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A BRIEF REVIEW ON ANTIMICROBIAL ACTIVITY OF OXAZOLE DERIVATIVES

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Abstract:

The usefulness of oxazole as intermediates for the synthesis of new chemical entities in medicinal chemistry has been increased in the past few years. Oxazole is a significant heterocyclic nucleus having a wide spectrum of biological activities which drew the consideration of researchers round the globe to synthesize various oxazole derivatives and monitor them for their various biological activities. The present review article aims to review the work reported on therapeutic potentials of oxazole scaffolds which are valuable for medical applications during new millennium.

Key Words: *Oxazole, Antimicrobial activity*

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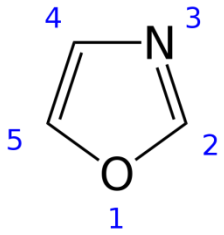
INTRODUCTION:

Heterocyclic compounds are cyclic compounds with the ring containing carbon and other element like oxygen, nitrogen and sulfur. Oxazole is the parent compound for a huge class of heterocyclic aromatic organic compounds. Oxazoles is a doubly unsaturated 5-membered ring having one oxygen atom at position 1 and a nitrogen at position 3 separated by a carbon in-between.[1] Substitution pattern in oxazole derivatives play a crucial role in the biological activities like antimicrobial, anticancer, antitubercular, anti-inflammatory, antidiabetic, antiobesity and antioxidant etc.



Oxazole compounds containing nitrogen and oxygen atoms in the five-membered aromatic ring are readily able to bind with a variety of enzymes and receptors in biological systems *via* diverse non-covalent interactions, and thus display versatile biological activities. Noticeably, a large number of oxazole compounds as clinical drugs or candidates have been frequently employed for the treatment of various types of diseases, which have shown their large development value and wide potential as medicinal agents.[2]

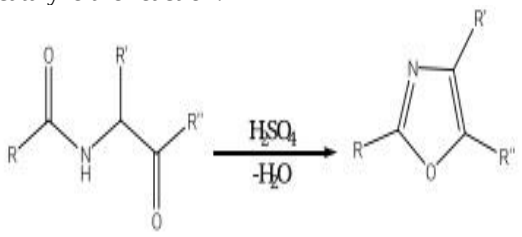
Oxazole is a π-electron-excessive heterocycle. The electronegativity of the N-atom attracts electrons so that C2 is partially electropositive and therefore susceptible to nucleophilic attack. However, electrophilic substitution of oxazoles takes place at the electron-rich position C5 preferentially.[3]

Preparation of oxazole derivatives

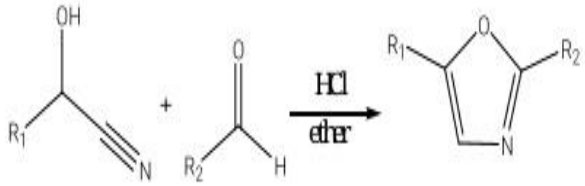
Due to the variety of therapeutic response profiles, the chemical synthesis of oxazole and its derivatives has become a key objective and has drawn a lot attention of current pharmacologists and chemists around the world to be explored thoroughly for the advantage of mankind.[4]

The first recorded oxazole was synthesized in the 1800s and the chemistry of this heterocycle was expanded during World War II as part of the penicillin effort, which was thought to contain an oxazole core. The parent compound is a stable liquid at room temperature, with a boiling point of 69° C, and was first prepared in 1947.[5]

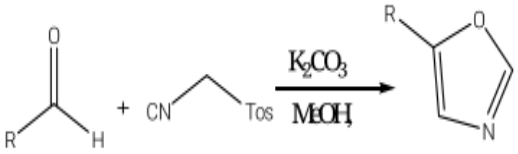
There are many reported procedures for the synthesis of oxazole, among them, The Robinson–Gabriel synthesis in which a 2-acylamino-ketone reacts intra-molecularly followed by a dehydration to give an oxazole. A cyclo-dehydrating agent is needed to catalyze the reaction.[6]



Fischer and coworker described an elegant synthesis of oxazole derivatives which was introduced in 1896 by reacting a cynohydrin and an aldehyde in the presence of anhydrous hydrochloric acid to give oxazole.[7]



There was the Van Leusen reaction which was first described in 1977 by Van Leusen and co-workers. Ketones reacted with TosMIC (Toluenesulfonylmethyl isocyanide) leading to the formation of a nitrile. When aldehydes are employed, the Van Leusen reaction is particularly useful to form oxazoles.[8]

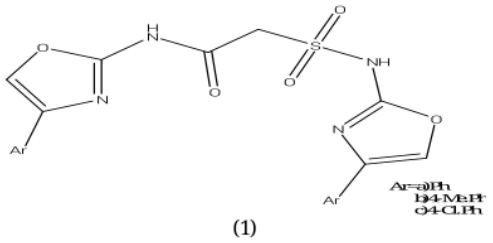


ANTIMICROBIAL ACTIVITY

The dramatically rising occurrence of multi-drug resistant microbial infections in the past few decades remains an important and challenging task for medicinal chemists to develop new antimicrobial agents with novel chemical structures and oxazoles are important component in antibacterial drug discovery.

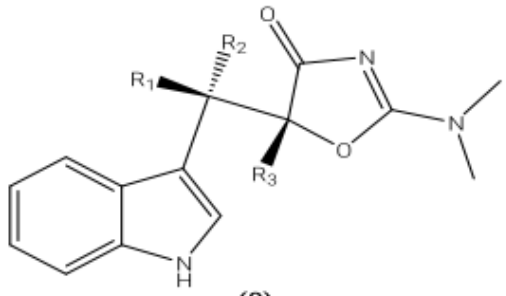
Chokkappagari et al. synthesized a new class of amido sulfonamido methane linked bisoxazoles, bisthiazoles, and bisimidazoles in simple and versatile synthetic methodologies. The lead compounds were assayed for antimicrobial activity.[9]

It is noteworthy that the tested compounds containing oxazole in their structure displayed comparable antibacterial activity towards gram-negative bacteria and gram-positive bacteria when compared to references (1).



(1)

Analogues of the aminoacyl tRNA synthetase inhibitor, indolmycin, have been synthesized by Witty et al. It has been found that antibacterial and enzyme inhibitory potency is related to steric properties and conformational preferences for these derivatives. It was observed from the inhibitory results that the better inhibitors were chromatographically the less polar isomers, and possessed the relative stereochemistry of indolmycin.[10]

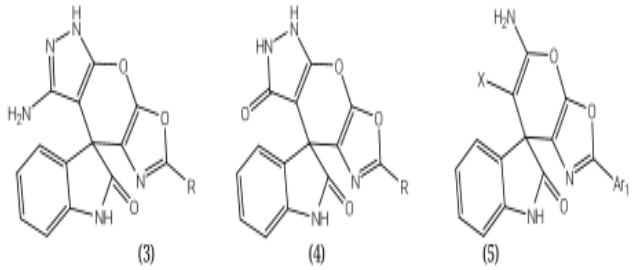


(2)

Abdel-Rahman et al. synthesized several new spiro indoline-based heterocycles by prior preparation of the 4-(20- oxo-indol-30-ylidene)-oxazol-5-one derivatives and subsequent reaction of the produced indol-3-ylidene based heterocycles with activated nitrile reagents.[11]

The obtained products were allowed to react with hydrazine hydrate in alcoholic basic to give the target compounds. The antibacterial as well as antifungal activities of a solution of the synthesized compounds in dimethyl formamide (DMF) were tested and evaluated against some gram positive (Bacillus subtilis and Bacillus megatherium), gram negative (Escherichia coli) and fungi (Aspergillus niger and Aspergillus oryzae) and compared with respect to some reference antibiotics.

The biological results revealed that while most of the prepared spiro 3H-indole-3,40-pyrano(30,20-d) oxazole derivatives showed comparable activity, the spiro 3H-indole-3,40-pyrazolo(30,40-b)pyrano(30,20-d)oxazole derivatives (3, 4, and 5) revealed very high activity with respect to the used references. On the other hand, nearly all of the prepared compounds exhibited an interesting high antifungal activity reaching to 90 mm zone of inhibition against the reference chemotherapeutics 22 mm.



(3) (4) (5)

CONCLUSION:

Several oxazole-containing natural products have been isolated and found to be biologically active. Much synthetic effort has been expended in their total synthesis. Oxazole derivatives are potentially pharmacologically active. They have antimicrobial, antioxidant, antitubercular and anticancer activities. Currently many compounds containing oxazole ring are using clinically. In addition to these many derivatives are under pre clinical and clinical trials. The pharmacological activity of the compound can be determined by using cup plate method using various strains of bacteria. The chemical properties can be determined and confirmed by using various analytical techniques like mass spectroscopy, IR spectroscopy and NMR spectroscopy.

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