Wasit Journal for Pure Science

Journal Homepage: https://wjps.uowasit.edu.iq/index.php/wjps/index
e-ISSN: 2790-5241 p-ISSN: 2790-5233

A Review of Modern Methods of Synthesis 1, 3, 4-Oxadiazole as a Bioactive Compounds

Hajar Adeeb Salim [1], Shaimaa Abed Saoud [2]*

[1] Department of Chemistry, College of education for pure science Ibn Al-Haitham, University of baghdad, IRAQ
Hajar.adeeb2105m@ihcoedu.uobaghdad.edu..iq

[2] Department of Chemistry, College of education for pure science Ibn Al-Haitham, University of baghdad, IRAQ
*Corresponding Author: Shaimaa Abed Saoud

DOI: https://doi.org/10.31185/wjps.262
Received 10 October 2023; Accepted 01 December 2023; Available online 30 December 2023

ABSTRACT: Oxadiazole ring is a heterocyclic molecule with an oxygen and two nitrogen atoms spread throughout its five-membered structure. There are four different isomers that have been discovered, Because of their wide applications in a range of sectors, including medications. Some of these biological activities are; anticonvulsant capacity, anticancer as well, antibacterial, antiviral, antifungal, antimalarial, antitubercular, anti-asthmatic, antidepressant, antidiabetic, antioxidant, antiparkinsonian, analgesic and anti-inflammatory, are just some of the therapeutic uses that have drawn attention to drug candidates containing an oxadiazole moiety. This review, we will examine the various methods of oxadiazole synthesis. The molecular docking of some oxadiazole compounds has been studied to investigate the active derivatives and to evaluate their activity. The synthesis of the oxadiazole ring has sparked a lot of attention since then. A large number of oxadiazole derivatives, as well and methods, were reported New antimicrobial drugs have been developed from a number of different areas in recent years in an effort to reduce the prevalence of drug-resistant bacteria. Furthermore, this review touches upon the importance of structural modification in fine-tuning the biological activities of 1,3,4-oxadiazole derivatives. By altering the substituents and the position of functional groups, researchers can tailor the pharmacological properties to target specific diseases or conditions, making them highly versatile and attractive in drug discovery.

Keywords: 1,3,4-Oxadiazole, Molecular Docking, biological activities.

1. INTRODUCTION

The five-member ring heterocyclic's exhibited various biological activities and among them are the 1,3,4-oxadiazole. furthermore, The oxadiazole and their 2,5-disubstituted derivatives are good for development materials due their large spectrum of various biological activity like, anti-inflammatory[1], anticancer , antibacterial [2][3] Antifungal [4][5] antihypertensive activities[6] , antitubercular [7] anti-HIV[8] , antimitotic[9]. Insecticidal [10][11], Anesthetic Activity[12], Chronic rhinosinusitis [13]Molecular Docking [14]and antioxidant activities[15]moreover, bisoxadiazole compounds was reported as a biological active compounds [16] ,also it show some physical property like electrochemical properties[17], electro-optical properties [18] and Luminescence property[19]. Inhibition of breast cancer cell growth, photosensitization of TiO2nanoparticles, control of rice sheath blight and sorghum anthracnose, and inhibition of Xanthomonas oryzae pv. oryzae (Xoo) using an in vitro turbidimeter assay[20], anti-tubercular agent[21], nematocidal activities, nematocidal activities[22].

The 1,3,4-oxadiazole heterocyclic scaffold has emerged as a fascinating and versatile class of compounds with a wide range of biological activities, making them highly sought-after in the realm of medicinal chemistry. These compounds have displayed remarkable potential in various therapeutic applications, such as anti-inflammatory, anti-cancer, anti-microbial, and anti-viral activities. The diverse biological activities exhibited by 1,3,4-oxadiazoles have spurred extensive research into developing efficient methods for their synthesis. This multitude of synthetic pathways reflects the urgency and significance of harnessing the unique pharmacological properties of 1,3,4-oxadiazoles for the development of novel pharmaceuticals. In this context, numerous innovative synthetic methods have been devised to access these compounds, each tailored to enhance yield, selectivity, and sustainability. This introduction sets the stage for an exploration of the

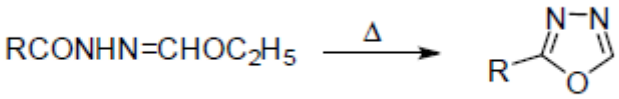
diverse biological activities of 1,3,4-oxadiazoles and the various synthetic methodologies that have emerged to harness their potential for drug discovery and development.

HIV (human immunodeficiency virus) XXO (Xanthomonas oryzae pv. Oryzae)

1.1 MATERIALS AND METHODS

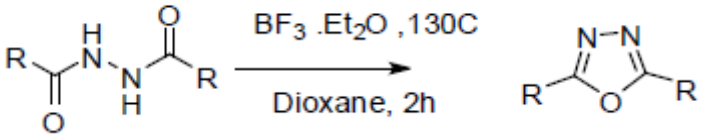
Literatures display several variety methods to synthesize 2,5 di -substitute -1,3,4-oxadiazole. Despite the wide range of approaches, the majority of these studies focused on the condensation of carboxylic acid and acid hydrazide . The first condensation to make heterocyclic reported in 1943 from R. A. Labriola and A. Felitte and 1n 1955 tow individual literatures report the synthesis of 1,3,4-Oxadiazole, below demonstrated for some these methods.

- Ainsworth and Hackler synthesised alkyl oxadiazole by heating 1-Acyl-2-ethoxymethylene hydrazines under ambient conditions [23].



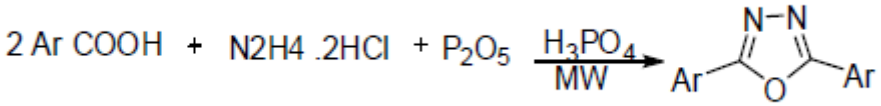
Scheme 1. Synthesis of oxadiazole

- Reaction of1,2-diacyl and 1,2-diaroyl hydrazines with BF_3.Et_2O, as cyclodehydration reagent[24].



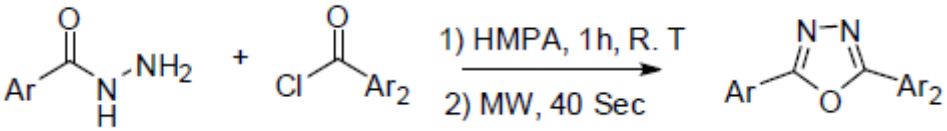
Scheme 2. Synthesisof2,5-dialkyl oxadiazole

- Reaction of tow mole of Aryl acid with Hydrazine dihydrochloridein presence o of phosphorus pentoxide and phosphoric acid, , 2-5 minutes (60 W) at 130 0C in a microwave oven with a reflux condenser[25].



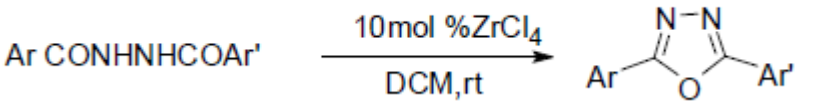
Scheme 3. Route of synthesis diaryl oxadiazole

- single aryl-hydrazides were condensed with acid chlorides in the presence of HMPA and microwaved to produce specific 2,5-disubstituted-1,3,4-oxa diazoles[26].



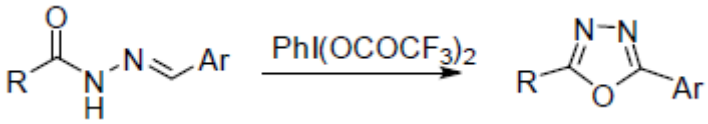
Scheme 4. Route of synthesis 2,5-disubstituted-oxadiazoles

- For the cyclodehydration of di-acyl-hydrazine, by mild catalyst that has been shown to be effective is zirconium(IV) chloride (10 mole%)[27].



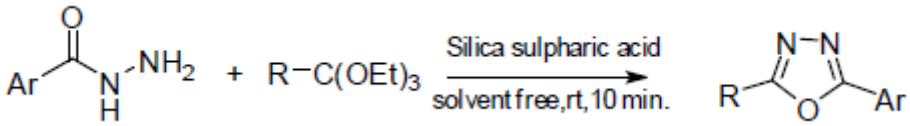
Scheme 5. Synthesisof oxadiazole

- Utilizing oxidizing Factor such as bis-(tri-fluoro acetoxy) iodobenzene with hydrazone may be cyclized in $CHCl_3$or DMSO at room temperature[28].



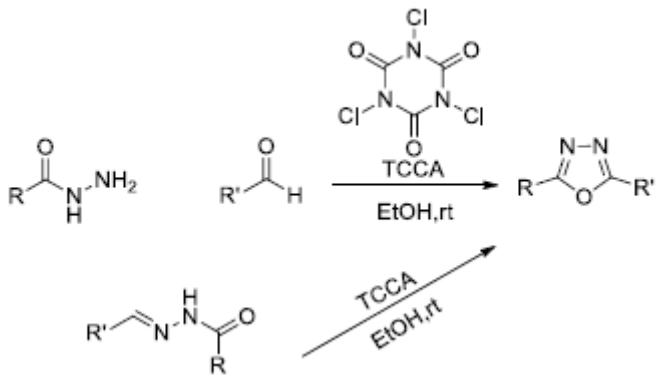
Scheme 6. Synthesisof oxadiazole by oxidised agent

- Solvent-free acyl hydrazide–orthoester condensation in existence of silica and H_2SO_4 [29].



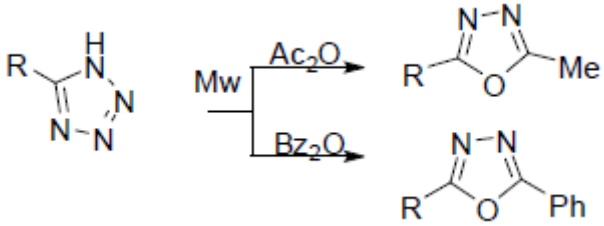
Scheme 7. Synthesisof oxadiazole by silica-sulfuric acid

- Trichloroisocyanuric acid (TCCA) is used to cyclize acylhydrazones and is also utilised to generate disubstituted-1,3,5-oxadiazole at room thermal reading by reacting acid hydrazide with aldehyde[30].



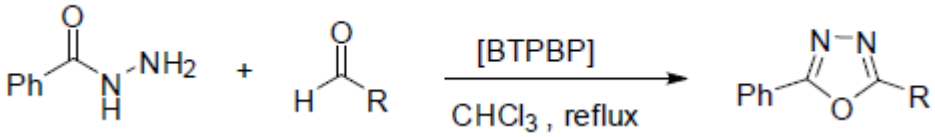
Scheme 8. Synthesisof oxadiazole by TCCA

- Under microwave irradiation, acetic or benzoic anhydride adding acyl group of 5-aryl(hetaryl)tetrazoles yielded the corresponding 5-Me and 5- Ph -1,3,4-oxadiazoles with 2 atoms of methyl orphenyl substituted[31].



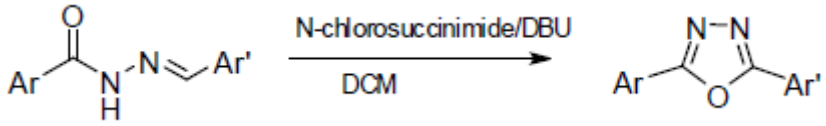
Scheme 9. Synthesisof 2,5-disubstituted-1,3,4-oxa diazoles Under microwave irradiation

- By combining aromatic aldehydes, acylhydrazide, and BTPBP[1,4-bis (triphenyl-phosphonium)-2-butene peroxodisulfate, one may create the oxadiazoles [32][33].



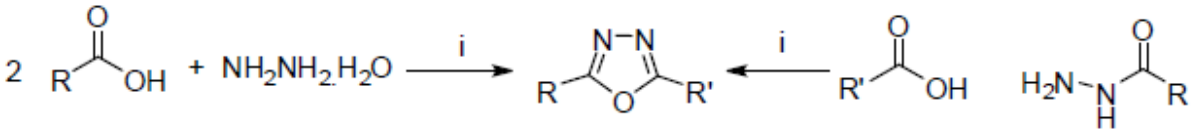
Scheme 10. Synthesisof 1,3,4-oxadiazole by BTPBP

- In order to get the necessary 2,5-disubstituted-1,3,5-oxadiazole, acyl hydrazone is oxidatively cyclized with the help of NCS and DBU as an efficient oxidant[34].



Scheme 11. Synthesisof 1,3,4-oxadiazole byDBU

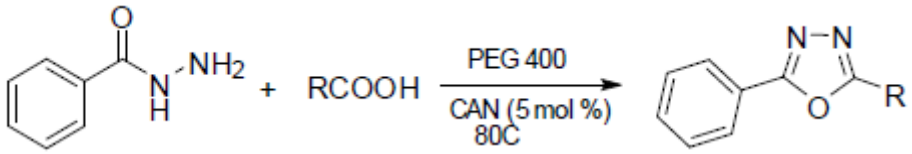
- M. Kidwai & R. Mohanin in 2003 reported synthesis symmetrical and un symmetrical oxadiazole from reaction carboxylic acid and hydrazine or acid hydrazide with carboxylic acid using acidic alumina or monomorillonite K10 clay under microwave irradiation condition as catalyst[35].



R=R' or R≠R', i) acidic alumina or monomorillonite K10 clay, MWI

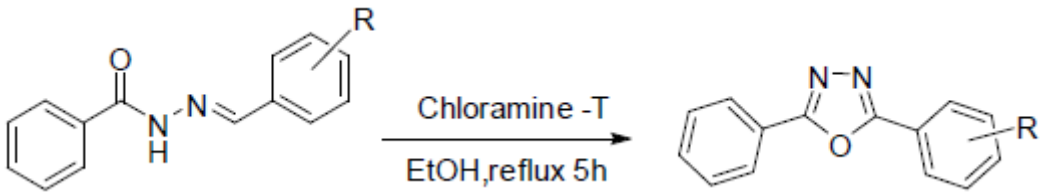
Scheme 12. Synthesisof symmetrical and un symmetrical oxa diazole

- Condensation ofacid hydrazide and carboxylic acid is catalysed using ceric ammonium nitrate (CAN) and Polyethyleneglycol (PEG) as catalysts in the synthesis of di-substituted oxadiazoles[36].



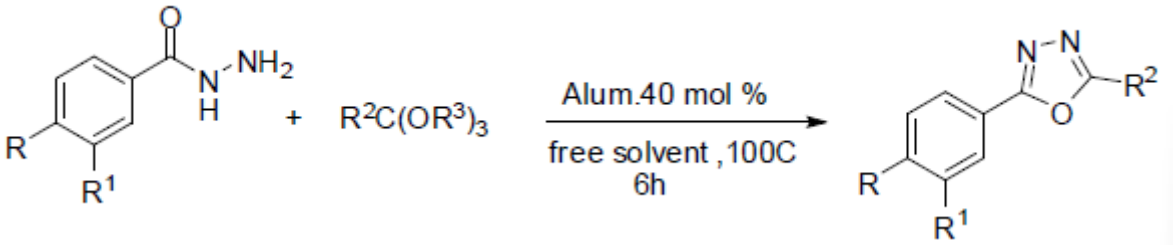
Scheme 13. Synthesisof oxadiazole by CAN & PEG

- Antibacterial study for synthesized oxadiazole had been reported, and this cyclization occured by using Chloramine-T as a cyclization agent towered the hydrazone [37].



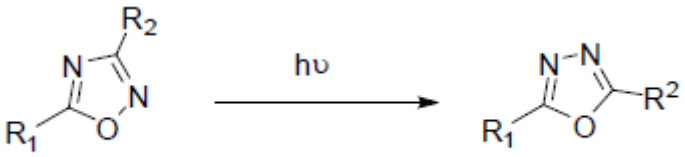
Scheme 14. Synthesisof oxadiazole by Chloramine-T

- Condensation of acyl hydrazides with orthoesters under solvent-free conditions at 100^0C catalyzed by g Alum ($KAl(SO_4)_2 .12H_2O$)[38].



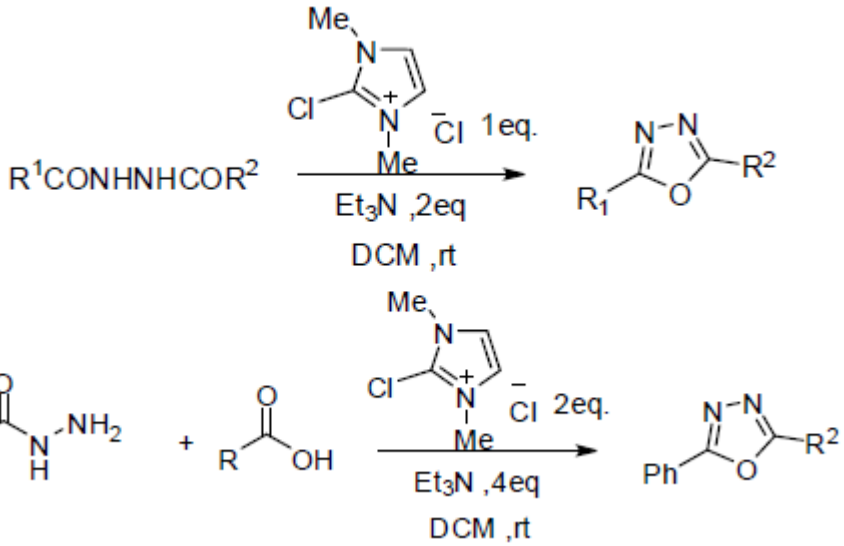
Scheme 15. Synthesisof oxadiazole by Alum

- 1,3,4 oxadiazole was synthesized from Photorearrangement of 1,2,4-Oxadiazoles[39].



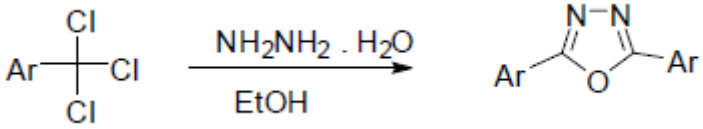
Scheme 16. Synthesisof 1,3,4-oxadiazole by Photorearrangement

- Using an ionic liquid 2-Chloro-1,3-dimethylimidazolinium Chloride as catalyst in presence of triethyl amine as catalyst to cyclization of Diacylhydrazines,also with Reaction of Acylhydrazines and Carboxylic Acids .



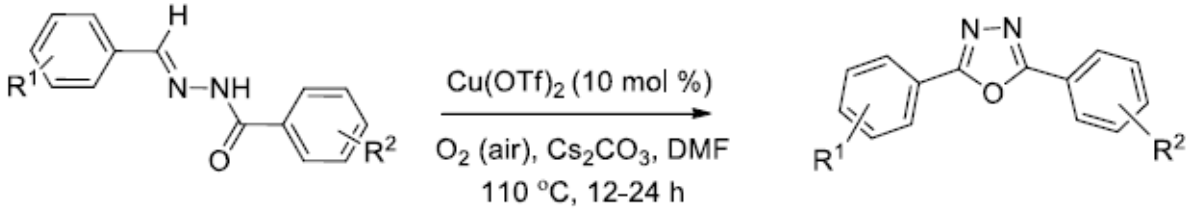
Scheme 17. Synthesisof oxadiazole by ionic liquid

- Symmetrical 2,5-diaryl-1,3,4-oxa diazole and 1,4-phenylene Bis oxadiazole were synthesized were synthesized from reaction of trichloromethylarenes with excess of hydrazine hydrate in ethanol.



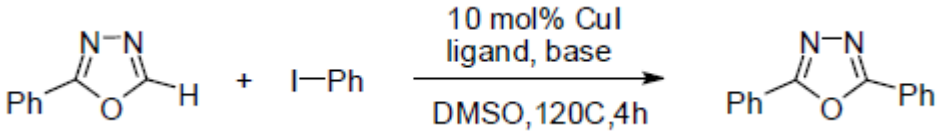
Scheme 18. Synthesisof Symmetrical 1,3,4-oxadiazole

- A catalytic amount of $Cu(OTf)_2$ was used to amine C-H functionalize N-arylidenearoylhydrazide, yielding asymmetric and unsymmetric disubstituted 1,3,4-oxa diazoles[40].



Scheme 19. Synthesisof 1,3,4-oxadiazole by $Cu(OTf)_2$

- Tsuyoshi Kawano et al [41] used new method for synthesis di substituted oxadiazole from reaction 2-phenyl 1,3,5-oxadiazole with phenyl iodide in presence of ligand and base with cupper iodide as a catalyst. In this investigation they used different base such as K_2CO_3, Li_2CO_3, Na_2CO_3, $CsCO_3$, and LiO-t-Bu, with various ligand like triphenyl phosphene(pph3),1,10 phenanthroline (phen) ,2,2'-bipyridine (bpy) ,N,N,N',N'-tetramethylethylene diamine (TMEDA) and N,N'- dimethylethylenediamine(DMEDA). The yield percentage demonstrated in table 2-1

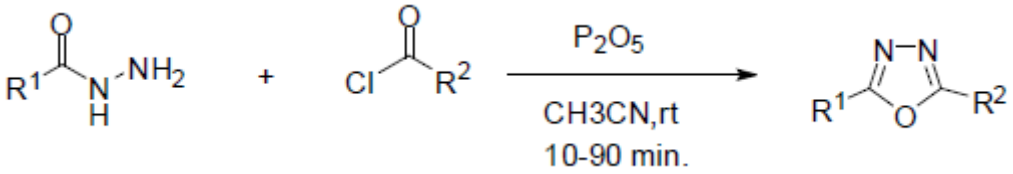


Scheme 20 Synthesisof 1,3,4-oxadiazole by using phenyl iodide

Table 1. -Some Physical Properties of Catalyst.

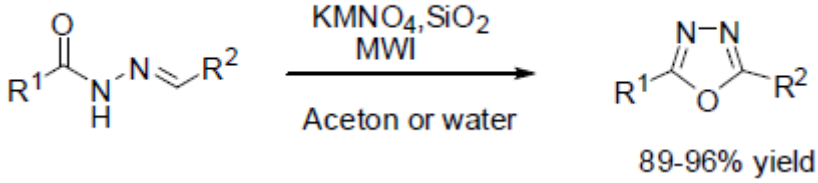
No.	Ligand	Base	Yield %	No.	ligand	Base	Yield%
1	pph_3	K_2CO_3	37	6	phen	Li_2CO_3	7
2	TMEDA	K_2CO_3	18	7	phen	Na_2CO_3	31
3	DMEDA	K_2CO_3	73	8	phen	CS_2CO_3	83at 100^0C
4	Bpy	K_2CO_3	33	9	phen	LiO-t-Bu	0
5	Phen	K_2CO_3	91				

- Di substituted oxadiazoles were synthesized via one pot at room temperature, from reaction of different of acid hydrazide and acyl halides in presence of phosphorus pentoxide in acetonitrile, this method shows excellent yield[42].



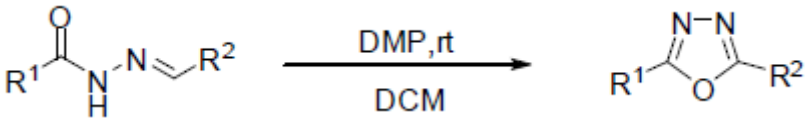
Scheme 21 Synthesisof oxadiazole by P_2O_5

- Treatment of aryl hydrazones with potassium permanganate on the surface of SiO_2 with aceton or water under microwave irradiation; lead to yield between 89%-97% from di substituted oxadiazole.



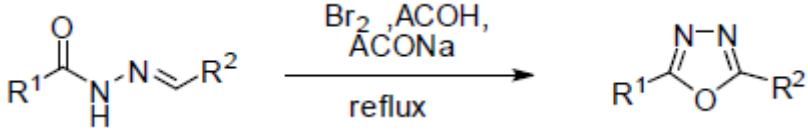
Scheme22 Synthesisof oxadiazole by using potassium permanganate on the surface of SiO_2

- The oxidative reagent activity of Dess-martin periodinane (DMP) in dicyclohexane (DCM) at room temperature on cyclic N-acylhydrazones [43].



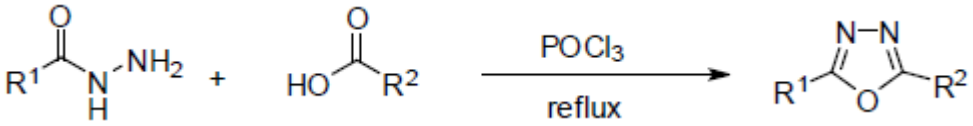
Scheme23 Synthesisof 1,3,4-oxa diazole by using DMP

- Cyclization ofN-Aryl hydrazones using Bromine in classier acetic acid and sodium acetate to formed di-substituted oxadiazole[44].



Scheme24 Synthesisof oxa diazole by using Bromine

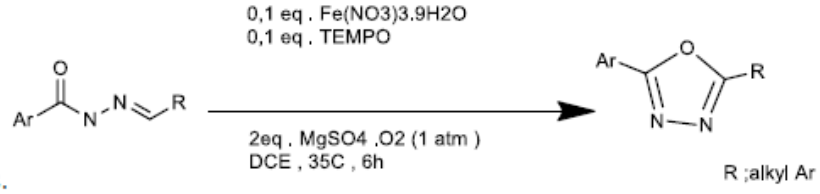
- Cyclizationof acid hydrazide and carboxylic acid in existence of Phosphorus oxychloride ($POCl_3$) [45][46][47] as a popular dehydration agent to attain 2,5-disubstituted -1,3,4-oxa diazole.



Scheme25 Synthesisof 1,3,4-oxadiazole by using $POCl_3$

This method was used to achieve our goal; eleven of 2, 6-di-*tert*-butyl-4- (5-Aryl-1,3,4-oxadiazol-2-yl) phenol and seven of 4,4'-(5,5'-(Substitute) bis (1,3,4-oxa diazole-5,2-diyl)) bis (2,6-di-*tert*-butylphenol) were synthesized according this method.

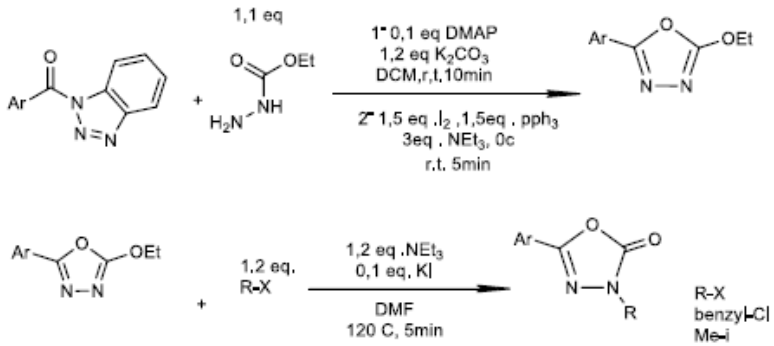
- Synthesis of 2,5-disubstituted 1,3,4-oxadiazole derivatives by oxidative cyclization of aroyl hydrazones in the presence of oxygen catalyzed by cationic Fe (III)/TEMPO yielded high to excellent percentages in 2017. The reaction might include a number of different functional groups.



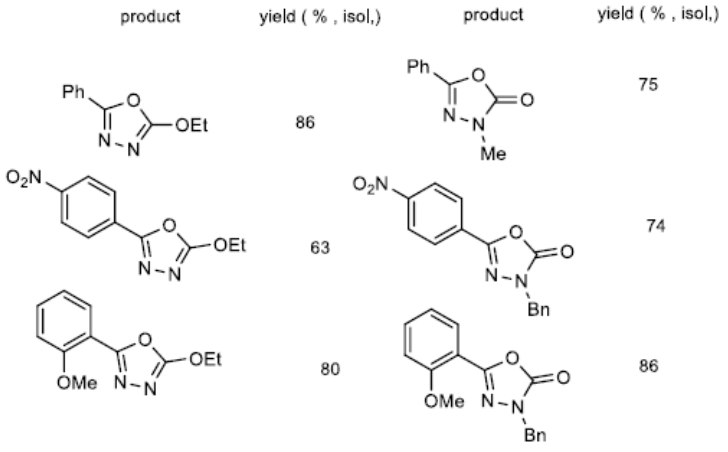
R1 = aryl, thienyl, 2-naphthyl, phenethyl, t-Bu, i-Bu, n-Pr, n-pentyl
R2 = H, Me, OMe, OH, CF_3, I, Br, Cl, NO_2

Scheme26 Synthesisof 1,3,4-oxadiazole by using Fe(III)/TEMPO

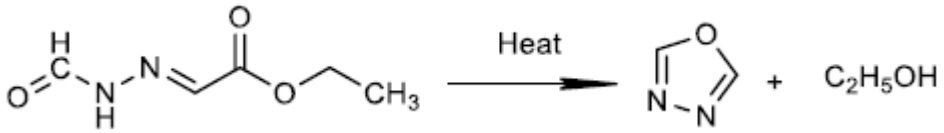
- Using sequential N-acylation/dehydrative cyclization of ethyl carbazate and N-acylbenzotriazoles with Ph3P-I2 as a dehydrating agent, it is now possible to quickly and efficiently synthesis 5-substituted-2-ethoxy-1,3,4-oxadiazoles in 2017. After reacting with stoichiometric quantities of alkyl halides, a large number of 3,5-disubstituted 1,3,4-oxadiazol-2(3H)-ones is produced. high above.



Scheme27 Synthesisof oxadiazole by using N-acylation

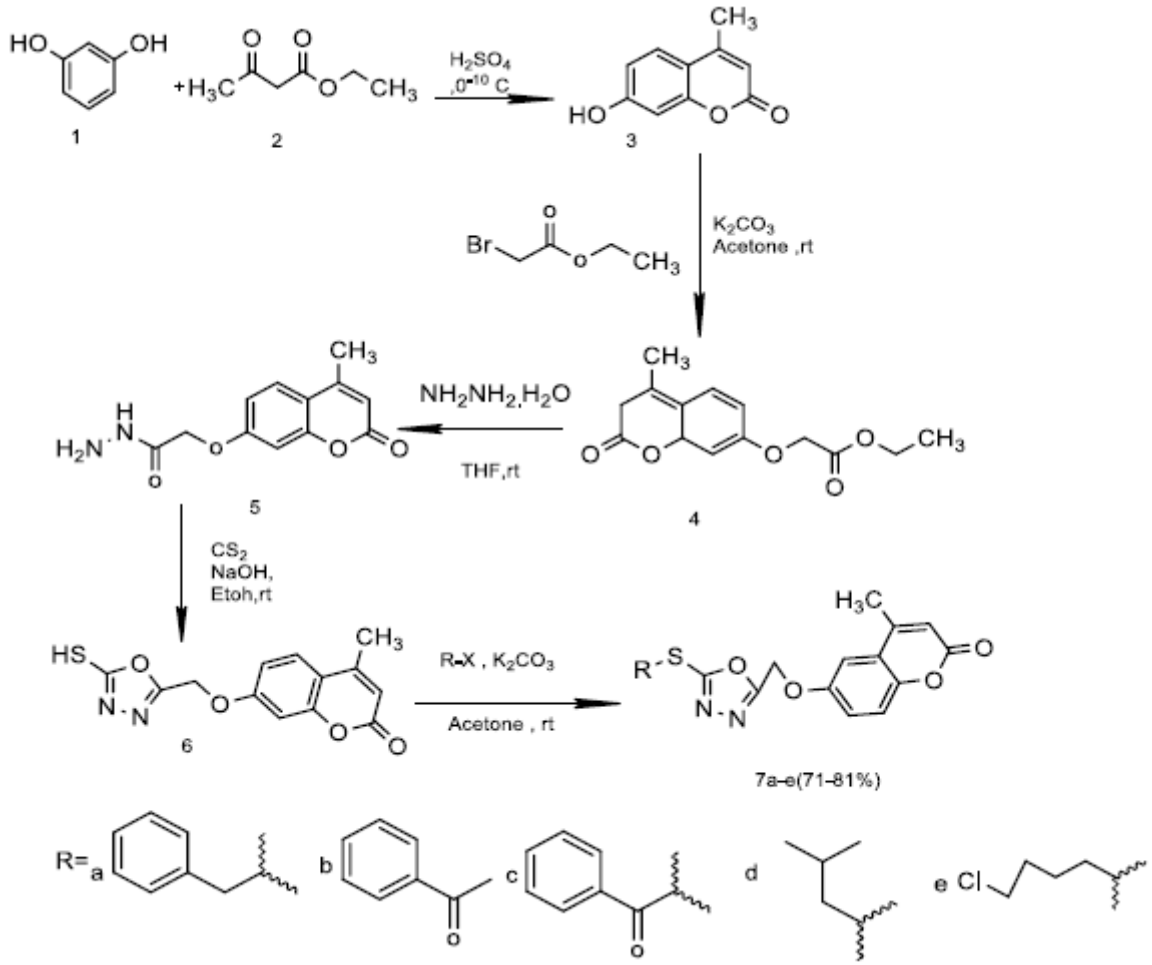


- In 2022, Ainsworth was the first to detail the process for making unsubstituted 1,3,4-oxadiazole. Formylhydrazone ethylformate was subjected to thermolysis at air pressure to complete the synthesis[48].



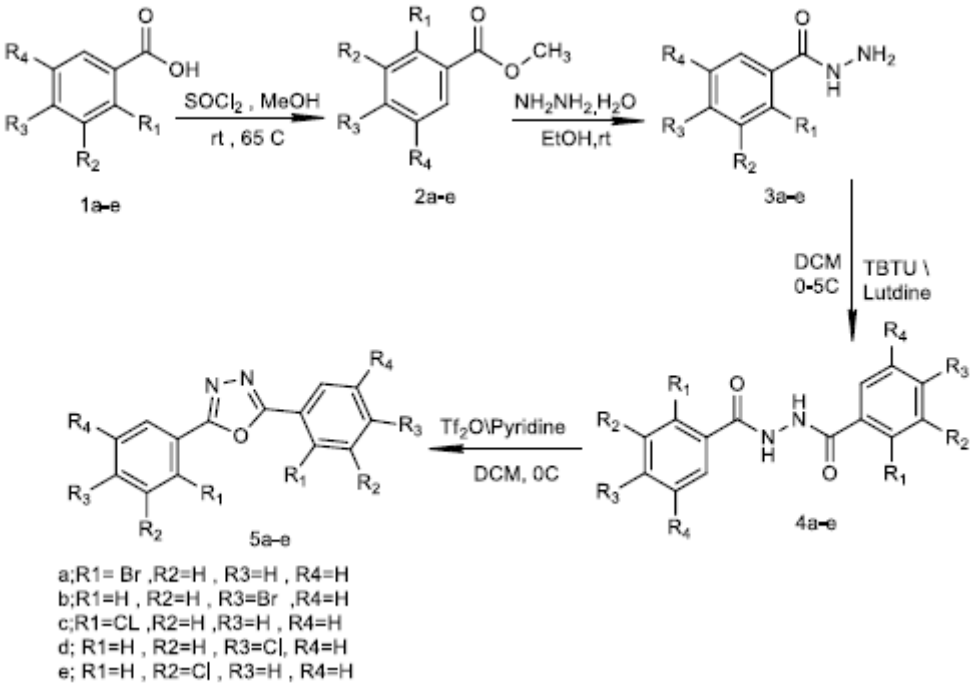
Scheme28 Synthesisof unsubstituted oxadiazole

- To create 2-aryl-1,3,4-oxadiazole with a p-bromophenylaminomethyl group substituted at position 5, Bhat et al. developed a method using mercury oxide and iodine[49].



Scheme29 Synthesisof oxadiazole by mercury oxide and iodine

- According to the strategy proposed by Zabiulla et al., 2,5-bisphenyl-1,3,4-oxa diazoles may be synthesised by the cyclization ofN,N′-diacylhydrazines using tri fluoromethanesulfonic anhydride as the main reagent[49].

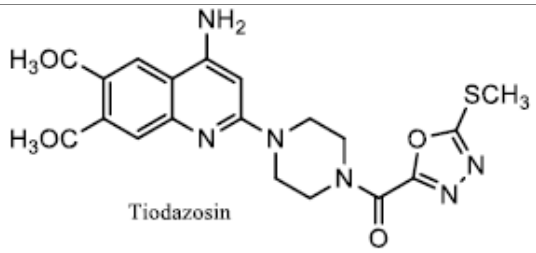
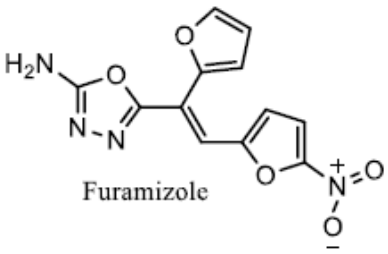


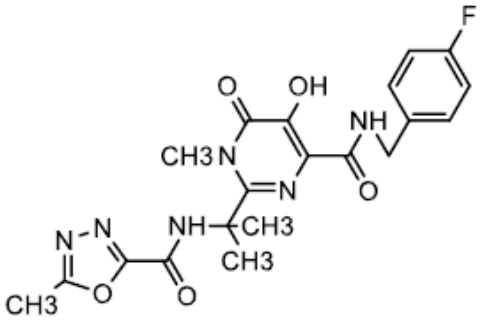
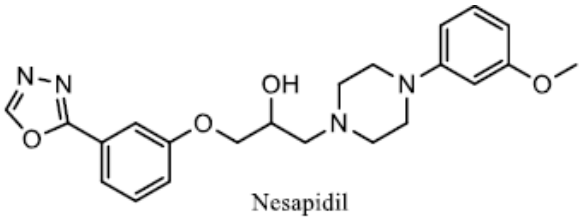
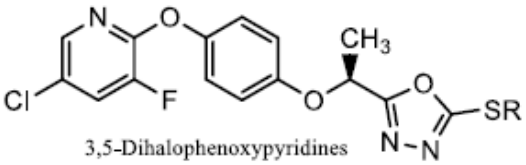
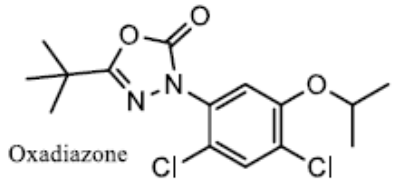
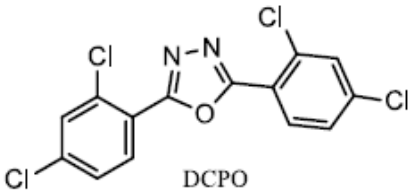
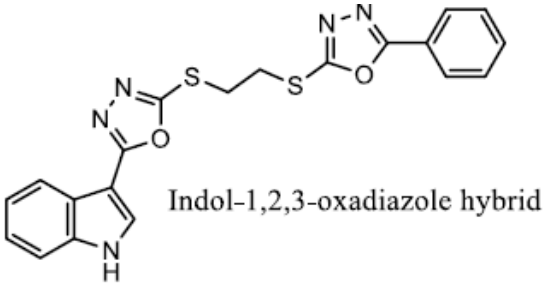
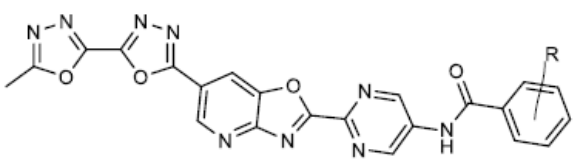
Scheme30 Synthesisof oxadiazole by using trifluoromethanesulfonic anhydride

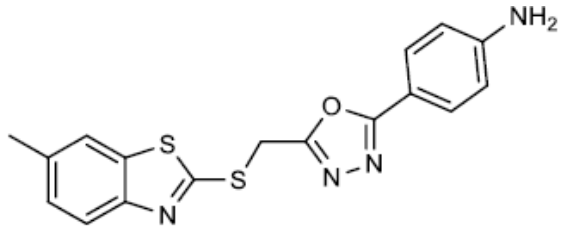
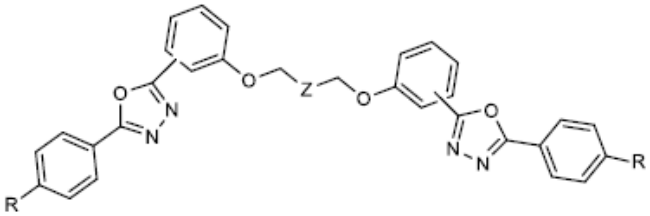
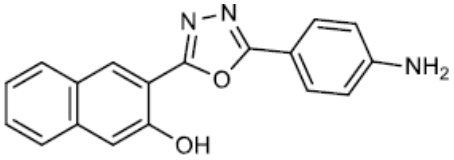
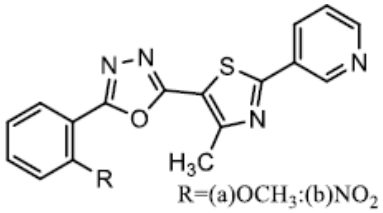
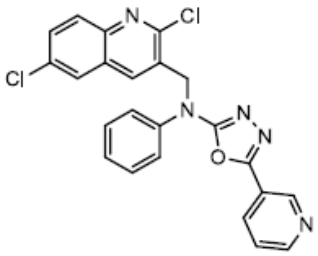
1.2 TABLES

Table 2 showed a wide range of biological activity for many oxadiazole derivatives due to the presence of the oxadiazole nucleus, which is involved in wide fields such as the pharmaceutical industry, dyes, materials science, and most organic compounds, in addition to the discovery of various biological agents such as anti-cancers, antihypertensive drugs, and in soothing sinuses, as well as in the physical field such as photoluminescence and others.

Table 2. - Some of Oxadiazoderivative with bioactive

No.	Structure	Biological activity	References
1	 Tiodazosin	Antihypertensive	[50]
2	 Furamizole	Antibacterial and anti-influenza	[51]

3	 Raltegravir(MK-0518)	Antiretroviral and HIV	[52]
4	 Nesapidil	Vasodilator	[53]
5	 3,5-Dihalophenoxypyridines	Herbicide	[49]
6	 Oxadiazone	Herbicidal	[54]
7	 DCPO	DNA and protein synthesis in insects are stymied.	[55]
8	 Indol-1,2,3-oxadiazole hybrid	Effective against Xanthomonas oryzae and Ralstonia solanacearum	[56]
9	 1a-j a;R=3,4,5-trimethoxy, b;R=3,5-dimethoxy, c;R=4-methoxy, d;R=4-nitro, e;R=3,5-dinitro, f;R=4-chloro, g;R=4-bromo, h;R=4-methyl, i;R=4-(dimethyl amino), j;R=4-cyano	Anticancer agent	[57][58]

10		Antidiabetic activity	[59]
11		antibacterial activity	[60][61]
12		antifungal activity	[62]
13		ant tubercular	[63]
15		Antimalarial	[64]

2.1 RESULTS AND DISCUSSION

The 1,3,4-oxadiazole derivatives with five atoms of ring structure are the building blocks of several molecules with beneficial biological activity [27] in medicine and agriculture . Evidence from studies evaluating the potency of these biological activities suggests that many systems of this kind have therapeutic potential against a wide range of infections. This has increased the tendency of researchers to study many of these compounds, diagnose them spectroscopically and physically, and search for new ways to prepare them and find raw materials. With the most reasonable prices, suitable environmental conditions, and available auxiliary factors.

Study data were collected to evaluate the effect of the prepared derivatives on different types of drugs, and studies showed their inhibitory effectiveness compared to pharmaceutical compounds on the nervous system as sedatives and anti-inflammatory substances and in many industrial applications, dyes, fluorinated materials, and heat resistance.

2.2 Conclusion

The urgent need to find new antifungal, antibacterial, anti-inflammatory in nature and analgesic molecules has prompted several research teams to investigate novel synthesis techniques of these substances. Research on 1,3,4-oxadiazole medications also focuses heavily on enhancing the structure and functionality of existing pharmaceuticals and insecticidesA molecule's solubility may affect its bioavailability and efficacy, and this can be achieved by the introduction of novel substituents or the development of new hybrid materials with existing physiologically active compounds Oxadiazole-based chemical designs are becoming more popular, and as a result, there is a growing library of physiologically active compounds that might be used in the future for medicines for humans and animals, as well as for the prevention of plant diseases.

Acknowledgment

I extend my thanks to the University of Baghdad and the College of Education for pure science Ibn al-Haitham, Department of Chemistry. I also thank Wasit University for providing the opportunity for researchers to exchange experiences

REFERENCES

[1] Z. M. Abbas, D. F. Hussain, and R. M. Shakir, "Synthesis of Some New Heterocyclic Fused Rings Compounds Based on 5-Aryl-1, 3, 4-Oxadiazole," *Ibn AL-Haitham J. Pure Appl. Sci.*, vol. 30, no. 2, pp. 161–176, 2017.

[2] H. I. Omar–Eldeen, "Synthesis and Antimicrobial Evaluation of Some Bis-1, 3, 4-Butane-1-3, 4-Oxadiazole Derivatives," *Ibn Al-Haitham J. Pure Appl. Sci.*, vol. 22, no. 3, 2009.

[3] I. Y. Majeed, S. A. Saoud, A. A. Ahmed, and E. F. Mustafa, "Synthesis, Characterization and Antibacterial Activity of Some New Five-Seven Membered Rings Attached to Sulfonamide Compounds," *Ibn AL-Haitham J. Pure Appl. Sci.*, vol. 27, no. 2, pp. 170–177, 2017.

[4] S. Bhatia and M. Gupta, "1, 3, 4-Oxadiazole as antimicrobial agents: An overview," *J. Chem. Pharm. Res*, vol. 3, no. 3, pp. 137–147, 2011.

[5] A. L. Jarallah, K. F. Ali, R. M. Shakir, and S. A. Saoud, "Synthesis, Antibacterial and Antifungal Activities for Novel Derivatives of 2, 2'-(((1-benzylbenzoimidazol-2-yl) methyl) azanediyl) bis (ethan-1-ol)," *Ibn AL-Haitham J. Pure Appl. Sci.*, vol. 32, no. 1, pp. 57–79, 2019.

[6] S. Vardan, H. Smulyan, S. Mookherjee, and R. Eich, "Effects of tiodazosin, a new antihypertensive, hemodynamics and clinical variables," *Clin. Pharmacol. Ther.*, vol. 34, no. 3, pp. 290–296, 1983.

[7] S. R. PATTAO, P. A. Rabara, J. S. PATTAN, A. A. Bukitagar, V. S. WAKALC, and D. S. MUSMADE, "Synthesis and evaluation of some novel substituted 1, 3, 4-oxadiazole and pyrazole derivatives for antitubercular activity," *Indian J. Chem. Sect. B Org. Chem. Incl. Med. Chem.*, vol. 48, no. 10, pp. 1453–1456, 2009.

[8] H. P. Shah, B. R. Shah, J. J. Bhatt, N. C. Desai, P. B. Trivedi, and N. K. Undavia, "Synthesis of 2, 5-disubstituted 1, 3, 4-oxadiazoles as potential antimicrobial, anticancer and anti-HIV agents," 1998.

[9] G. A. Pinna *et al.*, "Synthesis, Modelling, and Antimitotic Properties of Tricyclic Systems Characterised by a 2-(5-Phenyl-1H-pyrrol-3-yl)-1, 3, 4-oxadiazole Moiety," *ChemMedChem Chem. Enabling Drug Discov.*, vol. 4, no. 6, pp. 998–1009, 2009.

[10] X. Qian and R. Zhang, "Syntheses and insecticidal activities of novel 2, 5-disubstituted-1, 3, 4-oxadiazoles," *J. Chem. Technol. Biotechnol. Int. Res. Process. Environ. Clean Technol.*, vol. 67, no. 2, pp. 124–130, 1996.

[11] W. Wang *et al.*, "Synthesis and insecticidal evaluation of novel N-pyridylpyrazole derivatives containing diacylhydrazine/1, 3, 4-oxadiazole moieties," *J. Heterocycl. Chem.*, vol. 56, no. 4, pp. 1330–1336, 2019.

[12] H. Rajak, M. D. Kharya, and P. Mishra, "Synthesis and Local Anesthetic Activity of Some Novel N-[5-(4-Substituted) phenyl-1, 3, 4-oxadiazol-2-yl]-2-(Substituted)-Acetamides," *Arch. der Pharm. An Int. J. Pharm. Med. Chem.*, vol. 341, no. 4, pp. 247–261, 2008.

[13] H. S. Jasim, S. A. Saoud, and H. A. J. Almuslamawy, "Study of Acute and Chronic Sinusitis–Symptoms, Diagnosis and Treatment: A Review Article," *Ibn AL-Haitham J. Pure Appl. Sci.*, vol. 35, no. 3, pp. 83–90, 2022.

[14] D. Dewangan *et al.*, "Synthesis and Molecular Docking Study of Novel Hybrids of 1, 3, 4-Oxadiazoles and Quinoxaline as a Potential Analgesic and Anti-Inflammatory Agents," *J. Heterocycl. Chem.*, vol. 55, no. 12, pp. 2901–2910, 2018.

[15] R. Maheshwari, P. Chawla, and S. A. Saraf, "Comparison between antioxidant activity of 2, 5-disubstituted 1, 3, 4-oxadiazoles containing heteroaromatic ring and aromatic ring at 2nd position," *Med. Chem. Res.*, vol. 20, pp. 1650–1655, 2011.

[16] M. Shaban, A. E. Nasar, and S. M. EL-Badary, "Synthesis of some 1, 3, 4-oxadiazole and bis 1, 3, 4-oxadiazole that possess nematicidal insecticidal and herbicidal activity," *J. Islam. Acad. Sci.*, vol. 4, no. 3, pp. 184–191, 1991.

[17] X.-L. Wang, J. Li, H.-Y. Lin, H.-L. Hu, B.-K. Chen, and B. Mu, "Synthesis, structures and electrochemical properties of two novel metal–organic coordination complexes based on trimesic acid (H3BTC) and 2, 5-bis (3-pyridyl)-1, 3, 4-oxadiazole (BPO)," *Solid State Sci.*, vol. 11, no. 12, pp. 2118–2124, 2009.

[18] J. H. Kim, "Synthesis and electro-optical properties of poly (p-phenylenevinylene) derivative with conjugated 1, 3, 4-oxadiazole pendant and its AC electroluminescence," *Synth. Met.*, vol. 158, no. 21–24, pp. 1028–1036, 2008.

[19] M. K. Huda and S. K. Dolui, "Luminescence property of poly (1, 3-bis (phenyl-1, 3, 4-oxadiazole)) s containing polar groups in the main chain," *J. Lumin.*, vol. 130, no. 11, pp. 2242–2246, 2010.

[20] X. Song *et al.*, "Synthesis and investigation of the antibacterial activity and action mechanism of 1, 3, 4-oxadiazole thioether derivatives," *Pestic. Biochem. Physiol.*, vol. 147, pp. 11–19, 2018.

[21] A. N. Ambhore *et al.*, "Design, synthesis and in silico study of pyridine based 1, 3, 4-oxadiazole embedded hydrazinecarbothioamide derivatives as potent anti-tubercular agent," *Comput. Biol. Chem.*, vol. 80, pp. 54–65, 2019.

[22] P. Li *et al.*, "Novel bisthioether derivatives containing a 1, 3, 4-oxadiazole moiety: design, synthesis, antibacterial and nematocidal activities," *Pest Manag. Sci.*, vol. 74, no. 4, pp. 844–

852, 2018.

[23] C. Ainsworth and R. E. Hackler, “Alkyl-1, 3, 4-oxadiazoles,” *J. Org. Chem.*, vol. 31, no. 10, pp. 3442–3444, 1966.

[24] V. K. Tandon and R. B. Chhor, “An efficient one pot synthesis of 1, 3, 4-oxadiazoles,” *Synth. Commun.*, vol. 31, no. 11, pp. 1727–1732, 2001.

[25] F. Bentiss, M. Lagrenee, and D. Barbry, “Rapid synthesis of 2, 5-disubstituted 1, 3, 4-oxadiazoles under microwave irradiation,” *Synth. Commun.*, vol. 31, no. 6, pp. 935–938, 2001.

[26] S. H. Mashraqui, S. G. Ghadigaonkar, and R. S. Kenny, “An expeditious and convenient one pot synthesis of 2, 5-disubstituted-1, 3, 4-oxadiazoles,” *Synth. Commun.*, vol. 33, no. 14, pp. 2541–2545, 2003.

[27] G. V. M. Sharma, A. Begum, Rakesh, and P. R. Krishna, “Zirconium (IV) Chloride Mediated Cyclodehydration of 1, 2-Diacylhydrazines: A Convenient Synthesis of 2, 5-Diaryl 1, 3, 4-Oxadiazoles,” *Synth. Commun.*, vol. 34, no. 13, pp. 2387–2391, 2004.

[28] Z. Shang, “Oxidative Cyclization of Aromatic Aldehyde N-Acylhydrazones by bis (Trifluoroacetoxy) iodobenzene,” *Synth. Commun.*, vol. 36, no. 20, pp. 2927–2937, 2006.

[29] M. Dabiri, P. Salehi, M. Baghbanzadeh, M. A. Zolfigol, and M. Bahramnejad, “Silica Sulfuric Acid: An Efficient and Versatile Acidic Catalyst for the Rapid and Ecofriendly Synthesis of 1, 3, 4-Oxadiazoles at Ambient Temperature,” *Synth. Commun.*, vol. 37, no. 7, pp. 1201–1209, 2007.

[30] D. M. Pore, S. M. Mahadik, and U. V Desai, “Trichloroisocyanuric acid–mediated one-pot synthesis of unsymmetrical 2, 5-disubstituted 1, 3, 4-oxadiazoles at ambient temperature,” *Synth. Commun.*, vol. 38, no. 18, pp. 3121–3128, 2008.

[31] Y. A. Efimova, T. V Artamonova, and G. I. Koldobskii, “Tetrazoles: LIII. Microwave-activated acylation of 5-substituted tetrazoles,” *Russ. J. Org. Chem.*, vol. 44, pp. 1345–1347, 2008.

[32] R. Badri and M. Gorjizadeh, “A novel, one-pot synthesis of 2, 5-disubstituted-1, 3, 4-oxadiazoles using 1, 4-bis (triphenylphosphonium)-2-butene peroxodisulfate,” *Phosphorus, Sulfur, and Silicon*, vol. 185, no. 3, pp. 544–549, 2010.

[33] I. Y. Majeed, D. Al-Saady, and S. A. Saoud, “Synthesis and characterization of some new compounds derivatives from para-amino benzoic acid,” *Int. J. Sci. Technol.*, vol. 8, no. 3, 2013.

[34] S. P. Pardeshi, S. S. Patil, and V. D. Bobade, “N-Chlorosuccinimide/1, 8-Diazabicyclo [5.4. 0] undec-7-ene (DBU)–Mediated Synthesis of 2, 5-Disubstituted 1, 3, 4-Oxadiazoles,” *Synth.*

Commun., vol. 40, no. 11, pp. 1601–1606, 2010.

[35] M. Kidwai and R. Mohan, "Synthesis of 2, 5-disubstituted 1, 3, 4-oxadiazoles using dry media," *Org. Prep. Proced. Int.*, vol. 35, no. 4, pp. 426–429, 2003.

[36] M. Kidwai, D. Bhatnagar, and N. K. Mishra, "Polyethylene glycol (PEG) mediated green synthesis of 2, 5-disubstituted 1, 3, 4-oxadiazoles catalyzed by ceric ammonium nitrate (CAN)," *Green Chem. Lett. Rev.*, vol. 3, no. 1, pp. 55–59, 2010.

[37] I. Ali, "Chloramine-T mediated synthesis of 1, 3, 4-Oxadiazole as antibacterial agents," *Der Pharm. Sin.*, 2011.

[38] M. Dabiri, P. Salehi, M. Baghbanzadeh, and M. Bahramnejad, "Alum (KAl (SO 4) 2· 12H 2 O): an efficient and inexpensive catalyst for the one-pot synthesis of 1, 3, 4-oxadiazoles under solvent-free conditions," *Monatshefte für Chemie-Chemical Mon.*, vol. 138, pp. 1253–1255, 2007.

[39] A. Pace, S. Buscemi, and N. Vivona, "Heterocyclic rearrangements in constrained media. A zeolite-directed photorearrangement of 1, 2, 4-oxadiazoles," *J. Org. Chem.*, vol. 70, no. 6, pp. 2322–2324, 2005.

[40] S. Guin, T. Ghosh, S. K. Rout, A. Banerjee, and B. K. Patel, "Cu (II) catalyzed imine C–H functionalization leading to synthesis of 2, 5-substituted 1, 3, 4-oxadiazoles," *Org. Lett.*, vol. 13, no. 22, pp. 5976–5979, 2011.

[41] T. Kawano, T. Yoshizumi, K. Hirano, T. Satoh, and M. Miura, "Copper-mediated direct arylation of 1, 3, 4-oxadiazoles and 1, 2, 4-triazoles with aryl iodides," *Org. Lett.*, vol. 11, no. 14, pp. 3072–3075, 2009.

[42] S. Rostamizadeh and S. Ghamkhar, "A mild and facile method for one pot synthesis of 2, 5-di-substituted 1, 3, 4-oxadiazoles at room temperature," *Chinese Chem. Lett.*, vol. 19, no. 6, pp. 639–642, 2008.

[43] C. Dobrotă, C. C. Paraschivescu, I. Dumitru, M. Matache, I. Baciu, and L. L. Ruţă, "Convenient preparation of unsymmetrical 2, 5-disubstituted 1, 3, 4-oxadiazoles promoted by Dess–Martin reagent," *Tetrahedron Lett.*, vol. 50, no. 17, pp. 1886–1888, 2009.

[44] A. E.-G. E. Amr, S. F. Mohamed, N. A. Abdel-Hafez, and M. M. Abdalla, "Antianexiety activity of pyridine derivatives synthesized from 2-chloro-6-hydrazino-isonicotinic acid hydrazide," *Monatshefte für Chemie-Chemical Mon.*, vol. 139, pp. 1491–1498, 2008.

[45] M. Akhter, A. Husain, B. Azad, and M. Ajmal, "Aroylpropionic acid based 2, 5-disubstituted-1, 3, 4-oxadiazoles: Synthesis and their anti-inflammatory and analgesic activities," *Eur. J. Med. Chem.*, vol. 44, no. 6, pp. 2372–2378, 2009.

[46] R. M. Shakir, A. Ariffin, and M. A. Abdulla, "Synthesis of new 2, 5-di-substituted 1, 3, 4-

oxadiazoles bearing 2, 6-di-tert-butylphenol moieties and evaluation of their antioxidant activity," *molecules*, vol. 19, no. 3, pp. 3436–3449, 2014.

[47] S. A. Saoud, K. F. Ali, and R. M. Shakir, "Relationship Between the structure of Newly Synthesized derivatives of 1, 3, 4-oxadiazole Containing 2-Methylphenol and their Antioxidant and Antibacterial Activities," *Orient. J. Chem.*, vol. 33, no. 4, p. 1781, 2017.

[48] M. Luczynski and A. Kudelko, "Synthesis and biological activity of 1, 3, 4-oxadiazoles used in medicine and agriculture," *Appl. Sci.*, vol. 12, no. 8, p. 3756, 2022.

[49] B. K. Banik *et al.*, "Green synthetic approach: An efficient eco-friendly tool for synthesis of biologically active oxadiazole derivatives," *Molecules*, vol. 26, no. 4, p. 1163, 2021.

[50] W. Yu, L. P. Cheng, W. Pang, and L. L. Guo, "Design, synthesis and biological evaluation of novel 1, 3, 4-oxadiazole derivatives as potent neuraminidase inhibitors," *Bioorg. Med. Chem.*, vol. 57, p. 116647, 2022.

[51] I. K. Jóźwik, D. O. Passos, and D. Lyumkis, "Structural biology of HIV integrase strand transfer inhibitors," *Trends Pharmacol. Sci.*, vol. 41, no. 9, pp. 611–626, 2020.

[52] J. Crispim-Neto and M. C. S. de Mattos, "Tribromoisocyanuric acid as an alternative oxidant in the synthesis of 2-amino-1, 3, 4-oxadiazoles from 1-acylthiosemicarbazides," *Tetrahedron Lett.*, vol. 121, p. 154494, 2023.

[53] W.-G. Duan *et al.*, "Synthesis and herbicidal activity of 5-dehydroabietyl-1, 3, 4-oxadiazole derivatives," 2011.

[54] L. G. Maciel *et al.*, "Inhibition of 3-Hydroxykynurenine Transaminase from Aedes aegypti and Anopheles gambiae: A Mosquito-Specific Target to Combat the Transmission of Arboviruses," *ACS bio med Chem Au*, vol. 3, no. 2, pp. 211–222, 2023.

[55] Y. Yang, Q. Zhang, Y. Yu, G. Li, S. Xiao, and Z. Ma, "Improving crop health: Understanding the interaction mechanisms between crops and their pathogens," *Front. Plant Sci.*, vol. 14, p. 1161154, 2023.

[56] A. B. Syeda, M. Ferazoddin, M. Rajeswari, J. P. Paul, and B. Juluru, "Design, Synthesis and Anticancer Evaluation of Benzoxazole Resemble Substituted Arylamide Derivatives of Bis-1, 3, 4-Oxadiazole-oxazolo [4, 5-b] pyridin-2-yl) as Anticancer Agents," *Chem. Data Collect.*, vol. 43, p. 100971, 2023.

[57] Poonam, G. Bhasin, R. Srivastava, and R. Singh, "Oxadiazoles: moiety to synthesis and utilize," *J. Iran. Chem. Soc.*, pp. 1–13, 2022.

[58] B. D. Mohammad *et al.*, "Heterocyclic Compounds as Dipeptidyl Peptidase-IV Inhibitors with Special Emphasis on Oxadiazoles as Potent Anti-Diabetic Agents," *Molecules*, vol. 27, no. 18, p. 6001, 2022.

[59] A. M. Abdelfattah, A. E. M. Mekky, and S. M. H. Sanad, “Synthesis, antibacterial activity and in silico study of new bis (1, 3, 4-oxadiazoles),” *Synth. Commun.*, vol. 52, no. 11–12, pp. 1421–1440, 2022.

[60] R. F. Muslim, I. Y. Majeed, S. E. Saleh, M. M. Saleh, M. N. Owaid, and J. A. Abbas, “Preparation, Characterization and Antibacterial Activity of some New Oxazolidin-5-one Derivatives Derived from Imine Compounds,” *J. Chem. Heal. Risks*, vol. 12, no. 4, pp. 725–732, 2022, doi: 10.22034/jchr.2022.688557.

[61] J. Shi *et al.*, “Design, synthesis and antifungal evaluation of phenylthiazole-1, 3, 4-oxadiazole thione (ketone) derivatives inspired by natural thiasporine A,” *Pest Manag. Sci.*, 2023.

[62] T. Glomb and P. Świątek, “Antimicrobial activity of 1, 3, 4-oxadiazole derivatives,” *Int. J. Mol. Sci.*, vol. 22, no. 13, p. 6979, 2021.

[63] V. Adimule, A. H. Jagadeesha Gowda, S. S. Nandi, and D. Bowmik, “Antimalarial activity of novel class of 1, 3-benzoxaborole derivatives containing 1, 3, 4-oxadiazole moiety,” *Drug Dev. Malar. Nov. Approaches Prev. Treat.*, pp. 285–302, 2022.

[64] N. J. ABDULRADA, D. F. HUSSAIN, and S. SAOUD, “Synthesis, Characterization and Antibacterial of Some New 4, 4’-(pyridine-2, 6-diylbis (1, 3, 4-oxadiazole-5, 2-diyl)) bisphenolPolymer.,” *Int. J. Pharm. Res.*, vol. 11, no. 3, 2019.