

# Four-component Synthesis of 1,3,4-Oxadiazole Derivatives from (*N*-Isocyanimino)triphenylphosphorane, (*E*)-Cinnamic Acids, Acetaldehyde and Secondary Amines

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The 1:1 iminium intermediate, generated by the addition of a secondary amine to acetaldehyde is trapped by the (*N*-isocyanimino)triphenylphosphorane in the presence of an (*E*)-cinnamic acid derivative, leading to the formation of the corresponding iminophosphorane intermediate. Disubstituted 1,3,4-oxadiazole derivatives are formed *via* intramolecular *aza*-Wittig reaction of the iminophosphorane intermediates. The reactions were completed under neutral conditions at room temperature, and the corresponding disubstituted 1,3,4-oxadiazole derivatives were produced in excellent yields.

**Key words:** (*N*-Isocyanimino)triphenylphosphorane, (*E*)-Cinnamic Acid, Acetaldehyde, 1,3,4-Oxadiazole, *aza*-Wittig Reaction, Secondary Amine

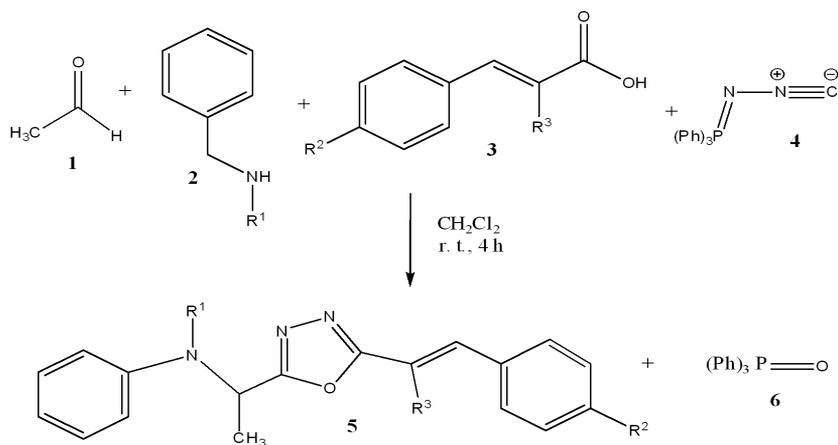
## Introduction

In recent years, multicomponent reactions (MCRs) have become important tools in modern preparative synthetic chemistry because these reactions increase the efficiency by combining several operational steps without any isolation of intermediates or changes of the conditions [1–6]. This principle, therefore, is highly efficient in terms of time as well as resources [7]. Among the multicomponent reactions known to date, the most valuable reactions are those based on isocyanides. Isocyanide-based multicomponent reactions (abbreviated to IMCRs by Ugi and Dömling) by virtue of their synthetic potential, their inherent atom efficiency, convergent nature, ease of implementation, and molecular diversity, have attracted much attention because of the advantages that they offer to the field of combinatorial chemistry [8].

Iminophosphoranes are a special class of zwitterions, which bear a strongly nucleophilic electron-rich nitrogen atom. The electron distribution around the P<sup>+</sup>–N<sup>–</sup> bond and its consequent chemical implications have been probed and assessed through theoretical, spectroscopic and crystallographic investigations [9]. The proton affinity of these iminophosphoranes can be

used as a molecular guide to assess their utility as synthetic reagents and their function as ligands in coordination and organometallic chemistry [9–17].

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. The nucleophilicity of the nitrogen atom 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 and of compounds with biological and pharmacological activity [9–15]. There are several reports for the use of (*N*-isocyanimino)triphenylphosphorane (**4**) in the preparation of metal complexes [16, 17] (Scheme 1). However, the role of (*N*-isocyanimino)triphenylphosphorane in organic chemistry remains almost unexplored [16, 17]. (*N*-isocyanimino)triphenylphosphorane is expected to have unique synthetic potential because it provides a reaction system in which the iminophosphorane group can react with a reagent having a carbonyl function-



Scheme 1. Four-component synthesis of sterically congested 1,3,4-oxadiazole derivatives **5** (see Table 1).

ality [16, 17]. In recent years, we have established a one-pot method for the synthesis of organophosphorus compounds [18–26]. As part of our ongoing program to develop efficient and robust methods for the preparation of heterocyclic compounds [27–35], we wish to report the synthesis of a new class of disubstituted 1,3,4-oxadiazole derivatives **5** by a novel four-component condensation of acetaldehyde (**1**), a secondary amine **2**, an *(E)*-cinnamic acid **3** and *(N*-isocyanimino)triphenylphosphorane (**4**) in excellent yields under neutral conditions (Scheme 1).

1,3,4-Oxadiazoles have attracted interest in medicinal chemistry as surrogates of carboxylic acids, esters, and carboxamides. They are an important class of heterocyclic compounds that have a wide range of pharmaceutical and biological activities including antimicrobial, anti-fungal, anti-inflammatory, antihypertensive, analgesic, antibacterial, hypoglycemic, antimalarial, antitubercular, and antidepressant [36–38] properties. Several methods have been reported in the literature for the synthesis of 1,3,4-oxadiazoles. These protocols are multi-step in nature [39–41]. The most general method involves the cyclization of diacylhydrazides with a variety of reagents, such as thionyl chloride, phosphorus oxychloride, or sulfuric acid, usually under harsh reaction conditions. Few reliable and operationally simple examples have been reported for the one-step synthesis of 1,3,4-oxadiazoles, especially from readily available carboxylic acids and acid hydrazides [40–42].

## Results and Discussion

The 1:1 imine intermediate generated by the addition of secondary amine **2** to acetaldehyde (**1**) is trapped by *(N*-isocyanimino)triphenylphosphorane in

the presence of an *(E)*-cinnamic acid derivative **3**, leading to the formation of a 1,3,4-oxadiazole derivative **5** and triphenylphosphine oxide (**6**) (Scheme 1 and Table 1). The reaction proceeds smoothly and cleanly under mild conditions, and no side reactions are observed.

The structures of the products were deduced from their IR,  $^1\text{H}$  NMR, and  $^{13}\text{C}$  NMR data and elemental analyses. For example the  $^1\text{H}$  NMR spectrum of **5a** consisted of a singlet for the three  $\text{CH}_3$  groups of the amine ( $\delta = 1.17$  ppm), a doublet for a  $\text{CH}_3$  group ( $\delta = 1.53$  ppm,  $^3J = 7.0$  Hz), a singlet for a  $\text{CH}_3$  group ( $\delta = 2.39$  ppm), an AB-quartet for the benzyl group ( $\delta = 3.99$  and 4.14 ppm,  $^2J = 17.3$  Hz), a quartet for the CH group ( $\delta = 4.76$  ppm,  $^3J = 7.0$  Hz) and a multiplet at  $\delta = 6.94$ – $7.47$  ppm for the aromatic and vinylic protons. The  $^1\text{H}$ -decoupled  $^{13}\text{C}$  NMR spectrum of **5a** showed 18 distinct resonances [ $\delta = 18.75$ , 21.43 and 28.62 (4  $\text{CH}_3$ ), 56.24 (C, aliphatic), 47.90 ( $\text{CH}_2\text{Ph}$ ), 48.41 (CH, aliphatic), 109.18 and 138.44 (2 CH, vinylic), 132.11, 140.20 and 143.80 (3 C, arom.), 126.05, 126.81, 127.41, 127.94 and 129.71 (9 CH, arom.), 164.07 and 168.59 (2 C=N, oxadiazole ring)]. The  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra of compounds **5b**–**i** are similar to those of **5a**, except for the aromatic or aliphatic moieties, which exhibited characteristic signals with appropriate chemical shifts.

A mechanistic rationalization for this reaction is provided in Scheme 2. It is conceivable that the initial event is the condensation of acetaldehyde (**1**), secondary amine **2**, and *(E)*-cinnamic acid **3** entities to an intermediate iminium ion **7**. Nucleophilic addition of phosphorane **4** to iminium ion **7** leads to the nitrilium intermediate **8**. This intermediate may be attacked by the conjugate base of the acid **3** to form the 1 : 1 : 1

<i>(E)</i> -cinnamic acid <b>3</b>	Secondary amine <b>2</b>	Product <b>5</b>	Yield (%) <sup>a</sup>
		<b>5a</b>	85
		<b>5b</b>	87
		<b>5c</b>	84
		<b>5d</b>	80
		<b>5e</b>	81
		<b>5f</b>	80
		<b>5g</b>	81
		<b>5h</b>	80
		<b>5i</b>	83

Table 1. Synthesis of sterically congested 1,3,4-oxadiazole derivatives **5** from *(E)*-cinnamic acid derivatives **3**, acetaldehyde (**1**) and secondary amines **2** in the presence of (*N*-isocyanimino)triphenylphosphorane (**4**) (see Scheme 1).

<sup>a</sup> Isolated yields.

adduct **9**. This adduct may undergo an intramolecular *aza*-Wittig reaction of the iminophosphorane moiety with the ester carbonyl group to afford the 2,5-disubstituted 1,3,4-oxadiazole **5** after elimination of triphenylphosphine oxide (**6**) from intermediate **10**.

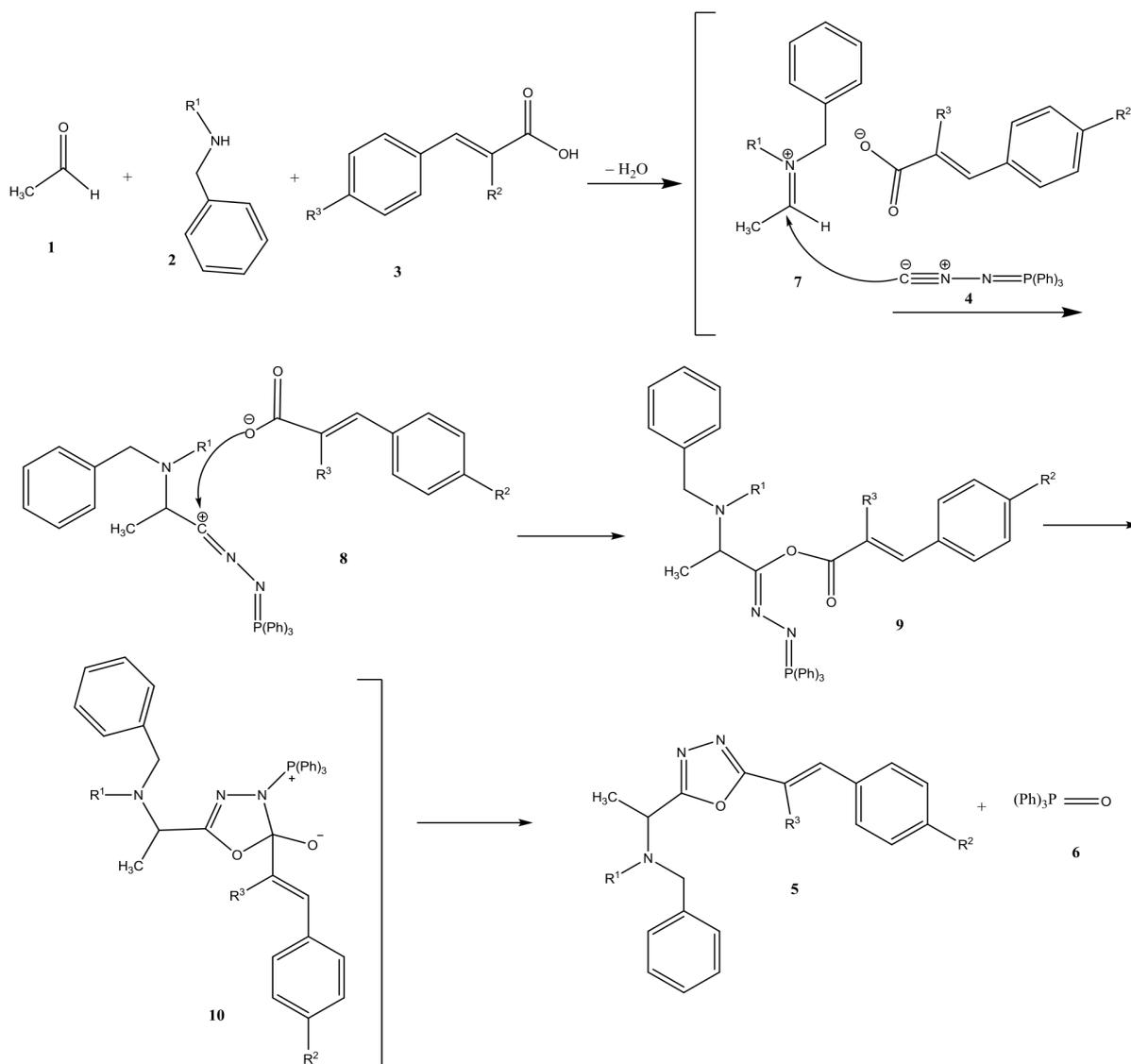
## Conclusions

We believe that the reported method offers a mild, simple, and efficient route for the preparation of sterically congested 1,3,4-oxadiazole derivatives, by a sequence of multicomponent reactions and an intramolecular *aza*-Wittig reaction. This synthetic approach and the neutral ring closure conditions have the

potential in the synthesis of various 2,5-disubstituted 1,3,4-oxadiazoles, which are of considerable interest as biologically active compounds or pharmaceuticals.

## Experimental Section

Starting materials and solvents were obtained from Merck (Germany) and Fluka (Switzerland) and were used without further purification. TLC and NMR spectroscopy were used to follow the reactions. Melting points were measured on an Electrothermal 9100 apparatus and are uncorrected. IR spectra were measured on a Jasco 6300 FTIR spectrometer. <sup>1</sup>H and <sup>13</sup>C NMR spectra were measured (CDCl<sub>3</sub> solution) with a Bruker DRX-250 Avance spectrometer at 250.0



Scheme 2. Proposed mechanism for the formation of sterically congested 1,3,4-oxadiazole derivatives **5a–i**.

and 62.5 MHz, respectively. Elemental analyses were performed using a Heraeus CHN-O-Rapid analyzer. Mass spectra were recorded on a Finnigan-MATT 8430 mass spectrometer operating at an ionization potential of 20 eV. Flash chromatography columns were prepared from Merck silica gel powder.

*Preparation of N-benzyl-N-(tert-butyl)-N-(1-[5-[(E)-2-(4-methylphenyl)-1-ethenyl]-1,3,4-oxadiazol-2-yl]ethyl)amine (5a). General procedure*

A mixture of (*N*-isocyanimino)triphenylphosphorane (**4**) (1.0 mmol), acetaldehyde (**1**) (1.0 mmol) and a secondary

amine **2** (1.0 mmol) in  $\text{CH}_2\text{Cl}_2$  (5 mL) was added dropwise to a solution of an (*E*)-cinnamic acid derivative **3** (1 mmol) in  $\text{CH}_2\text{Cl}_2$  (5 mL) at r. t. over 15 min. The mixture was stirred for 4 h. Then, the solvent was removed under reduced pressure, and the viscous residue was purified by flash column chromatography (silica gel powder; petroleum ether-ethyl acetate (2 : 1)). The solvent was removed under reduced pressure to give the product as a yellow oil. Yield: 85%. – IR (neat):  $\nu = 3456, 2977, 1644, 1533, 1454, 1150, 970, 808 \text{ cm}^{-1}$ . –  $^1\text{H NMR}$  ( $\text{CDCl}_3$ ):  $\delta = 1.17$  (s, 9 H,  $(\text{CH}_3)_3$ ), 1.53 (d, 3 H,  $^3J = 7.0 \text{ Hz}$ ,  $\text{CHCH}_3$ ), 2.39 (s, 3 H,  $\text{CH}_3$ ), 3.99 and 4.14 (AB quartet, 2 H,  $^2J = 17.3 \text{ Hz}$ ,  $\text{CH}_2$  of

benzyl group), 4.76 (q, 1 H,  $^3J = 7.0$  Hz, CH), 6.94–7.47 (m, 11 H, arom. and vinylic). –  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ ):  $\delta = 18.75, 21.43$  and  $28.62$  (4  $\text{CH}_3$ ),  $56.24$  (C, aliphatic),  $47.90$  ( $\text{CH}_2\text{Ph}$ ),  $48.41$  (CH),  $109.18$  and  $138.44$  (2 CH, vinylic),  $132.11, 140.20$  and  $143.80$  (3 C, arom.),  $126.05, 126.81, 127.41, 127.94$  and  $129.71$  (9 CH, arom.),  $164.07$  and  $168.59$  (2 C=N). – MS:  $m/z = 376$  (2)  $[\text{M}]^+$ ,  $360$  (6),  $213$  (76),  $162$  (72),  $145$  (50),  $105$  (37),  $91$  (100),  $83$  (48),  $69$  (17),  $56$  (66),  $43$  (48). –  $\text{C}_{24}\text{H}_{29}\text{N}_3\text{O}$  (375.51): calcd. C 76.76, H 7.78, N 11.19; found C 76.78, H 7.76, N 11.18.

*N*-Benzyl-*N*-(*tert*-butyl)-*N*-(1-[5-[(*E*)-1-methyl-2-phenyl-1-ethenyl]-1,3,4-oxadiazol-2-yl]ethyl)amine (**5b**)

Yellow oil, yield: 87%. – IR (neat):  $\nu = 3470, 2978, 1638, 1527, 1452, 1208, 924, 697$   $\text{cm}^{-1}$ . –  $^1\text{H}$  NMR ( $\text{CDCl}_3$ ):  $\delta = 1.17$  (s, 9 H,  $(\text{CH}_3)_3$ ),  $1.53$  (d, 3 H,  $^3J = 7.0$  Hz,  $\text{CHCH}_3$ ),  $2.37$  (s, 3 H,  $\text{CH}_3$ ),  $3.99$  and  $4.14$  (AB quartet, 2 H,  $^2J = 17.3$  Hz,  $\text{CH}_2$  of benzyl group),  $4.76$  (q, 1 H,  $^3J = 7.0$  Hz, CH),  $7.15$ – $7.45$  (m, 11 H, arom. and vinylic). –  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ ):  $\delta = 14.57, 18.85$  and  $28.64$  (5  $\text{CH}_3$ ),  $56.22$  (C, aliphatic),  $47.95$  ( $\text{CH}_2\text{Ph}$ ),  $48.49$  (CH),  $121.67$  (1 CH, vinylic),  $143.88$  (1 C, vinylic),  $133.79$  and  $135.65$  (2 C, arom.),  $126.01, 126.81, 127.93, 128.20, 128.48$  and  $129.53$  (10 CH, arom.),  $166.39$  and  $168.97$  (2 C=N). – MS:  $m/z = 376$  (2)  $[\text{M}]^+$ ,  $360$  (10),  $318$  (3),  $270$  (5),  $213$  (82),  $199$  (20),  $190$  (15),  $162$  (92),  $148$  (26),  $105$  (41),  $91$  (100),  $83$  (48),  $56$  (43),  $41$  (30). –  $\text{C}_{24}\text{H}_{29}\text{N}_3\text{O}$  (375.51): calcd. C 76.76, H 7.78, N 11.19; found C 76.77, H 7.75, N 11.20.

*N*-Benzyl-*N*-isopropyl-*N*-(1-[5-[(*E*)-1-methyl-2-phenyl-1-ethenyl]-1,3,4-oxadiazol-2-yl]ethyl)amine (**5c**)

Yellow oil, yield: 84%. – IR (neat):  $\nu = 3459, 2970, 2956, 1528, 1454, 1173, 1105, 956$   $\text{cm}^{-1}$ . –  $^1\text{H}$  NMR ( $\text{CDCl}_3$ ):  $\delta = 0.92$  (d, 3 H,  $^3J = 6.5$  Hz,  $\text{CH}_3$ ),  $1.02$  (d, 3 H,  $^3J = 6.5$  Hz,  $\text{CH}_3$ ),  $1.55$  (d, 3 H,  $^3J = 7.0$  Hz,  $\text{CH}_3$ ),  $2.39$  (s, 3 H,  $\text{CH}_3$ ),  $3.15$ – $3.23$  (m, 1 H, CH),  $3.77$  and  $3.90$  (AB quartet, 2 H,  $^2J = 15.0$  Hz,  $\text{CH}_2$  of benzyl group),  $4.26$  (q, 1 H,  $^3J = 7.0$  Hz, CH),  $7.22$ – $7.45$  (m, 11 H, arom. and vinylic). –  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ ):  $\delta = 14.58, 16.96, 19.50$  and  $21.14$  (4  $\text{CH}_3$ ),  $48.30$  ( $\text{CH}_2\text{Ph}$ ),  $48.95$  and  $49.63$  (2 CH),  $121.65$  (1 CH, vinylic),  $143.75$  (1 C, vinylic),  $133.92$  and  $135.75$  (2 C, arom.),  $126.05, 126.75, 127.85, 128.21, 128.50$  and  $129.55$  (10 CH, arom.),  $165.98$  and  $168.87$  (2 C=N). – MS:  $m/z = 360$  (2)  $[\text{M}]^+$ ,  $346$  (3),  $227$  (7),  $213$  (100),  $148$  (90),  $91$  (93),  $69$  (31),  $56$  (54),  $43$  (59). –  $\text{C}_{23}\text{H}_{27}\text{N}_3\text{O}$  (361.48): calcd. C 76.42, H 7.53, N 11.6; found C 76.37, H 7.57, N 11.62.

*N*-Benzyl-*N*-ethyl-*N*-(1-[5-[(*E*)-1-methyl-2-phenyl-1-ethenyl]-1,3,4-oxadiazol-2-yl]ethyl)amine (**5d**)

Yellow oil, yield: 80%. – IR (neat):  $\nu = 3459, 2974, 2932, 1527, 1454, 1107, 924, 767$   $\text{cm}^{-1}$ . –  $^1\text{H}$  NMR ( $\text{CDCl}_3$ ):  $\delta = 1.09$  (t, 3 H,  $^3J = 7.0$  Hz,  $\text{CH}_3$   $\text{CH}_2$ ),  $1.57$  (d, 3 H,  $^3J =$

$6.8$  Hz,  $\text{CH}_3$ ),  $2.39$  (s, 3 H,  $\text{CH}_3$ ),  $2.48$ – $2.53$  and  $2.71$ – $2.79$  (2 m, 2 H,  $\text{CH}_2\text{CH}_3$ ),  $3.54$  and  $3.87$  (AB quartet, 2 H,  $^2J = 14.3$  Hz,  $\text{CH}_2$  of benzyl group),  $4.26$  (q, 1 H,  $^3J = 6.8$  Hz, CH),  $7.24$ – $7.48$  (m, 11 H, arom. and vinylic). –  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ ):  $\delta = 13.75, 14.58$  and  $15.47$  (3  $\text{CH}_3$ ),  $44.45$  ( $\text{CH}_2\text{CH}_3$ ),  $50.80$  ( $\text{CH}_2\text{Ph}$ ),  $54.42$  (CH, aliphatic),  $121.60$  (1 CH, vinylic),  $143.75$  (1 C, vinylic),  $132.91$  and  $134.09$  (3 C, arom.),  $126.07, 126.92, 127.95, 128.25, 128.50$  and  $129.54$  (10 CH, arom.),  $165.92$  and  $168.55$  (2 C=N). – MS:  $m/z = 348$  (1)  $[\text{M}]^+$ ,  $213$  (44),  $162$  (6),  $145$  (9),  $134$  (100),  $115$  (12),  $91$  (86),  $41$  (10). –  $\text{C}_{22}\text{H}_{25}\text{N}_3\text{O}$  (347.45): calcd. C 76.05, H 7.25, N 12.09; found C 76.04, H 7.59, N 12.08.

*N*-Benzyl-*N*-ethyl-*N*-(1-[5-[(*E*)-2-(4-methylphenyl)-1-ethenyl]-1,3,4-oxadiazol-2-yl]ethyl)amine (**5e**)

Yellow oil, yield: 81%. – IR (neat):  $\nu = 3467, 2978, 2938, 1644, 1533, 1455, 971, 808$   $\text{cm}^{-1}$ . –  $^1\text{H}$  NMR ( $\text{CDCl}_3$ ):  $\delta = 1.09$  (t, 3 H,  $^3J = 7.0$  Hz,  $\text{CH}_3\text{CH}_2$ ),  $1.57$  (d, 3 H,  $^3J = 7.0$  Hz,  $\text{CH}_3$ ),  $2.39$  (s, 3 H,  $\text{CH}_3$ ),  $2.44$ – $2.55$  and  $2.67$ – $2.78$  (2 m, 2 H,  $\text{CH}_2\text{CH}_3$ ),  $3.54$  and  $3.87$  (AB quartet, 2 H,  $^2J = 14.3$  Hz,  $\text{CH}_2$  of benzyl group),  $4.26$  (q, 1 H,  $^3J = 7.0$  Hz, CH),  $6.99$ – $7.52$  (m, 11 H, arom. and vinylic). –  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ ):  $\delta = 13.77, 15.42$  and  $21.44$  (3  $\text{CH}_3$ ),  $44.45$  ( $\text{CH}_2\text{CH}_3$ ),  $50.75$  ( $\text{CH}_2\text{Ph}$ ),  $54.42$  (CH, aliphatic),  $109.14$  and  $138.78$  (2 CH, vinylic),  $132.06, 139.86$  and  $140.28$  (3 C, arom.),  $126.93, 127.44, 128.26, 128.51$  and  $129.72$  (9 CH, arom.),  $164.58$  and  $166.55$  (2 C=N). – MS:  $m/z = 348$  (1)  $[\text{M}]^+$ ,  $227$  (30),  $214$  (65),  $185$  (20),  $161$  (27),  $134$  (100),  $91$  (72),  $69$  (21),  $55$  (34). –  $\text{C}_{22}\text{H}_{25}\text{N}_3\text{O}$  (347.45): calcd. C 76.05, H 7.25, N 12.09; found C 76.02, H 7.28, N 12.10.

*N*-Benzyl-*N*-isopropyl-*N*-(1-[5-[(*E*)-2-phenyl-1-ethenyl]-1,3,4-oxadiazol-2-yl]ethyl)amine (**5f**)

Yellow oil, yield: 80%. – IR (neat):  $\nu = 3456, 2965, 2929, 1649, 1525, 1385, 1173, 990, 731$   $\text{cm}^{-1}$ . –  $^1\text{H}$  NMR ( $\text{CDCl}_3$ ):  $\delta = 0.90$  (d, 3 H,  $^3J = 6.3$  Hz,  $\text{CH}_3$ ),  $1.14$  (d, 3 H,  $^3J = 6.3$  Hz,  $\text{CH}_3$ ),  $1.56$  (d, 3 H,  $^3J = 6.8$  Hz,  $\text{CH}_3$ ),  $3.18$ – $3.23$  (m, 1 H, CH),  $3.78$  and  $3.89$  (AB quartet, 2 H,  $^2J = 15.0$  Hz,  $\text{CH}_2$  of benzyl group),  $4.26$  (q, 1 H,  $^3J = 6.8$  Hz, CH),  $6.99$ – $7.58$  (m, 12 H, arom. and vinylic). –  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ ):  $\delta = 16.92, 19.45$  and  $21.23$  (3  $\text{CH}_3$ ),  $48.31$  ( $\text{CH}_2\text{Ph}$ ),  $48.87$  and  $49.63$  (2 CH),  $110.23$  and  $138.60$  (2 CH, vinylic),  $134.79$  and  $139.30$  (2 C, arom.),  $126.78, 127.47, 128.23, 129$  and  $129.89$  (10 CH, arom.),  $164.49$  and  $167.72$  (2 C=N). –  $\text{C}_{22}\text{H}_{25}\text{N}_3\text{O}$  (347.45): calcd. C 76.05, H 7.25, N 12.0; found C 76.07, H 7.23, N 12.11.

*N*-Benzyl-*N*-(*tert*-butyl)-*N*-(1-[5-[(*E*)-2-phenyl-1-ethenyl]-1,3,4-oxadiazol-2-yl]ethyl)amine (**5g**)

Yellow oil, yield 81%. – IR (neat):  $\nu = 3467, 2977, 1647, 1529, 1207, 970, 756$   $\text{cm}^{-1}$ . –  $^1\text{H}$  NMR ( $\text{CDCl}_3$ ):  $\delta = 1.17$

(s, 9 H, (CH<sub>3</sub>)<sub>3</sub>), 1.53 (d, 3 H, <sup>3</sup>J = 7.0 Hz, CH<sub>3</sub>), 3.99 and 4.14 (AB quartet, 2 H, <sup>2</sup>J = 17.3 Hz, CH<sub>2</sub> of benzyl group), 4.76 (q, 1 H, <sup>3</sup>J = 7.0 Hz, CH), 6.96–7.56 (m, 12 H, arom. and vinylic). – <sup>13</sup>C NMR (CDCl<sub>3</sub>): δ = 18.68 and 28.63 (4 CH<sub>3</sub>), 56.24 (C, aliphatic), 47.89 (CH<sub>2</sub>Ph), 48.40 (CH), 110.21 and 138.45 (2 CH, vinylic), 134.81 and 136.30 (2 C, arom.), 126.06, 126.81, 127.44, 127.94, 128.99 and 129.84 (10 CH, arom.), 163.91 and 168.71 (2 C=N). – C<sub>23</sub>H<sub>27</sub>N<sub>3</sub>O (361.48): calcd. C 76.42, H 7.53, N 11.62; found C 76.45, H 7.51, N 11.65.

*N,N*-Dibenzyl-*N*-(1-[5-[(*E*)-2-phenyl]-1-ethenyl]-1,3,4-oxadiazol-2-yl)ethylamine (**5h**)

Yellow oil, yield: 80%. – IR (neat): ν = 3492, 2939, 1630, 1530, 1446, 970, 750 cm<sup>-1</sup>. – <sup>1</sup>H NMR (CDCl<sub>3</sub>): δ = 1.63 (d, 3 H, <sup>3</sup>J = 7.0 Hz, CH<sub>3</sub>), 3.54 and 3.89 (AB quartet, 4 H, <sup>2</sup>J = 13.8 Hz, 2 CH<sub>2</sub> of benzyl groups), 4.24 (q, 1 H, <sup>3</sup>J = 7.0 Hz, CH), 7.01–7.65 (m, 17 H, arom. and vinylic). – <sup>13</sup>C NMR (CDCl<sub>3</sub>): δ = 15.06 (CH<sub>3</sub>), 49.81 (CH), 54.26 (2 CH<sub>2</sub> of benzyl groups), 110.19 and 138.93 (2 CH, vinylic), 134.75 and 139.17 (3 C, arom.), 127.19, 127.52, 128.32, 128.70, 129.05 and 129.99 (15 CH, arom.), 164.48 and 166.34 (2 C=N). – C<sub>26</sub>H<sub>25</sub>N<sub>3</sub>O (395.50): calcd. C 78.96, H 6.37, N 10.62; found C 78.94, H 6.35, N 10.65.

*N*-Benzyl-*N*-isopropyl-*N*-(1-[5-[(*E*)-2-(4-methylphenyl)-1-ethenyl]-1,3,4-oxadiazol-2-yl]ethyl)amine (**5i**)

Yellow crystals, yield: 83%; m. p. 74.0–75.2 °C. – IR (KBr): ν = 3476, 2987, 2929, 1649, 1528, 1453, 1173, 988, 809 cm<sup>-1</sup>. – <sup>1</sup>H NMR (CDCl<sub>3</sub>): δ = 0.90 (d, 3 H, <sup>3</sup>J = 6.5 Hz, CH<sub>3</sub>), 1.14 (d, 3 H, <sup>3</sup>J = 6.5 Hz, CH<sub>3</sub>), 1.56 (d, 3 H, <sup>3</sup>J = 7.0 Hz, CH<sub>3</sub>), 2.40 (s, 3 H, CH<sub>3</sub>), 3.15–3.26 (m, 1 H, CH), 3.78 and 3.90 (AB quartet, 2 H, <sup>2</sup>J = 15.0 Hz, CH<sub>2</sub> of benzyl group), 4.25 (q, 1 H, <sup>3</sup>J = 7.0 Hz, CH), 6.98–7.50 (m, 11 H, arom. and vinylic). – <sup>13</sup>C NMR (CDCl<sub>3</sub>): δ = 16.96, 19.44, 21.28 and 21.45 (4 CH<sub>3</sub>), 48.28 (CH<sub>2</sub>Ph), 48.83 and 49.60 (2 CH); 109.17 and 138.58 (2 CH, vinylic), 132.08, 140.24 and 140.82 (3 C, arom.), 126.17, 127.43, 128.19, 128.21 and 129.72 (9 CH, arom.), 164.39 and 167.60 (2 C=N). – C<sub>23</sub>H<sub>27</sub>N<sub>3</sub>O (361.48): calcd. C 76.42, H 7.53, N 11.62; found C 76.38, H 7.56, N 11.63.

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