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"One pot Synthesis 1,3,4-oxadiazole Derivatives Under under ultrasonic irradiation with silica-supported "

Narendra P. Surse[1], Amol D. Kale [2], Ram Khalapure[2], Bharat. K. Dhotre[3*],

[1] Department of Chemistry, Dr. Babasaheb Ambedkar Marathwada University, Aurangabad, Maharashtra 431004, India

[2] Department of Chemistry, Lal Bahadur Shastri Senior College Partur, Maharashtra, India

[3] Department of Chemistry, Swami Vivekanand Senior College Mantha, Maharashtra, India.

Abstract:

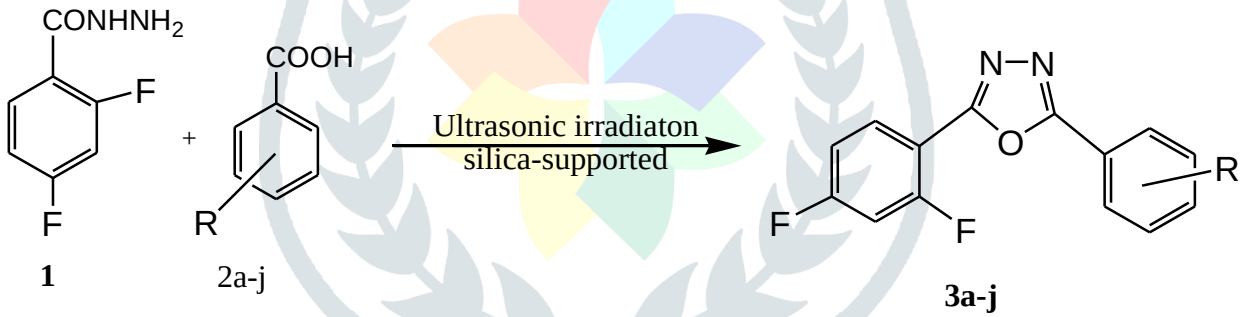
A rapid and efficient method for the one-pot synthesis of unsymmetrical 2,5- disubstituted 1,3,4-oxadiazoles has been developed using 2,4-difluorobenzohydrazide with substituted benzoic acid in presence in the presence of phosphorus oxychloride as a catalyst under ultrasonic irradiation with silica-supported. A wide variety of aromatic 2,4-difluorobenzohydrazide as well as substituted benzoic acid exhibit oxidative cyclization to yield corresponding unsymmetrical 2,5- disubstituted 1,3,4-oxadiazoles. The structures of these compounds are elucidated by their spectral data (IR, ^{1}H NMR, and MS). Maximum Yield, Short reaction time, and use of Silica and Ultrasonic are merits of the developed protocol.

Keywords. One Pot, ultrasonic irradiation, Silica, 1,3,4- oxadiazoles, 2,4- difluorobenzohydrazide

Introduction:

A large number of the market drug have contained heterocyclic entities, important for their key roles in medicinal Chemistry. The improvement of an efficient and practical synthesis of 2,5-disubstituted-1,3,4-oxadiazoles is an active matter of research organic synthesis. The presence of fluorine in organic molecules can frequently conclusion in significant changes in biological importance. It is owed to fluorine's blocking effect in metabolic transformations of enzyme substrates. The subsequent enhancement in the molecular lipophilicity to improve bioavailability. 1,3,4-Oxadiazoles derivative exhibits various biological activities such as antibacterial [1], antiviral [2], antidiabetic [3], anticonvulsant [4,5], anticancer [6], antimicrobial [7,8], anti-inflammatory [9], cytotoxic [10], antitumor [11], antifungal [12], anti-HIV [13], analgesic [14]. Due to the extensive commercial potential of 1, 3,4-oxadiazoles, numerous methods for their synthesis have been developed over the years. The common synthetic route to these compounds involves the cyclization of diacylhydrazines with a variety of reagents such as Silica-Supported Dichlorophosphate [15], Deoxo-Fluoro [16], $POCl_3$, [17], solvent-free [18], Polymer Supported [19], and Silica Supported [20].

Reaction Scheme



R= 4-NO_2,3-NO_2,H,4 -OCH_3, 4-Cl, 2-Cl,3-OH,4-CH_3,4-OH,4-NH_2

Experimental

All chemicals such as starting materials and reagents were commercially available and used without further purification. The reaction was monitored by thin-layer chromatography. Melting Points were determined by the open capillary method and were uncorrected. Column chromatography on silica gel (Merck, 70–230 mesh, and 400 mesh ASTH for flash chromatography) was applied when necessary to isolate and purify the reaction products.

Synthesis of 1,3,4-oxadiazoles from 2,4-difluorobenzohydrazide

A mixture of 2,4-difluorobenzohydrazide (1mmol)**(1)** with substituted benzoic acid **2 (a-j)** (1mmol) and Silica oxide and 5 ml of phosphorus oxychloride was added. The mixture was subjected to ultrasonic irradiation at 115 ^{0}C for 15–20 min. The completion of the reaction was monitored by TLC (ethyl acetate: n-hexane). After completion of the reaction, the mixture was cooled and poured onto crushed ice dropwise with continuous stirring. The resulting solid thus obtained was collected by filtration, washed well with cold water, dried, and recrystallized

from absolute ethanol.

Result and Discussion

We have described an efficient one-pot synthesis of 2,4-Difluoro-phenyl-5-(substituted phenyl)-[1,3,4] oxadiazol by reaction of 2,4-difluorobenzohydrazide with substituted benzoic acid in presence of the presence of phosphorus oxychloride as a catalyst under ultrasonic irradiation with silica-supported. The structure interpretations of the synthesized compounds were supported by different spectroscopic techniques like FTIR, ^{1}H NMR, and LC–MS. The structure of compound **(3a-3j)** was confirmed by the absence of hydrazide protons at δ 4.80 (NH_2) and δ 10.10 (NH) in the ^{1}H NMR spectrum; ^{1}H NMR spectrum of compound **(3a-3d)** displayed multiplets in the region between δ 7.07–8.9 for different aromatic protons. In the IR spectra of compound **3a** absorption band has been observed at 1645 cm^{-1} indicating the –C=N vibrations, which confirmed the formation of the oxadiazole ring. Stretching at 1174 cm^{-1} represents C–O–C bending vibration. Mass spectra of compound **3a** displayed a molecular ion base peak at m/z 304 which supports the structure of compound **3a**.

Spectroscopic data.

2-(2,4-Difluoro-phenyl)-5-(4-nitro-phenyl)-[1,3,4oxadiazole (3a). Yield 92%, m.p. 205°C; IR spectrum, ν, cm^{-1}: 1645 (C=N), 1174 (C–O–C) 1506 (C=C Ar), 1421 (N-O).^{1}H NMR spectrum, *δ*, ppm :7.05 (s, 1H), 7.06 (d, J=8.4 Hz, 1H), 8.19 (d, J=8.4 Hz, 1H), 8.2 (d, J=6.4, 2H), 8.4 (d, J=6.4, 2H). (MS: *m/z*: 304 $(M+H)^+$.

2-(2,4-Difluoro-phenyl)-5-(3-nitro-phenyl)-[1,3,4] ox diazole (3b). Yield 91%, m.p. 252°C; IR spectrum, ν, cm^{-1}: 1593 (C=N), 1177 (C–O–C), 1531 (C=C aromatic ring), 1450(N-O); ^{1}H NMR spectrum, *δ*, ppm: 7.4 (d, J=8.7Hz, 1H), 7.5(d, J=8.7 Hz, 1H), 7.8 (s, 1H), 8.5(d, J=7.6 Hz, 1H), 8.6 (d, J=7.6Hz, 1H), 9.01(s, 1H). (MS: *m/z*: 304 $(M+H)^+$.

2-(2,4-Difluoro-phenyl)-5-phenyl-[1,3,4] oxadiazole (3c).

Yield 90%, m.p.125°C; IR spectrum, ν, cm^{-1}: 1604 (C=N), 1146 (C–O–C), 3061 (Ar-CH), 1546 (Ar C=C). ^{1}H NMR spectrum, *δ*, ppm: 7.07 (d, J= 8.3 Hz,1H), 7.09 (d, J= 8.3 Hz, 1H), 7.5 (s, 1H), 7.6 (d, J= 7.3 Hz, 1H), 8.1(dd, J= 6.4, 7.3 Hz, 2H), 8.2 (d, J= 6.4Hz, 2H) .(MS: *m/z*: 259 $(M+H)^+$.

(2,4-Difluoro-phenyl)-5-(4-methoxy-phenyl)-[1,3,4]oxadiazole (3d).Yield 87%, m.p.139°C; IR spectrum, ν, cm^{-1}: 1606 (C=N), 995(C–O–C), 1507 (C=C aromatic ring), 2853(C-OCH_3). ^{1}H NMR spectrum, *δ*, ppm : 3.89 (s, 3H, OCH_3), 7.048 (d, J=8.7 Hz, 2H), 7.26(d, J=8.7 Hz, 2H), 8.07(d, J=6.73 Hz, 1H), 8.08 (s, J=6.4Hz,1H), 8.17 (s,1H). (MS: *m/z*: 289 (M +

Table 1. Physical data of synthesized compounds 3(a-j) using ultrasonic irradiation method

			Microwave Irradiation		
Entry	Compound	R	ReactionTime (min)	Yield (%)	M.P.(^{0}C)
1	3a	4-NO_2H	15	92	205
2	3b	3-NO_2	15	91	252
3	3c	H	20	90	125
4	3d	4-OCH_3	20	87	139
5	3e	4-Cl	20	86	155-160
6	3f	4-NH_2	20	89	87
7	3g	4-CH_3	15	87	235
8	3h	2-Cl	20	86	128
9	3i	4-OH	20	85	191
10	5j	3-OH	20	84	155-157

Conclusions

In summary, we have reported an efficient method for the synthesis of 1,3,4-oxadiazoles derivative. We achieved this derivative by using 2,4-difluorobenzohydrazide with substituted benzoic acid in presence in the presence of phosphorus oxychloride as a catalyst under ultrasonic irradiation with silica-supported. A wide variety of aromatic 2,4-difluorobenzohydrazide as well as substituted benzoic acid exhibit oxidative cyclization to yield corresponding 1,3,4-oxadiazoles. The structures of these compounds are elucidated by their spectral data (IR, ^{1}H NMR, and MS). Maximum Yield, Short reaction time, and use of Silica and Ultrasonic are merits of the developed protocol.

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Reference

1. Talath,S.,Gadad,A K.Eur.J.Med.Chem. 2006, vol. 41,no.8,p.918. doi.10.1016/j.ejmech.2006.03.027.

2. Iqbal, R., Zareef, M., Ahmed, S., Zaidi, J. H., Arfan, M., Shafique, M., Al-Masoudi, N. A. *J. Chin. Chem. Soc*. 2006, vol. 53, no. 3, p. 689. doi.10.1002/jccs.200600091.

3. Kavitha, Selvaraj, Kannan, Kulanthai, Gnanavel, Sadhasivam. *Saudi. Pharm.* J. 2017, vol. 25, no. 3, p. 337. doi.10.1016/j.jsps.2016.07.004.

4. Wang, Pei Yi, Shao, Wu Bin, Xue, Hai Tao, Fang, He Shu, Zhou, Jian, Wu, Zhi Bing, Song, BaoAn,Yang,Song. Res. Chem. Intermediat.2017, vol. 43, no. 11, p. 6115. doi.10.1007/s11164-017-2980-x.

5. Zarghi, A.; Tabatabai, S.A.; Faizi, M.; Ahadian, A.; Navabi, P.; Zanganeh, V.;Shafiee, A. **2005**, *15*, 1863–1865

6. He, X.; Li, X.; Liang, J.; Cao, C.; Li, S.; Zhang, T.; Meng, F. **2018**, *28*, 847–852.

7. Girish, V., Khanum N., Gurupadaswamy, H. D., Khanum S. A., Russ. *J. Bioorgan. Chem.* 2014, vol.40,no.3,p.330.doi.10.1134/S1068162014030066.

8. Iqbal, R., Zareef, M., Ahmed, S., Zaidi, J. H., Arfan, M., Shafique, M., Al-Masoudi, N. A. *J. Chin. Chem. Soc*. 2006, vol. 53, no. 3, p. 689. doi.10.1002/jccs.200600091.

9. Selvaraj, K.; Kulanthai, K.; Sadhasivam, G. **2017**, 337–345.

10. Padmavathi, V.; Reddy, G.S.; Padmaja, A.; Kondaiah, P. **2009**, *44*, 2106–2112.

11. Bondock, Samir, Adel, Shymaa, Etman, Hassan A., Badria, Farid A. *Eur.J. Med. Chem.* 2012, vol. 48, p. 192. doi.10.1016/j.ejmech.2011.12.013.

12 . Liao, Jun, Yang, Fan, Zhang, Lei, Chai, Xiaoyun, Zhao, Qingjie, Yu, Shichong, Zou, Yan, Meng, Qingguo, Wu, Qiuye. *Arch. Pharm. Res.*2015, vol. 38, no. 4. doi.10.1007/s12272-014-0378-5.

13. El-Emam, Ali A., Al-Deeb, Omar A., Al-Omar, Mohamed, Lehmann, Jochen.***Bioorg. Med. Chem***. 2004, vol. 12, no. 19, p. 5107. doi.10.1016/j.bmc.2004.07.033.

14. Almasirad, Ali, Shafiee, Abbas, Abdollahi, Mohammad, Noeparast, Amir, Shahrokhinejad, Nasir, Vousooghi, Nasim, Tabatabai, Sayyed Abbas, Khorasani, Reza. Med. Chem. Res 2011, vol. 20, no. 4, p. 435. doi.10.1007/s00044-010-9335-0.

15. Oliveira, Cledualdo Soares De, Lira, Bruno Freitas, Barbosa-filho, José Maria, Gonçalo, Jorge, Lorenzo, Fernandez, Athayde-filho, Petrônio Filgueiras De. 2012, 10192-10231p., ISBN5583321679.doi.10.3390/molecules170910192.

16. Kangani, Cyrous O., Kelley, David E., Day, Billy W.2006,vol.47,p.6497.doi.10.1016/j.tetlet.2006.07.032.
17. Guo, Shenghong A. Dai Yi-syuan. 2015. doi.10.1007/s11164-015-2128-9.

18. Montazeri, Nasser, Rad-moghadam, Kurosh. 2008,vol.19,p.1143.doi.10.1016/j.cclet.2008.06.050.

19. Stabile, Paolo, Lamonica, Alessandro, Ribecai, Arianna, Castoldi, Damiano, Guercio, Giuseppe, Curcuruto, Ornella. *Tetrahedron Lett* 2010, vol. 51,no.37,p.4801. doi.10.1016/j.tetlet.2010.06.139.

20. Rostamizadeh, Shahnaz, Housaini, S. A. Ghase. *Tetrahedron Lett*. 2004, vol. 45, no. 47, p. 8753. doi.10.1016 j.tetlet.2004.09.095.