

Article

# Green Hydroselenation of Aryl Alkynes: Divinyl Selenides as a Precursor of Resveratrol

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**Abstract:** A simple and efficient protocol to prepare divinyl selenides has been developed by the regio- and stereoselective addition of sodium selenide species to aryl alkynes. The nucleophilic species was generated in situ, from the reaction of elemental selenium with NaBH<sub>4</sub>, utilizing PEG-400 as the solvent. Several divinyl selenides were obtained in moderate to excellent yields with selectivity for the (*Z,Z*)-isomer by a one-step procedure that was carried out at 60 °C in short reaction times. The methodology was extended to tellurium, giving the desired divinyl tellurides in good yields. Furthermore, the Fe-catalyzed cross-coupling reaction of bis(3,5-dimethoxystyryl) selenide **3f** with (4-methoxyphenyl)magnesium bromide **5** afforded resveratrol trimethyl ether **6** in 57% yield.

**Keywords:** selenium; PEG-400; tellurium; resveratrol; chalcogen alkenes

## 1. Introduction

Chalcogen alkenes are attractive key intermediates in the synthesis of important compounds. They are useful synthons to access conjugated or isolated olefins with total control in the geometry of the double bond [1–5]. For instance, the iron- or nickel-catalyzed cross-coupling of divinyl chalcogenides with Grignard reagents [6], the direct coupling with terminal alkynes in the presence of a nickel/CuI catalyst [7], or similar transformations [8] are useful procedures to access functionalized alkenes. The synthesis of novel selenium heterocycles based on the reaction of selenium dichloride with divinyl sulfide [9–11] or divinyl selenide [12] was also reported.

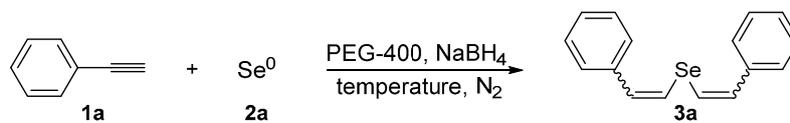
Divinyl selenides however, are less studied compared to synthetic intermediates, probably due to the limited number of general methods to prepare them in a selective way. They can be prepared by a stereoconservative three-step reaction of in situ generated vinyl selenide anions with (*E*)- or (*Z*)-bromo styrenes (Scheme 1A) [13]. Divinyl selenides of (*E,E*)-configuration were predominantly formed by the Wittig–Horner reaction of chalcogen diphosphonate derivatives with aldehydes [14–16] (Scheme 1B). Both approaches are very robust, despite the low atom efficiency and a high *E* factor [17]. A more atom-economic approach of preparing divinyl selenides and tellurides involves the electrophilic addition of chalcogen halides, such as selenium dichloride or dibromide and tellurium tetrachloride, to alkynes (Scheme 1C). In these reactions, however, halo-substituted products are obtained and a reduction step is necessary to prepare the halogen-free divinyl chalcogenides [18–22]. *Z,Z*-bis(acylvinyl) selenides were exclusively obtained in moderate yields by the reaction of sodium selenide with ethynyl



## 2. Results and Discussion

In our preliminary experiments, we chose phenylacetylene **1a** and selenium powder **2a** as standard starting materials to perform the optimization studies under a N<sub>2</sub> atmosphere and using PEG-400 as the solvent (Table 1). We evaluated the influence of temperature and the reaction time. Firstly, a mixture of selenium **2a** (0.5 mmol) and NaBH<sub>4</sub> (0.8 mmol) in PEG-400 (3.0 mL) was stirred at room temperature to generate in situ the nucleophilic selenium species. The selenium reduction was accompanied by a change in the color of the reaction mixture, from grey to colorless (30 min of stirring). After this time, phenylacetylene **1a** (1.0 mmol) was added in the reaction vessel and the desired product **3a** was obtained in 12% yield after 12 h at room temperature (Table 1, Entry 1). By increasing the temperature to 40 °C, the reaction proceeds smoothly and the desired product **3a** was obtained in 42% yield in 12 h (Table 1, Entry 2). The temperature had a positive influence in the reaction of the sodium selenide with phenyl acetylene, and a similar 40% yield of **3a** was obtained in 2 h at 60 °C (Table 1, Entry 3). Next, we investigated the reaction time and observed that 5 h gave the best result, with the desired divinyl selenide **3a** being isolated as a mixture of (*Z,Z*)- and (*Z,E*)-isomers (*Z,Z*:*Z,E* ratio of 80:20) in 92% yield (Table 1, Entries 4 and 5). An additional test was performed, setting a time of 5 h and increasing the temperature to 80 °C; however, the yield was lower than that under milder conditions (Table 1, Entry 6). Thus, analyzing the results showed in Table 1, we established the best reaction conditions as being the previous reaction of selenium **2a** (0.5 mmol) and NaBH<sub>4</sub> (0.8 mmol) in PEG-400 (3.0 mL) at 60 °C under N<sub>2</sub> for 30 min. Afterward, phenylacetylene **1a** (1.0 mmol) is added dropwise and the resulting mixture is stirred for additional 5 h at the same temperature.

Table 1. Optimization of the synthesis of divinyl selenide **3a**<sup>a</sup>.



Entry	Temperature	Time (h)	Yield (%) <sup>b</sup>
1	r.t.	12	12
2	40 °C	12	42
3	60 °C	2	40
4	60 °C	3	72
5	60 °C	5	92
6	80 °C	5	30

<sup>a</sup> Reactions performed in the presence of **1a** (1.0 mmol), **2a** (0.5 mmol), NaBH<sub>4</sub> (0.8 mmol) and solvent (3.0 mL) under N<sub>2</sub> atmosphere. <sup>b</sup> Yields are given for isolated product **3a**, which was obtained as a mixture of (*Z,Z*)- and (*Z,E*)-isomers.

In order to demonstrate the efficiency of this protocol, we attempted to apply the designed method to other aryl alkynes and the results are depicted in Table 2. A closer inspection of Table 2 reveals that our protocol worked well for a range of substrates, delivering products **3a–f** in good to excellent yields and high selectivity to the (*Z,Z*)-isomer. The reactions are sensitive to the electronic effect of the aromatic ring in the alkynes. The presence of strong electron-releasing group CH<sub>3</sub>O- in acetylenes **1c** and **1f** reduced the reactivity and a higher temperature (90 °C) was necessary to give good yields of the respective divinyl selenides **3c,f** (Table 2, Entries 3 and 6). This deactivating effect was less pronounced in 4-tolyl acetylene **1b**, which reacted under the standard conditions to afford the desired divinyl selenide **3b** after 5 h in 82% yield. In this example, a small amount of the (*E,E*)-isomer was detected in addition to (*Z,Z*)- and (*Z,E*)-ones (Table 2, Entry 2). The reaction is less affected by the presence of electron-withdrawing groups. 3,4-Dichlorophenyl acetylene **1e** afforded the respective (*Z,Z*)-divinyl selenide **3e** in 93% yield as the only isomer (Table 2, Entry 5), while 4-ethynylbenzonitrile **1d** produced **3d** in 74% yield as a mixture of (*Z,Z*)-, (*Z,E*)- and (*E,E*)-isomers in a 53:43:4 ratio (Table 2, Entry 4). In additional studies, the performance of the reaction using 1,1-dimethylpropargyl alcohol **1g**

and hept-1-yne **1h** was studied; however, there was no formation of the expected products and the starting materials were recovered (Table 2, Entries 7 and 8).

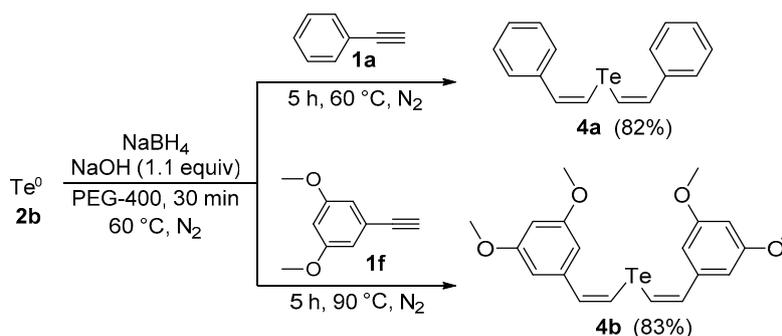
**Table 2.** Synthesis of divinyl selenides **3** by the hydroselenation of aryl alkynes **1**<sup>a</sup>.

Entry	Alkynes <b>1</b>	Product <b>3</b>	Yield (%) <sup>b</sup>	Ratio (Z,Z/E,E,E) <sup>c</sup>
1			92	80/20/00 <sup>c</sup>
2			82	71/15/14 <sup>d</sup>
3			77	77/23/00 <sup>d,e</sup>
4			74	53/43/04 <sup>c</sup>
5			93	100/00/00 <sup>c</sup>
6			78	80/20/00 <sup>c,e</sup>
7			nr	-
8			nr	-

<sup>a</sup> Reactions performed in the presence of aryl alkynes **1** (1.0 mmol), selenium **2a** (0.5 mmol), NaBH<sub>4</sub> (0.8 mmol), and PEG-400 (3.0 mL) under N<sub>2</sub> atmosphere. <sup>b</sup> Yields are given for isolated products **3a–f**. <sup>c</sup> Determined by <sup>1</sup>H-NMR of the purified product. <sup>d</sup> Determined by GC/MS of the purified product. <sup>e</sup> Reaction performed at 90 °C; nr = no reaction.

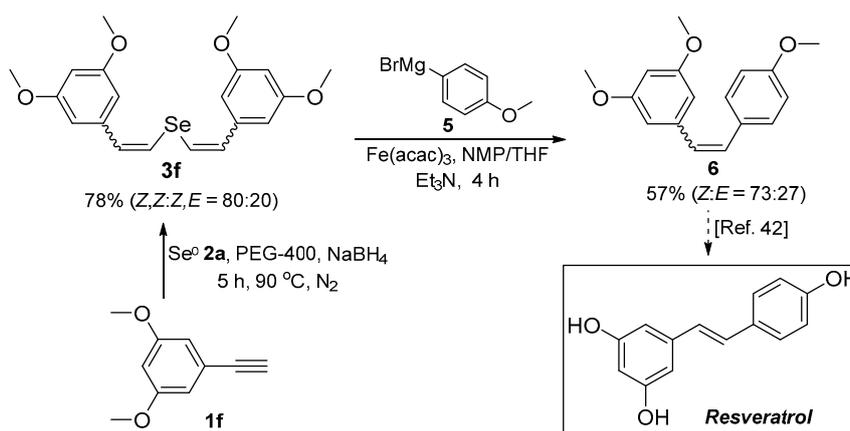
Afterward, we examined the possibility of using our protocol to prepare the divinyl tellurides analogues **4**. Firstly, we performed the reaction tellurium powder (0.5 mmol) with NaBH<sub>4</sub> (0.8 mmol)

in PEG-400 (3.0 mL) at 60 °C under N<sub>2</sub> atmosphere until consumption of the tellurium (30 min). Then, phenylacetylene **1a** (1.0 mmol) was added and the mixture was stirred under N<sub>2</sub> at the same temperature for an additional 5 h, affording the desired divinyl telluride **4a** in 40% yield (*Z,Z*-isomer, only). Interested in the excellent selectivity and aiming to improve the yield, the reaction was repeated in the presence of NaOH (1.1 equiv), similarly described by Tucci and co-workers in a closely related reaction [24], affording product **4a** in 82% yield after 5 h at 60 °C. By using the same strategy, bis(3,5-dimethoxystyryl) telluride **4b** was obtained in 83% yield from 3,5-dimethoxyphenylacetylene **1f** after 5 h at 90 °C (Scheme 2).



**Scheme 2.** Synthesis of divinyl tellurides by hydrotelluration of aryl alkynes.

In order to demonstrate the synthetic versatility of divinyl selenides, the Fe-catalyzed cross-coupling of bis(3,5-dimethoxystyryl) selenide **3f** with (4-methoxyphenyl)magnesium bromide **5** was investigated for the synthesis of resveratrol trimethyl ether **6**. Following the synthesis and purification of **3f**, it was reacted with Grignard's reagent **5** in the presence of catalytic Fe(acac)<sub>3</sub> at room temperature to afford, after 4 h, the expected resveratrol trimethyl ether **6** in 57% yield (Scheme 3). The reaction was stereoconservative, with compound **6** being obtained as a *Z/E* mixture (*Z/E* ratio of 73:27). The sequence shown in Scheme 3 is a straightforward way to polymethoxylated stilbenes, which are themselves biologically active and pharmaceutically relevant precursors (Scheme 3).



**Scheme 3.** Synthesis of resveratrol trimethyl ether **6**.

### 3. Materials and Methods

#### 3.1. General Information

The reactions were monitored by thin layer chromatography (TLC), which were performed using Merck (Merck, Darmstadt, Germany) silica gel (60 F<sub>254</sub>), with a 0.25 mm thickness. For visualization, TLC plates were either exposed to UV light, or stained with iodine vapor or in a 5% vanillin solution

in 10% aqueous H<sub>2</sub>SO<sub>4</sub> and heat. Column chromatography was performed using Merck Silica Gel (230–400 mesh). High-resolution mass spectra (HRMS) were recorded in positive ion mode (ESI) using a Bruker microQTOF spectrometer (Bruker, Billerica, MA, USA). Low-resolution mass spectra were obtained with a Shimadzu GC-MS-QP2010 mass spectrometer (Shimadzu Corporation, Kyoto, Japan). NMR spectra were recorded with Bruker DPX (Bruker). (<sup>1</sup>H-NMR = 400 and 500 MHz; <sup>13</sup>C-NMR = 100 and 126 MHz) instruments using CDCl<sub>3</sub> as solvent and calibrated using tetramethylsilane (TMS) as internal standard. Coupling constants (*J*) were reported in Hertz and chemical shifts ( $\delta$ ) in ppm. The NMR spectra are found in the Supplementary Materials. The reagents (substituted alkynes, sodium tetrahydroborate, elemental chalcogen) and PEG-400 were purchased from Sigma-Aldrich (Sigma-Aldrich, St. Louis, MO, USA).

### 3.2. General Procedure for the Preparation of Divinyl Selenides 3a–f

In a two necked round bottomed flask under nitrogen atmosphere, sodium selenide was generated by reaction of elemental selenium (Se<sup>0</sup>, 0.5 mmol) with sodium tetrahydroborate (0.8 mmol, 0.030 g) in PEG-400 (3.0 mL) at 60 °C. After 30 min, a colorless solution was obtained and the corresponding alkyne was added (1.0 mmol). After stirring for 5 h at 60 or 90 °C, the reaction mixture was quenched with water (10.0 mL) and extracted with ethyl acetate (3 × 15.0 mL). The combined organic layers were dried over MgSO<sub>4</sub>, filtered and concentrated under vacuum. The residue was purified by column chromatography over silica gel eluting with hexanes to yield the products as an inseparable mixture of isomers. All compounds were properly characterized by MS, <sup>1</sup>H-NMR, and <sup>13</sup>C-NMR, and the isomers ratios were determined by GC and NMR.

*Bis-(Z,Z)-styryl selenide 3a*: Yield: 0.132 g (92%) [13]; Orange solid; <sup>1</sup>H-NMR (CDCl<sub>3</sub>, 500 MHz)  $\delta$  (ppm): 7.20–7.38 (m, 10H), 6.92 (d, *J* = 10.4 Hz, 2H), 6.64 (d, *J* = 10.4 Hz, 2H). MS: *m/z* (rel. int.) 286 (M<sup>+</sup>, 22.2), 205 (100), 102 (36.7), 91 (42.8), 77 (50.4). *Z,E-3a*: [13] <sup>1</sup>H-NMR (CDCl<sub>3</sub>, 500 MHz)  $\delta$  (ppm): 7.14 (d, *J* = 10.4 Hz, 1H), 7.08 (d, *J* = 15.4 Hz, 1H), 6.85 (d, *J* = 15.4 Hz, 1H), 6.75 (d, *J* = 10.4 Hz, 1H), other peaks were overlapped with those of *Z,Z-3a*. MS: *m/z* (rel. int.) 286 (M<sup>+</sup>, 25.0), 205 (100), 102 (35.3), 91 (41.4), 77 (44.1). <sup>13</sup>C-NMR (125 MHz, CDCl<sub>3</sub>)  $\delta$  (ppm): (*Z,Z* + *Z,E*) 137.0, 136.7, 134.7, 134.1, 130.5, 130.2, 128.61, 128.57, 128.4, 128.2, 127.9, 127.6, 127.3, 126.3, 125.9, 123.4, 121.3, 119.5. HRMS (ESI): *m/z* calcd. for C<sub>16</sub>H<sub>14</sub>Se [M + H]<sup>+</sup>: 287.0339, found: 287.0328.

*Bis-(Z,Z)-4-methylstyryl selenide 3b*: Yield: 0.129 g (82%); Orange solid; <sup>1</sup>H-NMR (CDCl<sub>3</sub>, 400 MHz)  $\delta$  (ppm): 7.10–7.50 (m, 8H), 6.91 (d, *J* = 10.4 Hz, 2H), 6.60 (d, *J* = 10.4 Hz, 2H), 2.34 (s, 6H). MS: *m/z* (rel. int.) 314 (M<sup>+</sup>, 38.8), 219 (100), 204 (25.9), 102 (20.4), 91 (32.4), 77 (6.6). *Z,E-3b*: <sup>1</sup>H-NMR (CDCl<sub>3</sub>, 400 MHz)  $\delta$  (ppm): 6.96 (d, *J* = 10.3 Hz, 1H), 6.86 (d, *J* = 15.6 Hz, 1H), 6.76 (d, *J* = 15.6 Hz, 1H), 6.69 (d, *J* = 10.3 Hz, 1H), other peaks were overlapped with those of *E,E* and *Z,Z-3b*. MS: *m/z* (rel. int.) 314 (M<sup>+</sup>, 32.6), 219 (100), 204 (23.7), 102 (18.6), 91 (28.0), 77 (6.2). *E,E-3b*: [15] <sup>1</sup>H-NMR (CDCl<sub>3</sub>, 400 MHz)  $\delta$  (ppm): 7.04 (d, *J* = 15.8 Hz, 2H), 6.84 (d, *J* = 15.8 Hz, 2H), other peaks were overlapped with those of *Z,E* and *Z,Z-3b*. MS: *m/z* (rel. int.) 314 (M<sup>+</sup>, 39.3), 219 (100), 204 (25.0), 102 (17.4), 91 (29.4), 77 (7.0). <sup>13</sup>C-NMR (CDCl<sub>3</sub>, 100 MHz)  $\delta$  (ppm): (*Z,Z* + *Z,E* + *E,E*) 138.0, 137.5, 137.13, 137.11, 134.31, 134.29, 134.25, 130.4, 130.1, 129.34, 129.3, 129.1, 128.22, 128.17, 127.2, 126.5, 126.3, 126.1, 125.91, 125.87, 122.5, 120.5, 118.2, 116.6, 21.3, 21.2. HRMS (ESI): *m/z* calcd. for C<sub>18</sub>H<sub>18</sub>Se [M + H]<sup>+</sup>: 315.0652, found: 315.0648.

*Bis-(Z,Z)-4-methoxystyryl selenide 3c*: Yield: 0.133 g (77%); Orange solid; <sup>1</sup>H-NMR (CDCl<sub>3</sub>, 500 MHz)  $\delta$  (ppm): 6.72–7.34 (m, 10H), 6.52 (d, *J* = 9.9 Hz, 2H), 3.80 (s, 6H). MS: *m/z* (rel. int.) 346 (M<sup>+</sup>, 13.9), 266 (100), 235 (36.7), 77 (10.2). *Z,E-3c*: <sup>1</sup>H-NMR (CDCl<sub>3</sub>, 500 MHz)  $\delta$  (ppm): 6.61 (d, *J* = 10.2 Hz, 1H), 3.78 (s, 6H), other peaks were overlapped with those of *Z,Z-3c*. MS: *m/z* (rel. int.) 346 (M<sup>+</sup>, 14.8), 266 (100), 235 (35.6), 77 (10.7). <sup>13</sup>C-NMR (CDCl<sub>3</sub>, 100 MHz)  $\delta$  (ppm): (*Z,Z* + *Z,E*) 159.2, 158.7, 134.6, 134.2, 129.9, 129.8, 129.7, 129.63, 129.6, 127.2, 127.1, 121.0, 119.2, 116.5, 114.2, 114.0, 113.8, 113.7, 55.2. HRMS (ESI): *m/z* calcd. for C<sub>18</sub>H<sub>18</sub>O<sub>2</sub>Se [M + H]<sup>+</sup>: 347.0550, found: 347.0545.



*Bis-(Z,Z)-4-cyanostyryl selenide 3d*: Yield: 0.124 g (74%); Orange solid;  $^1\text{H-NMR}$  (DMSO- $d_6$ , 400 MHz)  $\delta$  (ppm): 6.68–7.03 (m, 8H), 6.47 (d,  $J = 10.5$  Hz, 2H), 6.30 (d,  $J = 10.5$  Hz, 2H). *Z,E-3d*:  $^1\text{H-NMR}$  (DMSO- $d_6$ , 400 MHz)  $\delta$  (ppm): 6.57 (d,  $J = 10.5$  Hz, 1H), 6.52 (d,  $J = 15.1$  Hz, 1H), 6.45 (d,  $J = 15.1$  Hz, 1H), 6.19 (d,  $J = 10.5$  Hz, 1H), other peaks were overlapped with those of *E,E* and *Z,E-3d*. *E,E-3d*:  $^1\text{H-NMR}$  (DMSO- $d_6$ , 400 MHz)  $\delta$  (ppm): 6.08 (d,  $J = 15.6$  Hz, 2H), other peaks were overlapped with those of *Z,Z* and *Z,E-3d*.  $^{13}\text{C-NMR}$  (DMSO- $d_6$ , 100 MHz)  $\delta$  (ppm): (*Z,Z* + *Z,E* + *E,E*) 141.1, 141.0, 140.6, 132.8, 132.4, 132.33, 132.26, 130.7, 130.5, 128.9, 128.8, 128.7, 128.4, 127.2, 127.1, 126.8, 126.42, 126.36, 125.7, 125.5, 118.5, 118.4, 110.2, 109.9, 109.6, 109.4, 109.38. MS:  $m/z$  (rel. int.) 336 ( $\text{M}^+$ , 19.0), 207 (100), 191 (13.8), 127 (40.4), 102 (9.0), 77 (11.6). HRMS (ESI):  $m/z$  calcd. for  $\text{C}_{18}\text{H}_{12}\text{N}_2\text{Se}$  [ $\text{M}$ ] $^+$ : 336.0166, found: 336.0150.

*Bis-(Z,Z)-3,4-dichlorostyryl selenide 3e*: Yield: 0.196 g (93%). Yellowish solid; m.p.: 152–155 °C.  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ , 400 MHz)  $\delta$  (ppm): 7.43–7.45 (m, 4H), 7.21 (dd,  $J = 8.2$  and 2.1 Hz, 2H), 6.86 (d,  $J = 10.4$  Hz, 2H), 6.73 (d,  $J = 10.4$  Hz, 2H).  $^{13}\text{C-NMR}$  ( $\text{CDCl}_3$ , 100 MHz)  $\delta$  (ppm):  $\delta$  136.8, 132.7, 131.4, 130.5, 130.1, 128.6, 127.2, 124.9. MS:  $m/z$  (rel. int.) 422 ( $\text{M}^+$ , 6.2), 207 (83.8), 40 (100). HRMS (ESI):  $m/z$  calcd. for  $\text{C}_{16}\text{H}_{10}\text{Cl}_4\text{Se}$  [ $\text{M} + \text{H}$ ] $^+$ : 422.8780, found: 422.8758.

*Bis-(Z,Z)-3,5-dimethoxystyryl selenide 3f*: Yield: 0.158 g (78%); Yellowish solid;  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ , 500 MHz)  $\delta$  (ppm): 6.88 (d,  $J = 10.3$  Hz, 2H), 6.67 (d,  $J = 10.3$  Hz, 2H), 6.54 (d,  $J = 2.3$  Hz, 4H), 6.38 (t,  $J = 2.3$  Hz, 2H), 3.79 (s, 12H).  $^{13}\text{C-NMR}$  ( $\text{CDCl}_3$ , 125 MHz)  $\delta$  (ppm): 160.7, 138.8, 130.2, 124.0, 106.1, 100.0, 55.3. *Z,E-3f*:  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ , 500 MHz)  $\delta$  (ppm): 7.11 (d,  $J = 15.7$  Hz, 1H), 6.93 (d,  $J = 10.3$  Hz, 1H), 6.79 (d,  $J = 15.7$  Hz, 1H), 6.77 (d,  $J = 10.3$  Hz, 1H), 6.48 (d,  $J = 2.3$  Hz, 4H), 6.34–6.35 (m, 2H), 3.81 (s, 12H). MS:  $m/z$  (rel. int.) 406 ( $\text{M}^+$ , 2.8), 325 (100), 207 (45.9), 77 (15.0). HRMS (ESI):  $m/z$  calcd. for  $\text{C}_{20}\text{H}_{22}\text{O}_4\text{Se}$  [ $\text{M} + \text{H}$ ] $^+$ : 407.0762, found: 407.0740.

### 3.3. General Procedure for the Preparation of Divinyl Tellurides **4a,b**

In a two-necked round bottomed flask under nitrogen atmosphere, sodium telluride was generated by reaction of elemental tellurium ( $\text{Te}^0$ , 0.5 mmol) with sodium tetrahydroborate (0.8 mmol, 0.030 g) and NaOH (0.55 mmol, 0.022 g) in PEG-400 (3.0 mL) at 60 °C. After 30 min, a violet solution was obtained and the corresponding alkyne was added (1.0 mmol). After stirring for 5 h at 60 or 90 °C, the reaction mixture was quenched with water (10.0 mL) and extracted with ethyl acetate (3  $\times$  15.0 mL). The combined organic layers were dried over  $\text{MgSO}_4$ , filtered, and concentrated under vacuum. The residue was purified by column chromatography over silica gel eluting with hexanes to yield the products. All compounds were properly characterized by MS,  $^1\text{H-NMR}$ , and  $^{13}\text{C-NMR}$ .

*Bis-(Z,Z)-styryl telluride 4a*: Yield: 0.138 g (82%); White solid; m.p.: 44–46 °C (Lit. [26]: 46–47 °C).  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ , 400 MHz)  $\delta$  (ppm): 7.43 (d,  $J = 10.6$  Hz, 2H), 7.33–7.36 (m, 4H), 7.22–7.24 (m, 6H), 6.99 (d,  $J = 10.6$  Hz, 2H).  $^{13}\text{C-NMR}$  ( $\text{CDCl}_3$ , 100 MHz)  $\delta$  (ppm): 138.8, 137.3, 128.4, 127.6, 127.4, 108.9. MS:  $m/z$  (rel. int.) 336 ( $\text{M}^+$ , 17.2), 206 (100), 91 (71.4), 77(67.1).

*Bis-(Z,Z)-3,5-dimethoxystyryl telluride 4b*: Yield: 0.189 g (83%); Orange solid; m.p.: 76–77 °C.  $^1\text{H-NMR}$  (DMSO- $d_6$ , 400 MHz)  $\delta$  (ppm): 7.45 (d,  $J = 10.5$  Hz, 2H), 7.23 (d,  $J = 10.5$  Hz, 2H), 6.42–6.47 (m, 6H), 3.76 (s, 12H).  $^{13}\text{C-NMR}$  (DMSO- $d_6$ , 100 MHz)  $\delta$  (ppm): 160.6, 140.5, 136.9, 110.1, 105.0, 99.6, 55.2. MS:  $m/z$  (rel. int.) 456 ( $\text{M}^+$ , 13.7), 325 (100), 175 (34.0). HRMS (ESI):  $m/z$  calcd. for  $\text{C}_{20}\text{H}_{22}\text{O}_4\text{Te}$  [ $\text{M} + \text{H}$ ] $^+$ : 457.0659, found: 457.0662.

### 3.4. Preparation of 3,4',5-Trimethoxystilbene **6**

To a two-necked 100 mL round bottomed flask under nitrogen, the dry solvent (NMP/THF 1:3, 20.0 mL), bis(3,5-dimethoxystyryl) selenide **3f** (0.406 g, 1 mmol),  $\text{Et}_3\text{N}$  (2.5 mL) and  $\text{Fe}(\text{acac})_3$  (71 mg, 20 mol %) was added. The mixture was stirred at room temperature, and after 15 min a solution of the Grignard reagent from 1-bromo-4-methoxybenzene (**5**, 10 mmol; 10.0 mL of a 1 mol/L sol. in THF) was added dropwise. The reactions were monitored by TLC until total disappearance of the starting material **3f**. After completion of the reaction, aqueous sat.  $\text{NH}_4\text{Cl}$  (15.0 mL) was added and the reaction

mixture was extracted with ethyl acetate (3 × 20.0 mL), the organic layer was washed with water and dried over MgSO<sub>4</sub>. After filtration, the solvent was removed under reduced pressure and the residue was purified by column chromatography on silica gel (ethyl acetate/hexanes, 10:90).

**3,4',5-Trimethoxystilbene 6:** Yield: 0.155 g (57%) [42]; Whitish oil; **Z-6:** <sup>1</sup>H-NMR (CDCl<sub>3</sub>, 400 MHz) δ (ppm): 7.11 (d, *J* = 8.7 Hz, 2H), 6.66 (d, *J* = 8.7 Hz, 2H), 6.42 (d, *J* = 12.0 Hz, 1H), 6.343 (d, *J* = 2.3 Hz, 2H), 6.337 (d, *J* = 12.0 Hz, 1H), 6.22 (t, *J* = 2.3 Hz, 1H), 3.66 (s, 3H), 3.56 (s, 6H). MS: *m/z* (rel. int.) 270 (M<sup>+</sup>, 100), 239 (23.6), 224 (15.6), 196 (7.9), 181 (4.9), 152 (7.8), 141 (4.7), 115 (6.0), 102 (1.2) 76 (2.9). **E-6:** <sup>1</sup>H-NMR (CDCl<sub>3</sub>, 400 MHz) δ (ppm): 7.33 (d, *J* = 8.8 Hz, 2H), 6.94 (d, *J* = 16.2 Hz, 1H), 6.80 (d, *J* = 16.2 Hz, 1H), 6.78 (d, *J* = 8.8 Hz, 2H), 6.55 (d, *J* = 2.3 Hz, 2H), 6.28 (t, *J* = 2.3 Hz, 1H), 3.71 (s, 6H), 3.70 (s, 3H). MS: *m/z* (rel. int.) 270 (M<sup>+</sup>, 100), 239 (21.3), 224 (10.8), 196 (6.5), 181 (4.1), 152 (6.0), 141 (3.5), 115 (4.2), 102 (0.9) 76 (2.4). <sup>13</sup>C-NMR (CDCl<sub>3</sub>, 100 MHz) δ (ppm): (*Z* + *E*) 160.9, 160.5, 159.3, 158.7, 139.6, 139.4, 130.2, 130.1, 129.8, 129.5, 128.65, 128.60, 127.7, 126.5, 114.1, 113.4, 106.5, 104.3, 99.8, 99.5, 55.22, 55.18, 55.1.

#### 4. Conclusions

An efficient methodology to prepare divinyl selenides from elemental selenium and arylalkynes was developed. The nucleophilic species of selenium was generated in situ from elemental selenium and NaBH<sub>4</sub>/PEG-400. The reactions proceeded at a gentle heating of 60 °C for only 5 h, affording the corresponding divinyl selenides in good to excellent yields with high selectivity to the *Z,Z*-isomer. The same strategy was used to prepare (*Z,Z*)-divinyl tellurides analogues from elemental tellurium, but good results were obtained only when NaOH was present in the reaction media. Divinyl selenides with the appropriate substitution pattern was used in a Fe-catalyzed cross-coupling reaction with a Grignard reagent to afford 3,4',5-trimethoxystilbene in moderate yield. Thus, this procedure could be used to access valuable polymethoxylated stilbenes.

**Supplementary Materials:** NMR spectra of synthesized compounds are available online.

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**Sample Availability:** Samples of the compounds **3**, **4** and **6** are available from the authors.



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