The Reaction of *N*-Isocyaniminotriphenylphosphorane with 2-Oxopropylbenzoate (or 4-Bromobenzoate) and a Primary Amine in the Presence of (*E*)-Cinnamic Acid Derivatives: A One-Pot Efficient Four-Component Reaction for the Synthesis of 2-(Arylamino)-2-(5-aryl-1-ethenyl-1,3,4-oxadiazol-2-yl) Propyl Benzoate (or 4-Bromobenzoate) Derivatives

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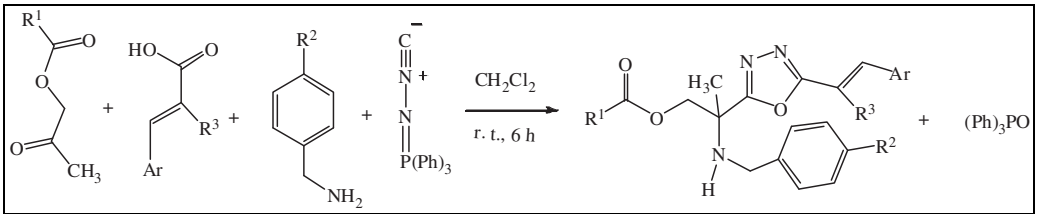

Reactions of *N*-isocyaniminotriphenylphosphorane with 2-oxopropylbenzoate (or 2-oxopropyl 4-bromobenzoate) in the presence of (*E*)-cinnamic acids and primary amines proceed smoothly at room temperature and in neutral conditions to afford sterically congested 1,3,4-oxadiazole derivatives in high yields. The reaction proceeds smoothly and cleanly under mild conditions and no side reactions were observed.

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INTRODUCTION

Multicomponent reaction (MCR) is a chemical reaction where three or more compounds react to form a single product. By definition, MCRs are those reactions whereby more than two reactants combine in a sequential manner to give highly selective products that retain majority of the atoms of the starting material. The development of novel MCRs is receiving growing interest from industrial chemistry research groups and represents a challenge for organic chemists [1,2]. The drive toward the ideal synthesis embracing step count, ideally just one, and yield, ideally 100%, has been pursued aggressively since scientists began to construct molecules. Of course, there are many other factors that affect these two aspects of synthesis, including cost; starting material availability; safety; environmental concerns; and overall ease of the process, including work up and purification [3]. The nature of the synthesis project also plays a role. Complex molecule total synthesis is often driven by step count while showcasing innovative chemistry. Traditional structure–activity relationship evaluations in medicinal chemistry typically involve the preparation of an advanced intermediate that can be analogued readily to introduce the molecular diversity necessary to prepare a collection, or library, of structurally related compounds. One strategy that potentially meets the goals of total synthesis and library production is MCR chemistry, in which three or more starting materials are brought together in a highly convergent approach to rapidly build up molecular structure and complexity [4].

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, antifungal, anti-inflammatory, and antihypertensive [5–9].

Several methods have been reported in the literature for the synthesis of 1,3,4-oxadiazoles. These protocols are multistep in nature [10–15]. 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 [16–21].

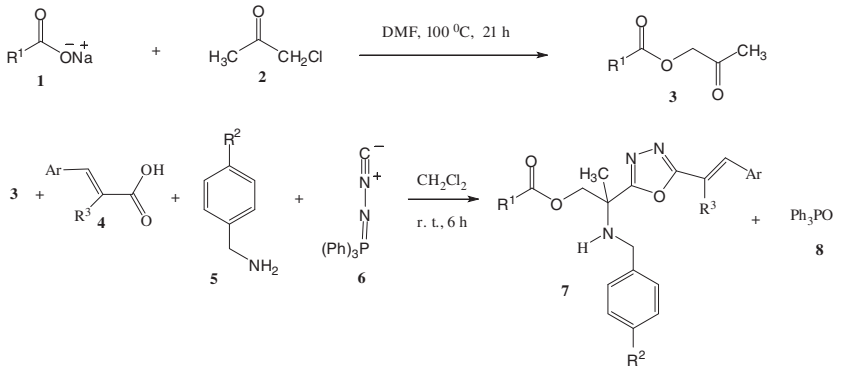
In recent years, several synthetic methods have been reported for the preparation of *N*-isocyaniminotriphenylphosphorane ($CNNPPh_3$) **6** [12,13]. There are several reports on the use of *N*-isocyaniminotriphenylphosphorane ($CNNPPh_3$) **6** in the synthesis of metal complexes [12,13]. However, application of **6** in the synthesis of organic compounds is

fairly rare [22–31]. In recent years, we have established a one-pot method for the synthesis of organophosphorus compounds [14–22]. As part of our ongoing program to develop efficient and robust methods for the preparation of heterocyclic compounds [23–35], we wish to report the synthesis of a disubstituted 1,3,4-oxadiazole derivatives **7** by a four-component condensation of *N*-isocyaniminotriphenylphosphorane **6** with 2-oxopropylbenzoate (or 2-oxopropyl 4-bromobenzoate) in the presence of (*E*)-cinnamic acids and primary amines (Scheme 1).

RESULTS AND DISCUSSION

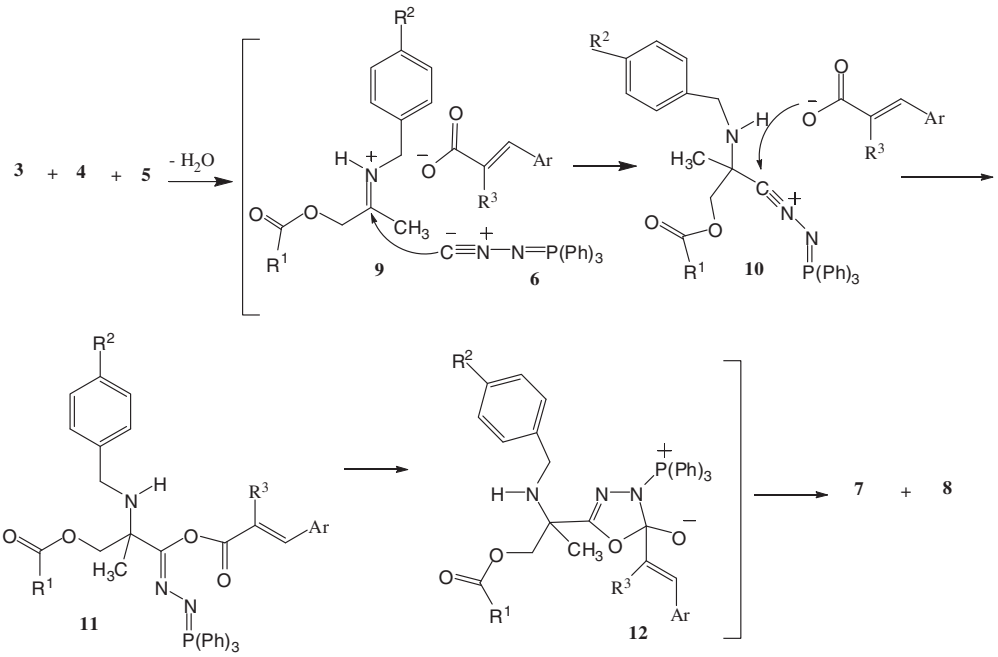
The imine intermediate generated by the reaction of primary amine **5** with 2-oxopropyl benzoate (or 4-bromobenzoate) **3** is trapped by the *N*-isocyaniminotriphenylphosphorane in the presence of an (*E*)-cinnamic acid derivative **4** to lead to the formation of disubstituted 1,3,4-oxadiazole derivatives **7** and triphenylphosphine oxide (**8**, Scheme 1). The reaction proceeds smoothly and cleanly under mild conditions and no side reactions were observed.

Scheme 1. Synthesis of 2-oxopropylbenzoate (or 4-bromobenzoate) **3** and four-component synthesis of disubstituted 1,3,4-oxadiazole derivatives **7a–l** (Experimental section).



7a: R^1=Ph, R^2=Me, R^3=H, Ar=C_6H_4; **7b**: R^1=Ph, R^2=Me, R^3=Me, Ar= C_6H_4; **7c**: R^1=4-BrC_6H_4, R^2=H, R^3=Me, Ar= C_6H_4; **7d**: R^1=Ph, R^2=H, R^3=H, Ar= C_6H_4; **7e**: R^1=Ph, R^2=H, R^3=Me, Ar= C_6H_4; **7f**: R^1=4-BrC_6H_4, R^2=Me, R^3=Me, Ar= C_6H_4; **7g**: R^1=Ph, R^2=H, R^3=H, Ar= 4-ClC_6H_4; **7h**: R^1=4-BrC_6H_4, R^2=H, R^3=H, Ar= C_6H_4; **7i**: R^1=Ph, R^2=OMe, R^3=Me, Ar= C_6H_4; **7j**: R^1=Ph, R^2=H, R^3=H, Ar= 4-MeC_6H_4; **7k**: R^1=Ph, R^2=Me, R^3=H, Ar= 3-ClC_6H_4; **7l**: R^1=4-BrC_6H_4, R^2=Me, R^3=H, Ar= C_6H_4

Scheme 2. Proposed mechanism for the formation of disubstituted 1,3,4-oxadiazole derivatives **7a–l**.



The structures of the products were deduced from their ^{1}H NMR, ^{13}C NMR, mass and IR spectra. For example the ^{1}H NMR spectrum of **7a** consisted of two singlet for the 2 CH_3 ($\delta = 1.81$ and 2.30 ppm), a singlet for the NH ($\delta = 2.25$), an AB quartet for CH_2 benzyl group at $\delta = 3.71$ and 3.80 ppm ($J = 12.1$ Hz), an AB quartet for CH_2 aliphatic at $\delta = 4.60$ and 4.71 ppm ($J = 11.0$ Hz) and a multiplet at $\delta = 6.98$–7.70 ppm (H-aromatic and vinylic) and a doublet at $\delta = 8.00$ ppm (d, 2H, $J = 7.8$ Hz, ortho protons of benzoate group). The aryl groups exhibited characteristic signals in the aromatic region of the spectrum. The ^{1}H-decoupled ^{13}C NMR spectrum of **7a** showed 21 distinct resonances, and partial assignment of these resonances is given in the Experimental section. The ^{1}H and ^{13}C NMR spectra of compounds **7b–l** were similar to those of **7a**, except for the aromatic and 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 reaction of the (*E*)-cinnamic acid derivative **4**, 2-oxopropyl benzoate (or 4-bromobenzoate) **3**, and primary amine **5** that leads to an intermediate iminium ion **9**. Nucleophilic addition of the *N*-isocyaniminotriphenylphosphorane **6** to the intermediate iminium ion **9** leads to nitrilium intermediate **10**. This intermediate may be attacked by the conjugate base of the acid **4** to form 1:1:1 adduct **11**. This adduct may undergo an intramolecular *aza*-Wittig reaction of an iminophosphorane moiety with the ester carbonyl group to afford the isolated disubstituted 1,3,4-oxadiazole **7** by removal of triphenylphosphine oxide **8** from intermediate **12**.

CONCLUSIONS

The reported method offers a mild, simple, and efficient route for the preparation of sterically congested 1,3,4-oxadiazole derivatives **7** from 2-oxopropyl benzoate (or 4-bromobenzoate) **3**, primary amine **5**, *N*-isocyaniminotriphenylphosphorane **6** and (*E*)-cinnamic acids **4**. Its ease of work-up, high yields, and fairly mild reaction conditions makes it a useful addition to modern synthetic methodologies.

EXPERIMENTAL

Starting materials and solvents were obtained from Merck (Germany) and Fluka (Switzerland) and were used without further purification. The methods used to follow the reactions are TLC and NMR, which indicated that there is no side product. Melting points were measured on an Electrothermal 9100 apparatus and are uncorrected. IR spectra were measured on a Jasco 6300 FTIR spectrometer (Tokyo, Japan). ^{1}H and ^{13}C NMR spectra were measured ($CDCl_3$) with a BRUKER DRX-250 AVANCE spectrometer (Billerica, MA) 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. Flash chromatography columns were prepared with Merck silica gel. 2-Oxopropyl benzoate (or 4-bromobenzoate) **3** [36] and *N*-isocyaniminotriphenylphosphorane **6** [12,13] were prepared based on known procedures.

General procedure for the preparation of 7a–l. To a magnetically stirred solution of primary amine **5** [1 mmol; 0.107 g ($C_6H_5CH_2NH_2$), 0.121 g (4-$MeC_6H_4CH_2NH_2$), and 0.137 g (4-$MeOC_6H_4CH_2NH_2$)], (2-oxopropyl benzoate and 2-oxopropyl 4-bromobenzoate) **3** [1 mmol; 0.178 g (R = Ph) and 0.257 g (R = 4-BrC_6H_4)], and *N*-isocyaniminotriphenylphosphorane **6** (1 mmol, 0.302 g) in CH_2Cl_2 (5 mL) was added dropwise a solution of an (*E*)-cinnamic acid **4** [1 mmol; 0.148 g (Ar = C_6H_4), 0.162 g (Ar = α-MeC_6H_4), 0.162 g (Ar = 4-MeC_6H_4), and 0.182 g (Ar = 4-ClC_6H_4)] in CH_2Cl_2 (5 mL) at room temperature over 15 min. The mixture was stirred for 6 h. The solvent was removed under reduced pressure, the viscous residue was purified by flash column chromatography [silica gel; petroleum ether–ethyl acetate (10:2)], and the products (**7a–l**) were obtained. The solvent was removed under reduced pressure to give product **6**. The characterization data of the compounds are given in the succeeding paragraphs.

2-[(4-Methylphenyl)amino]-2-{5-[(*E*)-2-phenyl-1-ethenyl]-1,3,4-oxadiazol-2-yl}propyl benzoate (7a). This compound was obtained as yellow oil, the yield was 403 mg (89%), ir (neat): 3388, 1720, 1642, 1447, 1266, 1105, 706 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 1.81, 2.30 (s, 6H, $2CH_3$), 2.25 (s, 1H, NH), 3.71, 3.80 (AB quartet, 2H, $J = 12.1$ Hz, CH_2 of benzyl group); 4.60, 4.71 (AB quartet, $J = 11.0$ Hz, 2H, CH_2 aliphatic), 6.98–7.70 (m, 14H, H-Ar and Vinylic), 8.00 (d, 2H, $J = 7.8$ Hz, H-Ar). ^{13}C NMR ($CDCl_3$): δ 21.07 ($2CH_3$), 47.50 (CH_2 of benzyl group), 56.70 (C aliphatic), 69.14 (CH_2 aliphatic), 109.84 and 136.90 (2 CH, vinylic), 129.52, 133.32, 134.61, 136.65 (4C arom), 127.48, 128.13, 128.50, 129.01, 129.19, 129.68, 130.03, 139.15 (14CH arom), 164.82, 165.83 (2C of oxadiazole), 167.58 (C of benzoate group). EI ms: *m/z*: 453 (M^+), 390 (5), 212 (29), 190 (34), 171 (100), 149 (16), 105 (81), 77 (21), 57 (9). *Anal*. Calcd. for $C_{28}H_{27}N_3O_3$ (453.53): C, 74.15; H, 6.00; N, 9.27. Found: C, 74.11; H, 6.03; N, 9.32.

2-[(4-Methylbenzyl)amino]-2-{5-[(*E*)-1-methyl-2-phenyl-1-ethenyl]-1,3,4-oxadiazol-2-yl}propyl benzoate (7b). This compound was obtained as yellow oil, the yield was 406 mg (87%), ir (neat): 3313, 2914, 1719, 1446, 1261, 1090, 704 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 1.80, 2.30, 2.38 (s, 9H, $3CH_3$), 2.27 (s, 1H, NH), 3.72, 3.80 (AB quartet, 2H, $J = 12.1$ Hz, CH_2 of benzyl group); 4.59, 4.70 (AB quartet, $J = 10.9$ Hz, 2H, CH_2 aliphatic), 6.97–7.70 (m, 13H, H-Ar and vinylic), 8.00 (d, 2H, $J = 7.8$ Hz, H-Ar). ^{13}C NMR ($CDCl_3$): δ 14.56, 21.07 ($3CH_3$), 47.54 (CH_2 of benzyl group), 56.67 (C aliphatic), 69.24 (CH_2 aliphatic), 121.36 (CH, vinylic), 128.34, 134.41, 135.41, 136.70 (4C arom), 128.16, 128.48, 129.18, 129.54, 129.68, 133.28 (14CH arom), 136.86 (C, vinylic), 165.83, 166.93 (2C of oxadiazole), 167.85 (C of benzoate group). EI ms: *m/z*: 467 (M^+), 313 (11), 226 (19), 185 (100), 149 (13), 105 (55), 77 (19). *Anal*. Calcd. for $C_{29}H_{29}N_3O_3$ (467.56): C, 74.50; H, 6.25; N, 8.99. Found: C, 74.53; H, 6.21; N, 9.02.

2-(Benzylamino)-2-{5-[(*E*)-1-methyl-2-phenyl-1-ethenyl]-1,3,4-oxadiazol-2-yl}propyl 4-bromobenzoate (7c). This compound was obtained as yellow oil, the yield was 452 mg (85%), ir (neat): 3350, 2920, 1721, 1447, 1268, 710 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 1.78, 2.38 (s, 6H, $2CH_3$), 2.23 (s, 1H, NH),

3.75, 3.82 (AB quartet, 2H, $J = 12.3$ Hz, CH_2 of benzyl group); 4.57, 4.70 (AB quartet, $J = 11.1$ Hz, 2H, CH_2 aliphatic), 7.27–7.70 (m, 13H, H-Ar and vinylic), 7.85 (d, 2H, $J = 8.3$ Hz, H-Ar). ^{13}C NMR ($CDCl_3$): δ 14.59, 21.05 ($2CH_3$), 47.80 (CH_2 of benzyl group), 56.69 (C aliphatic), 69.32 (CH_2 aliphatic), 121.30 (CH, vinylic), 128.41, 134.50, 135.32, 155.26 (4C arom), 127.26, 128.18, 128.53, 129.52, 131.17, 131.88 (14CH arom), 139.68 (C, vinylic), 165.13, 167.31 (2C of oxadiazole), 167.65 (C of benzoate group). EI ms: *m/z*: 533 (M^+, 26), 427 (70), 347 (20), 317 (100), 277 (34), 225 (96), 185 (95), 157 (68), 106 (92), 77 (28), 42 (8). *Anal*. Calcd. for $C_{28}H_{26}BrN_3O_3$ (532.43): C, 63.16; H, 4.92; N, 7.89. Found: C, 63.21; H, 4.95; N, 7.87.

2-(Benzylamino)-2-{5-[(*E*)-2-phenyl)-1-ethenyl]-1,3,4-oxadiazol-2-yl}propyl benzoate (7d). This compound was obtained as yellow oil, the yield was 364 mg (83%), ir (neat): 3431, 2923, 1719, 1589, 1266, 754 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 1.81 (s, 3H, CH_3), 2.26 (s, 1H, NH), 3.76, 3.84 (AB quartet, 2H, $J = 12.4$ Hz, CH_2 of benzyl group); 4.60, 4.73 (AB quartet, $J = 11.0$ Hz, 2H, CH_2 aliphatic), 7.02 (d, 1H, $J = 16.5$ Hz, H-vinyl); 7.10–7.70 (m, 14H, H-Ar and vinylic), 8.00 (d, 2H, $J = 7.8$ Hz, H-Ar). ^{13}C NMR ($CDCl_3$): δ 21.06 (CH_3), 47.76 (CH_2 of benzyl group), 56.76 (C aliphatic), 69.12 (CH_2 aliphatic), 109.84 and 134.60 (2CH, vinylic), 129.50, 133.33, 139.20 (3C arom), 127.26, 127.49, 128.18, 128.51, 129.01, 129.68, 130.04, 139.71 (15CH arom), 164.85, 165.83 (2C of oxadiazole), 167.53 (C of benzoate group). *Anal*. Calcd. for $C_{27}H_{25}N_3O_3$ (439.51): C, 73.78; H, 5.73; N, 9.56. Found: C, 73.74; H, 5.69; N, 9.59.

2-(Benzylamino)-2-{5-[(*E*)-1-methyl-2-phenyl)-1-ethenyl]-1,3,4-oxadiazol-2-yl}propyl benzoate (7e). This compound was obtained as yellow oil, the yield was 385 mg (85%), ir (neat): 3383, 1718, 1448, 1265, 707 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 1.80, 2.38 (s, 6H, $2CH_3$), 2.23 (s, 1H, NH), 3.77, 3.84 (AB quartet, 2H, $J = 12.4$ Hz, CH_2 of benzyl group); 4.60, 4.71 (AB quartet, $J = 10.9$ Hz, 2H, CH_2 aliphatic), 7.30–7.70 (m, 14H, H-Ar and vinylic), 8.00 (d, 2H, $J = 8.0$ Hz, H-Ar). ^{13}C NMR ($CDCl_3$): δ 14.58, 21.07 ($2CH_3$), 47.79 (CH_2 of benzyl group), 56.71 (C aliphatic), 69.19 (CH_2 aliphatic), 121.34 (CH, vinylic), 129.87, 134.45, 135.39 (3C arom), 127.21, 128.19, 128.35, 128.49, 129.53, 129.67, 129.87, 133.30 (15CH arom), 139.76 (C, vinylic), 165.82, 167.30 (2C of oxadiazole), 167.80 (C of benzoate group). *Anal*. Calcd. for $C_{28}H_{27}N_3O_3$ (453.53): C, 74.15; H, 6.0; N, 9.27. Found: C, 74.18; H, 6.05; N, 9.23.

2-[(4-Methylbenzyl)amino]-2-{5-[(*E*)-1-methyl-2-phenyl-1-ethenyl]-1,3,4-oxadiazol-2-yl}propyl 4-bromobenzoate (7f). This compound was obtained as yellow oil, the yield was 431 mg (79%), ir (neat): 3425, 2924, 1723, 1600, 1268, 756 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 1.77, 2.30, 2.38 (s, 9H, $3CH_3$), 2.24 (s, 1H, NH), 3.70, 3.78 (AB quartet, 2H, $J = 12.1$ Hz, CH_2 of benzyl group); 4.56, 4.69 (AB quartet, $J = 11.1$ Hz, 2H, CH_2 aliphatic), 7.02–7.70 (m, 12H, H-Ar and vinylic), 7.85 (d, 2H, $J = 7.9$ Hz, H-Ar). ^{13}C NMR ($CDCl_3$): δ 14.57, 14.69, 21.02 ($3CH_3$), 47.54 (CH_2 of benzyl group), 56.64 (C aliphatic), 69.35 (CH_2 aliphatic), 121.38 (CH, vinylic), 128.44, 134.45, 135.04, 135.34, 155.26 (5C arom), 128.16, 128.48, 128.53, 129.19, 129.52, 131.17, 131.87 (13CH arom), 136.61 (C, vinylic), 165.12, 167.28 (2C of oxadiazole), 167.69 (C of benzoate group). *Anal*. Calcd. for $C_{29}H_{28}BrN_3O_3$ (546.45): C, 63.74; H, 5.16; N, 7.69. Found: C, 63.70; H, 5.13; N, 7.72.

2-(Benzylamino)-2-{5-[(*E*)-2-(4-chlorophenyl)-1-ethenyl]-1,3,4-oxadiazol-2-yl}propyl benzoate (7g). This compound was obtained as yellow oil, the yield was 383 mg (81%), ir (neat): 3418, 1600, 1526, 1268, 709 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 1.80 (s, 3H, CH_3), 2.23 (s, 1H, NH), 3.76, 3.83 (AB quartet, 2H, $J = 12.4$ Hz, CH_2 of benzyl group); 4.58, 4.71 (AB quartet, $J = 10.6$ Hz, 2H, CH_2 aliphatic), 6.97 (d, 1H, $J = 16.5$ Hz, H-vinyl); 7.18–7.70 (m, 13H, H-Ar and vinylic), 8.00 (d, 2H, $J = 8.0$ Hz, H-Ar). ^{13}C NMR ($CDCl_3$): δ 21.0 (CH_3), 47.71 (CH_2 of benzyl group), 56.74 (C aliphatic), 69.08 (CH_2 aliphatic), 110.36 and 137.77 (2CH, vinylic), 129.46, 135.91, 139.65, 155.68 (4C arom), 127.26, 128.14, 128.51, 128.62, 129.28, 129.67, 133.07, 133.35 (14CH arom), 164.60, 165.81 (2C of oxadiazole), 167.63 (C of benzoate group). *Anal*. Calcd. for $C_{27}H_{24}ClN_3O_3$ (473.95): C, 68.42; H, 5.10; N, 8.87. Found: C, 68.37; H, 5.14; N, 8.90.

2-(Benzylamino)-2-{5-[(*E*)-2-phenyl-1-ethenyl]-1,3,4-oxadiazol-2-yl}propyl 4-bromobenzoate (7h). This compound was obtained as yellow oil, the yield was 414 mg (80%), ir (neat): 3429, 2926, 1723, 1450, 1248, 711 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 1.79 (s, 3H, CH_3), 2.23 (s, 1H, NH), 3.75, 3.82 (AB quartet, 2H, $J = 12.4$ Hz, CH_2 of benzyl group); 4.58, 4.72 (AB quartet, $J = 11.0$ Hz, 2H, CH_2 aliphatic), 6.99 (d, 1H, $J = 16.5$ Hz, H-vinyl); 7.12–7.70 (m, 13H, H-Ar and vinylic), 7.85 (d, 2H, $J = 7.9$ Hz, H-Ar). ^{13}C NMR ($CDCl_3$): δ 21.03 (CH_3), 47.76 (CH_2 of benzyl group), 56.73 (C aliphatic), 69.22 (CH_2 aliphatic), 109.75 and 139.26 (2CH, vinylic), 128.42, 134.53, 139.63, 155.25 (4C arom), 127.29, 127.48, 128.14, 128.52, 129.04, 130.08, 131.17, 131.88 (14CH arom), 164.85, 165.12 (2C of oxadiazole), 167.38 (C of benzoate group). *Anal*. Calcd. for $C_{27}H_{24}BrN_3O_3$ (518.40): C, 62.56; H, 4.67; N, 8.11. Found: C, 62.61; H, 4.63; N, 8.15.

2-[(4-Methoxybenzyl)amino]-2-{5-[(*E*)-1-methyl-2-phenyl-1-ethenyl]-1,3,4-oxadiazol-2-yl}propyl benzoate (7i). This compound was obtained as yellow oil, the yield was 398 mg (84%), ir (neat): 3436, 2923, 1722, 1589, 1447, 1266, 754 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 1.79, 2.38 (s, 6H, $2CH_3$), 2.21 (s, 1H, NH), 3.76 (s, 3H, OCH_3); 3.70, 3.80 (AB quartet, 2H, $J = 12.4$ Hz, CH_2 of benzyl group); 4.59, 4.70 (AB quartet, $J = 11.0$ Hz, 2H, CH_2 aliphatic), 6.80 (d, 2H, $J = 7.8$ Hz, H-arom); 7.10–7.70 (m, 11H, H-Ar and vinylic), 8.00 (d, 2H, $J = 7.9$ Hz, H-Ar). ^{13}C NMR ($CDCl_3$): δ 14.57, 21.08 ($2CH_3$), 47.22 (CH_2 of benzyl group), 55.24 (OCH_3), 56.64 (C aliphatic), 69.20 (CH_2 aliphatic), 121.37 (CH, vinylic), 128.33, 131.83, 134.42, 158.82 (4C arom), 113.89, 128.47, 129.40, 129.53, 129.67, 133.27 (14CH arom), 135.42 (C, vinylic), 165.82, 167.28 (2C of oxadiazole), 167.85 (C of benzoate group). *Anal*. Calcd. for $C_{29}H_{29}N_3O_4$ (483.60): C, 72.03; H, 6.04; N, 8.69. Found: C, 71.98; H, 6.09; N, 8.64.

2-(Benzylamino)-2-{5-[(*E*)-2-(4-methylphenyl)-1-ethenyl]-1,3,4-oxadiazol-2-yl}propyl benzoate (7j). This compound was obtained as yellow oil, the yield was 385 mg (85%), ir (neat): 3415, 1724, 1590, 1268, 709 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 1.80, 2.39 (s, 6H, $2CH_3$), 2.24 (s, 1H, NH), 3.76, 3.84 (AB quartet, 2H, $J = 12.4$ Hz, CH_2 of benzyl group); 4.60, 4.72 (AB quartet, $J = 10.9$ Hz, 2H, CH_2 aliphatic), 6.97 (d, 1H, $J = 16.5$ Hz, H-vinyl); 7.11–7.71 (m, 13H, H-Ar and vinylic), 8.00 (d, 2H, $J = 7.5$ Hz, H-Ar). ^{13}C NMR ($CDCl_3$): δ 21.05, 21.46 ($2CH_3$), 47.76 (CH_2 of benzyl group), 56.74 (C aliphatic), 69.14 (CH_2 aliphatic), 108.78 and 139.18 (2CH, vinylic), 129.52, 131.89, 139.73, 140.43 (4C arom), 127.24, 127.46, 128.18, 128.50, 129.68, 129.73, 133.31 (14CH arom), 165.02, 165.83 (2C of oxadiazole), 167.39 (C of benzoate group). *Anal*. Calcd. for $C_{28}H_{27}N_3O_3$ (453.53): C, 74.15; H, 6.0; N, 9.27. Found: C, 74.19; H, 6.06; N, 9.23.

2-{5-[(*E*)-2-(3-Chlorophenyl)-1-ethenyl]-1,3,4-oxadiazol-2-yl}-2-[(4-methylbenzyl)amino]- propyl benzoate (7k). This compound was obtained as yellow oil, the yield was 400 mg (82%), ir (neat): 3375, 1724, 1446, 1268, 705 cm^{-1}. ^1H NMR ($CDCl_3$): δ 1.80, 2.30 (s, 6H, $2CH_3$), 2.24 (s, 1H, NH), 3.70, 3.80 (AB quartet, 2H, $J = 11.$ Hz, CH_2 of benzyl group); 4.58, 4.71 (AB quartet, $J = 11.0$ Hz, 2H, CH_2 aliphatic), 6.99 (d, 1H, $J = 16.8$ Hz, H-vinyl); 7.07 (d, 2H, $J = 7.8$ Hz, H-arom), 7.19–7.70 (m, 10H, H-Ar and vinylic), 7.99 (d, 2H, $J = 7.8$ Hz, H-Ar). ^{13}C NMR ($CDCl_3$): δ 21.02 ($2CH_3$), 47.46 (CH_2 of benzyl group), 56.71 (C aliphatic), 69.07 (CH_2 aliphatic), 111.23 and 137.52 (2CH, vinylic), 129.85, 135.04, 136.40, 136.89, 155.58 (5C arom), 125.41, 127.44, 128.08, 128.51, 129.18, 129.67, 133.34, 136.62 (13CH arom), 165.25, 165.83 (2C of oxadiazole), 167.66 (C of benzoate group). *Anal*. Calcd. for $C_{28}H_{26}ClN_3O_3$ (488.0): C, 68.92; H, 5.37; N, 8.61. Found: C, 68.88; H, 5.34; N, 8.66.

2-[(4-Methylphenyl)amino]-2-{5-[(*E*)-2-phenyl-1-ethenyl]-1,3,4-oxadiazol-2-yl}propyl 4-bromobenzoate (7l). This compound was obtained as yellow oil, the yield was 415 mg (78%), ir (neat): 3428, 1721, 1447, 1268, 1109, 709 cm^{-1}. ^1H NMR ($CDCl_3$): δ 1.78, 2.29 (s, 6H, $2CH_3$), 2.25 (s, 1H, NH), 3.69, 3.77 (AB quartet, 2H, $J = 12.1$ Hz, CH_2 of benzyl group); 4.56, 4.70 (AB quartet, $J = 11.0$ Hz, 2H, CH_2 aliphatic), 6.96–7.70 (m, 13H, H-Ar and vinylic), 7.88 (d, 2H, J = 7.8 Hz, H-Ar). ^{13}C NMR ($CDCl_3$): δ 21.05 ($2CH_3$), 47.52 (CH_2 of benzyl group), 56.78 (C aliphatic), 69.18 (CH_2 aliphatic), 109.74 and 136.82 (2 CH, vinylic), 129.57, 130.15, 134.50, 135.36, 155.82 (5C arom), 127.47, 127.57, 128.10, 129.04, 129.19, 131.17, 131.87 (13CH arom), 165.72, 167.30 (2C of oxadiazole), 167.78 (C of benzoate group). *Anal*. Calcd. for $C_{28}H_{26}BrN_3O_3$ (532.43): C, 63.16; H, 4.92; N, 7.89. Found: C, 63.19; H, 4.96; N, 7.85.

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