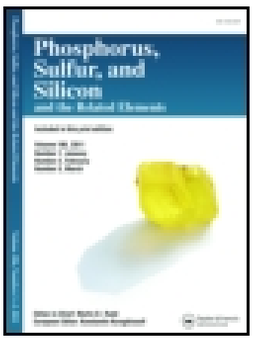

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ONE-POT THREE-COMPONENT REACTION OF *N*-ISOCYANIMINO-TRIPHENYLPHOSPHORANE (Ph_3PNNC), ACENAPHTHOQUINONE AND AN AROMATIC CARBOXYLIC ACID IN WATER

Ali Jafari[1], Ali Ramazani[*,1], Fariba Sadri[2] and Sang Woo Joo[3]

[1]Department of Chemistry, University of Zanjan, P O Box 45195-313, Zanjan, Iran,

[2]Department of Chemistry, Payame Noor University, P O BOX 19395-4697 Tehran, Iran

[3]School of Mechanical Engineering, Yeungnam University, Gyeongsan 712-749, Republic of Korea, E-mail: swjoo@yu.ac.kr

[*]Corresponding Author Email: aliramazani@gmail.com

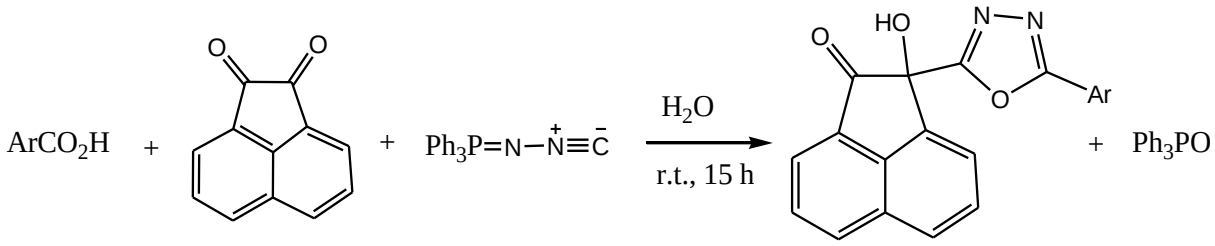
Keywords

N-isocyanimino-triphenylphosphorane (Ph_3PNNC); water; 1,3,4-oxadiazoles; *aza*-Wittig reaction; aromatic carboxylic acid.

Abstract

Water was used as an efficient green solvent for the synthesis of sterically congested 1,3,4-oxadiazoles derivatives via a one-pot, three component reaction of various aromatic carboxylic acids, acenaphthoquinone and N-isocyanimino-triphenylphosphorane (Ph_3PNNC) at RT (20–26 °C) for 15 h. The remarkable features of this “green” methodology include high yield of

products, water as the solvent, short reaction time, operational simplicity, environmentally benign and the absence of any volatile or hazardous organic solvents.



INTRODUCTION

The *aza*-Wittig-type reaction has attracted much attention recently because of its high potential for the synthesis of a wide variety of nitrogen heterocycles, which can be attributed in the preparation of functionalized iminophosphoranes.[1] Through *aza*-Wittig reaction, iminophosphoranes with isocyanates, carbon dioxide, or carbon disulfide can easily be converted into functionalized hetero-cumulenes.[1] The nucleophilicity at the nitrogen is an important factor in the use of these iminophosphoranes as *aza*-Wittig reagents. Iminophosphoranes are important reagents in organic chemistry, especially in the producing of naturally occurring products, compounds with biological and pharmacological activity.[1] In the last years, several preparative procedures have been reported for the preparations and synthetic applications of iminophosphoranes.[1] It is expected *N*-isocyanimino-triphenylphosphorane (Ph_3PNNC) **3** to have synthetic potential because it develops a reaction system in which the iminophosphorane group can react with a reagent having a carbonyl functionality. [1]

There is increasing interest in the chemistry of heterocyclic compounds because of their vast distribution in natural compounds, their applications in pharmaceuticals, agrochemicals, and industrial chemicals, *etc*. 1,3,4-Oxadiazole derivatives are an important class of heterocycles, which possess pharmaceutical and biological activities, such as antimicrobial,[2,3] antimycobacterial,[4] anti-inflammatory,[5] anti-allergic,[6] antifungal and genotoxic activities.[7] Nowadays, many organic compounds can be synthesized in multicomponent reactions (MCRs).[8] An important class of MCRs are the isocyanides-based multicomponent reactions (IMCRs). IMCRs are especially interesting because they are more diverse and versatile than non-IMCRs.[9–18] Several methods have been reported in the literature for the synthesis of 1,3,4-oxadiazoles.

These protocols are multistep in nature.[19–21] In recent years, a one-pot method for the synthesis of 1,3,4-oxadiazole derivatives from *N*-isocyanimino-triphenylphosphorane (Ph_3PNNC) has been established.[22–26]

One important aspect of green chemistry is the elimination of solvents in chemical processes or the replacement of hazardous solvents with relatively benign solvents. Water being the most environmentally benign, cleanest, cheapest, nonflammable, and naturally occurring solvent having high specific heat capacity is the primary choice. Moreover, in water significant rate enhancement was observed in many reactions,[27] because of hydrophobic interactions that induce a favorable aggregation of polar components in water.[28]

In continuation of our ongoing effort to develop new methods using water in organic synthesis,[29] in this paper we describe the one-pot reaction between various aromatic carboxylic acids **(1)**, acenaphthoquinone (**2)** and *N*-isocyanimino-triphenylphosphorane (Ph_3PNNC) **(3)** in water at RT (20–26 °C) to give sterically congested 1,3,4-oxadiazole derivatives (**4**, Scheme 1).

RESULTS AND DISCUSSION

Herein, the sterically congested 2,5-disubstituted 1,3,4-oxadiazoles derivatives **(4**) were synthesized *via* a one-pot three-component reaction of various aromatic carboxylic acids **(1)**, acenaphthoquinone (**2)** and *N*-isocyanimino-triphenylphosphorane (Ph_3PNNC) **(3)** in water as a green solvent at RT (20–26 °C) in 15 h (Scheme 1). The *N*-isocyanimino-triphenylphosphorane (Ph_3PNNC) **3** was prepared based on reported procedure.[30,31]

In our initial investigation to study the solvent effect, the reaction of benzoic acid, acenaphthoquinone and *N*-isocyanimino-triphenylphosphorane (as a model reaction) was studied in different solvents, like ethanol, methanol, dichloromethane, toluene, acetonitrile and water (Table 1, entries 1-6). Isolated yield of the desired product **(4a)** was 84% when the reaction was carried out in water as a solvent at RT (20–26 °C) for 15 h (Table 1, entry 6). Consequently, water was selected as the best reaction solvent. The results of this study are summarized in Table 1.

After selecting an appropriate solvent, to explore the scope of water effect as reaction solvent in the preparation of sterically congested 1,3,4-oxadiazoles derivatives, one-pot three-component reaction of an aromatic carboxylic acid derivative (1 mmol) with acenaphthoquinone (1 mmol) and *N*-isocyanimino-triphenylphosphorane (Ph_3PNNC) (1 mmol) were investigated in water at RT (20–26 °C). The reaction proceeds smoothly and cleanly under mild conditions in water that is considerable to be a green chemistry method.

All of the prepared products are known compounds and were identified by comparing their physical and spectral data with those reported in the literature.[32] The data of the prepared compounds are similar to their previously reported data[32] under the same analytical conditions.

A proposed mechanism for the formation of products **4a-p** is shown in Scheme 2. On the basis of the chemistry of isocyanides,[33] it is reasonable to assume that the first step may involve nucleophilic addition of the *N*-isocyanimino-triphenylphosphorane (Ph_3PNNC) **(3)** to acenaphthoquinone **(2)**, which is facilitated by its protonation with the aromatic acid **(1)**, leading to nitrilium intermediate **6**. This intermediate may be attacked by the conjugate base of acid **(1)**

to form 1:1:1 adduct **(7)**. This adduct may undergo intramolecular *aza*-Wittig reaction of iminophosphorane moiety with the ester carbonyl to afford the sterically congested 1,3,4-oxadiazole derivatives **(4)** by removal of triphenylphosphine oxide **(5)** from intermediate **(8)** (**See Scheme 2**).

EXPERIMENTAL

N-isocyanimino-triphenylphosphorane (Ph_3PNNC) **3** was prepared based on reported procedure.[30,31] Other starting materials and solvents were obtained from Merck (Germany) and Fluka (Switzerland) and were used without further purification. The progress of the reaction was monitored by thin layer chromatography (TLC) technique. Melting points were measured on an Electrothermal 9100 apparatus and are uncorrected. IR spectra were measured on a Jasco 6300 FT-IR spectrometer. ^1H and ^{13}C NMR spectra ($CDCl_3$) were recorded on a BRUKER DRX-250 AVANCE spectrometer at 250.0 and 62.5MHz, respectively. Mass spectra were recorded on a FINNIGAN-MATT 8430 mass spectrometer operating at an ionization potential of 20 eV. Preparative layer chromatography (PLC) plates were prepared from Merck silica gel (F_{254}) powder.

General Procedure for the synthesis of sterically congested 2,5-disubstituted 1,3,4-oxadiazoles derivatives (4a-p)

A mixture of *N*-isocyanimino-triphenylphosphorane (Ph_3PNNC) (1.0 mmol, 0.302 g), acenaphthoquinone (1.0 mmol, 0.182 g) and an aromatic carboxylic acid (1.0 mmol (**1a**: 0.136 g, **1b**: 0.201 g, **1c**: 0.147 g, **1d**: 0.136 g, **1e**: 0.178 g, **1f**: 0.173 g, **1g**: 0.214 g, **1h**: 0.215 g, **1i**: 0.172 g, **1j**: 0.157 g, **1k**: 0.140 g, **1l**: 0.136 g, **1m**: 0.152 g, **1n**: 0.182 g, **1o**: 0.136 g, **1p**: 0.150 g.)) in

distilled water (5 mL) was stirred at RT (20–26 °C) for 15 h. After completing the reaction, the resulting mixture was extracted in dichloromethane. The solvent was removed under reduced pressure, and the viscous residue was purified by preparative layer chromatography (PLC) (silica gel powder, F_{254}; petroleum ether-ethyl acetate (4:1)).

2-hydroxy-2-(5-phenyl-1,3,4-oxadiazol-2-yl)-1(2*H*)-acenaphthylenone (4a, $C_{20}H_{12}N_2O_3$)

Yellow powder; yield 84%; R_f = 0.36 (petroleum ether/ethyl acetate, 4/1); mp: 162-164 ºC. ^{1}H NMR (250.13 MHz, $CDCl_3$) δ = 4.59 (br s, OH); 7.40 - 8.30 (m, 11CH_{arom}) ppm. ^{13}C NMR (62.53 MHz, $CDCl_3$) δ = 87.74 (C-OH); 122.56, 123.88, 126.97, 127.13, 128.79 and 132.85 (6CH of naphthalene ring); 128.96, 129.07 and 132.02 (5CH of phenyl group); 129.60 (C of phenyl group); 123.22, 127.80, 135.12 and 142.96 (4C of naphthalene ring); 161.05 and 166.13 (2C=N of oxadiazole); 198.51 (C=O) ppm. IR (KBr, υ $_{max}$) = 3366, 3073, 1718, 1603, 1448 and 1012 cm^{-1}. MS (EI, 20 eV): *m/z* (%)= 328 (M^+), 198 (16), 182 (34), 154 (83), 126 (100), 98 (28), 85 (28), 76 (39), 62 (38) and 43 (45).

2-[5-(4–bromophenyl)-1,3,4–oxadiazol–2–yl]–2–hydroxy–1(2H)–acenaphthylenone (4b, $C_{20}H_{11}BrN_2O_3$)

Yellow powder; yield 81%; R_f = 0.33 (petroleum ether/ethyl acetate, 4/1); mp: 151-153 ºC. ^{1}H NMR (250.13 MHz, $CDCl_3$) δ = 4.57 (br s, OH); 7.57 (d, $^3J_{HH}$ = 8.3 Hz, 2CH_{arom}); 8.03 (d, $^3J_{HH}$ = 8.3 Hz, 2CH_{arom}); 7.69 - 7.86 and 8.09-8.30 (m, 6CH_{arom}) ppm. ^{13}C NMR (62.53 MHz, $CDCl_3$) δ = 86.50 (C-OH); 122.59, 123.96, 127.03, 128.51, 128.83 and 132.94 (6CH of naphthalene ring); 129.08 and 132.33 (4CH of benzene ring); 126.80 and 129.50 (2C of benzene ring); 122.12, 130.98, 134.22 and 140.25 (4C of naphthalene ring); 164.02 and 165.03 (2C=N of oxadiazole);

202.02 (C=O) ppm. IR (KBr, υ_{max}) = 3204, 3077, 1733, 1600, 1481 and 1007 cm^{-1}. MS (EI, 20 eV): *m/z* (%) = 407 (M^+), 198 (8), 182 (37), 154 (78), 126 (100), 98 (22), 85 (22), 75 (55), 62 (45) and 50 (18).

4-[5-(1-hydroxy-2-oxo-1,2-dihydro-1-acenaphthylenyl)-1,3,4-oxadiazol-2-yl]benzonitrile (4c, $C_{21}H_{11}N_3O_3$)

Yellow powder; yield 74%; R_f = 0.30 (petroleum ether/ethyl acetate, 4/1); mp: 161-163 ºC. ^{1}H NMR (250.13 MHz, $CDCl_3$) δ = 3.63 (s, OH); 7.71 - 8.33 (m, $10CH_{arom}$) ppm. ^{13}C NMR (62.53 MHz, $CDCl_3$) δ = 77.31 (C-OH); 122.07, 127.13, 127.60, 128.45, 129.09 and 132.75 (6CH of naphthalene ring); 115.51 and 132.62 (4CH of benzene ring); 109.98 and 128.90 (2C of benzene ring); 124.00, 133.02, 135.05 and 143.03 (4C of naphthalene ring); 161.03 and 165.13 (2C=N of oxadiazole); 192.21 (C=O) ppm. IR (KBr, υ_{max}) = 3439, 3209, 1729, 1604, 1495 and 1014 cm^{-1}. MS (EI, 20 eV): *m/z* (%) = 353 (M^+), 197 (17), 182 (32), 154 (73), 130 (100), 126 (85), 101 (90), 75 (86), 62 (47), 50 (48) and 42 (30).

2–hydroxy–2-[5-(3–methylphenyl)-1,3,4-oxadiazol–2-yl]-1(2H)–acenaphthylenone (4d, $C_{21}H_{14}N_2O_3$)

Yellow powder; yield 85%; R_f = 0.36 (petroleum ether/ethyl acetate, 4/1); mp: 169-171 ºC. ^{1}H NMR (250.13 MHz, $CDCl_3$) δ = 2.37 (s, CH_3); 4.50 (br s, OH); 7.26 - 8.30 (m, $10CH_{arom}$) ppm. ^{13}C NMR (62.53 MHz, $CDCl_3$) δ = 21.21 (CH_3); 76.57 (C-OH); 122.55, 124.29, 126.84, 128.44, 128.78 and 132.86 (6CH of naphthalene ring); 122.06, 127.58, 129.07 and 132.60 (4CH of benzene ring); 128.81 and 129.10 (2C of benzene ring); 123.82, 130.91, 134.80 and 143.35 (4C of naphthalene ring); 164.18 and 166.75 (2C=N of oxadiazole); 198.87 (C=O) ppm. IR (KBr, υ

$_{max}$) = 3399, 3073, 1723, 1603, 1490 and 1073 cm^{-1}. MS (EI, 20 eV): *m/z* (%) = 342 (M^+), 198 (6), 182 (24), 154 (54), 126 (60), 105 (100), 91 (18), 76 (54), 62 (23) and 50 (24).

2-{5-[4-(tert-butyl)phenyl]-1,3,4–oxadiazol–2-yl}–2-hydroxy-1(2H)–acenaphthylenone (4e, $C_{24}H_{20}N_2O_3$)

Yellow powder; yield 89%; R_f = 0.33 (petroleum ether/ethyl acetate, 4/1); mp: 176-178 ºC. ^{1}H NMR (250.13 MHz, $CDCl_3$) δ = 1.30 (s, $3CH_3$); 5.30 (br s, OH); 7.41 (d, $^3J_{HH}$ = 8.3 Hz, $2CH_{arom}$); 7.98 (d, $^3J_{HH}$ = 8.3 Hz, $2CH_{arom}$); 7.71 - 7.86 and 8.05-8.20 (m, $6CH_{arom}$) ppm. ^{13}C NMR (62.53 MHz, $CDCl_3$) δ = 31.03 ($3CH_3$); 35.03(C); 76.60 (C-OH); 122.53, 123.74, 126.98, 128.70, 129.03 and 132.73 (6CH of naphthalene ring); 125.89 and 126.79 (4CH of benzene ring); 128.43 and 129.75 (2C of benzene ring); 122.04, 130.88, 135.51 and 142.33 (4C of naphthalene ring); 164.28 and 166.00 (2C=N of oxadiazole); 198.17 (C=O) ppm. IR (KBr, υ $_{max}$) = 3209, 2965, 1738, 1614, 1495 and 1010 cm^{-1}. MS (EI, 20 eV): *m/z* (%) = 384 (M^+), 182 (11), 163 (25), 148 (14), 120 (38), 103 (17), 91 (73), 76 (35), 57 (18) and 43 (100).

2-[5-(3-chlorophenyl)–1,3,4-oxadiazol–2-yl]–2–hydroxy–1(2H)–acenaphthylenone (4f, $C_{20}H_{11}ClN_2O_3$)

Yellow powder; yield 79%; R_f = 0.30 (petroleum ether/ethyl acetate, 4/1); mp: 174-176 ºC. ^{1}H NMR (250.13 MHz, $CDCl_3$) δ = 4.06 (br s, OH); 7.33- 8.29 (m, $10CH_{arom}$) ppm. ^{13}C NMR (62.53 MHz, $CDCl_3$) δ = 77.25 (C-OH); 122.06, 123.98, 127.02, 128.44, 129.09 and 132.94 (6CH of naphthalene ring); 125.24, 130.34, 132.09 and 132.62 (4CH of benzene ring); 128.83 and 148.62 (2C of benzene ring); 122.59, 129.50, 133.82 and 135.12 (4C of naphthalene ring); 158.50 and 164.82 (2C=N of oxadiazole); 198.27 (C=O) ppm. IR (KBr, υ $_{max}$) = 3379, 3080,

1718, 1602, 1551 and 1068 cm^{-1}. MS (EI, 20 eV): *m/z* (%) = 362 (M^+), 197 (18), 182 (44), 154 (95), 126 (100), 98 (23), 85 (19), 75 (47), 62 (34) and 50 (17).

2–hydroxy–2-[5-(3–phenoxyphenyl)-1,3,4–oxadiazol–2-yl]-1(2H)–acenaphthylenone (4g, $C_{26}H_{16}N_2O_4$)

Yellow powder; yield 75%; R_f = 0.26 (petroleum ether/ethyl acetate, 4/1); mp: 153-155 ºC. ^1H NMR (250.13 MHz, $CDCl_3$) δ = 4.81 (br s, OH); 6.96- 8.29 (m, $15CH_{arom}$) ppm. ^{13}C NMR (62.53 MHz, $CDCl_3$) δ = 85.02 (C-OH); 117.19, 119.14, 121.80, 123.88, 129.95, 130.45 and 130.92 (9CH of benzene rings); 122.05, 123.97, 126.95, 128.77, 129.04 and 132.84 (6CH of naphthalene ring); 122.52, 129.62, 135.22 and 145.30 (4C of naphthalene ring); 128.44, 156.20 and 157.85 (3C of benzene rings); 165.45 and 164.71 (2C=N of oxadiazole); 198.17 (C=O) ppm. IR (KBr, υ_{max})= 3307, 3082, 1743, 1563, 1485 and 1225 cm^{-1}; MS (EI, 20 eV): *m/z* (%) = 420 (M^+), 214 (27), 197 (29), 182 (80), 154 (80), 126 (100), 98 (21), 85 (15), 76 (29), 62 (29) and 50 (22).

2-{5-[4-(bromomethyl)phenyl]-1,3,4–oxadiazol–2-yl}–2–hydroxy-1(2H)-acenaphthylenone (4h, $C_{21}H_{13}BrN_2O_3$)

Yellow powder; yield 85%; R_f = 0.33 (petroleum ether/ethyl acetate, 4/1); mp: 163-165 ºC. ^1H NMR (250.13 MHz, $CDCl_3$) δ: 4.46 (s, CH_2); 4.98 (br s, OH); 7.43 (d, $^3J_{HH}$ = 8.3 Hz, $2CH_{arom}$); 7.90 (d, $^3J_{HH}$ = 8.3 Hz, $2CH_{arom}$); 7.70- 7.86 and 7.99-8.29 (m, $6CH_{arom}$) ppm. ^{13}C NMR (62.53 MHz, $CDCl_3$) δ = 32.09 (CH_2); 76.77 (C-OH); 122.56, 123.89, 126.95, 127.55, 129.07 and 132.87 (6CH of naphthalene ring); 129.61 and 132.62 (4CH of benzene ring); 128.44 and 128.79 (2C of benzene ring); 123.10, 130.92, 135.24 and 141.80 (4C of naphthalene ring); 165.12 and

166.22 (2C=N of oxadiazole); 198.15 (C=O) ppm. IR (KBr, υ_{max}) = 3343, 3072, 1717, 1603, 1486 and 1012 cm^{-1}.

2-hydroxy-2-[5-(1-naphthyl)-1,3,4-oxadiazol-2-yl]-1(2H)-acenaphthylenone (4i, $C_{24}H_{14}N_2O_3$)

Yellow powder; yield 78%; R_f = 0.36 (petroleum ether/ethyl acetate, 4/1); mp: 154-156 ºC. ^1H NMR (250.13 MHz, $CDCl_3$) δ = 4.84 (br s, OH); 7.42- 9.07 (m, $13CH_{arom}$) ppm. ^{13}C NMR (62.53 MHz, $CDCl_3$) δ = 76.39 (C-OH); 122.60, 124.67, 125.95, 126.71, 126.96, 128.22, 128.59, 128.75, 128.79, 129.08 and 132.88 (13CH naphthalene rings); 123.91, 128.35, 129.90, 131.92, 133.80, 135.22 and 142.26 (7C of naphthalene rings); 162.32 and 166.25 (2C=N of oxadiazole); 198.17 (C=O) ppm. IR (KBr, υ_{max}) = 3433, 3186, 1741, 1604, 1538 and 1089 cm^{-1}.

2-[5-(4–chlorophenyl)-1,3,4–oxadiazol–2–yl]–2–hydroxy-1(2H)–acenaphthylenone (4j, $C_{20}H_{11}ClN_2O_3$)

Yellow powder; yield 73%; R_f = 0.30 (petroleum ether/ethyl acetate, 4/1); mp: 169-171 ºC. ^1H NMR (250.13 MHz, $CDCl_3$) δ = 4.58 (br s, OH); 7.77 (d, $^3J_{HH}$ = 8.3 Hz, $2CH_{arom}$); 8.24 (d, $^3J_{HH}$ = 8.3 Hz, $2CH_{arom}$); 7.40 - 7.73 and 7.83-8.13 (m, $6CH_{arom}$) ppm. ^{13}C NMR (62.53 MHz, $CDCl_3$) δ = 83.23 (C-OH); 122.07, 122.58, 128.40, 128.45, 129.09 and 132.94 (6CH of naphthalene ring); 129.37 and 132.63 (4CH of benzene ring); 127.02 and 137.52 (2C of benzene ring); 123.95, 128.83, 135.02 and 138.45 (4C of naphthalene ring); 164.12 and 165.23 (2C=N of oxadiazole); 202.12 (C=O) ppm. IR (KBr, υ_{max}) = 3227, 3022, 1732, 1604, 1486 and 1078 cm^{-1}.

2-[5-(4–fluorophenyl)-1,3,4–oxadiazol–2–yl]–2-hydroxy-1(2H)–acenaphthylenone (**4k**, **$C_{20}H_{11}FN_2O_3$**)

Yellow powder; yield 80%; R_f = 0.33 (petroleum ether/ethyl acetate, 4/1); mp: 156-158 ºC. ^{1}H NMR (250.13 MHz, $CDCl_3$) δ = 4.40 (s, OH); 7.10 - 8.31 (m, $10CH_{arom}$) ppm. ^{13}C NMR (62.53 MHz, $CDCl_3$) δ = 82.65 (C-OH); 116.38 (d, $^2J_{CF}$ = 20.1 Hz, 2CH of benzene ring); 122.06, 122.55, 127.00, 128.44, 129.09 and 132.62 (6CH of naphthalene ring); 129.53 (d, $^3J_{CF}$ = 12.5 Hz, 2CH of benzene ring); 123.93, 128.94, 135.02 and 140.74 (4C of naphthalene ring); 127.00 (C of benzene ring); 160.52 (d, $^1J_{CF}$ = 252.0 Hz, CF of benzene ring); 164.48 and 166.53 (2C=N of oxadiazole); 189.51 (C=O) ppm. IR (KBr, υ $_{max}$) = 3375, 3082, 1725, 1606, 1497 and 1013 cm^{-1}.

2–hydroxy–2-[5-(4–methylphenyl)-1,3,4-oxadiazol–2–yl]-1(2H)–acenaphthylenone (**4l**, **$C_{21}H_{14}N_2O_3$**)

Yellow powder; yield 83%; R_f = 0.36 (petroleum ether/ethyl acetate, 4/1); mp: 170-172 ºC. ^{1}H NMR (250.13 MHz, $CDCl_3$) δ= 2.37 (s, CH_3); 4.30 (br s, OH); 7.20 - 8.29 (m, $10CH_{arom}$) ppm. ^{13}C NMR (62.53 MHz, $CDCl_3$) δ= 21.61 (CH_3); 76.64 (C-OH); 122.05, 123.81, 127.07, 128.44, 129.05 and 132.80 (6CH of naphthalene ring); 129.64 and 132.61 (4CH of benzene ring); 122.52, 128.75, 135.22 and 142.85 (4C of naphthalene ring); 126.89 and 128.60 (2C of benzene ring); 162.08 and 164.13 (2C=N of oxadiazole); 198.10 (C=O) ppm. IR (KBr, υ $_{max}$) = 3355, 3068, 1725, 1603, 1498 and 1012 cm^{-1}.

2–hydroxy–2-[5-(4–methoxyphenyl)-1,3,4–oxadiazol–2–yl]-1(2H)-acenaphthylenone (**4m**, **$C_{21}H_{14}N_2O_4$**)

Yellow powder ; yield 73%; R_f = 0.26 (petroleum ether/ethyl acetate, 4/1); mp: 195-197 ºC. ^{1}H NMR (250.13 MHz, $CDCl_3$) δ= 3.84 (s, CH_3); 4.33 (s, OH); 6.85 - 8.31 (m, 10CH_{arom}) ppm. ^{13}C NMR (62.53 MHz, $CDCl_3$) δ = 55.55 (OCH_3); 77.55 (C-OH); 122.54, 123.92, 126.92, 128.93, 128.95 and 132.89 (6CH of naphthalene ring); 114.40 and 132.50 (4CH of benzene ring); 122.54, 131.04, 135.22 and 140.04 (4C of naphthalene ring); 128.86 and 158.82 (2C of benzene ring); 164.08 and 166.53 (2C=N of oxadiazole); 194.51 (C=O) ppm. IR (KBr, υ $_{max}$) = 3244, 3083, 1739, 1614, 1500 and 1185 cm^{-1}.

2-[5-(3,5–dimethoxyphenyl)-1,3,4–oxadiazol–2-yl]–2–hydroxy-1(2H)- acenaphthylenone (**4n**, **$C_{22}H_{16}N_2O_5$**)

Yellow powder; yield 71%; R_f = 0.20 (petroleum ether/ethyl acetate, 4/1); mp: 168-170 ºC. ^{1}H NMR (250.13 MHz, $CDCl_3$) δ= 3.80 (s, 2OCH_3); 4.43 (s, OH); 6.56 - 8.30 (m, 9CH_{arom}) ppm. ^{13}C NMR (62.53 MHz, $CDCl_3$) δ= 55.64 (2OCH_3); 87.00 (C-OH); 122.04, 123.94, 127.00, 128.43, 132.59 and 132.84 (6CH of naphthalene ring); 105.00 and 107.05 (3CH of benzene ring); 124.75, 131.04, 135.03 and 142.10 (4C of naphthalene ring); 127.00 and 162.15 (3C of benzene ring); 164.02 and 166.43 (2C=N of oxadiazole); 189.51 (C=O) ppm. IR (KBr, υ $_{max}$) = 3380, 3094, 1725, 1604, 1463 and 1162 cm^{-1}.

2–hydroxy–2-[5-(2–methylphenyl)-1,3,4–oxadiazol–2–yl]-1(2H)-acenaphthylenone (**4o**, **$C_{21}H_{14}N_2O_3$**)

Yellow powder; yield 77%; R_f = 0.34 (petroleum ether/ethyl acetate, 4/1); mp: 154-156 ºC. ^{1}H NMR (250.13 MHz, $CDCl_3$) δ= 2.57 (s, CH_3); 4.09 (br s, OH); 7.06 - 8.64 (m, $10CH_{arom}$) ppm. ^{13}C NMR (62.53 MHz, $CDCl_3$) δ= 22.32 (CH_3); 77.70 (C-OH); 122.06, 123.82, 126.98, 128.44, 129.09 and 132.80 (6CH of naphthalene ring); 126.06, 129.13, 131.50 and 132.61 (4CH of benzene ring); 123.82, 131.65, 138.62 and 140.35 (4C of naphthalene ring); 128.60 and 132.00 (2C of benzene ring); 164.18 and 166.73 (2C=N of oxadiazole); 198.03 (C=O) ppm. IR (KBr, υ_{max}) = 3416, 3072, 1725, 1604, 1491 and 1014 cm^{-1}.

2-[5-(3,4–dimethylphenyl)-1,3,4–oxadiazol–2–yl]–2–hydroxy-1(2H)–acenaphthylenone (**4p**, **$C_{22}H_{16}N_2O_3$**)

Yellow powder; yield 75%; R_f = 0.32 (petroleum ether/ethyl acetate, 4/1); mp: 167-169 ºC. ^{1}H NMR (250.13 MHz, $CDCl_3$): δ= 2.26 and 2.28 (s, $2CH_3$); 4.42 (br s, OH); 7.07 - 8.75 (m, $9CH_{arom}$) ppm. ^{13}C NMR (62.53 MHz, $CDCl_3$): δ= 19.65 and 19.93 ($2CH_3$); 80.00 (C-OH); 122.05, 122.54, 126.89, 128.59, 128.85 and 132.75 (6CH of naphthalene ring); 128.43, 130.16 and 132.61 (3CH of benzene ring); 122.05, 129.02, 135.32 and 145.90 (4C of naphthalene ring); 123.92, 127.50 and 128.05 (3C of benzene ring); 164.18 and 166.33 (2C=N of oxadiazole); 188.07 (C=O) ppm. IR (KBr, υ_{max}) = 3376, 3083, 1721, 1603, 1494 and 1184 cm^{-1}.

CONCLUSION

In conclusion, in the present paper an efficient green procedure for the synthesis of sterically congested 2,5-disubstituted 1,3,4-oxadiazole derivatives **(4)** *via* a one-pot three-component reaction of an aromatic carboxylic acid **(1)**, acenaphthoquinone **(2)** and *N*-isocyanimino-triphenylphosphorane (Ph_3PNNC) **(3)** in water as a green reaction solvent at RT (20–26 °C) for 15 h has been developed. The remarkable features of this "green" methodology include high yield of products, water as the solvent, short reaction time, operational simplicity, environmentally benign and the absence of any volatile or hazardous organic solvents.

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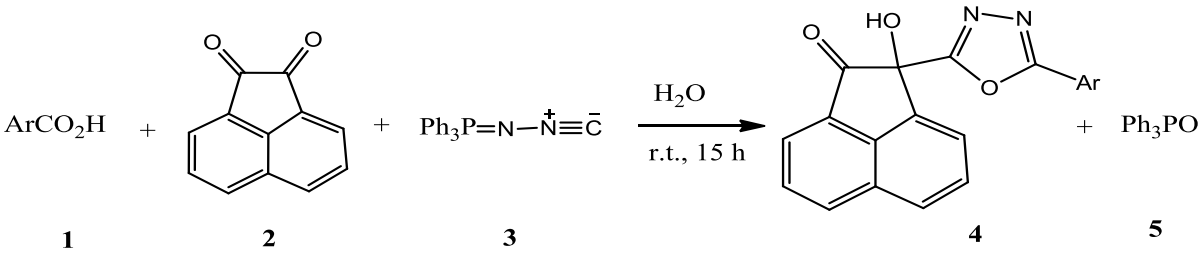
Table 1 Effect of solvent for the synthesis of sterically congested 1,3,4-oxadiazoles derivatives

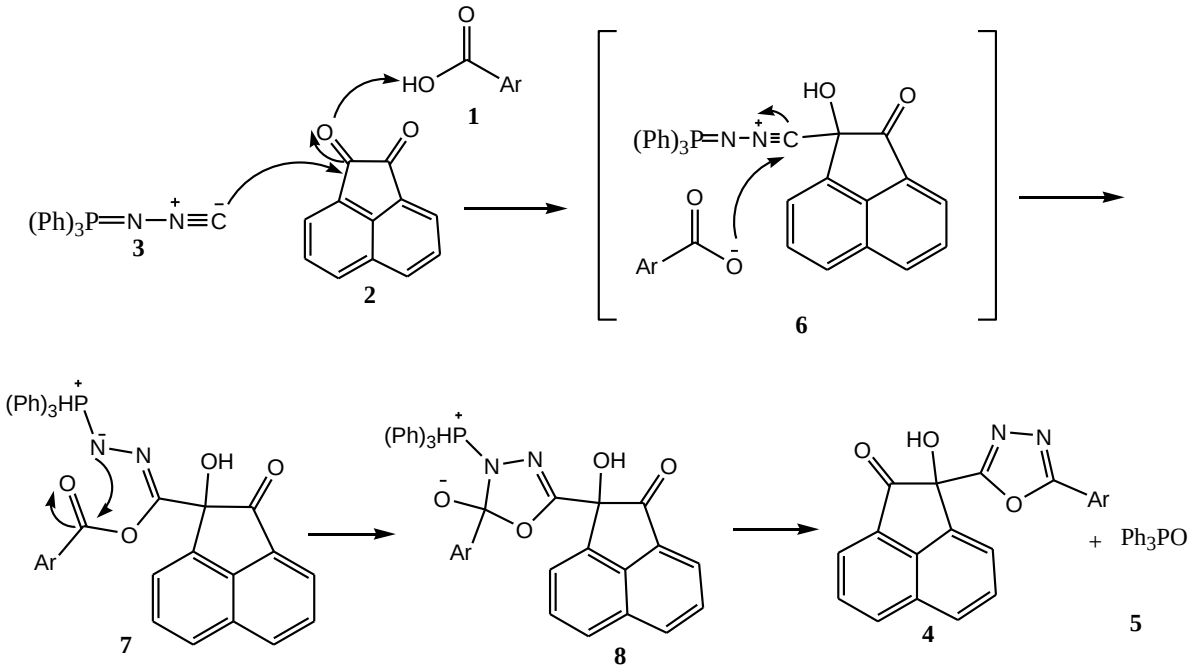
Entry	Solvent	Time (h)	Yield (%) [a, b]
1	EtOH	24	62
2	MeOH	24	41
3	CH_2Cl_2	24	59
4	Toluene	26	69
5	CH_3CN	24	80
6	Water	15	84

[a] Reaction conditions: *N*-isocyanimino-triphenylphosphorane (1.0 mmol), acenaphthoquinone (1.0 mmol) and benzoic acid (1.0 mmol) in solvent (5 mL) at RT (20–26 °C).

[b] Isolated yields.



Scheme 1 Synthesis of sterically congested 2,5-disubstituted 1,3,4-oxadiazole derivatives (**4a**: Ar=C_6H_5; **4b**: Ar=4-BrC_6H_4; **4c**: Ar=4-CNC_6H_4; **4d**: Ar=3-MeC_6H_4; **4e**: Ar=4-*t*-BuC_6H_4; **4f**: Ar=3-ClC_6H_4; **4g**: Ar=3-PhOC_6H_4; **4h**: Ar=4-Br$CH_2C_6H_4$; **4i**: Ar=$C_{10}H_7$ (1-Naphthyl); **4j**: Ar=4-ClC_6H_4; **4k**: Ar=4-FC_6H_4; **4l**: Ar=4-MeC_6H_4; **4m**: Ar=4-MeOC_6H_4; **4n**: Ar=3,5-diMeOC_6H_4; **4o**: Ar=2-MeC_6H_4; **4p**: Ar=3,4-diMeC_6H_4).



Scheme 2 Proposed mechanism for the formation of sterically congested 2,5-disubstituted 1,3,4-oxadiazole derivatives **4** in water.