Pharmacological Importance And Chemistry Of 1,3,4-Oxadiazole Derivatives

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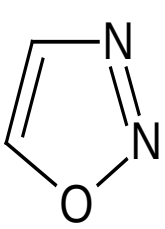
Abstract:
Oxadiazole is an important heterocyclic compound containing one oxygen and two nitrogen atoms in the five membered ring. 1,3,4-oxadiazole is a versatile heterocyclic nucleus having novel molecule which attract the medicinal chemist to search a new therapeutic molecule. The present review summarizes physicochemical properties, various synthetic procedures and various pharmacological activities of 1,3,4-oxadiazole moiety. 1,3,4-oxadiazole moiety is an important pharmacophore which plays a major role in the pharmaceutical chemistry and broad range of important biological activities such as anti-inflammatory, analgesic, ulcerogenic, antimicrobial, antifungal antitubercular, anticonvulsant, anticancer/antitumor, antiviral, and antihypertensive activities etc. as reported in the literature.
Keyword- Oxadiazole, Heterocyclic, Pharmaceutical, Biological

Introduction:

Oxadiazole is important heterocyclic compound containing one oxygen and two nitrogen atoms in five membered ring, which is considered to be derived from furan by the replacement of two methane (-CH=) group by two pyridine type nitrogen (-N=). Depending upon the position of N- atom in the heterocyclic ring, oxadiazoles may be divided into four isomers: (1) 1,2,3-oxadiazole, (2) 1,2,4-oxadiazole, (3) 1,2,5-oxadiazole and (4) 1,3,4-oxadiazole.



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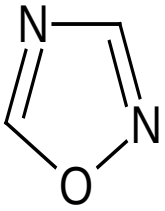

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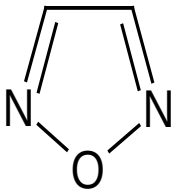

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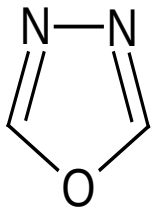
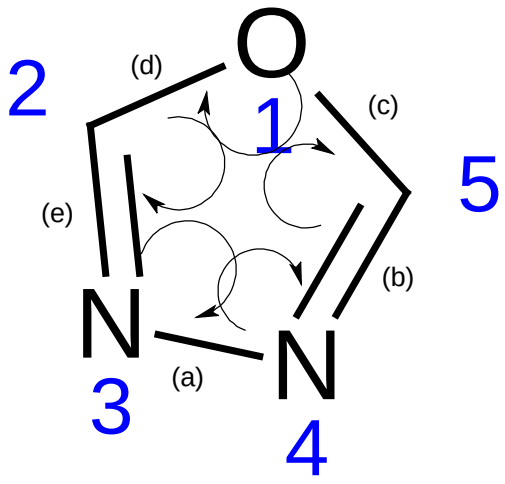


(4)

However, 1,3,4-oxadiazole and 1,2,4-oxadiazole are better known, and more widely studied by researchers because of their many important chemical and biological properties. Among heterocyclic compounds, 1, 3, 4-oxadiazole has become an important construction motif for the development of new drugs. Literature survey revealed that a minor modification in the structure can result in qualitative as well as quantitative changes in the activity, convinced us to begin on the synthesis of various new 1,3,4-oxadiazole derivatives with the aim of having improved activity and lesser toxicity. The synthesis of novel 1,3,4-oxadiazole derivatives and investigation of their chemical properties and biological behaviour has accelerated in the last two decades. In recent years the number of scientific studies with these compounds has increased considerably. Considering the period from 2002 to 2012, the Scifinder Scholar database records 2,577 references to 1,3,4-oxadiazole, demonstrating its relevance for heterocyclic chemistry. 1,3,4-oxadiazole derivatives is an important pharmacophore which play a major role in the pharmaceutical chemistry and broad range of important biological activities. We have decided to present the main synthesis approaches used for obtaining the heterocyclic nucleus, as well as the broad spectrum of pharmacological activities such as anti-inflammatory, analgesic, ulcerogenic, antimicrobial, antifungal antitubercular, anticonvulsant, anticancer/antitumor, antiviral, and Antihypertensive activities etc. as reported in the literature.[1]

PROPERTIES OF OXADIAZOLE RING

Physical properties



(5)

The first monosubstituted 1,3,4-Oxadiazoles were reported in 1955 by two independent laboratories. Since 1955 other workers have extended this reaction 1,3,4-Oxadiazole boils at 150°C. The percentage of C,H,N and bond angle present in 1,3,4-Oxadiazole are given in Table 1 & 2.

Table 1: Percentage of C, H, N present in 1,3,4-oxadiazole

	Calculated %	Found %
C	34.29	34.50
H	2.88	3.22
N	40.00	39.55

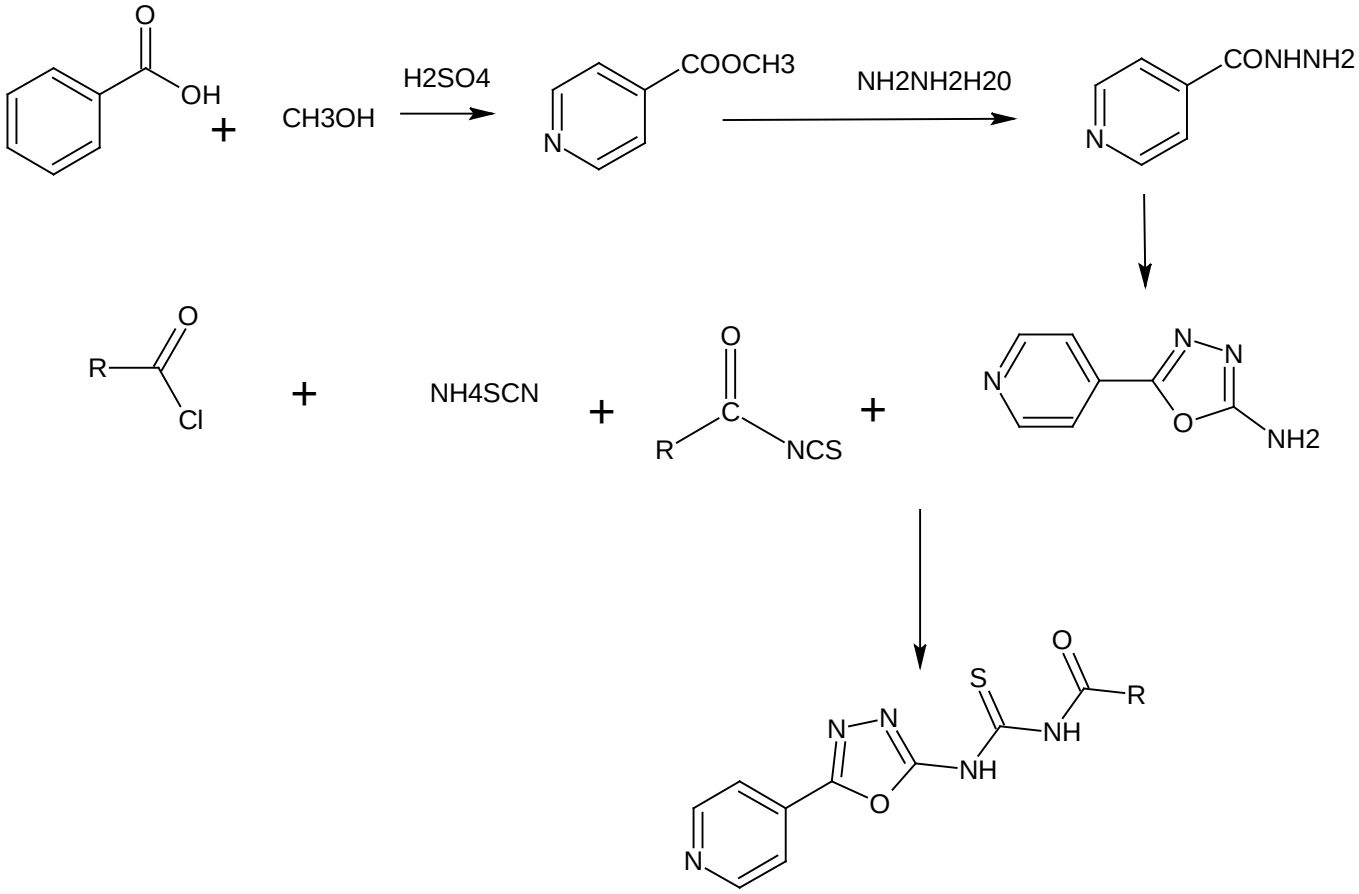
Table 2: Bond angle.

Bond/ Angle	Bond angle (°)	Bond length (pm)
A	105.6	139.7
B	113.4	129.9
C	102.0	134.8
D	113.4	134.8
E	105.6	19.7

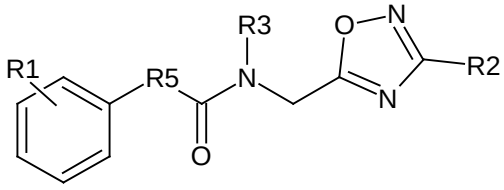
Chemistry of oxadiazole ring

Oxadiazole is a heterocyclic aromatic chemical compound having a five-member ring containing one oxygen and two nitrogen atoms and molecular formula of oxadiazole C H N O. There are four isomers of oxadiazole: (1) 1,2,3-oxadiazole (2) 1,2,4-oxadiazole, (3) 1,2,5- oxadiazole and (4) 1,3,4-oxadiazole are known, but the 1,2,3-isomer is unbalanced and reverts to the diazoketone tautomer. Name for oxadiazole ring such as 'Azoxime' (1,2,4-oxadiazole), 'Furazan' (1,2,5-oxadiazole), Furazans' (1,2,5-oxadiazole) and ˙Biazole, oxybiazole' (1,3,4- oxadiazole)[1-9]

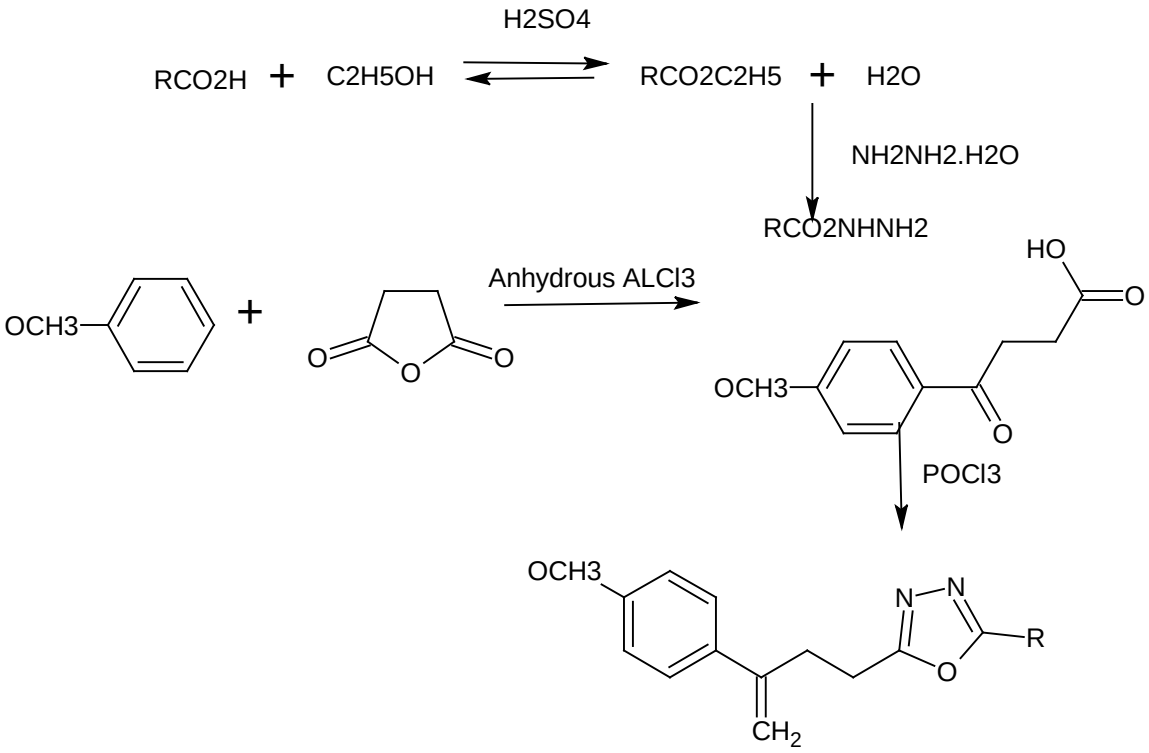
Asma Ambekari, et al., (2019): were synthesized Series of novel substituted Synthesis of N-{[5-(substituted)-1,3,4-oxadiazole-2-yl] carbamothioyl} derivatives containing 1,3,4-oxadiazole moiety were synthesized by microwave as a green chemistry method and conventional method by using pyridine 3- carboxylic acid as a starting material. The entire newly synthesized compound screened for their antimicrobial and In-vivo and In-vitro Anti-inflammatory studies. Anti-inflammatory studies revealed that Substituted[5-(pyridin-4-yl)-1,3,4-oxadiazol-2-yl]benzamide compound showed significant in-vivo and in-vitro anti-inflammatory activity as well potent antimicrobial activity.[2]



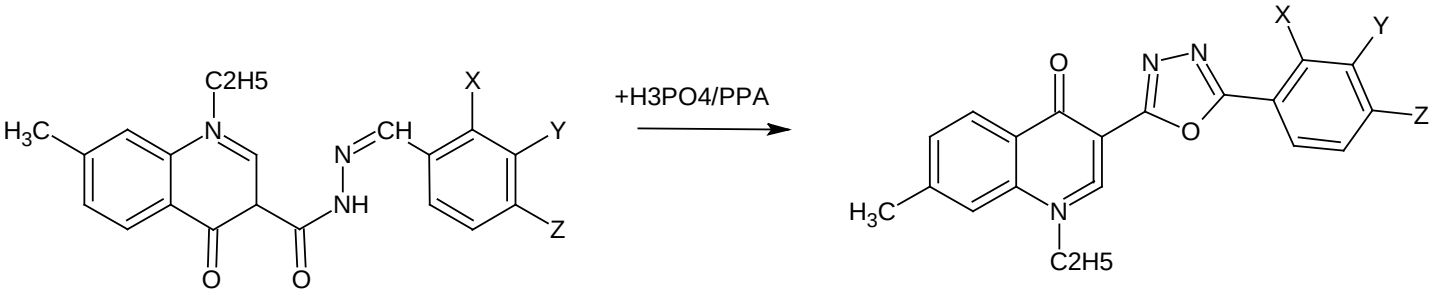
X. Maréchal et al., (2013): were synthesizes 1,2,4-oxadiazolederivatives for virtual ligand screening approach led to the identification of several relatively potent 1,2,4-oxadiazole derivatives acting selectively on the ChT-L activity of constitutive 20S proteasome. Oxadiazoles are pharmacophore of interest in medicinal chemistry. Different computational tools were used to screen the ChT-L active site of 20S proteasome leading to a selection of 300 compounds tested for their potential to inhibit the three catalytic activities of human 20S proteasome. Twenty of them were 1,2,4-oxadiazole derivatives that selectively inhibited the ChT-L activity. [4]



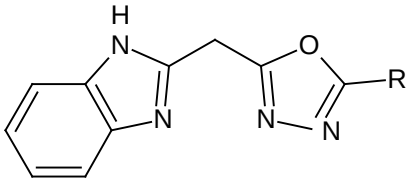
Suman Bala, et al., (2014): were synthesized 1,3,4-oxadiazole substituted 24 derivatives as novel, potential antibacterial agents. Among all the synthesized derivatives most of observed as the best antibacterial agents against all the selected microbial strains. While studying MIC against bacterial strains, compound containing p-chloro and m-methoxy and p-hydroxyl substitutions were found to be the most active among all the derivatives.[5]



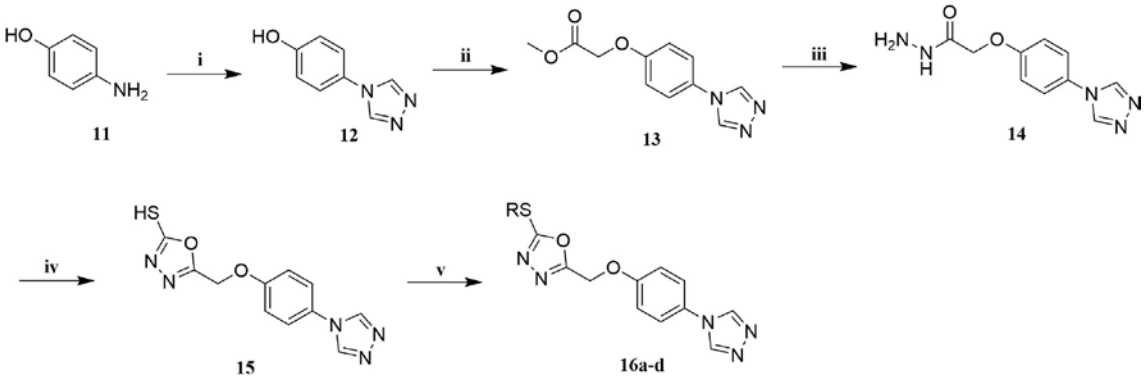
Farah Deeba et al., (2018): were synthesized A series of novel 1, 3, 4-oxadiazole analogues was synthesized from cyclization of hydrazones of substituted 1-ethyl-1,4-dihydro-7-methyl-4-oxo-1,8- naphthyridine-3-carbohydrazides were prepared from nalidixic acid. The structures of synthesized oxadiazole derivatives and their copper complexes were elucidated on the basis of FTIR, elemental analyses, 1H-NMR and atomic absorption spectral analysis. The synthesized compounds were further evaluated with biological activities and compared with parent hydrazones. Copper complexes possess antibacterial and antifungal activities better than the oxadiazoles while they have better antioxidant activity then copper complexes. Parent hydrazones were better in all biological activities than synthesized oxadiazoles.[6]



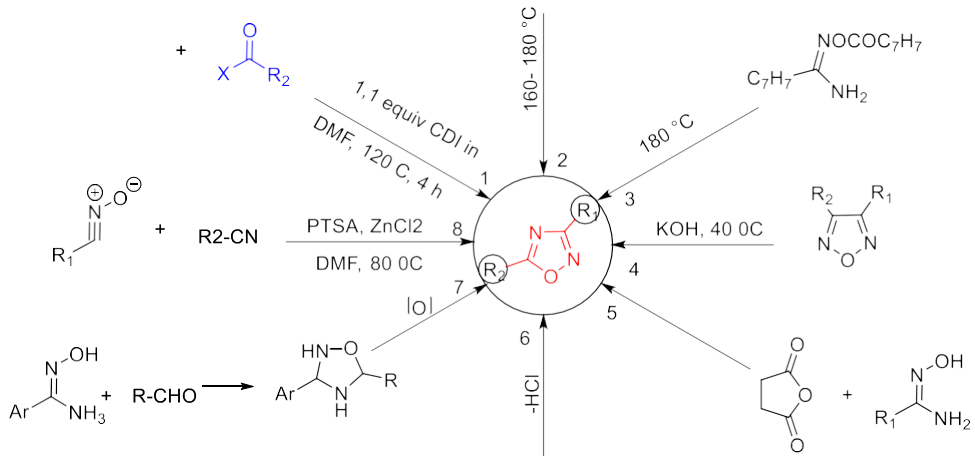
Teresa Glomb et al., (2018): were synthesized Compounds containing 1,3,4-oxadiazole ring in their structure are characterised by multidirectional biological activity. Their anti-proliferative effects associated with various mechanisms, such as inhibition of growth factors, enzymes, kinases and others, deserve attention. The activity of these compounds was tested on cell lines of various cancers. In most publications, the most active derivatives of 1,3,4-oxadiazole exceeded the effect of reference drugs, so they may become the main new anti-cancer drugs in the future.[7]



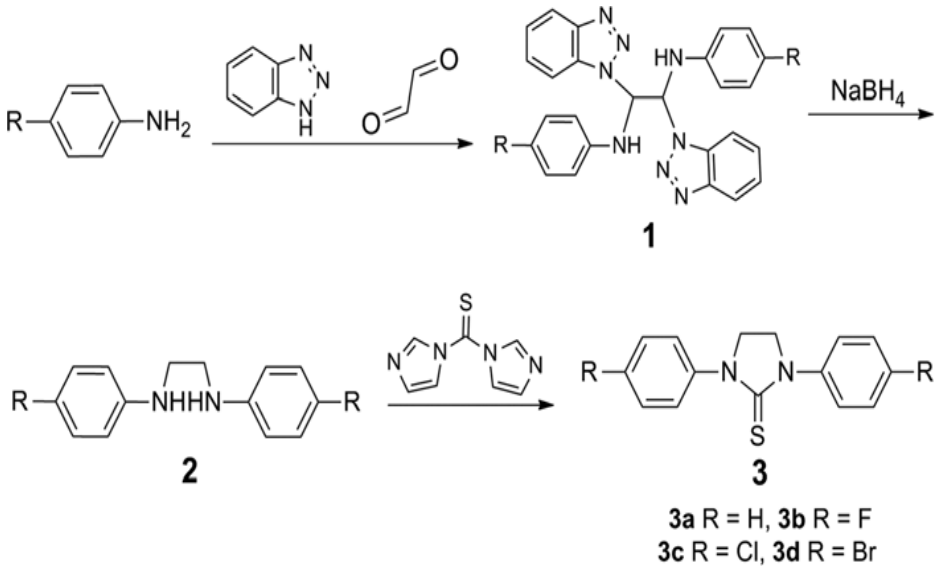
Shiben Wang et al., (2020): were synthesized series of 1,3,4-oxadiazole derivatives were designed, synthesized, and evaluated for their anticonvulsant activity. Most of the compounds showed significant anticonvulsant effects at different doses. Compound 6-((5-(pentylthio)-1,3,4- oxadiazol-2-yl)methoxy)-3,4-dihydroquinolin-2(1H)-one, showed the best anticonvulsant activity in the MES and scPTZ model. [8]



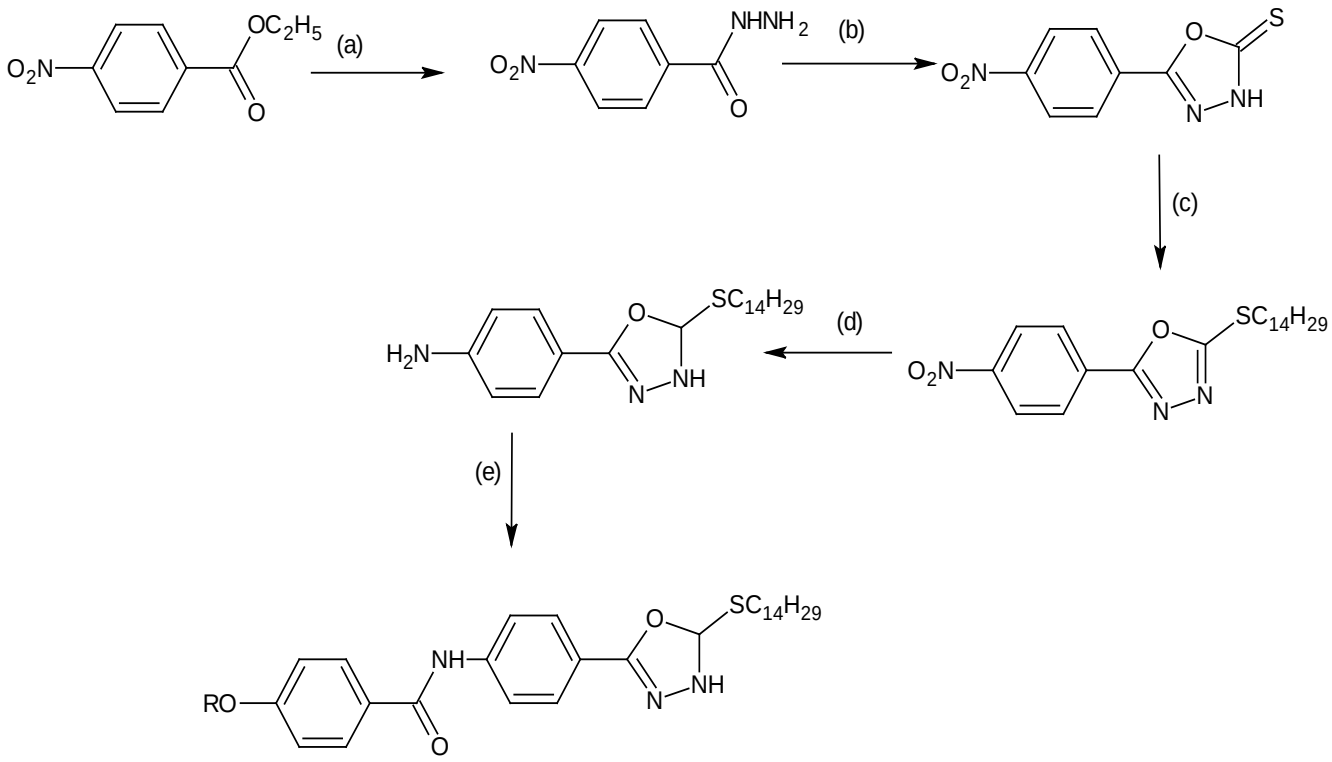
Upare Abhay Atmaram et al., (2021): were synthesized and tested 1,2,4-oxadiazole and 1,3,4-thiadiazole scaffolds are widely explored by researchers in medicinal chemistry, particularly as anti- tubercular and anticancer agents.[9]



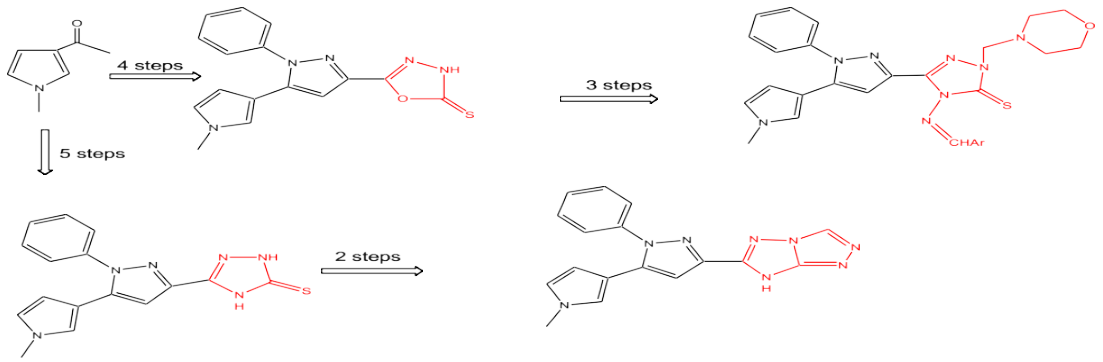
Bingqiong Yu et al., (2018): were synthesized the 1,3,4-oxadiazole derivatives having anti- tumour properties of new Au(I) metal complexes. The results demonstrated that these Au(I) oxadiazole derivatives obviously inhibited tumour cell growth, particularly $Au(I)(3c)_2OTf$.[10]



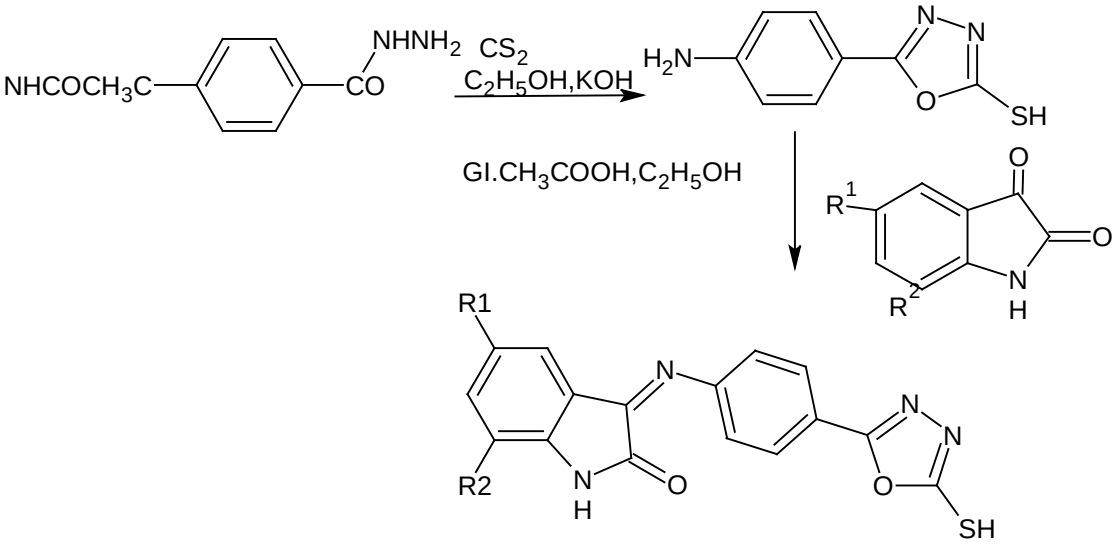
Vishal Modi et al., (2011): were synthesized a novel achiral and chiral amide incorporating 1,3,4-oxadiazole ring are reported. All the synthesized amides are characterized ^{1}H, ^{13}C, FTIR and elemental analysis techniques. Synthesized compounds are screened for microbial and cytotoxic activities. Shows potent activity. [12]



El-sayed M. Abdelrehim et al., (2021): were synthesized New derivatives of [1,3,4]oxadiazole-2-thione and triazole-3-thione were synthesized through the cyclocondensation of dicarbonyl ester 2 with phenyl hydrazine followed by hydrazinolysis to give the corresponding hydrazide, which reacted with carbon disulfide or ammonium thiocyanate to afford [1,3,4]oxadiazole 5 or triazole-3-thione 7, respectively. Hydrazinolysis of compound 5 gave [1,2,4]triazole-3-thiol 9 which was treated with different aromatic aldehydes to obtain Screening of some chosen synthesized compounds against the human colon carcinoma cancer cell lines showed that the compound [1,2,4]triazole-3-thiol 9 exhibiting cytotoxic activity was roughly equivalent to standard Vinblastine.[13]



Gudipati R, et al., (2011): were synthesised 5- or 7-substituted 3-{4-(5-mercapto-1,3,4-oxadiazol-2- yl)phenylimino}-indolin-2-one derivative having anticancer activity by treating 5-(4-aminophenyl)- 1,3,4-oxadiazole-2-thiol with different isatin derivatives.[14]



Conclusion: - This article summarizes the synthesis and biological activities of 1, 3, 4-oxadiazole derivatives. From this it is found that this five-member heterocyclic molecule can be synthesised by various methods and those derivatives are having verities of activities. Such as anticancer, antimicrobial, anti- inflammatory, anti- HIV, anti-tubercular, anti-diabetic, antifungal etc. So study on this molecule is useful to the mankind.

Acknowledgement:
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