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OXADIAZOLE: A BIOLOGICALLY ACTIVE SCAFFOLD

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ABSTRACT

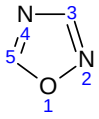
The extensive survey of literature has revealed that the oxadiazole possess wide range of biological activities including anticancer , anti-inflammatory , fungicidal , herbicidal , pesticidal, analgesic, anticonvulsant , anti-HIV , antibacterial and plant growth regulator activities .It is observed from that literature certain five membered heterocyclic compound possess interesting anti-inflammatory ,antimicrobial ,antibacterial ,anticonvulsant, antiviral and antifungal activity . It can act as an important tool for researchers to develop newer compounds possessing oxadiazole moiety that could be better agents in terms of efficacy and safety.

KEYWORDS: Oxadiazole, Biological activities.

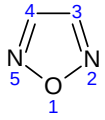
INTRODUCTION

Oxadiazole are considered to be derived from furan by the replacement of two methane (-CH=) groups by two pyridine type nitrogens (-N=). There are four isomeric type of oxadiazoles depending on the positions of the nitrogen atoms in the oxadiazole ring and are numbered as shown in following figure.

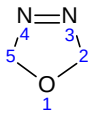
1,2,3-Oxadiazole



1,2,4-Oxadiazole



1,2,5-Oxadiazole

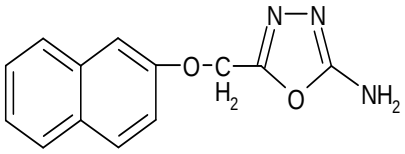


1,3,4-Oxadiazole

The replacement of two –CH= groups in furan by two pyridine type nitrogen (-N=) reduces aromaticity of the resulting oxadiazole ring to such an extent that the Oxadiazole ring exhibit character of the conjugated diene. The electrophilic substitutions in oxadiazole ring are extremely difficult at the carbon atoms because of relatively low electron density on the carbon atoms due to electron withdrawal effect of the pyridine –type nitrogen atoms; however the attack of electrophiles occurs at the nitrogens, if oxadiazole ring is substituted with an electron releasing group. Oxadiazole ring is generally resistant to the nucleophilic attack. Halogen substituted oxadiazoles however; undergo nucleophilic substitutions with the replacement of the halogen atom by nuclophiles. Oxadiazole undergo nucleophilic substitution similarly as occurring at an aliphatic sp^2-carbon atom, but not as aromatic nucleophilic substitution.[1,2]

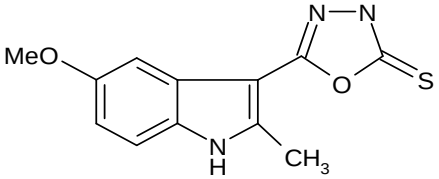
Antimicrobial Activity

Erhan Palaska et al[3] in 2002 reported the synthesis of some 1,3,4-oxadiazoles having antimicrobial activity.



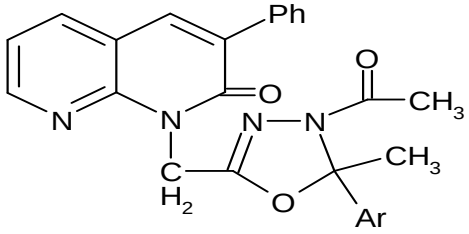
5-((naphthalen-2-yloxy)methyl)-1,3,4-oxadiazol-2-amine

Dundappa S Dondawade et al.[4] in 2006 reported the synthesis of Mercaptooxadiazoles with antimicrobial activity.



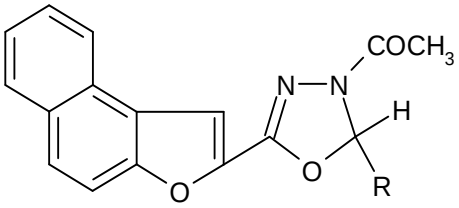
5-(5-methoxy-2-methyl-1*H*-indol-3-yl)-1,3,4-oxadiazole-2(3*H*)-thione

K. Mogilaian et al[5] in 2006 reported the synthesis of aryl oxadizoles having antibacterial activity.



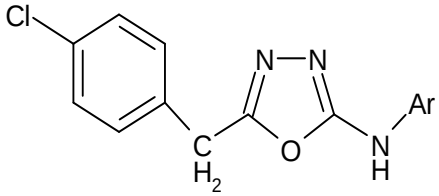
1-((4-acetyl-5,5-dimethyl-4,5-dihydro-1,3,4-oxadiazol-2-yl)methyl)-3-phenyl-1,8-naphthyridin-2(1*H*)-one

H. M. Vagdevi et al[6] in 2006 reported the synthesis of aryl oxadiazoles having antibacterial and anti-inflammatory activity.



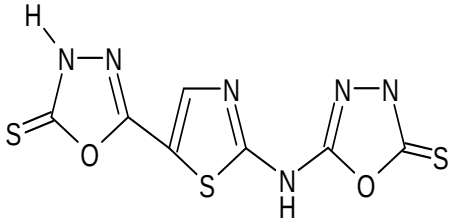
1-(2-methyl-5-(naphtho[2,1-*b*]furan-2-yl)-1,3,4-oxadiazol-3(2*H*)-yl)ethanone

N.C.Desai et al[7] in 2008 reported the synthesis of aryl oxadiazoles with antibacterial activity.



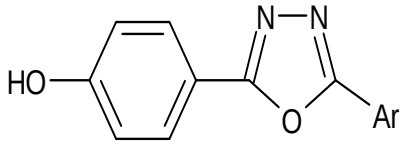
5-(4-chlorobenzyl)-*N*-methyl-1,3,4-oxadiazol-2-amine

B.H.M. Mruthyunjayaswamy et al.,[8] in 2009 reported the synthesis of Mercaptooxadiazoles with antimicrobial activity.



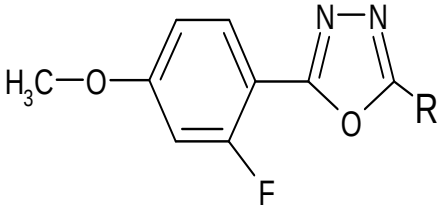
5-(5-(5-thioxo-4,5-dihydro-1,3,4-oxadiazol-2-yl)thiazol-2-ylamino)-1,3,4-oxadiazole-2(3*H*)-thione

Shashikant R Pattan et al[9] in 2009 reported the synthesis of Aryl oxadiazoles and Mercaptooxadiazoles having antimicrobial, antitubercular activity.



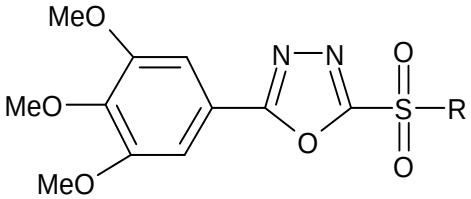
4-(5-methyl-1,3,4-oxadiazol-2-yl)phenol

B. Chandrakantha et al[10] in the year 2010 reported the synthesis of 1, 3, 4-oxadiazole derivatives containing 2-fluoro-4-methoxy and were screened for their antibacterial and antifungal activities.



2-(2-fluoro-4-methoxyphenyl)-5-methyl-1,3,4-oxadiazole

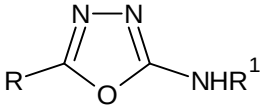
Cai-Jun Chen et al[11] in 2007 reported the Synthesis and antifungal activities of 5-(3,4,5-trimethoxyphenyl)-2-sulfonyl-1,3,4-thiadiazole and 5-(3,4,5-trimethoxyphenyl)-2-sulfonyl-1,3,4-oxadiazole derivatives.



2-(methylsulfonyl)-5-(3,4,5-trimethoxyphenyl)-1,3,4-oxadiazole

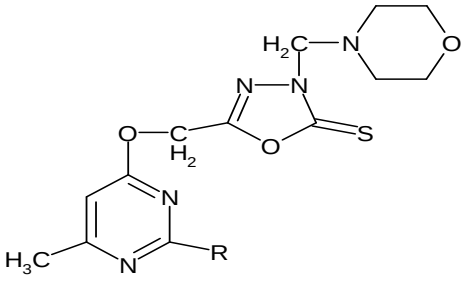
Anti-Inflammatory Activity

F.A. Omar et al[12] in the year 1996 have synthesized some 1, 3, 4-oxadiazole derivatives and evaluated it for Anti inflammatory activity.



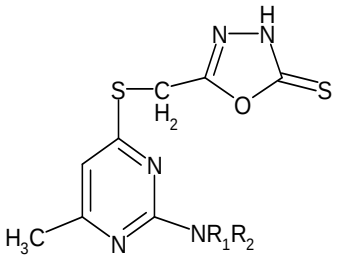
N,5-dimethyl-1,3,4-oxadiazol-2-amine

Virginija Jakubkiene et al[13] in 2003 reported the Synthesis and anti-inflammatory activity of 5-(6-methyl-2-substituted 4-pyrimidinyloxymethyl)-1,3,4-oxadiazole-2-thiones and their 3-morpholinomethyl derivatives.



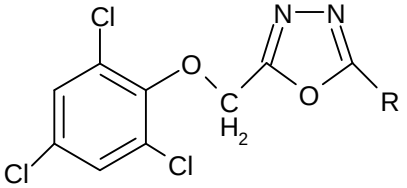
5-((2,6-dimethylpyrimidin-4-yloxy)methyl)-3-(morpholinomethyl)-1,3,4-oxadiazole-2(3*H*)-thione

Milda Malvina Burbuliene et al[14] in 2004 reported the Synthesis and anti-inflammatory activity of derivatives of 5-[(2-disubstitutedamino-6-methyl-pyrimidin-4-yl)-sulfanylmethyl]-3H-1,3,4-oxadiazole-2-thiones.



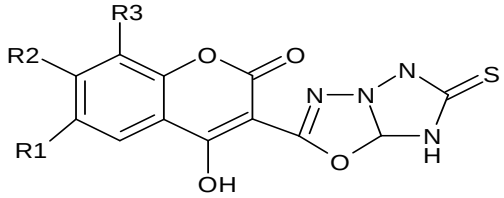
5-((2,6-dimethylpyrimidin-4-ylthio)methyl)-1,3,4-oxadiazole-2(3*H*)-thione

Mohd. Amir et al[15] in 2007 reported the synthesis of aryl oxadiazoles having anti-inflammatory activity.



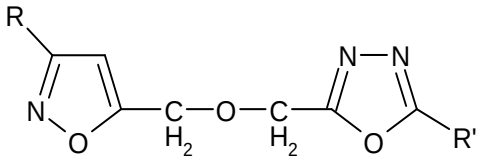
2-methyl-5-((2,4,6-trichlorophenoxy)methyl)-1,3,4-oxadiazole

Airody V.Adhikari et al[16] in 2008 reported the synthesis of Triazolooxadiazoles having analgesic and anti-inflammatory activity.



4-hydroxy-6,7,8-trimethyl-3-(6-thioxo-5,6,7,7a-tetrahydro-[1,2,4]triazolo[5,1-*b*][1,3,4]oxadiazol-2-yl)-2*H*-chromen-2-one

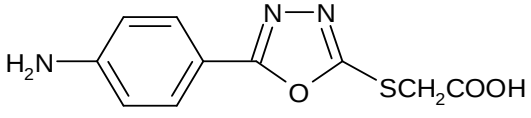
B. Jayashankar et al[17] in 2009 reported the synthesis and pharmacological evaluation of 1,3,4-oxadiazole bearing bis(heterocycle) derivatives as anti-inflammatory and analgesic agents.



2-methyl-5-(((3-methylisoxazol-5-yl)methoxy)methyl)-1,3,4-oxadiazole

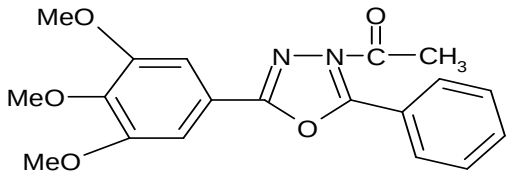
Anticancer Activity

T.K.Maity et al[18] in 2008 reported the synthesis of Mercaptooxadiazoles with anticancer activity.



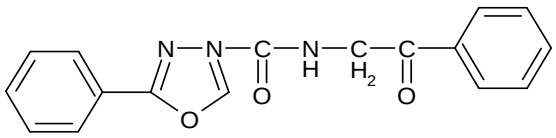
2-(5-(4-aminophenyl)-1,3,4-oxadiazol-2-ylthio)acetic acid

Baoan Song et al[19] in 2006 reported the Synthesis, structure, and bioactivity of N0-substituted benzylidene-3,4,5-trimethoxybenzohydrazide and 3-acetyl-2-substituted phenyl-5-(3,4,5- trimethoxyphenyl)-2,3-dihydro-1,3,4-oxadiazole derivatives.



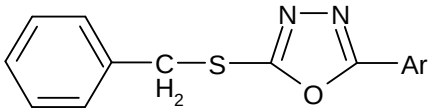
1-(2-phenyl-5-(3,4,5-trimethoxyphenyl)-1,3,4-oxadiazol-3(2*H*)-yl)ethanone

Zhong Li et al[20] in 2008 reported the synthesis 1,3,4-Oxadiazole-3(2H)-carboxamide derivatives as potential novel class of monoamine oxidase (MAO) inhibitors.



N-(2-oxo-2-phenylethyl)-5-phenyl-1,3,4-oxadiazole-3(2*H*)-carboxamide

Morihisa Saitoh et al[21] in 2009 reported the synthesis and structure–activity relationships of 1,3,4-oxadiazole derivatives as novel inhibitors of glycogen synthase kinase-3b.



2-(benzylthio)-5-methyl-1,3,4-oxadiazole

CONCLUSION

The review reports synthetic approaches to some of the oxadiazole derivatives and it highlights the use of oxadiazole derivatives having antimicrobial, anti-inflammatory and anticancer activity. This has been noticed that modifications on oxadiazole moiety displayed valuable biological activities.

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