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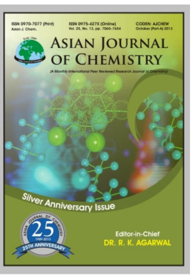

Microwave Promoted Synthesis of 2,5-Diaryl-1,3,4-oxadiazoles Using Melamine Formaldehyde Resin Supported Sulfuric Acid

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A simple and convenient procedure for the synthesis of some 2,5-diaryl-1,3,4-oxadiazoles by reaction of carboxylic acids with (un)substituted benzoic acid hydrazides using melamine formaldehyde resin supported sulfuric acid as dehydration reagent under microwave-accelerated solvent-free condition has been developed. Structures of the corresponding products were elucidated by IR and ^{1}H NMR spectra and elemental analysis. Results showed that most of the synthesized compounds displayed large Stokes shifts of fluorescence emission.

Key Words: 1,3,4-Oxadiazoles, Melamine formaldehyde resin, Sulfuric acid, Microwave irradiation.

INTRODUCTION

As a kind of cyclic compounds containing one oxygen and two nitrogen atoms in a five-membered ring, 1,3,4-oxadiazoles are known to possess an extensive spectrum of pharmacological activities, such as antiinflammatory, analgesic, antimicrobial, antitumor, anticonvulsant, herbicidal, antioxidant and antiviral effects *etc*.[1,2], in particularly, 2,5-disubstituted 1,3,4-oxadiazoles are of considerable interest due to their applications in organic light emitting diodes, photoluminescence, polymers and material science[3,4]. As a consequence of these characteristics, the synthesis of these compounds has attracted significant interest.

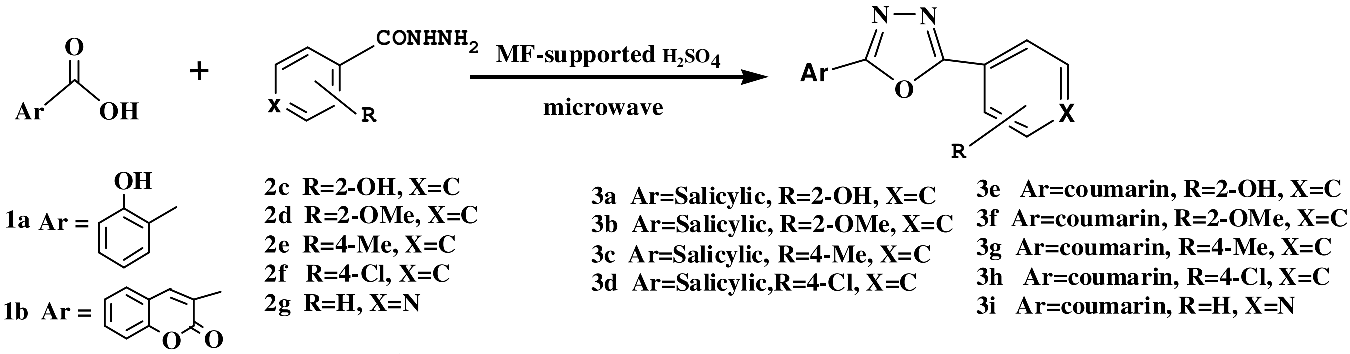
The most general procedure for the preparation of 2,5-disubstituted 1,3,4-oxadiazoles involves cyclization of diacylhydrazides in the presence of a dehydrating agent, such as boron trifluoride etherate, thionyl chloride and phosphorus oxychloride[5,6], usually under harsh reaction conditions. Several facile examples have been reported for the synthesis of 1,3,4- oxadiazoles[7,8], even though most of the procedures that have been described for the reaction use toxic reagents or solvents, or have long reaction times, which could not be adapted to the principles of green chemistry and furthermore repeatability is low.

Microwave irradiation may be considered to be an efficient tool in organic synthesis in terms of substantial reduction in time and considerable saving in the energy requirements. Meanwhile, the use of polymer-supported reagents to effect synthetic transformations in solution has received considerable attention, which could be conveniently removed from the reaction mixture by filtration and reactions may be monitored by conventional analytical techniques. A few examples have been reported to proceed by reacting carboxylic acids and acid hydrazides in the presence of polymer-supported reagents, such as Burgess reagent and PEG, under microwave heating conditions[9,10]. However, the widely usable polymer-supported heterogeneous catalysts are still in great demand. Melamine-formaldehyde resin (MF) is porous and has suitable chemical and physical properties allowing the supporting of sulfuric acid as a dehydrating agent for the synthesis of nitriles from aldoxime[11].

Herein, we report a procedure for the microwave-assisted synthesis of 2,5-disubstituted 1,3,4-oxadiazoles from carboxylic acids and acid hydrazides in the presence of catalytic amounts of melamine-formaldehyde-supported sulfuric acid under solvent-free condition (**Scheme-I**), together with the analysis for their spectroscopic properties.

EXPERIMENTAL

Melting points were determined with an electrothermal micromelting point apparatus and uncorrected. IR spectra were recorded using KBr pellets on a Nicolet Inpact 170S FT-IR spectrometer and ^{1}H-NMR spectra on a Braker AM 300 NMR spectrometer using Me_4Si as internal standard. Elemental analyses were performed on a Perkin-Elmer Model 240 analytical apparatus. UV spectra were taken on a UV-265 recording spectrophotometer and the emission spectra on a Hitachi F-4500 fluorescence spectrophotometer. The microwave irradiations were performed in an unmodified Galanz WD900M domestic microwave oven. All compounds were purified by thick layer chromatography using silica gel from Merck.



Scheme-I: Synthesis of 2,5-diaryl-1,3,4-oxadiazoles

Preparation of melamine-formaldehyde-supported sulfuric acid: The resin was prepared by mixing melamine and formaldehyde (with a mass ratio of 1: 0.76) at the alkaline solution of sodium hydroxide following a previously reported procedure[12] .

To a solution of melamine-formaldehyde resin (6 g) in 60 mL of acetone, commercial concentrated sulfuric acid (98 %, 6 mL) was added dropwise over a period of 0.5 h at room temperature. After the addition was complete, the mixture was shaken for 0.5 h. The precipitate was collected by filtration and a white solid of 11.5 g was obtained.

General procedure for the preparation of compounds 3a-3i: A mixture of carboxylic acid (**1a-1b**, 1 mmol), (un) substituted benzoic acid hydrazides (2c-2g, 1 mmol) and melamine-formaldehyde-supported sulfuric acid (1.2 mmol) was mixed using a pestle and mortar until a fine and homogeneous powder was obtained. Then the mixture was wrapped in an alumina bath and was irradiated inside a microwave oven for 6-8 min. On completion of the reaction, followed by TLC examination using petroleum ether-ethyl acetate (2:1), the reaction mixture was diluted with water (30 mL) and the precipitate was collected by filtration. The crude product was subjected to chromatography on silica gel to afford the 1,3,4-oxadiazoles **3a-3i**.

Ultraviolet and fluorescent spectra: All sample solutions were filtered through 0.45 μm Teflon membrane filters to remove interfering dust particles or fibers. For all measurements the path length was 1 cm with a cell volume of 3 mL. The absorption and emission spectra of these compounds were measured in methanol and have been corrected for the spectral response of the detection system. A solution of quinine hydrogen sulfate in 0.05 mol/L sulfuric acid (ϕ = 0.546) was used as the standard for determination of the quantum yield of fluorescence.

RESULTS AND DISCUSSION

Reaction of the corresponding benzoic acid with some readily available acid hydrazides upon treatment with a catalytic amount of melamine-formaldehyde-supported sulfuric acid under microwave irradiation gave 1,3,4-oxadiazoles **3a**-**3i** in good yields, with an optimum ratio of 10 mmol/g for sulfuric acid to the resin nearly. Thus, saving time, solvent and workup compared to their synthesis under conventional heating conditions.

Formation of 1,3,4-oxadiazoles was confirmed by the appearance of very strong absorption maxima nearly at 1675 cm^{-1} for C=N, at 1265 and 1020 cm^{-1} for characteristic stretching vibrations of the =C-O-C= fragment of the oxadiazole ring observed in each case in the IR spectra. The structures were further confirmed by ^1H NMR and all found of C, H, N of **3a-3i** are good agreement with the calculated values. The specific details of the products are listed below.

2,5-Di(2-hydroxyophenyl)-1,3,4-oxadiazole (3a): The reaction time is 5 min and the compound was obtained as white powder, 2.75 g, yielding in 88%. m.p. 207-209 °C; Anal. Calcd. for $C_{14}H_{10}N_2O_3$: C, 66.14; H, 3.96; N, 11.02. Found: C, 66.02; H, 3.90; N 10.94 %; IR (KBr, ν_{max}, cm^{-1}): 3452, 3200, 3052, 1682, 1527, 1270, 1026;^1H NMR (DMSO-d_6) δ:7.16 (m,4H,ArH), 7.47 (m,4H,Ar-H), 10.12- 10.19 (2H, s, OH).

2-[5-(2-Methoxy-phenyl)[1,3,4]oxadiazol-2-yl]phenol (3b): The reaction time is 6 min and the compound was obtained as white powder, 2.73 g, yielding in 80 %. m.p. 99-101 °C; Anal. Calcd. for $C_{15}H_{12}N_2O_3$: C, 67.16; H, 4.51; N, 10.44. Found: C, 66.92; H, 4.90; N 10.14 %; IR (KBr, ν_{max}, cm^{-1}): 3512, 3057, 1678, 1522, 1265, 1016; ^1H NMR (DMSO-d_6) δ: 3.89 (3H, s, CH_3O), 7.05-7.82 (4H, m, Ar-H), 7.84 (2H, d, *J* = 9.1Hz, Ar-H), 8.12(2H, d, *J* = 7.2Hz, Ar-H), 10.38 (1H, s, OH).

2-(5-*p*-Tolyl[1,3,4]oxadiazol-2-yl)phenol (3c): The reaction time is for 4 min and the compound was obtained as white powder, 2.06 g, yielding in 82 %. m.p. 163-165 °C; Anal. Calcd. for $C_{15}H_{12}N_2O_2$: C, 71.42; H, 4.79; N, 11.10. Found: C, 71.12; H, 4.99; N, 11.30 %; IR (KBr, ν_{max}, cm^{-1}): 3512, 3057, 1659, 1522, 1263, 1009; ^1H NMR (DMSO-d_6) δ: 2.54 (3H, s, CH_3), 7.12-8.22 (4H, m, Ar-H), 7.49 (2H, d, *J* = 9.1Hz, Ar-H), 7.79 (2H, d, *J* = 7.2 Hz, Ar-H), 10.18 (1H, s, OH)

2-[5-(4-Chloro-phenyl)[1,3,4]oxadiazol-2-yl]phenol (3d): The reaction time is 6 min and the compound was obtained as white powder, 2.31 g, yielding in 85 %. m.p. 211-213 °C; Anal. Calcd. for $C_{14}H_9ClN_2O_2$: C, 61.66; H, 3.33; N, 10.27. Found: C, 61.43; H, 3.18; N, 10.17 %; IR (KBr, ν_{max}, cm^{-1}): 3442, 3037, 1679, 1542, 1265, 1019; ^1H NMR (DMSO-d_6) δ: 7.22-7.42 (4H, m, Ar-H), 7.49 (2H, m, Ar-H), 7.59 (2H, m, Ar-H), 10.28 (1H, s, OH)

3-[5-(2-Hydroxy-phenyl)[1,3,4]oxadiazol-2-yl]chromen-2-one(3e): The reaction time is 5 min and the compound was obtained as white powder, 2.44 g, yielding in 80 %. m.p. 229-231 °C; Anal. Calcd. for $C_{17}H_{10}N_2O_4$: C, 66.67; H, 3.29; N, 9.15 %. Found: C, 66.53; H, 3.33; N, 9.08 %. IR (KBr, ν_{max}, cm^{-1}): 3155, 1744, 1673, 1607, 1258, 1024;^1H NMR (DMSO-d_6) δ: 7.04-7.12 (m, 2H, Ar-H), 7.40- 7.49 (m,3H, Ar-H), 7.82

TABLE-1
OPTICAL PARAMETERS OF 2,5-DIARYL-1,3,4-OXADIAZOLES

Compound	λ_{abs} (nm)	ε (L mol^{-1} cm^{-1})	λ_{em} (nm)	Stokes shift (nm)	Quantum yield (ϕ)
3a	323	25696	433	110	0.32
3b	313	20862	444	131	0.18
3c	330	30700	427	97	0.13
3d	315	30366	475	160	0.11
3e	345	35600	455	110	0.25
3f	342	33890	462	120	0.20
3g	344	34100	445	101	0.19
3h	318	31400	421	103	0.14
3i	321	32120	432	111	0.22

(m, 2H, Ar-H), 7.96 (m, 1H, Ar-H), 9.01(1H, s, 4-H), 10.20 (1H, s, OH).

3-[5-(2-Methoxy-phenyl)[1,3,4]oxadiazol-2-yl]chromen-2-one(3f): The reaction time is 7 min and the compound was obtained as white powder, 2.68 g, yielding in 84 %. m.p. 157-159 °C; Anal. Calcd. for $C_{18}H_{12}N_2O_4$: C, 67.50; H, 3.78; N, 8.75%. Found: C, 67.41; H, 3.70; N, 8.65 %. IR (KBr, ν_{max}, cm^{-1}): 1744, 1680, 1607, 1260, 1020; ^{1}H NMR (DMSO-d_6) δ: 3.95 (3H, s, OCH_3), 7.12-7.26 (m, 2H, Ar-H), 7.46-7.74 (m, 4H, Ar-H),7.93 (m, 2H, Ar-H), 8.91 (1H, s, 4-H).

3-(5-*p*-Tolyl-[1,3,4]oxadiazol-2-yl)chromen-2-one (3g): The reaction time is 4 min and the compound was obtained as white powder, 2.67 g, yielding in 88 %. m.p. 203-204 °C; Anal. calcd. for $C_{18}H_{12}N_2O_3$: C, 71.05; H, 3.97; N, 9.21 %. Found: C,70.94; H, 3.92; N, 9.17 %. IR (KBr, ν_{max}, cm^{-1}): 1747, 1677, 1605, 1262, 987; ^{1}H NMR (DMSO-d_6) δ: 2.23 (3H, s, CH_3), 7.10-7.24 (m, 2H, Ar-H), 7.44-7.78 (m, 4H, Ar-H), 7.84-7.90 (m, 2H, Ar-H), 8.81 (1H,s, 4-H).

3-[5-(4-Chloro-phenyl)[1,3,4]oxadiazol-2-yl]chromen-2-one(3h): The reaction time is 4 min and the compound was obtained as white powder, 2.72 g, yielding in 84 %. m.p. 259-260 °C; IR (KBr, ν_{max}, cm^{-1}): 1742, 1678, 1603, 1265, 1018; Anal. Calcd. for $C_{17}H_9ClN_2O_3$: C, 62.88; H, 2.79; N, 8.63 %. Found: C, 62.78; H, 2.71; N, 8.55 %. ^{1}H-NMR (DMSO-d_6) δ: 7.23-7.36 (m, 2H, Ar-H), 7.64-7.78 (m, 3H, Ar-H), 7.94-8.10 (m, 3H, Ar-H), 8.89 (1H,s,4-H).

3-(5-Pyridin-4-yl[1,3,4]oxadiazol-2-yl)chromen-2-one (3i): The reaction time is 5 min and the compound was obtained as pale yellow powder, 2.62 g, yielding in 90 %. mp. 279-280 °C; IR (KBr, ν_{max}, cm^{-1}): 1740, 1672, 1607, 1266, 1013; Anal. Calcd. for $C_{16}H_9N_3O_3$: C, 65.98; H, 3.11; N, 14.43 %. Found: C, 65.92; H, 3.15; N, 14.39 %. ^{1}H NMR (DMSO-d_6) δ: 7.23-7.42 (m, 2H, Ar-H), 7.68-7.80 (m, 2H, Ar-H), 8.00- 8.03 (m, 2H, Ar-H), 8.12-8.18 (m, 2H, Ar-H), 8.97 (1H, s, 4-H).

Spectral luminescence properties: Absorption spectra and fluorescence spectra with a concentration of 10 μmol/L were measured in methanol and the results were listed in Table-1. It is clearly demonstrated that all of the title compounds exhibit intense UV absorption bands with an absorption λ_{max} nearly at 330 nm and the maximum emission wavelength nearly at 475 nm with a Stokes shift of 97-160 nm for **3a-i**, respectively. Taking into account a large Stokes shift of the fluorescence spectra of molecules **3a-3i**, compounds of this type have potential for use as fluorescent probe for photoluminescence.

Conclusion

In summary, a one-step solvent-free microwave assisted protocol for the synthesis of 2,5-diaryl-1,3,4-oxadiazoles by dehydration of diacylhydrazides using supported sulfuric acid on melamine-formaldehyde resin has been developed, which was a green process and the catalyst could be reused for several uses.

REFERENCES

1. R. Franski, *Asian J. Chem.*, **17**, 2063 (2005).
2. A. Husain and M. Ajmal, *Acta Pharm.*, **59**, 223 (2009).
3. A.V. Gaenko, A. Devarajan, I.V. Tselinskii and U. Ryde, *J. Phys. Chem. A*, **110**, 7935 (2006).
4. S. Quan, F. Teng, Z. Xu, L. Qian, T. Zhang, D. Liu, Y. Hou, Y. Wang and X. Xu, *J. Luminescence*, **124**, 81 (2007).
5. S. Wang, Z.T. Li and W.T. Hua, *Synth. Commun.*, **32**, 3339 (2002).
6. M. Demina, G. Sarapulova, A. Borisova, L.I. Larina and A.S. Medvedeva, *Russ. J. Org. Chem.*, **10**, 1522 (2003).
7. F. Bentiss and M. Lagrenee, *J. Heterocycl. Chem.*, **36** 1029 (1999).
8. M. Dabiri, P. Salehi, M. Baghbanzadeh and M. Bahramnejad, *Tetrahedron Lett.*, **47**, 6983 (2006).
9. C.T. Brain, J.M. Paul, Y. Loong and P.J. Oakley, *Tetrahedron Lett.*, **40**, 3275 (1999).
10. Z. Li, J.L. Yu, R.B. Ding, Z.Y. Wang and X.C. Wang, *Synth. Commun.*, **34**, 2981 (2004).
11. R. Rezaei and M. Karami, *Chin. Chem. Lett.*, **22**, 815 (2011).
12. M. Gordon, A. Halliwell and T. Wilson, *Appl. Polym. Sci.*, **10**, 1153 (1966).