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ORIGINAL PAPER

Synthesis of sterically congested 1,3,4-oxadiazole derivatives from aromatic carboxylic acids, acenaphthoquinone, and (*N*-isocyanimino)triphenylphosphorane

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Abstract Reactions of (*N*-isocyanimino)triphenylphosphorane with acenaphthoquinone in the presence of aromatic carboxylic acids proceed smoothly at room temperature and under neutral conditions to afford sterically congested 1,3,4-oxadiazole derivatives in high yields. The reaction proceeds smoothly and cleanly under mild conditions and no side reactions are observed.

Keywords (*N*-Isocyanimino)triphenylphosphorane · Acenaphthoquinone · Aromatic carboxylic acid · 1,3,4-Oxadiazole · Aza-Wittig reaction

Introduction

Multicomponent reactions are capable of achieving high levels of brevity and diversity, as they allow more than two simple and flexible building blocks to be combined in practical, time-saving one-pot operations. Owing to their valued features such as atom economy, inherent simple experimental procedures, and their one-pot character, they are perfectly suited for automated synthesis. Thus, MCRs have attracted considerable interest owing to their exceptional synthetic efficiency [1–4]. Typically, the purification of products resulting from MCRs is also simple because all the organic reagents employed are consumed and incorporated into the target compound [5, 6]. MCRs leading to interesting heterocyclic scaffolds are particularly useful for the construction of diverse chemical libraries of drug-like molecules. The isocyanide-based MCRs are of special importance in this context [7–9].

The intramolecular version of the aza-Wittig-type reaction has attracted considerable attention recently because of its high potential for the synthesis of a wide variety of nitrogen heterocycles, which can be attributed, in good measure, to the rapid progress in the preparation of functionalized iminophosphoranes. Several interesting heterocyclization reactions involving iminophosphoranes have been reported [10–16]. These compounds can easily be converted through aza-Wittig reaction with isocyanates, carbon dioxide, or carbon disulfide into functionalized hetero-cumulenes which exhibit a rich chemistry of unusual synthetic promise [10–16]. The nucleophilicity at the nitrogen is a factor of essential mechanistic importance in the use of these iminophosphoranes as aza-Wittig reagents. Iminophosphoranes are important reagents in synthetic organic chemistry, especially in the synthesis of naturally occurring products, compounds with biological and pharmacological activity [10–16]. (*N*-Isocyanimino)triphenylphosphorane (**3**) is expected to have synthetic potential because it provides a reaction system in which the iminophosphorane group can react with a reagent having a carbonyl functionality [17, 18].

In recent years, several synthetic methods have been reported for the preparation of (*N*-isocyanimino)triphenylphosphorane ($CNNPPh_3$, **3**) (Scheme 1) [17, 18]. There are several reports on the use of (*N*-isocyanimino)triphenylphosphorane in the synthesis of metal complexes [17, 18]. However, application of **3** in the synthesis of organic compounds is rare [19–29]. As part of our ongoing program to develop efficient and robust methods for the preparation of heterocyclic compounds [19–33], we sought to develop a convenient preparation of sterically congested

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1,3,4-oxadiazole derivatives **4a**–**4p**. Herein, we report a hitherto unknown, one-pot three-component reaction, which, starting from readily available acenaphthoquinone (**2**), affords disubstituted 1,3,4-oxadiazole derivatives **4a**–**4p** (Scheme 1).

1,3,4-Oxadiazoles have attracted interest in medicinal chemistry as surrogates of carboxylic acids, esters, and carboxamides. 1,3,4-Oxadiazoles are an important class of heterocyclic compounds that have a wide range of pharmaceutical and biological activities including antimicrobial, antifungal, anti-inflammatory, and antihypertensive [34–38]. Several methods have been reported in the literature for the synthesis of 1,3,4-oxadiazoles. These protocols are multi-step in nature [39–45]. The most general method involves the cyclization of diacylhydrazides with a variety of reagents, such as $SOCl_2$, $POCl_3$, or H_2SO_4, usually under harsh reaction conditions. Few reliable and operationally simple examples have been reported for the one-pot synthesis of 1,3,4-oxadiazoles, especially from readily available carboxylic acids and acid hydrazides [46–50].

Results and discussion

The carboxylic acid derivatives **1** with acenaphthoquinone (**2**) and (*N*-isocyanimino)triphenylphosphorane (**3**) in CH_3CN react together in a 1:1:1 ratio at room temperature to produce sterically congested 1,3,4-oxadiazole derivatives **4** and triphenylphosphine oxide (**5**) (Scheme 1, Table 1). The reaction proceeds smoothly and cleanly under mild conditions and no side reactions are observed.

The suggested mechanism for the formation of products **4a**–**4p** is illustrated in Scheme 2. On the basis of the chemistry of isocyanides, it is reasonable to assume that the first step may involve nucleophilic addition of (*N*-isocyanimino)triphenylphosphorane (**3**) to acenaphthoquinone (**2**), which is facilitated by its protonation with the 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 the iminophosphorane moiety with the ester carbonyl to afford the isolated sterically congested 1,3,4-oxadiazole derivatives **4** by elimination of triphenylphosphine oxide (**5**) from intermediate **8**.

In summary, we believe that the reported method offers a mild, simple, and efficient route for the preparation of 1,3,4-oxadiazole derivatives **4**. Its ease of work-up, high yields, and fairly mild reaction conditions make it a useful addition to modern synthetic methodologies. Other aspects of this process are under investigation.

Experimental

(*N*-Isocyanimino)triphenylphosphorane (**3**) was prepared based on reported procedures [17, 18]. Other starting materials and solvents were obtained from Merck (Germany) and Fluka (Switzerland) and were used without further purification. The methods used to monitor the reactions are TLC and NMR. Melting points were measured on an Electrothermal 9100 apparatus. IR spectra were measured on a Jasco 6300 FTIR spectrometer. ^1H and ^{13}C NMR spectra ($CDCl_3$) were recorded on a Bruker DRX-250 Avance spectrometer at 250.0 and 62.5 MHz, respectively. Elemental analyses were performed using a Heraeus CHN-O-Rapid analyzer. Mass spectra were recorded on a Finnigan MAT-8430 mass spectrometer operating at an ionization potential of 70 eV. Preparative layer chromatography (PLC) plates were prepared from Merck silica gel (F_{254}) powder.

*General procedure for the preparation of compounds **4a**–**4p***

A mixture of (*N*-isocyanimino)triphenylphosphorane (1.0 mmol), acenaphthoquinone (1.0 mmol), and aromatic carboxylic acid (1.0 mmol) in 5 cm^3 CH_3CN was stirred at room temperature for 24 h. The solvent was removed under reduced pressure, and the viscous residue was purified by PLC [silica gel (F_{254}) powder; petroleum ether/ethyl acetate 4:1].

2-Hydroxy-2-(5-phenyl-1,3,4-oxadiazol-2-yl)-1(2H)-acenaphthylenone (**4a**, $C_{20}H_{12}N_2O_3$)
Yellow powder; yield 80%; $R_f = 0.36$ (petroleum ether/ethyl acetate 4:1); m.p.: 162–164 °C; ^1H NMR (250.13 MHz, $CDCl_3$): $\delta = 4.59$ (br s, OH), 7.40–8.30 (m, $11CH_{arom}$) ppm; ^{13}C NMR (62.53 MHz, $CDCl_3$): $\delta = 87.74$ (C–OH), 122.56, 123.88, 126.97, 127.13, 128.79, 128.96, 129.07, 132.02, 132.85 (11CH of arom),

Scheme 1

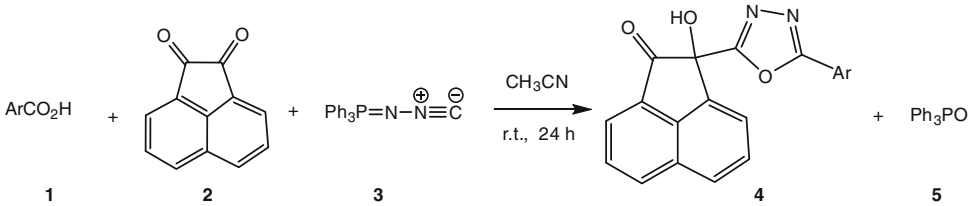
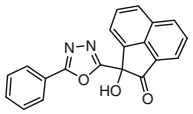
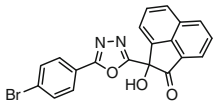
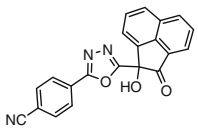
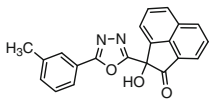
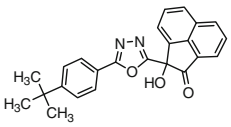
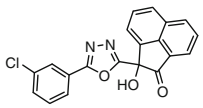
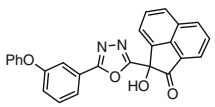
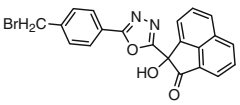
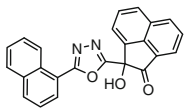
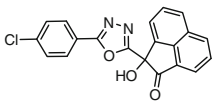
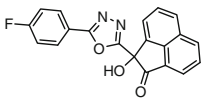
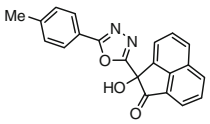
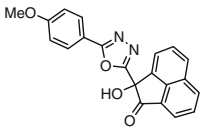
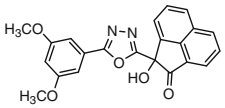
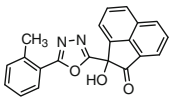
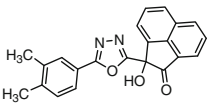


Table 1 Synthesis of sterically congested 1,3,4-oxadiazole derivatives **4a**–**4p** from carboxylic acids **1** and acenaphthoquinone (**2**) in the presence of (*N*-isocyanimino)triphenylphosphorane (**3**)

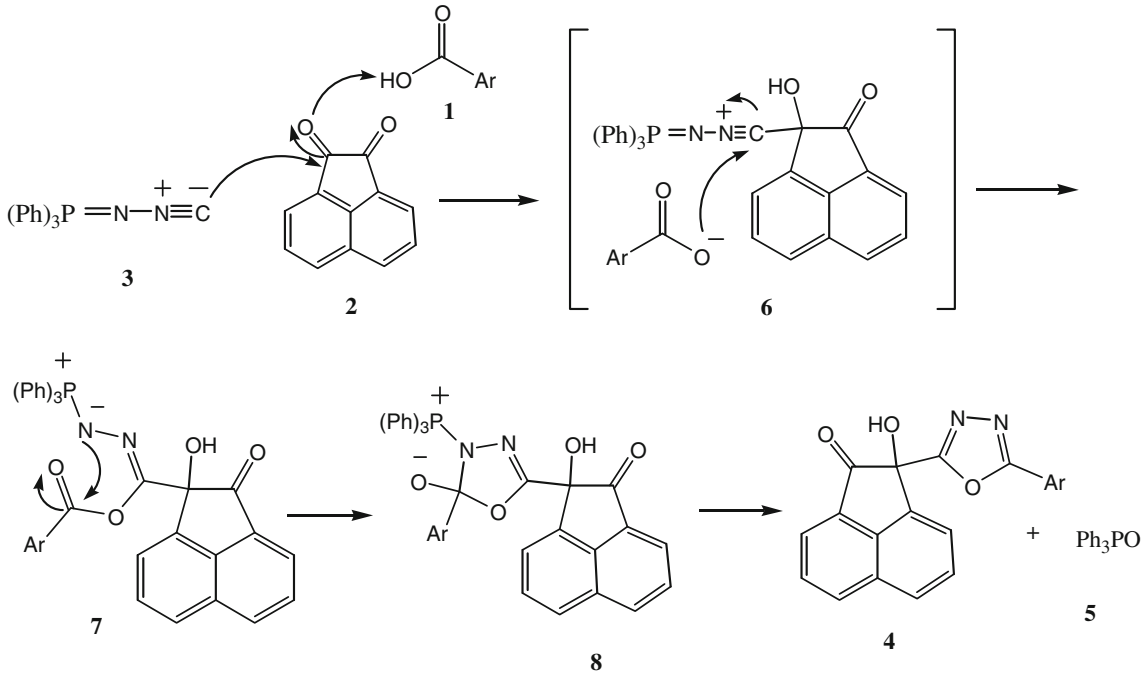
4	Ar	Product	Yield (%)[a]
a	C_6H_5		80
b	4-BrC_6H_4		78
c	4-CNC_6H_4		73
d	3-MeC_6H_4		83
e	4-*t*-BuC_6H_4		85
f	3-ClC_6H_4		76
g	3-$PhOC_6H_4$		72
h	4-$BrCH_2C_6H_4$		82
i	$C_{10}H_7$		75
j	4-ClC_6H_4		72
k	4-FC_6H_4		75
l	4-MeC_6H_4		80
m	4-$MeOC_6H_4$		68
n	3,5-di$MeOC_6H_3$		67
o	2-MeC_6H_4		72
p	3,4-diMeC_6H_3		70

[a] Yield of isolated **4**

123.22, 127.80, 129.60, 135.12, 142.96 (5C of arom), 161.05, 166.13 (2C=N of oxadiazole), 198.51 (C=O) ppm; IR (KBr): $\bar{\nu} = 3{,}366$, 3,073, 1,718, 1,603, 1,448, 1,012 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), 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 78%; $R_f = 0.33$ (petroleum ether/ethyl acetate 4:1); m.p.: 151–153 °C; ^{1}H NMR (250.13 MHz, $CDCl_3$): $\delta = 4.57$ (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, 8.09–8.30 (m, $6CH_{arom}$) ppm; ^{13}C NMR (62.53 MHz, $CDCl_3$): $\delta = 86.50$ (C–OH), 122.59, 123.96, 127.03, 128.51, 128.83, 129.08, 132.33, 132.94 (10CH of arom), 122.12, 126.80, 129.50, 130.98, 134.22, 140.25 (6C of arom), 164.02, 165.03 (2C=N of oxadiazole), 202.02 (C=O) ppm; IR (KBr): $\bar{\nu} = 3{,}204$, 3,077, 1,733, 1,600, 1,481, 1,007 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), 50 (18).

4-[5-(1,2-Dihydro-1-hydroxy-2-oxo-1-acenaphthylenyl)-1,3,4-oxadiazol-2-yl]benzonitrile (**4c**, $C_{21}H_{11}N_3O_3$)
Yellow powder; yield 73%; $R_f = 0.30$ (petroleum ether/ethyl acetate 4:1); m.p.: 161–163 °C; ^{1}H NMR (250.13 MHz, $CDCl_3$): $\delta = 3.63$ (s, OH), 7.71–8.33 (m, $10CH_{arom}$) ppm; ^{13}C NMR (62.53 MHz, $CDCl_3$): $\delta = 77.31$ (C–OH), 122.07, 127.13, 127.60, 128.45, 129.09, 132.62, 132.75 (10CH of arom), 109.98, 115.51, 124.00, 128.90, 133.02, 135.05, 143.03 (7C of arom), 161.03, 165.13 (2C=N of oxadiazole), 192.21 (C=O) ppm; IR (KBr): $\bar{\nu} = 3{,}439$, 3,209, 1,729, 1,604, 1,495, 1,014 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), 42 (30).



Scheme 2

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 83%; $R_f = 0.36$ (petroleum ether/ethyl acetate 4:1); m.p.: 169–171 °C; ^{1}H NMR (250.13 MHz, $CDCl_3$): $\delta = 2.37$ (s, CH_3), 4.50 (br s, OH), 7.26–8.30 (m, $10CH_{arom}$) ppm; ^{13}C NMR (62.53 MHz, $CDCl_3$): $\delta = 21.21$ (CH_3), 76.57 (C–OH), 122.06, 122.55, 124.29, 126.84, 127.58, 128.44, 128.78, 129.07, 132.60, 132.86 (10CH of arom),123.82, 128.81, 129.10, 130.91, 134.80, 143.35 (6C of arom), 164.18, 166.75 (2C=N of oxadiazole), 198.87 (C=O) ppm; IR (KBr): $\bar{\nu} = 3{,}399$, 3,073, 1,723, 1,603, 1,490, 1,073 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), 50 (24).

2-[5-(4-tert-Butylphenyl)-1,3,4-oxadiazol-2-yl]-2-hydroxy-1(2H)-acenaphthylenone (**4e**, $C_{24}H_{20}N_2O_3$)
Yellow powder; yield 85%; $R_f = 0.33$ (petroleum ether/ethyl acetate 4:1); m.p.: 176–178 °C; ^{1}H NMR (250.13 MHz, $CDCl_3$): $\delta = 1.30$ (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, 8.05–8.20 (m, $6CH_{arom}$) ppm; ^{13}C NMR (62.53 MHz, $CDCl_3$): $\delta = 31.03$ ($3CH_3$), 35.03 (C), 76.60 (C–OH), 122.53, 123.74, 125.89, 126.79, 126.98, 128.70, 129.03, 132.73 (10CH of arom), 122.04, 128.43, 129.75, 130.88, 135.51, 142.33 (6C of arom), 164.28, 166.00 (2C=N of oxadiazole), 198.17 (C=O) ppm; IR (KBr): $\bar{\nu} = 3{,}209$, 2,965, 1,738, 1,614, 1,495, 1,010 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), 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 76%; $R_f = 0.30$ (petroleum ether/ethyl acetate 4:1); m.p.: 174–176 °C; ^{1}H NMR (250.13 MHz, $CDCl_3$): $\delta = 4.06$ (br s, OH), 7.33–8.29 (m, $10CH_{arom}$) ppm; ^{13}C NMR (62.53 MHz, $CDCl_3$): $\delta = 77.25$ (C–OH), 122.06, 123.98, 125.24, 127.02, 128.44, 129.09, 130.34, 132.09, 132.62, 132.94 (10CH of arom), 122.59, 128.83, 129.50, 133.82, 135.12, 148.62 (6C of arom), 158.50, 164.82 (2C=N of oxadiazole), 198.27 (C=O) ppm; IR (KBr): $\bar{\nu} = 3{,}379$, 3,080, 1,718, 1,602, 1,551, 1,068 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), 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 72%; $R_f = 0.26$ (petroleum ether/ethyl acetate 4:1); m.p.: 153–155 °C; ^{1}H NMR (250.13 MHz, $CDCl_3$): $\delta = 4.81$ (br s, OH), 6.96–8.29 (m, $15CH_{arom}$) ppm; ^{13}C NMR (62.53 MHz, $CDCl_3$): $\delta = 85.02$ (C–OH), 117.19, 119.14, 121.80, 122.05, 123.88, 123.97, 126.95, 128.77, 129.04, 129.95, 130.45, 130.92, 132.84 (15CH of arom), 122.52, 128.44, 129.62, 135.22, 145.30, 156.20, 157.85 (7C of arom), 165.45, 164.71 (2C=N of oxadiazole), 198.17 (C=O) ppm; IR

(KBr): $\bar{\nu}$ = 3,307, 3,082, 1,743, 1,563, 1,485, 1,225 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), 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 82%; R_f = 0.33 (petroleum ether/ethyl acetate 4:1); m.p.: 163–165 °C; ^{1}H 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, 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, 129.61, 132.62, 132.87 (10CH of arom), 123.10, 128.44, 128.79, 130.92, 135.24, 141.80 (6C of arom), 165.12, 166.22 (2C=N of oxadiazole), 198.15 (C=O) ppm; IR (KBr): $\bar{\nu}$ = 3,343, 3,072, 1,717, 1,603, 1,486, 1,012 cm^{-1}.

2-Hydroxy-2-[5-(1-naphthalenyl)-1,3,4-oxadiazol-2-yl]-1(2H)-acenaphthylenone (**4i**, $C_{24}H_{14}N_2O_3$)
Yellow powder; yield 75%; R_f = 0.36 (petroleum ether/ethyl acetate 4:1); m.p.: 154–156 °C; ^{1}H 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, 132.88 (13CH of arom), 123.91, 128.35, 129.90, 131.92, 133.80, 135.22, 142.26 (7C of arom), 162.32, 166.25 (2C=N of oxadiazole), 198.17 (C=O) ppm; IR (KBr): $\bar{\nu}$ = 3,433, 3,186, 1,741, 1,604, 1,538, 1,089 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 72%; R_f = 0.30 (petroleum ether/ethyl acetate 4:1); m.p.: 169–171 °C; ^{1}H 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, 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, 129.37, 132.63, 132.94 (10CH of arom), 123.95, 127.02, 128.83, 135.02, 137.52, 138.45 (6C of arom), 164.12, 165.23 (2C=N of oxadiazole), 202.12 (C=O) ppm; IR (KBr): $\bar{\nu}$ = 3,227, 3,022, 1,732, 1,604, 1,486, 1,078 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 75%; R_f = 0.33 (petroleum ether/ethyl acetate 4:1); m.p.: 156–158 °C; ^{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 arom), 122.06, 122.55, 128.44, 129.09, 132.62 (6CH of arom), 129.53 (d, $^3J_{CF}$ = 12.5 Hz, 2CH of arom), 123.93, 127.00, 128.94, 135.02, 140.74 (5C of arom), 160.52 (d, $^1J_{CF}$ = 252.0 Hz, C of arom), 164.48, 166.53 (2C=N of oxadiazole), 189.51 (C=O) ppm; IR (KBr): $\bar{\nu}$ = 3,375, 3,082, 1,725, 1,606, 1,497, 1,013 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 80%; R_f = 0.36 (petroleum ether/ethyl acetate 4:1); m.p.: 170–172 °C; ^{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, 129.64, 132.61, 132.80 (10CH of arom), 122.52, 128.60, 128.75, 126.89, 135.22, 142.85 (6C of arom), 162.08, 164.13 (2C=N of oxadiazole), 198.10 (C=O) ppm; IR (KBr): $\bar{\nu}$ = 3,355, 3,068, 1,725, 1,603, 1,498, 1,012 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 68%; R_f = 0.26 (petroleum ether/ethyl acetate 4:1); m.p.: 195–197 °C; ^{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), 114.40, 122.54, 123.92, 126.92, 128.93, 128.95, 132.50, 132.89 (10CH of arom), 122.54, 128.86, 131.04, 135.22, 140.04, 158.82 (6C of arom), 164.08, 166.53 (2C=N of oxadiazole), 194.51 (C=O) ppm; IR (KBr): $\bar{\nu}$ = 3,244, 3,083, 1,739, 1,614, 1,500, 1,185 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 67%; R_f = 0.20 (petroleum ether/ethyl acetate 4:1); m.p.: 168–170 °C; ^{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), 105.00, 107.05, 122.04, 123.94, 128.43, 132.59, 132.84 (9CH of arom), 124.75, 127.00, 131.04, 135.03, 142.10, 162.15 (7C of arom), 164.02, 166.43 (2C=N of oxadiazole), 189.51 (C=O) ppm; IR (KBr): $\bar{\nu}$ = 3,380, 3,094, 1,725, 1,604, 1,463, 1,162 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 72%; R_f = 0.34 (petroleum ether/ethyl acetate 4:1); m.p.: 154–156 °C; ^{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, 126.06, 126.98, 128.44, 129.09, 129.13, 131.50, 132.61, 132.80 (10CH of arom), 123.82, 128.60, 131.65, 132.00, 138.62, 140.35 (6C of arom), 164.18, 166.73

(2C=N of oxadiazole), 198.03 (C=O) ppm; IR (KBr): $\bar{\nu}$ = 3,416, 3,072, 1,725, 1,604, 1,491, 1,014 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 70%; R_f = 0.32 (petroleum ether/ethyl acetate 4:1); m.p.: 167–169 °C; ^1H NMR (250.13 MHz, $CDCl_3$): δ = 2.26, 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, 19.93 ($2CH_3$), 80.00 (C–OH), 122.05, 122.54, 126.89, 128.43, 128.59, 128.85, 130.16, 132.61, 132.75 (9CH of arom), 122.05, 123.92, 127.50, 128.05, 129.02, 135.32, 145.90 (7C of arom), 164.18, 166.33 (2C=N of oxadiazole), 188.07 (C=O) ppm; IR (KBr): $\bar{\nu}$ = 3,376, 3,083, 1,721, 1,603, 1,494, 1,184 cm^{-1}.

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