

A review on Chemistry and Therapeutic effect of Pyrazole

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Abstract - Medicinal Chemistry Develops the new synthetic drug molecules or series has shown results in many other disciplines or branches of science are such as biochemistry, combinatorial chemistry,, photochemistry, pharmacology, medicinal chemistry. Focus on various studies medicinal chemists are also trying to develop new chemical active molecules or lead molecules against disease or disorder medicinal chemistry play an important role to drug discovery and development. Develops the new synthetic drug molecules or series has shown results in many other disciplines or branches of science are such as biochemistry, combinatorial chemistry,, photochemistry, pharmacology, medicinal chemistry.

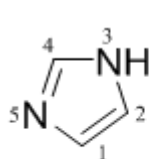
Keywords – Chemistry, Therapeutic effect

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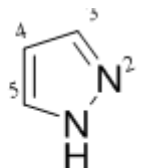
INTRODUCTION

In medicinal chemistry play an important role to drug discovery and development. Develops the new synthetic drug molecules or series has shown results in many other disciplines or branches of science are such as biochemistry, combinatorial chemistry,, photochemistry, pharmacology, medicinal chemistry. Focus on various studies medicinal chemists are also trying to develop new chemical active molecules or lead molecules against disease or disorder.

Diazoles are widely used as antibacterial and antifungal activities. They are of two types imidazoles and pyrazoles. Diazoles are of two isomeric forms with molecular formula $C_3H_3N_2$, having five-member cyclic aromatic ring consisting two Nitrogen (N) atoms on different positions and three carbon atoms².



Imidazole



Pyrazole

PYRAZOLES:

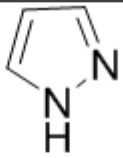
Pyrazoles is a aromatic five member heterocyclic compound are unique in chemical behavior. Pyrazole contains anomalous aromatic system characteristics, which are preferably pronounced in these derivatives having high ring liability that under some conditions..80 year before we known about Pyrazole derivatives, the exploration of their medicinal chemistry field purpose is very slowly. Earlier research were focused on organic molecules synthetic propose.

Recently studies focusing on the discovery and develops the synthesized derivatives for medicinal chemistry purpose against disease state to shows various pharmacological activities. Pyrazole derivatives have a various application in different fields are herbicides and insecticides are examples of agrochemicals and mainly in Pharma field to developed molecules acts as as antipyretic and anti-inflammatory and another pharmacological activities. Antipyrine is one of the earliest synthetic drug^{3,4}

CHEMISTRY OF PYRAZOLE:

The chemistry of heterocyclic pyrazole has been broadly investigated in last years. A series of aromatic heterocyclic contained a five member ring consist of 3-C atoms and 2 N atoms, and in derivatives are design from the imino group, the second position contains at another nitrogen. Pyrazole is crystalline and colorless in nature and very stable and act as weak base.

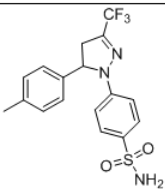
Pyrazole reactivity can be explains by the effect of each atoms or based on electronegativity and also stability. The nitrogen atom at position 2 is basic and acts as an electrophile because it has two electrons. The nitrogen atom at position 1 is unreactive, however the medium used as a base causes proton loss. Pyrazole is a Nucleophile in itself. Both N-atoms decrease the charge density of C-3 and C-5, facilitating electrophilic attack on C-4. Deprotonation happens at C-3 with in strong base, allowing the ring to open. Protonation caused pyrazolium cations to be less susceptible to electrophilic attack at C-4, but much more susceptible at C-3. Pyrazole anion has a low or non-reactive reactivity with nucleophiles, but a high reactivity with electron acceptors.⁵

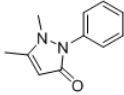
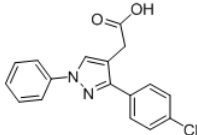
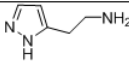

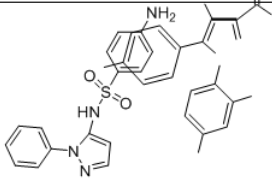
Structure	 Pyrazole
Chemical Name	1,2 diazole
Molecular formula	C ₃ H ₄ N ₂
Molecular mass	68.07 g/mol
M.P	66-70 °C
B.P	168-188 °C

Now in current research vast number of reported compounds with pyrazole moiety containing to shows many biological activity following as antimicrobial, antifungal, antiamoebic, neuroprotective, antiproliferative, and antiviral, anticancer, antiviral, anticonvulsant, anti-inflammatory etc. activities. Various wide range of pharmacological activities with pyrazoles core based a relevant synthetic importance in pharma industries.

Some of the marketed molecules to containing pyrazole moiety are following as:

Table 1: Pyrazole core based some marketed drugs

Marketed drugs	Structure
Celecoxib act as NSAIDS.	

Phenzone is used as an analgesic and antipyretic.	
Lonazolac used as NSAIDS.	
Betazole is a acts as H ₂ agonist.	
Fomepizole is used as an antidote in for methanol.	
Sulfaphenazole is used as a antibacterial.	

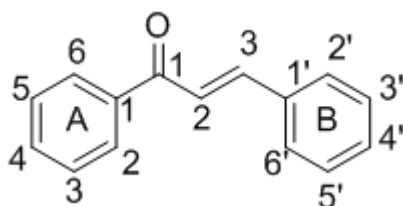
Current research on the heterocyclic compounds to containing pyrazole core are pharmacological active lead to play key role in medicinal chemistry field. Pyrazole cores in shows various pharmacological activities to helps to develop a novel lead molecules. Extensive literature survey related to 1,3,5-trisubstituted pyrazole core based in shows a particular considerable interest in current years. **We also planned to synthesize 1,3,5-trisubstitution novel pyrazole moiety based derivatives.** Current research shows the of 1,3,5-tri substituted pyrazole core based molecules synthesis approaches by various methods and reported in publications and patents of different pharmacological activities. Various methods reported of tri substituted pyrazole moiety based molecules for the laboratory scale involves mainly,

1. Substituted hydrazines react with 1, 3- dicarbonyl compounds
2. Cycloaddition reaction of substituted hydrazines with chalcones

Since chalcones can be easily synthesized by claisen Schmidt condensation, when compared to 1,3 dicarbonyl compounds. Various chalcone derivatives can be prepared with desired substitutions, which on cycloaddition reaction with substituted hydrazines leads to the formation of desired 1,3,5 tri substituted pyrazole based derivatives. Therefore in the present study various chalcone based derivatives were prepared and are used as intermediates for the synthesis and development core of tri substitutedpyrazole.

CHALCONES

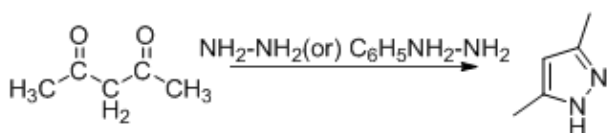
Chalcone molecules are 1,3-diphenylpropeneone core based in this molecule two aromatic benzene ring core are connected through a 3 carbon based α,β -unsaturated carbonyl linker.



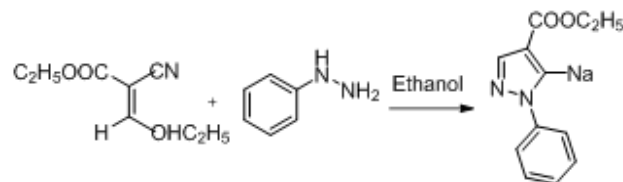
Chalcone are plethora in plants and precursors of flavonoids and isoflavonoids. Chalcone molecule contain a conjugated double bonds unsaturated and shows delocalization π -electron in benzene moiety have less intermolecular force and to goes through electron transfer.⁷ Chalcones method of preparation by catalysing the claisen-schmidt condensation reaction of an aromatic aldehyde and a ketone with a base or an acid, then dehydrating the product. Different substituents on the aromatic rings help in the backbone for the synthesis of different heterocyclic molecules to initiate different chemical reaction occur in the α, β -unsaturated part is necessary for antimicrobial property, and different substituent on aromatic rings help in the backbone for the synthesis of different heterocyclic molecules to undergo different chemical reactions. Chalcone play an key role in synthesis medicinal drugs or molecules^{8,9}. Literature review of chalcone revealed molecules of shows natural or synthetic origin based to exhibit different pharmacological evaluation activities following as antioxidant, antimicrobial agents, anti-inflammatory activity, cytotoxic activity, hypoglycemic activity, antihepatotoxic, antimalarial, antileishmanial, tyrosine inhibitors and antitumoractivities.

GENERAL METHODS FOR SYNTHESIZING PYRAZOLERING³

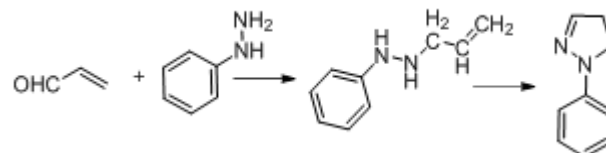
1. From dicarbonyl compounds: Direct method of pyrazole synthesis involved reaction in 1,3-dicarbonyl compound and hydrazine or its derivatives forms various substitutedpyrazoles.



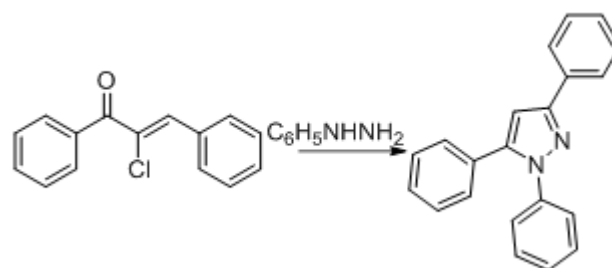
2. From ethyl ethoxy methyleno acetate: Synthesis of pyrazole moiety involves condensation of ethyl ethoxy methyleno acetate and phenyl hydrazine in presence of ethanol.



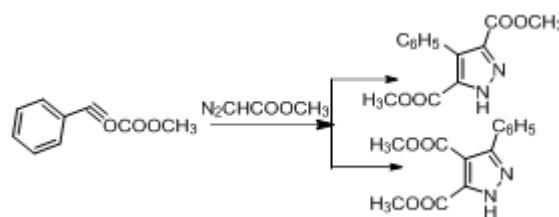
3. From acrolein: 1-phenylpyrazoline molecule was synthesized from the reaction between phenylhydrazine and acrolein.



4. From α,β -ethylene carbonyl compounds: Reaction between an α,β -ethylene carbonyl derivative and hydrazine to gives trisubstituted pyrazole.

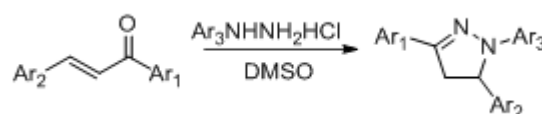


5. From 1,3-dipolar addition: azo molecule adds an acetylenic derivative in this reaction acetylenic triple bond activated by an electron withdrawing group, methyl diazoacetate and methyl phenyl propionate yields the isomeric pyrazoles in equimolaramounts.

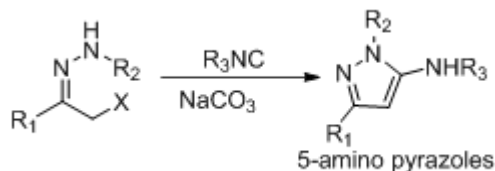


SYNTHESIS OF PYRAZOLEMOIETY

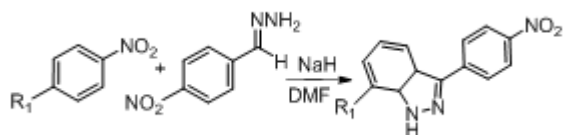
Ying R. Huang *et al*¹⁰ have synthesized dihydropyrazole by condensing of α,β - unsaturated ketones with aryl hydrazines.



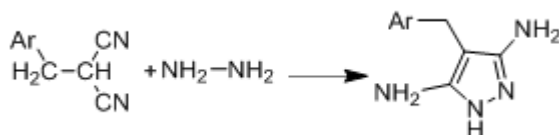
Altan *et al*¹¹ to have synthesized 5-aminopyrazoles from α - halogenoketone hydrazone reacted with isocyanides .



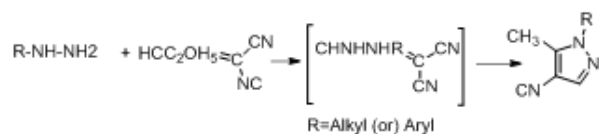
Takehiko *et al*¹² to synthesized reaction of nitrobenzene with aryl imines to gives aryl pyrazoles.



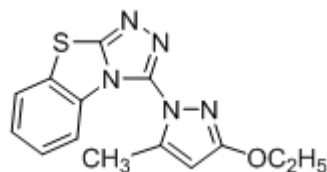
Ram *et al*¹³ have to synthesised and reported diamino substituted pyrazole.



Cheng *et al*^{14,15} synthesis of substituted cyanopyrazole from mono-substituted hydrazine, was reacted with ethoxymethylenemalononitrile in presence of boiling alcoholic solution.



Kapratwar *et al*¹⁶ reported the synthesis of substituted heterocyclic and benzothiazolyl-3-ethoxy-5-methylpyrazole and triazolo(3,4-b)benzothiazolyl-3,5-dimethylpyrazole.



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