ABSTRACT
SYNTHESIS, CHARACTERIZATION AND BIOLOGICAL ACTIVITY OF NOVEL HETEROCYCLIC COMPOUNDS

Introduction:

Heterocyclic compounds are widely distributed in nature and are essential for life. They play a vital role in the field of organic chemistry. Nitrogen and oxygen containing heterocyclic compounds are key building blocks used to develop compounds of biological or medicinal interest to chemists. A vast number of nitrogen containing heterocyclic building blocks have applications in pharmaceuticals and agrochemical research and drug discovery. Heterocyclic compounds also have a practical use as components in dyes, antioxidants, copolymers, bases, and ligands. Now a day’s nitrogen and oxygen containing heterocyclic compounds have gained attraction due to their great biological activities like Antimycobacterial, Antimicrobial, Antituberculosis, Antitumors, Anti-inflammatory, Antimalarial, Anticonvulsant, Anticancer, Anti HIV, Antimitotic agent, and Anti-proliferative activity against A 549 lung cancer cells.

The present work explains synthesis of hydrazones, Schiff bases, benzodiazepines, dipyrrromethanes, and imidazolines derivatives, and their biological activity such as Anti-bacterial activity.

Hydrazone is an important class in organic chemistry. These compounds have interesting biological activities such as Anti-mycobacterial, Antimicrobial, Anti-tuberculosis, Anti-tumors, Anti-inflammatory, Anti-malarial, Anti-convulsant, and Anticancer-Anti HIV.

The chemistry of the carbon-nitrogen double bond plays a vital role in the progress of chemistry science. Schiff-base compounds have been used as fine chemicals and medical substrates. Moreover, Schiff bases derived from various heterocycles have been reported to possess cytotoxic, anticonvulsant, antiproliferative, antimicrobial, anticancer, antifungal, anti-inflammatory. One of the important roles of Schiff bases is an intermediate in the biologically important transamination reaction. Schiff bases are used as protective agent in natural rubber. Schiff bases are used as amino protective group in organic synthesis.

Benzodiazepine is an important class of pharmacologically active organic compounds. Considerable interest has been focused on the synthesis of benzodiazepines because of their wide range of biological activities.
Dipyrromethanes are compounds known for more than a century and are widely being used as important building blocks for the synthesis of porphyrins, Calixpyrrols and Corroles, which have recent applications as chiral catalysts, chiral sensors, synthetic receptors for small molecular devices, potential sensitizers for photodynamic cancer therapy.

Imidazolines are important five membered heterocycles. According to the position of the double bond imidazolines are classified as 2-imidazoline, 3-imidazoline and 4-imidazoline.


CHAPTER-1: Synthesis of Hydrazones

1.1. Synthesis of hydrazones from 4,5-diazafluoren-9-hydrazone and aromatic aldehydes

The present scheme demonstrates the synthesis of hydrazones derived from 4,5-diazafluoren-9-hydrazone and tests their antibacterial activity. The salient feature of our strategy involves initial conversion of 1,10 phenanthroline (1) into 4,5-diazafluoren-9-one (2) by using potassium permanganate. The 4,5-diazafluoren-9-one is further transformed into from 4,5-diazafluoren-9-hydrazone (3) by using hydrazine hydrate in solid phase. The 4,5-diazafluoren-9-hydrazone molecule is further condensed with various substituted aldehydes (4). The obtained products (5) are well characterized by the spectroscopic methods like IR, $^1$HNMR, Mass and also assayed for antibacterial (Escherichia coli, Staphylococcus aureus, Bacillus subtilis, and Klebsiella pneumoniae) activities.

![Scheme 1.1]
1.2. Synthesis of hydrazones from 4,5-diazafluoren-9-hydrazone and aromatic ketones
In continuation of our studies on structure modifications we condensed 4,5-diazafluoren-9-hydrazone with different substituted aromatic ketones. The obtained products are well characterized by the spectroscopic methods like IR, $^1$HNMR, Mass and also assayed for antibacterial activities.

![Scheme 1.2](image)

1.3. Synthesis of hydrazones from substituted phenyl hydrazine and aldehydes.
The present scheme demonstrates the mechanistic synthesis of hydrazones derived from substituted phenyl hydrazine and various aldehydes under catalytically free condition. This protocol does not require any catalyst or any organic solvents. The obtained products are well characterized by the spectroscopic methods like IR, $^1$HNMR, Mass.

![Scheme 1.3](image)

1.4. Synthesis of hydrazones from substituted phenyl hydrazine and ketones.
In continuation of our studies on structure modifications we condensed substituted phenyl hydrazine with different substituted ketones under catalytically and solvent free condition. The obtained products are well characterized by the spectroscopic methods like IR, $^1$HNMR, Mass and also assayed for antibacterial activities.
CHAPTER-2: Synthesis of Schiff bases

2.1. Synthesis of Schiff bases from 4,5-diazafluoren-9-one

The present scheme deals with formation of Schiff bases from 4,5-diazafluoren-9-one and substituted amines. This scheme involves initial conversion of 1,10 phenanthroline (1) into 4,5-diazafluoren-9-one (2) by using potassium permanganate. The 4,5-diazafluoren-9-one is further condensed with substituted amines (3) under solvent free condition to get desired product. The obtained products (4) are well characterized by the spectroscopic methods like IR, $^1$HNMR, Mass and also assayed for antibacterial activities.

2.2. Synthesis of Schiff bases from 4-amino-3-methyl phenol

The present scheme demonstrates the solid phase synthesis of Schiff bases derived from 4-amino-3-methyl phenol under catalytically and solvent free condition. This protocol does not require any catalyst or any organic solvents. The obtained products are well characterized by the spectroscopic methods like IR, $^1$HNMR, Mass and also assayed for antibacterial activities. In this some synthesized compounds given good biological activity.
2.3. Synthesis of Schiff bases from 2-amino-4-methyl phenol

In continuation of our studies on structure modifications we condensed 2-amino-4-methyl phenol with substituted aldehydes and ketones under catalytically and solvent free condition. The result demonstrated that excellent yield of the products. The obtained products are well characterized by the spectroscopic methods like IR, $^1$HNMR, Mass and also assayed for antibacterial activities.

CHAPTER-3: Synthesis of Benzodiazepines and Benzimidazoles

3.1. SnCl$_2$·2H$_2$O catalyzed synthesis of benzodiazepines

SnCl$_2$·2H$_2$O is frequently used in organic synthesis as a catalyst due to its properties such as nontoxic nature, easy availability, inexpensiveness and easiness for work up. It plays excellent role as a Lewis acid. In this scheme we synthesized 1,5-benzodiazepine by using symmetrical and unsymmetrical diamines and substituted ketones in presence of SnCl$_2$·2H$_2$O as a catalyst under solvent free condition.
3.2. $K_4[Fe(CN)_6]$ catalyzed synthesis of benzimidazoles in water media
The metal co-ordinate complex $K_4[Fe(CN)_6]$ utilize carbon-nitrogen bond formation for the synthesis of benzimidazoles from aromatic aldehyde and diamines in water media at room temperature given product with excellent yield.

![Scheme 3.2](image)

3.3. $K_4[Fe(CN)_6]$ catalyzed synthesis of benzimidazoles on grinding
In continuation of our studies on rapid synthesis, we synthesized benzimidazoles from aromatic aldehyde and diamines under solvent free condition with excellent yield. The process is green, mild and inexpensive.

![Scheme 3.3](image)

CHAPTER-4: Synthesis of meso-Substituted Dipyrromethanes

4.1. $SnCl_2\cdot2H_2O$ catalyzed synthesis of meso-Substituted Dipyrromethanes
Highly rapid and simple methodology has been developed for the quantitative synthesis of meso-substituted dipyrromethanes from lowest pyrrole/aldehyde ratio. The method was carried out by using $SnCl_2\cdot2H_2O$ as a catalyst under solvent free condition. The method is environmentally friendly, easy to workup, and gives excellent yield of the products.

![Scheme 4.1](image)
4.2. Iodine catalyzed synthesis of meso-Substituted Dipyromethanes

Iodine plays an excellent role as a Lewis acid in many organic conversion reactions. I$_2$ in solvent free conditions was found to be an efficient catalyst in terms of handling, temperature, reaction time and yield for various organic transformations. In present scheme we got excellent yield of meso-Substituted Dipyromethanes under solvent free condition. This reaction was carried out under iodine catalysis.

4.3. Iodine catalyzed synthesis of meso-Substituted Dipyromethanes from substituted ketones

CHAPTER-5: Synthesis of Benzoxazoles and Benzothiazoles

5.1. K$_4$[Fe(CN)$_6$] catalyzed synthesis of benzoxazoles in water media

The metal co-ordinate complex K$_4$[Fe(CN)$_6$] utilize carbon-nitrogen bond formation for the synthesis of benzoxazoles from aromatic aldehyde and substituted 2-aminophenol in water media at room temperature given product with excellent yield.
5.2. $K_4[Fe(CN)_6]$ catalyzed synthesis of benzoxazoles on grinding

In continuation of our studies on rapid synthesis, we synthesized benzoxazoles from aromatic aldehyde and substituted 2-aminophenol under solvent free condition with excellent yield. The process is green, mild and inexpensive.

$$\text{CHO}$$

$\text{R}_2$

$\text{NH}_2$

$\text{OH}$

$\text{N}$

$\text{O}$

$\text{R}_1$

$k_4\text{Fe(CN)_6}$

grinding

$\text{R}_2$

$\text{R}_1$

1 2 3

Scheme 5.2

5.3. $K_4[Fe(CN)_6]$ catalyzed synthesis of benzothiazoles in water media

The metal co-ordinate complex $K_4[Fe(CN)_6]$ utilize carbon-nitrogen bond formation for the synthesis of benzothiazoles from aromatic aldehyde and 2-aminobenzenethiol in water media at room temperature given product with excellent yield.

$$\text{CHO}$$

$\text{R}_2$

$\text{NH}_2$

$\text{SH}$

$\text{N}$

$\text{S}$

$\text{R}_1$

$k_4\text{Fe(CN)_6}$

water

$\text{R}_2$

$\text{R}_1$

1 2 3

Scheme 5.3

5.4. $K_4[Fe(CN)_6]$ catalyzed synthesis of benzothiazoles on grinding

In continuation of our studies on rapid synthesis, we synthesized benzothiazoles from aromatic aldehyde and 2-aminobenzenethiol under solvent free condition with excellent yield. The process is green, mild and inexpensive.

$$\text{CHO}$$

$\text{R}_2$

$\text{NH}_2$

$\text{SH}$

$\text{N}$

$\text{S}$

$\text{R}_1$

$k_4\text{Fe(CN)_6}$

grinding

$\text{R}_2$

$\text{R}_1$

1 2 3

Scheme 5.4