# The Reaction of *N*-Isocyaniminotriphenylphosphorane with Ester Derivatives of 2-Oxopropyl Alcohol (2-Oxopropyl 4-Bromobenzoate, 2-Oxopropyl Benzoate, and 2-Oxopropyl Acetate) in the Presence of Aromatic Carboxylic Acids: A One-Pot Efficient Three-Component Reaction for the Synthesis of Fully Substituted 1,3,4-Oxadiazole Derivatives

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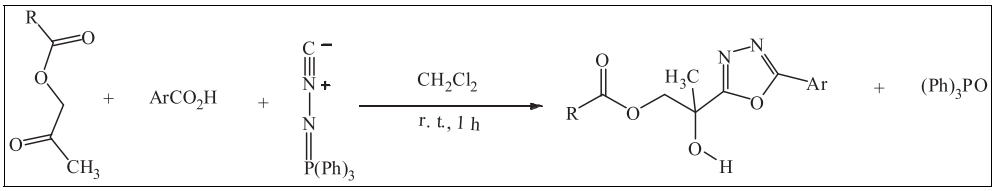


Reactions of *N*-isocyaniminotriphenylphosphorane with ester derivatives of 2-oxopropyl alcohol (2-oxopropyl 4-bromobenzoate, 2-oxopropyl benzoate, and 2-oxopropyl acetate) in the presence of aromatic carboxylic acids proceed smoothly at room temperature and in neutral conditions to afford sterically 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

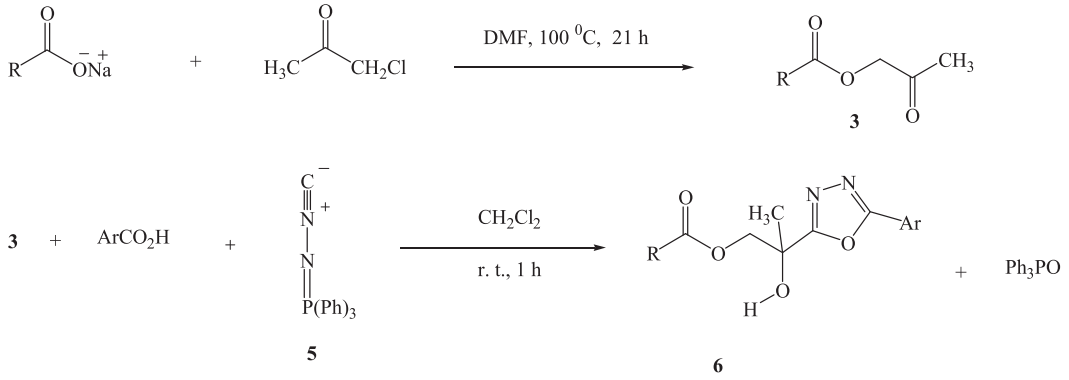
Multicomponent reactions (MCRs) have emerged as an efficient and powerful tool in modern synthetic organic chemistry because of their valued features such as atom economy, straightforward reaction design, and the opportunity to construct target compounds by the introduction of several diversity elements in a single chemical event. Typically, purification of products resulting from MCR is also simple because all the organic reagents used are consumed and are incorporated into the target compound [1]. 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 especially important in this area [2], [3].

Among the known multicomponent reactions 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 the generation of molecular diversity have attracted much attention because of the advantages that they offer to the field of combinatorial chemistry [4].

During recent years, there has been considerable investigation on different classes of oxadiazoles. In particular, compounds containing 1,3,4-oxadiazole nucleus have been shown to possess a wide range of pharmacological and therapeutic activities. Some 1,3,4-oxadiazoles have exhibited analgesic, anti-inflammatory, anticonvulsant, tranquilizing, myorelaxant, antidepressant, vasodilatatory, diuretic, antiulcer, antiarythmic, antiserotoninic, spasmolytic, hypotensive, antibronchocontrictive, anticholinergic, and antiemetic activities. Furthermore, many 1,3,4-oxadiazole derivatives have been reported as active inhibitors of several enzymes [5], [6].

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 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 [7–11]. However, the organic chemistry of *N*-isocyaniminotriphenylphosphorane **5** remains almost unexplored. *N*-isocyaniminotriphenylphosphorane **5** 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 [12], [13]. 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

**Scheme 1.** Synthesis of ester derivatives of 2-oxopropyl alcohol **3** (2-oxopropyl 4-bromobenzoate, 2-oxopropyl benzoate, and 2-oxopropyl acetate) and three-component synthesis of disubstituted 1,3,4-oxadiazole derivatives **6a–m** (see Experimental part).




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 **6** by a three-component condensation of *N*-isocyaniminotriphenylphosphorane **5**, aromatic carboxylic acid derivatives, and ester derivatives of 2-oxopropyl alcohol **3** (2-oxopropyl 4-bromobenzoate, 2-oxopropyl benzoate, and 2-oxopropyl acetate) (Scheme 1).

## RESULTS AND DISCUSSION

The carboxylic acid derivative with ester derivatives of 2-oxopropyl alcohol **3** (2-oxopropyl 4-bromobenzoate, 2-oxopropyl benzoate, and 2-oxopropyl acetate), and *N*-isocyaniminotriphenylphosphorane **5** in $CH_2Cl_2$ react together in a 1:1:1 ratio at room temperature to produce disubstituted 1,3,4-oxadiazole derivatives and triphenylphosphine oxide (Scheme 1). The reaction proceeds smoothly and cleanly under mild conditions and no side reactions were observed.**6a**: R = Ph, Ar = 3,5-di$MeC_6H_4$; **6b**: R = Ph, Ar = 4-$MeC_6H_4$; **6c**: R = Ph, Ar = 3,4-di$MeC_6H_4$; **6d**: R = Ph, Ar = 4-$ClC_6H_4$; **6e**: R = Ph, Ar = 4-$BrC_6H_4$; **6f**: R = $CH_3$, Ar = 3-$MeC_6H_4$; **6g**: R = Ph, Ar = 3-$MeC_6H_4$; **6h**: R = Ph, Ar = 4-$EtC_6H_4$; **6i**: R = $CH_3$, Ar = 4-$MeC_6H_4$; **6j**: R = 4-$BrC_6H_4$, Ar = 4-$ClC_6H_4$; **6k**: R = 4-$BrC_6H_4$, Ar = 4-$BrC_6H_4$; **6l**: R = 4-$BrC_6H_4$, Ar = 4-$MeC_6H_4$; **6m**: R = 4-$BrC_6H_4$, Ar = 3-$ClC_6H_4$

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 **6a** consisted of two singlet for the 3 $CH_3$ ($\delta$ = 1.85 and 2.33 ppm), a broad singlet for the OH ($\delta$ = 4.36), a AB-quartet for $CH_2$ aliphatic at $\delta$ = 4.65 and 4.71 ppm ($J$ = 11.50 Hz), and a multiplet at $\delta$ = 7.12–7.99 ppm for H-aromatic. The aryl groups exhibited characteristic signals in the aromatic region of the spectrum. The $^1$H decoupled $^{13}$C-NMR spectrum of **6a** showed 15 distinct resonances; partial assignment of these resonances is given in the experimental section. The $^1$H- and $^{13}$C-NMR spectra of compounds **6b–m** were similar to those of **6a**, except for the aromatic and aliphatic moieties, which exhibited characteristic signals with appropriate chemical shifts.

The suggested mechanism for the formation of products **6a–m** 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 the *N*-isocyaniminotriphenylphosphorane **5** to ester derivative of 2-oxopropyl alcohol **3** (2-oxopropyl 4-bromobenzoate, 2-oxopropyl benzoate, and 2-oxopropyl acetate), which facilitates by its protonation with the acid, leading to nitrilium intermediate **8**. This intermediate may be attacked by conjugate base of the acid to form 1:1:1 adduct **9**. This adduct may undergo intramolecular *aza*-Wittig reaction of iminophosphorane moiety with the ester carbonyl to afford the isolated sterically congested 1,3,4-oxadiazole derivatives **6** by removal of triphenylphosphine oxide from intermediate **10**.

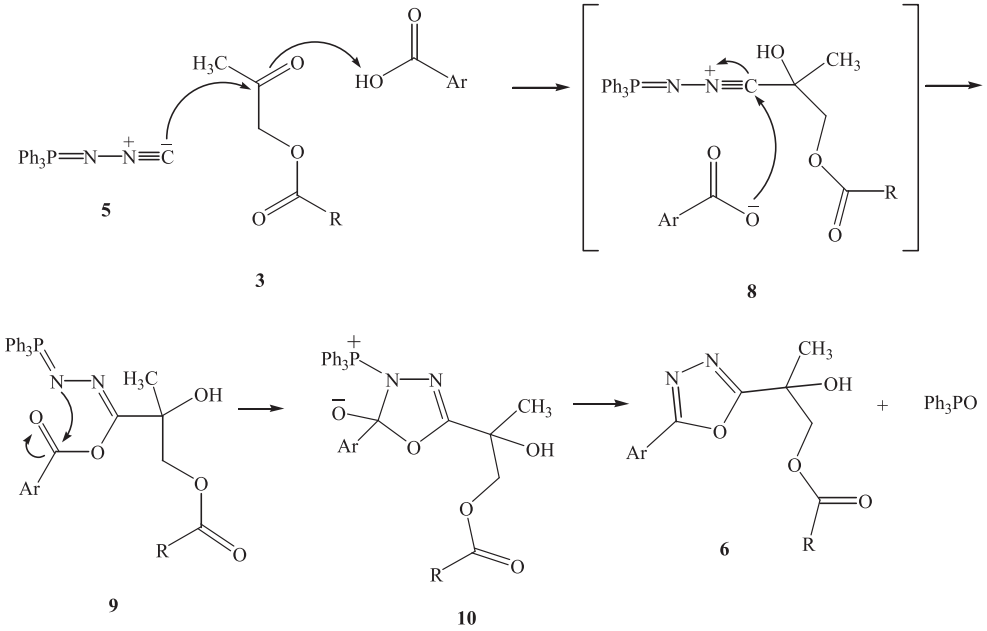
## CONCLUSIONS

We believe that the reported method offers a mild, simple, and efficient route for the preparation of sterically congested 1,3,4-oxadiazole derivatives **6** from ester derivatives of 2-oxopropyl alcohol **3** (2-oxopropyl 4-bromobenzoate, 2-oxopropyl benzoate, and 2-oxopropyl acetate), *N*-isocyaniminotriphenylphosphorane **5.** and aromatic carboxylic acids. Its ease of work-up, high yields, and fairly mild reaction conditions make 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 point were measured on an Electrothermal 9100 apparatus and are uncorrected. IR spectra were measured on a Jasco 6300 FTIR spectrometer. $^1$H- and $^{13}$C-NMR spectra were measured ($CDCl_3$)

**Scheme 2.** Proposed mechanism for the formation of disubstituted 1,3,4-oxadiazole derivatives **6a–m**.



with 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. Flash chromatography columns were prepared with Merck silica gel. Ester derivatives of 2-oxopropyl alcohol **3** (2-oxopropyl 4-bromobenzoate, 2-oxopropyl benzoate, and 2-oxopropyl acetate) were prepared based on known procedure [36].

**General procedure for the preparation of 6a–m.** A mixture of *N*-isocyaniminotriphenylphosphorane **5** (1 mmol, 0.302 g), ester derivative of 2-oxopropyl alcohol **3** (2-oxopropyl 4-bromobenzoate, 2-oxopropyl benzoate, and 2-oxopropyl acetate) [1 mmol; 0.116 g (R = $CH_3$), 0.178 g (R = Ph), and 0.257 g (R = 4-$BrC_6H_4$)], and carboxylic acid [1 mmol; 0.150 g (Ar = 3,5-di$MeC_6H_4$), 0.136 g (Ar = 4-$MeC_6H_4$), 0.150 g (Ar = 3,4-di$MeC_6H_4$), 0.157 g (Ar = 4-$ClC_6H_4$), 0.201 g (Ar = 4-$BrC_6H_4$), 0.136 g (Ar = 3-$MeC_6H_4$), 0.150 g (Ar = 4-$EtC_6H_4$), and 0.157 g (Ar = 3-$ClC_6H_4$)] in $CH_2Cl_2$ (5 mL) was stirred at room temperature for 1 h. Then, the solvent was removed under reduced pressure and the viscous residue was purified by flash column chromatography [silica gel; petroleum ether–ethyl acetate (4:1)]. The solvent was removed under reduced pressure to give product **6**. The characterization data of the compounds are given below.

***2-[5-(3,5-Dimethylphenyl)-1,3,4-oxadiazol-2-yl]-2-hydroxypropyl benzoate (6a).*** This compound was obtained as yellow oil, the yield was 306 mg (87%), IR (neat): 3490, 1725, 1274, 714 $cm^{-1}$. $^1$H-NMR ($CDCl_3$): δ 1.85, 2.33 (s, 9H, $3CH_3$), 4.36 (br s, 1H, OH), 4.65, 4.71 (AB quartet, *J* = 11.50 Hz, 2H, $CH_2$ aliphatic), 7.12–7.99 (m, 8H, H-Ar). $^{13}$C-NMR ($CDCl_3$): δ 21.16, 23.53 ($3CH_3$), 69.82 (C aliphatic), 70.35 ($CH_2$ aliphatic), 123.09, 129.18, 138.77 (4C arom), 124.68, 128.44, 129.77, 133.42, 133.69 (8CH arom), 165.74, 166.19 (2C of oxadiazole), 167.76 (C of benzoate group). EI ms: *m/z*: 352 ($M^+$), 217 (13.55), 167 (17.47), 149 (85.35), 132 (23.59), 104 (100), 91 (33.43), 77 (72.80), 43 (91.28). Anal. Calcd. for $C_{20}H_{20}N_2O_4$ (352.38): C, 68.17; H, 5.72; N, 7.95. Found: C, 68.13; H, 5.77; N 7.92

***2-Hydroxy-2-[5-(4-methylphenyl)-1,3,4-oxadiazol-2-yl]propyl benzoate (6b).*** This compound was obtained as white crystals, the yield was 287 mg (85%), m.p. 115.6–116.9°, IR (KBr): 3317, 2954, 1728, 1500, 1282, 711 $cm^{-1}$. $^1$H-NMR ($CDCl_3$): δ 1.84, 2.41 (s, 6H, $2CH_3$), 4.0 (br s, 1H, OH), 4.63, 4.72 (AB quartet, *J* = 11.37 Hz, 2H, $CH_2$ aliphatic), 7.29–7.99 (m, 9H, H-Ar). $^{13}$C-NMR ($CDCl_3$): δ 21.69, 23.51 ($2CH_3$), 69.83 (C aliphatic), 70.43 ($CH_2$ aliphatic), 120.59, 129.10, 142.62 (3C arom), 126.95, 128.49, 129.78, 129.81, 133.50 (9CH arom), 165.64, 166.15 (2C of oxadiazole), 167.75 (C of benzoate group). EI ms: *m/z*: 338 ($M^+$), 203 (18.08), 166 (83.81), 149 (64.30), 122 (31.18), 105 (72.16), 91 (27.54), 77 (72.66), 57 (62.76), 43 (100). Anal. Calcd. for $C_{19}H_{18}N_2O_4$ (338.36): C, 67.44; H, 5.36; N, 8.28. Found: C, 67.48; H, 5.33; N, 8.32.

***2-[5-(3,4-Dimethylphenyl)-1,3,4-oxadiazol-2-yl]-2-hydroxypropyl benzoate (6c).*** This compound was obtained as yellow oil, the yield was 303mg (86%), IR (neat): 3450, 2953, 1726, 1453, 1274, 713 $cm^{-1}$. $^1$H-NMR ($CDCl_3$): δ 1.84, 2.28, 2.30 (s, 9H, $3CH_3$), 4.22 (br s, 1H, OH), 4.64, 4.71 (AB quartet, *J* = 11.37 Hz, 2H, $CH_2$ aliphatic), 7.19–7.99 (m, 8H, H-Ar). $^{13}$C-NMR ($CDCl_3$): δ 19.69, 20.02, 23.52 ($3CH_3$), 69.83 (C aliphatic), 70.38 ($CH_2$ aliphatic), 120.83, 129.15, 137.55, 141.33 (4C arom), 124.51, 127.92, 128.46, 129.78, 130.24, 130.44 (8CH arom), 165.72, 166.20 (2C of oxadiazole), 167.57 (C of benzoate group). Anal. Calcd. for $C_{20}H_{20}N_2O_4$ (352.38): C, 68.17; H, 5.72; N, 7.95. Found: C, 68.20; H, 5.76; N, 7.90.

***2-[5-(4-Chlorophenyl)-1,3,4-oxadiazol-2-yl]-2-hydroxypropyl benzoate (6d).*** This compound was obtained as white crystals, the yield was 293 mg (82%), m.p. 123.3–124.7°, IR (KBr): 3397, 2953, 1726, 1607, 1486, 1281, 708 $cm^{-1}$. $^1$H-NMR ($CDCl_3$): δ 1.84 (s, 3H, $CH_3$), 3.87 (br s, 1H, OH), 4.64, 4.72 (AB quartet, *J* = 11.37 Hz, 2H, $CH_2$ aliphatic), 7.30–7.98 (m, 9H, H-Ar). $^{13}$C-NMR ($CDCl_3$): δ 23.52, ($CH_3$), 69.75 (C aliphatic), 70.45 ($CH_2$ aliphatic), 121.86, 129.04, 138.29 (3C arom), 128.26, 128.51, 129.44, 129.76, 133.57 (9CH arom), 165.66, 166.22 (2C

of oxadiazole), 167.98 (C of benzoate group). Anal. Calcd. for $C_{18}H_{15}ClN_2O_4$ (358.07): C, 60.26; H, 4.21; N, 7.81. Found: C, 60.29; H, 4.17; N, 7.85.

***2-[5-(4-Bromophenyl)-1,3,4-oxadiazol-2-yl]-2-hydroxypropyl benzoate (6e).*** This compound was obtained as white crystals, the yield was 350 mg (87%), m.p. 138.1–139.8°, IR (KBr): 3377, 2954, 1725, 1601, 1281, 1081, 709 $cm^{-1}$. $^1$H-NMR ($CDCl_3$): δ 1.84 (s, 3H, $CH_3$), 3.87 (br s, 1H, OH), 4.64, 4.72 (AB quartet, $J$ = 11.37 Hz, 2H, $CH_2$ aliphatic), 7.30–7.98 (m, 9H, H-Ar). $^{13}$C-NMR ($CDCl_3$): δ 23.52, ($CH_3$), 69.74 (C aliphatic), 70.45 ($CH_2$ aliphatic), 122.29, 126.76, 129.15 (3C arom), 128.38, 128.51, 129.76, 132.40, 133.57 (9CH arom), 165.64, 166.75 (2C of oxadiazole), 168.79 (C of benzoate group). Anal. Calcd. for $C_{18}H_{15}BrN_2O_4$ (403.23): C, 53.62; H, 3.75; N, 6.95. Found: C, 53.66; H, 3.77; N, 6.92.

***2-Hydroxy-2-[5-(3-methylphenyl)-1,3,4-oxadiazol-2-yl]propyl acetate (6f).*** This compound was obtained as yellow oil, the yield was 243 mg (88%), IR (neat): 3491, 2967, 1748, 1555, 1246, 1052, 722 $cm^{-1}$. $^1$H-NMR ($CDCl_3$): δ 1.75, 2.06, 2.42 (s, 9H, $3CH_3$), 4.11 (br s, 1H, OH), 4.36, 4.54 (AB quartet, $J$ = 11.50 Hz, 2H, $CH_2$ aliphatic), 7.36–7.85 (m, 4H, H-Ar).$^{13}$C-NMR ($CDCl_3$): δ 20.76, 21.35, 23.47 ($3CH_3$), 69.28 (C aliphatic), 70.21 ($CH_2$ aliphatic), 123.24, 139.03 (2C arom), 124.15, 127.50, 129.02, 132.87 (4CH arom), 165.56, 167.72 (2C of oxadiazole), 170.80 (C of acetate group). Anal. Calcd. for $C_{14}H_{16}N_2O_4$ (276.29): C, 60.86; H 5.84; N 10.14. Found: C, 60.83; H, 5.79; N, 10.18.

***2-Hydroxy-2-[5-(3-methylphenyl)-1,3,4-oxadiazol-2-yl]propyl benzoate (6g).*** This compound was obtained as yellow oil, the yield was 287 mg (85%), IR (neat): 3327, 2964, 1726, 1448, 1255, 710 $cm^{-1}$. $^1$H-NMR ($CDCl_3$): δ 1.84, 2.37 (s, 6H, $2CH_3$), 4.20 (br s, 1H, OH), 4.65, 4.71 (AB quartet, $J$ = 11.87 Hz, 2H, $CH_2$ aliphatic), 7.32–7.98 (m, 9H, H-Ar). $^{13}$C-NMR ($CDCl_3$): δ 21.28, 23.53 ($2CH_3$), 69.81 (C aliphatic), 70.37 ($CH_2$ aliphatic), 123.22, 129.16, 138.93 (3C arom), 124.15, 127.47, 128.45, 128.93, 129.77, 132.78, 133.43 (9CH arom), 165.59, 166.19 (2C of oxadiazole), 167.89 (C of benzoate group). Anal. Calcd. for $C_{19}H_{18}N_2O_4$ (338.36): C, 67.44; H, 5.36; N, 8.28. Found: C, 67.47; H, 5.40; N, 8.24.

***2-[5-(3-Methylphenyl)-1,3,4-oxadiazol-2-yl]-2-hydroxypropyl benzoate (6h).*** This compound was obtained as white crystals, the yield was 295 mg (84%), m.p. 240.1–241.3°, IR (KBr): 3369, 2977, 1725, 1282, 1084, 706 $cm^{-1}$. $^1$H-NMR ($CDCl_3$): δ 1.25 (t, $J$ = 7.2 Hz, 3H, $CH_3$ of Et), 1.84 (s, 3H, $CH_3$), 2.69 (q, $J$ = 7.2 Hz, 2H, $CH_2$ of Et), 4.18 (br s, 1H, OH), 4.64, 4.71 (AB quartet, 2H, $J$ = 11.50 Hz, $CH_2$ aliphatic), 7.29–7.98 (m, 9H, H-Ar). $^{13}$C-NMR ($CDCl_3$): δ 15.16, 23.52 ($2CH_3$), 28.89 ($CH_2$ of Et), 69.79 (C aliphatic), 70.38 ($CH_2$ aliphatic), 120.86, 129.23, 148.75 (3C arom), 127.07, 128.42, 128.53, 129.75, 133.36 (9CH arom), 165.59, 166.16 (2C of oxadiazole), 167.66 (C of benzoate group). Anal. Calcd. for $C_{20}H_{20}N_2O_4$ (352.38): C, 68.17; H, 5.72; N, 7.95. Found: C, 68.12; H, 5.75; N, 7.92.

***2-Hydroxy-2-[5-(4-methylphenyl)-1,3,4-oxadiazol-2-yl]propyl acetate (6i).*** This compound was obtained as yellow oil, the yield was 229 mg (83%), IR (neat): 3473, 1748, 1501, 1255, 1052, 727 $cm^{-1}$. $^1$H-NMR ($CDCl_3$): δ 1.74, 2.05, 2.42 (s, 9H, $3CH_3$), 4.11 (br s, 1H, OH), 4.36, 4.53 (AB quartet, J =11.12 Hz, 2H, $CH_2$ aliphatic), 7.29 (d, $J$ = 7.75 Hz, 2H, H-Ar), 7.91 (d, $J$ = 7.75 Hz, 2H, H-Ar). $^{13}$C-NMR ($CDCl_3$): δ 20.76, 21.70, 23.47 ($3CH_3$), 69.27 (C aliphatic), 70.16 ($CH_2$ aliphatic), 120.60, 142.66 (2C arom), 126.95, 129.80 (4CH arom), 165.54, 167.55 (2C of oxadiazole), 170.79 (C of acetate group). Anal. Calcd. for $C_{14}H_{16}N_2O_4$ (276.29): C, 60.86; H, 5.84; N, 10.14. Found: C, 60.81; H, 5.88; N, 10.11.

***2-[5-(4-Chlorophenyl)-1,3,4-oxadiazol-2-yl]-2-hydroxypropyl 4-bromobenzoate (6j).*** This compound was obtained as white crystals, the yield was 376 mg (86%), m.p. 168.3–169.8°, IR (KBr): 3386, 1725, 1621, 1467, 1256, 711 $cm^{-1}$. $^1$H-NMR ($CDCl_3$): δ 1.83 (s, 3H, $CH_3$), 3.30 (br s, 1H, OH), 4.62, 4.72 (AB quartet, $J$ = 11.12 Hz, 2H, $CH_2$ aliphatic), 7.47 (d, $J$ = 7.75 Hz, 2H, H-Ar), 7.53 (d, $J$ = 7.87 Hz, 2H, H-Ar), 7.82 (d, $J$ = 7.75 Hz, 2H, H-Ar), 7.95 (d, $J$ = 7.87 Hz, 2H, H-Ar).$^{13}$C-NMR ($CDCl_3$): δ 23.86 ($CH_3$), 69.07 (C aliphatic), 69.60 ($CH_2$ aliphatic), 122.51, 127.73, 128.14, 137.29 (4C arom), 128.79, 130.11, 131.69, 132.39 (8CH arom), 163.94, 165.02 (2C of oxadiazole), 168.81 (C of 4-bromobenzoate group). Anal. Calcd. for $C_{18}H_{14}BrClN_2O_4$ (437.67): C, 49.40; H, 3.22; N, 6.40. Found: C, 49.44; H, 3.18; N, 6.43.

***2-[5-(4-Bromophenyl)-1,3,4-oxadiazol-2-yl]-2-hydroxypropyl 4-bromobenzoate (6k).*** This compound was obtained as white crystals, the yield was 409 mg (85%), m.p. 173.4–174.7°, IR (KBr): 3352, 2991, 1727, 1556, 1487, 1266, 714 $cm^{-1}$. $^1$H-NMR ($CDCl_3$): δ 1.83 (s, 3H, $CH_3$), 3.61 (br s, 1H, OH), 4.63, 4.72 (AB quartet, $J$ = 11.37 Hz, 2H, $CH_2$ aliphatic), 7.55 (d, $J$ = 8.50 Hz, 2H, H-Ar), 7.67 (d, $J$ = 8.50 Hz, 2H, H-Ar), 7.83 (d, $J$ = 8.50 Hz, 2H, H-Ar), 7.88 (d, $J$ = 8.5 Hz, 2H, H-Ar).$^{13}$C-NMR ($CDCl_3$): δ 23.85 ($CH_3$), 69.06 (C aliphatic), 69.58 ($CH_2$ aliphatic), 122.82, 126.21, 128.15, 138.12 (4C arom), 128.90, 131.69, 132.39, 133.02 (8CH arom), 164.06, 165.02 (2C of oxadiazole), 168.81 (C of 4-bromobenzoate group). Anal. Calcd. for $C_{18}H_{14}Br_2N_2O_4$ (482.12): C, 44.84; H, 2.93; N, 5.81. Found: C, 44.79; H, 2.97; N, 5.84.

***2-Hydroxy-2-[5-(4-methylphenyl)-1,3,4-oxadiazol-2-yl]propyl 4-bromobenzoate (6l).*** This compound was obtained as white crystals, the yield was 350 mg (84%), m.p. 154.3–155.6°, IR (KBr): 3324, 2959, 1725, 1510, 1286, 714 $cm^{-1}$. $^1$H-NMR ($CDCl_3$): δ 1.70, 2.36 (s, 6H, $2CH_3$), 4.26 (br s, 1H, OH), 4.51, 4.60 (AB quartet, $J$ = 11.12 Hz, 2H, $CH_2$ aliphatic), 7.10–7.85 (m, 8H, H-Ar). $^{13}$C-NMR ($CDCl_3$): δ 21.58, 23.88 ($2CH_3$), 68.99 (C aliphatic), 69.61($CH_2$ aliphatic), 120.88, 128.13, 128.87, 142.71 (4C arom), 126.92, 130.43, 131.69, 132.38 (8CH arom), 164.75, 165.01 (2C of oxadiazole), 168.35 (C of 4-bromobenzoate group). Anal. Calcd. for $C_{19}H_{17}BrN_2O_4$ (417.25): C, 54.69; H, 4.11; N, 6.71. Found: C, 54.65; H, 4.07; N, 6.75.

***2-[5-(3-Chlorophenyl)-1,3,4-oxadiazol-2-yl]-2-hydroxypropyl 4-bromobenzoate (6m).*** This compound was obtained as white crystals, the yield was 376 mg (86%), m.p. 164.3–165.6°, IR (KBr): 3391, 1726, 1634, 1550, 1464, 1256, 710 $cm^{-1}$. $^1$H-NMR ($CDCl_3$): δ 1.84 (s, 3H, $CH_3$), 3.36 (br s, 1H, OH), 4.63, 4.71 (AB quartet, $J$ = 11.37 Hz, 2H, $CH_2$ aliphatic), 7.39–7.95 (m, 8H, H-Ar). $^{13}$C-NMR ($CDCl_3$): δ 23.51 ($CH_3$), 69.86 (C aliphatic), 70.45 ($CH_2$ aliphatic), 124.95, 127.95, 128.81, 135.24 (4C arom), 125.08, 126.92, 130.47, 131.22, 131.90, 132.11 (8CH arom), 164.35, 165.47 (2C of oxadiazole), 168.06 (C of 4-bromobenzoate group). Anal. Calcd. for $C_{18}H_{14}BrClN_2O_4$ (437.67): C, 49.40; H, 3.22; N, 6.40. Found: C, 49.45; H, 3.25; N, 6.36.

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