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Reviews of Synthesis and Characterization of Some Pyrazine Ring Containing Heterocycle's

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Abstract:*Heterocyclic chemistry has numbers of applications in the field of pharmaceutical chemistry. These compounds are synthesized worldwide by different synthetic methods. Two or more hetero elements containing heterocycles are synthesized and all these compounds were found stable. Chalcones a precursor has great importance in natural as well as synthetic heterocyclic compounds. Nitrogen atom containing heterocycles has very important role in medicinal field due to their biological activities. After reviewing literature, it was found that, nitrogen containing five membered heterocycle like pyrazoles, six membered Pyrimidines, seven membered benzodiazepines were synthesized by different synthetic methods. This literature survey promoted us to prepare highly stable five, six and seven membered ring structure using pyrazine ring containing derivatives and check their pharmacological activities. These compounds were characterized using IR, ^{1}H-NMR and Mass spectra and Elemental analysis. The compounds were found to be the most active against bacterial & fungal human pathogens.*

Keywords: Benzodiazepines, Chemistry, Heterocycles, Pyrazole, Pyrimidine, etc.

I. INTRODUCTION

Heterocyclic compounds were prepared in different synthetic methods. But if they are prepared from chalcones, found more stable and potent. Chalcones are common natural pigment & one of the most important classes of flavonoids & iso-flavonoids across the whole edible plant kingdom. [1, 2] It is one of the oldest but remain popular in 21st century due to the large number of replaceable hydrogens that allows a large number of derivatives and a variety of biological activities such as anticancer, anti-inflammatory, antioxidant, antiplatelet, antibacterial, antifungal, antileishmanial, antimalarial, antiviral etc. Chalcones are also key precursors in the synthesis of many biologically important heterocycles such as benzothiazepine, pyrazolines and flavones. Hence, the synthesis of chalcones has generated vast interest among organic as well as medicinal chemists. Some of their derivatives are used as sweeteners, drugs, and sunscreen agents. [3]

Several methods are available for the synthesis of chalcones. The most widely used method is the base-catalysed such as sodium hydroxide (NaOH), potassium hydroxide (KOH), barium hydroxide $Ba(OH)_2$ and lithium hydroxide($LiOH{\cdot}H_2O$). The acid-catalysts had been also used to synthesize chalcones includes aluminium trichloride ($AlCl_3$), dry HCl, boron trifluoride-etherate (BF_3-Et_2O), titanium tetrachloride ($TiCl_4$) and ruthenium trichloride ($RuCl_3$).

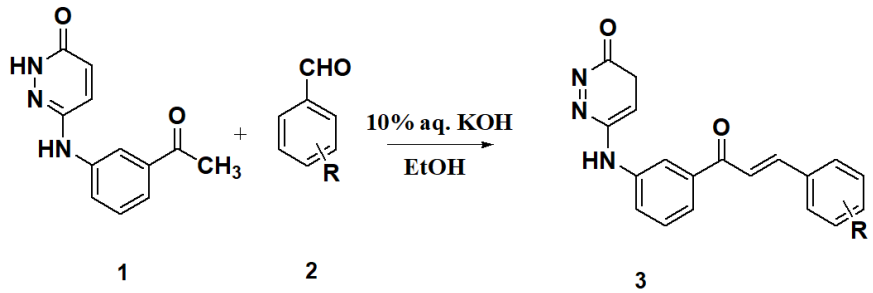

Figure 1

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Pyrazolines are five membered ring heterocyclic compounds containing three carbon atoms and two adjacent nitrogen atoms. Partially reduced form of pyrazole is called as pyrazoline which exists in tautomeric forms. These pyrazolines possess interesting pharmacological properties and hence they are used as raw materials in drug synthesis.

We have been synthesized Pyrazoline derivatives from heterocyclic chalcone derivatives using ethyl acetate as a solvent which help to reduces reaction time. 1, 3, 5 triphenyl -1H- Pyrazole containing 6-aminopyridazin-3(2H)-one derivatives [4], which possess potent biological activities.

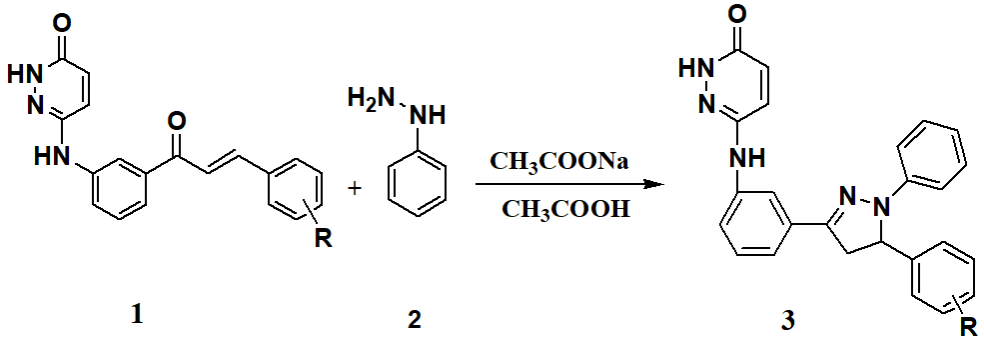

Figure 2

Benzodiazepines and benzodiazepines have been attracted as an important class of heterocyclic compounds in the field of clinical research. These compounds are widely used as anticonvulsant1, Antibacterial and antifungal 2-4 properties of 2, 4-diaryl, 2,3- dihydro-1,5-benzodiazepines have been reported. They also possess a wide range of pharmacological properties. [5-6] including anti-HIV [7], anticoagulant [8] and anti-allergenic [9]. The 1, 5 - benzodiazepines moiety is a privileged class of pharmacophores, as compounds bearing this structural unit possess a broad spectrum of biological activities. The common strategy for synthesis of the 1,5 -benzodiazepines moiety is the reaction of Chalcones with o-phenylene diamine [10].

The various methods of synthesis involve use of ethanol as a solvent, but we had used few drops of piperidine under reflux condition or microwave irradiation. Many of these processes suffer from some limitations such as requiring harsh conditions. Using this we have prepared some novel 1, 5]- benzodiazepines by using 6-(3-((E)-3-phenylacryloyl) phenyl amino) pyridazin-3(2H)-one [11] earlier prepared biologically active chalcones11 and o-phenylene diamine & few drops of piperidine in methoxy ethanol by microwave irradiation. TLC indicated formation of the products. The crude product was subjected to crystallization from benzene. This method represents a convenient, economic, green, highly efficient process for synthesis of 1, 5-Benzodiazepines under microwave irradiation. It also shows moderate to batter antibacterial activities.

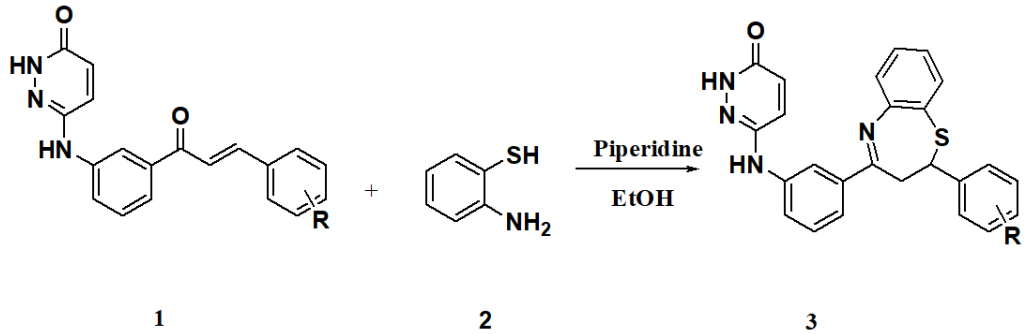

Figure 3

Organic compounds containing pyrimidines as a core unit are known to exhibit various biological and pharmaceutical activities [12]. In this regard we have synthesized some substituted pyridazone derivative of Chalcones are used for the synthesis of di-aryl pyrimidines. Organic compounds containing pyrimidines, thiopyrimidines as a core unit are known to exhibit various biological and pharmaceutical activities.[13]

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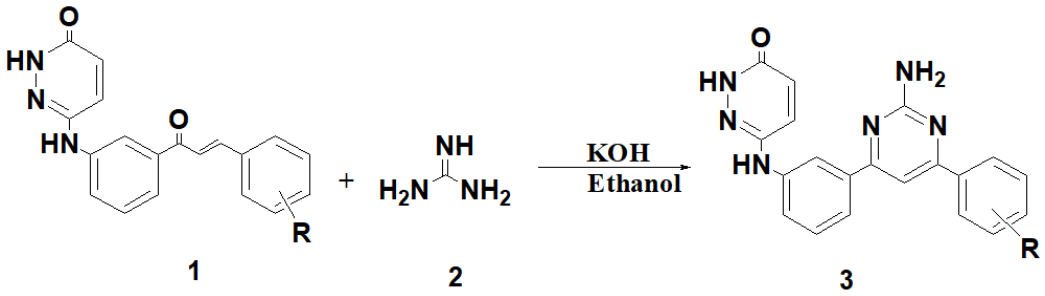

Figure 4

II. RESULT AND DISCUSSION

All of the novel synthesized pyrazoline compounds were screened for their antifungal and antibacterial activity against the Gram –ve bacteria Escherichia coli (ATCC 8739) and Gram +ve bacteria Staphylococcus aureus (ATCC 6538), in addition to their antifungal activity against Aspergillus Niger (ATCC 16404) Candida albicans (ATCC 10231) using ager diffusion method [14,15] at a concentration 20 mg/mL. DMSO used as a solvent. Some compounds show highly efficient antibacterial activity against S. aureus (ATCC 6538). We have synthesised 1,5-benzodiazepines by microwave irradiation method by using few drops of piperidine in methoxy ethanol as a solvent. This method of synthesis has many advantages over conventional methods of synthesis, including high yield, simple work-up shorter reaction span, no side reactions. So, it represents a convenient, economic, green, highly efficient process for synthesis of 1, 5-Benzodiazepines under microwave irradiation. It also shows moderate to batter antibacterial activities. Many synthetic methods of pyrimidine have been reported from urea, thiourea and Guanidine Chalcones.

But synthesis of pyrimidines from Guanidine gives very good yield as compared to urea & thiourea. In the present work, we describe the synthesis of 2-amino pyrimidines which have biological important in chemistry by using 6-(3-((E)-3-phenylacryloyl) phenyl amino) pyridazin-3(2H)-one to give 6-(-3-(-2 amino-6-phenyl pyrimidin-4yl) pyridazin-3(2H)-on. by conventional method. The product obtained in 55 to 72 % yield within around seven hours by refluxing. Best result in terms of yield and reaction time was reduced with small amount of alkali (Aqueous KOH).

III. CONCLUSION

All the heterocyclic compounds have wide application due to their pharmacological activities. In this short review we viewed some heterocyclic derivatives synthesized by condensing it with very active compound pyridazine through imido group which acts as electron releasing group. This methodology is maintaining environmentally friendly approach for the synthesis of pyridazin-3(2H)-one. Derivatives using sodium acetate and acetic acid. But by increasing the molar ratio to 1:2 and 1:3 the yields of increased, it may be that sodium acetate is in favour of release of phenyl hydrazine from phenyl hydrazine hydrochloride. So, reaction condition we chose were the molar ratio of chalcone: phenyl hydrazine: sodium acetate was 1.0:3.0:0.15. We have performed the reaction of chalcones with phenyl hydrazine hydrochloride by refluxing at 110˚C, the moderate to good % yield of pyrazoline derivatives is observed. The synthesized compounds were further subjected for biological screening.

All synthesized derivatives have good yield by conventional, greener and microwave irradiation methods. All these compounds were found active against anti-bacterial and anti-fungal activities.

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