Highly Stereoselective One-Pot Procedure to Prepare Unsymmetrical Bis- and Tris-chalcogenide Alkenes via Addition of Chalcogens to Alkynes

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We present here the reaction of unsymmetrical diorganoyl dichalcogenides (RSe−SR[1]) with terminal alkynes under catalyst-free conditions, by a one-pot procedure, to prepare bis- and tris-chalcogenide alkenes selectively, avoiding the previous preparation of chalcogen alkynes. The reaction proceeded cleanly under mild reaction conditions, and the addition of unsymmetrical dichalcogenides to alkynes occurred stereoselectively to give exclusively the corresponding *Z* isomers.

Introduction

In view of the fact that many biologically active compounds have the structure of substituted alkenes, the stereoselective synthesis of this function is an important goal in organic chemistry and is still being actively explored. In the last few decades, there has been remarkable interest in the synthesis of chalcogenide alkenes and their synthetic application in the development of methodologies for the synthesis of substituted alkenes.[1] There are several reasons for this, which include a widely varied synthetic organochemical potential and the fact that the chalcogen atom exercises a stabilizing effect on neighboring positive as well as negative charges. This makes the double bond in vinylic chalcogenides responsive toward both nucleophilic and electrophilic attack, an extremely useful feature for organic synthetic purposes.[2]

Organoselenium compounds have become attractive synthetic targets because of their chemo-, regio-, and stereoselective reactions and their useful biological activities.[3] Among organoselenium compounds the vinylic selenides play an important role in organic synthesis. Although various methods are mentioned for the preparation of vinylic selenides, a more useful procedure has centered on the nucleophilic or electrophilic organoselenium addition to terminal or internal alkynes.[4]

In addition to organoselenium, the scope and application of organosulfur chemistry has increased tremendously since sulfur-containing groups serve as an important auxiliary function in synthetic sequences. Most of the synthetic transformations using organosulfur compounds have involved the use of vinylic sulfides.[5] Many procedures for the preparation of vinyl sulfides have been developed.[6] In the course of our study on the preparation of vinyl chalcogenides and their application in organic synthesis, we have reported the introduction of two identical organochalcogen groups in the double bond.[7] In view of the fact that the organosulfur and organoselenium groups present a different reactivity, we became interested in the synthesis of bis- (**1**) and tris-chalcogenide alkenes (**2**). The challenge of this procedure is to build vinylic systems with two different organochalcogen groups in the double bond, which may allow us to use, efficiently and selectively, widely known reactions for these compounds.

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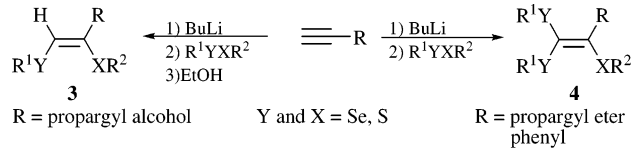
Results and Discussion

Since our initial studies have focused on the development of an optimum set of reaction conditions, we have initially chosen prop-2-yn-1-ol and unsymetrical diorganoyl dichalcogenides as standard starting materials (Scheme 1). In this way, *n*-butyllithium (3 mmol) was added to a solution of terminal alkyne (1mmol) and THF (2 mL), at 0 °C. After 30 min at room temperature, diorganoyl dichalcogenide (1.2 mmol) was added and the reaction was kept at room temperature for 3 h. After that, EtOH (0.5 mL) was added and the mixture was heated at 74 °C for 12 h. To demonstrate the efficiency of this reaction, we explored the generality of our method extending the conditions to various propargyl alcohols as well as different diorganoyl dichalcogenides, and the results are summarized in Table 1.

Scheme 1. Preparation of Bis- and Tris-chalcogene Alkenes



Analyzing Table 1 we observe that the reaction worked well for a variety of propargylic alcohols. Both hindered and nonhindered propargyl alcohols gave the desired vinylic products in good yields. A closer inspection of the results revealed that the reaction is not sensitive to the nature of functional groups present in the unsymmetrical diorganoyl dichalcogenide. Alkyl, unsubstituted aryl groups, and substituted aryl groups bonded to both sulfur and selenium atoms led to corresponding products in good yields. A plausible mechanism for the formation of the bis-chalcogenide alkenes **3a**−**m** is shown in Scheme 2. We believe that (a) the removal of acid hydrogens with *n*-BuLi from propargyl alcohol gave the lithium intermediate **a** and the reaction of **a** with unsymmetrical dichalcogenides afforded the species **b**, (b) the addition of EtOH led to the protonation of the intermediate **b** to give the acetylenic chalcogenide **c**, and (c) starting the reflux led to the addition of the chalcogenate anion onto the triple bond of the acetylenic chalcogenide **c**, and the subsequent trapping of the vinyl anion with a proton from the hydroxyl group, according to transition state **d**, leads to the desired vinyl compounds (Scheme 2). Although the intermediate

Scheme 2. Proposed Mechanism of Formation of Products 3a−n

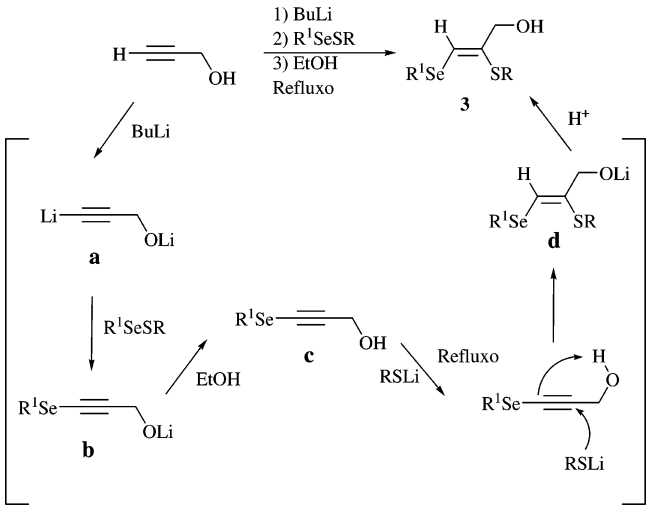
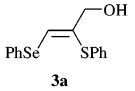
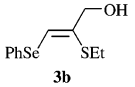
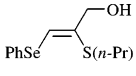
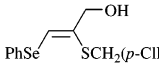
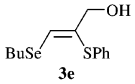
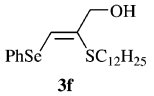
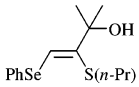
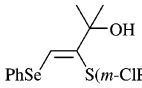
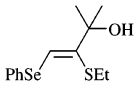
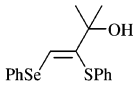
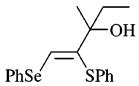
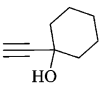
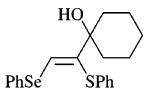
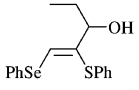
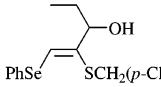
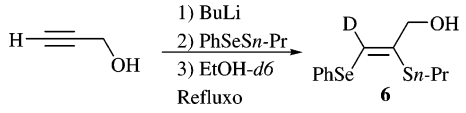


Table 1. Bis-chalcogene Alkenes Prepared from Alkynes and Unsymmetrical Diorganoyl Dichalcogenides

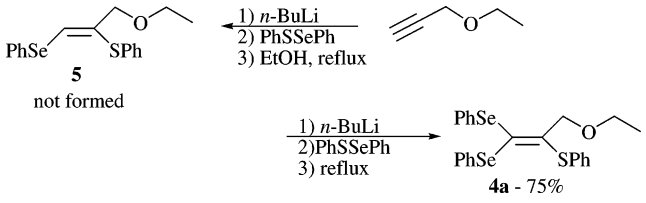
Entry	Alkyne	unsymmetrical chalcogenides	vinylic chalcogenides	Yield (%)
1		PhSeSPh	 **3a**	80
2		PhSeSEt	 **3b**	75
3		PhSeS(*n*-Pr)	 **3c**	80
4		$PhSeSCH_2$(*p*-ClPh)	 **3d**	60
5		BuSeSPh	 **3e**	82
6		$PhSeSC_{12}H_{25}$	 **3f**	64
7		PhSeS(*n*-Pr)	 **3g**	62
8		PhSeS(*m*-ClPh)	 **3h**	59
9		PhSeSEt	 **3i**	75
10		PhSeSPh	 **3j**	55
11		PhSeSPh	 **3k**	79
12		PhSeSPh	 **3l**	87
13		PhSeSPh	 **3m**	95
14		$PhSeSCH_2$(*p*-ClPh)	 **3n**	82

b could not be isolated from this reaction, several experimental data support the mechanism described in Scheme 2. First, when the reaction was stopped before starting the reflux (3 h at room temperature), a careful NMR analysis revealed the presence of

Scheme 3. Addition of Unsymmetrical Dichalcogenides Using EtOH-d_6 as Solvent



Scheme 4. Preparation of Tris-chalcogene Alkenes



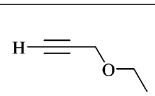
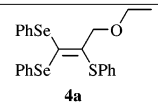
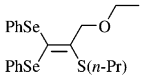
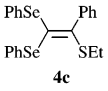
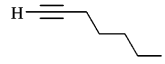
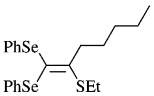
acetylenic selenide **c** as the major product. Second, when we carried out the addition of unsymmetrical dichalcogenides to prop-1-yn-3-ol in EtOH-d_6, vinylic deuterated **6** was isolated (Scheme 3).

Third, when this reaction condition was repeated with unsymmetrical chalcogenide and propargyl ether, without an acidic proton in the hydroxyl group, tris-chalcogen alkene **4** was obtained, instead of bis-phenylthio alkene **5**, even when using EtOH, a protic solvent (Scheme 4). Finally, the NOESY NMR experiment of compound **3a** showed only a correlation between the vinylic hydrogen and the methylene hydrogen bonded to the hydroxyl group. There was no correlation between the vinylic hydrogen and methylene hydrogen bonded to the sulfur atom. These experiments have shown that the addition of dichalcogenides to alkynes occurs stereoselectively to give exclusively the corresponding Z isomers (for NOESY NMR experiment, see the Supporting Information). These results strongly suggest that the addition of unsymmetrical dichalcogenides across the triple bond follows an anti-pathway addition, with the effective participation of the hydroxyl group from propargyl alcohols, as a proton source.

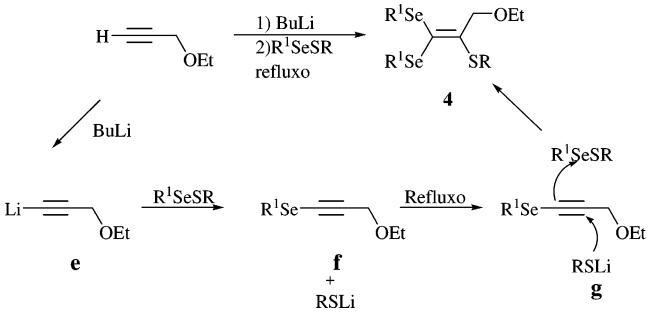
In an attempt to obtain other tris-chalcogen alkenes in good yields, a variety of conditions were investigated, including temperature, solvent, stoichiometry of alkynes, and unsymmetrical chalcogenides. Thus, the careful analysis of the optimized reactions revealed that the general synthetic procedure for the reaction is as follows: *n*-butyllithium (1.1 mmol) was added to a solution of alkyne (1 mmol) and THF (2 mL), at 0 °C. The resulting solution was stirred for 30 min at room temperature. After that, unsymmetrical dichalcogenide was added and the mixture was heated at 74 °C for 12 h. Next, we extended this condition to different alkynes without free hydrogen from the hydroxyl group, and the results are summarized in Table 2.

The results in Table 2 show that the reaction worked well with protected propargylic alcohols and phenylacetylene and was not sensitive to the nature of the unsymmetrical diorganoyl dichalcogenide (Table 2, entries 1−3). Concerning the structure of the alkynes, we found some limitations in this methodology. For example, no reaction was observed with alkynes bearing an alkyl group (Table 2, entry 4). The reaction pathways leading to tris-chalcogen alkene products **4** seem to depend on the amount of unsymmetrical dichalcogenides present in the reaction (1.2 and 2.2 mmol of dichalcogenides gave poor yields) and the absence of the acidic proton at the hydroxyl group in the structure of the alkynes. Thus, the removal of an acid hydrogen with *n*-BuLi from alkynes gave lithium intermediate **e**, and the reaction of this intermediate with dichalcogenide afforded acetylenic chalcogenide **f** together with lithium chalcogenate.

Table 2. Tris-chalcogenide Alkynes Prepared from Alkynes and Unsymmetrical Dichalcogenides

Entry	Alkyne	unsymmetrical chalcogenides	vinylic chalcogenides	Yield (%)
1		PhSeSPh	 **4a**	75
2		PhSeS(*n*-Pr)	 **4a**	74
3		PhSeSEt	 **4c**	70
4		PhSeSEt	 **4d**	N.R.

Scheme 5. Proposed Mechanism of Formation of Products 4a−d



Starting the reflux led to the addition of the chalcogenate anion onto the triple bond of acetylenic chalcogenide **f**, with concomitant attack on the dichalcogenides, according to intermediate **g**, leading to the desired vinyl chalcogenide **4** (Scheme 5).

Conclusion

In summary, we have presented here a highly selective and efficient introduction of two different chalcogen groups in alkynes by a one-pot procedure, avoiding the previous preparation of chalcogen alkynes. We observed that the selectivity control was governed by the effective participation of the hydroxyl group from propargyl alcohols. In addition, bis-vinylic chalcogenides were exclusively obtained with propargyl alcohols containing an acidic proton at the hydroxyl group. Conversely, alkynes with no potentially acidic protons at the propargyl positions gave exclusively tris-vinylic chalcogenide. The pharmacological activity of these compounds is under study in our laboratory.

Experimental Section

Instrumentation. Proton nuclear magnetic resonance spectra (^{1}H NMR) were obtained at 400 MHz. Spectra were recorded in $CDCl_3$ solutions. Chemical shifts are reported in ppm, referenced to the solvent peak of $CDCl_3$ or tetramethylsilane (TMS) as the external reference. Data are reported as follows: chemical shift (δ), multiplicity, coupling constant (J) in hertz, and integrated intensity. Carbon-13 nuclear magnetic resonance spectra (^{13}C NMR) were obtained at 100 MHz. Spectra were recorded in $CDCl_3$ solutions. Chemical shifts are reported in ppm, referenced to the solvent peak of $CDCl_3$. Abbreviations to denote the multiplicity of a particular

signal are s (singlet), d (doublet), t (triplet), q (quartet), quint (quintet), sex (sextet), and m (multiplet). High-resolution mass spectra were recorded on a double-focusing magnetic sector mass spectrometer using EI at 70 eV. Mass spectra were recorded in electron impact mode, and chemical ionization was in the positive ion mode. Reagents and solvents were handled using standard syringe techniques. Temperatures above room temperature were maintained by use of a mineral oil bath with an electrically heated coil connected to a controller.

Column chromatography was performed using silica gel (230−400 mesh) following the methods described by Still.[8] Thin-layer chromatography (TLC) was performed using silica gel GF_{254}, 0.25 mm thickness. For visualization, TLC plates were either placed under ultraviolet light or stained with iodine vapor or acidic vanillin.

Materials and Methods. General Procedure for the Preparation of the Unsymmetrical Bis-chalcogenide Alkenes. *n*-Butyllithium (1.91 mL of a 1.567 M solution in hexane, 3 mmol) was added, under argon, to a solution of alkyne (1 mmol) in THF (2 mL) previously cooled at 0 °C. The resulting solution was stirred for 30 min at room temperature. After this time, the mixture was cooled at 0 °C and the dichalcogenide (1.2 mmol) in THF (1 mL) was added. The reaction was warmed at room temperature, stirred for 3 h, and then treated with ethanol (0.5 mL). The mixture was then heated at reflux for 12 h. After this time, the mixture was cooled at room temperature, diluted with ethyl acetate (20 mL), and washed with brine (2 × 20 mL). The organic phase was separated, dried over $MgSO_4$, and concentrated under vacuum. The residue was purified by flash chromatography and eluted with hexane/ethyl acetate (80:20).

(*Z*)-3-(Phenylselenyl)-2-(phenylthio)prop-2-en-1-ol (3a). Yield: 0.257 g (80%). ^{1}H NMR, $CDCl_3$, 200 MHz, δ (ppm): 7.59−7.54 (m, 2H), 7.35−7.17 (m, 9H), 4.09 (s, 2H), 2.24 (s, 1H). ^{13}C NMR, $CDCl_3$, 100 MHz, δ (ppm): 135.57, 133.58, 133.05, 132.18, 130.79, 129.57, 129.25, 129.12, 127.74, 126.89, 65.63. MS (EI, 70 eV) *m*/*z* (relative intensity): 320 (100), 303 (77), 226 (33), 156 (49), 147 (22), 109 (48), 38 (15). HRMS: calcd for $C_{15}H_{14}OSSe$ 321.9930, found 321.9934. Anal. (%) Calcd for $C_{15}H_{14}OSSe$: C 56.07, H 4.39. Found: C 56.37, H 4.61.

(*Z*)-2-(Ethylthio)-3-(phenylselenyl)prop-2-en-1-ol (3b). Yield: 0.204 g (75%). ^{1}H NMR, $CDCl_3$, 200 MHz, δ (ppm): 7.57−7.52 (m, 2H), 7.30−7.27 (m, 3H), 7.00 (s, 1H), 4.20 (s, 2H), 2.82 (quart., J = 7.35 Hz, 2H), 2.28 (s, 1H), 1.30 (t, J = 7.35 Hz, 3H). ^{13}C NMR, $CDCl_3$, 50 MHz, δ (ppm): 133.60, 132.62, 131.99, 130.25, 129.03, 127.34, 65.46, 25.95, 14.94. MS (EI, 70 eV) *m*/*z* (relative intensity): 154 (100), 177 (31), 156 (76), 98 (12), 77 (21), 65 (44). HRMS: calcd for $C_{11}H_{14}OSSe$ 273.9930, found 273.9938. Anal. (%) Calcd for $C_{11}H_{14}OSSe$: C 48.35, H 5.16. Found: C 48.68, H 5.29.

(Z**)-3-(Phenylselenyl)-2-(propylthio)prop-2-en-1-ol (3c).** Yield: 0.229 g (80%). ^{1}H NMR, $CDCl_3$, 200 MHz, δ (ppm): 7.56−7.51 (m, 2H), 7.28−7.25 (m, 3H), 6.96 (s, 1H), 4.17 (s, 2H), 2.75 (t, J = 7.35 Hz, 2H), 2.52 (s, 1H), 1.64 (sex, J = 7.35 Hz, 2H), 1.01 (t, J = 7.35 Hz, 3H). ^{13}C NMR, $CDCl_3$, 50 MHz, δ (ppm): 133.88, 132.81, 132.17, 130.36, 129.15, 127.48, 65.57, 33.87, 23.31, 13.26. MS (EI, 70 eV) *m*/*z* (relative intensity): 287 (100), 270 (71), 193 (42), 156 (41), 114 (38), 85 (61), 77 (15), 75 (19), 43 (39). HRMS: calcd for $C_{12}H_{16}OSSe$ 288.0087, found 288.0092.

(*Z*)-2-(4-Chlorobenzylthio)-3-(phenylselenyl)prop-2-en-1-ol (3d). Yield: 0.221 g (60%). ^{1}H NMR, $CDCl_3$, 400 MHz, δ (ppm): 7.51−7.49 (m, 2H), 7.30−7.28 (m, 7H), 7.04 (s, 1H), 4.04 (s, 2H), 3.98 (s, 2H), 1.84 (s, 1H). ^{13}C NMR, $CDCl_3$, 50 MHz, δ (ppm): 136.22, 133.16, 132.84, 132.57, 130.26, 130.09, 129.33, 128.66, 127.83, 66.54, 35.85. MS (EI, 70 eV) *m*/*z* (relative intensity): 368 (100), 274 (85), 195 (62), 160 (44), 158 (38), 156 (32), 77 (21). HRMS: calcd for $C_{16}H_{15}ClOSSe$ 369.9697, found 369.9702. Anal. (%) calcd for $C_{16}H_{15}ClOSSe$: C 50.64, H 3.68. Found: C 50.79, H 3.81.

(*Z*)-3-(Butylselenyl)-2-(phenylthio)prop-2-en-1-ol (3e). Yield: 0.247 g (82%). ^{1}H NMR, $CDCl_3$, 400 MHz, δ (ppm): 7.42−7.40 (m, 1H), 7.32−7.16 (m, 5H), 4.06 (s, 2H), 2.76 (t, J = 7.28 Hz, 2H), 2.52 (s, 1H), 1.71 (quint, J = 7.44 Hz, 2H), 1.42 (sex, J = 7.44 Hz, 2H), 0.92 (t, J = 7.44 Hz, 3H). ^{13}C NMR, $CDCl_3$, 50 MHz, δ (ppm): 132.39, 131.91, 131.46, 128.95, 127.49, 126.38, 65.57, 32.79, 26.24, 22.54, 13.35. MS (EI, 70 eV) *m*/*z* (relative intensity): 284 (100), 227 (15), 148 (57), 136 (24), 109 (41), 77 (17), 43 (11). HRMS: calcd for $C_{13}H_{18}OSSe$ 302.0243, found 302.0237.

(*Z*)-2-(Dodecylthio)-3-(phenylselenyl)prop-2-en-1-ol (3f). Yield: 0.264 g (64%). ^{1}H NMR, $CDCl_3$, 200 MHz, δ (ppm): 7.55−7.50 (m, 2H), 7.28−7.25 (m, 3H), 6.96 (s, 1H), 4.17 (s, 2H), 2.77 (t, J = 7.35 Hz, 2H), 1.25 (m, 20H), 0.87 (t, J = 6.76 Hz, 3H). ^{13}C NMR, $CDCl_3$, 100 MHz, δ (ppm): 133.98, 132.80, 132.11, 130.43, 129.12, 127.43, 65.60, 33.86, 31.93, 31.78, 30.34, 29.90, 29.51, 29.41, 29.22, 29.09, 28.61, 22.55, 14.00. MS (EI, 70 eV) *m*/*z* (relative intensity): 413 (100), 398 (61), 319 (40), 240 (62), 225 (38), 211 (25), 201 (22), 197 (29), 182 (20), 167 (31), 156 (48), 152 (44), 137 (38), 77 (21), 28 (31). HRMS: calcd for $C_{21}H_{34}OSSe$ 414.1495, found 414.1498. Anal. (%) Calcd for $C_{21}H_{34}OSSe$: C 60.99, H 8.29. Found: C 60.72, H 8.02.

(*Z*)-2-Methyl-4-(phenylselenyl)-3-(propylthio)but-3-en-2-ol (3g). Yield: 0.195 g (62%). ^{1}H NMR, $CDCl_3$, 200 MHz, δ (ppm): 7.62−7.47 (m, 2H), 7.31−7.20 (m, 4H), 2.86 (t, J = 7.20 Hz, 2H), 2.34 (s, 1H), 2.20 (sex, J = 7.35 Hz, 2H), 1.44 (s, 3H), 1.42 (s, 3H), 1.04 (t, J = 7.35 Hz, 3H). ^{13}C NMR, $CDCl_3$, 100 MHz, δ (ppm): 136.61, 133.04, 129.74, 129.16, 127.64, 126.38, 75.19, 37.19, 29.27, 29.16, 13.28, 13.47. MS (EI, 70 eV) *m*/*z* (relative intensity): 315 (100), 298 (89), 221 (51), 156 (21), 142 (62), 113 (28), 77 (53), 75 (38), 43 (42). HRMS: calcd for $C_{14}H_{20}OSSe$ 316.0400, found 316.0405.

(*Z*)-3-(3-Chlorophenylthio)-2-methyl-4-(phenylselenyl)but-3-en-2-ol (3h). Yield: 0.226 g (59%). ^{1}H NMR, $CDCl_3$, 200 MHz, δ (ppm): 7.63 (s, 1H), 7.56−7.51 (m, 2H), 7.30−7.09 (m, 7H), 2.27 (s, 1H), 1.42 (s, 6H). ^{13}C NMR, $CDCl_3$, 100 MHz, δ (ppm): 138.32, 137.23, 136.61, 134.72, 133.24, 129.92, 129.28, 127.88, 126.48, 125.80, 124.94, 75.68, 29.13. MS (EI, 70 eV) *m*/*z* (relative intensity): 382 (100), 365 (78), 288 (64), 209 (35), 156 (29), 144 (71), 113 (28). HRMS: calcd for $C_{17}H_{17}ClOSSe$ 383.9853, found 383.9857. Anal. (%) Calcd for $C_{17}H_{17}ClOSSe$: C 53.20, H 4.46. Found: C 53.51, H 4.75.

(*Z*)-3-(Ethylthio)-2-methyl-4-(phenylselenyl)but-3-en-2-ol (3i). Yield: 0.225 g (75%). ^{1}H NMR, $CDCl_3$, 400 MHz, δ (ppm): 7.58−7.48 (m, 2H), 7.32−7.29 (m, 3H), 7.22 (s, 1H), 2.91 (q, J = 7.44 Hz, 2H), 2.34 (s, 1H), 1.45 (s, 3H), 1.43 (s, 3H), 1.33 (t, J = 7.44 Hz, 3H). ^{13}C NMR, $CDCl_3$, 100 MHz, δ (ppm): 136.78, 133.37, 129.93, 129.28, 127.71, 126.54, 75.18, 29.40, 29.27, 14.88. MS (EI, 70 eV) *m*/*z* (relative intensity): 301 (100), 284 (100), 207 (41), 156 (42), 128 (75), 77 (41), 61 (15), 29 (87). HRMS: calcd for $C_{13}H_{18}OSSe$ 302.0243, found 302.0246.

(*Z*)-2-Methyl-4-(phenylselenyl)-3-(phenylthio)but-3-en-2-ol (3j). Yield: 0.192 g (55%). ^{1}H NMR, $CDCl_3$, 200 MHz, δ (ppm): 7.59 (s, 1H), 7.52−7.50 (m, 2H), 7.36−7.22 (m, 8H), 2.37 (s, 1H), 1.42 (s, 6H). ^{13}C NMR, $CDCl_3$, 100 MHz, δ (ppm): 138.17, 137.10, 134.45, 133.07, 129.74, 129.20, 128.93, 127.69, 127.05, 125.70, 75.65, 29.13. MS (EI, 70 eV) *m*/*z* (relative intensity): 349 (100), 332 (75), 255 (61), 176 (32), 156 (49), 109 (23), 77 (41). HRMS: calcd for $C_{17}H_{18}OSSe$ 350.0243, found 350.0248.

(*Z*)-3-Methyl-1-(phenylselenyl)-2-(phenylthio)pent-1-en-3-ol (3k). Yield: 0.286 g (79%). ^{1}H NMR, $CDCl_3$, 200 MHz, δ (ppm): 7.54−7.49 (m, 3H), 7.38−7.13 (m, 8H), 2.22 (s, 1H), 1.67 (quart, J = 7.35, 2H), 1.35 (s, 3H), 0.84 (t, J = 7.35 Hz, 3H). ^{13}C NMR, $CDCl_3$, 100 MHz, δ (ppm): 138.13, 137.39, 134.40, 132.91, 130.38, 129.13, 128.83, 127.55, 127.40, 125.74, 78.16, 33.71, 26.44, 8.14.

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MS (EI, 70 eV) *m*/*z* (relative intensity): 363 (77), 346 (68), 269 (100), 190 (49), 156 (23), 109 (33), 77 (51), 42 (29). HRMS: calcd for $C_{18}H_{20}OSSe$ 364.0400, found 364.0402. Anal. (%) Calcd for $C_{18}H_{20}OSSe$: C 59.50, H 5.55. Found: C 59.71, H 5.69.

(*Z*)-1-(2-(Phenylselenyl)-1-(phenylthio)vinyl)cyclohexanol (3l). Yield: 0.338 g (87%). ^{1}H NMR, $CDCl_3$, 200 MHz, δ (ppm): 7.59 (s, 1H), 7.56−7.51 (m, 2H), 7.37−7.14 (m, 8H), 1.90 (s, 1H), 1.70−1.57 (m, 10H). ^{13}C NMR, $CDCl_3$, 100 MHz, δ (ppm): 138.79, 137.59, 134.68, 133.05, 130.42, 129.18, 128.89, 127.65, 126.94, 125.56, 71.98, 36.20, 25.17, 21.75. MS (EI, 70 eV) *m*/*z* (relative intensity): 389 (65), 372 (62), 295 (100), 216 (29), 156 (50), 109 (54), 82 (21). HRMS: calcd for $C_{20}H_{22}OSSe$ 390.0556, found 390.0560.

(*Z*)-1-(Phenylselenyl)-2-(phenylthio)pent-1-en-3-ol (3m). Yield: 0.331 g (95%). ^{1}H NMR, $CDCl_3$, 200 MHz, δ (ppm): 7.54−7.50 (m, 2H), 7.37−7.34 (m, 3H), 7.28−7.17 (m, 5H), 4.05 (t, J = 5.29 Hz, 1H), 2.48 (s, 1H), 1.78−1.49 (m, 2H), 0.85 (t, J = 7.20 Hz, 3H). ^{13}C NMR, $CDCl_3$, 100 MHz, δ (ppm): 136.18, 135.09, 133.78, 132.89, 130.18, 129.16, 128.96, 128.61, 127.59, 126.30, 76.71, 28.88, 9.69. MS (EI, 70 eV) *m*/*z* (relative intensity): 349 (66), 332 (71), 255 (100), 176 (44), 156 (59), 109 (52), 77 (21), 42 (15). HRMS: calcd for $C_{17}H_{18}OSSe$ 350.0243, found 350.0248. Anal. (%) Calcd for $C_{17}H_{18}OSSe$: C 58.45, H 5.19. Found: C 58.29, H 4.91.

(*Z*)-2-(4-Chlorobenzylsulfenyl)-1-phenylselenyl-pent-1-en-3-ol (3n). Yield: 0.326 g (82%). ^{1}H NMR, $CDCl_3$, 200 MHz, δ (ppm): 7.57−7.46 (m, 2H), 7.30−7.26 (m, 7H), 7.12 (s, 1H), 3.99 (s, 1H), 2.02 (s,1H), 1.70−1.49 (m, 2H), 0.85 (t, J = 7.30 Hz, 3H). ^{13}C NMR, $CDCl_3$, 50 MHz, δ (ppm): 136.28, 135.65, 134.74, 133.08, 131.95, 131.34, 130.38, 129.26, 128.55, 127.73, 77.66, 36.95, 28.85, 9.84. MS (EI, 70 eV) *m*/*z* (relative intensity): 379 (100), 344 (11), 303 (23), 224 (778), 223 (42), 156 (78), 125 (34), 91 (65), 77 (16). HRMS: calcd for $C_{18}H_{19}ClOSSe$ 398.0010, found 398.0015.

General Procedure for the Preparation of the Unsymmetrical Tris-chalcogenide Alkenes. *n*-Butyllithium (0.7 mL of a 1.567 M solution in hexane, 1.1 mmol) was added, under argon, to a solution of alkyne (1 mmol) in THF (2 mL) previously cooled at 0 °C. The resulting solution was stirred for 30 min at room temperature. After this time, the mixture was cooled at 0 °C, and the dichalcogenide (3 mmol) in THF (1 mL) was added. The mixture was then heated at reflux for 12 h, cooled at room temperature, diluted with ethyl acetate (20 mL), and washed with brine (2 × 20 mL). The organic phase was separated, dried over $MgSO_4$, and concentrated under vacuum. The residue was purified by flash chromatography and eluted with hexane/ethyl acetate (80:20).

(3-Ethoxy-1,1-bis(phenylselenyl)prop-1-en-2-yl)(phenyl)sulfane (4a). Yield: 0.378 g (75%). ^{1}H NMR, $CDCl_3$, 200 MHz, δ (ppm): 7.56−7.07 (m, 15H), 4.28 (s, 2H), 3.30 (q, J = 7.00 Hz, 2H), 1.09 (t, J = 7.00 Hz, 3H). ^{13}C NMR, $CDCl_3$, 100 MHz, δ (ppm): 141.42, 134.91, 133.68, 132.86, 131.79, 131.63, 129.79, 129.17, 128.79, 128.60, 128.33, 127.72, 127.46, 126.88, 71.92, 65.26, 15.01. MS (EI, 70 eV) *m*/*z* (relative intensity): 504 (52), 460 (62), 348 (100), 193 (38), 156 (32), 109 (63), 77 (31), 29 (35). HRMS: calcd for $C_{23}H_{22}OSSe_2$ 505.9721, found 505.9725. Anal. (%) Calcd for $C_{23}H_{22}OSSe_2$: C 54.77, H 4.40. Found: C 54.55, H 4.68.

(3-Ethoxy-1,1-bis(phenylselenyl)prop-1-en-2-yl)(propyl)sulfane (4b). Yield: 0.348 g (74%). ^{1}H NMR, $CDCl_3$, 400 MHz, δ (ppm): 7.32−7.07 (m, 10H), 4.56 (s, 2H), 3.50 (q, J = 6.90 Hz, 2H), 2.97 (t, J = 7.05 Hz, 2H), 1.67 (sex, J = 7.05 Hz, 2H), 1.19 (t, J = 6.90 Hz, 3H), 1.03 (t, J = 7.05 Hz, 3H). ^{13}C NMR, $CDCl_3$, 100 MHz, δ (ppm): 143.69, 134.93, 133.43, 132.54, 130.67, 128.51, 128.12, 127.53, 127.19, 126.38, 71.95, 64.97, 34.89, 23.06, 15.05, 13.30. MS (EI, 70 eV) *m*/*z* (relative intensity): 471 (62), 427 (32), 413 (100), 316 (28), 160 (63), 156 (29), 77 (12), 75 (41), 28 (17). HRMS: calcd for $C_{20}H_{24}OSSe$ 471.9878, found 471.9883.

Ethyl(1-phenyl-2,2-bis(phenylselenyl)vinyl)sulfane (4c). Yield: 0.332 g (70%). ^{1}H NMR, $CDCl_3$, 200 MHz, δ (ppm): 7.36−6.96 (m, 15H), 2.33 (q, J = 7.30 Hz, 2H), 1.08 (t, J = 7.30 Hz, 3H). ^{13}C NMR, $CDCl_3$, 100 MHz, δ (ppm): 139.59, 135.73, 133.82, 133.27, 132.59, 132.54, 131.98, 131.46, 128.97, 128.44, 127.99, 129.91, 127.34, 126.66, 28.34, 14.67. MS (EI, 70 eV) *m*/*z* (relative intensity): 523 (100), 446 (32), 367 (72), 211 (46), 156 (31), 109 (19), 77 (56). HRMS: calcd for $C_{22}H_{20}SSe_2$ 523.9616, found 523.9621. Anal. (%) Calcd for $C_{22}H_{20}SSe_2$: C 55.70, H 4.25. Found: C 55.49, H 4.38.

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Supporting Information Available: Experimental procedures, additional experimental details for the preparations of compounds **3a**−**n** and **4a**−**c**, and ^{1}H and ^{13}C NMR spectra for all reaction products. This material is available free of charge via the Internet at http://pubs.acs.org.

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