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The first synthesis of β-phenylchalcogeno-α,β-unsaturated esters via hydrochalcogenation of acetylenes using microwave and solvent-free conditions

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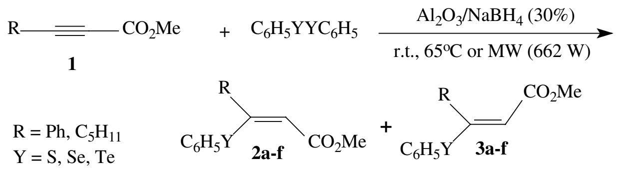
Abstract—A simple, clean, and efficient solvent-free protocol was developed for hydrochalcogenation of methyl propiolate derivatives with phenylchalcogenolate anion generated in situ from the respective diphenyl dichalcogenide (S, Se, Te) using alumina supported sodium borohydride. This efficient and improved method is general and furnishes the (*Z*)-β-phenylchalcogeno-α,β-unsaturated esters in yields and with selectivity comparable to those using organic solvent and inert atmosphere. The use of MW irradiation facilitates the procedure and accelerates the reaction.

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] Among the functionalized vinyl chalcogenides, those containing a Michael acceptor, like an ester group at the adjacent sp^2 carbon (a β-organylchalcogeno-α,β-unsaturated ester), are of greatest interest since they combine the chemical reactivity of the vinyl chalcogenides and the vinyl ester.[2]

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.[1,3] Despite the practicality 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,[4] selenolate,[2c,4,5] and tellurolate anions[2c,e,5,6] has solved the unpleasant smell problem. Unfortunately, these improvements were not extended to alkynes bearing electron-withdrawing groups, like esters, 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[7] and MW irradiation.[8,9] 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 synthesis of β-phenylchalcogeno esters **2** and **3** by



Scheme 1.

Keywords: Microwave irradiation; Solvent-free reaction; β-Phenylchalcogeno esters.

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hydrochalcogenation of acetylenes using $Al_2O_3/NaBH_4$ without any solvent[10,11] (Scheme 1, Table 1).

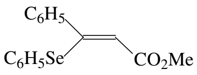
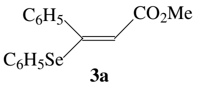
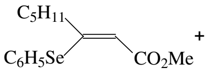
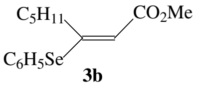
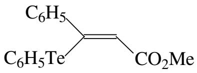
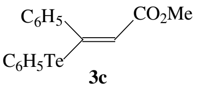
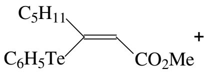
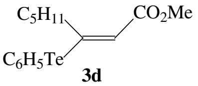
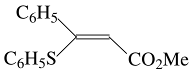
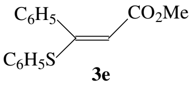
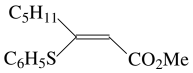
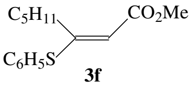
Our initial efforts were made toward the determination of the optimum conditions to perform the protocol. Thus, we chose methyl phenylpropiolate (1 equiv) and diphenyl diselenide (0.5 equiv) to establish the best conditions for the hydrochalcogenation reaction.

We examined the reaction time, amount of $Al_2O_3/NaBH_4$ (30%), temperature and use of microwave.[11] 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 ^1H NMR (6.32 and 5.64 ppm) indicated the formation of two isomers, which were identified as being **2a** and **3a**. The reaction was stereoselective, giving predominantly the (*Z*)-stereoisomer **2a** in a *Z*:*E* ratio = 79:21 (Table 1, entry 1, Method A). The use of 0.127 g of the catalytic system has not significantly increased the yield.

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 (662 W, Method B). Complete conversion was observed 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 (353 W), it was observed, after 20 min, incomplete conversion and the product could be isolated in 57% yield.

When the reaction was performed in the presence of alumina alone, without $NaBH_4$ no reaction took place in all the conditions tested and the starting materials were recovered. By using only $NaBH_4$, the desired products **2a** and **3a** were obtained only in 50% yield, together with several other byproducts (detected by GC).

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

Entry	R	Y	Products	Method[a]	Time (min)	Yield (%) 2+3[b]	Ratio[c] *Z*:*E*	δ_H (vinyl)	
								Z	*E*
1	C_6H_5	Se	 **2a** +  **3a**	A	360	83	79:21	6.32	5.64
2	C_6H_5	Se	**2a + 3a**	B	3	82	85:15		
3	C_6H_5	Se	**2a + 3a**	C	3	50	—		
4	C_6H_5	Se	**2a + 3a**	C	30	69	73:27		
5	C_5H_{11}	Se	 **2b** +  **3b**	A	240	69	87:13	6.17	5.48
6	C_5H_{11}	Se	**2b + 3b**	B	6	62	84:16		
7	C_6H_5	Te	 **2c** +  **3c**	A	300	73	98:2	6.72	5.90
8	C_6H_5	Te	**2c + 3c**	B	3	73	92:8		
9	C_5H_{11}	Te	 **2d** +  **3d**	A	600	50	90:10	6.61	5.89
10	C_5H_{11}	Te	**2d + 3d**	B	10	52	83:17		
11	C_6H_5	S	 **2e** +  **3e**	A	360	74	88:12	6.09	5.39
12	C_6H_5	S	**2e + 3e**	B	10	61	76:24		
13	C_5H_{11}	S	 **2f** +  **3f**	C	240	50	83:17	5.85	5.14
14	C_5H_{11}	S	**2f + 3f**	B	11	55	83:17		

[a] Method A: the experiments were performed at room temperature. Method B: the experiments were performed at 662 W. Method C: the reaction mixture was heated at 65 °C using an oil bath.[11]

[b] Yields of pure products isolated by column chromatography (AcOEt/hexanes) and identified by mass spectrometry, ^1H, ^{13}C NMR.[2]

[c] Determined by GC of the crude reaction mixture and confirmed after isolation of the individual isomers.