© INNOVATIVE RESEARCH THOUGHTS
Refereed | Peer Reviewed | Indexed
ISSN : 2454 – 308X | Volume : 09 , Issue : 01 | January - March 2023

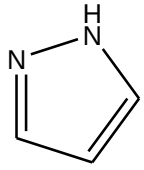
A SHORT REVIEW ON PYRAZOLE DERIVATIVES & THEIR APPLICATIONS

Dr. Poonam
Assistant Professor (Chemistry)
lohanpoonam@gmail.com
Dr. B.R. Ambedkar Govt. college, Jagdishpura (Kaithal)

Abstract: Pyrazole is a 2-neighbour nitrogen containing 5-membered heterocyclic organic compound with three carbon atoms. Pyrazole commonly known as 1,2 diazoles has been very popular now a days due to manifold uses. There are number of pyrazole derivative which has broad spectrum of biological activities like anti-bacterial, anti-microbial, anti-inflammatory, anti-convulsant, analgesic, anti-diabetic, anti-rheumatic, anti-cancer, and anti- tuberculosis. There are several applications of pyrazole core based organic molecules in various areas including pharmacy and agro-chemical industries. The purpose of the review was to collect various pharmacological actions which were reported in recent years made on its moiety. Pyrazole and its derivatives are prepared by dehydrogenating 2-pyrazoline or its derivative by processin which the reaction is carried out using sulfuric acid in the presence of iodine or of an iodine compound. This review highlights the different synthesis methods and the pharmacological properties of pyrazole derivatives.Development of pyrazole and its derivative has been reported by many scientists in decades.

Introduction:

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 $C_3H_4N_2$.



© INNOVATIVE RESEARCH THOUGHTS
Refereed | Peer Reviewed | Indexed
ISSN : 2454 – 308X | Volume : 09 , Issue : 01 | January - March 2023

Structure of Pyrazole

Physical Properties of Pyrazole

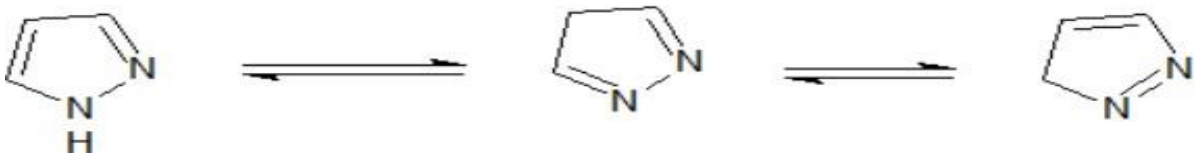
Pyrazole has a five-membered aromatic[1] ring structure consisting of two atoms of vicinal nitrogen, acidic pyrrole like nitrogen with a single pair of aromatic electrons, simple sp2 - hybridized nitrogen-like pyridine and three atoms of carbon, and these combined features must be carefully taken into account in the context of reactivity. In the first instance, N-unsubstituted pyrazoles possess amphotericproperties, acting as both acids and bases, considering the presence of nitrogen. While the proton is easily donated by the acidic pyrrole-like NH group, the simple pyridine-like nitrogen can accept protons even more readily, and thus the basic character is typically prevalent. Nevertheless, substitutions on the ring can modulate these properties[2-5], as, for instance, electron donating groups were shown to increase the acidity of the pyrrole-like -NH group. In addition to the previous, the combination of two dissimilar and adjacent nitrogen atoms in this azole allows it to simultaneously donate and accept hydrogen bonds, which favours the establishment of intermolecular interactions, either among pyrazole molecules themselves and the nature of the substituents in the ring or between pyrazoles and neighbouring molecules that participate in proton transfer processes.

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[6] 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 andforms organic salts with inorganic acids. The iminohydrogen group may be replaced by acyl group.

Therefore, important properties of these molecules were analysed by comparing with the properties of benzene derivatives Like other nitrogen involving heterocycles, different tautomeric structures can be written for pyrazoles[7-10]. unsubstituted pyrazole can be represented in three tautomeric forms

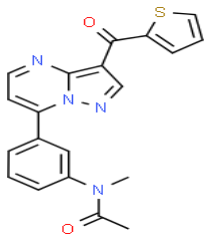
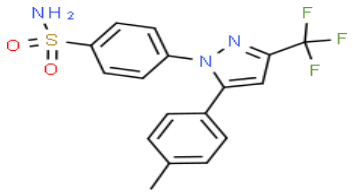
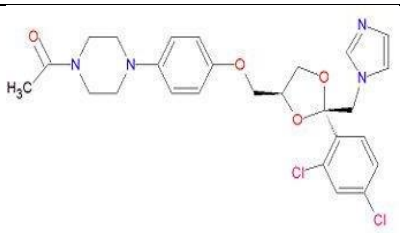
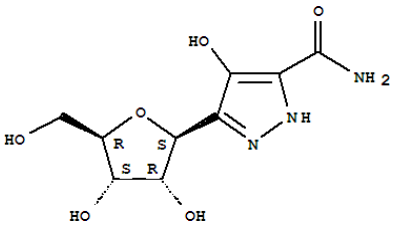
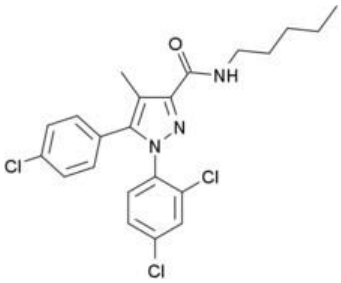
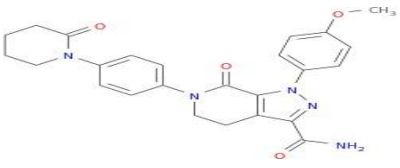
© INNOVATIVE RESEARCH THOUGHTS
Refereed | Peer Reviewed | Indexed
ISSN : 2454 – 308X | Volume : 09 , Issue : 01 | January - March 2023



The chemical properties of pyrazole can be explained by effect of individual atoms. the n- atom at position 2 with two electrons and therefore reacts with electrophile. the n- atom at position 1 is unreactive and 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. Protonation of pyrazoles leads toparazonium cations and that less goes electrophilic attack at position of C-4, but the attack at C-3 is more facilitated the pyrazole for more effective nucleophiles. The chemical reactivity of the pyrazole molecule can be explained by the effect of individualatoms. 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[11-13] at C-3 can 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 C-4, but attack at C3 is facilitated. The pyrazole anion is much less reactive toward nucleophiles, but the reactivity to electrophiles is increased. The pyrazole compounds are not known to occur in nature; they are usually prepared by reacting hydrazine's with 1,3 –diketones[14-18].

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. The presence of pyrazole nucleus in different structures leads to diversified applications[19-23] 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.

Table 1: Pyrazole derivatives having pharmacological activities

Drug	Activity	Structure
Indiplon	Antianxiety	
Celecoxib	Antinflammatory	
Lonazole	Nsaids	
Pyrazomycin	Anticancer	
Surinabant	Antiobesity	
Apixiban	Anticoagulant	

This review is a short description of an ongoing research area of pyrazole synthesis, though there are a lot of synthetic methods developed for generating novel pyrazole derivatives. However, generally these methods need organic solvents. In addition to the use of organic solvents, low yield percentage is another major challenge in pyrazole synthesis. Solventless reactions are rapid, regio- or chemo-selective. These reactions result in high yields, and have environmental and economic advantages. We believe that these solventless reactions represent a possible solution to the challenges in the synthesis of pyrazole derivatives. The use of water will also be helpful in overcoming some major issues of pyrazole derivative synthesis.

References

1. C. Ghosh, J. Haldar, Membrane-active small molecules: designs inspired by antimicrobial peptides, Chem.Med. Chem. 10 (2015) 1606-1624.
2. P. Kumar, S. Kumar, K. Husain, A. Kumar, An efficient synthesis of pyrazolo chalcones under solvent freeconditions at room temperature, Chin. Chem. Lett. 22 (2011) 37–40.
3. Yang Q, Zhang Z, Yang Y, Kuang C, Jin H. Efficient synthesis of 1,3-diaryl-4-halo-1H-pyrazoles from 3-arylsydnones and 2-aryl-1,1-dihalo-1-alkenes. Beilstein J Org Chem(7) (2011) 1658.
4. K. Kumar, P. Jayaroopa, Pyrazoles:synthetic strategies and their pharmaceutical applications-an overview.Int J PharmTech Res. 2013;5(4):1479
5. Takenaka, M.; Yamada, K.; Lu, T.; Kang, R.; Tanaka, T.; Noguchi, T. Eur. J. Biochem. 1996, 235, 366-371.
6. Samet M.; Rahmi K.; Salim Ok, A Short Review on Pyrazole Derivatives and their Applications, PostDocJournal (2014) 2(4), 68
7. Wannberg, J.; Dallinger, D.; Kappe, C. O.; Larhed, M. J. Comb. Chem. 2005, 7, 574
8. (a) Hartman, R. L.; Naber, J. R.; Zaborenko, N.; Buchwald, S. L.; Jensen, K. F. Org. Process Res. Dev.2010, 14, 1347.
   (b) Naber, J. R.; Buchwald, S. L. Angew. Chem., Int. Ed. 2010, 49, 9469.
9. Obermayer D.; Toma N.; Glasnov, and C. Oliver Kappe, The Journal of Organic Chemistry **2011** *76* (16),6664
10. Bishop, B.C.; Brands, K.M.; Gibb, A.D.; Kennedy, D.J. Regioselective synthesis of 1,3,5-substitutedpyrazoles from acetylenic ketones and hydrazines. Synthesis 2004, 2004, 43–52
11. Karrouchi K, Radi S, Ramli Y, Taoufik J, Mabkhot YN, Al-aizari FA, Ansar M. Synthesis andPharmacological Activities of Pyrazole Derivatives: A Review. Molecules. 2018; 23(1):134.

12. Da-Qing Shi, Jing-Wen Shi, Hao Yao. Three-component one-pot synthesis of indeno[2',1':5,6] pyrido[2,3-d]pyrazole derivatives in aqueous media. J Chinese Chem Soc 56 (2009) 505
13. K. Kumar, P. Jayaroopa, Pyrazoles:synthetic strategies and their pharmaceutical applications-an overview.Int J PharmTech Res. 2013;5(4):1475
14. Manikannan R, Venkatesan R, Muthusubramanian S. Synthesis of 1-(2.4-dinitrophenyl)-3-aryl-4- (arylsulfanyl)-1H-pyrazoles Vilsmeier reaction of 2,4-dinitrophenylhydrazones of phenacyl aryl sulfides. Ind J Chem 50B (2011) 1611-1618.
15. Selvi, S. and Perumal, P.T.; A comparative study on the synthesis of 4-alkyl-1,3-diarylpyrazoles using microwave irradiation and conventional thermal methods. Journal of Heterocyclic Chemistry, (2002), 39: 1129-1131
16. Ramesh P, Venkatesan R, Manikannan R, Muthsubramanian S &Ponnuswamy M N, Acta Cryst, E64, 2008,2093.
17. Parekh, N., Thomas,J., John,J., Kusurkar , R., De Borggraeve, W.M., Dehaen, W. J.org.chem., 2014,79(11),5338-5344.
18. Holzer, W., Kautsch, C.; Laggner, C.; claramunt, R.M.; Perez-Torralba,M.; Alkortac ,I.; Elguero,J. Tetrahedron 2004,60,6791.
19. Mariappan; G.; Sana, B.P.; Sutharson, L.; Garg, s.; Pandey, L.; Kumar.D.J.Pharm.Res.2010,3,2856.
20. Attanasi, O.A.; Filippone, P.; Guidi, B.; Hipper, T.; Mantellini, F.; Tietze,L.F.Tetrahedron let.1999,40,9277.
21. Corradi A, Leonelli C, RizzutiA,Rosa R, Veronesi P, Grandi R, Baldassari S and Villa C ,New "green" approaches to the synthesis of pyrazole derivatives molecule,2007,12(7),1482-1495.
22. Beyzaei H, Motraghi Z, Aryan R, Zahedi M M and Samzadeh- kermani A, Green one-pot synthesis of Novel Polysubstituted Pyrazole derivatives as potential Antimicrobial Agent Acta Chim. Slov. 2017,64,4,911.
23. Kumari, Simpal; Paliwal, Sarvesh; Chauhan, Rajani. Synthesis of Pyrazole Derivatives Possessing Anticancer Activity: Current Status. Synthetic Communications, 2014, 44 (11), 1521–1578.