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RECENT ADVANCES IN THE APPLICATION OF OXADIAZOLES IN MULTICOMPONENT REACTIONS FROM 2015-16: A REVIEW

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Abstract:

1,3,4-Oxadiazole is a thermally stable and neutral Heteroaromatic molecule having a wide variety of uses, particularly as biologically active compounds in medicine, agriculture, dye stuffs, UV absorbing and fluorescent materials, heat resistant polymers and scintillators. Oxadiazoles and their analogues can be considered as simple five membered heterocycles possessing one oxygen and two nitrogen atoms[1-5]. The oxadiazole exists in different isomeric forms such as 1,3,4- oxadiazole, 1,2,5-oxadiazole, 1,2,4-oxadiazole, and 1,2,3-oxadiazole, out of which 1,3,4-Oxadiazole is a thermally stable neutral aromatic molecule and its estimated resonance energy is 167.4 kJ/mol. particularly, aryl group at position 2 increases the thermal stability of 1,3,4-oxadiazole. The ring is stable to heat, a property which has been exploited in the production of heat-resistant poly-1,3,4-oxadiazoles[6-11]. UV spectra of substituted 1,3,4-oxadiazoles are similar to those of substituted benzenes, particularly in the case of 2-phenyl-1,3,4-oxadiazoles (λmax in ethanol = 247.5 nm, log ε 4.26).

Key words: ***1,3,4-oxadiazole, Polymers and Heteroaromatic molecule.***

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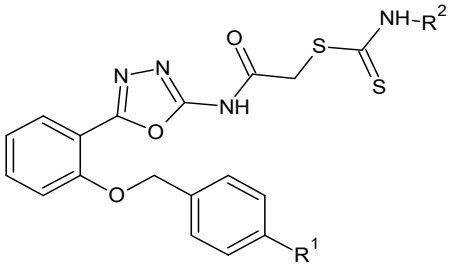
INTRODUCTION:

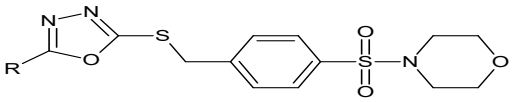
Basic information Oxadiazole is a heterocyclic nucleus, which gains heavy interest by many research scholars regarding invention of novel remedial molecules. There are possibly four isomers of oxadiazole in which 1,3,4-oxadiazole have enormous importance. Variety of therapeutically active agents e.g. raltagravir as HIV-integrase inhibitor, furamizole as nitrofuran anti-bacterial, nesapidil as antihypertensive agents, anti-microbial, anticancer activity, etc. are based on 1,3,4-oxadiazole moiety [12-19]. The 1,3,4-oxadiazole exhibit variety of reactions such as Studies of 1,3,4-oxadiazole derivatives, electrophilic substitution, nucleophilic substitution, thermal and photochemical reactions. Structural parameters of 1,3,4-oxadiazole 1,3,4-Oxadiazole is an aromatic molecule with resonance energy 167.4 kJ/mol. 1,3,4-oxadiazole ring is symmetrical and planar. We know oxadiazole consists of the two pyridine type nitrogen (-N=) hence, reduction in aromaticity of oxadiazole ring, which in turn leads the oxadiazole ring to exhibit the conjugated diene character. There is no or very less scope of electroplilic substitutions at the carbon atom in oxadiazole ring due to less electron density on the same carbon atom. Rather, electroplilic attack can occurs at nitrogen, but again there must be association of electron-releasing groups in oxadiazole ring, whereas for nucleophilic substitution like in halogen substituted oxadiazole there is replacement of halogen atom by nucleophiles [20,21].

DIFFERENT METHODS OF REACTIONS

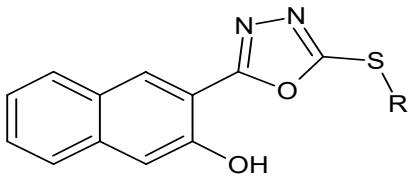
Rajak H. et al [22] (2015) reported antimicrobial potential of some novel n-aryl dithio carbamate based 1,3,4-oxadiazoles, The synthesized compounds were tested for their *in-vitro* antimicrobial activity against the Gram-positive bacteria *Staphylococcus aureus* (MTCC-96) and *Bacillus subtilis* (MTCC-619), the Gram negative bacteria *Proteus mirabilis* (MTCC-425) and *Pseudomonas aeruginosa* (MTCC-424), the fungal strain *Aspergillus niger* (MTCC-1344) and the yeast like pathogenic fungus *Candida albicans* (MTCC-227) using disk diffusion method.7-8 Norfloxacin and Clotrimazole were used as standard drug for antibacterial and antifungal studies, All the compounds exhibited significant antibacterial and moderate antifungal activities. Out of all the fourteen compounds evaluated for antimicrobial studies, compound showed significant antibacterial activity against all six microbial strains used.



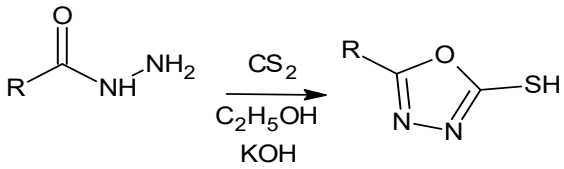
Aziz-ur-Rehman et a [23][3] (2015) reported synthesis and evaluation of some new 5-substituted-1,3,4-Oxadiazol-2yl-4-(morpholin-4yl sulfonyl)benzyl Sulfides as antibacterial agent, synthesized compounds biologically evaluated with antibacterial activity. One of the compounds inhibited the growth of four Gram negative (*S. typhi, E. coli, K. pneumoniae, P. aeruginosa*) and two Gram positive (*B. subtilis and S. aureus*) bacterial strains. Thus, the compounds are potential lead molecules in the search for potent agents for the treatment of bacterial infections.



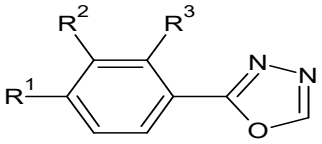
Shital A et al [24] (2015) reported microwave assisted synthesis, characterization and biological evaluation of novel 1,3,4-oxadiazole derivatives, The synthesized compounds shows good antimicrobial activity and good anti-inflammatory activity.



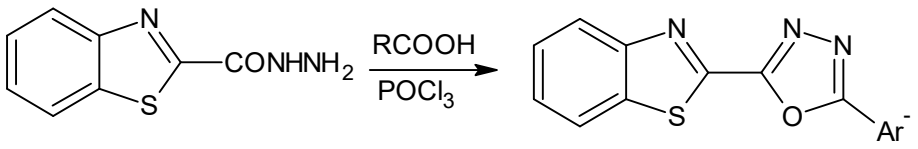
Gollapalli Naga Raju et al [25] (2015) reported synthesis, characterization and biological activity of some 1,3,4-oxadiazole derivatives with benzothiazole moiety, The synthesized compounds shows good antimicrobial activity.



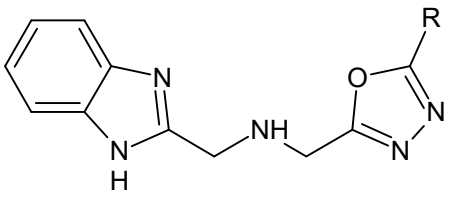
Ali Souldozi et al [26] (2015) reported one-pot synthesis of 2-aryl-1,3,4-oxadiazole derivatives as potential antibacterial agents, All the compounds have been screened for antibacterial activity against *Escherichia coli, Pseudomonas aeruginosa, Staphylococcus aureus, Listeria mono cytogenes* and antimycobacterial activity against *Mycobacterium smegmatis* by the broth dilution and well agar diffusion methods. The results revealed that compounds 5a and 5b have antibacterial activity against *E.coli* and compounds 5e and 5d showed anti-mycobacterial activity.



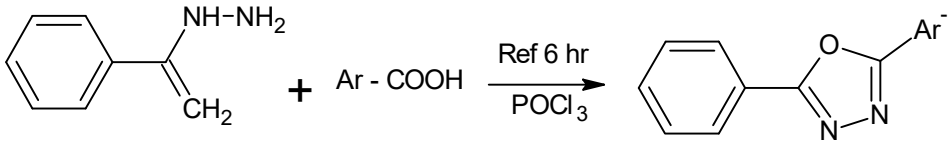
Kumar et al [27] (2015) reported synthesis and invivo anti-inflammatory and analgesic activities of oxadiazoles clubbed with benzothiazole nucleus, all the synthesized Compounds were assessed for their in*vivo* anti-inflammatory activity by the carrageen induced rat paw edema method. The compounds were assessed at an oral dose 200 mg/kg and differentiate with the standard drug Diclofenac Sodium. All the compounds showed good anti-inflammatory activities. All compounds were assessed at 10 mg/kg dose as a standard drug Pentazocin. Examination of the results showed that the compound having 1, 3-benzothiazole-2-carboxyhydrazide substitution at the 5th position of oxadiazole ring display outstanding analgesic activity.



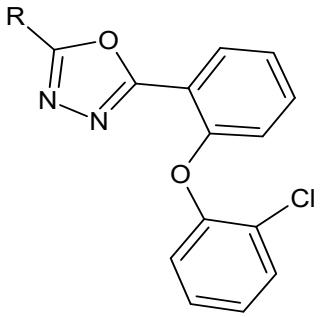
B. Vishwanathan et al [28] (2015) reported invitro antioxidant and invivo anti-inflammatory activity of 1,3,4-oxadiazole derivatives, all the synthesized compounds of the 1,3,4-oxadiazoles derivatives are biological evaluation for invitro antioxidant property and invivo anti-inflammatory efficacy have produced promising results. The result of invitro antioxidant activity correlates the importance of antioxidant property with respect to edema inhibition as seen in case of anti-inflammatory screening. The invivo anti-inflammatory activity was evaluated by carrageenan induced paw edema method at a dose of 25 mg kg-1 and the results were encouraging. The anti-inflammatory activity data indicated that the 1,3,4-oxadizole derivatives could be considered as possible hit as therapeutic agents.



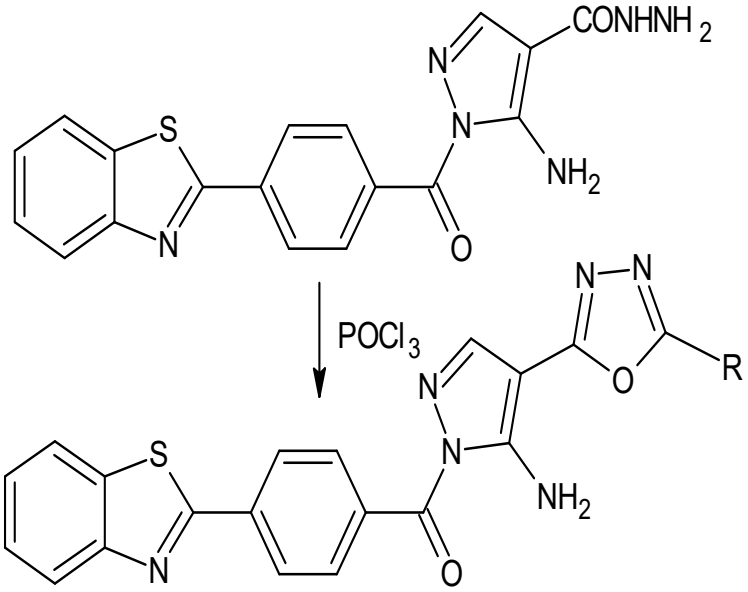
D. Bharathi et al [29] (2015) reported synthesis, characterization and biological evaluation of 2,5-disubstituted 1,3,4-oxadiazole derivative. The 2,5-disubstituted 1,3,4-Oxadiazole containing hydroxyl, chloro, amino groups possess significant anti-inflammatory activity and the compound containing methyl group possess significant anthelmintic activity.



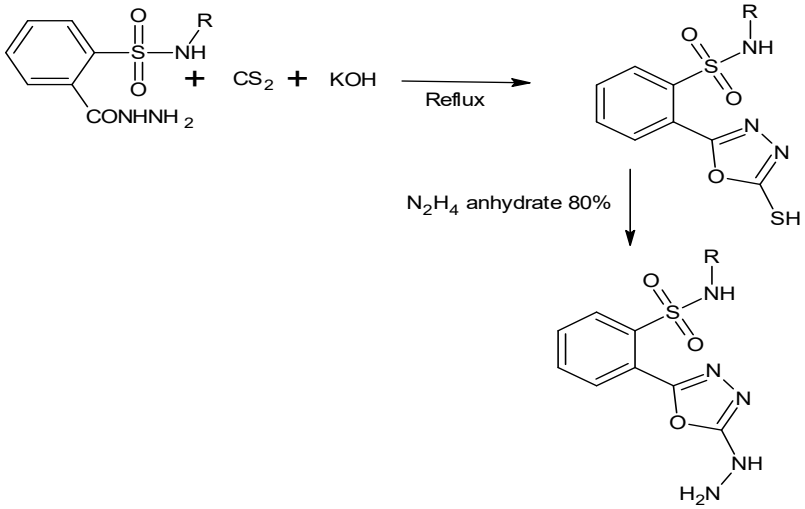
Tabatabai A et al [30] (2015) reported evaluation of anxiolytic, sedative-hypnotic and amnesic effects of novel 2-phenoxy phenyl-1,3,4-oxadizole derivatives using experimental models, Results of righting reflex test clearly indicated that the compounds with NH_2, SH, or SCH_3 groups on 2-position of 1,3,4-oxadiazole ring have shown considerable hypnotic effect. However, their potencies were less than diazepam and there was no significant difference among those of the three compounds. It means the compounds with NH_2, SCH_3, or SH groups have similar hypnotic effects and compound with OH group on 2-position of the heterocyclic ring did not show hypnotic effect.



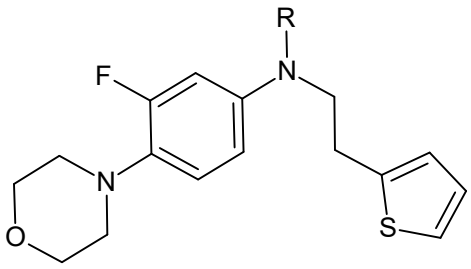
Eman AM et al [31] (2015) reported anticancer evaluation of some newly synthesized oxadiazol-2-yl-pyrazole derivatives attached to 4-benzothiazol-2-yl moiety, all of the newly synthesized compounds have been evaluated for their potential cytotoxicity against breast cancer cell line, and compounds are more potent than Tamoxifen a standard drug.



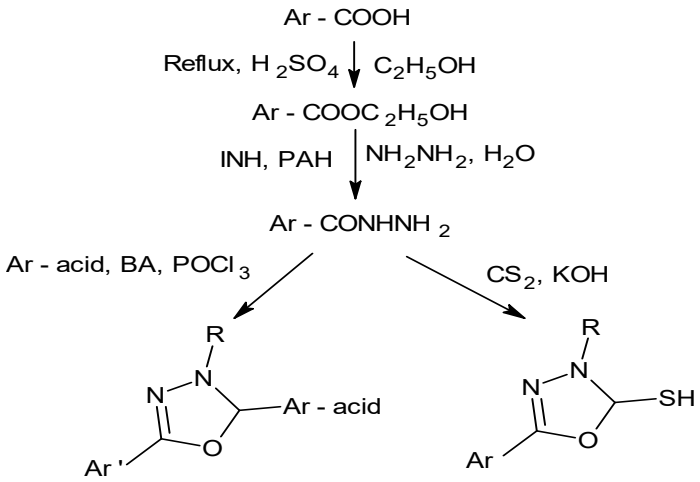
Ahmed Wahed Naser et al [32] (2015) reported synthesis of some new sulfonamide derivatives based on 1,3,4-oxadiazole, reported the good evidence for the formation of the aza-β-lactam derivatives.



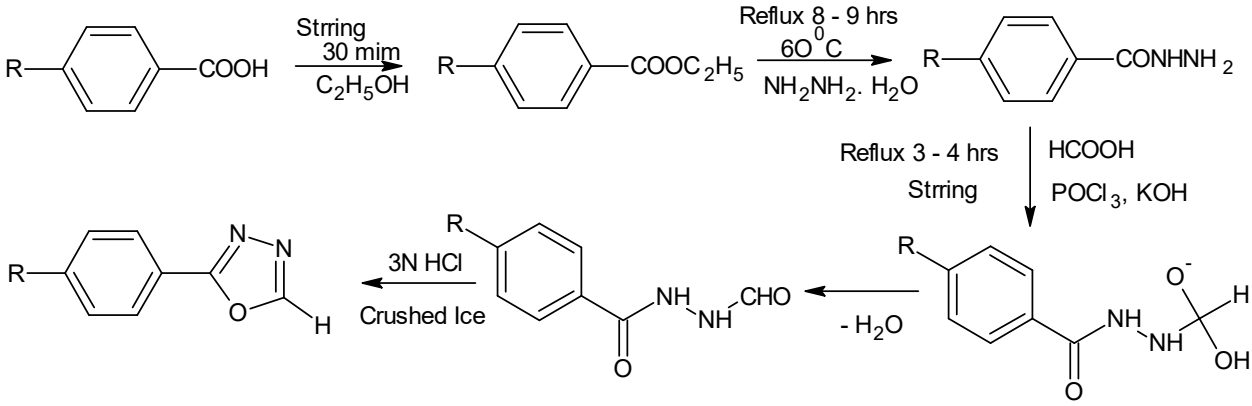
Loganathan et al [33] (2015) reported synthesis, characterization and biological evaluation of 3-fluoro-4-(morpholin-4-yl)-n-[2-(thiophene-2-yl) ethyl] aniline derivatives, the synthesized compounds were then examined for their antibacterial and antifungal activities. Some of them were found to possess good activity.



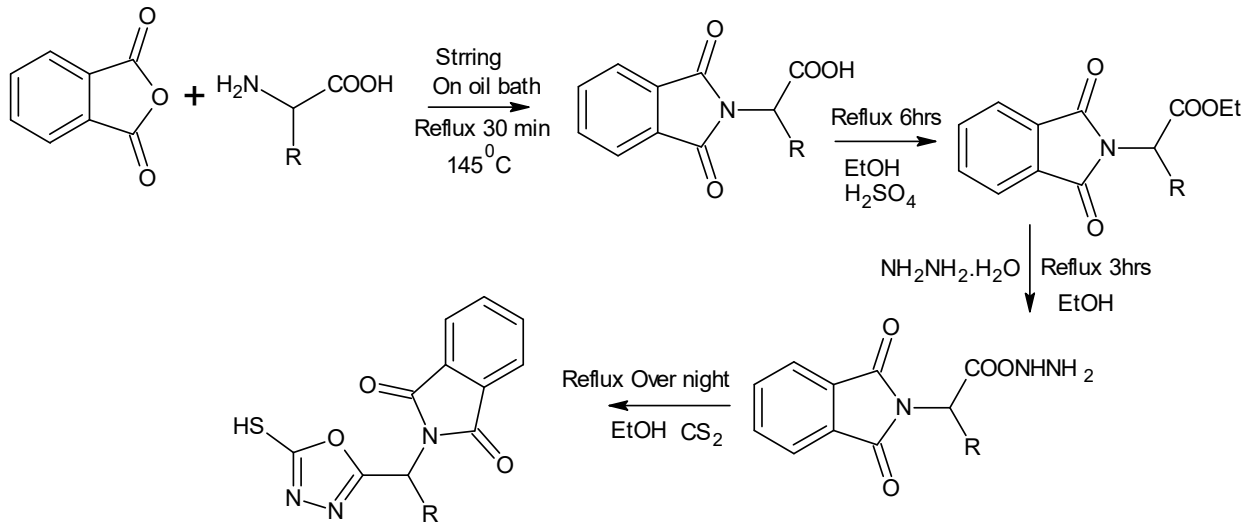
Annasaheb B. Jagnar et al [34] (2016) reported Design, synthesis and evaluation of some novel pyrazolidine-3-one, aryl oxadiazole and mercapto oxadiazole derivatives of biological interest. The present work synthesized of derivatives of pyrazolidine-3-one, aryl oxadiazole and mercapto oxadiazole and screened for antimicrobial, antitubercular, anti-inflammatory and antioxidant activities with the standard drugs.



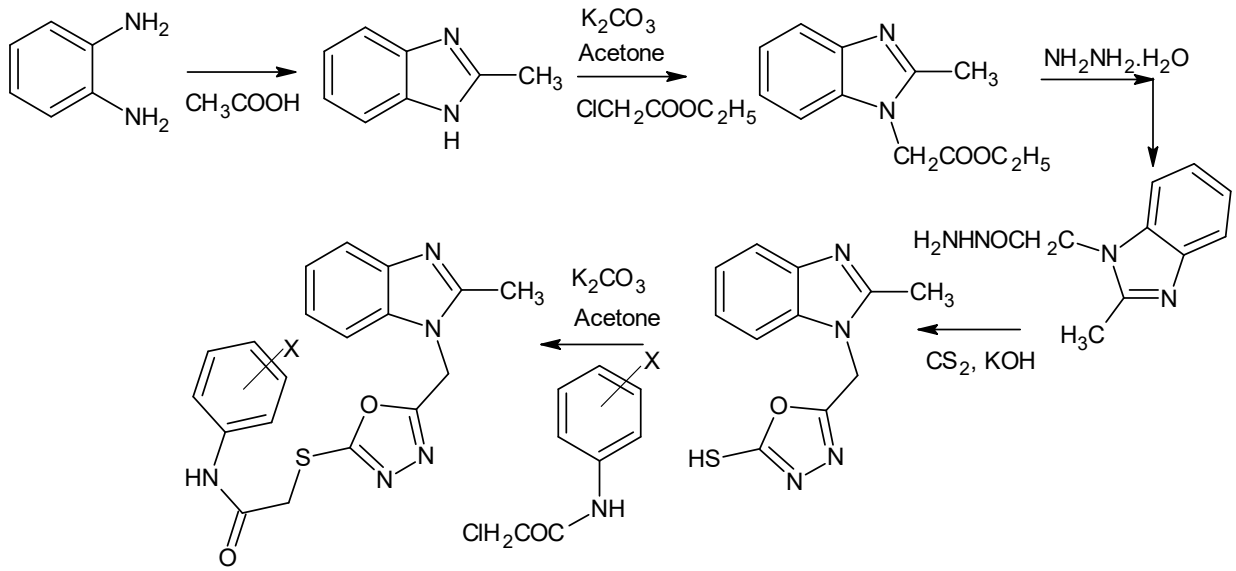
Pagare et al [35] (2016) reported Synthesis and Antimicrobial Evaluation of newer 1,3,4-Oxadiazole Derivatives containing R-phenyl moiety under Conventional conditions. The synthesized compounds showed excellent antimicrobial activity against various tested microorganisms.



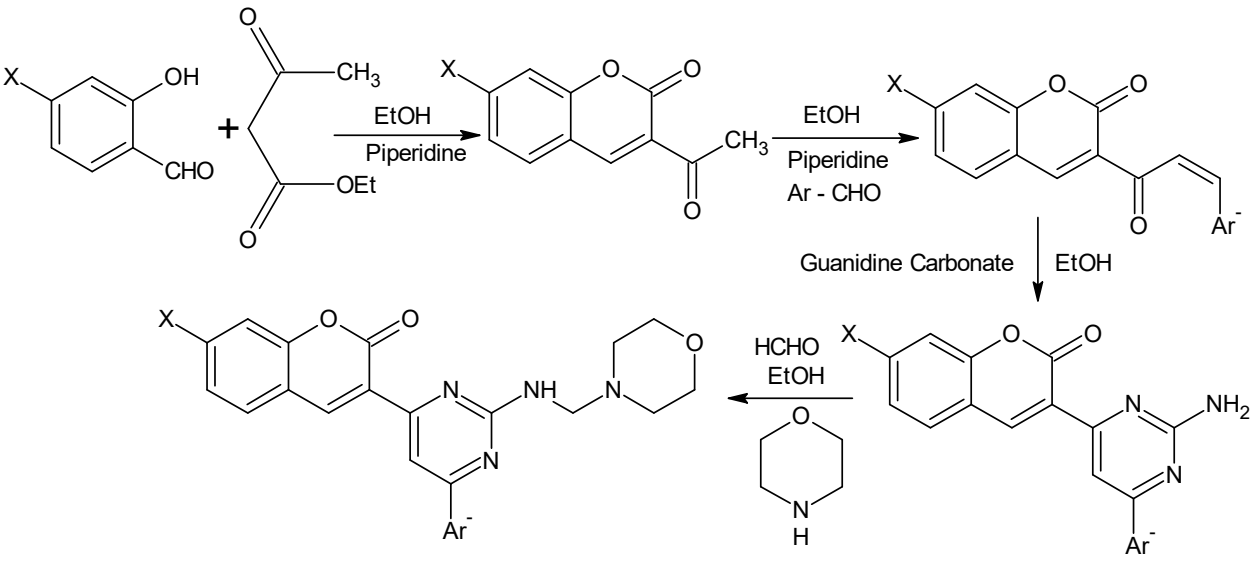
Siddiqui Roohi et al [36] (2016) reported Synthesis of some novel 1,3,4-oxadiazole. The synthesized compounds identified by FTIR and purified.



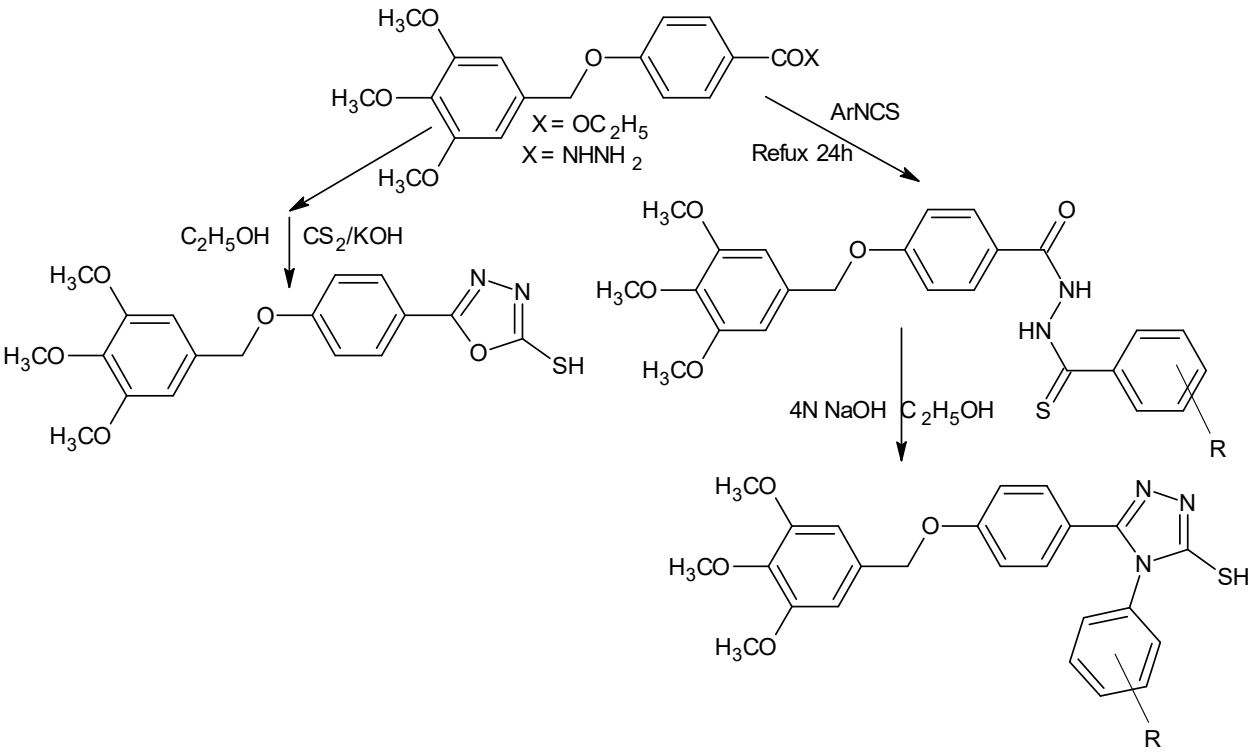
Ha Bui Manh et al [37] (2016) reported Synthesis and antibacterial activity of some derivatives of 2 methylbenzimidazole containing 1,3,4-oxadiazole or 1,2,4-triazole heterocycle. The compounds containing 1,3,4-oxadiazole or 1,2,4-triazole heterocycle has been tested for their antimicrobial activity against bacteria, mold, and yeast.



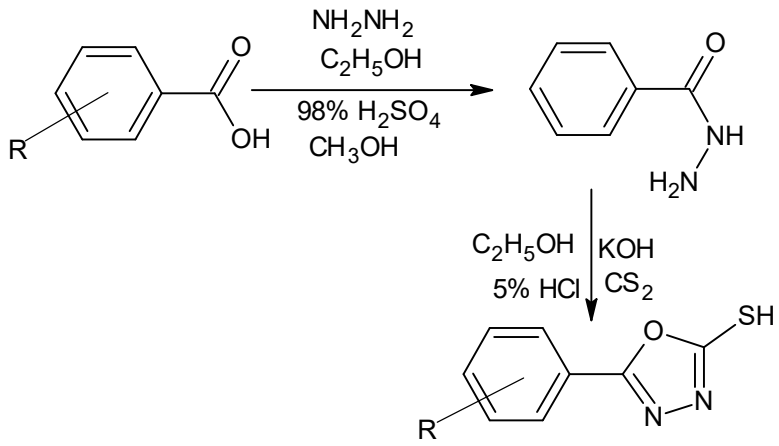
Imran et al [38] (2016) reported Synthesis and evaluation of antimicrobial activity of some 2-morpholinomethylamino-4-(7-unsubstituted/substituted-coumarin-3-yl)-6 chloro substituted phenyl pyrimidines. The synthesized compounds are relatively active antifungal agents but are weak antibacterial agents.



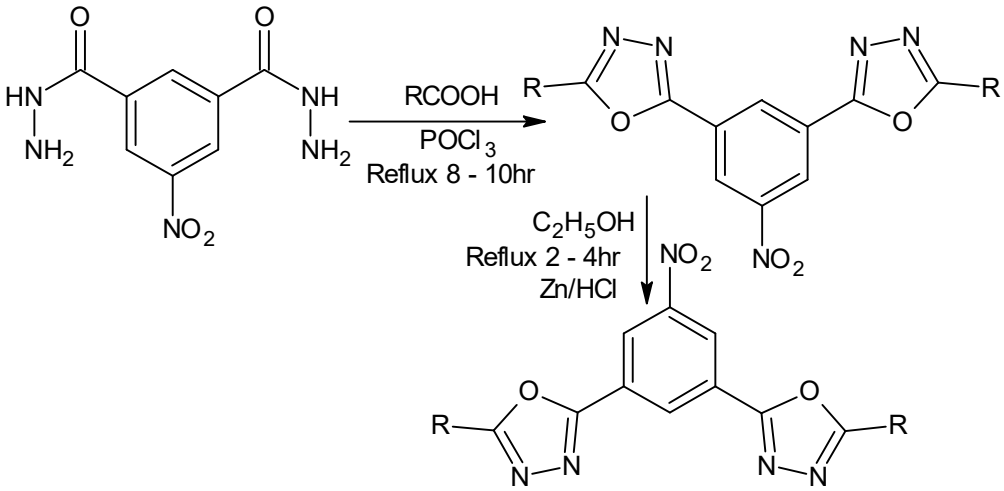
Huda S et al [39] (2016) were reported the thiosemicarbazide derivatives were highly active in both antioxidant assays with the lowest IC50 value for DPPH radical scavenging. Theoretical calculations based on density functional theory (DFT) were performed to understand the relative importance of NH, SH and CH hydrogens on the radical scavenging activities of these compounds.



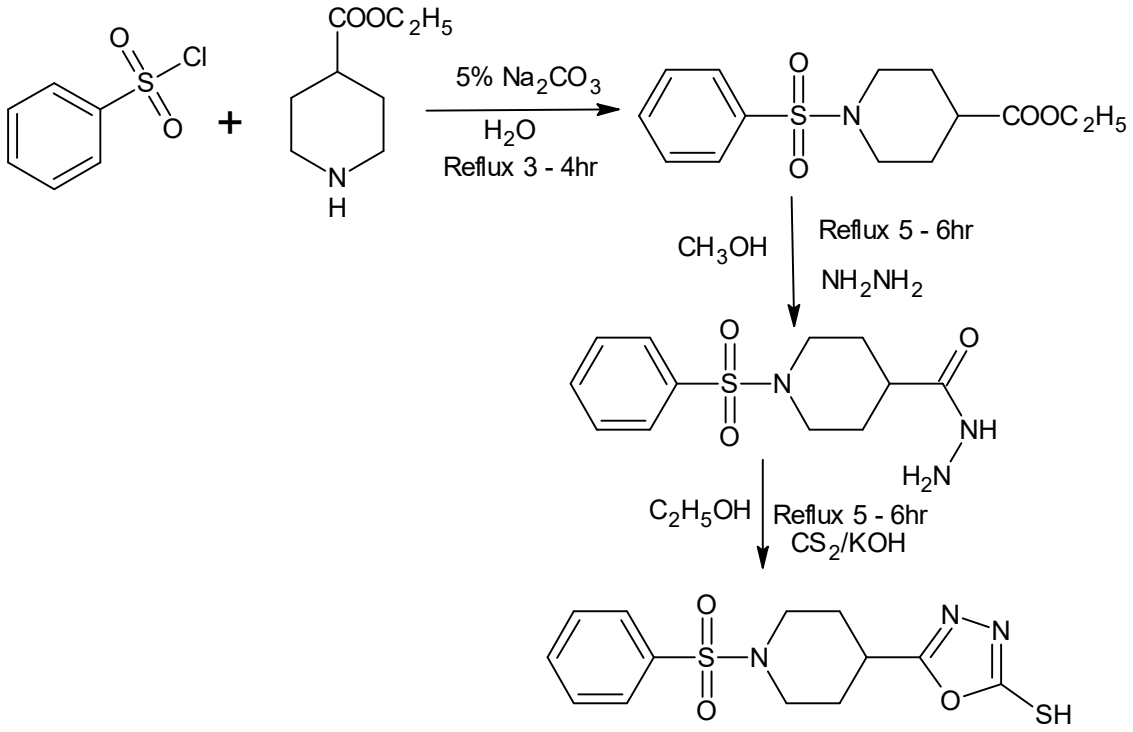
Wang PY et al [40] (2016) were reported a variety of 1-aryl-4-hydroxy-1H-pyrrol-2(5H)-one derivatives bearing 1,3,4-oxadiazole moiety were designed and synthesized. Preliminary bioassays suggested that these compounds not only exhibited favorable antibacterial activity toward plant pathogenic bacteria including Xanthomonas oryzae pv. Oryzae (Xoo), Ralstonia solanacearum (R. solanacearum), and Xanthomonas axonopodis pv. Citri. (Xac), but also demonstrated certain curative and protective activities against Tobacco mosaic virus (TMV).



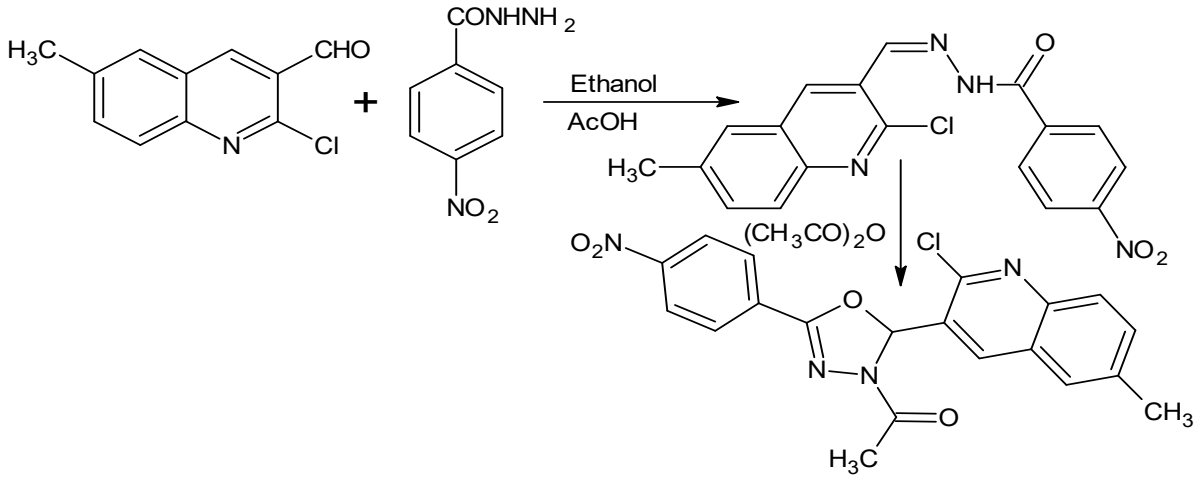
Shridhar AH et al [41] (2016) were reported the synthesized compounds were screened for their antimicrobial and in vitro antioxidant properties. The results of this investigation revealed that the newly synthesized compounds were potent antibacterial and antioxidant agents. All the synthesized compounds exhibit significant biological activity and certainly hold a greater promise for discovering potent biologically active molecules.



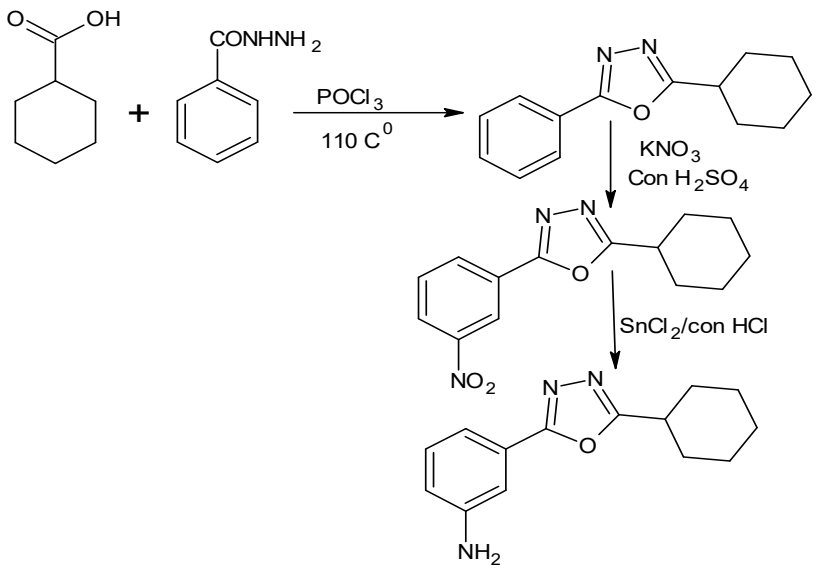
Khalid H et al [42] (2016) were reported the synthesized compounds were screened against Gram-negative and Gram-positive bacteria and exhibited moderate to talented activity.



Desai NC et al [43] (2016) were reported newly synthesized 1,3,4-oxadiazole derivatives screened for vitro antimicrobial activity on different strains of bacteria and fungi. Compound 4h showed the highest activity.



Kavithav S et al [44] (2016) were reported and screened for their antidiabetic, anti-inflammatory and anticancer activities.



CONCLUSION:

The present review highlights that the 1,3,4-oxadiazole moiety as a template for the development of newer therapeutic agents. Modified 1,3,4-oxadiazole moiety displayed the various synthetic methods and valuable biological activities.

ACKNOWLEDGMENTS:

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