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A Mini Review on Biological Activities and synthetic approaches for 1,3,4-Oxadiazoles

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Abstract:
This mini-review presents a summary of literature survey on the synthetic approaches for the preparation of 1,3,4-oxadiazoles and their derivatives. Further, various biological activities of these derivatives were also summarized.

Keywords: 1,3,4-Oxadiazoles, synthesis, biological activity

Introduction:

Oxadiazole is a heterocyclic aromatic compound consisting of 2 nitrogen atoms, 2 carbon atoms, and 1 oxygen atom with 2 double bonds in a five membered ring. It consists of four possible isomers (Figure 1), namely 1,2,3-, 1,2,4-, 1,2,5- and 1,3,4-oxadiazoles. They are one of the most valuable pharmacological, pesticide and polymeric products in heterocyclic chemistry.[1-3]

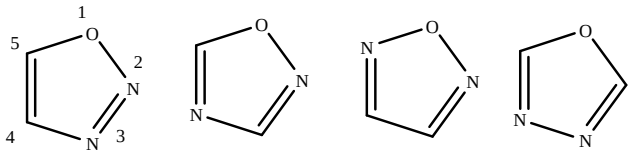


Figure 1

The 1,3,4-oxadiazole derivatives may act as ester and amide bioisosteres and hence are of interest in pharmaceutical, agrochemical, organic light-emitting diodes (OLEDs) fields.[4-5] Owing to possessing conjugate diene type character, electrophilic substitution at carbon is very difficult. Among four isomers, 1,3,4-oxadiazole isomer shows lower magnitude lipophilicity. This moiety is susceptible for electrophilic, nucleophilic, thermal and photochemical reactions.[6]

Biological significance of 1, 3, 4-Oxadiazoles

Several 1,3,4-oxadiazoles are found to have characteristic drug activity in related studies, makes the medicinal chemists concentrate on the preparation and pharmacological evolution of novel 1,3,4-oxadiazole derivatives.

The following are a few examples of the 1,3,4-oxadiazole derivatives consists of biological significance.

Anti-inflammatory activity

Jayashankar *et al*[7] reported the preparation and biological evaluation of 1,3,4-oxadiazole bearing bis(heterocycle) analogues as anti-inflammatory and analgesic agents (Figure 2).

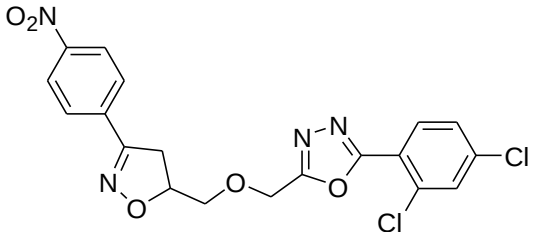


Figure 2

Antimicrobial activity

Farshori *et al*[8] developed and synthesized oxadiazoles and thiadiazoles, were screened for antibacterial and antifungal activities (Figure 3).

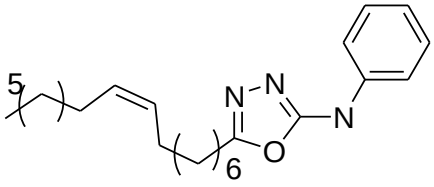


Figure 3

Anti-Fungal activity

Some novel 2,5-disubstituted 1,3,4-oxadiazoles were evaluated for their *in-vitro* antifungal activity by Sangshetti *et al*[9] (Figure 4).

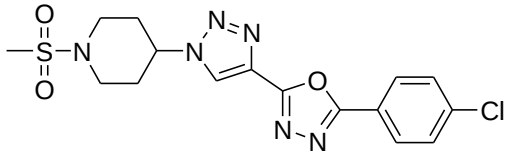


Figure 4

Anti-Bacterial activity

Chandrakantha *et al*[10] developed a series of new 1,3,4-oxadiazole derivatives containing 2-fluoro-4-methoxy moiety and evaluated for their antimicrobial studies (Figure 5).

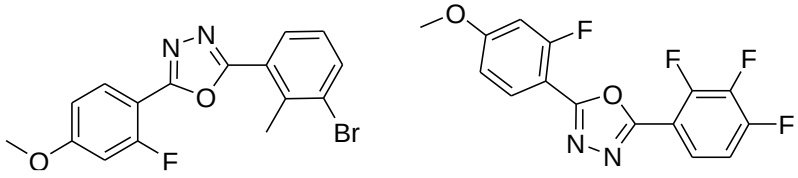


Figure 5

Antioxidant activity

Musad *et al*[11] described the synthesis and evaluation of antioxidant and antibacterial activities of 4-[5-[[5-[4-(dimethylamino)phenyl]-1,3,4-oxadiazol-2-yl]methyl]-1,3,4-oxadiazol-2-yl]-N,N-dimethyl-aniline (Figure 6) has shown moderate antioxidant and antibacterial activity.

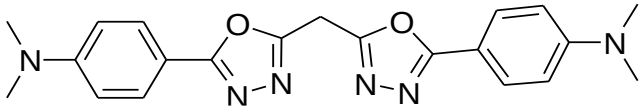


Figure 6

Antitumor activity

Rajak *et al*[12] developed a series of novel 2, 5-disubstituted-1,3,4-oxadiazoles/ thiadiazole as surface recognition moiety and screened for the antiproliferative activities.2-[[5-(4-chlorophenyl)-1,3,4-oxadiazol-2-yl]amino]pyrimidine-5-carbohydroxamic acid (Figure 7) is found to have the best antitumor activity against Ehrlich ascites carcinoma.

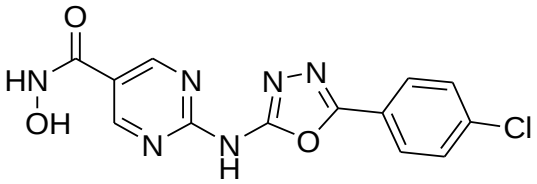


Figure 7

Anticonvulsant activity

Rajak *et al*[13] identified that 4-[5-[[(E)-[(5R)-5-isopropenyl-2-methyl-cyclohex-2-en-1-ylidene] amino] carbalmoylamino]-1,3,4-oxadiazol-2-yl]phenyl] azinicacid (Figure 9) has shown remarkable anticonvulsant activity.

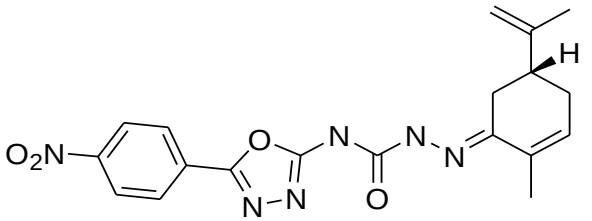


Figure 8

Anti-Hepatitis-B Virus activity

Tan *et al*[14] discovered the synthesis and the biological evaluation of 2-benzene sulfonyl alkyl-5-substituted-sulfanyl-[1,3,4]-oxadiazoles as potential anti-hepatitis B virus agents (Figure 9).

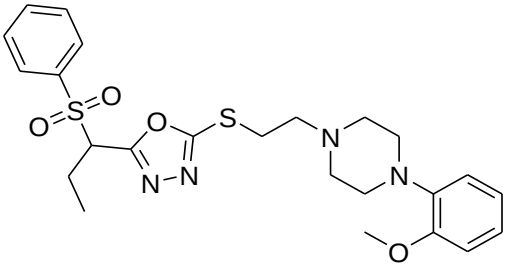


Figure 9

Cytotoxic activity

Gurupadaswamy *et al*[15] synthesized a series of 2,5-di (4-aryloylaryloxy-methyl)-1,3,4-oxadiazoles which were screened for the cytotoxicity (Figure 10).

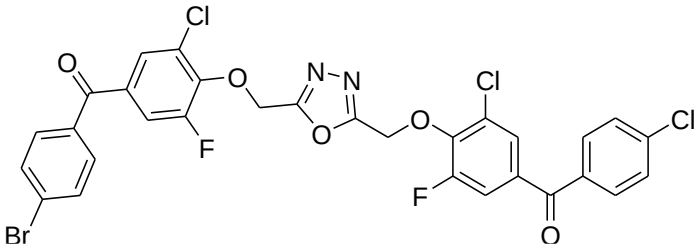
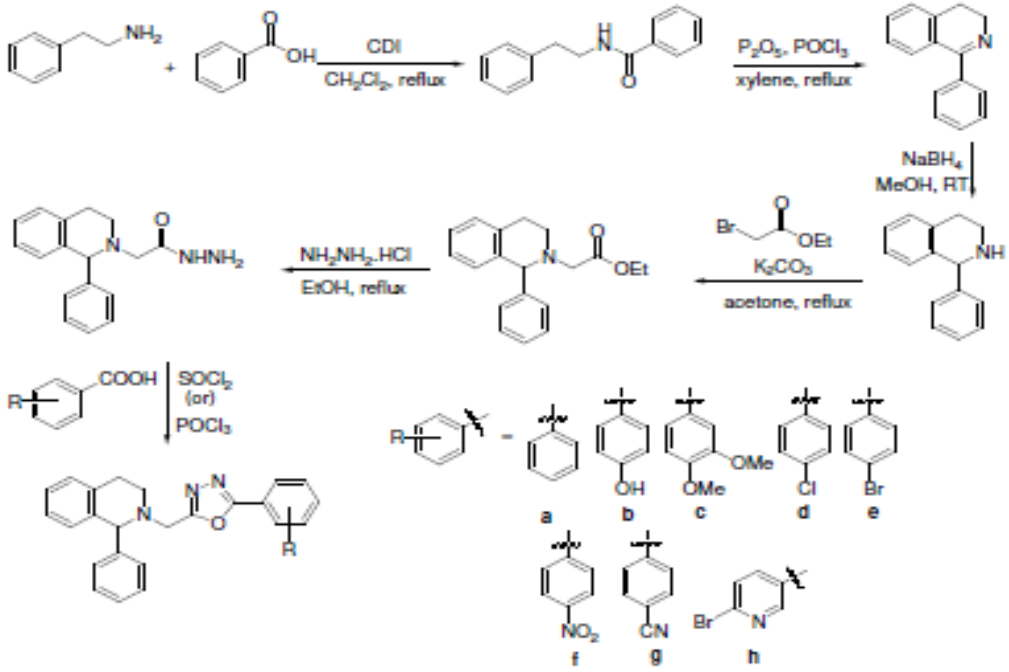


Figure 10

Existing synthetic approaches

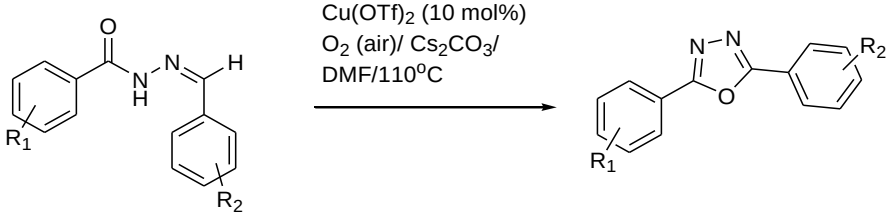
The synthesis of 1,3,4-oxadiazoles using various Lewis, bronsted catalysts, ionic liquids, acidic reagents has been performed. The following are the recent developments for the synthesis of 1,3,4- oxadiazoles over the recent years have been briefly discussed below

Surendra Babu *et al*[16] reported the preparation and characterization of 1,3,4-oxadiazoles derivatives from 1,2,3,4-tetrahydroisoquinoline and evaluated successfully for their antibacterial & antifungal activities (Scheme 1).



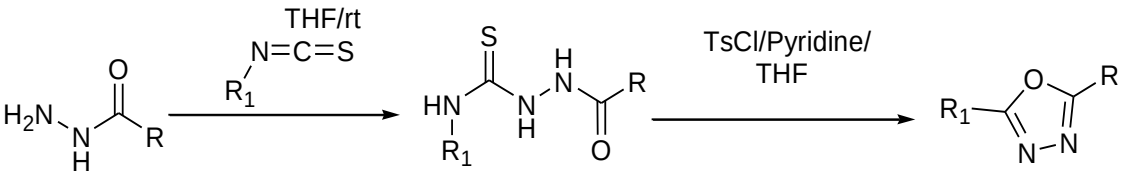
Scheme 1

Guin *et al*[17] developed Cu (II) catalyzed imine C-H functionalization leading to the synthesis of 2,5-substituted-1,3,4-oxadiazoles as shown in Scheme 2.



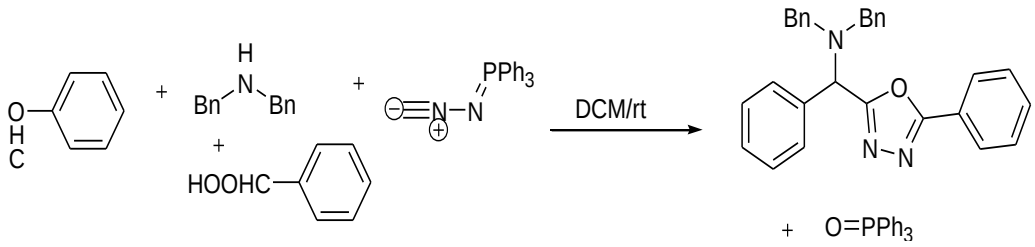
Scheme 2

Superior reactivity of thiosemicarbazides in the synthesis of 2-amino-1,3,4-oxadiazoles has been described by Dolman *et al*[18] using thiosemicarbazides (Scheme 3).



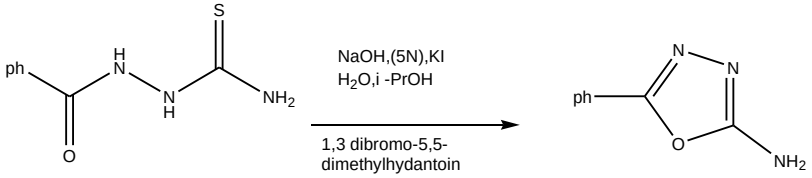
Scheme 3

As shown in Scheme 4, Ramazani *et al*[19] developed a new one-pot and efficient method for the synthesis of the 2,5-disubstituted 1,3,4-oxadiazole .



Scheme 4

Rivera *et al*[20] reported that 1,3-dibromo-5,5-dimethylhydantoin is an effective oxidizing agent for cyclization reactions of acylthiosemicarbazide (Scheme 5).

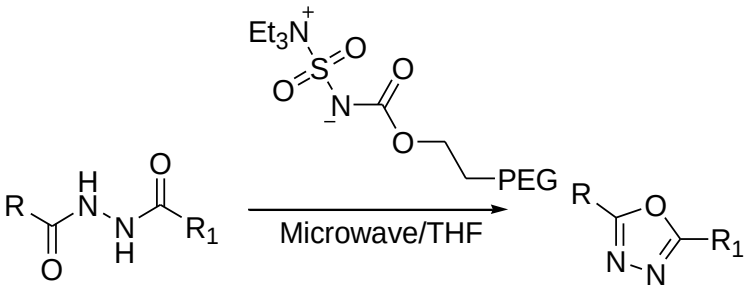


Scheme 5

Stabilea *et al*[21] described a mild and convenient one-pot synthesis of 2-phenyl-5-substituted-1,3,4-oxadiazoles (Scheme 6).

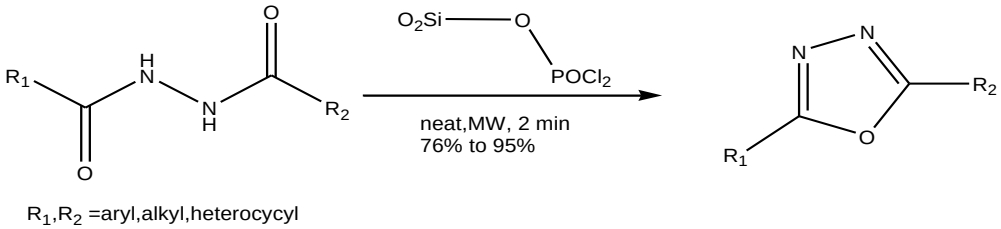
Scheme 6

Brain *et al*[22] described a novel procedure for the synthesis of 1,3,4-oxadiazoles from 1,2-diacylhydrazines using polymer-supported Burgess reagent under microwave conditions in combination with single-mode microwave heating with considerable yields (Scheme 7).



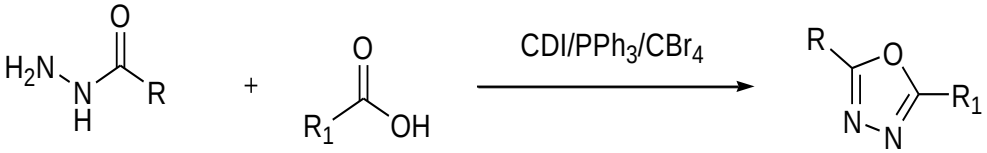
Scheme 7

Li and Dickson [23] developed a convenient one-pot protocol for the synthesis of 1,3,4-oxadiazoles from carboxylic acids and hydrazides as described in Scheme 8.



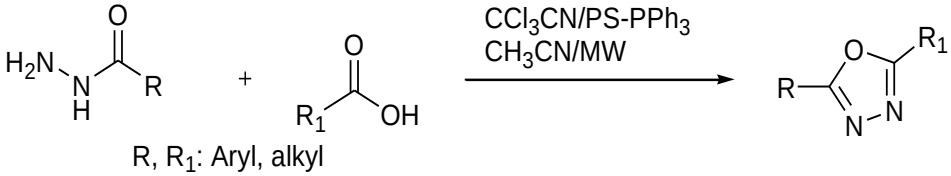
Scheme 8

Rajapakse *et al*[24] described a mild and efficient one pot synthesis of 1,3,4-oxadiazoles from carboxylic acids and acyl hydrazides (Scheme 9).



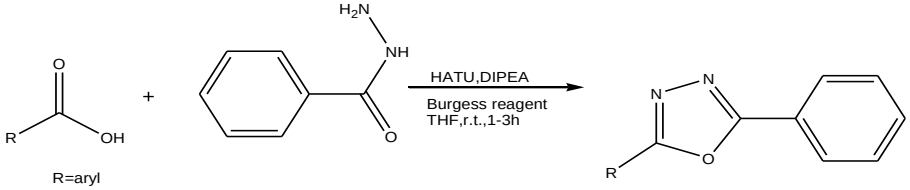
Scheme 9

Wang *et al*[25] described a very productive one step synthesis of 1,3,4-oxadiazoles utilizing polymer supported reagents and microwave heating from a variety of carboxylic acids and acid hydrazides in one simple step (Scheme 10).



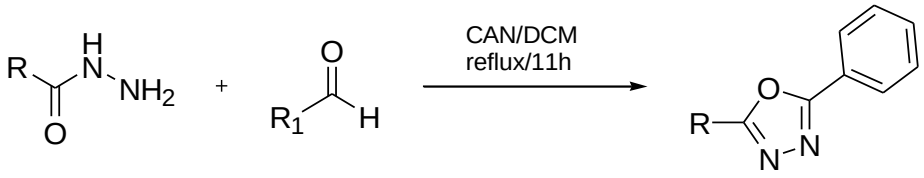
Scheme 10

Li *et al*[26] reported that silica-supported dichlorophosphate is an efficient cyclodehydration agent for the synthesis of 2,5-disubstituted 1,3,4-oxadiazoles from 1,2-diacylhydrazines in a solvent-free medium under microwave irradiation (Scheme 11).



Scheme 11

Dabiri *et al*[27] described a facile procedure for the one-pot synthesis of unsymmetrical 2,5-disubstituted 1,3,4-oxadiazoles from the cyclizationoxidation reaction of acyl hydrazones (Scheme 12).



Scheme 12

Conclusion:

In this mini-review, authors tried to outline the synthetic approaches and biological activities of 1,3,4-oxadiazoles upto 2018. Hope this will be a valuable addition in the field of synthetic as well as medicinal chemistry.

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