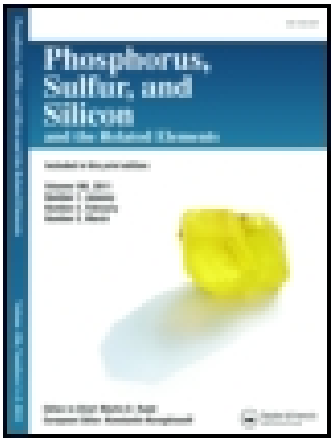


Phosphorus, Sulfur, and Silicon and the Related Elements

Publication details, including instructions for authors and subscription information:
http://www.tandfonline.com/loi/gpss20

Ultrasound-Promoted Three-Component Reaction of N-Isocyaniminotriphenyl-Phosphorane, (E)-Cinnamic Acids, and Biacetyl

Ali Ramazani[a], Morteza Rouhani[b], Fatemeh Zeinali Nasrabadi[c] & Farideh Gouranlou[d]

[a] Department of Chemistry, Zanjan Branch, Islamic Azad University, Zanjan, Iran

[b] Department of Chemistry, University of Zanjan, Zanjan, Iran

[c] Department of Chemistry, Payame Noor University, Tehran, Iran

[d] Science and Biotechnology Research Center, Malek Ashtar University of Technology, Tehran, Iran

Accepted author version posted online: 18 Jun 2014.Published online: 02 Dec 2014.

To cite this article: Ali Ramazani, Morteza Rouhani, Fatemeh Zeinali Nasrabadi & Farideh Gouranlou (2014): Ultrasound-Promoted Three-Component Reaction of N-Isocyaniminotriphenyl-Phosphorane, (E)-Cinnamic Acids, and Biacetyl, Phosphorus, Sulfur, and Silicon and the Related Elements, DOI: 10.1080/10426507.2014.909428

To link to this article: http://dx.doi.org/10.1080/10426507.2014.909428

Phosphorus, Sulfur, and Silicon, 189:1–9, 2014

ISSN: 1042-6507 print / 1563-5325 online
DOI: 10.1080/10426507.2014.909428

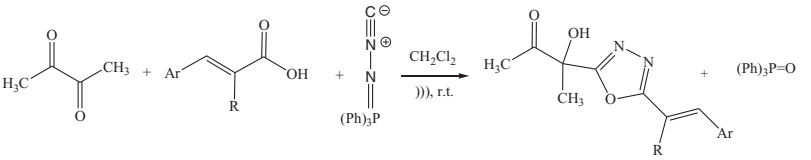
Taylor & Francis
Taylor & Francis Group

ULTRASOUND-PROMOTED THREE-COMPONENT REACTION OF *N*-ISOCYANIMINOTRIPHENYL-PHOSPHORANE, (*E*)-CINNAMIC ACIDS, AND BIACETYL

Ali Ramazani,[1] Morteza Rouhani,[2] Fatemeh Zeinali Nasrabadi,[3] and Farideh Gouranlou[4]

[1]*Department of Chemistry, Zanjan Branch, Islamic Azad University, Zanjan, Iran*
[2]*Department of Chemistry, University of Zanjan, Zanjan, Iran*
[3]*Department of Chemistry, Payame Noor University, Tehran, Iran*
[4]*Science and Biotechnology Research Center, Malek Ashtar University of Technology, Tehran, Iran*

GRAPHICAL ABSTRACT



Abstract *Fully substituted 1,3,4-oxadiazole derivatives were obtained in a one-pot three-component reaction of N-isocyaniminotriphenylphosphorane, biacetyl, and (E)-cinnamic acids in dichloromethane under ultrasound irradiation. This rapid method produced the products in short reaction times (16–27 min) and excellent yields (91–97%).*

Keywords 1,3,4-oxadiazole; *N*-isocyaniminotriphenylphosphorane; biacetyl; (*E*)-cinnamic acid; ultrasound irradiation; aza-Wittig reaction

INTRODUCTION

Throughout the past decade, isocyanide-based multicomponent reactions (IMCR) earned considerable concern within the scientific community as an efficient, convenient, time-saving, and atom-economical approach to rapidly generate chemical diversity. IMCRs are easily performed using readily available starting materials and bear a diversity range of functional groups. Variations and following transformations give approach to a clearly large number of unique structures that would otherwise demand lengthy preparations.[1,2]

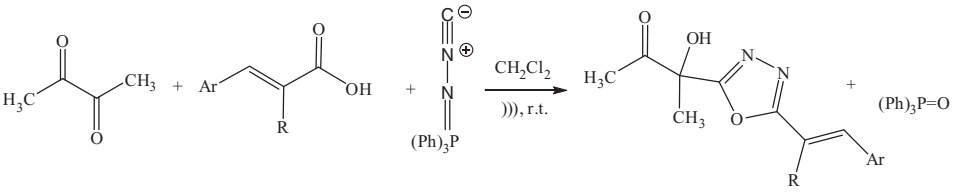
In recent times, the intramolecular version of the aza-Wittig–type reaction has attracted much attention because it has showed high potential for the synthesis of a broad

Received 30 January 2014; accepted 25 March 2014.
Address correspondence to Ali Ramazani, Department of Chemistry, Zanjan Branch, Islamic Azad University, P O Box 49195-467, Zanjan, Iran. E-mail: aliramazani@gmail.com

diversity of nitrogen heterocycles, which can be ascribed, in good measure, to the rapid development in the preparation of functionalized iminophosphoranes. Existence of the nucleophilicity at the nitrogen is a factor of necessary mechanistic significance 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[3,4]. In recent years, we have explored a synthetic ability of *N*-isocyaniminotriphenylphosphorane in the synthesis of various organic compounds[5–13]. It looks that the *N*-isocyaniminotriphenylphosphorane has excellent synthetic potential because it provides a reaction system in which the iminophosphorane group can react with a reagent having a carbonyl functionality.

In recent years there has been important investigation on different classes of oxadiazoles. Especially, compounds including 1,3,4-oxadiazole nucleus have been shown to own a wide range of pharmacological and therapeutic activities. Different 1,3,4-oxadiazoles have been reported to have a wide spectrum of biological activity, involving antimicrobial[14–16], antifungal[17,18], anti-inflammatory[19], and hypotensive activity[20]. Few credible and functionally simple examples have been reported for the one-pot synthesis of 1,3,4- oxadiazoles, especially from readily available carboxylic acids and acid hydrazides.[21–25]

Ultrasonic-assisted organic synthesis as a green synthetic path is a powerful technique that is being used more and more to accelerate organic reactions[26,27]. While the last three decades, ultrasound-accelerated organic chemical reactions have been increasingly improved by researchers beyond the globe for the synthesis of organic molecules. Ultrasound irradiation offers an optional energy source for organic reactions. Ultrasound-assisted reactions continue by the formation, growth, and collapse of acoustic bubbles in the reaction medium. These clearly help in shortening the time span of reactions and increasing the yield of products. Many homogeneous and heterogeneous organic reactions have been directed efficiently by sonication. A large number of organic reactions can be carried out in higher yields, shorter reaction time, or milder conditions under ultrasound irradiation and considered a processing aid in terms of energy conservation and waste minimization which compared with traditional methods[28–31]. As in continuation of our work on the synthesis of heterocycles[32–35] and in order to enlarge the application of ultrasound irradiation in the synthesis of heterocyclic compounds, we report herein a simple and efficient method for the preparation of fully substituted 1,3,4-oxadiazole derivatives under ultrasonic irradiation (Scheme 1).



Scheme 1

Table 1 Effect of different solvents for synthesis of **4a** under ultrasound irradiation at room temperature

Entry[a]	Solvent	Time (min)	Yield (%)[b]
1	DMF	30	34
2	THF	25	52
3	CH_3CN	20	72
4	1,4-dioxane	30	48
5	EtOH	30	54
6	CH_2Cl_2	16	97

[a]Reaction conditions: 1 mmol 4-methylcinnamic acid, 1 mmol *N*-isocyaniminotriphenylphosphorane, and 1 mmol biacetyl in 15 mL solvent.
[b]Isolated yield.

RESULTS AND DISCUSSION

In our initial research, 4-methylcinnamic acid was selected as a representative reactant in order to optimize the reaction conditions. We conducted the one-pot three-component condensation reaction of *N*-isocyaniminotriphenylphosphorane, biacetyl, and 4-methylcinnamic acid in the presence of various solvents. We examined the effect of different solvents such as CH_2Cl_2, DMF, THF, CH_3CN, 1,4-dioxane, and EtOH on a model reaction under ultrasound irradiation at room temperature. The results are listed in Table 1. The reaction using CH_2Cl_2 as solvent gave the best result (Table 1, entry 6). The reaction failed to give poor yields in DMF, THF, CH_3CN, 1,4-dioxane, and EtOH (Table 1, entries 1–5).

To demonstrate the effect of ultrasound, the synthesis of 4a as a model was investigated under stirring and ultrasound conditions. The results are shown in Table 2. Under stirring conditions, the reaction can be completed within 12 h to give 4a in 92% yield (Table 2, entry 1). Whereas under ultrasonic irradiation in 100 W, 4a was obtained in 97% yield within 16 min (Table 2, entry 3). We also observed the effect of power of the ultrasound irradiation on the reaction. The yield with 100 W irradiation for 16 min (Entry 3) was better than that with 150 W irradiation for 16 min (Entry 4). The reason may be that the lower power irradiation produces the better cavitations[36]. As shown in Tables 1 and 2, we selected the CH_2Cl_2 as solvent under ultrasound irradiation conditions with 100 W power for the one-pot reaction of *N*-isocyaniminotriphenylphosphorane, biacetyl, and (*E*)-cinnamic acids to give corresponding 1,3,4-oxadiazole derivatives at room temperature.

Thus, we have carried out a series of experiments and the results are summarized in Table 3. In order to show the advantages of the present experimental conditions, in Table 3

Table 2 Comparison of the yields for the synthesis of **4a** as a model

Entry	Condition	Time (min)	Yield (%)[a]
1	Stirring in CH_2Cl_2 at room temperature	12 h	92
2	Ultrasonic in CH_2Cl_2 at room temperature (50 W)	16	62
3	Ultrasonic in CH_2Cl_2 at room temperature (100 W)	16	97
4	Ultrasonic in CH_2Cl_2 at room temperature (150 W)	16	79

[a]Isolated yield.

Table 3 The synthesis of fully substituted 1,3,4-oxadiazole derivatives **(4a–g)** under ultrasound irradiation and stirring condition at room temperature

		US		Conventional stirring	
Product[a]	R, Ar	*t* (min)	Yield (%)[b]	*t* (h)	Yield (%)[b]
4a	H, 4-MeC_6H_4	16	97	12	92
4b	H, 4-F-C_6H_4	18	96	12	90
4c	H, 4-Cl-C_6H_4	20	94	12	88
4d	H, C_6H_5	27	91	12	85
4e	Me, C_6H_5	23	92	12	85
4f	H, 3-ClC_6H_4	19	94	12	86
4g	H, 3-MeOC_6H_4	22	93	12	87

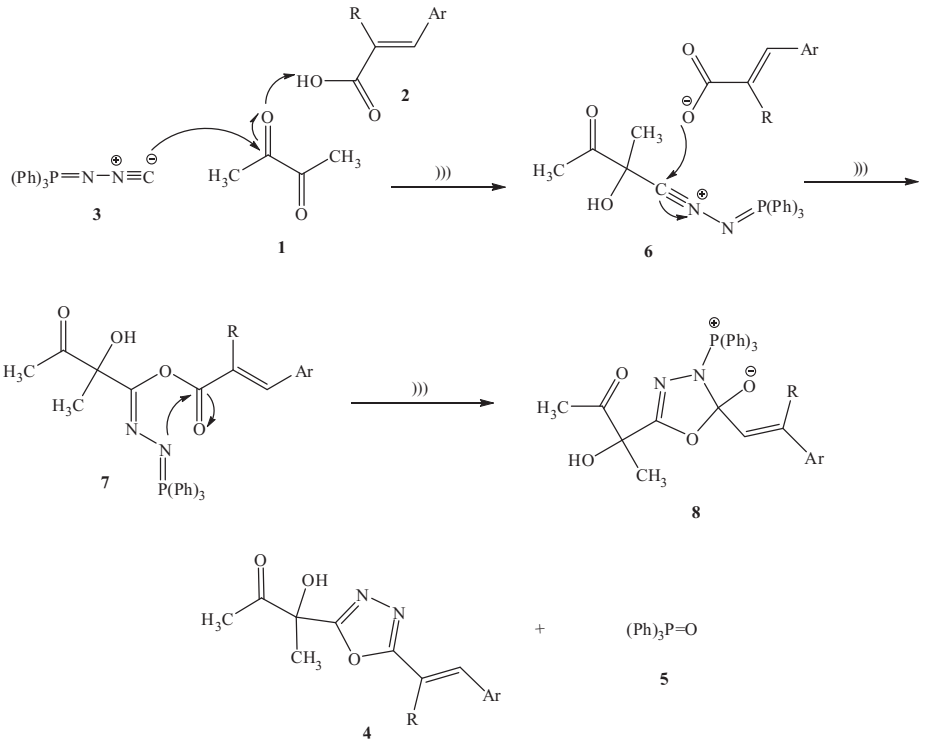
[a]Reaction conditions: 1 mmol (*E*)-cinnamic acid, 1 mmol *N*-isocyaniminotriphenylphosphorane, and 1 mmol biacetyl in CH_2Cl_2.
[b]Isolated yield.

we have also collected the results under conventional conditions by stirring in CH_2Cl_2 as well as under ultrasound irradiation. As shown in Table 3, the condensation of a variety of substituted (*E*)-cinnamic acids, *N*-isocyaniminotriphenylphosphorane, and biacetyl in CH_2Cl_2 proceeds smoothly to afford the respective products in excellent yields (91–97%) within 16–27 min.

The method to obtain fully substituted 1,3,4-oxadiazole derivatives (4a–g) under ultrasonic irradiation offers several significant advantages including faster reaction rates, higher yields, higher purity, and the smoothly reaction proceeds at room temperature. In comparison with routine methods, the main benefit of ultrasound application is the significant decline in the reaction times. Thus, while conventional method using stirring in CH_2Cl_2 requires 12 h, ultrasonic irradiation affords the respective products in only 16–27 min (see Table 3).

These results encourage that the energy provided by ultrasound accelerates these reactions. The distinction in yields and reaction times may be a result of the particular effects of ultrasound. The effect observed on the reaction is due to cavitation, a physical process that creates, enlarges, and collapses gaseous and vaporous cavities in an irradiated liquid, therefore improving the mass transfer and permitting chemical reactions to happen. The creation of the so-called hot spots in the reaction mixture produces great local temperatures and high pressures created inside the cavitation bubble and its interfaces when it collapses[37]. Under these situations, very reactive chemical species are produced, with a very short lifetime, giving rise to the 1,3,4-oxadiazole derivatives (**4a–g**) in shorter times, thus facilitating the deprotonation step that is critical in this type of multi-component reactions. Moreover, compared with traditional methods (see Table 3), this technique is more efficient and less time consuming.

The reaction consists in several successive steps (Scheme 2). On the basis of the chemistry of isocyanides[38], it is reasonable to assume that the first step may involve nucleophilic addition of the *N*-isocyaniminotriphenylphosphorane **3** to biacetyl **1**, which facilitates by its protonation with the acid **2**, leading to nitrilium intermediate **6**. This intermediate may be attacked by conjugate base of the acid **2** to form 1:1:1 adduct **7**. This adduct may undergo intramolecular *aza*-Wittig reaction[39–41] of iminophosphorane moiety with the ester carbonyl to afford the isolated sterically congested 1,3,4-oxadiazole derivatives **4** by removal of triphenylphosphine oxide **5** from intermediate **8**.



Scheme 2

As it is known, the nucleophilic addition of the *N*-isocyaniminotriphenylphosphorane to biacetyl has negative activation volume owing to the condensation of the molecules into a reactive intermediate. In this regard, it is well-known that reactions with negative activation volumes are accelerated with pressure[42] On the other hand, ultrasound irradiation[37,43] as well as solvophobic interactions of ionic liquids generate a microscopic internal pressure in the solvent cavity[44]. Our reaction, owning to the ultrasonic cavitations generates a microscopic internal high pressure and high temperature. Accordingly, it is reasonable to assume that these effects should accelerate this type of one-pot three-component reaction.

As shown in Table 3, the electronic effect and the nature of the substituent on the (*E*)-cinnamic acids aromatic ring did not show any remarkable effect in terms of yields, under the same reaction conditions. Obviously, the presence of different groups in (*E*)-cinnamic acids **2** do not alter significantly the yields obtained. To the best of our knowledge, this new procedure provides the first example of an efficient and ultrasound-promoted approach for the synthesis of fully stituted 1,3,4-oxadiazole derivatives. This method is the most simple and convenient and would be applicable for the synthesis of different types of 1,3,4-oxadiazoles.

CONCLUSION

In this work, we have developed a mild, highly efficient, and improved protocol for the preparation of a series of fully substituted 1,3,4-oxadiazoles. Our sonochemical method

offers several advantages over existing methods, including improved yields, cleaner reactions, simple work-up, and short-reaction times, which makes it a useful and environmentally attractive strategy for the synthesis of 1,3,4-oxadiazole derivatives, compounds with promising bioactivity.

EXPERIMENTAL

General Considerations

All reagents were obtained from Merck (Germany) and Fluka (Switzerland) and used without further purification. Infrared spectra were recorded on a Jasco 6300 FTIR spectrometer. ^{1}H and ^{13}C NMR spectra of $CDCl_3$ solutions were obtained with a BRUKER DRX-250 AVANCE spectrometer at 250.0 and 62.5 MHz, respectively using tetramethylsilane (TMS) as the internal standard. Elemental analysis was performed with 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. Melting points were measured on an Electrothermal 9100 apparatus and are uncorrected. Sonication was performed in a Bandelin SONOPULS ultrasonic homogenizers (made in Germany) with 20 kHz processing frequency, a nominal power 250 W, uniform sonic waves. Preparative layer chromatography (PLC) plates were prepared from Merck silica gel (F_{254}) powder. *N*-Isocyaniminotriphenylphosphorane **3** was prepared on the basis of reported procedures.[4]

Synthesis of 1,3,4-Oxadiazoles 4a–g by Conventional Method

A mixture of *N*-isocyaniminotriphenylphosphorane (1.0 mmol; 0.300 g), biacetyl (1.0 mmol; 0.10 mL), and (*E*)-cinnamic acid (1.0 mmol) in CH_2Cl_2 (5 mL) was stirred at room temperature for 12 h. The solvent was removed under reduced pressure, and the viscous residue was purified by PLC [silica gel (F_{254}) powder; petroleum ether/ethyl acetate 4:1].

Synthesis of 1,3,4-Oxadiazoles 4a–g by Ultrasound Irradiation

In a 25 mL beaker, *N*-isocyaniminotriphenylphosphorane (1.0 mmol; 0.300 g), biacetyl (1.0 mmol; 0.10 mL), and (*E*)-cinnamic acid (1.0 mmol) were mixed with CH_2Cl_2 (15 mL). The reaction mixtures were then sonicated by an ultrasonic probe with a power of 100 W at room temperature. The complete consumption of reagents occurred after 16–27 min, as monitored by TLC. The solvent was removed, and the viscous residue was purified by PLC [silica gel (F_{254}) powder; petroleum ether/ethyl acetate 4:1].

SPECTRAL DATA OF PRODUCTS

3-Hydroxy-3-{5-[(E)-2-(4-Methylphenyl)-1-Ethenyl]-1,3,4-Oxadiazol-2-yl}-2-Butanone (4a)

White powder (291 mg, yield 97%), m.p 125–127°C, ^{1}H NMR ($CDCl_3$, 250 MHz): δ_H (ppm) 1.92, 2.35, 2.38 (s, 9H, $3CH_3$), 4.70 (s, 1H, OH), 6.95 (d, $^3J_{HH}$ = 16.5 Hz, =CH), 7.21 (d, 2H, $^3J_{HH}$ = 7.5 Hz, $CH_{arom,}$), 7.43 (d, 2H, $^3J_{HH}$ = 7.5 Hz, $CH_{arom,}$), 7.53 (d, $^3J_{HH}$ = 16.5 Hz, =CH). ^{13}C NMR ($CDCl_3$, 62.5 MHz): δ_C (ppm) 21.47, 23.24, 23.75 ($3CH_3$), 75.72 (C−OH), 108.20, 140.20, (2CH=), 127.58, 129.77 (4CH, arom),

131.71140.69 (2C, arom), 164.67, 165.56 (2C=N), 204.65 (C=O). IR (Neat) (υ_{max}, cm^{-1}): 3298, 2998, 2918, 1723, 1644, 1532, 1363, 1180, 833. Ms *m/z* (%) 272 (M^+, 20), 229 (100), 187 (72), 160 (32), 143 (68), 115 (52), 91 (24), 43 (96). Anal. Calcd for $C_{15}H_{16}N_2O_3$ (272.12): C, 66.16; H, 5.92; N, 10.29. Found: C, 66.24; H, 5.97; N, 10.24.

3-{5-[(E)-2-(4-Fluorophenyl)-1-Ethenyl]-1,3,4-Oxadiazol-2-yl}-3-Hydroxy-2-Butanone (4b)

White powder (288 mg, yield 96%), m.p 84–86°C, ^{1}H NMR ($CDCl_3$, 250 MHz): δ_H (ppm) 1.87, 2.35 (s, 6H, $2CH_3$), 4.70 (s, 1H, OH), 6.92 (d, $^3J_{HH} = 16.5$ Hz, =CH), 7.01–7.55 (m, 5H, CH_{arom} and =CH). ^{13}C NMR ($CDCl_3$, 62.5 MHz): δ_C (ppm) 23.25, 23.74, ($2CH_3$), 75.74 (C−OH), 109.02, 138.89 (2CH=), 116.22 (d, $^2J_{CF} = 28.3$ Hz, $2CH_{arom}$), 129.44 (d, $^3J_{CF} = 8.2$ Hz, $2CH_{arom}$), 130.70 (C, arom), 162.50 (d, $^1J_{CF} = 440.3$ Hz, C_{arom}), 164.85, 165.22 (2C=N), 204.60 (C=O). IR (Neat) (υ_{max}, cm^{-1}): 3372, 2923, 1731, 1670, 1529, 1505, 1163, 818. Ms *m/z* (%) 276 (M^+, 12), 234 (100), 191 (56), 164 (32), 147 (60), 121 (20), 101 (24), 43 (68). Anal. Calcd for $C_{14}H_{13}FN_2O_3$ (276.09): C, 60.87; H, 4.74; N, 10.14. Found: C, 60.81; H, 4.80; N, 10.08.

3-{5-[(E)-2-(4-Chlorophenyl)-1-Ethenyl]-1,3,4-Oxadiazol-2-yl}-3-Hydroxy-2-Butanone (4c)

White powder (282 mg, yield 94%), m.p 148–150°C, ^{1}H NMR ($CDCl_3$, 250 MHz): δ_H (ppm) 1.92, 2.35, (s, 6H, $2CH_3$), 4.67 (s, 1H, OH), 6.97 (d, $^3J_{HH} = 16.8$ Hz, =CH), 7.25 -7.54 (m, 5H, CH_{arom} and =CH). ^{13}C NMR ($CDCl_3$, 62.5 MHz): δ_C (ppm) 23.26, 23.72, ($2CH_3$), 75.72 (C−OH), 109.84, 138.76 (2CH=), 128.73, 129.34 (4CH, arom), 132.90, 136.15 (2C, arom), 164.85, 165.12 (2C=N), 204.51 (C=O). IR (Neat) (υ_{max}, cm^{-1}): 3363, 2921, 1726, 1648, 1523, 1406, 1152, 815. Anal. Calcd for $C_{14}H_{13}ClN_2O_3$ (292.06): C, 57.44; H, 4.48; N, 9.57. Found: C, 57.39; H, 4.53; N, 9.52.

3-Hydroxy-3-{5-[(E)-2-Phenyl-1-Ethenyl]-1,3,4-Oxadiazol-2-yl}-2-Butanone (4d)

White powder (273 mg, yield 91%), m.p 79–81°C, ^{1}H NMR ($CDCl_3$, 250 MHz): δ_H (ppm) 1.93, 2.36 (s, 6H, $2CH_3$), 4.69 (s, 1H, OH), 7.01 (d, $^3J_{HH} = 16.5$ Hz, =CH), 7.40–7.60 (m, 6H, CH_{arom} and =CH). ^{13}C NMR ($CDCl_3$, 62.5 MHz): δ_C (ppm) 23.26, 23.73 ($2CH_3$), 75.71 (C−OH), 109.28, 140.22 (2CH=), 127.60, 129.05, 130.24 (5CH), 134.41 (C, arom), 164.95, 165.35 (2C=N), 202.6 (C=O). IR (Neat) (υ_{max}, cm^{-1}): 3311, 2923, 1726, 1649, 1528, 1449, 1150, 759, 693. Anal. Calcd for $C_{14}H_{14}N_2O_3$ (258.10): C, 65.11; H, 5.46; N, 10.85. Found: C, 65.05; H, 5.40; N, 10.91.

3-Hydroxy-3-{5-[(E)-1-Methyl-2-Phenyl-1-Ethenyl]-1,3,4-Oxadiazol-2-yl}-2-Butanone (4e)

Yellow viscous oil (276 mg, yield 92%), ^{1}H NMR ($CDCl_3$, 250 MHz): δ_H (ppm) 1.93, 2.36, 2.39 (s, 9H, $3CH_3$), 4.66 (s, 1H, OH), 7.36–7.51 (m, 6H, CH_{arom} and =CH). ^{13}C NMR ($CDCl_3$, 62.5 MHz): δ_C (ppm) 14.56, 23.25, 23.75 ($3CH_3$), 75.75 (C−OH), 128.52, 129.59, 135.25, 135.38 (4CH, arom), 120.90 (C, arom), 167.83, 170.00 (2C=N), 204.68 (C=O). IR (Neat) (υ_{max}, cm^{-1}): 3298, 2994, 2926, 1720, 1601, 1526, 1447, 1093, 713,

695. Anal. Calcd for $C_{15}H_{16}N_2O_3$ (272.12): C, 66.16; H, 5.92; N, 10.29. Found: C, 66.24; H, 5.84; N, 10.37.

3-{5-[(E)-2-(3-Chlorophenyl)-1-Ethenyl]-1,3,4-Oxadiazol-2-yl}-3-Hydroxy-2-Butanone (4f)

White powder (282 mg, yield 94%), m.p 62–64°C, ^{1}H NMR ($CDCl_3$, 250 MHz): δ_H (ppm) 1.93, 2.36 (s, 6H, $2CH_3$), 4.69 (s, 1H, OH), 7.01 (d, $^3J_{HH}$ = 16.5 Hz, =CH), 7.36–7.52 (m, 5H, CH_{arom} and =CH). ^{13}C NMR ($CDCl_3$, 62.5 MHz): δ_C (ppm) 23.28, 23.73, ($2CH_3$), 75.72 (C−OH), 110.71135.10 (2CH=), 125.71, 127.41, 130.11, 130.29 (4CH, arom), 136.20, 138.58 (2C, arom), 162.83, 164.95 (2C=N), 204.87 (C=O). IR (Neat) (υ_{max}, cm^{-1}): 3274, 2923, 1728, 1650, 1528, 1426, 1110, 840, 789, 691. Anal. Calcd for $C_{14}H_{13}ClN_2O_3$ (292.06): C, 57.44; H, 4.48; N, 9.57. Found: C, 57.49; H, 4.53; N, 9.52.

3-Hydroxy-3-{5-[(E)-2-(3-Methoxyphenyl)-1-Ethenyl]-1,3,4-Oxadiazol-2-yl}-2-Butanone (4g)

White powder (279 mg, yield 93%), m.p 70–72, ^{1}H NMR ($CDCl_3$, 250 MHz): δ_H (ppm) 1.93, 2.35 (s, 6H, $2CH_3$), 3.83 (s, 3H, OCH_3), 4.73 (s, 1H, OH), 6.91–7.35 (m, 5H, CH_{arom} and =CH), 7.52 (d, $^3J_{HH}$ = 16.5 Hz, =CH). ^{13}C NMR ($CDCl_3$, 62.5 MHz): δ_C (ppm) 23.26, 23.76 ($2CH_3$), 55.31 (s, 3H, OCH_3), 75.75 (C−OH), 109.57, 140.12 (2CH=), 112.54, 116.05, 120.25, 130.04 (4CH), 135.77, 159.98 (2C), 164.87, 165.31 (2C=N), 204.61 (C=O). IR (Neat) (υ_{max}, cm^{-1}): 3236, 3004, 2922, 1730, 1650, 1580, 1466, 1108, 876, 795, 687. Anal. Calcd for $C_{15}H_{16}N_2O_4$ (288.11): C, 62.49; H, 5.59; N, 9.72. Found: C, 62.44; H, 5.64; N, 9.67.

ACKNOWLEDGMENTS

The authors thank Zanjan Islamic Azad University for the support and guidance.

REFERENCES

1. Akritopoulou-Zanze, I. *Curr. Opin. Chem. Biol.* **2008,** 12, 324-331.
2. (a) Domling, A. *Chem. Rev.* **2006,** 106, 17-89. (b) Jida, M.; Soueidan, M.; Willand, N.; Agbossou-Niedercorn, F.; Pelinski, L.; Laconde, G.; Deprez-Poulain, R.; Deprez, B. *Tetrahedron Lett.* **2011,** 52, 1705-1708. (c) Jida, M.; Malaquin, S.; Deprez-Poulain, R.; Laconde, G.; Deprez, B. *Tetrahedron Lett.* **2010,** 51, 5109-5111. (d) Malaquin, S.; Jida, M.; Gesquiere, J. C.; Deprez-Poulain, R.; Deprez, B.; Laconde, G. *Tetrahedron Lett.* **2010,** 51, 2983-2985.
3. Palacios, F.; Aparicio, D.; Rubiales, G.; Alonso, C.; de los Santos, J. M. *Curr. Org. Chem.* **2009,** 13, 810-828.
4. Stolzenberg, H.; Weinberger, B.; Fehlhammer, W. P.; Pühlhofer, F. G.; Weiss, R. *Eur. J. Inorg. Chem.* **2005,** 4263-4271.
5. Souldozi, A.; Ramazani, A. *Tetrahedron Lett.* **2007,** 48, 1549-1551.
6. Ramazani, A.; Rezaei, A. *Org. Lett.* **2010,** 12, 2852-2855.
7. Ramazani, A.; Souldozi, A. *Arkivoc.* **2008,** xvi, 235-242.
8. Souldozi, A.; Slepokura, K.; Lis, T.; Ramazani, A. *Z. Naturforsch.* **2007,** 62b, 835-840.
9. Ramazani, A.; Ahmadi, Y.; Tarasi, R. *Heteroat. Chem.* **2011,** 22, 79-84.
10. Ramazani, A.; Shajari, N.; Mahyari, A.; Ahmadi, Y. *Mol. Divers.* **2011,** 15, 521-527.

11. Ramazani, A.; Ahmadi, Y.; Nasrabadi, F. Z. *Z. Naturforsch.* **2011,** 66b, 184-190.
12. Ramazani, A.; Salmanpour, S.; Souldozi, A. *Phosphorus, Sulfur, Silicon Relat. Elem.* **2010,** 185, 97-102.
13. Ramazani, A.; Shajari, N.; Tofangchi Mahyari, A.; Khoobi, M.; Ahmadi, Y.; Souldozi, A. *Phosphorus, Sulfur, Silicon Relat. Elem.* **2010,** 185, 2496-2502.
14. Holla, B. S.; Gonaslaves, R.; Shenoy, S. *Eur. J. Med. Chem.* **2000,** 35, 267-271.
15. Ramazani, A.; Zeinali Nasrabadi, F.; Abdian, B.; Rouhani, M. *Bull. Korean Chem. Soc.* **2012,** 33, 453-458.
16. Burbuliene, M.; Jakubkiene, V.; Mekuskiene, G.; Udrenaite, E.; Smicius, R.; Vainilavicius, P. *Farmaco* **2004,** 59, 767-774.
17. Şahin, G.; Palaska, E.; Ekizoğlu, M.; Özalp, M. *Farmaco* **2002,** 57, 539-542.
18. Zou, X. J.; Lai, L. H.; Jin, G. Y.; Zhang, Z. X. *J. Agric. Food Chem.* **2002,** 50, 3757-3760.
19. Palaska, E.; Sohin, G.; Kalicen, P.; Darlu, N. T.; Altinok, G. *Farmaco* **2002,** 57, 101-107.
20. Coppo, F. T.; Evans, K. A.; Graybill, T. D. Burton, G. *Tetrahedron Lett*. **2004,** 45, 3257-3260.
21. Tandon, V. K.; Chhor, R. B. *Synth. Commun.* **2001,** 31, 1727-1732.
22. Mashraqui, S. H.; Ghadigaonkar, S. G.; Kenny, R. S. *Synth. Commun.* **2003,** 33, 2541-2545.
23. Bentiss, F.; Lagrenee, M.; Barbry, D. *Synth. Commun.* **2001,** 31, 935-938.
24. Jedlovska, E.; Lesko, J. *Synth. Commun.* 1994, 24, 1879-1885.
25. Wang, Y.; Sauer, D. R.; Djuric, S. W. *Tetrahedron Lett*. **2006,** 47, 105-108.
26. Xu, H.; Liao, W. M.; Li, H. F. *Ultrason. Sonochem.* **2007,** 14, 779-782.
27. Guzen, K. P.; Guarezemini, A. S.; Orfao, A. T. G.; Cella, R.; Pereiraa, C. M. P.; Stefani, H. A. *Tetrahedron Lett.* **2007,** 48, 1845-1848.
28. Li, J. T.; Meng, X. T.; Zhai, X. L. *Ultrason. Sonochem.* **2009,** 16, 590-592.
29. Zeng, H. Y.; Li, H.; Shao, H. W. *Ultrason. Sonochem.* **2009,** 16, 758-762.
30. Xa, M.; Lu, Y. D. *Ultrason. Sonochem.* **2007,** 14, 235-240.
31. Li, J. T.; Liu, X. F. *Ultrason. Sonochem.* **2008,** 15, 330-335.
32. Ramazani, A.; Zeinali Nasrabadi, F.; Karimi, Z.; Rouhani, M. *Bull. Korean Chem. Soc.* **2011,** 32, 2700-2704.
33. Ramazani, A.; Rouhani, M.; Rezaei, A.; Shajari, N.; Souldozi, A. *Helv. Chim. Acta.* **2011,** 94, 282-288.
34. Ramazani, A.; Ahmadi, Y.; Rouhani, M.; Shajari, N.; Souldozi, A. *Heteroatom Chem*. **2010,** 21, 368-372.
35. Ramazani, A.; Zeinali Nasrabadi, F.; Ahmadi, Y. *Helv. Chim. Acta.* **2011,** 94, 1024-1029.
36. Li, J. T.; Lin, Z. P.; Li, T. S. *Ultrason. Sonochem.* **2005,** 12, 349-352.
37. Ruiz, E.; Rodriguez, H.; Coro, J.; Slafran, E.; Suarez, M.; Martinez-Alvarez, R.; Martin, N. *Ultrason. Sonochem.* **2011,** 18, 32-36.
38. Dömling, A.; Ugi, I. *Angew. Chem. Int. Ed. Engl.* **2000,** 39, 3168-3210.
39. Souldozi, A.; Ramazani, A.; Bouslimani, N.; Welter, R. *Tetrahedron Lett.* **2007,** 48, 2617-2620.
40. Souldozi, A.; Ramazani, A. *Phosphorus, Sulfur, Silicon Relat. Elem.* 2009, 184, 3191-3198.
41. Souldozi, A.; Ramazani, A. *Phosphorus, Sulfur, Silicon Relat. Elem.* **2009,** 184, 2344-2350.
42. Shaabani, A.; Rezayan, A. H.; Rahmati, A.; Sharifi, M. *Monatsh Chem*. **2006,** 137, 77-81.
43. Cintas, P.; Luche, J. L. *Green Chem.* **1999,** 1, 115-125.
44. Welton, T. *Chem. Rev.* **1999,** 99, 2071-2084.