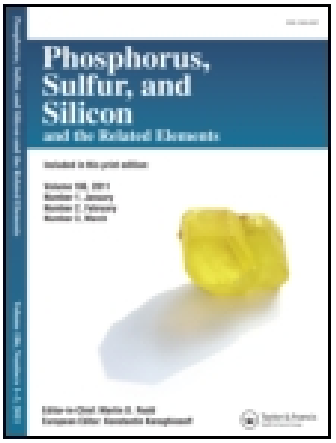

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N-Isocyaniminotriphenylphosphorane (Ph3PNNC) as an Efficient Reagent for the Synthesis of Fully Substituted 1,3,4-Oxadiazoles from 3-Phenyl-2-Propynoic Acid, Secondary Amines and Aromatic Bis-Aldehydes

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N-ISOCYANIMINOTRIPHENYLPHOSPHORANE (PH3PNNC) AS AN EFFICIENT REAGENT FOR THE SYNTHESIS OF FULLY SUBSTITUTED 1,3,4-OXADIAZOLES FROM 3-PHENYL-2-PROPYNOIC ACID, SECONDARY AMINES AND AROMATIC BIS-ALDEHYDES

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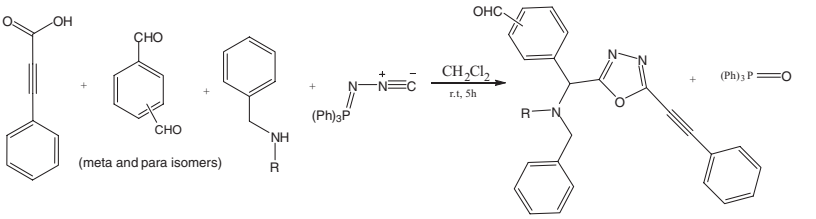
GRAPHICAL ABSTRACT



Abstract *Reactions of N-isocyaniminotriphenylphosphorane (Ph_3PNNC) with aromatic bis-aldehydes (isophthalaldehyde and terphthalaldehyde) in the presence of 3-phenyl-2-propynoic acid and secondary 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.*

Keywords *N*-isocyaniminotriphenylphosphorane; bis-aldehydes; 3-phenyl-2-propynoic acid; secondary amines; 1,3,4-oxadiazole

INTRODUCTION

A 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

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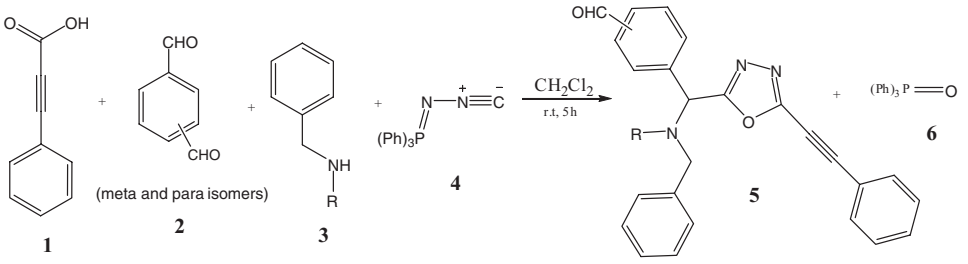
is receiving growing interest from industrial chemistry research groups and represents a challenge for organic chemists.[1,2] The drive toward the ideal synthesis embracing step count, ideally just one, and yield, ideally 100%, has been pursued aggressively since scientists began to construct molecules. 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 analoged 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, anti-fungal, 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 (Ph_3PNNC) **4**.[12,13] There are several reports on the use of *N*-isocyaniminotriphenylphosphorane (Ph_3PNNC) **4** in the synthesis of metal complexes.[12,13] However, the application of **4** 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 **5** by a four-component condensation of *N*-isocyaniminotriphenylphosphorane (Ph_3PNNC) **4** with bis-aldehydes (isophthalaldehyde and terphthalaldehyde) in the presence of 3-phenyl-2-propynoic acid and secondary amines followed by a aza-Wittig cyclization in CH_2Cl_2 at ambient temperature in excellent yields (Scheme 1).



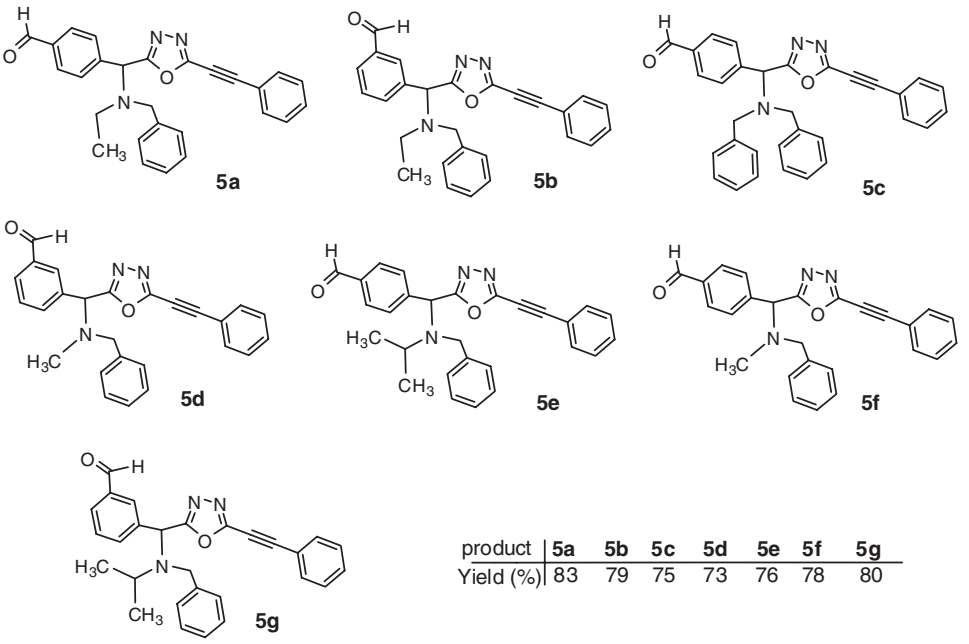
Scheme 1

RESULTS AND DISCUSSION

The imine intermediate generated by the reaction of secondary amine derivatives **3** with bis-aldehydes (isophthalaldehyde and terphthalaldehyde) **2** is trapped by the *N*-isocyaniminotriphenylphosphorane (Ph_3PNNC) **4** in the presence of an 3-phenyl-2-propynoic acid **1** to lead to the formation of disubstituted 1,3,4-oxadiazole derivatives **5** and triphenylphosphine oxide **6** (Scheme 1 and Figure 1). The reaction proceeds smoothly and cleanly under mild conditions and no side reactions were observed.

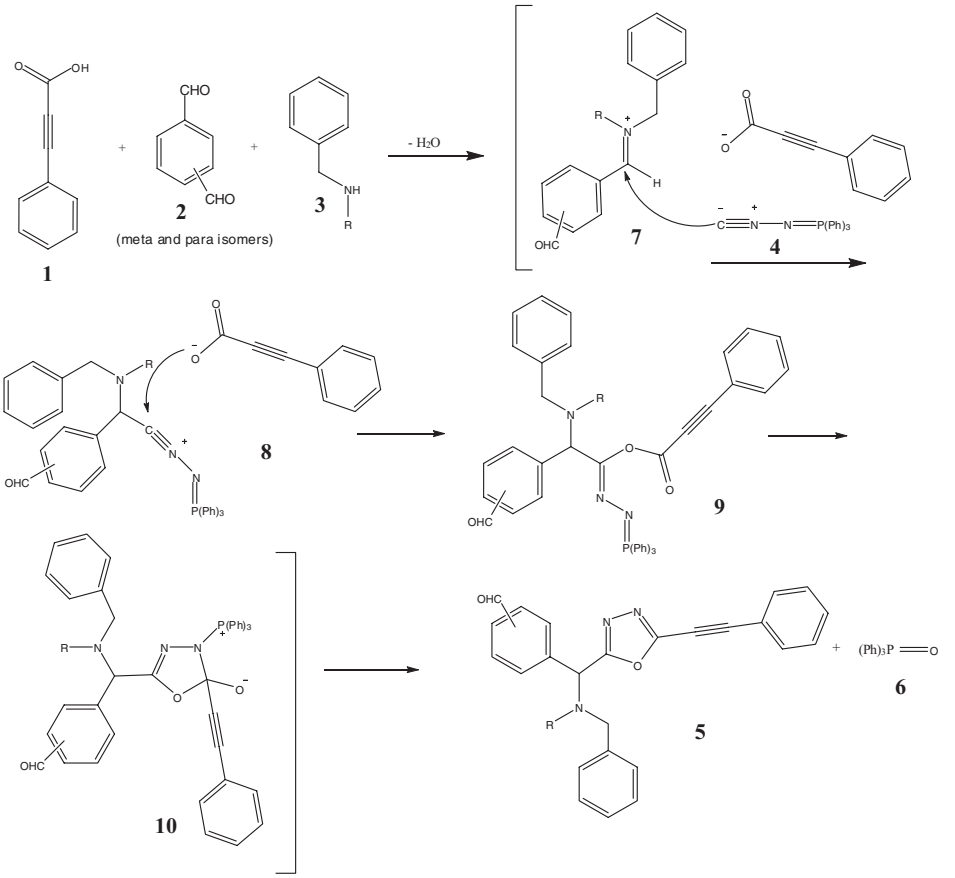
The structures of the products were deduced from their IR, Mass, H NMR, and ^3C NMR spectra. The mass spectra of these compounds displayed molecular ion peaks at the appropriate m/z values. The H NMR spectrum of **5a** consisted of a triplet at $\delta = 1.14$ ($^3J_{HH} = 7$ Hz) for CH_3 of ethyl group, tow multiplet at 2.44–2.57 and 2.70–2.79 for CH_2 of ethyl group, a AB-quartet for CH_2 of benzyl group ($\delta = 3.56$ and 3.89, $^2J_{HH} = 14$ Hz), a singlet at $\delta = 5.47$ for CH aliphatic, a multiplet at 7.28–7.90 for the aromatic protons and a singlet for CH of aldehyde group ($\delta = 10.13$). The ^{1}H-decoupled ^{13}C NMR spectrum of **5a** is in agreement with the proposed structure. In view of the success of the above-mentioned reaction, we explored the scope of this promising reaction by varying the structure of the bis-aldehyde, and secondary amine component (Table 1). Owing to the great diversity of substitution patterns, this reaction may be used in the production of combinatorial libraries.

A mechanistic rationalization for this reaction is provided in Scheme 2. It is conceivable that, the initial event is the condensation of the bis-aldehydes **2**, Secondary amine derivatives **3**, and 3-phenyl-2-propynoic acid **1** entities to an iminium intermediate **7**. Nucleophilic addition of the *N*-isocyaniminotriphenylphosphorane (Ph_3PNNC) **4** to the iminium intermediate **7**, leading to nitrilium intermediate **8**. This intermediate may be attacked by



product	5a	5b	5c	5d	5e	5f	5g
Yield (%)	83	79	75	73	76	78	80

Figure 1 Synthesis of disubstituted 1,3,4-oxadiazole derivatives **5a–g**.



Scheme 2

conjugate base of the acid **1** to form 1:1:1 adduct **9**. This adduct may undergo intramolecular *aza*-Wittig reaction of iminophosphorane moiety with the ester carbonyl group to afford the isolated 2,5-disubstituted 1,3,4-oxadiazole **5** by removal of triphenylphosphine oxide **6** from intermediate **10**.

Table 1 Synthesis of disubstituted 1,3,4-oxadiazole derivatives **5a–g** from 3-phenyl-2-propynoic acid **1**, bis-aldehyde **2** and Secondary amine **3** in the presence of *N*-isocyaniminotriphenylphosphorane **4**

Compounds	Acid **1**	Bis-aldehyde **2**	Secondary amine **3**	Yield[a] (%)
5a	3-phenyl-2-propynoic acid	Terephthalaldehyde	*N*-benzyl-*N*-ethylamine	**83**
5b	3-phenyl-2-propynoic acid	Isophthalaldehyde	*N*-benzyl-*N*-ethylamine	**79**
5c	3-phenyl-2-propynoic acid	Terephthalaldehyde	*N*,*N*-dibenzylamine	**75**
5d	3-phenyl-2-propynoic acid	Isophthalaldehyde	*N*-benzyl-*N*-methylamine	**73**
5e	3-phenyl-2-propynoic acid	Terephthalaldehyde	*N*-benzyl-*N*-isopropylamine	**76**
5f	3-phenyl-2-propynoic acid	Terephthalaldehyde	*N*-benzyl-*N*-methylamine	**78**
5g	3-phenyl-2-propynoic acid	Isophthalaldehyde	*N*-benzyl-*N*-isopropylamine	**80**

[a]Yield of isolated products.

EXPERIMENTAL

General

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 (thin layer chromatography) and NMR, which indicated that there is no side product. IR spectra were measured on a Jasco 6300 FTIRspectrometer. ^{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 70 eV. Flash chromatography columns were prepared with Merck silica gel powder.

General Procedure for the Preparation of Compounds 5a–g

A mixture of *N*-isocyaniminotriphenylphosphorane **4** (1 mmol, 0.302 g), aromatic bis-aldehyde **2** (1 mmol; 0.134 g), and secondary amine **3** (1 mmol; 0.121 g (R = methyl), 0.197 g (R = benzyl), 0.149 g (R = Isopropyl), and 0.135 g (R = ethyl)) in CH_2Cl_2 (5 mL) was added dropwise a solution of 3-phenyl-2-propynoic acid **1** (1 mmol; 0.146 g) in CH_2Cl_2 (5 mL) at room temperature over 15 min. The mixture was stirred for 5 h. The solvent was removed under reduced pressure and the viscous residue was purified by flash column chromatography (silica gel (F_{254}); petroleum ether–AcOEt (10:2). The solvent was removed under reduced pressure and the products were obtained. The characterization data of the compounds are given below:

4–{[Benzyl(ethyl)amino][(5-(2-phenyl-1-ethynyl)-1,3,4-oxadiazol-2-yl]methyl}benzaldehyde 5a. Yellow oil, Yield 349 mg (83%); $R_f = 0.25$ (petroleum ether–AcOEt (10:2); IR (neat) (ν_{max} /cm^{-1}): 3066 (m), 2864 (m), 2235 (m), 1704 (s), 1542 (m), and 760 (m) cm^{-1}. ^{1}H NMR ($CDCl_3$, 250 MHz): δ_H (ppm) 1.14 (t, 3H, $^{3}J_{HH} = 7$ Hz, CH_3 of Et), 2.44–2.57 and 2.70–2.79 (2m, 2H, CH_2 of Et), 3.56 and 3.89 (AB quartet, 2H, $^{2}J_{HH} = 14$Hz, CH_2 of benzyl group), 5.47 (s, 1H, CH aliphatic), 7.28–7.90 (m, 14H, H-arom), 10.13 (s, 1H, CHO). ^{13}C NMR ($CDCl_3$, 62.5 MHz): δ_C (ppm) 12.7 (CH_3), 44.6 (CH_2 of Ethyl group), 54.5 (CH_2 of benzyl group), 60.2 (CH, aliphatic), 72.9 and 97.3 (2C, acetylene), 127.3, 128.5, 128.7, 128.7, 128.8, 129.9, 130.8, and 132.4 (14CH–Ar), 119.6, 136.2, 138.5, and 143.6 (4C–Ar), 151.5 and 164.9 (2C=N of oxadiazole), 191.6 (C=O of aldehyde). MS: m/e (%) 422 (M^+, 4), 342 (33), 288 (72), 252 (12), 134 (100), 91 (93), 65 (9). Anal. Calcd for $C_{27}H_{23}N_3O_2$ (421.49): C, 76.94; H, 5.50; N, 9.97. Found: C, 76.88; H, 5.54; N, 9.92.

3–{[Benzyl(ethyl)amino][(5-(2-phenyl-1-ethynyl)-1,3,4-oxadiazol-2-yl]methyl}benzaldehyde 5b. Yellow oil, Yield 333 mg (79%); $R_f = 0.28$ (petroleum ether–AcOEt (10:2); IR (neat) (ν_{max} /cm^{-1}): 2982 (m), 2861 (m), 2234 (m), 1700 (s), 1540 (m), and 760 (m) cm^{-1}. ^{1}H NMR ($CDCl_3$, 250 MHz): δ_H (ppm) 1.14 (t, 3H, $^{3}J_{HH} = 7$ Hz, CH_3 of Et), 2.47–2.55 and 2.71–2.79 (2m, 2H, CH_2 of Et), 3.57 and 3.88 (AB quartet, 2H, $^{2}J_{HH} = 14$Hz, CH_2 of benzyl group), 5.48 (s, 1H, CH aliphatic), 7.28–7.96 (m, 14H, H-arom), 10.12 (s, 1H, CHO). ^{13}C NMR ($CDCl_3$, 62.5 MHz): δ_C (ppm) 12.5 (CH_3), 44.6 (CH_2 of Ethyl group), 54.4 (CH_2 of benzyl group), 59.9 (CH, aliphatic), 72.6 and 97.6 (2C, acetylene), 128.5, 128.7, 129.4, 129.6, 129.9, 130.8, 131.0, 132.4, 134.6, and 136.0 (14CH-Ar), 119.6, 127.4, 134.2, and 136.7 (4C-Ar), 151.5 and 164.9 (2C=N of oxadiazole), 191.9 (C=O of aldehyde). MS: m/e (%) 421 (M^+, 3), 288 (11), 262 (7), 170

(15), 134 (100), 105 (59), 91 (33), 77 (54), 51 (43), 43 (15). Anal. Calcd for $C_{27}H_{23}N_3O_2$ (421.49): C, 76.94; H, 5.50; N, 9.97. Found: C, 76.90; H, 5.47; N, 9.91.

4–{(diBenzylamino)[(5-(2-phenyl-1-ethynyl)-1,3,4-oxadiazol-2-yl]methyl}benzaldehyde 5c. Yellow oil, Yield 362 mg (75%); $R_f = 0.38$ (petroleum ether–AcOEt (10:2); IR (neat) (ν_{max} /cm^{-1}): 2865 (m), 2233 (m), 1704 (m), 1541 (m), and 758 (m) cm^{-1}. ^{1}H NMR ($CDCl_3$, 250 MHz): δ_H (ppm) 3.58 and 3.86 (AB quartet, 4H, $^2J_{HH} = 13.75$Hz, 2CH_2 of dibenzyl group), 5.46 (s, 1H, CH aliphatic), 7.33–8.06 (m, 19H, H-arom), 10.02 (s, 1H, CHO). ^{13}C NMR ($CDCl_3$, 62.5 MHz): δ_C (ppm) 54.6 (2CH_2 of benzyl group), 59.7 (CH, aliphatic), 71.9 and 97.1 (2C, acetylene), 127.5, 128.2, 128.6, 128.8, 128.8, 129.3, 129.0 and 132.4 (19CH-Ar), 128.6, 128.0, 129.0, and 138.1 (5C-Ar), 152.7 and 164.8 (2C=N of oxadiazole), 191.6 (C=O of aldehyde). Anal. Calcd for $C_{32}H_{25}N_3O_2$ (483.56): C, 79.48; H, 5.21; N, 8.69. Found: C, 79.52; H, 5.27; N, 8.65.

3–{[Benzyl(methyl)amino][(5-(2-phenyl-1-ethynyl)-1,3,4-oxadiazol-2-yl]methyl}benzaldehyde 5d. Yellow oil, Yield 297 mg (73%); $R_f = 0.34$ (petroleum ether–AcOEt (10:2); IR (neat) (ν_{max} /cm^{-1}): 2859 (m), 2234 (m), 1702 (s), 1540 (m), and 759 (m) cm^{-1}. ^{1}H NMR ($CDCl_3$, 250 MHz): δ_H (ppm) 2.30 (s, 3H, CH_3), 3.63 and 3.70 (AB quartet, 2H, $^2J_{HH} = 13.75$Hz, CH_2 of benzyl group), 5.31 (s, 1H, CH aliphatic), 7.28–8.08 (m, 14H, H-arom), 10.04 (s, 1H, CHO). ^{13}C NMR ($CDCl_3$, 62.5 MHz): δ_C (ppm) 39.2 (CH_3), 58.9 (CH_2 of benzyl group), 63.6 (CH, aliphatic), 71.0 and 98.2 (2C, acetylene), 127.5, 128.4 (CH and C), 128.5, 128.8, 129.6, 129.6, 129.8, 132.5 (CH and C), 134.4 and 136.8 (14CH-Ar), 122.5 and 126.7, (2C-Ar), 152.3 and 164.7 (2C=N of oxadiazole), 191.8 (C=O of aldehyde). Anal. Calcd for $C_{26}H_{21}N_3O_2$ (407.46): C, 76.64; H, 5.19; N, 10.31. Found: C, 76.69; H, 5.22; N, 10.24.

4–{[benzyl(Isopropyl)amino][(5-(2-phenyl-1-ethynyl)-1,3,4-oxadiazol-2-yl]methyl}benzaldehyde 5e. Yellow oil, Yield 331 mg (76%); $R_f = 0.29$ (petroleum ether–AcOEt (10:2); IR (neat) (ν_{max} /cm^{-1}): 2976 (m), 2877 (m), 2235 (m), 1703 (s), 1540 (m), and 758 (m) cm^{-1}. ^{1}H NMR ($CDCl_3$, 250 MHz): δ_H (ppm) 0.93 (d, 3H, $^3J_{HH} = 6.62$ Hz, CH_3 amin), 1.16 (d, 3H, $^3J_{HH} = 6.62$ Hz, CH_3 amin), 3.09–3.20 (m, 1H, CH amin), 3.80 and 3.89 (AB quartet, 2H, $^2J_{HH} = 14.75$Hz, CH_2 of benzyl group), 5.48 (s, 1H, CH aliphatic), 7.28–8.09 (m, 14H, H-arom), 10.14 (s, 1H, CHO). ^{13}C NMR ($CDCl_3$, 62.5 MHz): δ_C (ppm) 18.8 and 19.7 (2CH_3), 49.9 and 58.8 (2CH, aliphatic), 51.3 (CH_2 of benzyl group), 71.7 and 97.2 (2C, acetylene), 127.3, 128.3, 128.3, 128.7, 128.0, 130.1 (CH and C), 132.3 and 139.0 (14CH-Ar), 119.6, 131.7 and 136.2 (3C-Ar), 151.7 and 163.3 (2C=N of oxadiazole), 191.5 (C=O of aldehyde). Anal. Calcd for $C_{28}H_{25}N_3O_2$ (435.52): C, 77.22; H, 5.79; N, 9.65. Found: C, 77.27; H, 5.74; N, 9.68.

4–{[Benzyl(methyl)amino][(5-(2-phenyl-1-ethynyl)-1,3,4-oxadiazol-2-yl]methyl}benzaldehyde 5f. Yellow oil, Yield 317 mg (78%); $R_f = 0.38$ (petroleum ether–AcOEt (10:2); IR (neat) (ν_{max} /cm^{-1}): 2855 (m), 2235 (m), 1701 (s), 1542 (m) and 760 (m) cm^{-1}. ^{1}H NMR ($CDCl_3$, 250 MHz): δ_H (ppm) 2.28 (s, 3H, CH_3), 3.61 and 3.68 (AB quartet, 2H, $^2J_{HH} = 13.37$Hz, CH_2 of benzyl group), 5.29 (s, 1H, CH aliphatic), 7.29–7.93 (m, 14H, H-arom), 10.05 (s, 1H, CHO). ^{13}C NMR ($CDCl_3$, 62.5 MHz): δ_C (ppm) 39.2 (CH_3), 58.9 (CH_2 of benzyl group), 63.9 (CH, aliphatic), 72.9 and 97.4 (2C, acetylene), 127.5, 128.5, 128.7 (CH and C), 128.8, 129.1, 130.1, 130.8 and 132.4 (14CH-Ar), 119.6, 136.4 and 137.8 (3C-Ar), 151.9 and 164.5 (2C=N of oxadiazole), 191.6 (C=O of aldehyde). Anal. Calcd for $C_{26}H_{21}N_3O_2$ (407.46): C, 76.64; H, 5.19; N, 10.31. Found: C, 76.59; H, 5.24; N, 10.35.

3–{[benzyl(Isopropyl)amino][(5-(2-phenyl-1-ethynyl)-1,3,4-oxadiazol-2-yl]methyl}benzaldehyde 5g. Yellow oil, Yield 348 mg (80%); $R_f = 0.32$ (petroleum

ether–AcOEt (10:2); IR (neat) (ν_{max} /cm^{-1}): 2981 (m), 2867 (m), 2237 (m), 1701 (s), 1542 (m), and 760 (m) cm^{-1}. ^{1}H NMR ($CDCl_3$, 250 MHz): δ_H (ppm) 0.94 (d, 3H, $^3J_{HH}$ = 6.50 Hz, CH_3 amin), 1.17 (d, 3H, $^3J_{HH}$ = 6.50 Hz, CH_3 amin), 3.10–3.20 (m, 1H, CH amin), 3.80 and 3.88 (AB quartet, 2H, $^2J_{HH}$ = 14.75Hz, CH_2 of benzyl group), 5.49 (s, 1H, CH aliphatic), 7.28–8.18 (m, 14H, H-arom), 10.12 (s, 1H, CHO). ^{13}C NMR ($CDCl_3$, 62.5 MHz): δ_C (ppm) 18.7 and 19.4 ($2CH_3$), 48.9 and 58.7 (2CH, aliphatic), 50.1 (CH_2 of benzyl group), 72.9 and 98.1 (2C, acetylene), 126.0, 128.3, 128.3, 128.7, 129.4, 129.5, 129.6, 130.7, 132.3 and 136.7 (14CH-Ar), 119.6, 132.4, 134.2 and 136.5 (4C-Ar), 152.9 and 165.1 (2C=N of oxadiazole), 191.9 (C=O of aldehyde). Anal. Calcd for $C_{28}H_{25}N_3O_2$ (435.52): C, 77.22; H, 5.79; N, 9.65. Found: C, 77.19; H, 5.85; N, 9.58.

CONCLUSIONS

The reported method offers a mild, simple, and efficient route for the preparation of sterically congested 1,3,4-oxadiazole derivatives **5** from aromatic bis-aldehydes **2**, secondry amines **3**, *N*-isocyaniminotriphenylphosphorane **4** and 3-phenyl-2-propynoic acid **1**. Its ease of work-up, high yields and fairly mild reaction conditions make it a useful addition to modern synthetic methodologies.

REFERENCES

1. Zhu, J.; Bienayme, H. *Multicomponent Reactions*; Wiley-VCH: Weinheim, **2005**.
2. (a) Dömling, A. *Chem. Rev.* **2006**, 106, 17-89; (b) Massoudi, A.; Amini, I.; Ramazani, A.; Nasrabadi, F. Z.; Ahmadi, Y. *Bull. Korean Chem. Soc.* **2012**, 33, 39-42; (c) Vessally, E.; Ramazani, A.; Yaaghubi, E. *Monatsh. Chem.* **2011**, 142, 1143-1147; (d) Shoaei, S. M.; Kazemizadeh, A. R.; Ramazani, A. *Chinese J. Struct. Chem.* **2011**, 30, 568-574; (e) Ramazani, A.; Dolatyari, L.; Morsali, A.; Yilmaz, V. T.; Büyükgüngör, O. J. *Iran. Chem. Soc.* **2006**, 3, 367-370.
3. Dömling, A.; Ugi, I. *Angew. Chem. Int. Ed.* **2000,** 39, 3168-3210.
4. Ugi, I.; Werner, B.; Dömling, A. *Molecules*. **2003,** 8, 53-66.
5. Hill J. In: A. R. Katritzky, C. W. Rees, E. F. V. Scriven (Eds.), *Comprehensive Heterocyclic Chemistry II, Vol. 4*; Pergamon: London, **1996**, Chap. 6, 267, and references cited therein.
6. Suwiński, J.; Szczepankiewicz, W. In: A. R. Katritzky, C. A. Ramsden, E. F. V. Scriven, R. J. K. Taylor (Eds.), *Comprehensive Heterocyclic Chemistry III*, Vol. 5; Elsevier Science: Oxford, **2008**, Chap. 6, 396, and references cited therein.
7. Ramazani, A.; Ahmadi, Y.; Tarasi, R. *Heteroat. Chem.* **2011,** 1, 79-84.
8. Molina, P.; Vilaplana, M. J. *Synthesis* **1994**, 1197-1218.
9. Palacios, F.; Aparicio, D.; Rubiales, G.*;* Alonso, C.; de los Santos, J. M. *Curr. Org. Chem.* **2009,** 13, 808-826.
10. Ramazani, A.; Ahmadi, Y.; Rouhani, M.; Shajari, N.; Souldozi, A. *Heteroat. Chem*. **2010,** 21, 368-372.
11. Ramazani, A.; Shajari, N.; Mahyari, A.; Ahmadi, Y. *Mol. Divers* **2011,** 15, 521-527.
12. Stolzenberg, H.; Weinberger, B.; Fehlhammer, W. P.; Pühlhofer, F. G.; Weiss, R. *Eur. J. Inorg. Chem*. **2005,** 21, 4263-4271.
13. Chiu, T. W.; Liu, Y. H.; Chi, K. M.; Wen, Y. S.; Lu, K. L. *Inorg Chem.* **2005,** 44, 6425-6430.
14. Ramazani, A.; Ahmadi, Y.; Mashhadi Malekzadeh, A.; Rezaei, A. *Heteroat. Chem.* **2010,** 22, 692-698.
15. Ramazani, A.; Salmanpour, S.; Souldozi, A. *Phosphorus, Sulfur, Silicon Relat. Elem*. **2010,** 185, 97-102.
16. Ramazani, A.; Bodaghi, A. *Tetrahedron Lett.* **2000,** 41, 567-568.

17. Pakravan, P.; Ramazani, A.; Noshiranzadeh, N.; Sedrpoushan, A. *Phosphorus, Sulfur, Silicon Relat. Elem*. **2007,** 182, 545-549.
18. Ramazani, A.; Rahimifard, M.; Souldozi, A. *Phosphorus, Sulfur, Silicon Relat. Elem*. **2007,** 182, 1-5.
19. Ramazani, A.; Rahimifard, M.; Noshiranzadeh, N.; Souldozi, A. *Phosphorus, Sulfur, Silicon Relat. Elem*. **2007,** 182, 413-417.
20. Ramazani, A.; Rouhani, M.; Rezaei, A.; Shajari, N.; Souldozi, A. *Helv. Chim. Acta* **2011,** 94, 282-288.
21. Ghomi, J. S.; Salimi, F.; Ahmadi, Y.; Ramazani, A.; Nasrabadi, F. Z. *Chemija.* **2012,** 23, 43-47.
22. Ramazani, A.; Amini, I.; Massoudi, A. *Phosphorus, Sulfur, Silicon Relat. Elem.* 2006, 181, 2225-2229.
23. Souldozi, A.; Ramazani, A.; Bouslimani, N.; Welter, R. *Tetrahedron Lett.* **2007,** 48, 2617-2620.
24. Souldozi, A.; Ramazani, A. *Tetrahedron Lett*. **2007,** 48, 1549-1551.
25. Souldozi, A.; Ramazani, A. *Phosphorus, Sulfur, Silicon Relat. Elem*. **2009,** 184, 3191-3198.
26. Ahankar, H.; Ramazani, A.; Amini, I.; Ahmadi, Y.; Souldozi, A. *Heteroat. Chem.* **2011,** 22, 612-616.
27. (a) Ramazani, A.; Souldozi, A., *Arkivoc* **2008,** xvi, 235-242; (b) Ramazani, A.; Nasrabadi, F. Z.; Ahmadi, Y. *Helv. Chim. Acta* **2011,** 94, 1024-1029; (c) Ramazani, A.; Ahmadi, Y.; Nasrabadi, F. Z. *Z. Naturforsch.* **2011,** 66b, 184-190; (d) Ramazani, A.; Ahmadi, Y.; Mahyari, A. *Synth. Commun.* **2011,** 41, 2273-2282; (e) Ramazani, A.; Nasrabadi, F. Z.; Mashhadi Malekzadeh, A.; Ahmadi, Y. *Monatsh. Chem.* **2011,** 142, 625-630; (f) Nasrabadi, F. Z.; Ramazani, A.; Ahmadi, Y. *Mol. Divers.* **2011,** 15, 791-798; (g) Shajari, N.; Ramazani, A.; Ahmadi, Y. *Bull. Chem. Soc. Ethiop.* **2011,** 25, 1-6; (h) Ramazani, A.; Nasrabadi, F. Z.; Karimi, Z.; Rouhani, M. *Bull. Korean Chem. Soc.* **2011,** 32, 2700-2704.
28. Ramazani, A.; Farshadi, A.; Mahyari, A.; Ślepokura, K.; Lis, T.; Rouhani, M. *J. Chem. Crystallogr.* **2011,** 41, 1376-1385.
29. Ramazani, A.; Rezaei, A. *Org. Lett.* **2010,** 12, 2852-2855.
30. Souldozi, A.; Ślepokura, K.; Lis, T.; Ramazani, A. *Z. Naturforsch.* **2007,** 62b, 835-840.
31. Ramazani, A.; Kazemizadeh, A. R.; Marandi, F. *Phosphorus, Sulfur Silicon Relat. Elem.* **2005,** 180, 1541-1544.
32. Ramazani, A.; Noshiranzadeh, N.; Ghamkhari, A.; Slepokura, K.; Lis, T. *Helv. Chim. Acta* **2008,** 91, 2252-2261.
33. Ramazani, A.; Rezaei, A.; Mahyari, A. T.; Rouhani, M.; Khoobi, M. *Helv. Chim. Acta* **2010,** 93, 2033-2036.
34. (a) Ramazani, A.; Mahyari, A. *Helv. Chim. Acta* **2010**, 93, 2203-2209; (b) Ramazani, A.; Nasrabadi, F. Z.; Abdian, B.; Rouhani, M. *Bull. Korean Chem. Soc.* **2012**, 33, 453-458; (c) Khoobi, M.; Foroumadi, A.; Emami, S.; Safavi, M.; Dehghan, G.; Alizadeh, B. H.; Ramazani, A.; Ardestani, S. K.; Shafiee, A. *Chem Biol Drug Des* **2011**; 78, 580-586; (d) Yavari, I.; Esmaili, A. A.; Ramazani, A.; Bolbol-Amiri, A. R. *Monatsh. Chem.* **1997**, 128, 927-931; (e) Kazemizadeh, A. R.; Ramazani, A. *Curr. Org. Chem.* **2012**, 16, 418-450; (f) Ramazani, A.; Kazemizadeh, A. R.; *Curr. Org. Chem.* **2011**, 15, 3986-4020; (h) Ramazani, A.; Noshiranzadeh, N.; Eskandari, I.; Morsali, A. *JDUBS* **2009**, 2, 1-8; (i) Noshiranzadeh, N.; Ramazani, A.; Morsali, A.; Hunter, A. D.; Zeller, M. *Inorg. Chem. Commun.* **2007**, 10, 738-742; (j) Noshiranzadeh, N.; Ramazani, A.; Morsali, A.; Hunter, A. D.; Zeller, M. *Inorg. Chim. Acta* **2007**, 360, 3603-3609; (k) Ganjali1, M. R.; Aghabalazadeh, S.; Khoobi, M.; Ramazani, A.; Foroumadi, A.; Shafiee, A.; Norouzi, P.; *Int. J. Electrochem. Sci.* **2011**, 6, 52-62; (l) Khoobi, M.; Ramazani, A.; Foroumadi, A. R.; Hamadi, H.; Hojjati, Z.; Shafiee, A. *J. Iran. Chem. Soc.* **2011**, 8,1036-1042; (m) Yavari, I.; Ramazani, A.; Esmaili, A. A. *J. Chem. Research (S)* **1997**, 208-209; (n) Yavari, I.; Ramazani, A. *J. Chem. Res. (S)* **1996**, 382-383; (o) Yavari, I.; Ramazani, A.; Yahya-Zadeh, A. *Synth. Commun.* **1996**, 26, 4495-4499; (p) Morsali, A.; Ramazani, A.; J. *Coord. Chem.* **2005**, 58, 751-758; (q) Ramazani, A.; Dolatyari, L.; Morsali, A.; Kassaee, M. Z. *J. Coord. Chem.* **2009**, 62, 1784-1790; (r) Ahankar, H.; Taheri, S.; Morsali, A.; Ramazai, A.; Zhu, L-G. *J. Coord. Chem.* **2006**, 59,

2039-2045; (s) Morsali, A.; Mahjoub, A. R.; Ramazai, A. *J. Coord. Chem.* **2004**, 57, 347-352; (t) Morsali, A.; Ramazai, A.; Mahjoub, A. R.; *J. Coord. Chem.* **2003**, 56, 1555-1566; (u) Ghomi, J. S.; Salimi, F.; Ramazani, A.; Nasrabadi, F. Z.; Ahmadi, Y. *J. Sulfur Chem.* **2012**, 33, 87-92; (v) Zareai, Z.; Khoobi, M.; Ramazani, A.; Foroumadi, A.; Souldozi, A.; Slepokura, K.; Lis, T.; Shafiee, A. *Tetrahedron* **2012**, 68, 6721-6726.

35. (a) Ramazani, A.; Yousefi, L.; Ahmadi, E.; Souldozi, A. *Phosphorus, Sulfur Silicon Relat. Elem.* **2004,** 179, 1459-1464; (b) Noshiranzadeh, N.; Ramazani, A.; Tofangchi Mahyari, A.; Ślepokura, K.; Lis, T. *Z. Naturforsch.* **2008,** 63b, 65-70; (c) Tofangchi Mahyari, A.; Shajari, N.; Kazemizadeh, A. R.; Ślepokura, K.; Lis, T.; Ramazani, A. Z. *Naturforsch.* **2007,** 62b, 829-834; (d) Kazemizadeh, A. R.; Ramazani, A. *J. Braz. Chem. Soc.* **2009,** 20, 309-312; (e) Noshiranzadeh, N.; Ramazani, A. *Synth. Commun.* **2007,** 37, 3181-3189; (f) Ramazani, A.; Kardan, M.; Noshiranzadeh, N. *Synth. Commun.* **2008,** 38, 383-390; (g) Noshiranzadeh, N.; Ramazani, A.; Ślepokura, K.; Lis, T. *Synth. Commun.* **2008,** 38, 1560-1568; (h) Ramazani, A.; Noshiranzadeh, N. *Synth. Commun.* **2009,** 39, 1204-1214; (i) Ramazani, A.; Shajari, N.; Tofangchi Mahyari, A.; Khoobi, M.; Ahmadi, Y.; Souldozi, A. *Phosphorus, Sulfur, Silicon Relat. Elem.* **2010,** 185, 2496-2502; (j) Ramazani, A.; Souldozi, A. *Phosphorus, Sulfur, Silicon Relat. Elem.* **2009,** 184, 2344-2350; (k) Souldozi, A.; Ramazani, A.; Noshiranzadeh, N. *Phosphorus, Sulfur Silicon Relat. Elem.* **2006,** 181, 587-589; (l) Souldozi, A.; Ramazani, A.; Noshiranzadeh, N. *Phosphorus, Sulfur Silicon Relat. Elem.* **2006,** 181, 1271-1275; (m) Ramazani, A.; Amini, I.; Massoudi, A. *Phosphorus, Sulfur Silicon Relat. Elem.* **2006,** 181, 2373-2376; (n) Morsali, A.; Ramazani, A. Z *Anorg. Allg. Chem.* **2005,** 631, 1759-1760; (o) Morsali, A.; Ramazani, A. *J. Coord. Chem.* **2005,** 58, 751-758; (v) Morsali, A.; Mahjoub, A. R.; Ramazani, A. *J. Coord. Chem.* **2004,** 57, 347-352; (p) Morsali, A.; Ramazani, A.; Mahjoub, A. R.; Soudi, A. A. *Z. Anorg. Allg. Chem.* **2003,** 629, 2058-2061; (q) Ramazani, A.; Souldozi, A. *Phosphorus, Sulfur Silicon Relat. Elem.* **2003,** 178, 2189-2192; (r) Ramazani, A.; Souldozi, A. *Phosphorus, Sulfur Silicon Relat. Elem.* **2003,** 178, 1329-1332; (s) Ramazani, A.; Souldozi, A. *Phosphorus, Sulfur Silicon Relat. Elem.* **2003,** 178, 1325-1328; (t) Ramazani, A.; Souldozi, A. *Phosphorus, Sulfur Silicon Relat. Elem.* **2003,** 178, 2663-2666; (u) Ramazani, A.; Rahimifard, M. *Phosphorus, Sulfur Silicon Relat. Elem.* **2006,** 181, 2675-2678; (v) Ramazani, A.; Mahyari, A. *Helv. Chim. Acta* **2010,** 93, 2203-2209; (w) Shajari, N.; Ramazani, A. *Phosphorus, Sulfur, Silicon Relat. Elem.* **2010,** 185, 1850-1857; (x) Kazemizadeh, A. R.; Ramazani, A. *Arkivoc* **2008,** xv, 159-165; (y) Heshmati-Gonbari, M.; Ramazani, A.; Souldozi, A. *Phosphorus, Sulfur, Silicon Relat. Elem.* **2009,** 184, 309-314; (z) Ramazani, A.; Bodaghi, A. *Phosphorus, Sulfur, Silicon Relat. Elem.* **2004,** 179, 1615-1620.