

## Addition of chalcogenolate anions to terminal alkynes using microwave and solvent-free conditions: easy access to bis-organochalcogen alkenes

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**Abstract**—We present here the reaction of diphenyl dichalcogenides (Se and Te) with propargyl alcohols using alumina supported sodium borohydride under solvent-free conditions. This efficient and improved method is general and furnishes the corresponding vinyl chalcogenide preferentially with a *Z* configuration. We also observed that when the same protocol was applied to phenyl acetylene, the (*E*)-bis-organochalcogen alkenes were obtained in good yields and high selectivity. The use of MW irradiation facilitates the procedure and accelerates the reaction.

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Vinyl chalcogenides have been found to be a very useful tool in organic synthesis, since they are very versatile intermediates for the selective construction of isolated or conjugated olefins.<sup>1</sup> Among the vinyl chalcogenides, 1,2-bis-organochalcogen alkenes are very useful synthons in organic synthesis, because they can be used as precursor to enediyne and other functionalized olefins. However, the number of methodologies for accessing 1,2-bis chalcogenide alkenes is limited and the development of protocols for rigorous regio- and stereochemical controlled synthesis of these compounds remains yet a challenge.

Vinyl chalcogenides have been prepared by the addition of organo chalcogenols, or the respective chalcogenolate anions, to acetylenes.<sup>1,2</sup> Besides, it is known that diselenides<sup>3</sup> and ditellurides<sup>4</sup> add to terminal alkynes, in the presence of UV irradiation<sup>3a-d,4</sup> or a transition-metal catalyst<sup>3e,f</sup> to afford the respective 1,2-bis(organylchalcogenide) alkenes in moderate to good yields. Recently, the in situ addition of chalcogenides to propargylic alcohols (alkynyl-lithium species) to afford bis-chalcogenide alkenes (S and Se) in very good yields was described.<sup>5</sup>

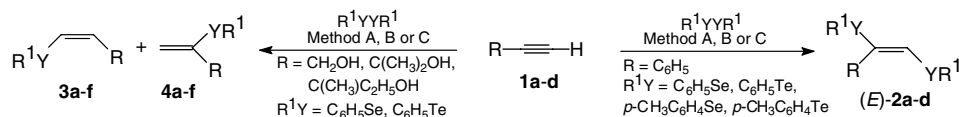
The authors observed that the presence of the acidic hydrogen from hydroxyl group is essential for the selectivity control of the addition. They also described that with diorganoyl ditelluride the reaction failed completely and in a similar condition, terminal acetylenes afforded the respective tris-organochalcogen alkenes. Due to the increasing use of vinyl chalcogenides,<sup>1,2</sup> the development of new and efficient methods for the preparation of bis-organochalcogen alkenes 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<sup>6</sup> and MW irradiation.<sup>7</sup> As a continuation of our studies toward the development of new methods for the synthesis of vinyl chalcogenides,<sup>6,7a</sup> we report herein the results of the hydrochalcogenation of propargylic alcohols and chalcogenolate anion in addition to phenyl acetylene using  $\text{Al}_2\text{O}_3/\text{NaBH}_4$  without any solvent (Scheme 1).<sup>8,9</sup>

Initially, we chose propargyl alcohol **1a** (1.5 equiv) and diphenyl diselenide (0.5 equiv) to establish the best conditions for the hydrochalcogenation reaction. We examined the reaction time, the amount of  $\text{Al}_2\text{O}_3/\text{NaBH}_4$  (50%) and the use of microwave.<sup>9</sup> It was found that

**Keywords:** Microwave irradiation; Solvent-free reaction; Bis(organo-chalcogen)alkenes; Vinyl chalcogenides.

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**Scheme 1.** Method A:  $\text{Al}_2\text{O}_3/\text{NaBH}_4$  (50%), stirring, rt, 3–72 h; Method B:  $\text{Al}_2\text{O}_3/\text{NaBH}_4$  (50%), MW (548 W), 6–35 min; Method C:  $\text{Al}_2\text{O}_3/\text{NaBH}_4$  (50%), stirring, 60 °C (oil bath), 1.5–42 h.

using 0.050 g of  $\text{Al}_2\text{O}_3/\text{NaBH}_4$ , at room temperature, the reaction proceeded slowly and in 30% yield after stirring for 72 h. However, by using 0.076 g of  $\text{Al}_2\text{O}_3/\text{NaBH}_4$ , the desired products **3a** and **4a** were obtained in good yield (76%) after 46 h (Table 1, entry 1, Method A). Aiming to reduce the reaction time, the mixture was irradiated with MW (548 W). It was observed there was complete consumption of the starting materials after 10 min and the products were obtained in comparable yield and selectivity (Table 1, entry 2, Method B). When the same protocol was performed at reduced MW power (353 W) it was observed, after 10 min, there was incomplete consumption of diphenyl diselenide, and the product was isolated in 51% yield.

When the reaction was performed in the presence of alumina alone, without  $\text{NaBH}_4$ , no reaction took place in

all conditions tested and the starting materials were recovered. By using only  $\text{NaBH}_4$ , the desired products **3a** and **4a** were obtained only in 32% yield.

In order to check the possibility of intervention of specific (non-purely thermal) microwave effects, the reaction with  $\text{Al}_2\text{O}_3/\text{NaBH}_4$  (50%) was also examined using a pre-heated oil bath for the same final temperature (60 °C), as measured at the end of exposure during the MW-assisted synthesis (Table 1, entry 3, Method C). However, it was observed that 22 h was required for complete consumption of diphenyl diselenide.

Since the best conditions were established, the protocols were extended to other propargylic alcohols with diphenyl diselenide and also with diphenyl ditelluride (Scheme 1). In all the cases studied, a mixture of **3** and **4** was

**Table 1.** Synthesis of vinyl chalcogenides **3** and **4** under solvent-free conditions

Entry	Alkyne <b>1</b>	$\text{R}^1\text{Y}_2$	Products <b>3</b> + <b>4</b>	Method <sup>a</sup>	Time	Yield <sup>b</sup> (%)	Ratio <sup>c</sup> <b>3</b> : <b>4</b>
1		$\text{C}_6\text{H}_5\text{Se}_2$	 + 	A	46 h	76	75:25
2	<b>1a</b>	$\text{C}_6\text{H}_5\text{Se}_2$	<b>3a</b> + <b>4a</b>	B	10 min	79	70:30
3	<b>1a</b>	$\text{C}_6\text{H}_5\text{Se}_2$	<b>3a</b> + <b>4a</b>	C	22 h	77	73:27
4	<b>1a</b>	$\text{C}_6\text{H}_5\text{Te}_2$	 + 	A	72 h	73	80:20
5	<b>1a</b>	$\text{C}_6\text{H}_5\text{Te}_2$	<b>3b</b> + <b>4b</b>	B	6 min	84	80:20
6		$\text{C}_6\text{H}_5\text{Se}_2$	 + 	A	48 h	68	93:07
7	<b>1b</b>	$\text{C}_6\text{H}_5\text{Se}_2$	<b>3c</b> + <b>4c</b>	B	13 min	71	90:10
8	<b>1b</b>	$\text{C}_6\text{H}_5\text{Te}_2$	 + 	B	15 min	85	90:10
9	<b>1b</b>	$\text{C}_6\text{H}_5\text{Te}_2$	<b>3d</b> + <b>4d</b>	C	27 h	91	91:09
10		$\text{C}_6\text{H}_5\text{Se}_2$	 + 	A	48 h	65	81:19
11	<b>1c</b>	$\text{C}_6\text{H}_5\text{Se}_2$	<b>3e</b> + <b>4e</b>	B	14 min	82	84:16
12	<b>1c</b>	$\text{C}_6\text{H}_5\text{Te}_2$	 + 	B	13 min	63	91:09
13	<b>1c</b>	$\text{C}_6\text{H}_5\text{Te}_2$	<b>3f</b> + <b>4f</b>	C	42 h	68	88:12

<sup>a</sup> Method A: The experiments were performed at room temperature. Method B: The experiments were performed at 548 W. Method C: The reaction mixture was heated at 60 °C using an oil bath.<sup>9</sup>

<sup>b</sup> Yields of pure products isolated by column chromatography (AcOEt/hexanes) and identified by mass spectrometry,  $^1\text{H}$ ,  $^{13}\text{C}$  NMR.

<sup>c</sup> Determined by GC of the crude reaction mixture and confirmed after isolation of the individual isomers.

obtained in good yields by using the optimized conditions described above for the preparation of **3a** and **4a** (Table 1, entries 4–13).<sup>9</sup> The anti-Markovnikov adduct **3** was obtained in a higher amount than the Markovnikov one **4** in all the tested examples. It was observed that steric factors are important, because the **3**:**4** ratio increases with the group R size. This regioselectivity is similar to that reported for the methods which use organic solvents and inert atmosphere.<sup>1,2</sup> It was observed that for the reaction of phenyltelluroate anions with the sterically hindered alcohols **1b** and **1c** the Method A was not efficient, even after stirring for 72 h (yield < 35%). However, when the reaction was performed under heating at 60 °C, the respective tellurides **3** and **4** were obtained in good yields (Table 1, entries 9 and 13). Probably, that happens because temperature  $\geq 60$  °C is necessary for the diphenyl ditelluride/acetylene mixture to become homogeneous.<sup>3c</sup>

When the same protocol (Method A) was applied to phenyl acetylene **1d** and diphenyl diselenide, 1,2-bis-phenylseleno alkenes **2a** were obtained in good yield (95%) after 3 h at room temperature.<sup>10</sup> This is a new and unexpected result that allows to obtain bis-organochalcogen alkenes in an easy and clean way. The structure of **2a** was confirmed by the appearance of two different signals in the olefinic region of the <sup>1</sup>H NMR spectrum (7.08 and 7.60 ppm) indicating the formation of two isomers, which were identified as being (*E*)-**2a** and (*Z*)-**2a**.<sup>3c</sup> The reaction was stereoselective, giving predominantly the (*E*)-stereoisomer in a *E*:*Z* ratio = 80:20 (Table 2, entry 1). Aiming to reduce the reaction time, the mixture

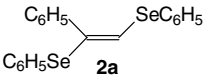
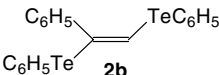
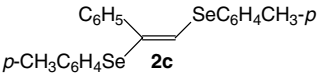
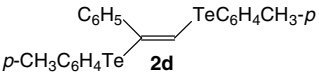
was irradiated with MW (548 W, Method B). It was observed there was complete consumption of diphenyl diselenide after 6 min and the product was obtained in comparable yield and selectivity (Table 2, entry 2).

When the same reaction was performed using a pre-heated oil bath (60 °C), **2a** was obtained with similar yield after 1.5 h (Table 2, entry 4, Method C). The reaction was extended to other diaryl dichalcogenides, and in all the tested cases the respective bis-arylchalcogenide alkenes **2** were obtained in good yields and preferentially with *E* configuration (Scheme 1, Table 2). Although the energy transfer and distribution in a domestic microwave oven is not controlled as in professional chemistry one, we found that the microwave-assisted reactions are more efficient, more convenient and cleaner.

A possible mechanism for explaining the formation of the (*E*)-bis-organochalcogen alkenes **2a–d** from phenyl acetylene is depicted in Scheme 2 and involves the intermediate **5**. This mechanism is similar to that reported recently to explain the synthesis of tris-phenylchalcogen alkenes by hydrochalcogenation of acetylenes.<sup>5</sup> A free-radical chain addition mechanism could also be involved. However, the fact that propargylic alcohols do not afford the respective bis-chalcogen alkenes suggests that the intermediates **6** and **7** are involved in the formation of **3** and **4**, respectively.<sup>2c</sup>

In conclusion, we have presented here a new methodology for the addition of chalcogenolate anions to propargylic alcohols and phenyl acetylene under solid

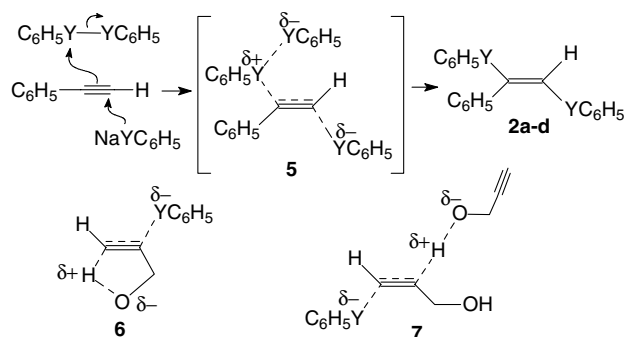
**Table 2.** Synthesis of bis-organochalcogen alkenes **2a–d** starting from phenylacetylene (**1d**) under solvent-free conditions

Entry	R <sup>1</sup> Y <sub>2</sub>	Products <b>2</b>	Method <sup>a</sup>	Time	Yield <sup>b</sup> (%)	Ratio <sup>c</sup> <i>E</i> : <i>Z</i>	$\delta_{\text{H}}$ vinyl (or CH <sub>3</sub> )	
							<i>E</i>	<i>Z</i>
1	C <sub>6</sub> H <sub>5</sub> Se) <sub>2</sub>		A	3 h	95	80:20	7.08	7.60
2	C <sub>6</sub> H <sub>5</sub> Se) <sub>2</sub>	<b>2a</b>	B	6 min	94	74:26		
3	C <sub>6</sub> H <sub>5</sub> Se) <sub>2</sub>	<b>2a</b>	C	6 min	22	—		
4	C <sub>6</sub> H <sub>5</sub> Se) <sub>2</sub>	<b>2a</b>	C	1.5 h	94	71:29		
5	C <sub>6</sub> H <sub>5</sub> Te) <sub>2</sub>		A	48 h	20	—	7.36	8.37
6	C <sub>6</sub> H <sub>5</sub> Te) <sub>2</sub>	<b>2b</b>	B	25 min	72	83:17		
7	C <sub>6</sub> H <sub>5</sub> Te) <sub>2</sub>	<b>2b</b>	C	18 h	75	82:18		
8	<i>p</i> -CH <sub>3</sub> C <sub>6</sub> H <sub>4</sub> Se) <sub>2</sub>		A	19 h	72	87:13	(2.26 and 2.30)	(2.22 and 2.33)
9	<i>p</i> -CH <sub>3</sub> C <sub>6</sub> H <sub>4</sub> Se) <sub>2</sub>	<b>2c</b>	B	35 min	85	85:15		
10	<i>p</i> -CH <sub>3</sub> C <sub>6</sub> H <sub>4</sub> Te) <sub>2</sub>		C	24 h	80	88:12	(2.31 and 2.32)	(2.26 and 2.35)
11	<i>p</i> -CH <sub>3</sub> C <sub>6</sub> H <sub>4</sub> Te) <sub>2</sub>	<b>2d</b>	B	30 min	75	85:15		

<sup>a</sup> Method A: The experiments were performed at room temperature. Method B: The experiments were performed at 548 W. Method C: The reaction mixture was heated at 60 °C using an oil bath.<sup>9</sup>

<sup>b</sup> Yields of pure products isolated by column chromatography (AcOEt/hexanes) and identified by mass spectrometry, <sup>1</sup>H, <sup>13</sup>C NMR.<sup>3,4</sup>

<sup>c</sup> Determined by GC of the crude reaction mixture and confirmed after isolation of the individual isomers.



Scheme 2.

supported catalyst. This improved, simple, fast and clean protocol eliminates the use of inert atmosphere and minimizes the organic solvent and energy demands, as well as, affords selectively mono- and bis-organochalcogen alkenes. Besides these advantages, the reaction time could be reduced from hours to a few minutes (when MW was employed), under milder conditions and with non-aqueous work-up.

### Acknowledgements

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- The solid supported catalysts were prepared by the following procedure: To a pestle mortar was added alumina (0.038 g of Al<sub>2</sub>O<sub>3</sub>, 90, 0.063–0.200 mm, Merck) and NaBH<sub>4</sub> (0.038 g). The mixture was stirred for 1 min and immediately used in the reaction.<sup>11</sup>
- General procedure for the synthesis of vinyl chalcogenides **3a–f** and **4a–f**. Method A: A mixture of propargyl alcohol **1a** (0.084 g; 1.5 mmol) and diphenyl diselenide (0.157 g; 0.5 mmol) was added to aluminum oxide impregnated with NaBH<sub>4</sub> (0.076 g). The mixture was stirred at room temperature. The reaction progress was followed by TLC, and after 46 h (see Table 1) the product was filtered off the aluminum oxide by washing with ethyl acetate (10 mL). The solvent was evaporated under reduced pressure and the residue was purified by column chromatography over silica gel (SiO<sub>2</sub>) eluting with hexane/ethyl acetate (90:10), yielding the product **3a** (0.121 g, 57%) and **4a** (0.040 g, 19%). (Z)-**3a**: <sup>1</sup>H NMR (200 MHz, CDCl<sub>3</sub>) δ (ppm) 7.43–7.54 (m, 2H); 7.22–7.27 (m, 3H); 6.58 (dt, *J* = 9.4 and 1.4 Hz, 1H); 6.19 (dt, *J* = 9.4 and 6.0 Hz, 1H); 4.24 (dd, *J* = 6.0 and 1.0 Hz, 2H); 3.02 (broad s, 1H); **4a**: 7.43–7.54 (m, 2H); 7.22–7.27 (m, 3H); 5.86 (s, 1H); 5.40 (s, 1H); 4.15 (s, 2H); 3.02 (broad s, 1H). Method B: The aforementioned whole mixture was previously stirred for 1 min and then irradiated with microwave (used a domestic Panasonic model Piccolo NN-S42BK, operating at 2.45 MHz) at 548 W<sup>12</sup> for 6–15 min (Table 1) and the product extracted and purified according to the described Method A. Method C: The procedure described in Method A was followed and the reaction mixture was stirred under heating at 60 °C (oil bath) for 22 h (Table 1).
- General procedure for the synthesis of bis-chalcogen alkenes **2a–d**. Method A: A mixture of phenyl acetylene **1d** (0.153 g; 1.5 mmol) and diphenyl diselenide (0.314 g; 1.0 mmol) was added to aluminum oxide impregnated with NaBH<sub>4</sub> (0.076 g).<sup>8</sup> The mixture was stirred at room temperature. The reaction progress was followed by TLC, and after 3 h (see Table 2) the product was filtered off the aluminum oxide by washing with ethyl acetate (10 mL). The solvent was evaporated under reduced pressure and the residue was purified by column chromatography over silica gel (SiO<sub>2</sub>) eluting with hexane/ethyl acetate (98:2), yielding the product **2a** (0.395 g, 95%, *E:Z* = 80:20). <sup>1</sup>H NMR (200 MHz, CDCl<sub>3</sub>) δ (ppm) (*E* + *Z*) 7.36–7.48 (m, 6H); 7.10–7.29 (m, 9H); 7.60 (s, 1H, *Z* isomer); 7.08 (s, 1H, *E* isomer).<sup>3e</sup>
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