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A Review On Pyrazole An Its Derivative

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Abstract: Pyrazole and its derivatives are a class of organic compounds that have garnered significant attention in medicinal chemistry and organic synthesis due to their diverse biological activities and versatile applications. These five-membered heterocyclic rings, containing two nitrogen atoms, serve as valuable scaffolds for developing a wide range of therapeutic agents. There are several applications of pyrazole core based organic molecules in various areas including pharmacy and agro-chemical industries. There is various method used for manufacture of pyrazole and its derivative. The purpose of the review was to collect various pharmacological actions which was reported in recent years made on its moiety. Pyrazole and its derivatives are prepared by dehydrogenating 2-pyrazoline or its derivative by process in which the reaction is carried out using sulfuric acid in the presence of iodine or of an iodine compound. Taking into considerations diversity in the biological activity, this nucleus has attracted attention of many researchers to study its skeleton chemically and biologically. This review highlights the different synthesis methods and the pharmacological properties of pyrazole derivatives. Development of pyrazole an its derivative has been reported by many scientists in decades.

Keywords: Pyrazole, Synthesis, Scheme of pyrazole.

Introduction

Medicinal or pharmaceutical chemistry is a discipline at the intersection of chemistry that involves identification, synthesis and development of new chemical entities suitable for therapeutic use. It also includes the study of existing drugs, their biological properties, and their quantitative structure-activity relationships (QSAR). Heterocyclic compounds are cyclic organic substances which contain at least one atom other than carbon in the ring system. It is evident that more than a third of the known organic compounds are heterocyclic.[1] Many anticancer, anti-inflammatory, antidiabetics, antimalarial, alkaloids, vitamins, antibiotics and dye stuffs are heterocyclic, including building blocks of life like nucleic acid also. Five and six-membered heterocyclic ring containing compounds form an important part of medicinal

chemistry as large number of drugs which exist as of today bear these nuclei. Cancer, a major health impediment for both developed and underdeveloped countries, involves abnormal cell growth with the potential to invade or spread to other parts of the body. According to the World Health Organization (WHO) report, 8.8 million people died of cancer globally in 2015 [1]. Most cancers are recognized by uninhibited growth of cells without demarcation due to the deregulation of crucial enzymes and proteins controlling cell division and proliferation. obesity, poor nutrition, physical inactivity and /or excess alcohol consumption are responsible for 20% of all cancers diagnosed. Infection due to Human papilloma virus (HPV), hepatitis B virus (HBV), hepatitis C virus (HCV), human immunodeficiency virus (HIV), and Helicobacter pylori (H. pylori) are also a cause of cancer. Although much progress has been aspired from the identification to the treatment of cancer, factors like poor patient compliance, drug resistance and drug induced toxicities has provided a strong impetus for the discovery and development of novel cancer chemotherapeutic hybrids of clinical significance [2]. Consequently, in the development of effectual and discerning anticancer drugs having low incidence of side effects, toxicity and emergence of drug resistance is of high priority [3]. To address this issue, combination therapy was considered, where numerous cytotoxic hybrids were pooled in anticancer behaviour regimes that endorse improved results with fewer side effects. The efficient and rapid synthesis of biologically active molecules has stimulated synthetic chemists to explore and develop novel strategies which could be certainly useful to the academia and industry.[4] In the past decade the diversity-oriented synthesis and versatile concepts of multi-component processes have extensively motivated the synthetic scientific community. The synthesis of pyrazole and isoxazole derivatives has been the subject of consistent interest because of the widespread applications of such heterocycles in pharmaceutical as well as agrochemical industry. Pyrazoles and isoxazoles are well known for their anti-inflammatory activity. In order to develop potent anticaner agents, a novel series of 3-(1H-indol-3-yl)-2,3,3a,4-tetrahydrothiochromeno[4,3-c]pyrazole derivatives were synthesized. Structures of all compounds were confirmed. MTT assay has been employed to study antiproliferative activity of these compounds with four human cancer cell lines [5] and a normal cell line L929. Most of these compounds showed potential anticancer activity and low cytotoxicity on normal cell in vitro. Numerous compounds containing pyrazole and isoxazole moieties have been shown to exhibit anticancer, integrin avb3 receptor antagonists, antimicrobial, molluscicidal, glycine agonists, 20-hydroxyeicosatetraeonic acid (20-HETE) synthase inhibitory, histone deacetylase 3 and 8 (HDAC3 and HDAC8) gene inhibitory, and antioxidant activities [6]. Furthermore, 1,5-benzoxazepine derivatives have been recognized as novel microtubule-targeting agents. Some substituted benzoxazepine and benzothiazepine were found to exhibit antipsychotic and anticonvulsant activity. Moreover, there are some reports for benzothiazepine and benzodiazepine derivatives as anti-inflammatory agents. Several benzothiazepine derivatives have been reported to have potential calcium channel blocker activity. Benzodiazepines were found to show sentrin- specific protease (SENP1) and p53-mouse double minute 2 (p53-MDM2) inhibitory activities. On the other hand, the heterocyclic compounds containing aryl sulfonate moiety are known to exhibit marked antimicrobial activity[7]. In addition, they are possessed of potential papillomavirus microbicidal, anti-human immunodeficiency virus-1, antineoplastic and

anticancer activity[8]. These observations have encouraged us to synthesize some new pyrazole, isoxazole, benzoxazepine, benzothiazepine and benzodiazepine derivatives containing aryl sulfonate moiety via the cyclo-condensation reaction in aqueous medium under microwave irradiation conditions by an efficient and general one pot-three component procedure in the hope to evaluate their potential antimicrobial and anti-inflammatory activities. Pyrazole may be any class of organic compound having heterocyclic ring composed of carbon atom an nitrogen atom in adjacent position of its structure. The simplest member of pyrazole family is pyrazole itself, a compound with molecular formulae C3H4N2. The chemical reactivity of the pyrazole molecule can be explained by the effect of individual atoms. The N-atom at position 2 with two electrons is basic and therefore reacts with electrophiles. The N-atom at position 1 is unreactive, but loses its proton in the presence of base. The combined two N-atoms reduce the charge density at C3 and C5, making C4 available for electrophilic attack. Deprotonation at C3can occur in the presence of strong base, leading to ring opening. Protonation of pyrazoles leads to parazonium cations that are less likely to undergo electrophilic attack at C4, but attack at C3 is facilitated.[8]

Pyrazole derivatives play an important role in antitumor agents because of their good inhibitory activity against BRAF (V600E), GFR, telomerase, ROS Receptor Tyrosine kinase
and Aurora-A kinase.[9] In the addition, pyrazole derivatives also show good anti-nflammatory
and anti-bacterial activities. Pyrazole are five membered heterocycle that constitute a class of compounds particularly useful in organic synthesis. They are one of the most studied groups of compounds among the azole family. Indeed, a huge variety of synthesis methods and synthetic analogues have been reported over the years.[10] The presence of pyrazole nucleus in different structures leads to diversified applications in different structures leads to diversified areas such as technology, medicine and agriculture. In particular, they are described as inhibitors of protein glycation, antibacterial, antifungal, anti-cancer, antidepressant, anti-inflammatory, anti-tuberculosis, antioxidant as well as antiviral agents. Pyrazole or isoxazole derivatives are prepared by a palladium- catalysed four- component coupling of terminal alkaline, hydrazine (hydroxylamine), carbon monoxide under ambient pressure, and an aryl iodide.[11]

Physical Properties of Pyrazole

Pyrazole has a five-membered aromatic ring structure consisting of two atoms of vicinal nitrogen, acidic pyrrole like nitrogen with a single pair of aromatic electrons, simple sp2 -hybridized nitrogen-like pyridine and three atoms of carbon, 7 and these combined features must be carefully taken into account in the context of reactivity. In the first instance, N-unsubstituted pyrazoles possess amphoteric properties, acting as both acids and bases, considering the presence of nitrogen. While the proton is easily donated by the acidic pyrrole-like NH group.[12]

Properties

1. Pyrazole is a colourless solid.
2. With boiling point of 186-188°C,
3. Melting point of 67-70°C,
4. Pyrazole is having Pkb = 11.5.
5. Molecular weight 68.0776g/mol.

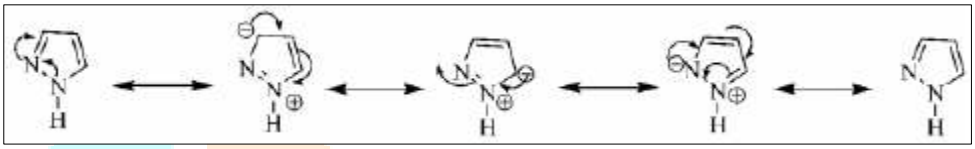
6. Pyrazole is usually soluble in water

Chemistry of Pyrazole

The high melting points and boiling point of pyrazole with 1-alkyl or 1- aryl substituent are due to the intermolecular hydrogen bonding which forms dimmer molecules. It is tautomeric in nature (each of two molecules or isomers of compound which exist together in equilibrium, and are ready to get interchanged by migration of one or two atoms present within the molecules. pyrazole is weak In nature and forms organic salts with inorganic acids. The imino hydrogen group may be replaced by acyl group.[12]

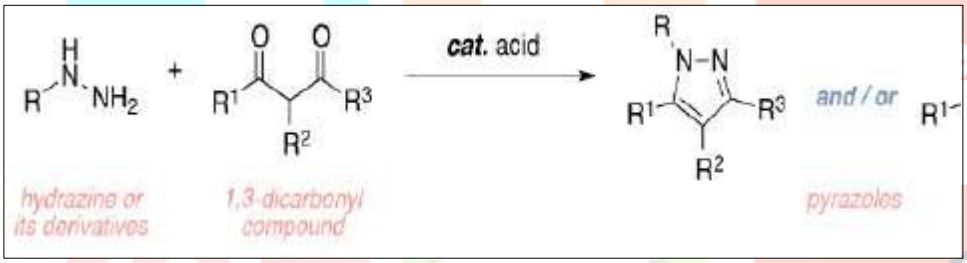
Resonating Structure of Pyrazole

Pyrazole resist oxidation and reduction reaction due to loss of aromaticity, but may be hydrogenate catalytically, first to pyrazoline, and then to pyrazolidine. Both of these compounds are stronger bases than pyrazole.[13]



Scheme 1

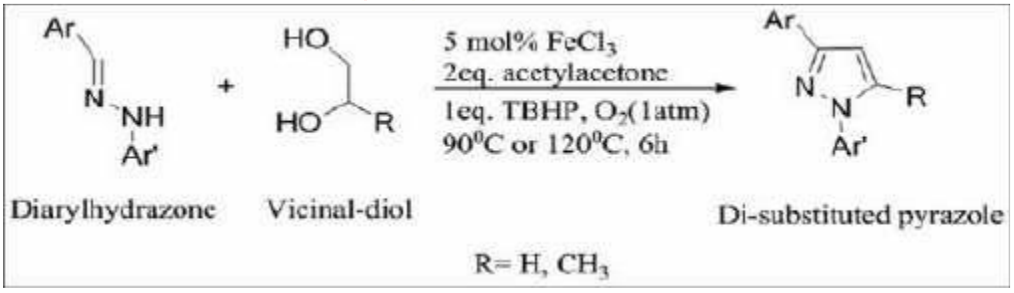
$CH_3C(O)CH_2C(O)CH_3 + N_2H_4 \rightarrow (CH_3)_2C_3HN_2H + 2\ H_2O$



Scheme 2

Synthesis of 1, 3 Substituted Pyrazol

An iron catalysed route for region selective synthesis of 1, 3 substituted pyrazoles from the reaction of diarylhydrazones and vicinal diol.

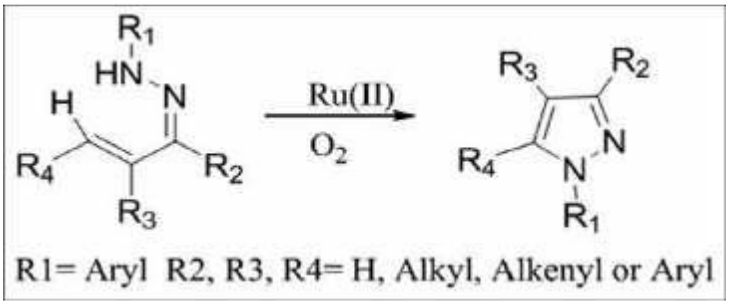


Synthesis of 1,3- and 1,3,5-substituted pyrazoles

Scheme3

Synthesis of Tri an Tetra Substituted Pyrazoles

A ruthenium (ii) – catalysed intramolecular oxidative CN couling method for the facile synthesis of tri- an tetrasubstituted pyrazoles. Dioxygen gas is employed as oxidant in this transformation and the reaction demonstrates excellent reactivity, functional group tolerance, and high yields.[14]

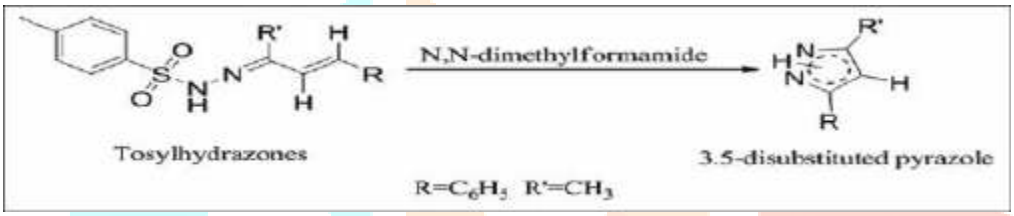


Synthesis of tri- and tetra-substituted pyrazoles

Scheme 4

Syntheisis of 3, 5 Substituted 1h- Pyrazole Synthesis-

A novel approach to the synthesis of pyrazole derivatives from tosylhydrazones of α, β-unsaturated carbonyl compounds possessing a β-hydrogen is proposed, exploiting microwave activation coupled with solvent free reaction conditions.[15]



Synthesis of 3,5-substituted-1H-pyrazole.

Conclusion

Pyrazole represents a major pharmacophore with various biological properties, and some pyrazole-containing derivatives have already been used for therapeutic purposes. This shows that pyrazole derivatives are pharmacologically very potent and, therefore their design and synthesis is the potential area of research. It has been noted so far that the structural modifications of the basic structure of pyrazole, have allowed the preparation of new derivatives with a broad spectrum of biological activity, with the most important structural variations concerning the substituent at the 1- position, the carbon at the 3-position and the substituents at the 5-position.

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