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Article

Synthesis of β-Phenylchalcogeno-α,β-Unsaturated Esters, Ketones and Nitriles using Microwave and Solvent-free Conditions

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Um método simples e eficiente foi desenvolvido para a hidrocalcogenação de alquinos contendo um aceptor de Michael (éster, cetona e nitrila) com ânions fenilcalcogenolatos gerados *in situ* a partir do respectivo dicalcogeneto de difenila (Se, Te, S), usando hidreto de boro e sódio suportado em alumina e meio livre de solvente. Este método é geral e permite a obtenção de ésteres, cetonas e nitrilas (Z)-β-fenilcalcogeno-α,β-insaturados, com rendimentos e seletividade comparados aos obtidos quando se utiliza solvente orgânico e atmosfera inerte. O uso de irradiação de microondas facilitou o procedimento e acelerou a reação.

A simple, clean and efficient solvent-free protocol was developed for hydrochalcogenation of alkynes containing a Michael acceptor (ester, ketone and nitrile) with phenylchalcogenolate anions generated *in situ* from the respective diphenyl dichalcogenide (Se, Te, S), using alumina supported sodium borohydride. This efficient and improved method is general and furnishes the respective (Z)-β-phenylchalcogeno-α,β-unsaturated esters, ketones and nitriles, in good yield and higher selectivity, compared with those that use organic solvent and inert atmosphere. The use of microwave (MW) irradiation facilitates the procedure and accelerates the reaction.

Keywords: microwave irradiation, solvent-free reaction, β-phenylchalcogeno esters, β-phenylchalcogeno ketones, β-phenylchalcogeno nitriles

Introduction

Functionalized vinyl chalcogenides (S, Se and Te) have been found to be a potential tool in organic synthesis, since they are very versatile intermediates for the selective construction of isolated or conjugated olefins.[1-7] Among the functionalized vinyl chalcogenides, those containing a Michael acceptor, like an ester,[8-12] a keto[13-19] or a nitrile group[20-22] at the adjacent sp^2 carbon are of greatest interest since they combine the chemical reactivity of the vinyl chalcogenides and the vinyl acceptor group.

The method of choice to prepare (*Z*)-1,2-disubstituted vinyl chalcogenides is the addition of organo chalcogenols, or the respective chalcogenolate anions, to acetylenes.[1-7,10,23-25] Despite the simplicity of experimental procedure and high regio- and stereoselectivity, this method shows some disadvantages, such as, the use of stinking, volatile and toxic thiophenol, unstable and air sensitive tellurolate and selenolate anions, use of long heating time and inert atmosphere. The "*in situ*" generation of organyl thiolate,[26] selenolate[10,26,27] and tellurolate anions[10,12,27,28] has solved the unpleasant smell problem. Unfortunately, these improvements were not extended to alkynes bearing electron-withdrawing groups and have not eliminated the use of organic solvents and inert atmosphere. Due to the increasing interest on functionalized vinyl chalcogenides, the development of new and efficient methods for the preparation of these compounds with defined regio- and stereochemistry is of general interest in organic synthesis.

Looking for cleaner approaches to classical syntheses, we have developed several protocols involving solid supported catalyst under solvent-free conditions[29] and MW irradiation.[30-35] As a continuation of our studies toward the development of new methods for the synthesis of vinyl sulfides, selenides and tellurides, we report herein the full results on the synthesis of β-phenylchalcogeno esters, ketones and nitriles **3** by hydrochalcogenation of acetylenes using $Al_2O_3/NaBH_4$ without any solvent (Scheme 1, Table 1).

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Results and Discussion

Our initial efforts were made towards the determination of the optimum conditions to perform the protocol. Thus, we chose methyl phenylpropiolate (**1a**, 1 equiv.) and diphenyl diselenide (**2a**, 0.5 equiv.) to establish the best conditions for the hydrochalcogenation reaction.

We examined the reaction time, amount of Al_2O_3/$NaBH_4$ (30%), temperature and use of MW. It was found that using 0.050 g of Al_2O_3/$NaBH_4$, at room temperature, the reaction proceeded slowly in 60% yield after 6 h. However, by using 0.080 g of sodium borohydride supported on alumina, the desired product was obtained in very good yield (83%). The appearance of two different signals in the olefinic region of the ^{1}H NMR (6.32 and 5.64 ppm) indicated the formation of two isomers, which were identified as being (*Z*)-**3a** and (*E*)-**3a**.[11] The reaction was stereoselective, giving predominantly the (*Z*)-stereoisomer **3a** in a *Z*:*E* ratio = 79:21 (Table 1, entry 1, Method A). The use of 0.127g of the catalytic system has not significantly increased the yield.

When the same conditions (Method A) were used for the reaction of 4-phenyl-3-butyn-2-one (**1c**) or phenylpropiolonitrile (**1e**) with diphenyl diselenide (**2a**), (*Z*)-β-phenylseleno-α,β-unsaturated ketone **3g** and (*Z*)-β-phenylselenocinnamonitrile **3m** were obtained, respectively. It was found that using **1c** (1 equiv.), diphenyl diselenide (0.5 equiv.) and 0.050 g of Al_2O_3/$NaBH_4$ (30%), at room temperature, the reaction proceeded slowly in 30% yield after stirring for 2.5 h. However, by using 0.080 g of sodium borohydride supported on alumina, the desired product **3g** was obtained in good yield (62%) after 1.5 h (Table 1, entry 15). The appearance of two different signals in the olefinic region of the ^{1}H NMR spectrum (6.81 and 5.92 ppm) indicated the formation of two isomers, which were identified as being (*Z*)-**3g** and (*E*)-**3g**.[36] The reaction was stereoselective, giving predominantly the (*Z*)-stereoisomer in a *Z*:*E* ratio = 96:4 (Table 1, entry 15, Method A). The use of 0.127 g of the catalytic system has not significantly increased the yield.

For phenylpropiolonitrile (**1e**) it was necessary 0.080 g of Al_2O_3/$NaBH_4$ (50%) and stirring for 6 h to obtain a mixture of (*Z*)- and (*E*)-β-phenylselenocinnamonitrile (**3m**, *Z*:*E* ratio = 97:3) in 85% yield (Table 1, entry 27).

Aiming to reduce the reaction time, the mixture of ester, diphenyl diselenide and Al_2O_3/$NaBH_4$ (0.080 g) was irradiated with MW (662W, Method B). It was observed complete conversion after 3 min and the product was obtained in comparable yield and higher selectivity (Table 1, entry 2). When the same protocol was performed at reduced MW power (353W), it was observed, after 20 min, incomplete conversion and the product could be isolated in 57% yield.

When the mixture of 4-phenyl-3-butyn-2-one (**1c**), diphenyl diselenide (**2a**) and Al_2O_3/$NaBH_4$ (0.080 g) was irradiated with MW (548W, Method B), it was observed complete conversion after 1.5 min and the product was obtained in comparable yield and selectivity (Table 1, entry 16). When the same protocol was performed at reduced MW power (353W), it was observed, after 3 min, incomplete conversion and the product could be isolated in 40% yield. For phenylpropiolonitrile (**1e**), it was necessary only 15 min at 548W to produce **3m** in 72% yield and comparable selectivity (Table 1, entry 28).

When the reactions were performed in the presence of alumina alone, without $NaBH_4$, no reaction took place in all conditions tested and the starting materials were recovered. By using only $NaBH_4$, the desired products **3a** and **3g** were obtained only in 50% and 43% yields, respectively, together with several others byproducts (detected by GC).

In order to check the possibility of intervention of specific (no purely thermal) MW effects, the reactions were also examined using a pre-heated oil-bath for the same time and final temperature, as measured at the end of exposure during the MW-assisted synthesis. Thus, when a mixture of diphenyl diselenide (**2a**), methyl phenylpropiolate (**1a**) and Al_2O_3/$NaBH_4$ (30%) was heated at 65 °C for 3 min, (*Z*)- and (*E*)-**3a** were obtained only in 50% yield (Table 1, entry 3, Method C). It was observed that 30 min were required to complete consume of the starting materials, but the yield and selectivity of (*Z*)-**3a** decreased (Table 1, entry 4). The same reaction was performed with 4-phenyl-3-butyn-2-one (**1c**, 1.5 min, 42 °C, Table 1, entry 17) and it was observed that 40 min were required to consume completely the starting materials, but the yield (51%) and selectivity of (*Z*)-**3g** decreased (Table 1, entry 18) when compared with the Method A (entry 15). Although the energy transfer and distribution in a domestic MW oven is not controlled as in professional chemistry oven, we found that the MW-assisted reactions are more efficient, more convenient and cleaner.

Once the best conditions were established, the protocols were extended to methyl 2-octynoate (**1b**), 3-nonyn-2-one (**1d**), phenylpropiolonitrile (**1e**) and diphenyl chalcogenides. In all the studied cases, the β-organylchalcogeno-α,β-unsaturated esters (*Z*)-**3b**-**f** and (*E*)-**3b**-**f** were obtained from reasonable to good yields by using the optimized conditions described above for preparation of **3a**. However, for the synthesis of β-organyltelluro- and thio-α,β-unsaturated esters (Table 1, entries 7-14) it was necessary a larger amount of the Al_2O_3/$NaBH_4$ system.

It was found that using 0.080 g of $Al_2O_3/NaBH_4$, the reaction of methyl phenylpropiolate (**1a**) with diphenyl ditelluride (**2b**) at room temperature (Method A) occurred slowly (7 h), in 62% yield. However, the yield could be increased (73%) and the time reduced (5 h) by using 0.127 g of the supported hydride (entry 7, Table 1). The product was obtained almost exclusively with the *Z*-configuration (*Z*:*E* ratio = 98:2), as detected by GC and ^{1}H NMR. Otherwise, the use of argon atmosphere has displayed no significant increasing in yield and selectivity of the product. When the same reaction was performed under MW irradiation (Method B), it was observed complete conversion after 3 min of irradiation (Table 1, entry 8).

A search in literature[9] showed that the hydrotelluration of phenylpropiolate esters with methyl phenyltellurolate anion in presence of EtOH/THF under inert atmosphere yielded exclusively the methyl (*Z*)-3-phenyl-3-(phenyltelluro)propenoate (**3c**). On the other hand, by using our solventless protocols (Methods A and B), we have obtained two isomers ((*Z*)-**3c** and (*E*)-**3c**), with a large predominance of the *Z* isomer. In the attempt to explain this apparent lost of control in selectivity, we repeated the described procedure using solvent (THF/ethanol) and argon atmosphere. Surprisingly and in contrast to the reported data,[9] in our experiment **3c** was obtained in 75% yield as a mixture of isomers (*Z*:*E* ratio = 96:4). The *Z* and *E* esters were separated easily by column chromatography (AcOEt/hexanes as eluent), with the more polar isomer showing the *E*-configuration (*E*)-**3c**, according to GC analysis and their ^{1}H and ^{13}C NMR spectra.

The protocols were extended to other diphenyl chalcogenides and to 4-phenyl-3-butyn-2-one (**1c**) and 3-nonyn-2-one (**1d**, Scheme 1) and in all the studied cases, the β-organylchalcogeno-α,β-unsaturated ketones **3h**-**j** (Y = Se and Te) were obtained in good yield by using the optimized conditions described above for preparation of **3g** (Table 1, entries 15 and 16). The slightly inferior yield of the β-phenylchalcogeno-α,β-unsaturated ketones obtained by our methodology, when compared with methods using organic solvents and inert atmosphere, can be explained by the intermolecular competition between the dichalcogenide and the carbonyl compound for $NaBH_4$.[37] In the case of the Se- and Te-derivatives, the bond cleavage at the dichalcogenides happens preferentially in relation to the carbonyl reduction, favoring the formation of the vinyl ketone **3g**-**j**.

In order to validate the generality of our method, we have also carried out few experiments employing phenyl thiolate anion, generated "*in situ*" from diphenyl disulfide (**2c**). It was found that the hydrosulfurylation of methyl phenylpropiolate (**1a**) using 0.080 g or 0.127 g of $Al_2O_3/NaBH_4$ furnished **3e** respectively in 40 and 44% yield, after stirring for 6 h at room temperature. Although, the yield could be increased to 74% by using 0.253 g of $Al_2O_3/NaBH_4$ (Table 1, entry 11, Method A), for the hydrosulfurylation of methyl 2-octynoate (**1b**), it was observed that the reaction occurs only under heating or microwave. The respective β-phenylthio esters (*Z*)-**3f** and (*E*)-**3f** were obtained only in modest yields (entries 13 and 14, Table 1). In all the studied cases, the *Z* and *E* isomers can be easily separated by column chromatography (hexane/AcOEt as eluent).

In contrast with the observed for the Se and Te analogs, the hydrosulfuryllation reaction of ketones **1c**-**d** was not effective, with formation of **3k** and **3l** in very low yields (*ca*. 10% yield after stirring for 2.5 h). The major components of the crude reaction mixture were unreacted diphenyl disulfide and alcohols derived from total and partial reduction of the starting 4-organyl-3-butyn-ketones by $NaBH_4$. To avoid this problem, commercially available sodium phenylthiolate (PhSNa) was used as starting material. The simple stirring of the mixture of the ketone with PhSNa at room temperature afforded **3k** or **3l** after 10 to 15 min in good yields (Table 1, entries 25 and 26).

The β-phenylseleno- and β-phenylthio-α,β-unsaturated ketones were obtained almost exclusively on the *Z*-configuration, while the reaction with diphenyl ditelluride was 100% stereoselective, affording only the (*Z*)-β-phenyltelluro ketones **3i**-**j**.

In conclusion, several (*Z*)-β-phenylchalcogeno esters, ketones and cinnamonitriles **3** could be prepared in a stereoselective manner from moderate to good yield by hydrochalcogenation of acetylenes **1** under solid supported ($Al_2O_3/NaBH_4$) and solvent-free conditions at room temperature, gently heating or under MW irradiation. This improved, simple, fast and clean protocol eliminates the use of inert atmosphere and minimizes the organic solvent and energy demands. Besides these advantages, the reaction time could be reduced from hours to few minutes (when MW was employed), under milder conditions and with non-aqueous work-up.

Experimental

General remarks

^{1}H and ^{13}C NMR spectra of $CDCl_3$ solutions were recorded with a 200 MHz (Bruker DPX 200) or a 400 MHz (Bruker DPX 400) spectrometer as noted. Chemical shifts are expressed as ppm, downfield from tetramethylsilane as an internal standard. Mass spectra (EI) were

obtained at 70 eV with a Hewlett Packard EM/CG HP-5988A spectrometer. Merck's silica gel (230-400 mesh) was used for flash chromatography.

General procedure for the synthesis of β*-phenylchalcogeno esters* ***3a-f****, ketones* ***3g-j*** *and nitriles* ***3m-o***

Method A

A mixture of the acetylene **1** (1 mmol) and diphenyl chalcogenide **2** (0.5 mmol) was added to aluminum oxide impregnated with $NaBH_4$[38] (0.080 g). The mixture was stirred at room temperature. The reaction progress was followed by TLC, and after 40 min-10 h (see Table 1) ethyl acetate (10 mL) was then added and the organic solution was separated of the aluminum oxide by filtration. The solvent was evaporated under reduced pressure and the residue was purified by column chromatography over silica gel (SiO_2) using hexane/ethyl acetate (99:1) as eluent.

Method B

For β-phenylchalcogeno esters (**3a**-**f**) the aforementioned whole mixture was previously stirred for 1 min and then irradiated with MW (used a domestic Brastemp model VIP-38 Sensor Crisp operating at 2.45 GHz) at 662W[39] for 3.0-11.0 min (Table 1). For the ketones (**3g**-**j**) and nitriles (**3m**-**o**), the mixture was irradiated with a MW domestic Panasonic model Píccolo NN-S42BK, operating at 2.45 MHz at 548W[39] for 1.0-30 min (Table 1) and the product extracted and purified according to described on Method A. Spectral data of **3a**-**j** and **3m**-**o** are listed below.

Method C

The procedure described on Method A was followed and the reaction mixture was stirred under heating (oil bath) at 65 °C (Table 1, entries 3, 4 and 13) and at 42 °C (Table 1, entries 17 and 18).

*Methyl 3-phenyl-3-(phenylseleno)propenoate (**3a**)*[11]

Yield: 0.264 g (83%, Method A); *Z*:*E* ratio = 79:21. *Z* + *E* isomers: ^{1}H NMR (200 MHz, $CDCl_3$) δ (ppm) 3.57 and 3.77 (2s, 3H, *E* and *Z* respectively), 5.64 and 6.32 (2s, 1H, *E* and *Z* respectively), 6.90-7.03 (m, 8H), 7.18-7.35 (m, 2H). *Z* isomer: MS *m*/*z* (rel. int., %) 318 (M^+, 67.5), 259 (28.8), 161 (100.0), 77 (18.0). *E* isomer: 318 (M^+, 70.0), 259 (27.5), 161 (100.0), 77 (20.0).

*Methyl 3-pentyl-3-(phenylseleno)propenoate (**3b**)*[11]

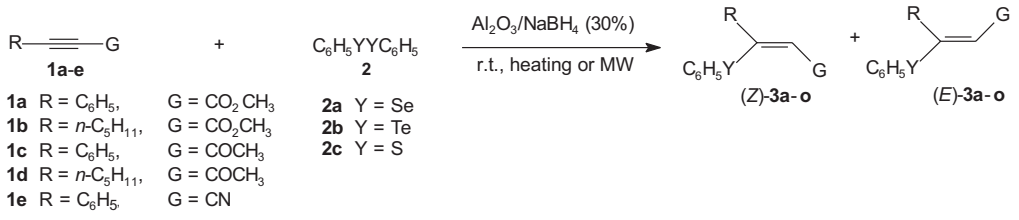
Yield: 0.215 g (69%, Method A); *Z*:*E* ratio = 87:13. *Z* + *E* isomers: ^{1}H NMR (200 MHz, $CDCl_3$) δ (ppm) 0.76 (t, *J* 6.6 Hz, 3H), 0.87-1.14 (m, 4H), 1.24-1.40 (m, 2H), 2.16 and 2.89 (2t, *J* 8.0 Hz, 2H, *Z* and *E* respectively), 3.60 and 3.76 (2s, 3H, *E* and *Z* respectively), 5.48 and 6.17 (2s, 1H, *E* and *Z* respectively), 7.21-7.31 and 7.32-7.45 (2m, 3H, *E* and *Z* respectively), 7.57-7.63 and 7.64-7.70 (2m, 2H, *E* and *Z* respectively); *Z* isomer: ^{13}C NMR (50 MHz, $CDCl_3$) δ 13.7, 22.0, 29.3, 30.8, 37.7, 51.2, 104.5, 113.0, 127.5, 129.0, 137.5, 164.1, 167.4. *E* isomer: 14.3, 22.3, 29.6, 31.5, 37.7, 50.7, 102.1, 113.4, 127.5, 128.9, 136.7, 163.6, 167.0. *Z* isomer: MS *m*/*z* (rel. int., %) 312 (M^+, 86.0), 256 (37.0), 155 (100.0), 95 (92.0). *E* isomer: 312 (M^+, 37.4), 256 (39.5), 155 (100.0), 95 (92.4).

*Methyl 3-phenyl-3-(phenyltelluro)propenoate (**3c**)*[9,40]

Yield: 0.269 g (73%, Method A); *Z*:*E* ratio = 98:2. *Z* isomer: ^{1}H NMR (200 MHz, $CDCl_3$) δ (ppm) 3.86 (s, 3H); 6.72 (s, 1H); 6.88-7.14 (m, 8H); 7.38-7.43 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 52.0, 113.9, 118.8, 120.9, 127.2, 127.5, 127.8, 128.0 (2C), 128.4, 133.6, 140.4 (2C), 140.9, 156.1, 168.4. MS *m*/*z* (rel. int., %) 368 (M^+, 58.0), 205 (45.0), 161 (100.0), 77 (31.0). *E* isomer: ^{1}H NMR (200 MHz, $CDCl_3$) δ 3.46 (s, 3H); 5.90 (s, 1H); 7.25-7.43 (m, 8H); 7.83-7.88 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 51.0, 114.9, 122.6, 126.8, 127.2, 127.9, 128.1, 128.4, 129.5, 130.0, 140.4, 140.5, 140.9. MS *m*/*z* (rel. int., %) 368 (M^+, 40.0), 205 (100.0), 161 (87.0), 77 (85.0).

*Methyl 3-pentyl-3-(phenyltelluro)propenoate (**3d**)*[40]

Yield: 0.181 g (50%, Method A); *Z*:*E* ratio = 90:10. *Z* + *E* isomers: ^{1}H NMR (200 MHz, $CDCl_3$) δ (ppm) 0.76 (t, *J* 6.6 Hz, 3H), 0.84-1.15 (m, 4H), 1.23-1.38 (m, 2H), 2.27 and 2.91 (2t, *J* 7.2 Hz, 2H, *Z* and *E* respectively), 3.61 and 3.79 (2s, 3H, *E* and *Z* respectively), 5.89 and 6.61 (2s, 1H, *Z* and *E* respectively), 7.20-7.33 and 7.34-7.45 (2m, 3H, *Z* and *E* respectively), 7.80-7.87 and 7.89-



Scheme 1.

Table 1. Synthesis of β-phenylchalcogeno-α,β-unsaturated esters, ketones and nitriles under solvent-free conditions

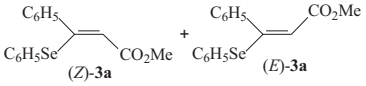
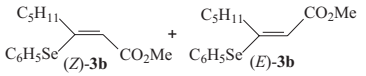
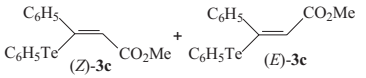
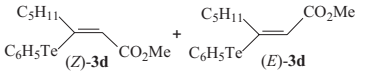
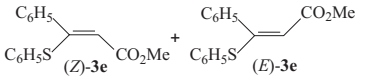
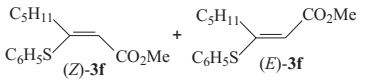
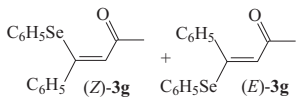
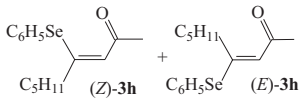
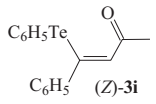
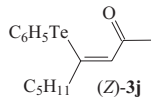
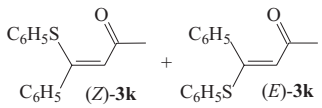
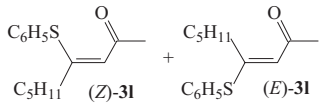
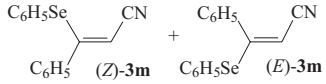
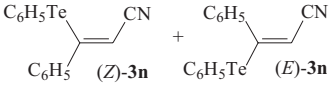
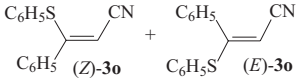
Entry	R **1**	Y **2**	G	Products **3**	Method[a]	time	Yield[b] (%)	Ratio[c] *Z* : *E*	δ_H (vinyl) *Z*	*E*
1	C_6H_5	Se	CO_2CH_3	 (*Z*)-**3a** + (*E*)-**3a**	A	6 h	83	79 : 21	6.32	5.64
2	C_6H_5	Se	CO_2CH_3	(*Z*)-**3a** + (*E*)-**3a**	B	3 min	82	85 : 15		
3	C_6H_5	Se	CO_2CH_3	(*Z*)-**3a** + (*E*)-**3a**	C	3 min	50	-		
4	C_6H_5	Se	CO_2CH_3	(*Z*)-**3a** + (*E*)-**3a**	C	0.5 h	69	73 : 27		
5	C_5H_{11}	Se	CO_2CH_3	 (*Z*)-**3b** + (*E*)-**3b**	A	4 h	69	87 : 13	6.17	5.48
6	C_5H_{11}	Se	CO_2CH_3	(*Z*)-**3b** + (*E*)-**3b**	B	6 min	62	84 : 16		
7	C_6H_5	Te	CO_2CH_3	 (*Z*)-**3c** + (*E*)-**3c**	A	5 h	73	98 : 2	6.72	5.90
8	C_6H_5	Te	CO_2CH_3	(*Z*)-**3c** + (*E*)-**3c**	B	3 min	73	92 : 8		
9	C_5H_{11}	Te	CO_2CH_3	 (*Z*)-**3d** + (*E*)-**3d**	A	10 h	50	90 : 10	6.61	5.89
10	C_5H_{11}	Te	CO_2CH_3	(*Z*)-**3d** + (*E*)-**3d**	B	10 min	52	83 : 17		
11	C_6H_5	S	CO_2CH_3	 (*Z*)-**3e** + (*E*)-**3e**	A	6 h	74	88 : 12	6.09	5.39
12	C_6H_5	S	CO_2CH_3	(*Z*)-**3e** + (*E*)-**3e**	B	10 min	61	76 : 24		
13	C_5H_{11}	S	CO_2CH_3	 (*Z*)-**3f** + (*E*)-**3f**	C	4 h	50	83 : 17	5.85	5.14
14	C_5H_{11}	S	CO_2CH_3	(*Z*)-**3f** + (*E*)-**3f**	B	11 min	55	83 : 17		
15	C_6H_5	Se	$COCH_3$	 (*Z*)-**3g** + (*E*)-**3g**	A	1.5 h	62	96 : 4	6.81	5.92
16	C_6H_5	Se	$COCH_3$	(*Z*)-**3g** + (*E*)-**3g**	B	1.5 min	64	95 : 5		
17	C_6H_5	Se	$COCH_3$	(*Z*)-**3g** + (*E*)-**3g**	C	1.5 min	34	-		
18	C_6H_5	Se	$COCH_3$	(*Z*)-**3g** + (*E*)-**3g**	C	40 min	51	90 : 10		
19	C_5H_{11}	Se	$COCH_3$	 (*Z*)-**3h** + (*E*)-**3h**	A	1.5 h	60	87 : 13	6.67	5.91
20	C_5H_{11}	Se	$COCH_3$	(*Z*)-**3h** + (*E*)-**3h**	B	1.5 min	70	85 : 15		
21	C_6H_5	Te	$COCH_3$	 (*Z*)-**3i**	A	40 min	61	100 : 0	7.32	-
22	C_6H_5	Te	$COCH_3$	(*Z*)-**3i**	B	1.0 min	68	100 : 0		
23	C_5H_{11}	Te	$COCH_3$	 (*Z*)-**3j**	A	2 h	63	100 : 0	7.22	-
24	C_5H_{11}	Te	$COCH_3$	(*Z*)-**3j**	B	1.5 min	65	100 : 0		
25	C_6H_5	S	$COCH_3$	 (*Z*)-**3k** + (*E*)-**3k**	D	10 min	92	78 : 22	6.47	5.73
26	C_5H_{11}	S	$COCH_3$	 (*Z*)-**3l** + (*E*)-**3l**	D	15 min	90	76 : 24	6.31	5.58

Table 1. cont.

Entry	R **1**	Y **2**	G	Products **3**	Method[a]	time	Yield[b] (%)	Ratio[c] *Z* : *E*	δ_H (vinyl) *Z*	*E*
27	C_6H_5	Se	CN	 (*Z*)-**3m** + (*E*)-**3m**	A	6 h	85	97 : 3	5.82	4.95
28	C_6H_5	Se	CN	(*Z*)-**3m** + (*E*)-**3m**	B	15 min	72	96 : 4		
29	C_6H_5	Te	CN	 (*Z*)-**3n** + (*E*)-**3n**	A	9 h	64	100 : 0	6.11	
30	C_6H_5	Te	CN	(*Z*)-**3n** + (*E*)-**3n**	B	20 min	66	100 : 0		
31	C_6H_5	S	CN	 (*Z*)-**3o** + (*E*)-**3o**	A	10 h	32	96 : 4	5.64	4.73
32	C_6H_5	S	CN	(*Z*)-**3o** + (*E*)-**3o**	B	30 min	31	94 : 6		

[a]Method A: The experiments were performed at room temperature. Method B: For β-phenylchalcogeno-α,β-unsaturated esters the experiments were performed at 662W and at 548W for ketones and nitriles. Method C: The reaction mixture was heated at 65 °C (entries 3, 4 and 13) and 42 °C (entries 17 and 18) using an oil bath. Method D: The experiments were performed using C_6H_5SNa and at room temperature. [b]Yields of pure products isolated by column chromatography (AcOEt/hexanes); the spectral data are showed in the experimental section. [c]Determined by GC of the crude reaction mixture and confirmed after isolation of the individual isomers.

7.95 (2m, 2H, *E* and *Z* respectively); *Z* isomer: ^{13}C NMR (50 MHz, $CDCl_3$) δ 13.7, 22.0, 30.1, 30.7, 39.6, 51.5, 116.7, 118.0, 128.6, 128.9, 141.5, 158.3, 168.7. *E* isomer: 14.2, 22.2, 29.9, 31.2, 36.7, 53.3, 106.8, 118.4, 128.5, 128.6, 140.9, 157.7, 168.4. *Z* isomer: MS *m/z* (rel. int., %) 361 (M^+ -1, 100.0), 254 (30.0), 205 (7.5), 155 (27.5), 95 (61.0). *E* isomer: 362 (M^+, 65.0), 205 (43.0), 155 (92.5), 95 (100.0).

*Methyl 3-phenyl-3-(phenylthio)propenoate (**3e**)[41]*

Yield: 0.200 g (74%, Method A); *Z*:*E* ratio = 88:12. *Z* + *E* isomers: ^{1}H NMR (200 MHz, $CDCl_3$) δ (ppm) 3.47 and 3.81 (2s, 3H, *E* and *Z* respectively), 5.39 and 6.09 (2s, 1H, *E* and *Z* respectively), 7.02-7.19 (m, 8H), 7.37-7.45 (m, 2H). *Z* isomer: MS *m/z* (rel. int., %) 270 (M^+, 68.8), 240 (40.0), 212 (100.0). *E* isomer: 270 (M^+, 30.0), 240 (24.5), 211 (100.0).

*Methyl 3-pentyl-3-(phenylthio)propenoate (**3f**)[42]*

Yield: 0.132 g (50%, Method A); *Z*:*E* ratio = 83:17. *Z* isomer: ^{1}H NMR (200 MHz, $CDCl_3$) δ (ppm) 0.77 (t, *J* 7.2 Hz, 3H); 0.90-1.60 (br m, 6H); 2.09 (t, *J* 8.0 Hz, 2H); 3.75 (s, 3H); 5.85 (s, 1H); 7.36-7.57 (m, 5H). *E* isomer: 0.90-1.68 (br m, 9H); 2.84 (t, *J* 8.0 Hz, 2H); 3.60 (s, 3H); 5.14 (s, 1H); 7.36-7.57 (m, 5H). *Z* isomer: MS *m/z* (rel. int., %) 264 (M^+, 87.5), 161 (100.0), 95 (41.5). *E* isomer: 264 (M^+, 100.0), 161 (87.5), 95 (40.0).

*4-Phenyl-4-(phenylseleno)-3-buten-2-one (**3g**)[36]*

Yield: 0.187 g (62%, Method A); *Z*:*E* ratio = 96:4. *Z* isomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 2.33 (s, 3H); 6.81 (s, 1H); 6.97-7.10 (m, 6H); 7.19-7.22 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 30.3, 127.3, 127.7, 127.9, 128.2, 128.6, 129.7, 136.1, 139.1, 162.4, 196.4. MS *m/z* (rel. int., %) 302 (M^+, 58.5), 156 (19.2), 77 (100.0). *E* isomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 2.04 (s, 3H); 5.92 (s, 1H); 6.80-7.10 (m, 6H); 7.20-7.16 (m, 4H). MS *m/z* (rel. int., %) 302 (M^+, 47.2), 157 (37.4), 77 (100.0).

*4-Pentyl-4-(phenylseleno)-3-buten-2-one (**3h**)[36]*

Yield: 0.178 g (60%, Method A); *Z*:*E* ratio = 87:13. *Z* + *E* isomers: ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 0.76 (t, *J* 7.2 Hz, 3H); 0.87-1.01 (m, 2H); 1.04-1.11 (m, 2H); 1.28-1.36 (m, 2H); 2.24 and 1.99 (2s, 3H, *Z* and *E* respectively); 2.82 and 2.19 (2t, *J* 7.6 Hz, 2H, *E* and *Z* respectively); 6.67 and 5.91 (2s, 1H, *Z* and *E* respectively); 7.24-7.41 (m, 3H); 7.63-7.66 (m, 2H); *Z* isomer: ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.7, 22.0, 29.8, 30.0, 30.9, 37.7, 121.4, 128.3, 128.8, 128.9, 137.2, 165.4, 196.4. *Z* isomer: MS *m/z* (rel. int., %) 296 (M^+, 14.1), 154 (10.2), 139 (70.3), 81 (100.0). *E* isomer: 296 (M^+, 8.6), 158 (15.6), 139 (73.4), 81 (100.0).

*4-Phenyl-4-(phenyltelluro)-3-buten-2-one (**3i**)[43]*

Yield: 0.215 g (61%, Method A); *Z*:*E* ratio = 100:0. *Z* isomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 2.34 (s, 3H); 6.91-7.99 (m, 7H); 7.05-7.09 (m, 1H); 7.32 (s, 1H); 7.35-7.37 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 29.9, 120.8, 127.1, 127.5, 128.1, 128.2, 128.6, 128.7, 139.8, 141.0, 159.8, 196.6. MS *m/z* (rel. int., %) 350 (M^+ -2, 5.5), 275 (10.2), 207 (5.5), 77 (100.0).

*4-Pentyl-4-(phenyltelluro)-3-buten-2-one (**3j**)*[36]

Yield: 0.218 g (63%); *Z*:*E* ratio = 100:0. *Z* isomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 0.76 (t, *J* 6.8 Hz, 3H); 0.93-0.99 (m, 2H); 1.03-1.10 (m, 2H); 1.28-1.36 (m, 2H); 2.25 (s, 3H); 2.35 (t, *J* 8.0 Hz, 2H); 7.22 (s, 1H); 7.25-7.29 (m, 2H); 7.35-7.40 (m, 1H); 7.86-7.89 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.7, 22.0, 29.7, 30.8, 30.9, 39.7, 119.1, 126.6, 128.5, 128.9, 141.0, 162.9, 196.6. MS *m*/*z* (rel. int., %) 346 (M^+, 28.1), 267 (43.0), 77 (100.0).

*3-Phenylselenocinnamonitrile (**3m**)*[20]

Yield: 0.242 g (85%, Method A); *Z*:*E* ratio = 97:3. *Z* + *E* isomers: ^{1}H NMR (200 MHz, $CDCl_3$) δ (ppm) 4.95 and 5.82 (2s, 1H, *E* and *Z* respectively); 7.00-7.70 (m, 10H).

*3-Phenyltellurocinnamonitrile (**3n**)*

Yield: 0.214 g (64%, Method A); *Z*:*E* ratio = 100:0. *Z* isomer: ^{1}H NMR (200 MHz, $CDCl_3$) δ (ppm) 6.11 (s, 1H); 7.01-7.56 (m, 10H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 110.1, 118.9, 131.7, 133.3, 133.4, 133.8, 134.4, 134.7, 144.8, 145.2, 157.6.

*3-Phenylthiocinnamonitrile (**3o**)*[22]

Yield: 0.076 g (32%, Method A); *Z*:*E* ratio = 96:4. *Z* + *E* isomers: ^{1}H NMR (200 MHz, $CDCl_3$) δ (ppm) 4.73 and 5.64 (2s, 1H, *E* and *Z* respectively); 7.16-7.67 (m, 10H).

General procedure for the synthesis of β*-phenylthio ketones **3k**-**l** (Method D)*

A mixture of sodium phenylthiolate (0.130 g; 1 mmol) and 4-organyl-3-butyn-2-one **1c**-**d** (1 mmol) was stirred at room temperature for 10-15 min and the product purified by column chromatography over silica gel (SiO_2) eluting with hexane/ethyl acetate. The ketones **3k** and **3l** were obtained as a mixture of *Z* and *E* isomers (Table 1, entries 25 and 26). Spectral data of **3k**-**l** are listed below.

*4-Phenyl-4-(phenylthio)-3-buten-2-one (**3k**)*[19]

Yield: 0.234 g (92%); *Z*:*E* ratio = 78:22. *Z* + *E* isomers: ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 2.32 and 1.71 (2s, 3H, *Z* and *E* respectively); 6.47 and 5.73 (2s, 1H, *Z* and *E* respectively); 7.00-7.15 (m, 8H); 7.37-7.57 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 30.0, 30.6, 123.0, 123.4, 127.7, 127.8, 128.2, 128.3, 128.3, 128.4, 128.8, 128.9, 129.5, 129.8, 129.9, 130.0, 132.5, 134.1, 135.3, 138.2, 159.0, 159.1, 196.1, 196.2.

*4-Pentyl-4-(phenylthio)-3-buten-2-one (**3l**)*[36]

Yield: 0.223 g (90%); *Z*:*E* ratio = 76:24. *Z* isomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 0.76 (t, *J* 6.8 Hz, 3H); 0.88-1.16 (m, 4H); 1.27-1.40 (m, 2H); 2.10 (t, *J* 7.2 Hz, 2H); 2.24 (s, 3H); 6.31 (s, 1H); 7.35-7.37 (m, 3H); 7.51-7.54 (m, 2H). *E* isomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 0.85-0.95 (m, 5H); 1.27-140 (m, 2H); 1.60-1.65 (m, 2H); 1.97 (s, 3H); 2.80 (t, *J* 7.6 Hz, 2H); 5.58 (s, 1H); 7.41-7.45 (m, 3H); 7.46-7.53 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.7, 13.9, 21.9, 22.3, 29.3, 29.3, 30.4, 30.9, 31.5, 31.6, 33.6, 36.5, 117.6, 119.3, 128.9, 129.2, 129.6, 129.7, 130.4, 130.9, 135.4, 135.7, 162.4, 165.5, 194.4, 196.0.

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References

1. Zeni, G.; Lüdtke, D. S.; Panatieri, R. B.; Braga, A. L.; *Chem. Rev*. **2006**, *106*, 1032.
2. Comasseto, J. V.; Ling, L. W.; Petragnani, N.; Stefani, H. A.; *Synthesis* **1997**, 373.
3. Comasseto, J. V.; Barrientos-Astigarraga, R. E.; *Aldrich Acta* **2000**, *33*, 66.
4. Harmata, M.; Jones, D.; *Tetrahedron Lett*. **1996**, *37*, 783.
5. Trost, B. M.; Ornstein, P. L.; *Tetrahedron Lett*. **1981**, *22*, 3463.
6. Wenkert, E.; Ferreira, T. W.; *J. Chem. Soc., Chem. Commun*. **1982**, 840.
7. Bohlmann, F.; Bresinsky, E.; *Chem. Ber*. **1964**, *97*, 2109.
8. Wadsworth, D. H.; Detty. M. R.; *J. Org. Chem*. **1980**, *45*, 4611.
9. Detty, M. R.; Murray, B. J.; Smith, D. L.; Zumbulyadis, N.; *J. Am. Chem. Soc*. **1983**, *105*, 875.
10. Detty, M. R.; Murray, B. J.; *J. Am. Chem. Soc*. **1983**, *105*, 883.
11. Huang, X.; Zhao, C.-Q.; *Synth. Commun*. **1997**, *27*, 3491.
12. Uemura, S.; Fukuzawa, S.; *Tetrahedron Lett*. **1982**, *23*, 1181.
13. Zhao, C.-Q.; Huang, X.; Meng, J.-B.; *Tetrahedron Lett.* **1998**, *39*, 1933.
14. Barrientos-Astigarraga, R. E.; Castelani, P.; Sumida, C. Y.; Comasseto, J. V.; *Tetrahedron Lett.* **1999**, *40*, 7717.
15. Hamaguchi, M.; Nagai, T.; *J. Org. Chem.* **1989**, *54*, 3957.
16. Buzilova, S. R.; Sadekov, I. D.; Lipovich, T. V.; Fillipova, T. M.; Vereshchagin, L. I.; *J. Org. Chem. (USSR)* **1977**, *47*, 1828.
17. Omar, M. T.; Basyouni, M. N.; *Bull. Chem. Soc. Jpn.* **1974**, *47*, 2325.
18. Takehiko, N.; Yoshimore, O.; *J. Chem. Soc., Perkin Trans. 1* **1981**, 934.
19. Takehiko, N.; Yoshimore, O.; *Chem. Lett.* **1979**, 365.
20. Zhao, C.-Q.; Huang, X.; *Synth. Commun*. **1996**, *26*, 3607.
21. Le Guillanton, G.; Simonet, J.; *Acta Chem. Scand. B: Org. Chem. Biochem.* **1983**, *B37*, 437.

22. Kamiya, I.; Kawakami, J.-I.; Yano, S; Nomoto, A.; Ogawa, A.; *Organomet*. **2006**, *25*, 3562.
23. Truce, W. E.; Goldhamer, D. L.; *J. Am. Chem. Soc.* **1959**, *81*, 5795.
24. Uemura, S.; Fukuzawa, S.; *Tetrahedron Lett.* **1982**, *23*, 1181.
25. Lenardão, E. J.; Cella, R.; Jacob, R. G.; Silva, T. B.; Perin, G. *J. Braz. Chem. Soc.* **2006**, *17*, 1031.
26. Braga, A. L.; Alves, E. F.; Silveira, C. C.; Andrade, L. H.; *Tetrahedron Lett*. **2000**, *41*, 161.
27. Dabdoub, M. J.; Baroni, A. C. M.; Lenardão, E. J.; Gianeti, T. R.; Hurtado, G. R.; *Tetrahedron* **2001**, *57*, 4271.
28. Zeni, G.; Formiga, H. B.; Comasseto, J. V.; *Tetrahedron Lett.* **2000**, *41*, 1311.
29. Perin, G.; Jacob, R. G.; Botteselle, G. V.; Kublik, E. L.; Lenardão, E. J.; Cella, R.; Santos, P. C. S.; *J. Braz. Chem. Soc.* **2005**, *16*, 857.
30. Jacob, R. G.; Perin, G.; Loi, L. N.; Pinno, C. S.; Lenardão, E. J.; *Tetrahedron Lett*. **2003**, *44*, 3605.
31. Jacob, R. G.; Perin, G.; Botteselle, G. V.; Lenardão, E. J.; *Tetrahedron Lett*. **2003**, *44*, 6809.
32. Perin, G.; Jacob, R. G.; Azambuja, F.; Botteselle, G. V.; Siqueira, G. M.; Freitag, R. A.; Lenardão, E. J.; *Tetrahedron Lett*. **2005**, *46*, 1679.
33. Perin, G.; Mendes, S. R.; Silva, M. S.; Lenardão, E. J.; Jacob, R. G.; Santos, P. C.; *Synth. Commun*. **2006**, *36*, 2587.
34. Perin, G.; Jacob, R. G.; Dutra, L. G.; Azambuja, F.; Santos, G. F. F.; Lenardão, E. J.; *Tetrahedron Lett*. **2006**, *47*, 935.
35. Lenardão, E. J.; Mendes, S. R.; Ferreira, P. C.; Perin, G.; Silveira, C. C.; Jacob, R. G.; *Tetrahedron Lett*. **2006**, *47*, 7439.
36. Proidakov, A. G.; Kalabin, G. A.; Buzilova, S. R.; Vereshchagin, L. I.; Panov, A. M.; Ratovskii, G. V.; *Zh. Org. Khim.* **1981**, *17*, 2414.
37. Varma, R. S.; Saini, R. K.; *Tetrahedron Lett*. **1997**, *38*, 4337.
38. The solid supported catalysts were prepared by the following procedure: To a pestle mortar alumina (0.7 g of Al_2O_3 90, 0.063-0.200 mm, Merck) and $NaBH_4$ (0.3 g) was added and the mixture was stirred for 1 min and immediately used in the reaction.
39. The oven powers were determined as described by Kingston, H. M. In *Introduction to Microwave Sample Preparation-Theory and Practice*; Jassie, L. B., ed.; American Chemical Society: Washington, DC, 1988.
40. Takahashi, H.; Ohe, K.; Uemura, S.; Sugita, N.; *Nippon Kagaku Kaishi* **1987**, *7*, 1508.
41. Bates, C. G.; Saejueng, P.; Doherty, M. Q.; Venkataraman, D.; *Org. Lett*. **2004**, *6*, 5005.
42. Rossi, R.; Bellina, F.; Mannina, L.; *Tetrahedron* **1997**, *53*, 1025.
43. Zhao, C.-Q.; Li, J.-L.; Meng, J.-B.; Wang, Y.-M.; *J. Org. Chem*. **1998**, *63*, 4170.

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