Zinc oxide as a new, highly efficient, green, and reusable catalyst for microwave-assisted Michael addition of sulfonamides to α,β-unsaturated esters in ionic liquids

Abdolkarim Zare, Alireza Hasaninejad, Ahmad Reza Moosavi Zare, Abolfath Parhami, Hashem Sharghi, and Ali Khalafi-Nezhad

Abstract: A simple, clean, and efficient procedure for the green synthesis of some *N*-alkyl derivatives of sulfonamides is described. Microwave-assisted Michael addition of sulfonamides to α,β-unsaturated esters, in the presence of catalytic amount of zinc oxide (ZnO) in 1-butyl-3-methylimidazolium bromide ([bmim]Br), affords the title compounds in high yields and short reaction times.

Key words: zinc oxide, green chemistry, microwave, Michael addition, sulfonamide, ionic liquid.

Résumé : On décrit une méthode simple, propre et efficace pour la synthèse verte de quelques dérivés *N*-alkyles des sulfonamides. L'addition de Michael assistée par micro-ondes de sulfonamides sur des esters α,β-insaturés, en présence d'une quantité catalytique d'oxyde de zinc (ZnO) dans le bromure de 1-butyl-3-méthylimidazolium ([bmim]Br) conduit à la formation des produits mentionnés dans le titre, avec des rendements élevés et de courts temps de réaction.

Mots-clés : oxyde de zinc, chimie verte, micro-onde, addition de Michael, sulfonamide, liquide ionique.

[Traduit par la Rédaction]

Introduction

Currently, ionic liquids are the subject of considerable interest as benign reaction media in organic synthesis because of their unique properties, such as non-volatility, non-flammability, recyclability, and ability to dissolve a wide range of materials (1). During the past decade, a variety of ionic liquids have been demonstrated as efficient and practical alternatives to organic solvents for many important organic transformations (1). Catalytic activity has been also reported for these green solvents (2). Together with the substitution of common molecular solvents, non-conventional activation methods, mainly microwave irradiation (MWI), have emerged as powerful techniques to reduce reaction times and to enhance reaction rates (3). As part of our drive to avoid the use of volatile organic solvents in reactions (4), we have initiated a program to explore the use of ionic liquids as efficient reaction media for useful organic transformations at room temperature.

N-Alkyl derivatives of sulfonamides are important because they have various biological activities, including their antidepressant, psychostimulant, analgesic, anti-ulcer, antiemetic, and anti-inflammatory properties (5). These compounds can be prepared via aza-conjugate addition of sulfonamides to α,β-unsaturated compounds (6). Michael reaction of sulfonamides with α,β-unsaturated esters also affords protected β-amino acids. This class of compounds (β-amino acids) are essential components in many bioactive compounds and drugs scaffolds, such as β-peptides (7), imeriamine (hypoglycemic and antiketogenic agent, Fig. 1) (8), vitamin B_3 (Fig. 1) (9), cryptophycin (antitumor) (10), and TAN-1057 A (antibiotic) (11). Indeed, to the best of our knowledge, there are only a few reports of Michael addition of sulfonamides. Reitz et. al have used alumina to carry out this reaction (6). However, in their report, the reaction times are long, and the yields are moderate. Moreover, they applied more reactive α,β-unsaturated ketones.

In aza-conjugate reactions, the nucleophilic nitrogen is usually among the powerful nucleophiles, such as amines (12), which, if used in the reaction, can lead to side products, e.g., amides via nucleophilic attack of amine to carbonyl group of α,β-unsaturated esters (12*a*). Furthermore, 1,2- and 1,4-condensation of a β-amino residue to α,β-unsaturated esters caused polymerization or tar formation (12*a*). Moreover, some procedures often require a large excess of reagents (12*b*). Therefore, in this context, using sulfonamides instead of amines in Michael reaction with

Received 6 March 2007. Accepted 9 May 2007. Published on the NRC Research Press Web site at canjchem.nrc.ca on 12 June 2007.

A. Zare.[1] Department of Chemistry, Payam Noor University of Bushehr, Bushehr 1698, Iran.
A. Hasaninejad.[2] Department of Chemistry, Faculty of Sciences, Persian Gulf University, Bushehr 75169, Iran.
A.R. Moosavi Zare, A. Parhami, H. Sharghi, and A. Khalafi-Nezhad. Department of Chemistry, College of Sciences, Shiraz University, Shiraz 71454, Iran.

[1]Corresponding author (e-mail: abdolkarimzare@yahoo.com).
[2]Corresponding author (e-mail: ahassaninejad@yahoo.com).

 doi:10.1139/V07-050

Scheme 1. Michael addition of benzenesulfonamide to *n*-butyl acrylate.

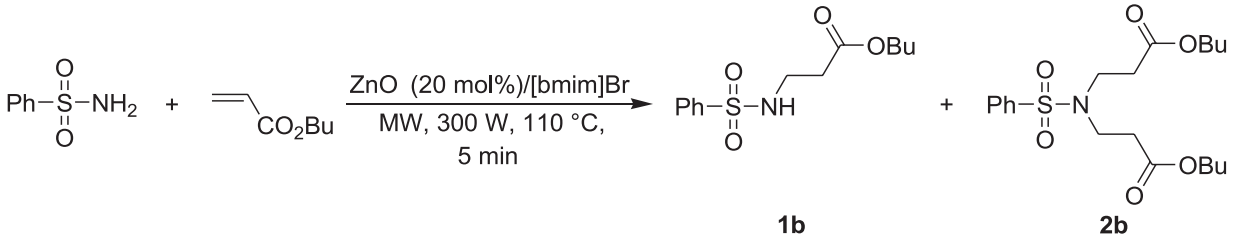
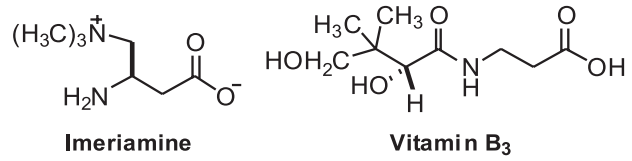


Fig. 1. The structures of imeriamine and vitamin B_3.



α,β-unsaturated esters seems to be more favorable, since lower nucleophilicity of nitrogen leads to less side reactions.

Recently, mineral oxides have proved to be useful to chemists both in the laboratory and in the industry because of the good activation of adsorbed compounds, reaction rate enhancement, selectivity, easier workup, recyclability of the supports, and the eco-friendly reaction conditions (13, 14). Zinc oxide (ZnO) is certainly one of the most interesting of these oxides because it has surface properties that can accomodate rich organic reactions (14). Zinc oxide is an inexpensive, moisture stable, reusable, commercially available, and environmentally benign catalyst. This catalyst has been used in several transformations, such as Beckmann rearrangement (14*a*), Friedel–Crafts acylation (14*b*), benzylic oxidation (14*c*), conversion of oximes to nitriles (14*d*), synthesis of cyclic ureas (14*e*), and acylation of alcohols and amines (14*f*, 14*g*).

Herein, we report a clean, facile, and rapid method for Michael addition of sulfonamides to α,β-unsaturated esters in the presence of catalytic amount of zinc oxide in [bmim]Br under MWI (Scheme 1). In this method, *N*,*N*-dialkyl sulfonamides formed together with the N-alkylated products in very low yields.

Results and discussion

To optimize reaction conditions, Michael addition of benzenesulfonamide to *n*-butyl acrylate was studied as a model reaction to provide compounds **1b** and **2b** (Scheme 1). First, the efficiency of several ionic liquids, including [bmim]Br, [bmim]Cl, [bmim]BF_4, and [bmim]PF_6, was investigated in the presence of ZnO (20 mol%) under MWI (300 W, max. 110 °C). Interestingly, all examined ionic liquids afforded almost similar yields and reaction times. However, [bmim]Br was applied as solvent for all reactions because the preparation of this ionic liquid was easy, compared with other ionic liquids.

In another study, the influence of various inorganic and organic basic catalysts on the model reaction was studied. The results are summarized in Table 1. Clearly, higher selectivity in shorter reaction time was attained when ZnO was used. Therefore, ZnO was the catalyst of choice in all reactions. Moreover, the effect of using different amounts of ZnO was investigated (Table 1). The optimum amount of ZnO was found to be 20 mol%.

Table 1. The effect of different basic catalysts on Michael addition of benzenesulfonamide (2 mmol) with *n*-butyl acrylate (2.2 mmol) in [bmim]Br (2 g) under MW conditions (300 W, max. 110 °C).

		Yield[a] (%)	
Catalyst	Time (min)	N-Alkylated product	N,N-Dialkylated product
ZnO (10%)	8	67	6
ZnO (15%)	8	75	8
ZnO (20%)	5	86	9
ZnO (30%)	5	77	13
ZnO (50%)	5	63	22
ZnO (100%)	5	50	29
K_2CO_3 (20%)	6	57	8
Cs_2CO_3 (20%)	5	68	13
t-BuOK (20%)	5	67	11
Basic Al_2O_3 (20%)	7	58	9
NBu_3 (20%)	8	22	<3
DABCO (20%)	8	17	<3

[a]Isolated yield.

To select the appropriate MW power, conjugate addition of benzenesulfonamide to *n*-butyl acrylate was examined at different MW powers (100–600 W), with controlled temperature (max. 110 °C), in the presence of ZnO, and in [bmim]Br. The best results were observed at 300 W.

To compare the efficiency of the ionic liquid with that of the conventional solvents, the model reaction was examined in various conventional solvents. Thus, a mixture of benzenesulfonamide (2 mmol), ZnO (0.4 mmol), and *n*-butyl acrylate (2.2 mmol) was irradiated in a MW oven (300 W, max. 110 °C) in different solvents (5 mL) (Table 2). Clearly, conventional solvents exhibited lower selectivities and longer reaction times compared with [bmim]Br. Therefore, the ionic-liquid-accelerated method is more efficient.

The capability and efficiency of MW heating, compared with conventional heating, on Michael reaction was also investigated. For this purpose, compounds **1b** and **2b** as well as **1g** and **2g** were prepared via Michael reaction between benzenesulfonamide and α,β-unsaturated esters in the presence of ZnO in [bmim]Br under thermal conditions (110 °C) (Table 3). As Table 3 demonstrates, MW conditions gave better results compared with thermal conditions. This can be attributed to the efficient performance of the reactions with more polar transition state relative to the ground state under MWI (3*a*–3*c*).

Table 2. Comparative Michael addition of benzenesulfonamide (2 mmol) to *n*-butyl acrylate (2.2 mmol) in the presence of ZnO (0.4 mmol) in conventional solvents (5 mL) vs. [bmim]Br (2 g) under MWI (300 W, max. 110 °C).

		Yield[a] (%)	
Solvent	Time (min)	N-Alkylated product	N,N-Dialkylated product
—	25	37	8
DMSO	20	68	12
DMF	20	63	10
HMPTA	25	50	9
o-Xylene	25	44	11
[bmim]Br	5	86	9

[a]Isolated yield.

Table 3. Comparative synthesis of compounds **1b** and **2b** as well as **1g** and **2g** using conventional heating (Δ, 110 °C) vs. the MW method (MW, 300 W, max. 110 °C).

Compound	Time (min)		Yield[a] (%)	
	Δ	MW	Δ	MW
1b	240	5	65	86
2b			16	9
1g	300	9	53	78
2g			9	6

[a]Isolated yield.

After optimizing the reaction conditions, Michael addition of sulfonamides was examined with structurally diverse α,β-unsaturated esters. The results are depicted in Table 4. The reactions proceeded efficiently, and the desired Michael adducts were obtained in high yields.

To study the structural influence of the alkoxy groups (–OR) of α,β-unsaturated esters (Michael acceptors) on the reaction, we have investigated the reaction of benzenesulfonamide with esters containing sterically hindered alkoxy groups. The results showed that the bulkiness of the alkoxy group had no significant effect on the yields, the selectivities, and the reaction times (Table 4, entries 1–6). The structural effect of α,β-unsaturated esters on Michael-addition reaction was also studied. Lower yields of the products and longer reaction times were observed when benzenesulfonamide was added to sterically hindered α,β-unsaturated esters (ethyl methacrylate and ethyl crotonate) (Table 4, entries 7 and 8). However, in these cases, the selectivity increased. Interestingly, the reaction of benzenesulfonamide as well as naphthalene-2-sulfonamide with ethyl crotonate afforded only the monoalkylated product (Table 4, entries 8 and 10). When 4-methylbenzenesulfonamide was used instead of benzenesulfonamide, the yields decreased (Table 4, entries 2 and 9).

The interesting behavior of [bmim]Br–ZnO system lies in the fact that it can be re-used after simple washing with Et_2O, thus rendering the process more economic. The yields of compounds **1b** and **2b** (model compounds) in the second, third, fourth, and fifth uses of the [bmim]Br/ZnO were almost as high as in the first use.

In conclusion, we have introduced a highly efficient catalyst for ionic-liquid-accelerated Michael addition of sulfonamides with α,β-unsaturated esters under MWI. The promising points for the presented methodology are high conversion, ease of handling and low cost of the catalyst, cleaner reaction profile, and short reaction times, which makes it a useful and attractive process for the rapid synthesis of *N*-alkyl sulfonamides as biologically interesting compounds.

Experimental

All chemicals were purchased from Merck or Fluka chemical companies. The progress of the reactions was followed with TLC using silica gel SILG/UV 254 plates. Silica gel 60, 0.063–0.200 mm (70–230 mesh ASTM) was used for column chromatography. All reactions were carried out using CEM MARS 5^{TM} MW oven. IR spectra were run on a Shimadzu FTIR-8300 spectrophotometer; ν_{max} values are reported in cm^{-1}. The ^1H NMR (250 MHz) and ^{13}C NMR (62.5 MHz) were run on a Bruker AVANCE DPX-250 FTNMR spectrometer. Mass spectra were recorded on a Shimadzu GC MS-QP 1000 EX apparatus. Microanalyses were performed on a PerkinElmer 240-B microanalyzer. Melting points were recorded on a Büchi B-545 apparatus in open capillary tubes and are uncorrected.

General procedure for the preparation of compounds 1b and 2b

To a mixture of benzenesulfonamide (0.31 g, 2 mmol), well-ground ZnO (0.033 g, 0.4 mmol), and *n*-butyl acrylate (0.28 g, 2.2 mmol) in a MW vessel was added [bmim]Br (2 g) and mixed carefully. The resulting mixture was irradiated in a MW oven at 300 W for 5 min. The oven was programmed to give a maximum internal temperature of 110 °C. Afterward, the reaction mixture was cooled to room temperature and was extracted with Et_2O (3 × 25 mL). The organic extracts were then combined. After the removal of the solvent, the crude product was purified by column chromatography on silica gel with EtOAc–*n*-hexane (1:3) to give **1b** and **2b** as colorless oils. After isolating the products and evaporating the remainder Et_2O in ionic liquid, the ionic liquid containing the catalyst ZnO ([bmim]Br–ZnO) was used for the next run under identical reaction conditions.

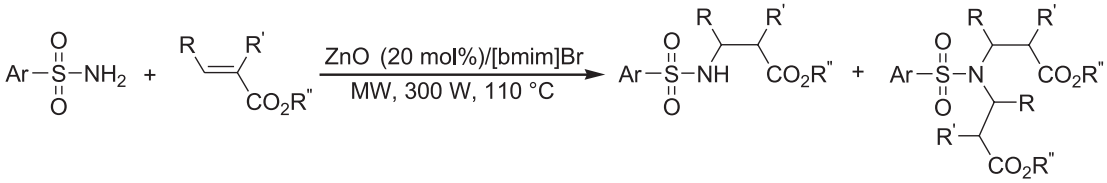
Ethyl 3-(phenylsulfonamido)propanoate (1a)

Colorless oil; isolated yield: 0.433 g (84%). IR (neat, cm^{-1}): 3286, 3059, 2975, 1732, 1447, 1329. ^1H NMR ($CDCl_3$, ppm) δ: 1.16 (t, 3H, J = 7.0 Hz, CH_3), 2.48 (t, 2H, J = 5.0 Hz, O=CCH_2), 3.15 (t, 2H, J = 5.0 Hz, O=CCH$_2$CH_2), 4.02 (q, 2H, J = 7.0 Hz, OCH_2), 5.56 (s, 1H, N*H*, exchangeable with D_2O), 7.42–7.52 (complex, 3H, H_3–H_5 of the aromatic ring), 7.80 (m, 2H, H_2 and H_6 of the aromatic ring). ^{13}C NMR ($CDCl_3$) δ: 14.0, 34.1, 38.7, 60.7, 127.0, 128.7, 132.6, 138.8, 171.7. MS *m/z*: 257 [M^+]. Anal. calcd. for $C_{11}H_{15}NO_4S$: C 51.35, H 5.88, N 5.44; found: C 51.52, H 6.01, N 5.30.

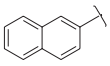
Compound 2a

Colorless oil; isolated yield: 0.072 g (10%). IR (neat, cm^{-1}): 3028, 2984, 1733, 1447, 1317. ^1H NMR ($CDCl_3$, ppm) δ: 1.22 (t, 6H, J = 7.1 Hz, 2CH_3), 2.59 (t, 4H, J = 5.0 Hz, 2O=CCH_2), 3.45 (t, 4H, J = 5.0 Hz, 2O=CCH$_2$CH_2), 4.08 (q, 4H, J = 7.1 Hz, 2OCH_2), 7.46–7.57 (complex, 3H, H_3–H_5 of

Table 4. Ionic-liquid-accelerated Michael addition of sulfonamides to α,β-unsaturated esters using ZnO under MWI (300 W, 110 °C).



1a–1j **2a–2g and 2i**

Entry	Ar	R	R'	R"	Product	Time (min)	Yield[a] (%)
1[b]	C_6H_5	H	H	CH_3CH_2	**1a**	5	84
					2a	5	10
2	C_6H_5	H	H	$CH_3(CH_2)_2CH_2$	**1b**	5	86
					2b	5	9
3	C_6H_5	H	H	$CH_3(CH_2)_4CH_2$	**1c**	5	85
					2c	5	9
4	C_6H_5	H	H	$C_6H_5CH_2$	**1d**	6	84
					2d	6	8
5	C_6H_5	H	H	$C_6H_5CH_2CH_2$	**1e**	6	85
					2e	6	8
6	C_6H_5	H	H	$C_6H_5CH{=}CHCH_2$	**1f**	7	82
					2f	7	9
7	C_6H_5	H	CH_3	CH_3CH_2	**1g**	9	78
					2g	9	6
8[c]	C_6H_5	CH_3	H	CH_3CH_2	**1h**	12	73
9	*p*-$CH_3C_6H_4$	H	H	$CH_3(CH_2)_2CH_2$	**1i**	7	77
					2i	7	8
10[c]		CH_3	H	CH_3CH_2	**1j**	12	70

[a]Isolated yield.
[b]In this reaction, the molar ratio of α,β-unsaturated ester/sulfonamide was 1.3:1.
[c]In this case, only monosubstituted Michael adduct was produced.

the aromatic ring), 7.87 (m, 2H, H_2 and H_6 of the aromatic ring). ^{13}C NMR ($CDCl_3$) δ: 13.9, 32.8, 44.7, 60.4, 127.2, 129.1, 132.6, 138.9, 170.9. MS *m/z*: 357 [M^+]. Anal. calcd. for $C_{16}H_{23}NO_6S$: C 53.77, H 6.49, N 3.92; found: C 53.98, H 6.33, N 4.08.

Butyl 3-(phenylsulfonamido)propanoate (1b)

Colorless oil; isolated yield: 0.492 g (86%). IR (neat, cm^{-1}): 3271, 3048, 2960, 1733, 1447, 1330. ^{1}H NMR ($CDCl_3$, ppm) δ: 0.90 (t, 3H, *J* = 6.5 Hz, CH_3), 1.34 (m, 2H, CH_3CH_2), 1.56 (m, 2H, $CH_3CH_2CH_2$), 2.51 (t, 2H, *J* = 5.0 Hz, O=CCH_2), 3.19 (t, 2H, *J* = 5.0 Hz, O=CCH_2CH_2), 4.03 (t, 2H, *J* = 7.0 Hz, OCH_2), 5.68 (s, 1H, N*H*, exchangeable with D_2O), 7.48–7.57 (complex, 3H, H_3–H_5 of the aromatic ring), 7.79 (m, 2H, H_2 and H_6 of the aromatic ring). ^{13}C NMR ($CDCl_3$) δ: 13.5, 18.9, 30.4, 34.1, 38.7, 64.6, 126.8, 129.0, 132.5, 139.9, 172.7. MS *m/z*: 285 [M^+]. Anal. calcd. for $C_{13}H_{19}NO_4S$: C 54.72, H 6.71, N 4.91; found: C 54.48, H 6.92, N 5.06.

Compound 2b

Colorless oil; isolated yield: 0.075 g (9%). IR (neat, cm^{-1}): 3036, 2966, 1732, 1447, 1317. ^{1}H NMR ($CDCl_3$, ppm) δ: 0.92 (t, 6H, *J* = 6.5 Hz, 2CH_3), 1.33 (m, 4H, 2CH_3CH_2),

1.56 (m, 4H, $2CH_3CH_2CH_2$), 2.63 (t, 4H, J = 5.1 Hz, $2O{=}CCH_2$), 3.45 (t, 4H, J = 5.1 Hz, $2O{=}CCH_2CH_2$), 4.06 (t, 4H, J = 6.9 Hz, $2OCH_2$), 7.51–7.60 (complex, 3H, H_3–H_5 of the aromatic ring), 7.82 (m, 2H, H_2 and H_6 of the aromatic ring). ^{13}C NMR ($CDCl_3$) δ: 13.5, 18.9, 30.5, 34.2, 44.4, 64.2, 126.9, 129.0, 132.4, 138.9, 171.1. MS *m/z*: 413 [M^+]. Anal. calcd. for $C_{20}H_{31}NO_6S$: C 58.09, H 7.56, N 3.39; found: C 58.20, H 7.69, N 3.25.

Hexyl 3-(phenylsulfonamido)propanoate (1c)

Colorless oil; isolated yield: 0.532 g (85%). IR (neat, cm^{-1}): 3275, 3044, 2967, 1732, 1447, 1328. ^{1}H NMR ($CDCl_3$, ppm) δ: 0.90 (t, 3H, J = 6.7 Hz, CH_3), 1.28–1.34 (complex, 6H, CH_3CH_2, $CH_3CH_2CH_2$ and $CH_3(CH_2)_2CH_2$), 1.57 (m, 2H, $CH_3(CH_2)_3CH_2$), 2.56 (t, 2H, J = 5.1 Hz, $O{=}CCH_2$), 3.16 (t, 2H, J = 5.1 Hz, $O{=}CCH_2CH_2$), 4.09 (t, 2H, J = 6.9 Hz, OCH_2), 5.63 (s, 1H, NH), 7.41–7.48 (complex, 3H, H_3–H_5 of the aromatic ring), 7.78 (m, 2H, H_2 and H_6 of the aromatic ring). ^{13}C NMR ($CDCl_3$) δ: 13.5, 22.5, 25.5, 27.9, 30.6, 34.1, 38.5, 64.9, 126.5, 128.7, 132.2, 139.5, 171.8. MS *m/z*: 313 [M^+]. Anal. calcd. for $C_{15}H_{23}NO_4S$: C 57.48, H 7.40, N 4.47; found: C 57.26, H 7.58, N 4.62.

Compound 2c

Colorless oil; isolated yield: 0.084 g (9%). IR (neat, cm^{-1}): 3031, 2974, 1733, 1447, 1316. ^{1}H NMR ($CDCl_3$, ppm) δ: 0.89 (t, 6H, J = 6.6 Hz, $2CH_3$), 1.26–1.32 (complex, 12H, $2CH_3CH_2$, $2CH_3CH_2CH_2$ and $2CH_3(CH_2)_2CH_2$), 1.58 (m, 4H, $2CH_3(CH_2)_3CH_2$), 2.61 (t, 4H, J = 5.0 Hz, $2O{=}CCH_2$), 3.41 (t, 4H, J = 5.0 Hz, $2O{=}CCH_2CH_2$), 4.05 (t, 4H, J = 6.9 Hz, $2OCH_2$), 7.43–7.50 (complex, 3H, H_3–H_5 of the aromatic ring), 7.74 (m, 2H, H_2 and H_6 of the aromatic ring). ^{13}C NMR ($CDCl_3$) δ: 13.8, 22.3, 25.5, 28.0, 30.4, 33.9, 44.5, 64.4, 126.4, 128.9, 132.1, 139.4, 171.4. MS *m/z*: 392 [$M^+ - C_6H_5$], 368 [$M^+ - C_6H_{13}O$), 328 [$M^+ - C_6H_5SO_2$]. Anal. calcd. for $C_{24}H_{39}NO_6S$: C 61.38, H 8.37, N 2.98; found: C 61.13, H 8.23, N 3.11.

Benzyl 3-(phenylsulfonamido)propanoate (1d)

Pale yellow oil; isolated yield: 0.535 g (84%). IR (neat, cm^{-1}): 3286, 3031, 2954, 1733, 1447, 1328. ^{1}H NMR ($CDCl_3$, ppm) δ: 2.65 (t, 2H, J = 5.1 Hz, $O{=}CCH_2$), 3.17 (t, 2H, J = 5.1 Hz, $O{=}CCH_2CH_2$), 5.00 (s, 2H, OCH_2), 5.71 (s, 1H, NH), 7.26–7.31 (complex, 5H, H_1–H_5 of the alkoxy groups of the aromatic ring), 7.45–7.51 (complex, 3H, H_3–H_5 of the aromatic ring of sulfonamide), 7.82 (m, 2H, H_2 and H_6 of the aromatic ring of sulfonamide). ^{13}C NMR ($CDCl_3$) δ: 34.2, 38.7, 66.6, 126.9, 128.2, 128.4, 128.6, 129.2, 132.7, 135.4, 139.9, 171.7. MS *m/z*: 319 [M^+]. Anal. calcd. for $C_{16}H_{17}NO_4S$: C 60.17, H 5.37, N 4.39; found: C 59.94, H 5.56, N 4.26.

Compound 2d

Pale yellow oil; isolated yield: 0.081 g (8%). IR (neat, cm^{-1}): 3051, 2965, 1734, 1447, 1316. ^{1}H NMR ($CDCl_3$, ppm) δ: 2.58 (t, 4H, J = 5.0 Hz, $2O{=}CCH_2$), 3.36 (t, 4H, J = 5.0 Hz, $2O{=}CCH_2CH_2$), 5.00 (s, 4H, $2OCH_2$), 7.22–7.25 (complex, 10H, H_1–H_5 of the alkoxy groups of the aromatic ring), 7.39–7.48 (complex, 3H, H_3–H_5 of the aromatic ring of sulfonamide), 7.72 (m, 2H, H_2 and H_6 of the aromatic ring of sulfonamide). ^{13}C NMR ($CDCl_3$) δ: 33.3, 43.9, 65.5, 126.2, 127.7, 128.1, 128.9, 129.5, 131.8, 134.4, 137.8, 171.4. MS *m/z*: 404 [$M^+ - C_6H_5$], 374 [$M^+ - C_7H_7O$], 340 [$M^+ - C_6H_5SO_2$). Anal. calcd. for $C_{26}H_{27}NO_6S$: C 64.85, H 5.65, N 2.91; found: C 65.04, H 5.48, N 2.80.

Phenethyl 3-(phenylsulfonamido)propanoate (1e)

Pale yellow oil; isolated yield: 0.564 g (85%). IR (neat, cm^{-1}): 3285, 3063, 2957, 1732, 1447, 1329. ^{1}H NMR ($CDCl_3$, ppm) δ: 2.48 (t, 2H, J = 5.2, $O{=}CCH_2$), 2.88 (t, 2H, J = 6.8 Hz, $ArCH_2$), 3.14 (t, 2H, J = 5.2 Hz, $O{=}CCH_2CH_2$), 4.24 (t, 2H, J = 6.8 Hz, OCH_2), 5.43 (s, 1H, NH), 7.15–7.28 (complex, 5H, H_1–H_5 of the alkoxy groups of the aromatic ring), 7.47–7.52 (complex, 3H, H_3–H_5 of the aromatic ring of sulfonamide), 7.84 (m, 2H, H_2 and H_6 of the aromatic ring of sulfonamide). ^{13}C NMR ($CDCl_3$) δ: 34.1, 34.9, 38.7, 65.2, 126.6, 126.9, 128.5, 128.8, 129.1, 132.7, 137.5, 139.9, 171.7. MS *m/z*: 333 [M^+]. Anal. calcd. for $C_{17}H_{19}NO_4S$: C 61.24, H 5.74, N 4.20; found: C 60.97, H 5.89, N 4.29.

Compound 2e

Pale yellow oil; isolated yield: 0.083 g (8%). IR (neat, cm^{-1}): 3045, 2942, 1733, 1447, 1331. ^{1}H NMR ($CDCl_3$, ppm) δ: 2.51 (t, 4H, J = 5.2 Hz, $2O{=}CCH_2$), 2.82 (t, 4H, J = 6.9 Hz, $2ArCH_2$), 3.30 (t, 4H, J = 5.2 Hz, $2O{=}CCH_2CH_2$), 4.19 (t, 4H, J = 6.9 Hz, $2OCH_2$), 7.10–7.19 (complex, 10H, H_1–H_5 of the alkoxy groups of the aromatic ring), 7.42–7.45 (complex, 3H, H_3–H_5 of the aromatic ring of sulfonamide), 7.78 (m, 2H, H_2 and H_6 of the aromatic ring of sulfonamide). ^{13}C NMR ($CDCl_3$) δ: 34.3, 34.9, 44.9, 65.2, 126.6, 126.7, 126.9, 128.6, 128.8, 129.2, 132.8, 137.5, 171.0. MS *m/z*: 432 [$M^+ - C_6H_5$], 388 [$M^+ - C_8H_9O$], 368 [$M^+ - C_6H_5SO_2$]. Anal. calcd. for $C_{28}H_{31}NO_6S$: C 65.99, H 6.13, N 2.75; found: C 65.87, H 6.26, N 2.89.

Cinnamyl 3-(phenylsulfonamido)propanoate (1f)

Pale yellow oil; isolated yield: 0.568 g (82%). IR (neat, cm^{-1}): 3287, 3059, 2964, 1732, 1447, 1329. ^{1}H NMR ($CDCl_3$, ppm) δ: 2.55 (t, 2H, J = 5.2 Hz, $O{=}CCH_2$), 3.19 (t, 2H, J = 5.2 Hz, $O{=}CCH_2CH_2$), 4.69 (m, 2H, OCH_2), 5.50 (s, 1H, NH), 6.23 (m, 1H, PhCH=CH), 6.63 (d, 1H, J = 15.7 Hz, PhCH), 7.29–7.35 (complex, 5H, H_1–H_5 of the alkoxy groups of the aromatic ring), 7.45–7.50 (complex, 3H, H_3–H_5 of the aromatic ring of sulfonamide), 7.95 (m, 2H, H_2 and H_6 of the aromatic ring of sulfonamide). ^{13}C NMR ($CDCl_3$) δ: 34.2, 38.8, 65.8, 122.6, 122.9, 126.6, 126.9, 128.1, 128.6, 129.0, 132.7, 134.6, 139.9, 171.7. MS *m/z*: 345 [M^+]. Anal. calcd. for $C_{18}H_{19}NO_4S$: C 62.59, H 5.54, N 4.06; found: C 62.82, H 5.39, N 4.21.

Compound 2f

Pale yellow oil; isolated yield: 0.094 g (9%). IR (neat, cm^{-1}): 3026, 2981, 1732, 1448, 1317. ^{1}H NMR ($CDCl_3$, ppm) δ: 2.51 (t, 4H, J = 5.1 Hz, $2O{=}CCH_2$), 3.41 (t, 4H, J = 5.1 Hz, $2O{=}CCH_2CH_2$), 4.73 (m, 4H, $2OCH_2$), 6.15 (m, 2H, 2PhCH=CH), 6.54 (d, 2H, J = 15.7 Hz, 2PhCH), 7.28–7.36 (complex, 10H, H_1–H_5 of the alkoxy groups of the aromatic ring), 7.41–7.47 (complex, 3H, H_3–H_5 of the aromatic ring of sulfonamide), 7.94 (m, 2H, H_2 and H_6 of the aromatic ring of sulfonamide). ^{13}C NMR ($CDCl_3$) δ: 33.8, 43.2, 65.4, 122.4, 123.0, 126.7, 126.9, 127.9, 128.5, 129.4, 132.4, 134.1, 139.3, 171.5. MS *m/z*: 400 [M^+ –

C_9H_9O], 392 [$M^+ - C_6H_5SO_2$]. Anal. calcd. for $C_{30}H_{31}NO_6S$: C 67.52, H 5.86, N 2.62; found: C 67.40, H 5.71, N 2.78.

Ethyl 2-methyl-3-(phenylsulfonamido)propanoate (1g)

Pale yellow oil; isolated yield: 0.421 g (78%). IR (neat, cm^{-1}): 3283, 3034, 2966, 1732, 1447, 1328. ^1H NMR ($CDCl_3$, ppm) δ: 1.17–1.26 (complex, 6H, $2CH_3$), 2.73 (m, 1H, O=CC*H*), 3.14–3.20 (complex, 2H, O=CCH(CH_3)CH_2), 4.12 (q, 2H, *J* = 7.0 Hz, OCH_2), 5.65 (s, 1H, N*H*), 7.55–7.64 (complex, 3H, H_3–H_5 of the aromatic ring), 7.93 (m, 2H, H_2 and H_6 of the aromatic ring). ^{13}C NMR ($CDCl_3$) δ: 14.0, 14.7, 39.6, 45.4, 60.8, 126.8, 129.1, 132.5, 139.9, 174.7. MS *m*/*z*: 271 [M^+]. Anal. calcd. for $C_{12}H_{17}NO_4S$: C 53.12, H 6.32, N 5.16; found: C 53.31, H 6.57, N 5.01.

Compound 2g

Pale yellow oil; isolated yield: 0.048 g (6%). IR (neat, cm^{-1}): 3042, 2982, 1732, 1447, 1316. ^1H NMR ($CDCl_3$, ppm) δ: 1.09–1.19 (complex, 12H, $4CH_3$), 2.78 (m, 2H, 2O=CC*H*), 3.22–3.27 (complex, 4H, 2O=CCH(CH_3)CH_2), 4.03 (q, 4H, *J* = 7.0 Hz, 2OCH_2), 7.44–7.53 (complex, 3H, H_3–H_5 of the aromatic ring), 7.75 (m, 2H, H_2 and H_6 of the aromatic ring). ^{13}C NMR ($CDCl_3$) δ: 14.1, 15.3, 39.2, 52.4, 60.7, 127.3, 129.1, 132.7, 139.0, 174.7. MS *m*/*z*: 385 [M^+]. Anal. calcd. for $C_{18}H_{27}NO_6S$: C 56.08, H 7.06, N 3.63; found: C 55.80, H 7.23, N 3.77.

Ethyl 3-(phenylsulfonamido)butanoate (1h)

Pale yellow solid; isolated yield: 0.394 g (73%); mp 60–62 °C. IR (KBr, cm^{-1}): 3285, 3044, 2953, 1732, 1447, 1329. ^1H NMR ($CDCl_3$, ppm) δ: 1.14–1.23 (complex, 6H, $2CH_3$), 2.38–2.43 (complex, 2H, O=CCH_2), 3.68 (m, 1H, O=CCH_2C*H*), 4.04 (q, 2H, *J* = 7.1 Hz, OCH_2), 5.39 (s, 1H, N*H*), 7.49–7.59 (complex, 3H, H_3–H_5 of the aromatic ring), 7.89 (m, 2H, H_2 and H_6 of the aromatic ring). ^{13}C NMR ($CDCl_3$) δ: 14.0, 21.0, 40.7, 46.6, 60.7, 126.9, 129.0, 132.5, 140.9, 171.1. MS *m*/*z*: 271 [M^+]. Anal. calcd. for $C_{12}H_{17}NO_4S$: C 53.12, H 6.32, N 5.16; found: C 53.30, H 6.19, N 5.31.

Butyl 3-(4-methylphenylsulfonamido)propanoate (1i)

Pale yellow oil; isolated yield: 0.460 g (77%). IR (neat, cm^{-1}): 3286, 3044, 2960, 1732, 1330. ^1H NMR ($CDCl_3$, ppm) δ: 0.89 (t, 3H, *J* = 6.8 Hz, $CH_2(CH_2)_2CH_3$), 1.33 (m, 2H, CH_3CH_2), 1.56 (m, 2H, $CH_3CH_2CH_2$), 2.40 (s, 3H, ArCH_3), 2.51 (t, 2H, *J* = 5.3 Hz, O=CCH_2), 3.16 (t, 2H, *J* = 5.3 Hz, O=CCH_2CH_2), 4.04 (t, 2H, *J* = 7.0 Hz, OCH_2), 5.76 (s, 1H, N*H*), 7.33 (d, 2H, *J* = 7.9 Hz, H_3 and H_5 of the aromatic ring), 7.72 (d, 2H, *J* = 7.9 Hz, H_2 and H_6 of the aromatic ring). ^{13}C NMR ($CDCl_3$) δ: 13.5, 18.9, 21.3, 30.3, 34.1, 38.7, 64.5, 126.9, 129.6, 135.8, 143.2, 172.7. MS *m*/*z*: 299 [M^+]. Anal. calcd. for $C_{14}H_{21}NO_4S$: C 56.16, H 7.07, N 4.68; found: C 55.97, H 7.18, N 4.55.

Compound 2i

Pale yellow oil; isolated yield: 0.071 g (8%). IR (neat, cm^{-1}): 3056, 2975, 1734, 1317. ^1H NMR ($CDCl_3$, ppm) δ: 0.92 (t, 6H, *J* = 6.9 Hz, $2CH_2(CH_2)_2CH_3$), 1.32 (m, 4H, $2CH_3CH_2$), 1.57 (m, 4H, $2CH_3CH_2CH_2$), 2.42 (s, 3H, ArCH_3), 2.63 (t, 4H, *J* = 5.2 Hz, 2O=CCH_2), 3.43 (t, 4H, *J* = 5.2 Hz, 2O=CCH_2CH_2), 4.02 (t, 4H, *J* = 7.0 Hz, 2OCH_2), 7.31 (d, 2H, *J* = 7.9 Hz, H_3 and H_5 of the aromatic ring), 7.72 (d, 2H, *J* = 7.9 Hz, H_2 and H_6 of the aromatic ring). ^{13}C NMR ($CDCl_3$) δ: 13.6, 19.0, 21.4, 30.4, 33.9, 45.0, 64.5, 126.9, 129.5, 135.9, 143.5, 172.5. MS *m*/*z*: 427 [M^+]. Anal. calcd. for $C_{21}H_{33}NO_6S$: C 58.99, H 7.78, N 3.28; found: C 59.15, H 7.68, N 3.14.

Ethyl 3-(naphthalene-2-sulfonamido)butanoate (1j)

Colorless buff; isolated yield: 0.453 g (70%). IR (neat, cm^{-1}): 3284, 3051, 2970, 1732, 1447, 1329. ^1H NMR ($CDCl_3$, ppm) δ: 1.07–1.12 (complex, 6H, $2CH_3$), 2.31–2.35 (complex, 2H, O=CCH_2), 3.67 (m, 1H, O=CCH_2C*H*), 3.99 (q, 2H, *J* = 7.0 Hz, OCH_2), 5.38 (s, 1H, N*H*), 7.52–7.57 (complex, 4H), 7.79–7.90 (complex, 3H). ^{13}C NMR ($CDCl_3$) δ: 14.0, 21.1, 40.6, 46.7, 60.7, 122.3, 127.5, 127.7, 127.9, 128.1, 128.3, 128.8, 129.2, 129.5, 132.1, 171.1. MS *m*/*z*: 321 [M^+]. Anal. calcd. for $C_{16}H_{19}NO_4S$: C 59.79, H 5.96, N 4.36; found: C 59.90, H 6.11, N 4.51.

Acknowledgements

We are grateful to Payam Noor University of Bushehr, Persian Gulf University, and Shiraz University Research Councils for the financial support of this work.

References

1. (*a*) K. Mikami. Green reaction media in organic synthesis. Blackwell Publishing, Oxford, UK. 2005; (*b*) R. D. Rogers. Ionic Liquids as green solvents: progress and prospects. An American Chemical Society Publication. 2005; (*c*) P. Wasserscheid and T. Welton. Ionic liquids in synthesis. Wiley-VCH, Weinheim. 2003; (*d*) T. Welton. Chem. Rev. **99**, 2071 (1999); (*e*) M.S. Rasalkar, S.V. Bhilare, A.R. Deorukhkar, N.B. Darvatkar, and M.M. Salunkhe. Can. J. Chem. **85**, 1 (2007); (*f*) X. Fan, Y. Li, X. Zhang, G. Qu, and J. Wang. Can. J. Chem. **84**, 794 (2006); (*g*) G. Karthikeyan and P.T. Perumal. Can. J. Chem. **83**, 1746 (2005).
2. (*a*) J.R. Harjani, S.J. Nara, and M.M. Salunkhe. Tetrahedron Lett. **43**, 1127 (2002); (*b*) V.V. Namboodiri and R.S. Varma. Chem. Commun. 342 (2002); (C) V.R. Koch, L.L. Miller, and R.A. Osteryoung. J. Am. Chem. Soc. **98**, 5277 (1976); (*d*) D.S. Kim and W.S. Ahn. Korean J. Chem. Eng. **39**, 20 (2003); (*e*) D.S. Newman, R.E. Winans, and R.L. McBeth. J. Electrochem. Soc. **131**, 1079 (1984); (*f*) C.J. Adams, M.J. Earle, G. Roberts, and K.R. Seddon. Chem. Commun. 2097 (1998); (*g*) P.A.Z. Suarez, J.E.L. Dullius, S. Einloft, R.F. de Souza, and J. Dupont. Polyhedron, **15**, 1217(1996).
3. (*a*) A. Loupy. Microwaves in organic synthesis. Wiley-VCH, Weinheim. 2004; (*b*) L. Perreux and A. Loupy. Tetrahedron, **57**, 9199 (2001); (C) A. Dandia, M. Sati, K. Arya, R. Sharma, A. Loupy. Chem. Pharm. Bull. **10**, 1137 (2003); (*d*) A. Loupy. Microwaves in organic synthesis. Wiley-VCH, Weinheim. 2006; (*e*) K. Tanaka. Solvent-free organic synthesis. Wiley-VCH, GmbH and KGaA, Weinheim. 2004; (*f*) A. Khalafi-Nezhad, A. Zare, A. Parhami, M.N. Soltani Rad, and G.R. Nejabat. Can. J. Chem. **84**, 979 (2006); (*g*) R.S. Varma. Advances in green chemistry: chemical synthesis using microwave irradiation. Astra Zeneca Research Foundation, Kavitha Printers, Bangalore, India. 2002; (*h*) B.L. Hayes. Microwave synthesis: chemistry at the speed of light. CEM Publishing: Mathews, NC. 2002; (*i*) H.M. Kingston and S.J. Haswell. Microwave-enhanced chemistry: fundamentasls, sample prepa-

ration, and applications. American Chemical Society: Washington, D.C. 1997; (*j*) J. Yin, X. Li, X. Wu, B. Chen, Z. Liu, and Q. Song. Can. J. Chem. **83**, 2140 (2005); (*k*) B. P. Joshi, A. Sharma, and A. K. Sinha. Can. J. Chem. **83**, 1826 (2005); (*l*) G. Qu, S. Han, Z. Zhang, M. Geng, and F. Xue. Can. J. Chem. **84**, 819 (2006); (*m*) S. Singh, M.P.S. Ishar, G. Singh, and R. Singh. Can. J. Chem. **83**, 260 (2005); (*n*) M. Kidwai, and R. Mohan. Can. J. Chem. **82**, 427 (2004).

4. (*a*) A. Khalafi-Nezhad, A. Zare, A. Parhami, M.N, Soltani Rad, and G.R. Nejabat. J. Iran. Chem. Soc. In press; (*b*) G.H. Imanzadeh, A. Khalafi-Nezhad, A. Zare, A. Hasaninejad, A.R. Moosavi Zare, and A. Parhami. J. Iran. Chem. Soc. **4**, 229 (2007); (*c*) A. Khalafi-Nezhad, A. Zare, A. Parhami, M.N. Soltani Rad and G.R. Nejabat. Phosphorus, Sulfur Silicon Relat. Elem. **182**, 657 (2007); (*d*) A. Khalafi-Nezhad, A. Zare, A. Parhami, M.N. Soltani Rad, and G.R. Nejabat. Synth. Commun. **36**, 3549 (2006); (*e*) A. Khalafi-Nezhad, A. Parhami, M.N. Soltani Rad, and A. Zare, Tetrahedron Lett. **46**, 6879 (2005); (*f*) A. Khalafi-Nezhad, A. Zare, M.N. Soltani Rad, B. Mokhtari, and A. Parhami. Synthesis, 419 (2005); (*g*) A. Khalafi-Nezhad, M.N. Soltani Rad, and A. Khoshnood. Synthesis, 583 (2004); (*h*) A. Khalafi-Nezhad, M.N. Soltani Rad, and G.H. Hakimelahi. Helv. Chim. Acta. **86**, 2396 (2003); (*i*) A. Khalafi-Nezhad, B. Mokhtari, and M.N. Soltani Rad. Tetrahedron Lett. **44**, 7325 (2003); (*j*) A. Khalafi-Nezhad, and A. Hashemi. Iran. J. Chem. Chem. Eng. **20**, 9 (2001); (*k*) A. Khalafi-Nezhad, F. Alamdari, and N. Zekri. Tetrahedron, **56**, 7503 (2000); (*l*) A. Khalafi-Nezhad, and A. Hashemi. J. Chem. Res. Synop. 720 (1999).
5. M.J. O'Neil, A. Smith, T.E. Heckelman, and F. Dudavari (*Editors*). The Merck index: an encyclopedia of chemicals, drugs, and biologicals. 13th Ed. Merck: Whitehouse Station, NJ. 2001.
6. A. Reitz, M. Verlander, and M. Goodman. Tetrahedron Lett. **23**, 751 (1982).
7. S. H. Gellman. Acc. Chem. Res. **31**, 173 (1998).
8. S. Shinagawa, T. Kanamaru, S. Harada, M. Asai, and H. Okazaki. J. Med. Chem. **30**, 1458 (1987).
9. M. Windholz, S. Budavari, L.Y. Stroumtsos, and M.N. Fertig (*Editors*). The Merck index, an encyclopedia of chemicals and drugs. 9th ed. Merck, Rahway, NJ. 1976.
10. C. Shih, L.S. Gossett, J.M. Gruber, C.S. Grossman, S.L. Andis, R.M. Schultz, J.F. Wor.0zalla, T.H. Corbett, and J.T. Metz. Bioorg. Med. Chem. Lett. **9**, 69 (1999).
11. C. Yuan and R.M. Williams. J. Am. Chem. Soc. **119**, 11777 (1997).
12. (*a*) N. Azizi and M.R. Saidi. Tetrahedron, **60**, 383 (2004); (*b*) F. Palacios, D. Aparicio, Y. Lopez, and J.M. de los Santos. Tetrahedron Lett. **45**, 4345 (2004); (C) C. Magnier-Bouvier, J.-C. Blazejewski, C. Larpent, and E. Magnier. Tetrahedron Lett. **47**, 9121 (2006); (*d*) H. Firouzabadi, N. Iranpoor, M. Jafarpour, and A. Ghaderi. J. Mol. Catal. A.: Chem. **252**, 150 (2006); (*e*) M. Molteni, A. Volonterio, G. Fossati, P. Lazzarib, and M. Zandac. Tetrahedron Lett. **48**, 589 (2007); (*f*) H. Firouzabadi, N. Iranpoor, and F. Nowrouzi. Chem. Commun. 789 (2005); (*g*) H. Firouzabadi, N. Iranpoor, and A. A. Jafari. Adv. Synth. Cat. **347**, 655 (2005); (*h*) B. Tamami, A. Fadavi, and M. Tamami. Iran. Polym. J. **15**, 799 (2006).
13. (*a*) M.M. Khodaei, K. Bahrami, and M. Khedri. Can. J. Chem. **85**, 7 (2007); (*b*) R.S. Varma. Tetrahedron, **58**, 1235 (2002); (C) B.M. Choudary, R.S. Mulukutla, and K. Klabunde. J. Am. Chem. Soc. **125**, 2020 (2003); (*d*) T.F. Dossin, M.-F. Reyniers, R.J. Berger, and G.B. Marin. Appl. Catal. B. **67**, 136 (2006); (*e*) B.M. Choudary, L. Chakrapani, T. Ramani, K.V. Kumar, and M.L. Kantam. Tetrahedron, **62**, 9571 (2006); (*f*) T. Seki, H. Tachikawa, T. Yamada, and H. Hattori. J. Catal. **217**, 117 (2003); (*g*) B.M. Choudary, M.L. Kantam, K.V.S. Ranganath, K. Mahendar, and B. Sreedhar. J. Am. Chem. Soc. **126**, 3396 (2004); (*h*) B.M. Choudary, K.V.S. Ranganath, U. Pal, M.L. Kantam, and B. Sreedhar. J. Am. Chem. Soc. **127**, 13167 (2005).
14. (*a*) H. Sharghi, and M. Hosseini. Synthesis, 1057 (2002); (*b*) M. Hosseini Sarvari, and H. Sharghi. J. Org. Chem. **69**, 6953 (2004); (C) M. Gupta, S. Paul, R. Gupta, and A. Loupy. Tetrahedron Lett. **46**, 4957 (2005); (*d*) M. Hosseini Sarvari. Synthesis, 787 (2005); (*e*) Y.J. Kim and R.S. Varma. Tetrahedron Lett. **45**, 7205 (2004); (*f*) M. Hosseini Sarvari and H. Sharghi. Tetrahedron, **61**, 10903 (2005); (*g*) F. Tamaddon. M.A. Amrollahi, and L. Sharafat, Tetrahedron Lett. 46, 7841 (2005).