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OXADIZOLE: A SYNTHETIC AND BIOLOGICALLY ACTIVE MOIETY

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ABSTRACT

Oxadiazole is a five membered heterocyclic nucleus and it having wide range of attention of the chemist. Substituted 1,3,4- oxadiazole are found to exhibit diverse biological activities such as antibacterial, antifungal, anti-inflammatory, analgesic and anticancer activity. The present review attempts to summarize the various routes of synthesis and the reaction of 1,3,4 and 1,2,4- oxadiazole and its derivatives and focus on their biological activity.

KEYWORDS: Oxadiazole, antimicrobial activity, anti-inflammatory activity, anticancer activity, anticonvulsant activity, antiviral activity.

INTRODUCTION

Heterocyclic compounds possess a cyclic structure with two or more different kinds of atoms in the ring known a heteroatom. Heterocyclic compounds are very widely distributed in nature and are essential to life, playing a vital role in the metabolism of all living cells. Among the wide variety of heterocycles that have been explored for developing pharmaceutically important molecules oxadiazole derivatives have played an vital role in medicinal chemistry.[1]

Oxadiazole chemistry has become more and more important over the years, which is documented by number of papers and patents on oxadiazole. This is mainly because the discovery of their varied biochemical properties. The oxadiazole chemistry has been developed extensively and is still developing. Presently there are a number of drugs used clinically, which comprise oxadiazole moiety in association with various heterocyclic rings.[2]

1,3,4-Oxadiazoles have attracted interest in medicinal chemistry as surrogates of carboxylic acids, esters, and carboxamides. They are an important class of heterocyclic compounds that have a wide range of pharmaceutical and biological activities including antimicrobial[3,9], antifungal[32,33], anticancer[34,35], anti-inflammatory[37,38] and antiviral activity.[44]

Several methods have been reported in the literature for the synthesis of 1,3,4-oxadiazoles. The major routes are-

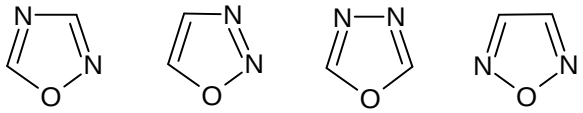
1) The formation of oxadiazole by cyclodehydration of diacylhydrazines.
2) The formation of oxadiazole by oxidation of acylhydrazones.
3) The formation of oxadiazolidinone, oxadiazolinethiones and aminooxiadiazole by action of hydrazide of phosgene, carbon disulphide and cynogen bromide respectively.

The most general method involves the cyclization of diacylhydrazides with a variety of reagents, such as thionyl chloride, carbon disulphide, phosphorus oxychloride, or sulfuric acid, usually under harsh reaction conditions. Few reliable and operationally simple examples have been reported for the one-step**.** Synthesis of 1,3,4-oxadiazoles, especially from readily available carboxylic acids and acid hydrazides.

The present review specially emphasizes on chemistry, methods of synthesis and biological activity of 1, 3, 4-oxadiazole and its derivatives.

Chemistry of Oxadiazole

Oxadiazole is a very weak base due to the inductive effect of the extra heteroatom. The replacement of two -CH= groups in furan by two pyridine type nitrogen (-N=) reduces aromaticity of resulting oxadiazole ring to such an extent that the oxadiazole ring exhibit character of conjugated diene. The electrophilic substitutions in oxadiazole ring are extremely difficult at the carbon atom because of the relatively low electron density on the carbon atom which can be attributed to electron withdrawal effect of the pyridine type nitrogen atom. However, the attack of electrophiles occurs at nitrogen, if oxadiazole ring is substituted with electron-releasing groups. Oxadiazole ring is generally resistant to nucleophilic attack. Halogen substituted oxadiazole, however, undergo nucleophilic substitution with replacement of halogen atom by nucleophiles. Oxadiazole undergo nucleophilic substitution similarly as occurring at an aliphatic sp2 carbon atom. There are four possible isomers of oxadiazole, depending on the position of nitrogen atom in the ring and are numbered as shown below.[1,2]



Sar of Oxadiazole

Oxadiazole molecule originates five membered ring of heterocyclic. They are important place in organic chemistry. It is common observation that combination of two or more biologically active heterocyclic ring either in condensed form or coupled form result in the enhancement of biological profile of such compound by many fold.

1,3,4- oxadiazole exhibit various activity possibly due to the presence of –N=C-O moiety.

(i) All compounds with an allyl group adjacent to an oxadiazole ring were mutagenic in at least one strain.

(ii) All compounds with the oxadiazole ring in the `O-N' arrangement showed at least weak mutagenic effects in strain TA100, preincubation version, independent of the side chain used.

(iii) Compounds containing allyl group in the side chain and O-N arrangement in the aromatic heterocycle are more strongly positive than N-O arranged heteroaromatics.

(iv) Longer chains, *i.e.* a C2 bridge, between the allyl groups and the oxadiazole ring reduces the mutagenic effect.

(V) In 3rd and ^{2nd} position aromatic compounds are attached it increases the antifungal activity and further this aromatic ring substituted with electron donating group it will more effective against *Fusarium lateritium* and *Fusarium decemcellulare.*

(Vi) If electron donating groups substituted at 2nd position in 1,3,4- oxadiazole it will increases the anti-inflammatory, analgesic and anti-microbial activity.

Ir Spectroscopic Studies

The IR spectrum of the compound showed absorption peak at 1609- 1609 cm^{-1}, 1870- 1550 cm^{-1}, 1199- 1019 cm^{-1} due to the stretching of the C=N, C=O, C-O-C. IR Spectra (KBr) were recorded on shimadzu IR spectrophotometer.

Synthesis of Oxadiazole

Oxadiazole can be synthesized from mainly thiosemicarbazide or hydrazide that is oxadiazole can cyclized from thiosemicarbazide or hydrazide by methods like conventional method, ultrasound or microwave using catalyst like $POCl_3$, $SOCl_2$, CS_2, Chloramine-T, *etc*.

Methods of synthesis of 2,5-disubstituted-1,3,4-oxadiazoles

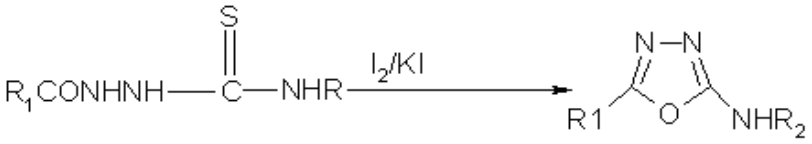
No important new general routes to 1,3,4-oxadiazoles have been reported since, the mid-1980s. The major routes are:

- The formation of oxadiazole by cyclodehydration of diacylhydrazines $R_1CONHNHCOR_2$.
- The formation of oxadiazole by oxidation of acylhydrazones $RCH{=}NNHCOR_1$.
- The formation of oxadiazolinones, oxadiazolinethiones and amino-oxadiazole by the action on hydrazide $RCONHNH_2$ of phosgene, carbon disulphide (or thiophosgene) and cyanogens bromide, potassium thiocyanate, $POCl_3$ respectively.

1. From Thiosemicarbazides

a. Using Iodine in the presence of Potassium Iodide

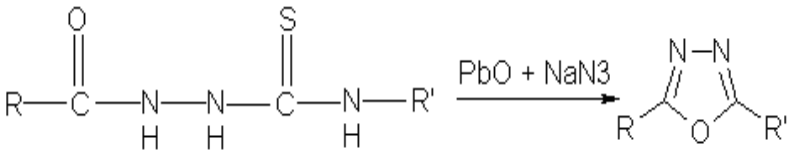
1,3,4-oxadiazoles were generally synthesized from thiosemicarbazides by oxidation with iodine in the presence of potassium iodide and sodium hydroxide.[11]



Whereas, R_1 & R_2 is any alkyl or aryl group

b. Oxidation by PbO

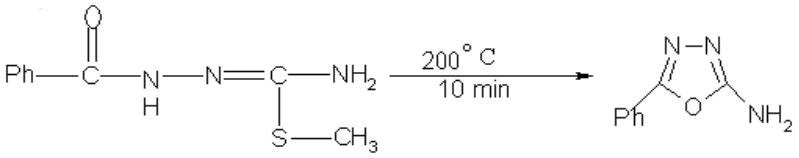
Thiosemicarbazides were easily cyclized by lead oxide and NaN_3 in ethanol to give 2-substituted-5-aryl-1,3,4-oxadiazoles.[12]



Whereas, R = aryl; R_1 = arylamino.

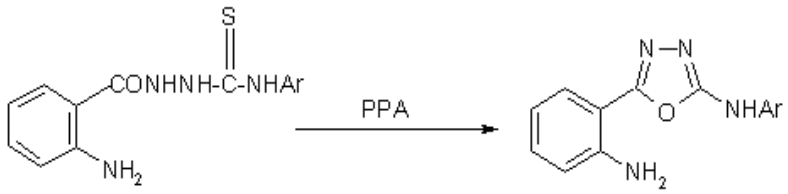
c. By Thermal Cyclization

Hoggarth[13] synthesized 2-amino-5-phenyl-1,3,4-oxadiazoles by heating 1-benzolyl-5-methyl-isothiosemicarbazide at 200° C for 10 min.



d. By PPA Cyclization

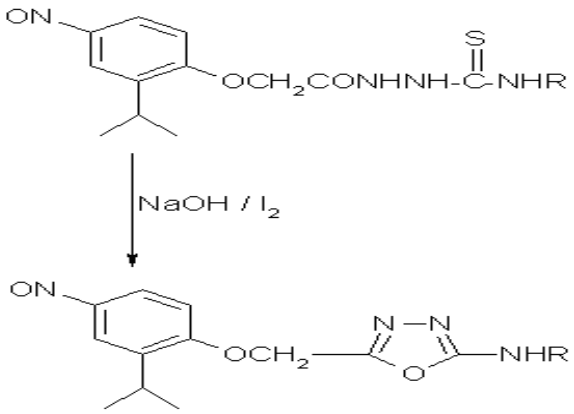
Peet *et al*[14] reported the formation of 2-arylamino-5-(2-aminophenyl)-1,3,4-oxadiazoles by cyclization of 1-(2-aminobenzoyl)-4-aryl-3-thiosemicarbazides.



Whereas, Ar = substituted phenyl groups.

e. By Cyclization with Iodine in Sodium Hydroxide

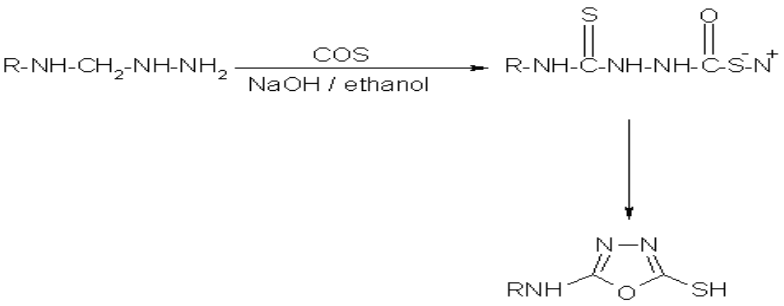
Shah *et al*[15] synthesized 2-arylamino-5-substituted-1,3,4-oxadiazoles by the reaction of appropriately substituted thiosemicarbazides in presence of iodine in sodium hydroxide.



Whereas, R is any aliphatic group.

f. Carbonoxysulphide in the presence of Sodium Hydroxide

Chande *et al*[16] synthesized 5-substituted-2-mercapto-1,3,4-oxadiazoles from sodium (N-arylthiocarbamyl) thiocarbaoxizinate which was further obtained from 4-substituted thiosemicarbazide in the presence of carbonoxysulphide.

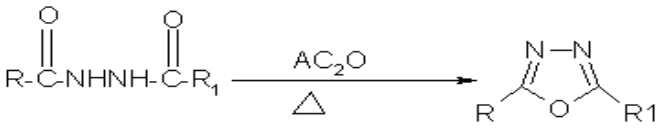


R is methyl or substituted alkyl group

2. Synthesis starting from hydrazides

a. By dehydrocyclization

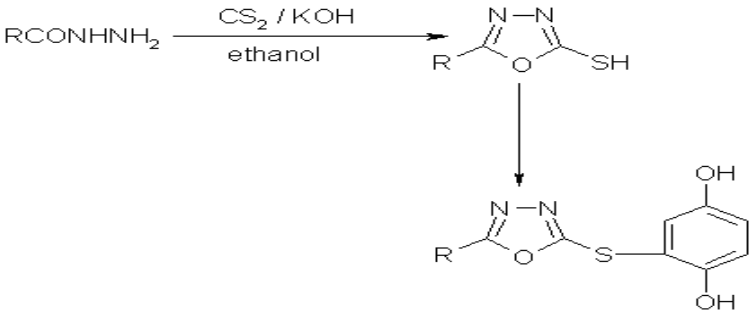
2,5-diaryl-1,3,4-oxadiazole were prepared by dehydrocyclization of corresponding 1,2-diaryl hydrazide in the presence of acetic anhydride.[17]



Whereas, R_1 and R_2 are any aromatic groups.

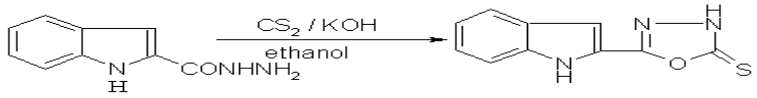
b. By condensation with carbondisulphide in the presence of KOH

i) Hosur *et al*[18] reported synthesis of 2-(2,5-dihydroxyphenylthio)-5-N-alkyl-1,3,4-oxadiazoles from properly substituted acid hydrazide in the presence of carbon disulphide and potassium hydroxide.

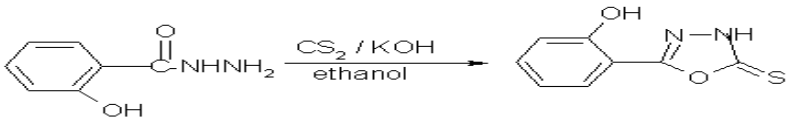


Whereas, R is any aromatic group.

ii) Anisworth[19] synthesized indolyl-1,3,4-oxadiazol-5-thione derivatives from 2-indole carboxylic hydrazide.

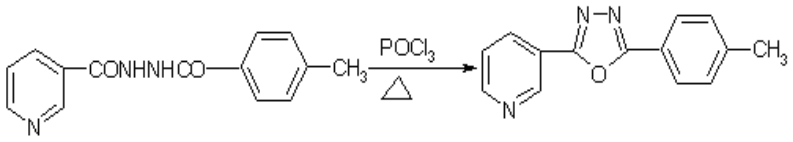


iii) Motti[20] synthesized 5-(2-hydroxyphenyl)-2-mercapto-1,3,4-oxadiazoles from 1-(2-hydroxybenzoyl) hydrazine.



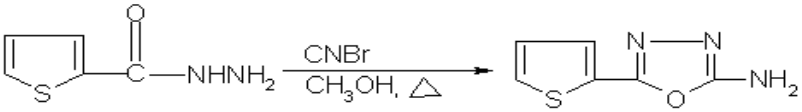
c. Using $POCl_3$

Grekov[21] synthesized 2-(*p*-tolyl)-5-(3-pyridyl)-1,3,4-oxadiazole from 1-(*p*-tolyl)-2-nicotinyl hydrazine using boiling $POCl_3$ as cyclizing agent.



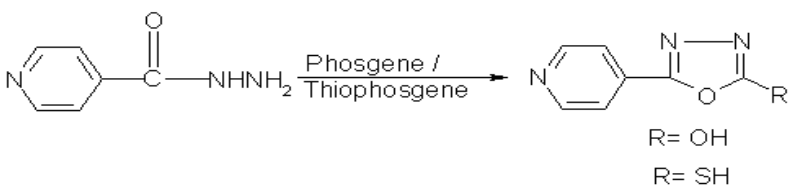
d. By Cyanogen Bromide

Borai *et al*[22] reported synthesis of 2-amino-5-(2'-thienyl)-1,3,4-oxadiazole by the condensation of 2-thienyl hydrazide with cyanogen bromide. It is a very convenient method of synthesis of imino-1,3,4-oxadiazoles.



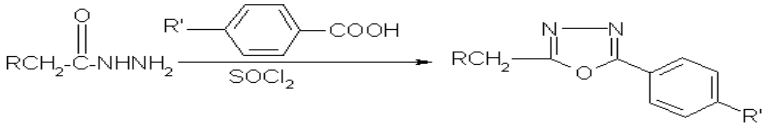
e. Using Phosgene or Thiophosgene

Konig[23] prepared 2-hydroxy-5-(4-pyridyl)-1,3,4-oxadiazole and 2-mercapto-5-(4-pyridyl)-1,3,4-oxadiazole by reacting isonicotinic acid hydrazide with phosgene or thiophosgene, respectively.



f. Aromatic acids in presence of thionyl chloride under microwave irradiation

Acid hydrazide on cyclocondensation with aromatic acids in the presence of thionyl chloride under microwave irradiation gave 2,5-disubstituted-1,3,4-oxadiazoles in good yields. This method[24] is useful due to its substantial reduction in reaction time.



Whereas, R is aromatic group & R' is aliphatic group.

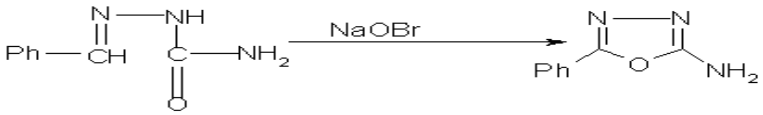
g. Using Chloramine-T as an oxidant with hydrazide

Singh *et al*[25] reported a one-pot synthesis of 1,3,4-oxadiazole from 2-benzothiazolyl carbohydrazide in presence of Chloramine-T which was found to be efficient oxidizing agent.

Whereas, R and R' are any aromatic groups.

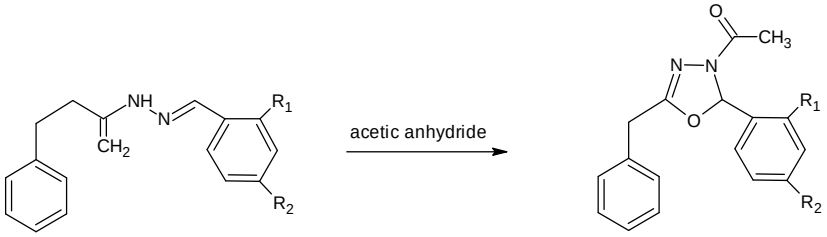
h. Oxidative Cyclization of hydrazones and semicarbazones

2-Amino-5-phenyl-1,3,4-oxadiazoles were prepared from benzaldehyde semicarbazones and sodium hypobromite.[26]



Scheme:1 Cyclization of imines.

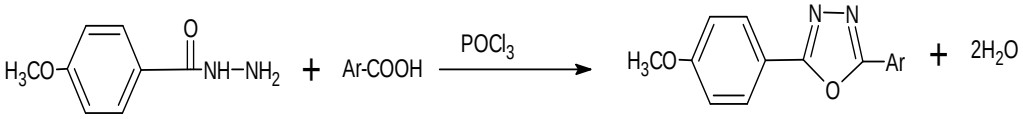
Using acetic anhydride was reported by Neeraj Kumar Fuloria.[3] The carbonylamino and imino groups in imine compounds were found to cyclize to form oxadiazole.



R_1= H, OH and R_2= $N(CH_3)_2$, Cl, OH, H

Scheme: 2 Condensation of 4-methoxybenzohydrazide.

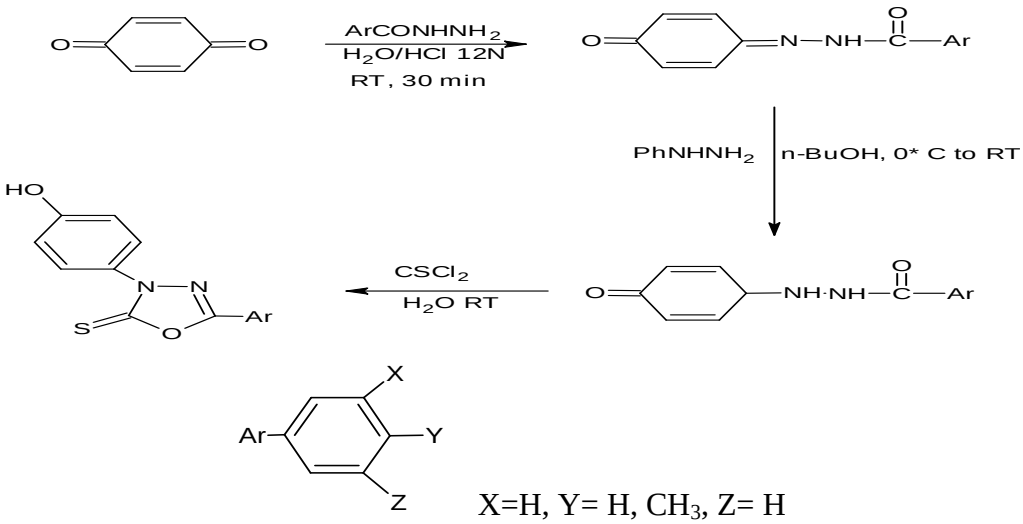
Nagalakshmi[4] reported the synthesis of various 2,5- disubstituted- 1,3,4- oxadiazole via condensation of 4-methoxybenzohydrazide with various aromatic acids in presence of phosphoryl chloride.



Ar = C_6H_5, 4- $CH_3C_6H_4$, C_5H_4N

Scheme: 3.

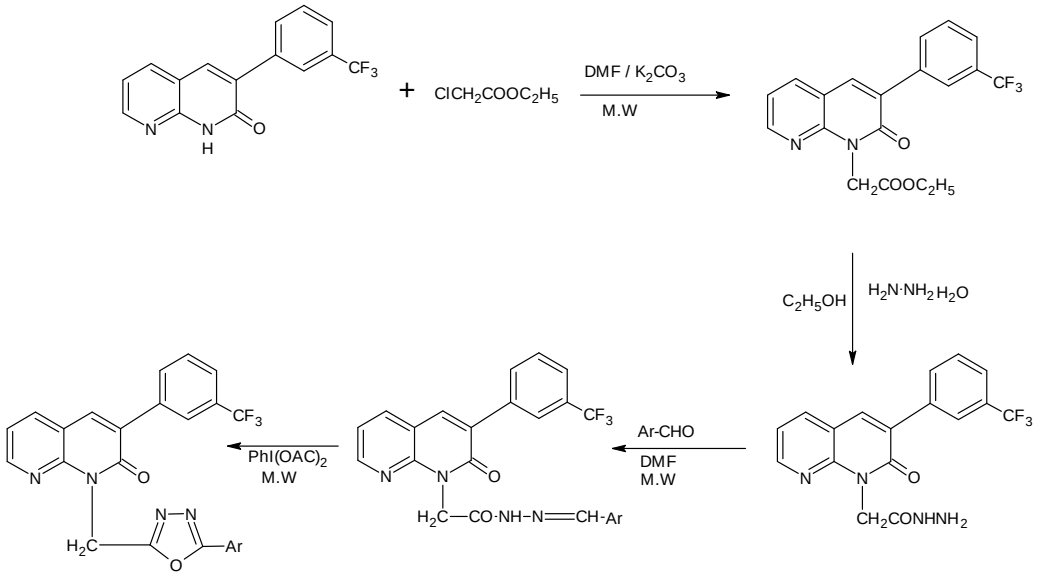
Condensation of substituted benzoic acid hydrazide with 1,4-benzoquinone to obtain benzoic acid (cyclohexadien-1-ylidene) hydrazide substituted derivatives. Which were reduced with phenylhydrazine to afford corresponding substituted benzoic acid 2- (4-hydroxyl phenyl) hydrazide. Further, cyclocondensation with thiophosgene in water yielded the 5-aryl-3-(4-hydroxyphenyl)-1,3,4- oxadiazole-2(3H) thiones.[5]



X=H, Y= H, CH_3, Z= H

Scheme: 4.

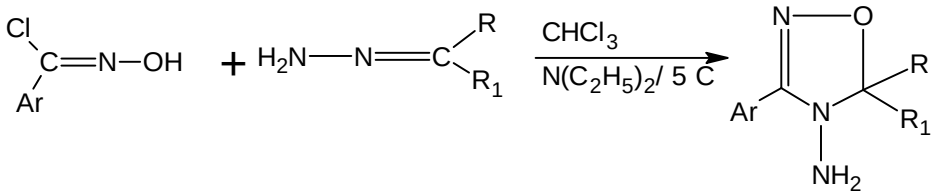
Hydrazinolysis of ethyl(2-oxo-3-(3-trifluoromethylphenyl)-2H- (1,8 naphthyridin-1-yl) acetate with hydrazine hydrate afforded (2-oxo-3-(3-trifluoromethyl phenyl)2H-(1,8) naphthyridin-1-yl) acetic acid hydrazide. Further condensation with various aromatic aldehydes under microwave irradiation afforded (2-oxo-3-(3-trifluoromethyl phenyl)-2H-(1,8) naphthyridin-1-yl)acetic acid arylidenehydrazides which on further oxidative cyclization with $PhI(OAc)_2$ furnished the respective 1- (5-aryl-(1,3,4- oxadiazole-2-yl-methyl)- 3- (3-trifluoromethyl phenyl)-1,4-(1,8) naphthyridin-2-ones.[6]



Ar = C_6H_5, p-$CH_3C_6H_4$,

Scheme: 5 Cycloaddition Reaction.

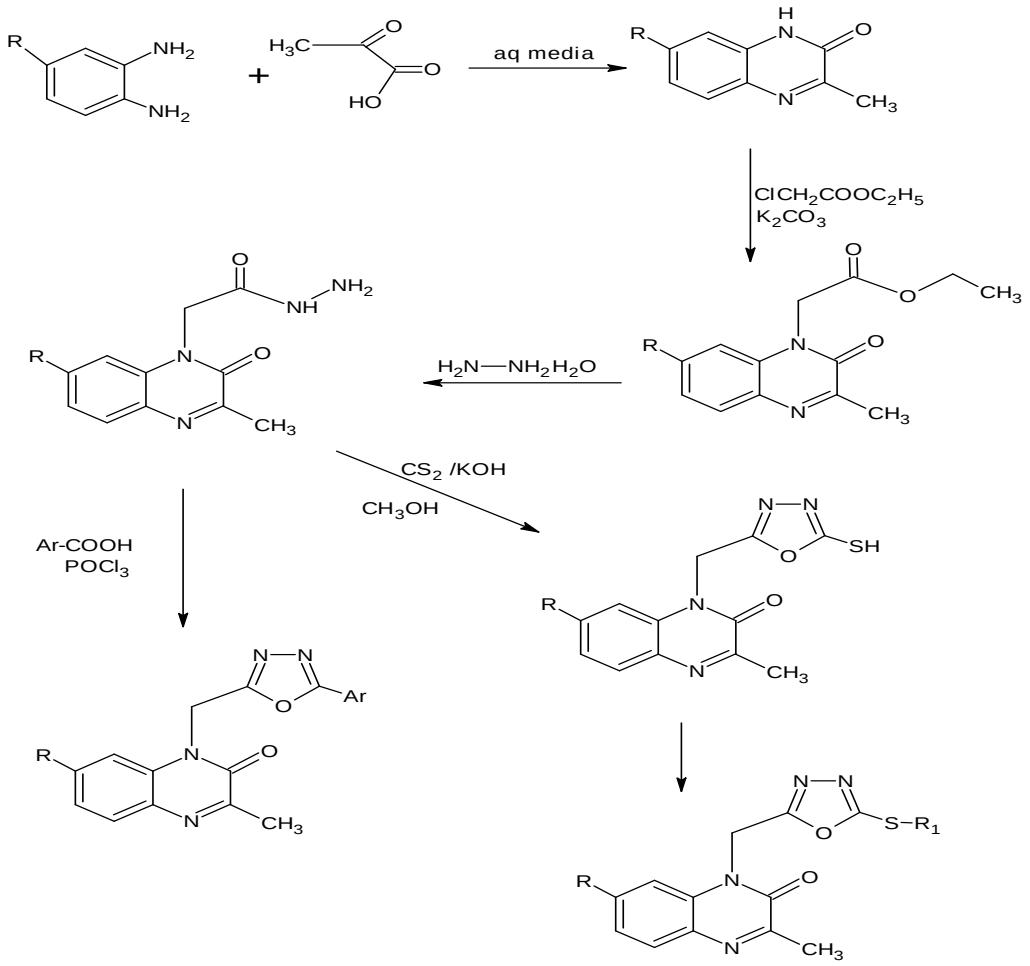
Rademacher[7] reported the synthesis of 4-amino-Δ^2- 1,2,4-oxadiazolines *via* 1,3-dipolar cycloaddition of aliphatic ketohydrazones to aryl nitrile oxides, generated from hydroxamoyl chloride.



R= $(CH_2)_4$, $(CH_2)_5$, R_1= CH_3 and Ar = *p*-$(NO_2)C_2H_4$

Scheme: 6.

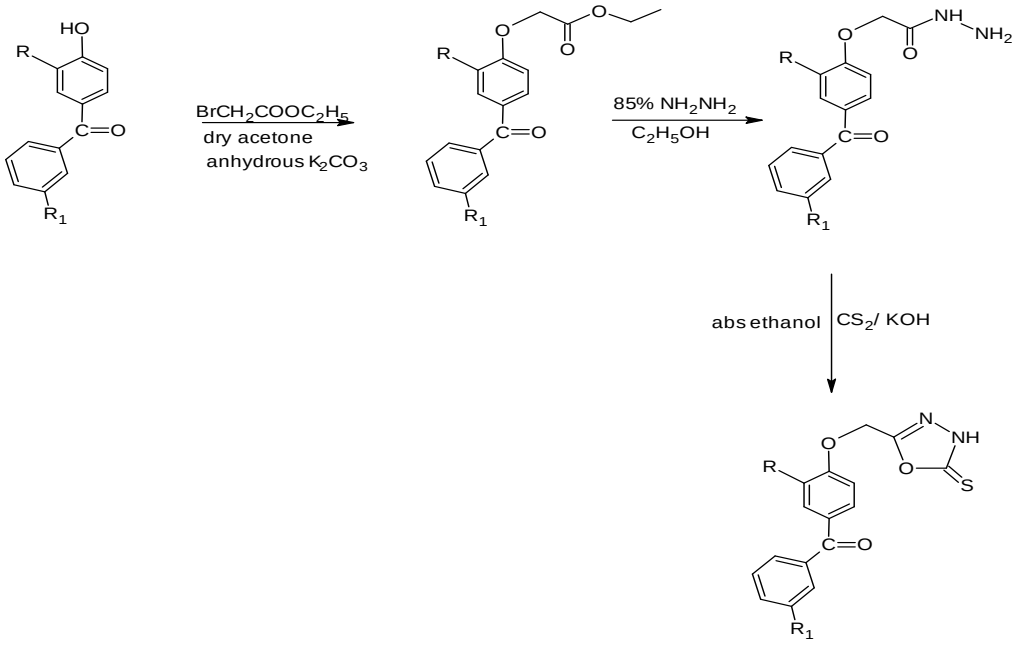
Condensation of 3,4- diaminotoluene with pyruvic acid at acidic p^H to obtain 3,7-dimethylquinoxalin-2-(1H)-one. Then this compound is reacted with ethyl chloroacetate in the presence of potassium carbonate under refluxing condition yielded ethyl (3,7-dimethyl-2-oxoquinoxalin-1(2H)-yl) acetate, which on reaction with hydrazine hydrate in methanol at 65^{o}C gave 2-(3,7- dimethyl-2-oxoquinoxalin-1(2H)-yl) acetohydrazide and then cyclization by using different aromatic acid in the presence of phosphorous oxychloride gives the compounds 3,7 –dimethyl -1-[(5-substituted phenyl-1,3,4- oxadiazol-2-yl) methyl]-quinoxalin-2(1H)-one.[9]



$R=CH_3$, H, Cl $R_1= CH_3$, C_2H_5 and Ar = C_6H_5, $4(NO_2)C_6H_4$

Scheme: 7 Fries Rearrangement reaction.

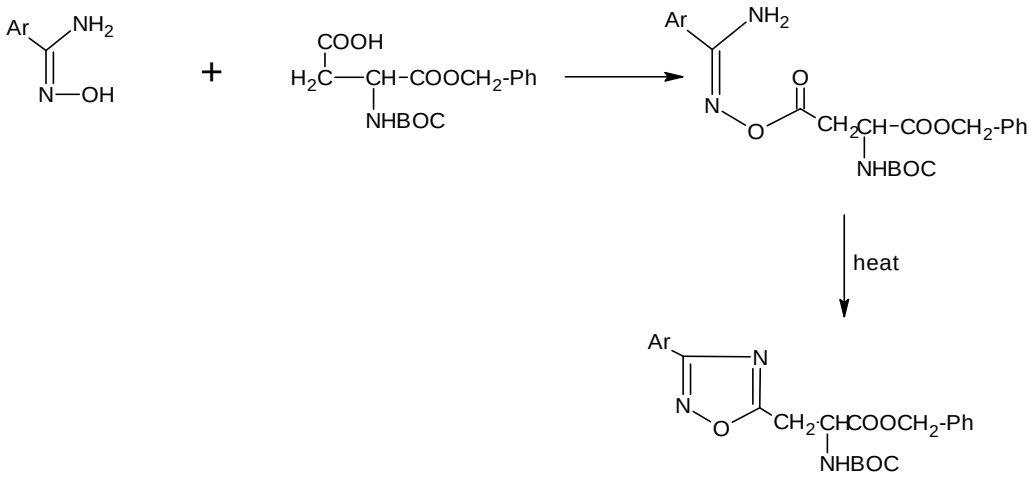
Substituted 4- hydroxybenzophenones were synthesized by the benzoylation of phenols followed by fries rearrangement. And this 4- hydroxybenzophenones on treatment with ethyl bromoacetate in the presence of anhydrous potassium carbonate and dry acetone gave the corresponding aroyl aryloxy esters. This esters are treated with hydrazine monohydrate gave acid hydrazides and then mixture of potassium hydroxide and carbon disulphide in absolute alcohol used to get 2-thio-1,3,4-oxadiazoles.[46]



R= H, CH_3 R_1= H, Cl

Scheme 8.

The synthesis of some 1,2,4- oxadiazole derivatives starting from arylamidoximes and N- *t*-butoxycarbonyl-*o*- benzyl- L- aspartic acid is described. The structures of these new products have been determined by spectroscopic methods.[8]



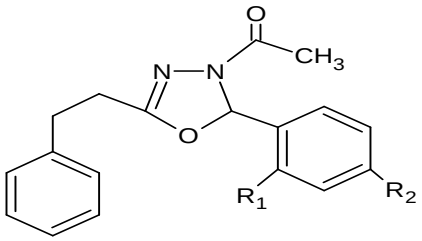
Ar = C_6H_5,*m*-$CH_3C_6H_5$, *p*-$CH_3C_6H_5$

BIOLOGICAL ACTIVITIES OF OXDIAZOLE

Antimicrobial Activity

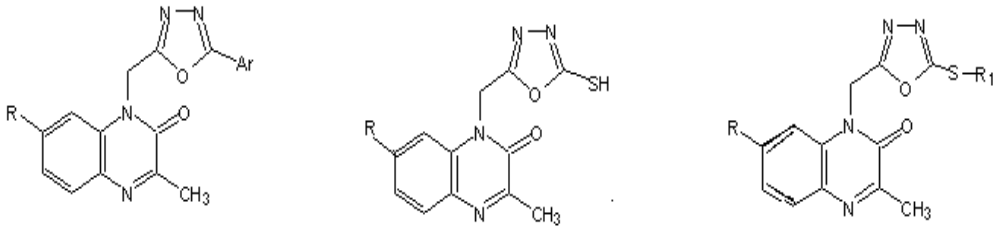
Antimicrobial activity has been exhaustively studied for oxadiazole over the years. It shows wide spectrum of chemotherapeutic activity and considerable amount of work has been done on synthesis of new potent antibacterial, antifungal, anti Tubercular acting oxadiazole.

Neeraj Kumar Fuloria *et al*[3] synthesized phenylpropionohydrazides as potent biological active agent. a, d and e are prominent antibacterial and antifungal activity against *S. aureus* and *P. aeruginosa* at a concentration of 1 mg per ml by using standard drug as Ampicillin and Fluconazole.



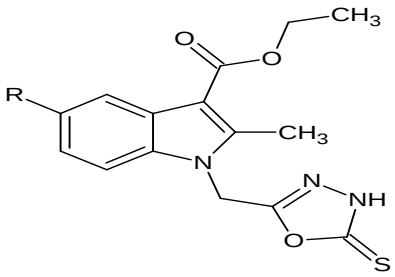
a: R_1=H, R_2= $N(CH_3)_2$, d: R_1= H, R_2= H, e: R_1=H,R_2= OH.

Waghale *et al*[9] synthesized 2-(3-methyl-7-substituted-2-oxoquinoxalinyl)-5-(aryl)-1,3,4-oxadiazole possessing anti-inflammatory and analgesic activity. 7-methyl quinoxaline was found to posses maximum activity than unsubstituted quinoxaline. 4-OCH_3 and 3,4,5-$(OCH_3)_3$ in aromatic ring significantly increases analgesic activity. The Anti-inflammatory activity of the compounds were evaluated by carrageenan- induced paw edema method at a concentration of 2 mg/ kg by using standard drug Indomethacin. The analgesic activity were evaluated by hot- plate method by using standard drug Pethidine at concentration of 5 mg/ kg.



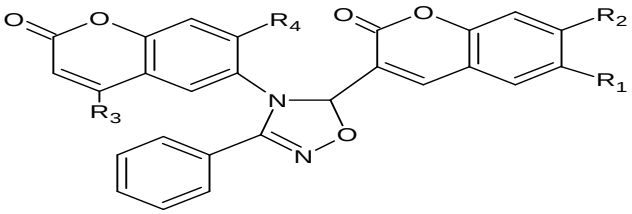
Ia) R_1=R=CH_3, II b)R=-CH_3, R_1=-C_2H_5, IIIa) Ar =4-OCH_3-C_6H_4, R= CH_3,
IIIb) Ar =3,4,5-$(OCH_3)_3$-C_6H_4, R= CH_3; IIIc) Ar =3,4,5-$(OCH_3)_3$-C_6H_4, R= H;
IIId) Ar=4-OCH_3-C_6H_4, R= H; IIIe) 3,4,5-$(OCH_3)_3$-C_6H_4, R= Cl

Bhovi *et al*[10] synthesized 2-methyl-3-ethoxycarbonyl-1-oxadiazolyl-amino carbonyl methylindole having antimicrobial. (*a*) posses highest antibacterial activity towards *Micrococcus* and *E.coli*. (*b*): weak activity towards *E.coli* and moderate activity towards *Micrococcus*. (*a*) and (*b*) moderate activity towards *penicillium*. (*a*): moderate activity towards *A. niger* but (*b*) has weak activity at concentration of 1 mg/ ml by using standard drug Norfloxacin.



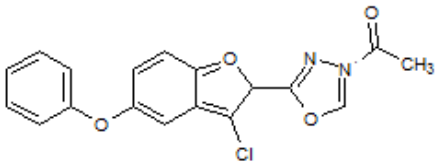
(a) R—OH, (b): R—OCH_3

Sanket P Chaudhari *et al*[27] synthesized 1,2,4-oxadiazolines bearing coumarin nucleus as potent biological active agent. e and h are more effective against *S. aureus* and *E. coli* at concentration of 5 mcg/ ml by using standard drug Ciprofloxacin.



(e) R_1= H, R_2= Cl, R_3= R_4= H, (f) R_1= H, R_2= Cl, R_3= CH3, R_4= OCH3.

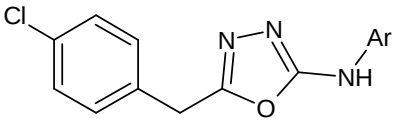
Vasoya *et al*[28] synthesized acetyl oxadiazole bearing Benzo [b] thiophene nucleus as potent biological active agent. *a, e, f* are prominent antiTubercular activity against *mycobacterium tuberculosis strain* at concentration of 6.25 mcg/ ml in BACTEC 12B medium using the ALAMAR radiometric system. *e, b, c*: good antifungal activity. *d* has good antibacterial activity towards *E. coli* and *S. aureus* at 40 mcg/ml concentration and standard drugs like Amoxycillin, Benzyl Penicillin, Ciprofloxacin, Erythromycin, Griseofulvin were used for comparison purpose.



a: 4-Cl-C_6H_4

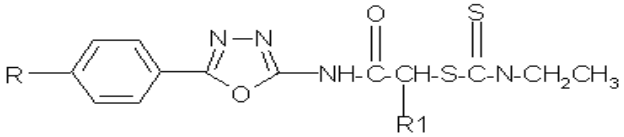
b: 4-OH-C_6H_4, c: 4-OH-3-OCH_3-C_6H_3, d: 3,4-$(OCH_3)_2$-C_6H_3, e: 2,3,4-$(OCH_3)_3$-C_6H_2, f: 3-OC_6H_5-C_6H_4

Desai *et al*[29] synthesized 1,3,4-oxadiazole derivative that having antibacterial activity. *(a)* show good activity towards *E. coli* and *S. aureus*. *(b)* good activity towards *E. coli* but less activity towards *S. aureus.* (*c*) and (*d)* better activity towards *S. aureus* using Ciprofloxacin as standard drug at concentration of MIC mcg/ml.



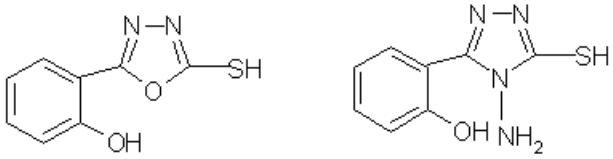
Ar = (a) 2,5$(OCH_3)_2$-C_6H_3, (b) 3-CH_3- C_6H_4, (c) 2-OC_2H_5- C_6H_4, (d) 4-CH_3-C_6H_4

Ates *et al*[30] synthesized some 5-aryl-2-[(N, N-disubstituted thiocarbamoylthio) acylamine]-1,3,4-oxadiazoles and screened them for antimicrobial activity.

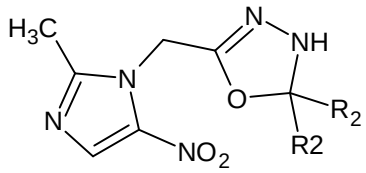


R is methyl or chloromethyl group & R_1 is aliphatic group

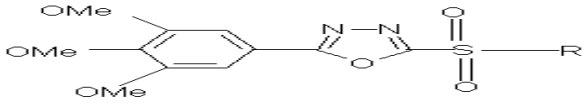
Othman and Guessas *et al*[31] reported the synthesis of 1,3,4-oxadiazole and 1,2,4-triazole derivatives and investigated antibacterial activity against *E.coli, S. aureus and P. aeruginosa* at concentration of 2 mg/ml by using standard drug Gentamycin.



Frank *et al*[32] synthesized 1,3,4-oxadiazole carrying imidazole moiety possessing antibacterial and antifungal activity. Changing R by H or CH_3 and changing R' by *p*-tolyl, *p*-anisyl, *p*-chlorophenyl, *p*-bromophenyl, *p*-nitrophenyl or by 3,4-methylene dioxyphenyl all compounds show good antibacterial and antifungal activity.



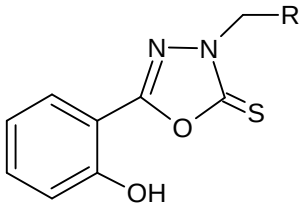
Song B *et al*[33] synthesized novel sulfone derivatives contain trimethoxy phenyl substituted 1,3,4-oxadiazole and thiadiazole moiety and screened for antifungal activity. Most of the compounds showed good activity.



R is aliphatic or aromatic group

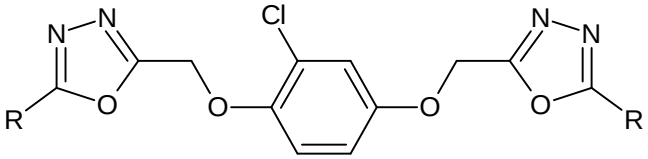
Anticancer Activity

Aboraia *et al*[34] synthesized series of 5-(2-hydroxyphenyl)-3-substituted-2,3-dihydro-1,3,4-oxadiazole-2-thione derivatives and evaluated for their *in-vitro* anticancer activity, where seven out of twenty two synthesized compounds displayed high anticancer activity, in the primary assay. These seven oxadiazole compounds were selected for a full anticancer screening against a 60-cell panel assay where they showed non-selective broad spectrum and promising activity against all cancer cell lines. As a result of 60-cell panel assay two oxadiazole compounds were identified as promising lead compounds.



R= 1-morpholine, 1-phenylpiperazine, -NH-C_6H_4(2-Cl), -NH-C_6H_4(3-Cl) -NH-C_6H_4(4-Cl)

Holla *et al*[35] synthesized 2-chloro-1,4-bis-(5-substituted-1,3,4-oxadiazol-2-methyleneoxy) phenylene derivatives possessing anticancer activity. Most of derivatives show significant activity against cell lines with G 150 values < 100 µm concentration.



a) R= 2,4-dichloro-C_6H_3-OCH_2, b) R= 4-Cl-C_6H_4NH-CH_2

Anti-inflammatory Activity

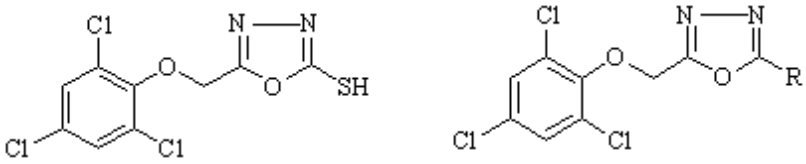
Mechanism of action

NSAIDs inhibit the Cyclooxygenases, the enzyme that catalyses the synthesis of cyclic endopeoxidases from the arachidonic acid to form Prostaglandins (PG). The two COX isoenzymes are COX-1 and COX-2. COX-2 is responsible for the production of PG's at inflammation site. Selective COX-2 inhibitors may eliminate the side effects associated with NSAIDs due to COX-1 inhibition such as gastric and renal effect.

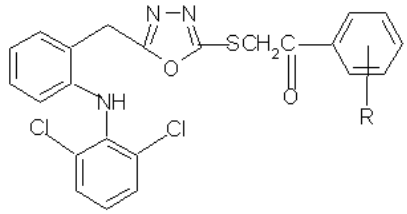
NSAIDS (Non steroidal anti-inflammatory drugs) are widely used for the treatment of pain, fever and inflammation particularly arthritis. NSAIDS reduce the inflammation and pain associated with arthritis by blocking metabolism of archidonic acid by the enzyme cyclooxygenase (COX) and thereby the production of prostaglandins on chronis use of

NSAIDS one of the prominent side effect is formation of gastric ulcers. This adverse effect may be attenuated in the presence of an inhibitor of 5-lipoxygenase (5-LOX). 1,3,4-oxadiazoles found to posses anti-inflammatory properties by virtue of dual mechanism, *i.e.*, inhibit both COX and LOX reducing the gastric ulcer formation.

Amir *et al*[37] synthesized some 1,3,4-oxadiazole derivative possessing potent anti-inflammatory action. Compounds R= 2,4-dichlorophenyl and R= 1-(4-isobutylphenyl) ethyl show good anti-inflammatory action. These above groups when replaced by 4-aminophenyl or 4-nitrophenyl, it minimized activity. In case ulcerogenic activity, compound with R= 2-acetoxyphenyl shows maximum activity.

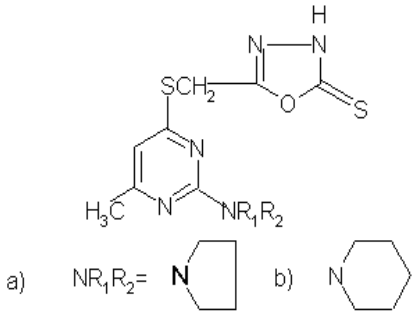


Bhandari *et al*[38] reported novel S-substituted phenyl-1,3,4-oxadiazol-2-thiol and Schiff bases of diclofenac and evaluated for anti-inflammatory, analgesic and ulcerogenic activity.

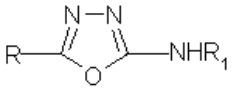


Whereas, R is methyl, methoxy or haloalkane.

Burbuliene *et al*[39] synthesized 5-{(2-disubstitutedamino-6-methyl-pyrimidin-4-yl)-sulfanylmethyl-3*H*-1,3,4-oxadiazol-2-thiones and tested these compounds as anti-inflammatory agents by using carrageenan-induced paw oedema method at concentration of 1 mg/ kg using standard drug Ibuprofen.

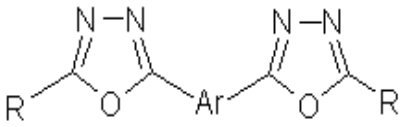


Mahfouz *et al*[40] reported same series of substituted 1,3,4-oxadiazole derivatives and screened them for anti-inflammatory activity by using carrageenan-induced paw oedema method.



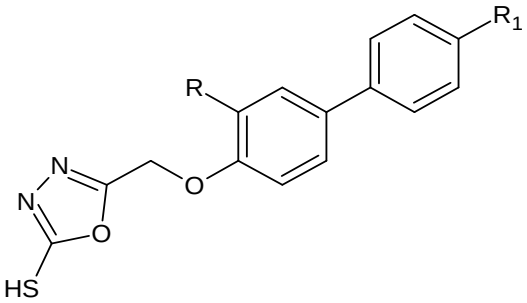
R= Pyridyl, R=Phenyl

Wang *et al*[41] reported synthesis of substituted 1,3,4-oxadiazoles under microwave irradiation and screened for anti-inflammatory, anticancer and antifungal activity.



Ar= Pyridyl & R= Substuent Phenyl

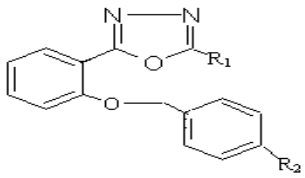
Sudha *et al*[42] synthesized 5-(4-aroyl)-aryl oxy methyl-2-thio-1,3,4-oxadiazole and screened for their anti-inflammatory was measured using the carageenan-induced paw oedema method at concentration of 1 mg/ kg by using standard drug Ibuprofen.



Whereas, R and R_1 are alkyl groups

Anticonvulsant Activity

Zarghi *et al*[43] designed and synthesized a series of new 2-substituted-5-(2-benzylthiophenyl)-1,3,4-oxadiazoles and 2-substituted-5-[2-(2-halo-benzyloxy) phenyl]-1,3,4-oxadiazole tested them for possible anticonvulsant activity. Most of synthesized compounds posses anticonvulsant activity.



R_1 is any substituted phenyl groups and R_2 is any aliphatic group.

Antiviral Activity

Zareef *et al*[44] synthesized new benzenesulfonamides bearing the 2,5-disubstituted-1,3,4-oxadiazole moiety and screened for anti-HIV and antifungal activity.

CONCLUSION

Above mentioned research work confirms the potential of 1,3,4-oxadiazole as lead for development of novel and better compounds possessing excellent biological activities. In conclusion, with proper designing and structure activity relationship studies of compounds having 1,3,4-oxadiazole nucleus, prospective compounds can be synthesized for a particular biological activity. The complete exploitation of oxadiazole lead may be expected from scientific community, to discover the safe, potent drug candidates with lesser side effects.

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