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An Environmentally Friendly Approach to Pyrazole And 1,2,3- Triazole Chemistry: Novel Clay Catalysis, Bioactive Schiff Bases, And Polymer Design: A ReviewCH. Sreedhar Reddy, S. Kavitha²¹Research scholar, Department of Chemistry, Chaitanya Deemed University Hyderabad, India.²Professor, Department of Chemistry, Chaitanya Deemed University Hyderabad, India**Article Information**

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Keywords*Alhagi maurorum*, Azide-Alkyne Cycloaddition, CuAAC reactions**ABSTRACT**

Heterocyclic compounds, especially the nitrogen-containing scaffolds pyrazole and 1,2,3- triazole, are important building blocks in organic chemistry because they are used in so many ways to find new drugs and make useful molecules. In the past, many medicinal plants, like *Alhagi maurorum*, had a lot of these substances. For example, the plant itself has pyrano flavonoids, which are anti-inflammatory and antioxidant. Because of the high demand for these chemicals, one of the main goals of this study was to find ways to make them that are greener, cheaper, and more selective for specific regions. The main focus of the study was on the CuAAC reaction, which is an Azide-Alkyne Cycloaddition. It was important to make a new catalyst system that works very well and is easy to make: clay-supported copper(II) nitrate activated with hydrazine hydrate. This catalyst did a great job of speeding up the CuAAC reactions in just 1 to 10 minutes at room temperature and, most importantly, without any solvents. It provides a better and more long-lasting option to current methods. In addition to making triazoles, the project also included making and testing pyrazole-linked Schiff bases for their antibacterial and antioxidant qualities and coming up with pyrazole-derived polymers for use in sensors.

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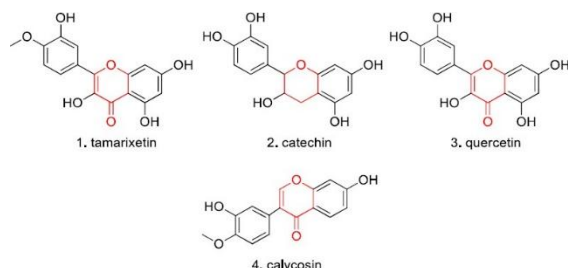
1. INTRODUCTION:

Because of its extensive coverage of organic molecules, its remarkable characteristics, its ease of synthesis, and the wide range of applications it provides, heterocyclic chemistry is an essential branch in organic chemistry. Heterocyclic compounds are abundant and find use in many fields, from business to medicine. Polymers, food processing, supramolecular chemistry, veterinary goods, pharmaceuticals, sanitizers, anti-ordinaters, surfactants, anti-corrosion products, semiconductors, waterproofing agents, and a host of other fields make use of them.

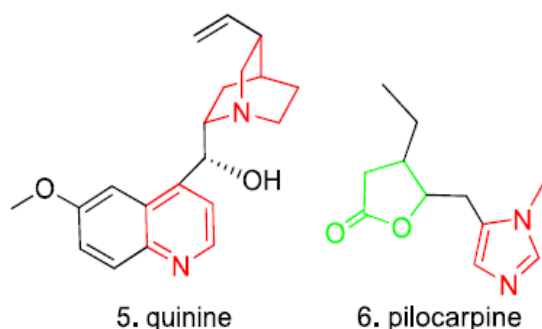
1.1 Historical Background of Heterocyclic Compounds**1.1.1 The Natural Heterocyclic Compounds**

In recent years, it has been found that many plants and herbs used for medicinal purposes in ancient times contained a high concentration of heterocyclic compounds. One such herb is *Alhagi maurorum* Medik, which the ancient Egyptians, Greeks, and Romans used to treat a variety of ailments, such as fever, anorexia, dermatosis, bloody diarrhea, asthma, epistaxis, rheumatism, hemorrhoids, liver diseases, digestive disorders, kidney stones (Al-Douri et al., 2010), and more (Duke et al., 2008; Al-Douri et al., 2010; Al-Douri et al., 2010; Al-Douri et al., 2010; Al-Douri et al., 2010; Al-Douri et al., 2010; Al-Douri et al., 2006). *Alhagi maurorum* plant mostly contains heterocyclic compounds called pyranoflavonoids. These compounds are non-aromatic and include pyran as an oxygen atom (Memon et al., 2014). Tamaroxetin, catechin, quercetin, and calycosin are some of the pyranoflavonoids found in *A. maurorum*. They have

anti-inflammatory and antioxidant properties. Quercetin and calycosin also have anticancer properties and can treat neurological illnesses (Gao et al., 2014).

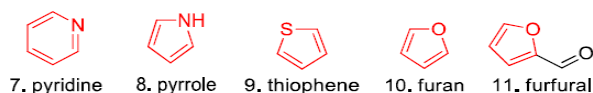


Cinchona bark tree extract, which contains quinine [5], was used to cure fever and malaria in the seventeenth century. The structure of the isolated quinine compound was also unknown at that time (Achan et al. 2011). Pelletier et al. (1820) were the first to isolate quinine from cinchona tree bark, which was subsequently employed as an anti-malarial drug. A basic alkaloid with an L-histidine derivative structure, imidazole acts as an active heterocyclic ring in pilocarpine [6]. The medication pilocarpine has been in use since 1875 to treat a variety of medical issues, such as skin disorders, muscle discomfort, cardiovascular ailments, and more, after being taken from the Pilocarpus Jaborandi plant (Herbert et al., 1904). Xerostomia, or dry mouth, is a symptom that can develop in patients with head and neck cancer; pilocarpine has mostly been used to treat acute and chronic instances of open angle glaucoma (Patten et al., 2010).



The discovery and subsequent widespread knowledge of heterocycle rings and their ring configurations occurred in the latter part of the nineteenth century. Among the first heterocycles found in an oily combination created by intense heating of bones were pyridines [7] and pyrroles [8], which contained nitrogen (Encyclopaedia Britannica). The sulfur-containing heterocycle thiophene was found as a by-product in an 1882 experiment that purified benzene from natural resources. At the tail end of the nineteenth century, scientists found two heterocyclic compounds that included oxygen: thiophene and furan [10] (Steinkopf et al., 1941). Natural heterocycles have been postulated for thiophene and furan. In addition to thiophene and its derivatives, which have been

identified in cool tar, furan and its close chemical relatives were found in oat hulls and corncobs. Subsequently, furan and its derivatives were found in a wide variety of natural products, including alkaloids, polyketides, terpenes, and various plants and marine organisms (Weinreb et al., 2009; Nicolaou et al., 2009; Gaich et al., 2009; Weinreb et al., 2009; Gaich et al., 2009; Weinreb et al., 2009; Nicolaou et al., 2009; Gaich et al., 2009; Weinreb et al., 2009; & Gaich, 2009). Conversion to the other compounds has also made use of both rings as scaffolds or intermediates.

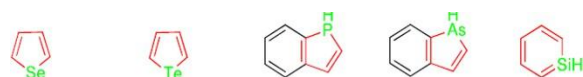


The 20th century saw an uptick in the discovery of natural heterocycles following WWII. Discoveries in the field of heterocyclic rings and their derivatives and compounds have led to a plethora of research into the biological activities and medicinal treatment potential of various plant, terrestrial, and marine-derived heterocyclic compounds. One example is the heterocyclic ring with two heteroatoms, often known as thiaziridine.

1.2 The Definition and Classification of Heterocycles

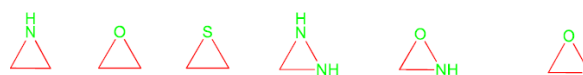
The common definition of heterocyclic compound is:

Any class organic compounds whose molecules contain one or more rings of atoms with at least one atom (the heteroatom) being an element other than carbon, most frequently nitrogen, oxygen, or sulfur. Beside N, O and S heteroatoms, there are other heteroatoms that can participate, though not so common, these appear in configuration of the heterocyclic ring as selenium selenophene 12, tellurophene 13, phosphindole 14, arsinidole 15, silabenzene 16. The heterocyclic ring type is the foundation for heterocyclic compound categorization. The structure of the heterocyclic ring might be either aromatic or non-aromatic.



1.2.1 Non-Aromatic Heterocycles:

Aliphatic heterocycles are another name for non-aromatic heterocycles. Amines, ethers, thio-ethers, amides, and so on all have cyclic counterparts in this group. Examples of non-aromatic heterocycles include aziridine [17], oxirane [18], and thiirane [19], as well as diaziridine [20], 1,2-oxaziridine [21], and 1,2-oxathiirane [22], which are all three-membered rings.



1.3 Nitrogen Containing Heterocycles:

Compounds containing nitrogen are part of a vast family known as heterocyclic compounds. As mentioned in sections 1.1.1 and 1.1.2, they can be found in a wide range of organic and synthetic substances. Over the past few decades, N-containing heterocycles have found widespread use in bioactive compounds, medicines, therapeutic chemicals, and more as a result of their significant biological properties. It is common practice to employ N-containing heterocycles as structural components in compounds that exhibit bioactivity or participate in supramolecular applications. While N-containing heterocycles have been involved in coordination chemistry, chiral ligands of N-heterocycles have shown great productivity in organic synthesis, industrial applications, and environmental concerns. An example of an N-heterocyclic ligand in the context of N-heterocyclic carbenes (NHCs) is the imidazole ring [23]. Some researchers in the domains of hydrogenation reaction catalysis and coordination chemistry have taken an interest in these ligands (Fantasia et al., 2007). Diazine ligands [24] were developed in the beginning of the 1900s, and the N-N bond in diazine functions as a bridge. Dinuclear complexes involving diazine and conjugated aromatic heterocycles can be formed by a variety of transition metals (Xu et al., 2003).

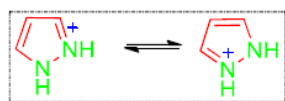
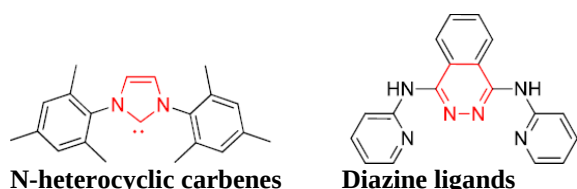


Figure 1.1: The resonance configuration of pyrazole ring



1.4 N-Containing Aromatic Heterocyclic Five Membered Ring:

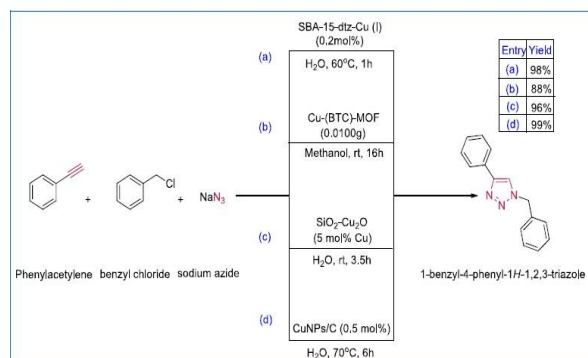
1.4.1 Pyrazole:

On the first and second places of a five-member aromatic heterocycle ring are the nitrogen atoms found in pyrazole. Among the 1,2-azoles, pyrazole is a member, as are isothiazole and isoxalazole. Physical properties of the pyrazole ring include its resonance, which is shown in Figure 1.1, its solid state at room temperature, its melting point of 70 °C, and its boiling point of 187 °C. Additionally, pyrazole is planar and has regular pentagonal geometry, as stated by Joule et al. (2000).

2. LITERATURE REVIEW:

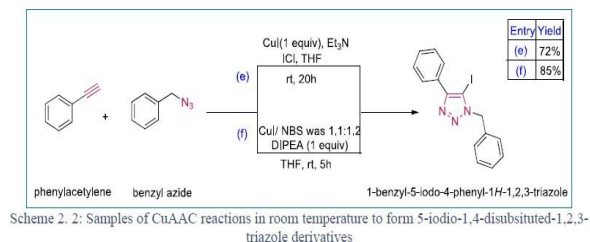
1,2,3- Triazole New Protocol to Synthesize 1,4-

Disubstituted 1,2,3- Triazole from Azide-Alkyne Cycloaddition Reaction. In this chapter, we will show you how to make 1H-1,2,3-triazole derivatives by using a 1,3-dipolar cycloaddition procedure using azides and alkynes. The 1,4-disubstituted-1H-1,2,3-triazole exhibited favorable regioselectivity compared to 1,5-1H-1,2,3-triazole when treated with copper (I). Almost all of the necessary 1,4-1H-1,2,3-triazole derivatives were produced in a very short amount of time using the newly designed Cu(I) catalytic system. There is no way to regulate the regioselectivity in the thermal azide-alkyne cycloaddition process, and it is quite slow. According to Tornøe et al. (2002) and Rostovtsev et al. (2002), Meldal and Sharpless independently discovered that Cu (I) may enhance the cycloaddition reaction of azide and alkyne at room temperature, leading to the production of regioselective 1,4-disubstituted-1,2,3-triazole. On their own, they accomplished this. Copper (I) has been the focus of many protocol advancements since then because of its exceptional regioselectivity and great efficiency in increasing reaction speeds and yields. Utilizing a range of Cu catalytic techniques, the production of homogeneous, heterogeneous, and nanoparticle 1,2,3-triazole derivatives has been achieved. Other solvent systems, such as water, ionic liquid, or alcoholic solvents, have also been shown to improve the cycloaddition process. Regardless, a number of Cu(I) sources have been used in the multi-component processes. The first plan involves a multi-component method that uses Cu (I) as a catalyst to synthesize 1,4-disubstituted-1,2,3-triazoles (Gupta et al., 2015; Alonso et al., 2010).



Scheme 2. 1: Cu (I) as catalyst in multicomponent reaction to synthesize 1,4-disubstituted 1,2,3- triazoles

Using azo compounds and terminal alkynes, the 1,3-dipolar cycloaddition process invariably adheres to Scheme 2. 2. At room temperature, 5-Iodio-1,4-disubstituted-1,2,3-triazole compounds were synthesized from CuAAC reaction samples.



2.1. A Method for Making Clay-Cu (II)

Montmorillonite K10 clay, often known as Mont K10, has found use as a metal support in a number of chemical syntheses because of its intense characteristics. There are several benefits to using K10 clay, including its low cost, minimal environmental effect, ease of handling, and great flexibility. Mont K10 is an aluminosilicate chemical with cationic characteristics due to its acidity. To name only a few of its many outstanding features, Mont K10 clay stands out. Impressive recovery and reuse, swelling, ease of work up, milder usage conditions, high cation exchange capacity, and a long list of other benefits are just a few of the numerous. If the surface reactant concentration increases, it might mean that the clay is providing support for something. These further characteristics make K10 clay suitable for metal intercalation, namely copper (II).

nitrate trihydrate $\text{Cu}(\text{NO}_2)_3 \cdot 3\text{H}_2\text{O}$ catalyse The cycloaddition of azides to alkynes is a step in this process, as stated by Kumar et al. (2014). A method that has been described in great length in the literature was used to synthesize claycop. By adding 10 grams of copper (II) nitrate trihydrate to 250 ml of acetone and stirring for 10 minutes, a solution was formed. To remove the solvent from the product in suspension, a rotating vacuum evaporator was employed. After the 50-minute evaporation process at 50°C , a reactive powder that was brilliant blue in color was produced. This powder maintained its reactive properties for months to come. Measurements of BET surface area and powder XRD were used to characterize Claycop. Powder X-ray diffraction analyses verified that the clay's surface contained $\text{Cu}(\text{NO}_2)_3 \cdot 3\text{H}_2\text{O}$. Four separate peaks at the refraction angles shown in the picture were visible in the XRD pattern.

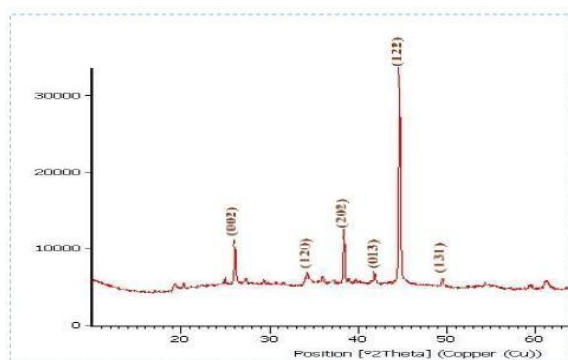


Figure 2. 1: Powder-XRD pattern of claycop

2.2. Synthesis Hybrids of Pyrazole and 1,2,3-triazole:

In order to produce molecules with improved bioactivity, there has been a recent push in the literature to find more efficient, regioselective, and ecologically friendly ways to synthesize these heterocyclic scaffolds.

- **Revolutionary Hybrid Frameworks:** Molecular hybridization, which involves linking pyrazole with other heterocycles such as 1,2,3-triazole and isoxazole, remains a primary area of research. A number of cancer cell lines, including MCF7, HEPG2, and HELA, have been tested for their ability to proliferate in response to newly synthesized 1,2,3-triazole and isoxazole-linked pyrazole derivatives.

- **Eco-Friendly Catalysis and Chemistry:** In 2024, a more environmentally friendly approach to synthesizing 1,2,3-triazole was found, which satisfied your target of using less toxic and more cost-effective water. The synthesis and assessment of new 1,2,4-triazole clubbed pyrazole derivatives for antibacterial and antioxidant activities is described in another research from 2025. It was reported in a September 2025 publication that oxazole hybridized with pyrazole and/or thiazole molecules were designed and synthesized using computational drug design methods. In order to forecast and validate binding affinities to biological targets, such as human carbonic anhydrase II, these investigations frequently employ molecular docking and density-functional theory (DFT) analysis.

2.3 Biological Activity of Schiff Bases Based on Pyrazole

One important area of investigation is the multi-target agent potential of pyrazole-linked Schiff bases. Multi-Target medications (2024): A study conducted in May 2024 investigated Schiff bases based on pyrazoles as potential novel medications that target multiple human diseases. The compounds were tested in vitro for their anti-diabetic properties. An article published in 2025 details the synthesis of copper(II) complexes with pyrazole-linked Schiff bases, as well as other metal complexes and potent therapeutics. These metal complexes were highly effective and selective against *Plasmodium falciparum* when used as Antimalarial drugs. A class of anticancer medicines known as "compounds" outperformed standard treatments like cisplatin in their ability to selectively target A549 lung cancer cells.

2.5 Study of the Phytochemicals in Alhagi maurorum:

By examining the active secondary metabolites of *Alhagi maurorum*, such as pyranoflavonoids, modern science has provided credence to the plant's long history of usage in traditional medicine.

- **Increase of Phytochemical Activity (2025):** The possibility of increasing the yield of medicinal metabolites, such as total flavonoids and total phenolic

compounds, in *Acinetobacter maurorum* tissue culture was explored in a study conducted in August 2025 utilizing copper oxide nanoparticles (CuO NPs) that were green-synthesized. This exemplifies a cutting-edge biotechnology strategy for extracting the most therapeutic benefits from the plant.

• **Compound Identification (2025):** It was reported in February 2025 that the root extract of *A. maurorum* contained active phytochemical compounds, which were identified using Gas Chromatography-Mass Spectroscopy (GC-MS). Along with the traditional usage indicated in your document, the discovered chemicals are known to possess anti-inflammatory, anti-cancer, antibacterial, and anti-ulcerogenic actions. Anti-biofilm properties in the year 2024: The anti-infective potential of *Alhagi maurorum* extract in combination with lytic phage cocktails was investigated in a recent study (2024), which demonstrated a promising treatment approach against biofilms of *Proteus mirabilis*, a multi-drug-resistant bacterium. These medicinal effects are believed to be attributable to the plant's known active components, such as flavonoids.

3. SCOPE

Considering the wide range of uses for pyrazole and 1, 2, 3-triazole compounds, there is a significant demand for their manufacturing. New approaches to improving the yield of highly regioselectivity target molecules in shorter time frames have been explored. The goal of developing new methods is to produce the necessary goods at a reasonable cost while adhering to the principles of green chemistry.

Consequently, there is a critical need for, and great potential for, the development of safer methods for the synthesis of pyrazole and 1, 2, 3-triazole scaffold.

4. OBJECTIVES

1. Creating environmentally friendly processes for making nitrogen-containing heterocycles like pyrazoles and 1, 2, 3-triazoles

2. The synthesis and biological assessment of Schiff bases containing pyrazole for their antioxidant, antibacterial, and anti-inflammatory properties.

3. pyrazole-derived polymer design and synthesis.

4. Investigations using fluorescent and anion sensing techniques on the synthetic polymers.

5. CONCLUSION:

After reviewing several published protocols, this study was compared to a range of others and was determined to be the most beneficial and best. The catalyst system for the synthesis of 1,4-distributed 1,2,3 -triazoles, which consisted of clay-supported copper(II) nitrate and hydrazine hydrate, was found to be both quickly

manufactured and tolerable to a wide variety of azides and alkynes. In a brief time frame of 1-10 minutes at room temperature and without the presence of solvent, the CuAAC reactions were satisfactorily catalyzed by the catalyst. This catalyst, which was created via a gentle process, has several potential useful uses.

Here are the 25 references, including author name(s), paper title, journal name, and year of publication, presented in a single-line format and sorted in ascending order of the publication year.

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