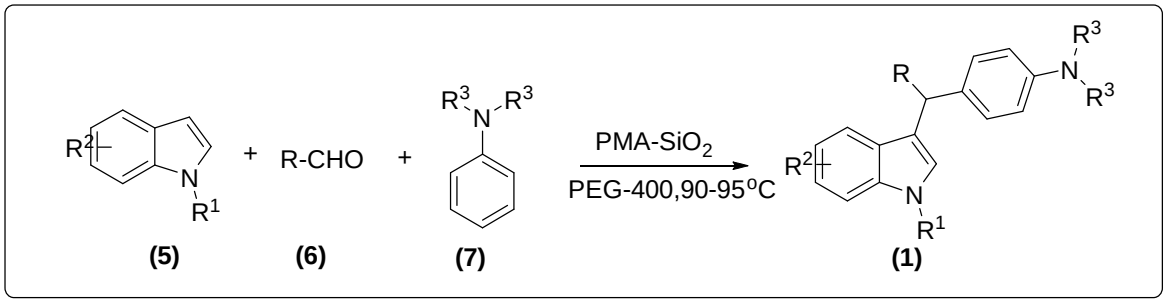
Figure1: Core area of the present research work.

Chapter 2

The present chapter provides the reviews on synthetic approaches for 3-alkyl/arylmethyl indole derivatives (**1**), 4-oxo-4, 5, 6, 7-tetrahydroindole derivatives (**2**), *N*-substituted 2-amino-3-cyanopyridine derivatives (**3**) and *N*-substituted 2-amino-3-cyano-6-arylpyridine derivatives (**4**).

Chapter 3

This chapter deals with development of a simple, efficient and multicomponent synthesis of 3-arylmethyl/diarylmethyl indole derivatives (**1**) by PMA-SiO_2 catalyzed reaction of indole **(5)**, aldehyde **(6)** and *N*, *N*-dialkyl aniline (**7**) by in PEG-400 as shown in below **Scheme 1.**



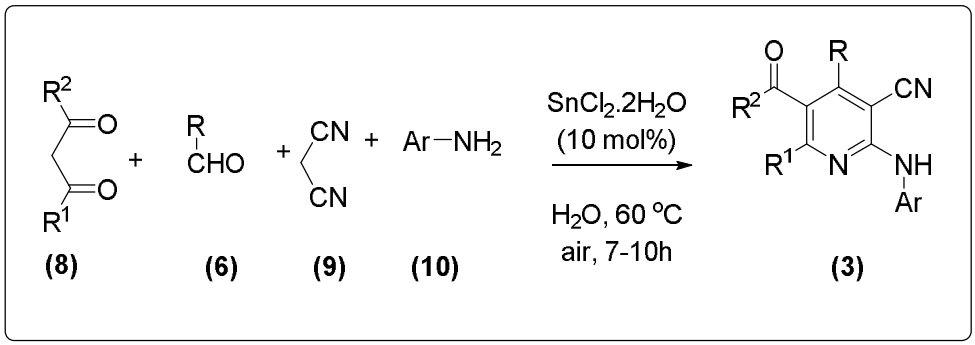
Scheme 1: PMA-SiO_2 catalyzed synthesis of 3-arylmethyl/diarylmethyl indole derivatives.

By using this methodology, a variety of 3-arylmethyl/diarylmethyl indole derivatives were prepared with various indoles, aldehydes and *N*, *N*- dialkyl anilines.

This current methodology represents a safer alternative to the existing methods leading to 3-diarylmethyl/arylmethyl indoles and might find the usage towards the preparation of more complex indole derivatives of pharmacutical interest.

Chapter 4

This chapter provides an efficient synthesis of 2-arylamino-3-cyanopyridine derivatives (**3**) by $SnCl_2.2H_2O$ catalyzed four-component reaction of *β*-keto esters or 1, 3-diketones **(8)**, aryl/heteroaryl/alkyl aldehydes **(6)**, malononitrile **(9)** and anilines **(10)** in water as shown in below **sheme 2.**



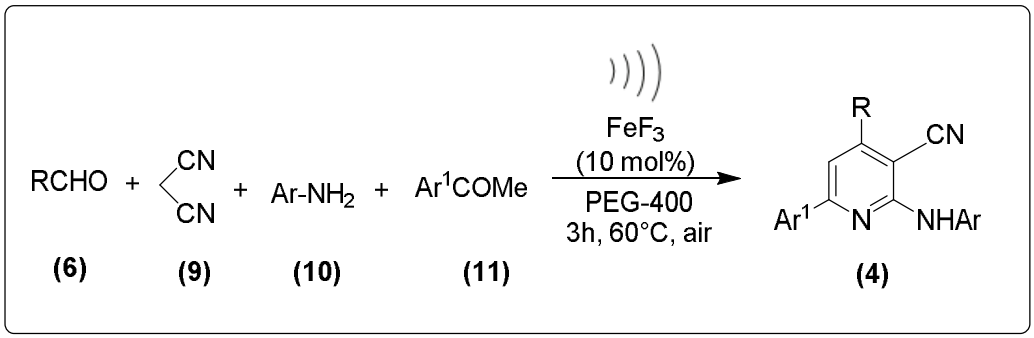
Scheme 2: $SnCl_2.2H_2O$ catalysed synthesis of 2-arylamino-3-cyanopyridine derivatives.

By using this methodology, a variety of 2-arylamino-3-cyanopyridine derivatives were prepared with various *β*-keto esters or 1, 3-diketones, aldehydes and anilines.

$SnCl_2 \cdot 2H_2O$ was found to be an efficient precatalyst for the synthesis of 2-arylamino-3-cyanopyridine derivatives *via* multicomponent reaction in water. The use of less expensive catalyst in water media, good yield of products and wider substrate scope are the main features of this present methodology.

Chapter 5

This chapter provides an ultrasound assisted synthesis of 2-arylamino-3-cyano-6-arylpyridine derivatives (**4**) by FeF_3 catalyzed four-component reaction of acetophenones **(11)**, aryl/heteroaryl/alkyl aldehydes **(6)**, malononitrile **(9)** and anilines **(10)** in PEG-400 as shown in below **sheme 3**.



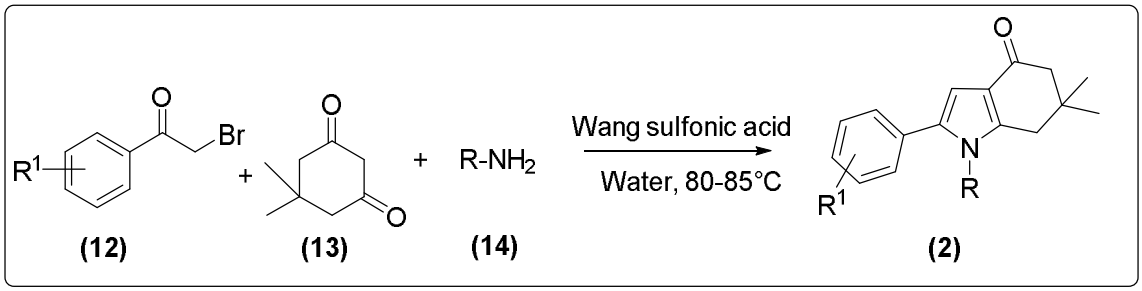
Scheme 3: FeF_3 catalyzed ultrasound assisted synthesis of 2-arylamino-3-cyano-6-arylpyridine derivatives

By using this methodology, a variety of 2-arylamino-3-cyano-6-arylpyridine derivatives were prepared with various acetophenones, aldehydes and anilines.

Ultrasound assisted 4-component methodology has been developed for the synthesis of 2-arylamino-3-cyano-6-aryl pyridine derivatives. This methodology is free from anhydrous or inert atmosphere and involved the use of easily available starting materials to give the desired pyridine derivatives under very mild reaction conditions. A variety of 2-arylamino-3-cyano-6-arylpyridine derivatives were prepared by using this methodology in good to excellent yields.

Chapter 6

This chapter provides an efficient and greener synthesis of 4-oxo-4, 5, 6, 7-tetrahydroindole (**2**) derivatives with Wang resin supported sulfonic acid catalysed three-component reaction of phenacyl bromide (**12**), primary amines (**14**) and dimedone (**13**) in water as shown in below **sheme 4**.



Scheme 4: Synthesis of 4-oxo-4, 5, 6, 7-tetrahydroindole derivatives catalyzed by Wang-OSO_3H in water.

By using this methodology, a variety of 4-oxo-4, 5, 6, 7-tetrahydroindole derivatives were prepared with various phenacyl bromides, alkyl/aryl/cycloalkyl amines and dimedone.

Wang-OSO_3H was found to be an efficient and reusable catalyst for the synthesis of 4-oxo-4, 5, 6, 7-tetrahydroindole derivatives *via* three-component reaction in water. The use of recyclable, less expensive and environmentally benign catalyst in water medium, wider substrate scope and good yield of products are the key features of this methodology.

Chapter 7

This chapter includes overall summary, conclusion and recommendations of the present research work.