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A One-Pot Efficient Four-Component Reaction for the Synthesis of 2-(Arylamino)-2-(5-aryl-1,3,4-oxadiazol-2-yl)propyl Benzoate (or Acetate) Derivatives

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ABSTRACT: *Reactions of (N-isocyanimino) triphenylphosphorane with 2-oxopropylbenzoate (or acetate) in the presence of aromatic carboxylic 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.* © 2011 Wiley Periodicals, Inc. Heteroatom Chem 22:692–698, 2011; View this article online at wileyonlinelibrary.com. DOI 10.1002/hc.20735

INTRODUCTION

Multicomponent reactions (MCRs) have emerged as an efficient and powerful tool in modern synthetic organic chemistry due to their valued features such as atom economy, straightforward reaction design, and the opportunity to construct target compounds by the introduction of several diverse elements in a single chemical event. Typically, purification of products resulting from MCRs is also simple since all the organic reagents employed 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 MCRs to date, the most valuable reactions are those based on isocyanides. Isocyanide-based MCRs (abbreviated to IMCRs by Ugi and Dömling) by virtue of their synthetic potential, inherent atom efficiency, convergent nature, ease of implementation, and 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 a 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, antiinflammatory, anticonvulsant, tranquilizing, myorelaxant, antidepressant, vasodilatatory, diuretic, antiulcer, antiarythmic, antiserotonin, spasmolytic, hypotensive, antibronchoconstrictive, anticholinergic, and antiemetic activities. Furthermore, many 1,3,4-oxadiazole derivatives have been

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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 of 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*-isocyanimino)triphenylphosphorane **6** remains almost unexplored. (*N*-Isocyanimino) triphenylphosphorane **6** is expected to have synthetic potential because it provides a reaction system in which the iminophosphorane group can react with a reagent having carbonyl functionality [12,13]. In this paper, we report an interesting four-component reaction of (*N*-isocyanimino)triphenylphosphorane **6** (Scheme 1).

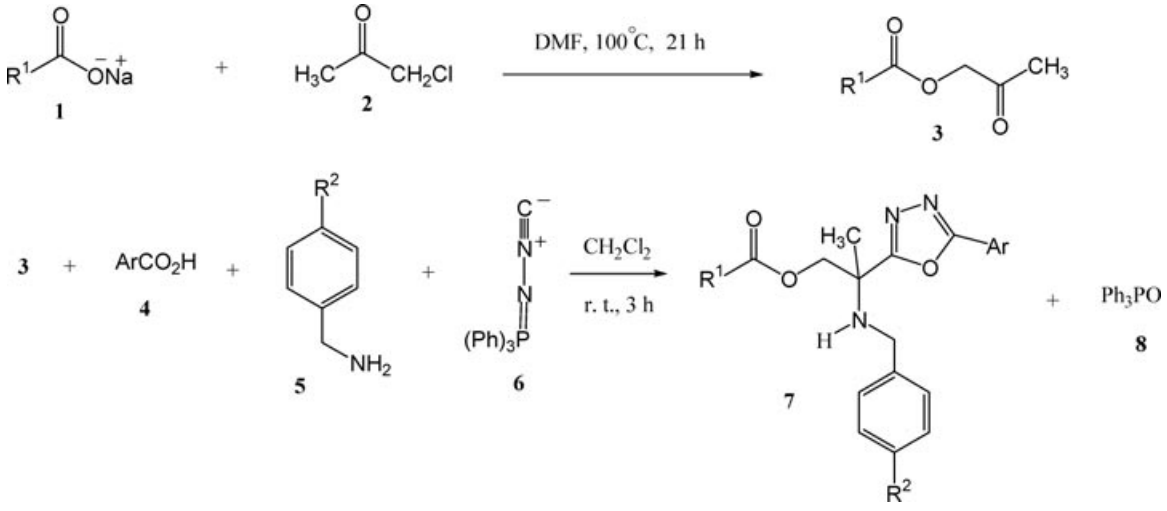
RESULTS AND DISCUSSION

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 disubstituted 1,3,4-oxadiazole derivatives **7** by a four-component condensation of primary amine **5,** (*N*-isocyanimino)triphenylphosphorane **6**, aromatic carboxylic acid derivatives **4**, and 2-oxopropyl benzoate (or acetate) **3** (Scheme 1). The imine intermediate generated by the reaction of primary amine **5** with 2-oxopropyl benzoate (or acetate) **3** is trapped by the (*N*-isocyanimino)triphenylphosphorane in the presence of an aromatic carboxylic acid derivative **4** leading to the formation of disubstituted 1,3,4-oxadiazole derivatives **7** and triphenylphosphine oxide (**8**; Scheme 1 and Table 1). The reaction proceeds smoothly and cleanly under mild conditions, and no side reactions were observed.

TABLE 1 Synthesis of Disubstituted 1,3,4-Oxadiazole Derivatives **7** (See Scheme 1)

7	R^1	R^2	*Ar*	*Yield of* **7** *(%)*[a]
a	Ph	H	3,5-diMeC_6H_4	85
b	Ph	CH_3	3,5-diMeC_6H_4	87
c	Ph	CH_3	3,4-diMeC_6H_4	82
d	Ph	H	3,4-diMeC_6H_4	86
e	CH_3	H	3,5-diMeC_6H_4	87
f	CH_3	H	4-MeC_6H_4	88
g	Ph	CH_3	4-MeC_6H_4	85
h	Ph	F	3,5-diMeC_6H_4	84
i	Ph	F	2-BrC_6H_4	81
j	Ph	H	4-BrC_6H_4	86
k	Ph	H	4-ClC_6H_4	85
l	Ph	OCH_3	4-ClC_6H_4	83
m	Ph	OCH_3	3,5-diMeC_6H_4	85

[a]Yield of isolated products.



SCHEME 1 Synthesis of 2-oxopropylbenzoate (or acetate) **3** and four-component synthesis of disubstituted 1,3,4-oxadiazole derivatives **7a–m** (see Table 1 and the Experimental section).

The structures of the products were deduced from their ^{1}H NMR, ^{13}C NMR, and mass and IR spectra. For example, the ^{1}H NMR spectrum of **7a** consisted of two singlets for the 3 CH_3($\delta = 1.83$ and 2.36 ppm), a singlet for the NH ($\delta = 2.08$, exchangeable by D_2O), an AB-quartet for the CH_2 of a benzyl group at δ = 3.74 and 3.83 ppm ($^2J_{HH}$ = 12.4 Hz), an AB-quartet for the CH_2 aliphatic at $\delta = 4.60$ and 4.73 ppm ($^2J_{HH}$ = 10.9 Hz), and a multiplet at δ = 7.15–8.01 ppm for the H-aromatic. The aryl groups exhibited characteristic signals in the aromatic region of the spectrum. The ^{1}H decoupled ^{13}C NMR spectrum of **7a** showed 20 distinct resonances; partial assignment of these resonances is given in the Experimental section. The ^{1}H and ^{13}C NMR spectra of compounds **7b–m** 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 carboxylic acid **4**, 2-oxopropyl benzoate (or acetate) **3**, and primary amine **5** that leads to an intermediate iminium ion **9**. The nucleophilic addition of the (*N*-isocyanimino)triphenylphosphorane **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 the 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 acetate) **3**, primary amine **5**, (*N*-isocyanimino)triphenylphosphorane **6**, and aromatic carboxylic acid **4**. Its ease of work-up, high yields, and fairly mild reaction conditions make it a useful addition to modern synthetic methodologies.

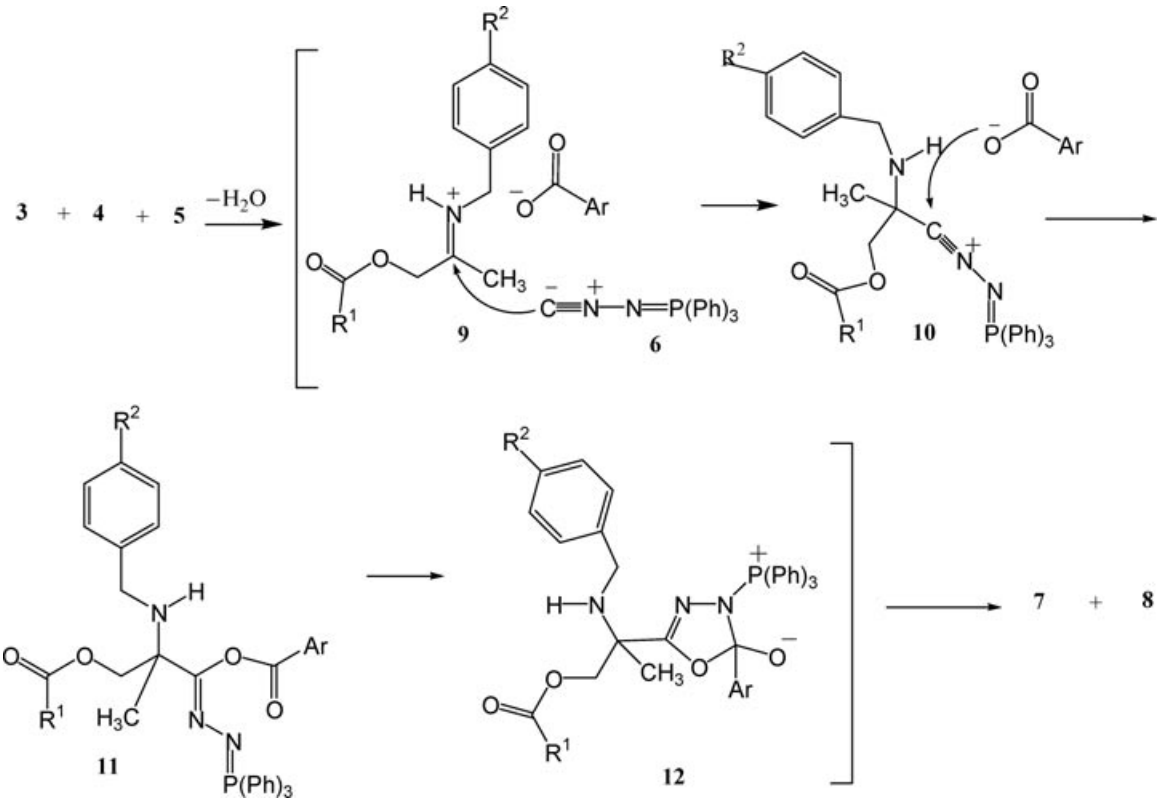
EXPERIMENTAL

Starting materials and solvents were obtained from Merck (Darmstadt, Germany) and Fluka (Buchs, 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 (mp) 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 ($CDCl_3$) 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 20 eV. Flash chromatography columns were prepared with Merck silica gel. 2-Oxopropyl benzoate (or acetate) **3** was prepared based on the known procedure [36].

General Procedure for the Preparation of **7a − m**

To a magnetically stirred solution of primary amine **5** (1 mmol; 0.107 g ($C_6H_5CH_2NH_2$), 0.121 g (4-$MeC_6H_4CH_2NH_2$), 0.125 g (4-$FC_6H_4CH_2NH_2$), and 0.137 g (4-$MeOC_6H_4CH_2NH_2$)), an ester derivative of 2-oxopropyl alcohol **3** (2-oxopropyl acetate and 2-oxopropyl benzoate) (1 mmol; 0.116 g (R = CH_3) and 0.178 g (R = Ph)) and (*N*-isocyanimino)triphenylphosphorane **6** (1 mmol, 0.302 g) in CH_2Cl_2 (5 mL) was added dropwise a solution of an aromatic carboxylic acid **4** (1 mmol; 0.150 g (Ar = 3,5-diMeC_6H_4), 0.150 g (Ar = 3,4-diMeC_6H_4), 0.136 g (Ar = 4-MeC_6H_4), 0.201 g (Ar = 4-BrC_6H_4), and 0.157 g (Ar = 4-ClC_6H_4)) in CH_2Cl_2 (5 mL) at room temperature for more than 15 min. The mixture was stirred for 3 h. The solvent was removed under reduced pressure, and the viscous residue was purified by flash column chromatography (silica gel; petroleum ether–ethyl acetate (10:1)), and the products **(7a–m)** were obtained. The physical and spectral data of the compounds are given below.

*2-(Benzylamino)-2-[5-(3,5-dimethylphenyl)- 1,3, 4-oxadiazol-2-yl]propyl benzoate (***7a***).* Yellow oil, yield: 375 mg (85%). ^{1}H NMR: 1.83, 2.36 (s, 9H, $3CH_3$); 2.08 (s, 1H, NH of amine exchangeable by D_2O); 3.74, 3.83 (AB quartet, 2H, $^2J_{HH}$ = 12.37 Hz, CH_2 of the benzyl group); 4.60, 4.73 (AB quartet, 2H, $^2J_{HH}$ = 10.87 Hz, CH_2 aliphatic); 7.15–8.01 (m, 13H, H-Ar).^{13}C NMR: 20.97, 21.21 ($3CH_3$); 47.80 (CH_2 of the benzyl group); 56.79 (C aliphatic); 69.20 (CH_2 aliphatic); 129.45, 133.33, 133.55, 138.79 (5C arom); 123.42, 124.28, 127.28, 128.25, 128.49, 128.55, 129.71, 129.90 (13CH arom); 165.58, 165.83 (2C of oxadiazole); 168.21 (C of the benzoate group). IR (neat): 3467, 2961, 2364, 2354, 1726, 1430, 1273, 712 cm^{-1}. Anal. calcd for $C_{27}H_{27}N_3O_3$ (441.52): C 73.45, H 6.16, N 9.52; Found: C 73.40, H 6.12, N 9.55. MS (EI): 441 (M^+), 279 (3.67), 174 (9.77), 167 (21.20), 149 (89.29), 132 (29.75), 104 (89.27), 91 (27.20), 76 (79.92), 57 (97.95), 43 (100).



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

*2-[5-(3,5-Dimethylphenyl)-1,3,4-oxadiazol-2-yl]-2-[(4-methylbenzyl)amino)]propyl Benzoate (***7b***).* Yellow oil, yield: 396 mg (87%). ^{1}H NMR: 1.87, 2.24, 2.36 (s, 12H, 4CH_3); 2.12 (s, 1H, NH of amine); 3.75, 3.85 (AB quartet, 2H, $^2J_{HH}$ = 12 Hz, CH_2 of the benzyl group); 4.66, 4.76 (AB quartet, 2H, $^2J_{HH}$ = 11 Hz, CH_2 aliphatic); 7.06–8.02 (m, 12H, H-Ar).^{13}C NMR: 21.02, 21.12, 21.21 (4CH_3); 47.54 (CH_2 of the benzyl group); 56.95 (C aliphatic); 69.45 (CH_2 aliphatic); 129.43, 133.33, 133.55, 137.09, 138.76 (6C arom); 123.33, 124.67, 128.41, 128.47, 129.21, 129.72, 129.75 (12CH arom); 165.64, 165.76 (2C of oxadiazole); 167.78 (C of the benzoate group). IR (neat): 3495, 2427, 2369, 1728, 1459, 1279,1118, 716 cm^{-1}. Anal. calcd for $C_{28}H_{29}N_3O_3$ (455.22): C 73.82, H 6.42, N 9.22; Found: C 73.88, H 6.47, N 9.18. MS (EI): 455.55 (M^+), 174 (1.06), 105 (4.82), 58 (14.63), 43 (100).

*2-[5-(3,4-Dimethylphenyl)- 1,3,4-oxadiazol-2-yl]-2-[(4-methylbenzyl)amino)]propyl Benzoate (***7c***).* Yellow oil, yield: 373 mg (82%). ^{1}H NMR: 1.82, 2.25, 2.31 (s, 12H, 4CH_3); 2.10 (s, 1H, NH of amine); 3.71, 3.81 (AB quartet, 2H, $^2J_{HH}$ = 11.37 Hz, CH_2 of the benzyl group); 4.62, 4.71 (AB quartet, 2H, $^2J_{HH}$ = 10.12 Hz, CH_2 aliphatic); 7.09–8.07 (m, 12H, H-Ar).^{13}C NMR: 19.75, 20.05, 20.89, 21.07 (4CH_3); 47.56 (CH_2 of the benzyl group); 56.79 (C aliphatic); 69.25 (CH_2 aliphatic); 129.41, 130.24, 133.33, 137.03, 137.53, 141.13 (6C arom); 121.14, 124.45, 127.88, 128.32, 128.48, 129.21, 129.59, 129.72 (12CH arom); 165.55, 165.82 (2C of oxadiazole); 167.89 (C of the benzoate group). IR (neat): 3467, 2952, 2417, 2377, 1725, 1452, 1271, 1114, 715 cm^{-1}. Anal. calcd for $C_{28}H_{29}N_3O_3$ (455.22): C 73.82, H 6.42, N 9.22; Found: C 73.78, H 6.46, N 9.17.

*2-(Benzylamino)-2-[5-(3,4-dimethylphenyl)- 1,3, 4-oxadiazol-2-yl]propyl Benzoate (***7d***).* Yellow oil, yield: 380 mg (86%). ^{1}H NMR: 1.84, 2.31, 2.32 (s, 9H, 3CH_3); 2.10 (s, 1H, NH of amine); 3.79, 3.88 (AB quartet, 2H, $^2J_{HH}$ = 12.37 Hz, CH_2 of the benzyl group); 4.65, 4.75 (AB quartet, 2H, $^2J_{HH}$ = 11 Hz, CH_2 aliphatic); 7.22–8.08 (m, 13H, H-Ar).^{13}C NMR: 19.73, 20.03, 20.83 (3CH_3); 47.82 (CH_2 of the benzyl group); 56.91 (C aliphatic); 69.23 (CH_2 aliphatic); 129.48, 130.26, 133.33, 137.55, 141.18 (5C arom); 121.09, 124.47, 127.42, 127.89, 128.48, 128.53, 128.64, 129.33, 129.72 (13CH arom); 165.60, 165.80 (2C of oxadiazole); 168.72 (C of the benzoate group). IR (neat): 3441, 2956, 2369, 2359, 1725, 1453, 1272, 1115, 711 cm^{-1}. Anal. calcd for $C_{27}H_{27}N_3O_3$

(441.52): C 73.45, H 6.16, N 9.52; Found: C 73.41, H 6.11, N 9.56.

*2-(Benzylamino)-2-[5-(3,5-dimethylphenyl)-1,3,4-oxadiazol-2-yl]propyl Acetate (**7e**)*. Yellow oil, yield: 330 mg (87%). ^{1}H NMR: 1.72, 2.04, 2.40 (s, 9H, $3CH_3$); 2.11 (s, 1H, NH of amine); 3.75 (s, 2H, CH_2 of the benzyl group); 4.35, 4.53 (AB quartet, 2H, $^2J_{HH}$ = 11 Hz, CH_2 aliphatic); 7.17–7.65 (m, 8H, H-Ar).^{13}C NMR: 20.72, 20.92, 21.18.80 ($4CH_3$); 47.77 (CH_2 of the benzyl group); 56.54 (C aliphatic); 68.67 (CH_2 aliphatic); 133.51, 138.82, 139.71 (4C arom); 123.54, 124.63, 127.21, 128.23, 128.47 (8CH arom); 165.78, 167.74 (2C of oxadiazole); 170.34 (C of the benzoate group). IR (neat): 3339, 2929, 1754, 1455, 1249, 1051, 741 cm^{-1}. Anal. calcd for $C_{22}H_{25}N_3O_3$ (379.45): C 69.64, H 6.64, N 11.07; Found: C 69.60, H 6.73, N 11.11.

*2 -(Benzylamino)-2-[5-(4-methylphenyl)-1,3,4-oxadiazol-2-yl]propyl Acetate (**7f**)*. Yellow oil, yield: 321 mg (88%). ^{1}H NMR: 1.67, 2.04, 2.43 (s, 9H, $3CH_3$); 2.06 (s, 1H, NH of amine); 3.72, 3.78 (AB quartet, 2H, $^2J_{HH}$ = 12.37 Hz, CH_2 of the benzyl group); 4.33, 4.51 (AB quartet, 2H, $^2J_{HH}$ = 11 Hz, CH_2 aliphatic); 7.23–7.94 (m, 9H, H-Ar).^{13}C NMR: 20.80, 20.91, 21.68 ($3CH_3$); 47.79 (CH_2 of the benzyl group); 56.48 (C aliphatic); 68.76 (CH_2 aliphatic); 120.97, 139.65, 142.41 (3C arom); 126.87, 127.25, 128.28, 128.51, 129.78 (9CH arom); 165.33, 167.64 (2C of oxadiazole); 170.42 (C of the benzoate group). IR (neat): 3468, 2969, 2374, 2360, 1726, 1489, 1276, 1115, 717 cm^{-1}. Anal. calcd for $C_{21}H_{23}N_3O_3$ (365.43): C 69.02, H 6.34, N 11.50; Found: C 69.07, H 6.29, N 11.47.

*2-[(4-Methylbenzyl)amino)]2-[5-(4-methylphenyl)-1,3,4-oxadiazol-2-yl]propyl Benzoate (**7g**)*. Yellow oil, yield: 375 mg (85%). IR (neat): 3461, 2961, 2381, 2366, 1725, 1499, 1271, 1115, 713 cm^{-1}. ^{1}H NMR: 1.84, 2.25, 2.43 (s, 9H, $3CH_3$); 2.09 (s, 1H, NH of amine); 3.74, 3.83 (AB quartet, 2H, $^2J_{HH}$ = 12 Hz, CH_2 of the benzyl group); 4.65, 4.73 (AB quartet, 2H, $^2J_{HH}$ = 11 Hz, CH_2 aliphatic); 7.06–8.0 (m, 13H, H-Ar).^{13}C NMR: 20.85, 21.04, 21.67 ($3CH_3$); 47.56 (CH_2 of the benzyl group); 56.86 (C aliphatic); 69.31 (CH_2 aliphatic); 129.40, 133.31, 133.55, 137.09, 142.38 (5C arom); 120.89, 126.90, 128.37, 128.47, 129.21, 129.72, 129.79 (13CH arom); 165.43, 165.43 (2C of oxadiazole); 167.80 (C of the benzoate group). IR (neat): 3468, 2969, 2374, 2360, 1726, 1489, 1276, 1115, 717 cm^{-1}. Anal. calcd for $C_{27}H_{27}N_3O_3$ (441.52): C 73.45, H 6.16, N 9.52; Found: C 73.48, H 6.12, N 9.57.

*2-[5-(3,5-Dimethylphenyl)-1,3,4-oxadiazol-2-yl]-2-[(4-fluorobenzyl)amino]propyl Benzoate (**7h**)*. Yellow oil, yield: 386 mg (84%). ^{1}H NMR: 1.84, 2.36 (s, 9H, $3CH_3$); 2.08 (s, 1H, NH of amine); 3.73, 3.79 (AB quartet, 2H, $^2J_{HH}$ = 12.25 Hz, CH_2 of the benzyl group); 4.58, 4.72 (AB quartet, 2H, $^2J_{HH}$ = 11 Hz, CH_2 aliphatic); 6.93–8.01 (m, 12H, H-Ar).^{13}C NMR: 20.95, 21.20 ($3CH_3$); 47.06 (CH_2 of the benzyl group); 56.82 (C aliphatic); 69.21 (CH_2 aliphatic); 115.33 (d,$^2J_{CF}$ = 21.39 Hz, 2CH, arom), 129.83 (d,$^3J_{CF}$ = 8.8 Hz, 2CH, arom), 124.64, 128.50, 129.69, 129.72, 130.02 (8CH arom); 129.79, 133.39, 133.65, 138.83 (4C arom); 162.81 (d,$^1J_{CF}$ = 212.17 Hz, C, arom), 165.62, 165.79 (2C of oxadiazole); 167.83 (C of the benzoate group). IR (neat): 3471, 2380, 2373, 1725, 1509, 1273, 1117, 713 cm^{-1}. Anal. calcd for $C_{27}H_{26}FN_3O_3$ (459.51): C 70.57, H 5.70, N 9.14; Found: C 70.53, H 5.74, N 9.10.

*2-[5-(2-Bromophenyl)-1,3,4-oxadiazol-2-yl]-2-[(4-fluorobenzyl)amino]propyl Benzoate (**7i**)*. Yellow oil, yield: 413 mg (81%). ^{1}H NMR: 1.82 (s, 3H, CH_3); 2.07 (s, 1H, NH of amine); 3.82 (s, 2H, CH_2 of the benzyl group); 4.61, 4.72 (AB quartet, 2H, $^2J_{HH}$ = 10.87 Hz, CH_2 aliphatic); 6.99–7.90 (m, 13H, H-Ar).^{13}C NMR: 21.05 (CH_3); 47.07 (CH_2 of the benzyl group); 56.88 (C aliphatic); 69.18 (CH_2 aliphatic); 115.29 (d,$^2J_{CF}$ = 20.80 Hz, 2CH, arom), 129.86 (d,$^3J_{CF}$ = 8.1 Hz, 2CH, arom), 127.66, 128.48, 129.35, 129.69, 129.73, 132.74, 133.35 (9CH arom); 121.61, 131.74, 132.70, 134.44 (4C arom); 162.03 (d,$^1J_{CF}$ = 244.7 Hz, C, arom), 164.29, 165.82 (2C of oxadiazole); 168.62 (C of the benzoate group). IR (neat): 3469, 2387, 2381, 1725, 1455, 1273, 1117, 716 cm^{-1}. Anal. calcd for $C_{25}H_{21}BrFN_3O_3$ (510.35): C 58.84, H 4.15, N 8.23; Found: C 58.88, H 4.10, N 8.27.

*2-(Benzylamino)-2-[5-(4-bromophenyl)-1,3,4-oxadiazol-2-yl]propyl Benzoate (**7j**)*. Yellow oil, yield: 423 mg (86%). ^{1}H NMR: 1.83 (s, 3H, CH_3); 2.18 (s, 1H, NH of amine exchangeable by D_2O); 3.82 (s, 2H, CH_2 of the benzyl group); 4.62, 4.73 (AB quartet, 2H, $^2J_{HH}$ = 11 Hz, CH_2 aliphatic); 7.24–7.99 (m, 14H, H-Ar).^{13}C NMR: 21.00 (CH_3); 47.78 (CH_2 of the benzyl group); 56.86 (C aliphatic); 69.00 (CH_2 aliphatic); 121.81, 129.36, 133.40, 137.20 (4C arom); 122.57, 126.54, 127.33, 128.25, 128.32, 128.52, 129.68, 132.37 (14CH arom); 164.56, 165.78 (2C of oxadiazole); 168.02 (C of the benzoate group). IR (neat): 3485, 2411, 2369, 1726, 1482, 1273, 1115, 712 cm^{-1}. Anal. calcd for $C_{25}H_{22}BrN_3O_3$ (492.36): C 60.98, H 4.50, N 8.53; Found: C 60.93, H 4.53, N 8.50.

*2 - (Benzylamino) - 2- [5- (4 - chlorophenyl) - 1,3,4 - oxadiazol-2-yl]propyl Benzoate (***7k***).* Yellow oil, yield: 380 mg (85%). IR (neat): 3472, 2387, 2385, 1726, 1484, 1273, 1095, 712 cm^{-1}. ^1H NMR: 1.83 (s, 3H, CH_3); 2.24 (s, 1H, NH of amine); 3.78, 3.86 (AB quartet, 2H, $^2J_{HH} = 12.37$ Hz, CH_2 of the benzyl group); 4.63, 4.74 (AB quartet, 2H, $^2J_{HH} = 11$ Hz, CH_2 aliphatic); 7.21–8.09 (m, 14H, H-Ar).^{13}C NMR: 21.01 (CH_3); 47.79 (CH_2 of the benzyl group); 56.85 (C aliphatic); 69.02 (CH_2 aliphatic); 122.16, 129.38, 133.40, 138.09 (4C arom); 127.32, 128.20, 128.22, 128.49, 128.52, 129.38, 129.42, 129.68 (14CH arom); 164.47, 165.79 (2C of oxadiazole); 168.03 (C of the benzoate group). IR (neat): 3485, 2411, 2369, 1726, 1482, 1273, 1115, 712 cm^{-1}. Anal. calcd for $C_{25}H_{22}ClN_3O_3$ (447.91): C 67.04, H 4.95, N 9.38; Found: C 67.07, H 4.90, N 9.35.

*2 - [5 - (4 - Chlorophenyl) - 1,3,4 - oxadiazol - 2 - yl]- 2-[(4-methoxybenzyl)amino]propyl Benzoate (***7l***).* Yellow oil, yield: 396 mg (83%). ^1H NMR: 1.81 (s, 3H, CH_3); 2.07 (s, 1H, NH of amine); 3.73 (s, 3H, OCH_3); 3.68, 3.78 (AB quartet, 2H, $^2J_{HH} = 12.12$ Hz, CH_2 of the benzyl group); 4.60, 4.71 (AB quartet, 2H, $^2J_{HH} = 11$ Hz, CH_2 aliphatic); 6.72–8.07 (m, 13H, H-Ar).^{13}C NMR: 21.03 (CH_3); 47.18 (CH_2 of the benzyl group); 55.21 (OCH_3); 56.69 (C aliphatic); 69.09 (CH_2 aliphatic); 129.72, 131.60, 133.28, 133.37, 158.78 (5C arom); 113.87, 124.17, 128.16, 128.50, 129.39, 129.65, 129.72 (13CH arom); 165.55, 165.78 (2C of oxadiazole); 168.27 (C of the benzoate group). IR (neat): 3476, 2989, 2389, 2378, 1729, 1480, 1276, 1115, 715 cm^{-1}. Anal. calcd for $C_{26}H_{24}ClN_3O_4$ (477.94): C 65.34, H 5.06, N 8.79; Found: C 65.29, H 5.10, N 8.83.

*2-[5-(3,5-Dimethylphenyl)-1,3,4-oxadiazol-2-yl]- 2-[(4-methoxybenzyl)amino]propyl Benzoate (***7m***).* Yellow oil, yield: 400 mg (85%). ^1H NMR: 1.81, 2.35 (s, 9H, $3CH_3$); 2.10 (s, 1H, NH of amine); 3.73 (s, 3H, OCH_3); 3.68, 3.78 (AB quartet, 2H, $^2J_{HH} = 12.12$ Hz, CH_2 of the benzyl group); 4.59, 4.71 (AB quartet, 2H, $^2J_{HH} = 10.89$ Hz, CH_2 aliphatic); 6.76-8.08 (m, 12H, H-Ar).^{13}C NMR: 20.99, 21.20 ($3CH_3$); 47.20 (CH_2 of the benzyl group); 55.22 (OCH_3); 56.66 (C aliphatic); 69.21 (CH_2 aliphatic); 131.72, 133.31, 133.52, 138.78, 158.77 (6C arom); 113.87, 124.62, 128.47, 129.43, 129.47, 129.70, 129.78 (12CH arom); 165.54, 165.84 (2C of oxadiazole); 167.94 (C of the benzoate group). IR (neat): 3472, 2377, 2369, 1479, 1281, 1116, 715 cm^{-1}. Anal. calcd for $C_{28}H_{29}N_3O_4$ (471.55): C 71.32, H 6.20, N 8.91; Found: C 71.36, H 6.16, N 8.88.

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