SYNTHESIS AND REACTIVITY OF SOME PYRAZOLE DERIVATIVES

The designing and synthesis of new pyrazole derivatives is very important for biological and pharmacological activities. This derivative is behaving as anti-cancer, anti-inflammatory, anti-oxidant, anti-fungal, anti-glycemis, anti-amoebic and anti-depressive. Pharmacological activities of some of the drug molecules improved due to pyrazole nucleus directly attached to heterocyclic moieties. Most of the pyrazole containing heterocyclic compounds existed in market as drugs like cartazolate, zaleplon, sildenafil, allopurinol, indiplon, etazolate, etc. Fused pyrazole derivatives, particularly pyrazoloazines were reported to mimic purine bases, present in DNA and RNA because of their close structure resemblance.

Pyrazole is a five membered heteroaromatic compound which contains two adjacent nitrogen atoms. NH-Pyrazoles as weak bases and moderately weak acids because of having a pyridine type proton acceptor nitrogen atom (C=N) and proton donating behaviour of one pyrrole-type nitrogen atom (N-H). The metal complex is prepared with different type of pyrazoles derivatives due to pyridine -like N-atom present in the respective ligand. Pyrazoles compounds can react with electrophilic reagents at fourth position easily and will react to nucleophiles poorly at position of 3 and 5 due to π-excess aromatic heterocyclic. However, pyrazole reactivity can be increased in both electrophiles and nucleophiles by introducing electron withdrawing (EWG) or electron donating groups (EDG) attached to pyrazole derivative. Physicochemical properties of pyrazole are mainly depends on nitrogen atoms and electronic effects of substituents attached to the ring system.

Many pyrazole derivatives also exist sensor activity. The physicochemical properties of molecular system change between chemical species interaction called as chemosensor. The possible guest species are called as cations, anions or neutral molecules. The chemosensors

components are fluorophore, a spacer and a receptor unit. The central processing unit (CPU) of chemosensor called as a receptor. While designing of chemosensor, need to give importance for both receptor and signalling moieties, in this selectivity is responsible for receptor unit and capability of binding while signalling moiety behave as signal transducer, i.e., during binding of analyte, the sensor compound shows different absorption/fluorescence signals compare with free sensor in the solution, permitting the guest species quantitative determination.

Based on the above discussion, the research work was carried out to target the synthesis of new series of pyrazole derivatives and these derivatives are studied on biological activity, chemosensor study and the results are presented in the thesis. The introductory chapter explains a general background about the synthesis, biological activity and application of heterocyclic chemistry, pyrazole contain oxazole and pyrazole derivatives, while the second chapters explain about the details of material, method, instruments and software which was used throughout the study. The remaining four chapters explained about the results and conclusions of the research work carried out in the current study.

Chapter-I: Introduction

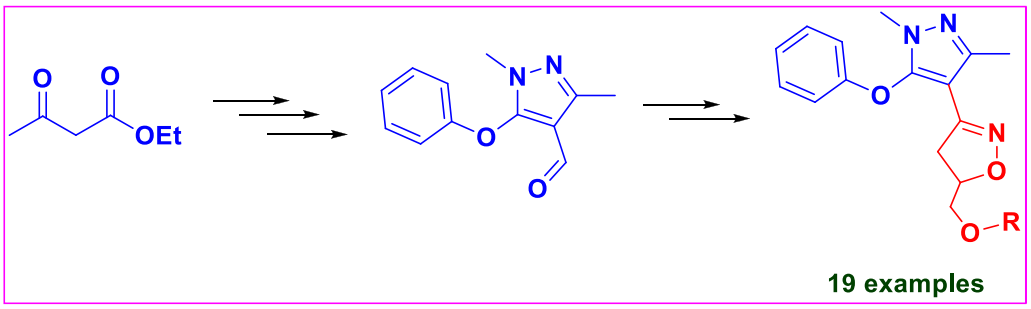
A general introduction about Heterocyclic chemistry, Isoxazole, imine, palladium catalyst chemistry, sensors is presented in Chapter-I in which describes the overview of synthesis, biological activities and other application.

Chapter-II: Materials and Methods

This chapter presents details of the chemicals, methods, instruments and software employed throughout the research study.

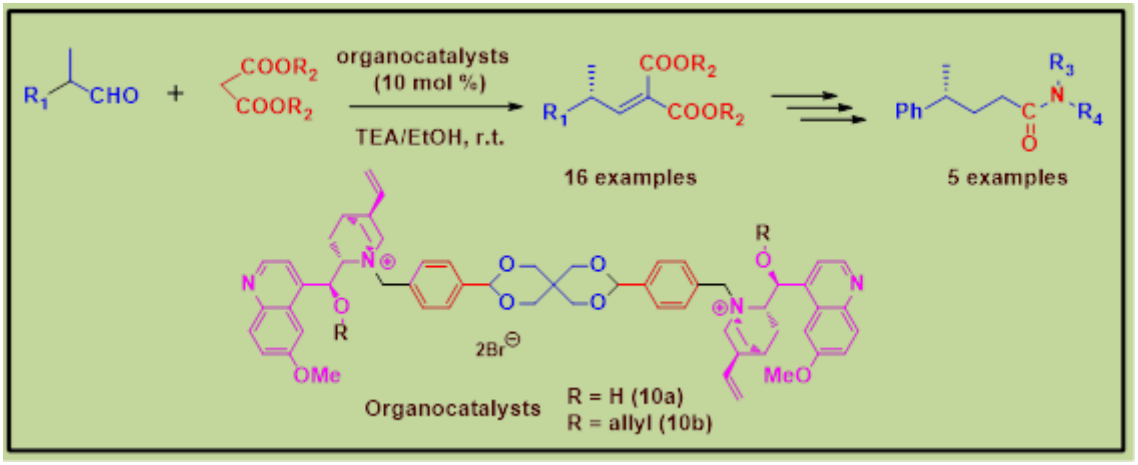
Chapter-III: Design, simple and efficient synthesis of bio active novel pyrazolyl-isoxazoline hybrids

A simple and new methodology introduced for the synthesis of novel bioactive pyrazolyl-isoxazoline hybrids has been described from the reactions of pyrazoline substituted oximes and various substituted allyoxy benzene through easily available inexpensive starting materials. All the novel synthesized target hybrids were characterized by NMR, IR, and Mass spectroscopic techniques. We were applying the some of the hybrid materials for anti-bacterial and anti-fungal studies. The hybrid materials **6m** and **6p** having the best anti-bacterial and antifungal activities.



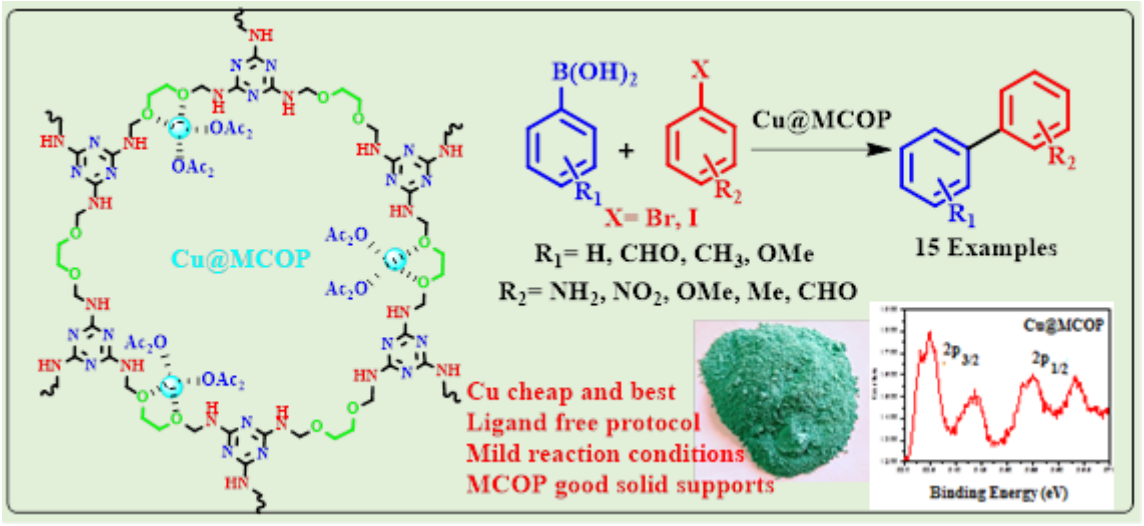
Chapter-IV: The Organocatalytic Highly Enantioselective Knoevenagel Condensation: Applications in the Synthesis of Various Chiral Amide Derivatives

In this work, efficient organocatalysts were designed, synthesized and successfully applied to the Knoevenagel condensation. In this reaction, different α-branched aldehydes were treated with various malonate compounds to give the desired products up to 97 % yield and excellent e.r up to 99.68: 0.32 under the mild reaction conditions. Moreover, the Knoevenagel product was converted into different chiral amide derivatives in higher enantioselectivity



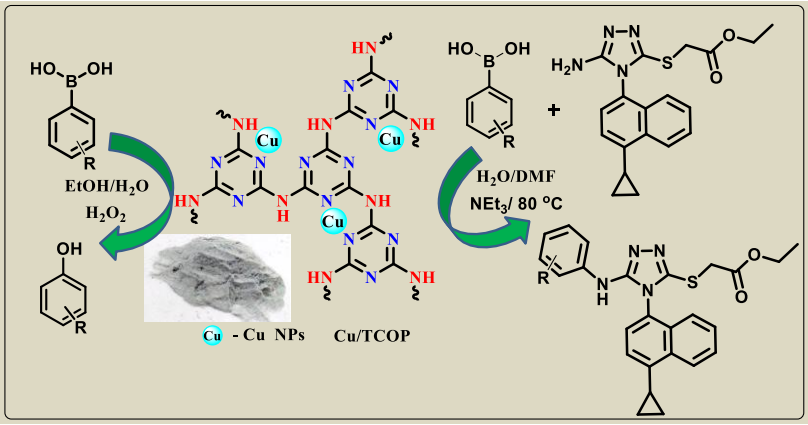
Chapter-V: Cu(OAc)2-entrapped on ethylene glycol modified melamine-formaldehyde polymer as an efficient heterogeneous catalyst for Suzuki-Miyaura coupling reactions

$Cu(OAc)_2$-entrapped on ethylene glycol modified melamine-formaldehyde polymeric material (Cu@MCOP) have been successfully synthesized in a simple procedure using commercial available starting materials via solvothermal approaches. Powder X-ray diffraction, FT-IR, UV-DRS, X-ray photo electron spectroscopy, SEM and elemental mapping have been used to authenticate the polymeric materials Cu@MCOP.In addition, the prepared and characterized Cu@MCOP were applied to check the heterogeneous catalytic application for the formation of C-C bond through Suzuki-Miyaura cross coupling of various aryl halides and substituted organoboranes under normal reaction conditions. Furthermore, the copper source was easily available, low cost, cheap and best instead of palladium. Which shows good catalytic activity and excellent yield (up to 86%), the catalyst can be separated easily and recycle for five times.



Chapter-VI: Copper Nanoparticles Supported on Highly Nitrogen-Rich Containing Covalent Organic Polymers as Heterogeneous Catalyst for N-Arylation and Oxidation of Phenylboronic acid

Here we have demonstrated facile synthesis of nitrogen-rich triazine containing covalent organic polymers (Cu/TCOP) which has been prepared by the nucleophilic substitution reaction between melamine and cyanuric chloride then mixture of DMSO and 1,4-dioxane (1:1) at 90 ºC for about 48 h under solvothermal techniques. Further, the synthesized materials were thoroughly characterized by different analytical techniques. The prepared Cu/TCOP heterogeneous catalysts exhibited high catalytic activity for promoting to oxidation reaction of variety of aryl boronic acid and H_2O_2 as an oxidant in a EtOH/water (1:1) medium for about 25 minutes at ambient temperature to obtain excellent yield (up to 99%) and then same catalyst was carried out for N-arylation of phenyl boronic acid with triazole derivative **S1-a** in DMF/water (1:1) ratio solvent, triethylamine as a base for about 10 h at 80 °C to give very good yield up to 90% and high turnover number under less reaction time, phosphine-free catalyst, and mild reaction conditions.



Chapter-VII: Incredible Colorimetric Sensing Behavior of Pyrazole-Based Imine Chemosensor Towards Copper(II) Ion Detection: Synthesis, Characterization and Theoretical Investigations

Herein, we synthesize more conjugated compounds like as substituted phenyl, fluorene, anthracene, and pyrene based pyrazole derivatives with good yield. All the compounds were thoroughly characterized by various spectral techniques such as NMR and mass analysis. Further, we studied the photophysical behavior of some strained/sterically hindered pyrazole derivatives (hybrids) upon the addition of analytes using UV-visible spectroscopic techniques. All the hybrid compounds are good colorimetric sensor for copper(II) ion. AS1, AS2 and AS3 hybrid compounds limit of detections are 0.62 mM, 0.47 mM, and 4.4 mM respectively. The Binding constant of the hybrid compounds of AS1, AS2 and AS3 are 3.1 x 10^{-2} M, 2.3 x 10^{-2} M and 3.9 x 10^{-2} M respectively. The detection limit and binding constant of anthracene based hybrid AS2 are superior when compared to AS1 and AS3. In addition to that we found ligand to metal charge transfer in AS1 and AS2. Further, ligand to the metal charge transition of the probe with analyte were confirmed by density function theory (DFT) through Gaussian 09 Software.