



# Copper-catalyzed synthesis of $\beta$ -haloalkenyl chalcogenides by addition of dichalcogenides to internal alkynes and its application to synthesis of (Z)-tamoxifen

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## ABSTRACT

A copper-catalyzed synthesis of  $\beta$ -haloalkenyl sulfides or selenides was carried out by addition of dichalcogenides and tetrabutylammonium halides to internal alkynes. The present reaction *anti*- and *regio*-selectively afforded the corresponding alkenyl chalcogenides, and took advantage of both organochalcogenide-groups on dichalcogenide. Furthermore, the reaction under oxygen atmosphere could employ thiols. The use of the procedure could easily synthesize (Z)-tamoxifen from diphenyl acetylene in three steps.

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## 1. Introduction

A transition-metal-catalyzed preparation of alkenyl sulfides from alkynes was carried out by numerous methods so far.<sup>1,2,3</sup> Herein produced compounds have found a widespread utilization as convenient intermediates in organic synthesis.<sup>4</sup>

As a general rule, to synthesize alkenyl sulfides, disulfidations<sup>5</sup> or hydrosulfidations<sup>6</sup> of terminal alkynes using disulfides or thiols have been performed. In these reactions, the use of a palladium or a rhodium catalyst affords *syn*-adducts, and a stoichiometric gallium chloride as a Lewis acid gives *anti*-adducts.<sup>7</sup> However, a transition-metal-catalyzed preparation of *anti*-additive products has been rarely exploited.<sup>8</sup> Moreover, an employment of internal alkyne is very limited though various reactions using terminal alkynes are reported.<sup>6</sup>

Although  $\beta$ -haloalkenyl sulfides are useful intermediates to prepare various alkenes, an advance of its synthetic method has not been performed to date. In particular, previous methods can synthesize only simple derivatives. For instance, these are usually prepared by addition of sulfonyl halides to alkynes<sup>9,10</sup> or decarboxylative dehydrohalogenation of  $\beta$ -arylmercapto- $\alpha,\beta$ -dihalopropionic acids.<sup>11</sup> Problems in these reactions are the use of chlorine gas or the separation of stereoisomers, and these methods cannot construct intricate structures. Therefore, an efficient and

a stereoselective procedure to prepare  $\beta$ -haloalkenyl sulfides from internal alkynes are desired now.

To synthesize  $\beta$ -haloalkenyl sulfides from alkynes, I researched a reaction using disulfides. These disulfides are stable and useful compounds, but the utilization is less than that of thiols. In addition, previously developed procedures using disulfides cannot efficiently synthesize expected alkenyl sulfides. To solve this problem, it is required to explore a system producing a sulfonyl cation and reusing a metal-thiolate complex generated as an intermediates.<sup>12</sup> From various investigations, I found that a synthesis of  $\beta$ -haloalkenyl sulfides from disulfides with internal alkynes could carry out by a copper catalyst in air.<sup>13</sup> In this paper, I wish to describe the methodology.

## 2. Results and discussion

To carry out the introduction of halide and sulfide-groups to alkynes, conditions using 4-octyne **1a** with diphenyl disulfide **2a** were initially researched in the presence of copper catalyst (Table 1). In the selection of various additions, when KBr or dibromoethane were used, the yield of 4-bromo-5-phenylthio-4-octene **3a** was low yield (entries 1–2). Fortunately, when *n*-Bu<sub>4</sub>NBr was employed, the corresponding  $\beta$ -bromoalkenyl sulfide **3a** could be obtained in 81% yield without other isomers (entry 3).

This reaction could lead to good results by the use of bpy or 1,10-phenanthroline (o-Phen) as a ligand (entries 3 and 5), though the use of TMEDA or Ph<sub>3</sub>P was unexpected result (entries 6 and 7). In the investigation of copper catalysts, when Cu(I)I or Cu(I)Br was

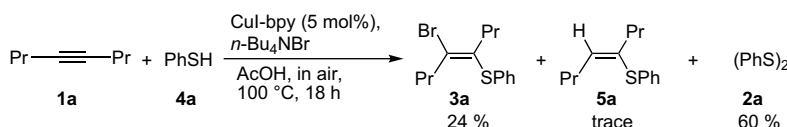
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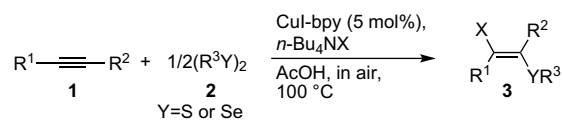
$$\text{Pr}\text{---}\text{C}\equiv\text{C}\text{---}\text{Pr} + (\text{PhS})_2 \xrightarrow[\text{Solvent, in air, } 100^\circ\text{C, 18 h}]{\text{cat. [Cu] (5 mol\%), \text{Additive}}} \text{Pr}\text{---}\text{C}(\text{Br})=\text{C}(\text{SPh})\text{---}\text{Pr}$$
<sup>a</sup> Isolated yields after silica gel chromatography.

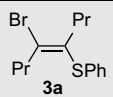
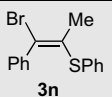
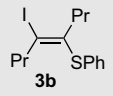
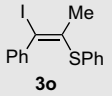
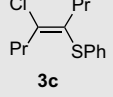
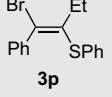
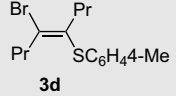
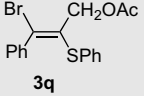
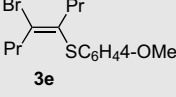
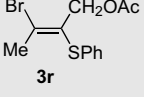
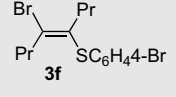
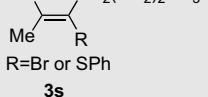
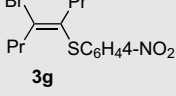
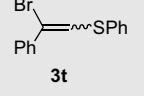
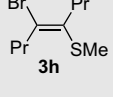
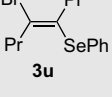
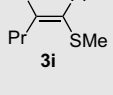
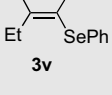
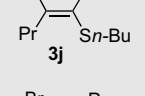
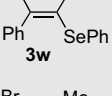
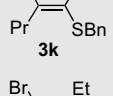
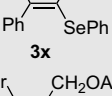
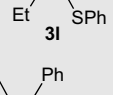
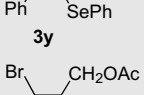
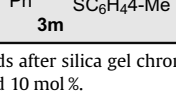
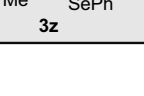
The present procedure could also employ unsymmetrical internal alkynes, and *regio*- and *anti*-selectively produced the corresponding  $\beta$ -bromo or iodoalkenyl sulfides (entries 14–18).<sup>15,16</sup> Although a reaction using 1-phenyl-1-propyne or 2-butyne-1-ol afforded good yields, the *anti*-selectivity decreased slightly (entries 14 and 18).<sup>16</sup> On the contrary, a reaction of 2-octyne indicated no *regio*-selectivity (entry 19), and the use of terminal alkyne resulted in lower yield owing to the formation of various products (entry 20).

Therefore, a reaction mechanism is considered as follows (Fig. 1). After the Cu(I)-catalyst acted on the disulfide as the oxidant in air or Lewis acid,<sup>13,18,19</sup> a sulfenium ion **9** and PhSCu(I)L<sub>n</sub> **11** are



**Scheme 1.** Reaction of 4-octyne with benzenethiol.

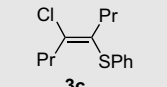
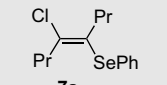
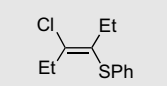
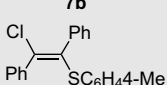
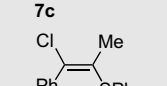
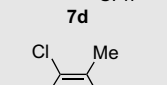
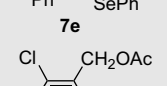
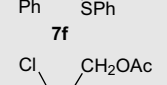
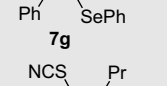
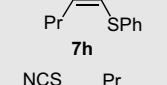
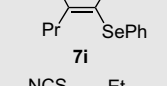
**Table 2**Copper-catalyzed synthesis of  $\beta$ -haloalkenyl chalcogenides using dichalcogenides

| Entry | <b>3</b>                                                                            | Time (h) | <b>3</b> (%) <sup>a</sup> | Entry             | <b>3</b>                                                                             | Time (h) | <b>3</b> (%) <sup>a</sup> (E/Z) <sup>c</sup> |
|-------|-------------------------------------------------------------------------------------|----------|---------------------------|-------------------|--------------------------------------------------------------------------------------|----------|----------------------------------------------|
| 1     |    | 18       | 81                        | 14                |    | 18       | 94 (98/2) <sup>c,d</sup>                     |
| 2     |    | 18       | 80                        | 15                |    | 18       | 66                                           |
| 3     |    | 18       | 42                        | 16                |    | 18       | 86                                           |
| 4     |    | 18       | 85                        | 17 <sup>f</sup>   |    | 48       | 69                                           |
| 5     |    | 18       | 87                        | 18 <sup>g</sup>   |    | 36       | 85 (87/13) <sup>c,d</sup>                    |
| 6     |   | 18       | 65                        | 19                |   | 40       | 73 <sup>e</sup>                              |
| 7     |  | 24       | 45                        | 20 <sup>b</sup>   |  | 18       | 28 (65/35) <sup>c</sup>                      |
| 8     |  | 18       | 74                        | 21                |  | 18       | 94                                           |
| 9     |  | 18       | 77                        | 22                |  | 18       | 80                                           |
| 10    |  | 18       | 76                        | 23                |  | 40       | 81                                           |
| 11    |  | 18       | 81                        | 24                |  | 18       | 80                                           |
| 12    |  | 18       | 71                        | 25 <sup>b,f</sup> |  | 48       | 84                                           |
| 13    |  | 42       | 70                        | 26 <sup>g</sup>   |  | 48       | 87(87/13) <sup>c,d</sup>                     |

<sup>a</sup> Isolated yields after silica gel chromatography.<sup>b</sup> Cul was used 10 mol %.<sup>c</sup> Determined by <sup>1</sup>H NMR.<sup>d</sup> These isomers can separate by silica gel chromatography.<sup>e</sup> Regio-isomers were obtained in the ratio of 1:1.<sup>f</sup> 3-Phenyl-2-propyn-1-ol was used as a starting material.<sup>g</sup> 2-Butyn-1-ol was used as a starting material.

**Table 3**

Copper-catalyzed introduction of chloride or thiocyanide and chalcogenide-groups to alkynes

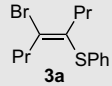
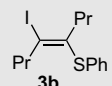
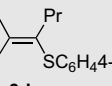
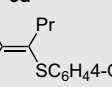
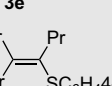
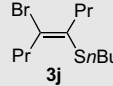
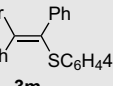
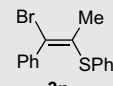
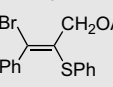
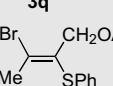
| $\text{R}^1\text{—}\text{C}\equiv\text{C—R}^2 + \frac{1}{2}(\text{R}^3\text{Y})_2 \xrightarrow[\text{AcOH, in air, 100 }^\circ\text{C}]{\text{CsCl or NH}_4\text{SCN, Cul-bpy (5 mol\%)}} \text{R}^1\text{—}\text{C}(\text{X})=\text{C}(\text{R}^2)\text{—YR}^3$ |                                                                                     |          |                    |
|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------|----------|--------------------|
| 1                                                                                                                                                                                                                                                                | 2 or 6                                                                              | 3c or 7  | X = Cl or SCN      |
| Entry                                                                                                                                                                                                                                                            | 7                                                                                   | Time (h) | 7 (%) <sup>a</sup> |
| 1                                                                                                                                                                                                                                                                |    | 40       | 76                 |
| 2                                                                                                                                                                                                                                                                |    | 42       | 86                 |
| 3                                                                                                                                                                                                                                                                |    | 43       | 67                 |
| 4                                                                                                                                                                                                                                                                |    | 40       | 75                 |
| 5                                                                                                                                                                                                                                                                |    | 42       | 75                 |
| 6                                                                                                                                                                                                                                                                |    | 42       | 78                 |
| 7 <sup>b</sup>                                                                                                                                                                                                                                                   |   | 72       | 52                 |
| 8 <sup>b</sup>                                                                                                                                                                                                                                                   |  | 72       | 70                 |
| 9                                                                                                                                                                                                                                                                |  | 18       | 90                 |
| 10                                                                                                                                                                                                                                                               |  | 18       | 63                 |
| 11                                                                                                                                                                                                                                                               |  | 18       | 66                 |

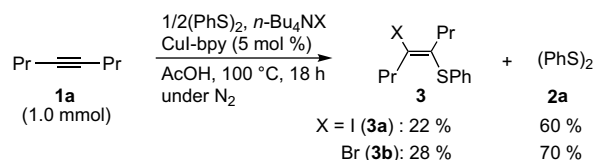
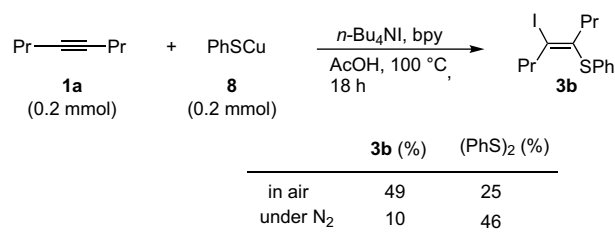
<sup>a</sup> Isolated yields after silica gel chromatography.<sup>b</sup> 3-Phenyl-2-propyn-1-ol was used as a starting material.

produced from intermediates **10** with alkyne **1**. Sequentially,  $\beta$ -haloalkenyl sulfides **3** are formed by a reaction of **9** with  $\text{X}^-$ .<sup>19</sup> On the other hand, the disproportionation of  $\text{PhSCu(I)}\text{L}_n$  **11** under acidic conditions gave  $(\text{PhS})_2\text{Cu(II)}\text{L}_n$  **12** and  $\text{Cu(0)}\text{L}_n$ . Finally, the oxidation of the complex **12** produces disulfide **2a** and  $\text{Cu(I)}\text{L}_n$  again in air.<sup>12,20</sup>

Herein developed method can be carried out on a larger preparative scale. The copper-catalyzed bromosulfonylation of 4-octyne **1a** (1.1 g, 10 mmol) or 1-phenyl-1-propyne **1m** (1.2 g, 10 mmol) using  $(\text{PhS})_2$  **2a** (1.1 g, 5 mmol) and  $n\text{-Bu}_4\text{NBr}$  (3.5 g, 11 mmol) afforded (*E*)-4-bromo-5-phenylthio-4-octene **3a** (2.3 g)

**Table 4**Copper-catalyzed synthesis of  $\beta$ -haloalkenyl chalcogenides using thiol

| $\text{R}^1\text{—}\text{C}\equiv\text{C—R}^2 + \text{R}^3\text{SH} \xrightarrow[\text{AcOH, under O}_2, 100^\circ\text{C}]{\text{Cul-bpy (10 mol\%), } n\text{-Bu}_4\text{NX}} \text{R}^1\text{—}\text{C}(\text{X})=\text{C}(\text{R}^2)\text{—SR}^3$ |                                                                                     |          |                          |
|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------|----------|--------------------------|
| Entry                                                                                                                                                                                                                                                  | 3                                                                                   | Time (h) | 3 (%) <sup>a</sup>       |
| 1                                                                                                                                                                                                                                                      |   | 18       | 60                       |
| 2                                                                                                                                                                                                                                                      |   | 18       | 24                       |
| 4                                                                                                                                                                                                                                                      |   | 18       | 57                       |
| 4                                                                                                                                                                                                                                                      |   | 18       | 52                       |
| 5                                                                                                                                                                                                                                                      |   | 18       | 60                       |
| 6                                                                                                                                                                                                                                                      |  | 18       | 45                       |
| 7                                                                                                                                                                                                                                                      |  | 24       | 77                       |
| 8                                                                                                                                                                                                                                                      |  | 18       | 90 (98/2) <sup>b,c</sup> |
| 9 <sup>d</sup>                                                                                                                                                                                                                                         |  | 46       | 74                       |
| 10 <sup>e</sup>                                                                                                                                                                                                                                        |  | 40       | 68 (91/9) <sup>b,c</sup> |

<sup>a</sup> Isolated yields after silica gel chromatography.<sup>b</sup> Determined by <sup>1</sup>H NMR.<sup>c</sup> These isomers can separate by silica gel chromatography.<sup>d</sup> 3-Phenyl-2-propyn-1-ol was used as a starting material.<sup>e</sup> 2-Butyn-1-ol was used as a starting material.**Scheme 2.** Reaction in the absence of oxygen.**Scheme 3.** Reactivity of  $\text{PhSCu}$ .**Table 5** $\text{PhSCu(I)}$  in various solvents

| $\text{PhSCu} \xrightarrow[\text{in air, 18 h}]{\text{bpy, Solv., 100 }^\circ\text{C}} \frac{1}{2}(\text{PhS})_2$ |         |                            |
|-------------------------------------------------------------------------------------------------------------------|---------|----------------------------|
| Entry                                                                                                             | Solvent | <b>2a</b> (%) <sup>a</sup> |
| 1                                                                                                                 | AcOH    | 92                         |
| 2 <sup>b</sup>                                                                                                    |         | 48                         |
| 3 <sup>c</sup>                                                                                                    |         | 57                         |
| 4                                                                                                                 | DMF     | 43                         |
| 5                                                                                                                 | DMSO    | 35                         |

<sup>a</sup> Isolated yield after silica gel chromatography.<sup>b</sup> bpy was not added.<sup>c</sup> This reaction was carried out at room temperature.

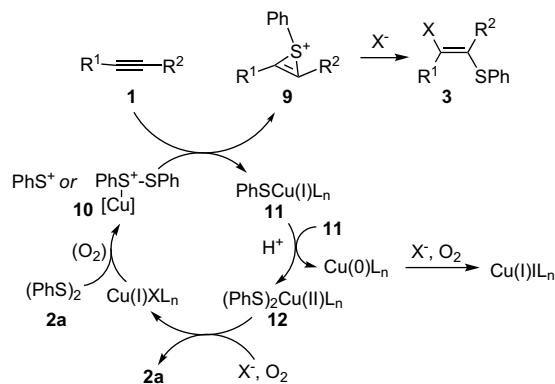
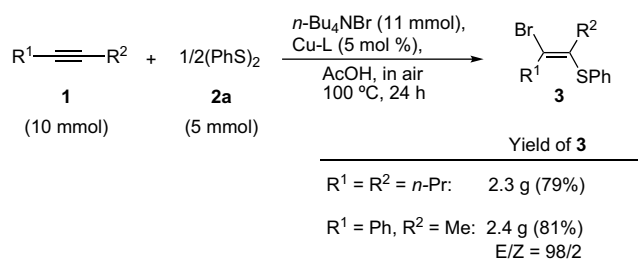


Figure 1. Plausible reaction mechanism.



Scheme 4. Large scale reaction.

or (*E*)-1-bromo-2-phenylthio-2-methylstyrene **3n** (2.4 g) in 79% or 81% yield, respectively (Scheme 4).

The present procedure can be accessible to the synthesis of numerous polysubstituted alkenes.<sup>21</sup> For example, (*Z*)-tamoxifen is known as an estrogen antagonist, and is effective for metastatic breast cancer.<sup>22</sup> Previous syntheses have been carried out by a classical synthesis using stoichiometric reagents or a stereospecific synthesis by multi-steps.<sup>23</sup>

However, as shown in Scheme 5, the use of my developed procedure can synthesized (*Z*)-tamoxifen from diphenyl acetylene in three steps.

Initially, β-bromoalkenyl sulfide **3m** was derived in 94% yield from diphenyl acetylene **1m** by CuI catalyst. Herein the obtained **3m** was converted to the corresponding alkenyl sulfide **13** in 72% yield by Suzuki–Miyaura coupling. Finally, (*Z*)-tamoxifen **14** could be synthesized in 75% yield (*Z*/*E*=93/7) by a nickel-catalyzed coupling of **13** with EtMgBr.

Thus, β-haloalkenyl sulfides can use as very convenient intermediates for the purpose of preparations of various polysubstituted alkenes.

### 3. Conclusion

In conclusion, I achieved a copper-catalyzed introduction of halide and sulfide or selenide-groups to internal alkynes using

dichalcogenide with tetrabutylammonium halide in air. The present reaction could prepare the corresponding β-haloalkenyl chalcogenide in *anti*-selectively, and use both chalcogenide-groups on dichalcogenide. Herein obtained compounds can take advantage of preparations of various polysubstituted alkenes.

## 4. Experimental section

### 4.1. General procedure

All reactions of dichalcogenides with alkynes were carried out in air. NMR spectra were recorded on a JEOL EX-270 spectrometer (270 MHz for <sup>1</sup>H, 67.5 MHz for <sup>13</sup>C). Chemical shifts are reported in δ parts per million referenced to an internal tetramethylsilane standard for <sup>1</sup>H NMR and chloroform-*d* (δ 77.0) for <sup>13</sup>C NMR. IR spectra were measured by Perkin–Elmer Spectrum One FT-IR spectrometer. Melting points were measured on a BÜCHI Melting Point B-540 apparatus. Elemental analysis was performed at the Instrumental Analysis Center for Chemistry, Tohoku University (Japan).

### 4.2. Copper-catalyzed synthesis of β-bromoalkenyl sulfide (Table 2)

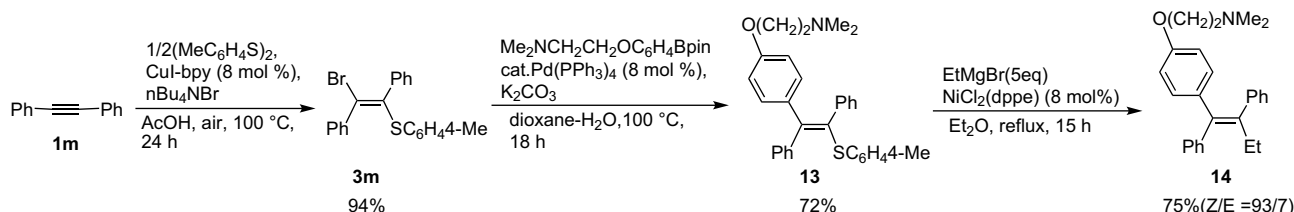
To a mixture of CuI (1.9 mg, 0.01 mmol), bpy (1.6 mg, 0.01 mmol), diphenyl disulfide **2a** (21.8 mg, 0.1 mmol), and *n*-Bu<sub>4</sub>NBr (70.9 mg, 0.22 mmol) in AcOH (0.3 mL) was added 4-octyne **1a** (22.0 mg, 0.2 mmol), and the mixture was stirred at 100 °C for 18 h in air. After the residue was dissolved in Et<sub>2</sub>O, the solution was washed with H<sub>2</sub>O and saturated sodium chloride and dried over anhydrous magnesium sulfate. Chromatography on silica gel (Hexane) gave (*E*)-4-bromo-5-phenylthio-4-octene **3a** (48.7 mg, 81%). <sup>1</sup>H NMR (270 MHz, CDCl<sub>3</sub>) δ 7.31–7.16 (m, 5H), 2.90 (t, *J*=7.5 Hz, 2H), 2.38 (t, *J*=7.5 Hz, 2H), 1.67–1.51 (m, 4H), 0.92 (t, *J*=7.5 Hz, 3H), 0.86 (t, *J*=7.5 Hz, 3H); <sup>13</sup>C NMR (67.5 MHz, CDCl<sub>3</sub>) δ 135.3, 132.8, 131.5, 129.2, 128.9, 126.2, 41.2, 38.8, 21.9, 21.0, 13.6, 13.1; IR (neat) 2960, 2870, 1582, 1476, 1461 cm<sup>-1</sup>. Anal. Calcd for C<sub>14</sub>H<sub>19</sub>SBr: C, 56.19; H, 6.40. Found: C, 56.09; H, 6.27.

#### 4.2.1. (*E*)-4-Iodo-5-phenylthio-4-octene (**3b**)

<sup>1</sup>H NMR (270 MHz, CDCl<sub>3</sub>) δ 7.31–7.16 (m, 5H), 2.94 (t, *J*=7.3 Hz, 2H), 2.39 (t, *J*=7.3 Hz, 2H), 1.66–1.50 (m, 4H), 0.92 (t, *J*=7.3 Hz, 3H), 0.87 (t, *J*=7.3 Hz, 3H); <sup>13</sup>C NMR (67.5 MHz, CDCl<sub>3</sub>) δ 135.5, 135.4, 129.3, 128.9, 126.4, 113.0, 45.4, 43.9, 22.9, 21.3, 13.5, 12.9; IR (neat) 2959, 1582, 1476, 1461 cm<sup>-1</sup>. Anal. Calcd for C<sub>14</sub>H<sub>19</sub>SI: C, 48.56; H, 5.53. Found: C, 48.48; H, 5.47.

#### 4.2.2. (*E*)-4-Chloro-5-phenylthio-4-octene (**3c**)

<sup>1</sup>H NMR (270 MHz, CDCl<sub>3</sub>) δ 7.31–7.15 (m, 5H), 2.79 (t, *J*=7.4 Hz, 2H), 2.36 (t, *J*=7.4 Hz, 2H), 1.70–1.47 (m, 4H), 0.92 (t, *J*=7.4 Hz, 3H), 0.86 (t, *J*=7.4 Hz, 3H); <sup>13</sup>C NMR (67.5 MHz, CDCl<sub>3</sub>) δ 139.9, 135.5, 129.5, 128.9, 128.8, 126.1, 39.0, 35.9, 21.3, 21.0, 13.6, 13.2; IR (neat) 2961, 1582, 1477, 1462 cm<sup>-1</sup>. Anal. Calcd for C<sub>14</sub>H<sub>19</sub>SCl: C, 65.99; H, 7.52. Found: C, 65.90; H, 7.15.

Scheme 5. Synthesis of (*Z*)-tamoxifen from diphenyl acetylene.

**4.2.3. (E)-4-Bromo-5-(4-tolyl)thio-4-octene (3d)**

$^1\text{H}$  NMR (270 MHz,  $\text{CDCl}_3$ )  $\delta$  7.15 (d,  $J=8.3$  Hz, 2H), 7.09 (d,  $J=8.3$  Hz, 2H), 2.90 (t,  $J=7.4$  Hz, 2H), 2.34 (t,  $J=7.4$  Hz, 2H), 2.32 (s, 3H), 1.49–1.67 (m, 4H), 0.93 (t,  $J=7.4$  Hz, 3H), 0.86 (t,  $J=7.4$  Hz, 3H);  $^{13}\text{C}$  NMR (67.5 MHz,  $\text{CDCl}_3$ )  $\delta$  136.5, 132.2, 131.5, 131.4, 130.1, 129.8, 41.2, 38.5, 21.9, 21.0 (2C), 13.6, 13.1; IR (neat) 2960, 2929, 1894, 1602, 1491  $\text{cm}^{-1}$ . Anal. Calcd for  $\text{C}_{15}\text{H}_{21}\text{SBr}$ : C, 57.50; H, 6.76. Found: C, 57.21; H, 6.67.

**4.2.4. (E)-4-Bromo-5-(4-methoxyphenyl)thio-4-octene (3e)**

$^1\text{H}$  NMR (270 MHz,  $\text{CDCl}_3$ )  $\delta$  7.24 (d,  $J=8.9$  Hz, 2H), 6.84 (d,  $J=8.9$  Hz, 2H), 3.79 (s, 3H), 2.91 (t,  $J=7.3$  Hz, 2H), 2.28 (t,  $J=7.5$  Hz, 2H), 1.48–1.68 (m, 4H), 0.94 (t,  $J=7.4$  Hz, 3H), 0.85 (t,  $J=7.4$  Hz, 3H);  $^{13}\text{C}$  NMR (67.5 MHz,  $\text{CDCl}_3$ )  $\delta$  159.2, 133.3, 132.8, 129.5, 125.1, 114.6, 55.3, 41.1, 38.0, 21.9, 20.9, 13.6, 13.1; IR (neat) 2960, 2930, 1592, 1493  $\text{cm}^{-1}$ . Anal. Calcd for  $\text{C}_{15}\text{H}_{21}\text{OSBr}$ : C, 54.71; H, 6.43. Found: C, 54.53; H, 6.38.

**4.2.5. (E)-4-Bromo-5-(4-bromophenyl)thio-4-octene (3f)**

$^1\text{H}$  NMR (270 MHz,  $\text{CDCl}_3$ )  $\delta$  7.40 (d,  $J=8.6$  Hz, 2H), 7.08 (d,  $J=8.6$  Hz, 2H), 2.87 (t,  $J=7.2$  Hz, 2H), 2.37 (t,  $J=7.7$  Hz, 2H), 1.67–1.49 (m, 4H), 0.92 (t,  $J=7.4$  Hz, 3H), 0.87 (t,  $J=7.4$  Hz, 3H);  $^{13}\text{C}$  NMR (67.5 MHz,  $\text{CDCl}_3$ )  $\delta$  134.7, 133.7, 132.0, 130.9, 130.2, 120.1, 41.3, 38.8, 21.9, 21.0, 13.6, 13.0; IR (neat) 2960, 2929, 1889, 1603, 1471  $\text{cm}^{-1}$ . Anal. Calcd for  $\text{C}_{14}\text{H}_{18}\text{SBr}_2$ : C, 44.46; H, 4.80. Found: C, 44.32; H, 4.89.

**4.2.6. (E)-4-Bromo-5-(4-nitrophenyl)thio-4-octene (3g)**

$^1\text{H}$  NMR (270 MHz,  $\text{CDCl}_3$ )  $\delta$  8.14 (d,  $J=9.2$  Hz, 2H), 7.25 (d,  $J=9.2$  Hz, 2H), 2.85 (t,  $J=7.2$  Hz, 2H), 2.48 (t,  $J=7.6$  Hz, 2H), 1.67–1.53 (m, 4H), 0.94–0.88 (m, 6H);  $^{13}\text{C}$  NMR (67.5 MHz,  $\text{CDCl}_3$ )  $\delta$  146.1, 145.5, 137.5, 128.6, 126.6, 124.2, 41.5, 39.7, 21.9, 21.1, 13.6, 13.0; IR (neat) 2960, 2930, 1918, 1580, 1515  $\text{cm}^{-1}$ . Anal. Calcd for  $\text{C}_{14}\text{H}_{18}\text{NO}_2\text{SBr}$ : C, 48.84; H, 5.27. Found: C, 48.49; H, 5.20.

**4.2.7. (E)-4-Bromo-5-methylthio-4-octene (3h)**

$^1\text{H}$  NMR (270 MHz,  $\text{CDCl}_3$ )  $\delta$  2.81 (t,  $J=7.2$  Hz, 2H), 2.48 (t,  $J=7.7$  Hz, 2H), 2.20 (s, 3H), 1.63–1.54 (m, 4H), 0.95 (t,  $J=5.3$  Hz, 3H), 0.91 (t,  $J=5.3$  Hz, 3H);  $^{13}\text{C}$  NMR (67.5 MHz,  $\text{CDCl}_3$ )  $\delta$  133.4, 127.4, 40.8, 37.4, 21.7, 21.0, 16.4, 13.6, 12.9; IR (neat) 2960, 2928, 1602, 1459  $\text{cm}^{-1}$ . Anal. Calcd for  $\text{C}_9\text{H}_{17}\text{SBr}$ : C, 45.57; H, 7.22. Found: C, 45.60; H, 6.93.

**4.2.8. (E)-4-Iodo-5-methylthio-4-octene (3i)**

$^1\text{H}$  NMR (270 MHz,  $\text{CDCl}_3$ )  $\delta$  2.85 (t,  $J=7.5$  Hz, 2H), 2.51 (t,  $J=7.5$  Hz, 2H), 2.21 (s, 3H), 1.62–1.51 (m, 4H), 0.97 (t,  $J=7.5$  Hz, 3H), 0.91 (t,  $J=7.5$  Hz, 3H);  $^{13}\text{C}$  NMR (67.5 MHz,  $\text{CDCl}_3$ )  $\delta$  137.2, 106.8, 44.8, 42.5, 22.5, 21.2, 16.7, 13.6, 12.8; IR (neat) 2958, 2926, 1455, 1462  $\text{cm}^{-1}$ . Anal. Calcd for  $\text{C}_9\text{H}_{17}\text{SI}$ : C, 38.03; H, 6.03. Found: C, 38.10; H, 6.05.

**4.2.9. (E)-4-Bromo-5-(n-butyl)thio-4-octene (3j)**

$^1\text{H}$  NMR (270 MHz,  $\text{CDCl}_3$ )  $\delta$  2.84 (t,  $J=7.4$  Hz, 2H), 2.61 (t,  $J=7.1$  Hz, 2H), 2.45 (t,  $J=7.6$  Hz, 2H), 1.65–1.51 (m, 6H), 1.48–1.36 (m, 2H), 0.94–0.88 (m, 9H);  $^{13}\text{C}$  NMR (67.5 MHz,  $\text{CDCl}_3$ )  $\delta$  132.4, 128.9, 40.9, 37.8, 32.5, 31.9, 21.9, 21.8, 21.1, 13.6 (2C), 13.0; IR (neat) 2960, 2929, 1601, 1462  $\text{cm}^{-1}$ . Anal. Calcd for  $\text{C}_{12}\text{H}_{23}\text{SBr}$ : C, 51.61; H, 8.30. Found: C, 51.36; H, 8.17.

**4.2.10. (E)-4-Bromo-5-benzylthio-4-octene (3k)**

$^1\text{H}$  NMR (270 MHz,  $\text{CDCl}_3$ )  $\delta$  7.31–7.19 (m, 5H), 3.80 (s, 2H), 2.65 (t,  $J=7.2$  Hz, 2H), 2.48 (t,  $J=7.5$  Hz, 2H), 1.67–1.53 (m, 2H), 1.49–1.36 (m, 2H), 0.94 (t,  $J=7.4$  Hz, 3H), 0.81 (t,  $J=7.4$  Hz, 3H);  $^{13}\text{C}$  NMR (67.5 MHz,  $\text{CDCl}_3$ )  $\delta$  137.8, 131.8, 131.5, 128.8, 128.5, 127.0, 40.7, 38.5, 37.9, 21.7, 21.0, 13.6, 12.9; IR (neat) 2960, 2929, 1601, 1494, 1453  $\text{cm}^{-1}$ . Anal. Calcd for  $\text{C}_{15}\text{H}_{21}\text{SBr}$ : C, 57.50; H, 6.76. Found: C, 57.15; H, 6.85.

**4.2.11. (E)-3-Bromo-4-phenylthio-3-hexene (3l)**

$^1\text{H}$  NMR (270 MHz,  $\text{CDCl}_3$ )  $\delta$  7.31–7.15 (m, 5H), 2.91 (q,  $J=7.2$  Hz, 2H), 2.41 (t,  $J=7.2$  Hz, 2H), 1.13 (t,  $J=7.2$  Hz, 3H), 1.05 (t,  $J=7.2$  Hz, 3H);  $^{13}\text{C}$  NMR (67.5 MHz,  $\text{CDCl}_3$ )  $\delta$  135.3, 133.9, 131.8, 129.0, 128.9, 126.2, 33.3, 30.6, 13.5, 12.0; IR (neat) 2970, 2932, 1606, 1582, 1476, 1457, 1438  $\text{cm}^{-1}$ . Anal. Calcd for  $\text{C}_{12}\text{H}_{15}\text{SBr}$ : C, 53.14; H, 5.57. Found: C, 52.91; H, 5.56.

**4.2.12. (E)-1-Bromo-1,2-diphenyl-2-(4-tolyl)thioethene (3m)**

Mp 116–117  $^{\circ}\text{C}$ ;  $^1\text{H}$  NMR (270 MHz,  $\text{CDCl}_3$ )  $\delta$  7.57–7.53 (m, 2H), 7.43–7.32 (m, 4H), 7.25–7.16 (m, 4H), 7.00 (d,  $J=7.9$  Hz, 2H), 6.88 (t,  $J=7.9$  Hz, 2H), 2.18 (s, 3H);  $^{13}\text{C}$  NMR (67.5 MHz,  $\text{CDCl}_3$ )  $\delta$  140.7, 139.6, 137.2, 136.3, 131.8, 130.0, 129.7, 129.3, 129.2, 128.7, 128.2, 127.7, 127.6, 121.5, 21.0; IR ( $\text{CHCl}_3$ ) 3019, 1598, 1492  $\text{cm}^{-1}$ . Anal. Calcd for  $\text{C}_{21}\text{H}_{17}\text{SBr}$ : C, 66.14; H, 4.49. Found: C, 66.53; H, 4.53.

**4.2.13. (E)-1-Bromo-2-phenylthio-2-methylstyrene (3n)**

$^1\text{H}$  NMR (270 MHz,  $\text{CDCl}_3$ )  $\delta$  7.41–7.24 (m, 10H), 2.21 (s, 3H);  $^{13}\text{C}$  NMR (67.5 MHz,  $\text{CDCl}_3$ )  $\delta$  140.5, 134.5, 130.5, 130.2, 129.1, 129.0, 128.5, 128.1, 126.9, 123.3, 24.9; IR (neat) 3057, 1581, 1475, 1439  $\text{cm}^{-1}$ . Anal. Calcd for  $\text{C}_{15}\text{H}_{13}\text{SBr}$ : C, 59.02; H, 4.29. Found: C, 58.94; H, 4.37.

**4.2.14. (E)-1-Iodo-2-phenylthio-2-methylstyrene (3o)**

$^1\text{H}$  NMR (270 MHz,  $\text{CDCl}_3$ )  $\delta$  7.33–7.22 (m, 10H), 2.27 (s, 3H);  $^{13}\text{C}$  NMR (67.5 MHz,  $\text{CDCl}_3$ )  $\delta$  144.3, 134.9, 131.0, 129.0, 128.9, 128.7, 128.1, 128.0, 127.2, 99.6, 29.9; IR (neat) 3072, 3056, 1582, 1475, 1439  $\text{cm}^{-1}$ . Anal. Calcd for  $\text{C}_{15}\text{H}_{13}\text{SI}$ : C, 51.15; H, 3.72. Found: C, 51.10; H, 3.42.

**4.2.15. (E)-1-Bromo-1-phenyl-2-phenylthio-1-butene (3p)**

$^1\text{H}$  NMR (270 MHz,  $\text{CDCl}_3$ )  $\delta$  7.38–7.18 (m, 10H), 2.56 (q,  $J=7.4$  Hz, 2H), 1.16 (t,  $J=7.4$  Hz, 3H);  $^{13}\text{C}$  NMR (67.5 MHz,  $\text{CDCl}_3$ )  $\delta$  140.7, 136.3, 134.9, 130.1, 129.1, 128.9, 128.4, 128.0, 126.7, 123.6, 30.3, 12.1; IR (neat) 3057, 1581, 1475, 1439  $\text{cm}^{-1}$ . Anal. Calcd for  $\text{C}_{16}\text{H}_{15}\text{SBr}$ : C, 60.19; H, 4.74. Found: C, 59.97; H, 4.70.

**4.2.16. (E)-1-Bromo-1-phenyl-2-phenylthio-1-propenyl acetate (3q)**

$^1\text{H}$  NMR (270 MHz,  $\text{CDCl}_3$ )  $\delta$  7.41–7.20 (m, 10H), 4.96 (s, 2H), 2.00 (s, 3H);  $^{13}\text{C}$  NMR (67.5 MHz,  $\text{CDCl}_3$ )  $\delta$  170.4, 139.7, 133.9, 130.8, 130.3, 129.4, 129.3, 129.0, 128.8, 128.1, 127.2, 66.2, 20.6; IR (neat) 3058, 1743, 1581, 1477, 1440  $\text{cm}^{-1}$ . Anal. Calcd for  $\text{C}_{17}\text{H}_{15}\text{O}_2\text{SBr}$ : C, 56.21; H, 4.16. Found: C, 56.32; H, 4.25.

**4.2.17. (E)-2-Bromo-3-phenylthio-2-butenyl acetate (3r)**

$^1\text{H}$  NMR (270 MHz,  $\text{CDCl}_3$ )  $\delta$  7.32–7.21 (m, 5H), 4.87 (d,  $J=0.7$  Hz, 2H), 2.67 (s, 3H), 1.95 (s, 3H);  $^{13}\text{C}$  NMR (67.5 MHz,  $\text{CDCl}_3$ )  $\delta$  170.4, 134.3, 132.3, 129.2, 129.1, 126.8, 126.4, 66.7, 27.9, 20.5; IR (neat) 3058, 1743, 1610, 1581, 1477, 1440  $\text{cm}^{-1}$ . Anal. Calcd for  $\text{C}_{12}\text{H}_{13}\text{O}_2\text{SBr}$ : C, 47.85; H, 4.35. Found: C, 47.88; H, 4.59.

**4.2.18. (E)-4-Bromo-5-phenylseleno-4-octene (3u)**

$^1\text{H}$  NMR (270 MHz,  $\text{CDCl}_3$ )  $\delta$  7.42–7.36 (m, 2H), 7.28–7.23 (m, 3H), 2.89 (t,  $J=7.4$  Hz, 2H), 2.41 (t,  $J=7.4$  Hz, 2H), 1.69–1.46 (m, 4H), 0.92 (t,  $J=7.2$  Hz, 3H), 0.86 (t,  $J=7.2$  Hz, 3H);  $^{13}\text{C}$  NMR (67.5 MHz,  $\text{CDCl}_3$ )  $\delta$  132.1, 130.6, 129.5, 129.3, 129.2, 127.1, 43.3, 40.7, 21.9, 21.3, 13.5, 13.0; IR (neat) 2959, 2929, 1608, 1577, 1475  $\text{cm}^{-1}$ . Anal. Calcd for  $\text{C}_{14}\text{H}_{19}\text{SeBr}$ : C, 48.58; H, 5.53. Found: C, 48.82; H, 5.54.

**4.2.19. (E)-3-Bromo-4-phenylseleno-3-hexene (3v)**

$^1\text{H}$  NMR (270 MHz,  $\text{CDCl}_3$ )  $\delta$  7.42–7.38 (m, 2H), 7.28–7.23 (m, 3H), 2.90 (q,  $J=7.4$  Hz, 2H), 2.46 (q,  $J=7.4$  Hz, 2H), 1.12 (t,  $J=7.4$  Hz, 3H), 1.03 (t,  $J=7.4$  Hz, 3H);  $^{13}\text{C}$  NMR (67.5 MHz,  $\text{CDCl}_3$ )  $\delta$  132.1, 131.9, 130.6, 129.8, 129.2, 127.1, 35.4, 32.7, 13.5, 12.3; IR (neat) 2969, 2931,



1610, 1577, 1475, 1456, 1437  $\text{cm}^{-1}$ . Anal. Calcd for  $\text{C}_{12}\text{H}_{15}\text{SeBr}$ : C, 45.31; H, 4.75. Found: C, 45.02; H, 4.70.

#### 4.2.20. (*E*)-1-Bromo-1,2-diphenyl-2-phenylselenoethene (**3w**)

Mp 98–99 °C;  $^1\text{H}$  NMR (270 MHz,  $\text{CDCl}_3$ )  $\delta$  7.55–7.40 (m, 2H), 7.38–7.34 (m, 4H), 7.21–6.97 (m, 9H);  $^{13}\text{C}$  NMR (67.5 MHz,  $\text{CDCl}_3$ )  $\delta$  141.2, 140.5, 135.0, 133.3, 129.5, 129.3, 129.1, 128.8, 128.5, 128.3, 127.8, 127.6, 127.4, 117.7; IR ( $\text{CHCl}_3$ ) 3019, 1578, 1476, 1443  $\text{cm}^{-1}$ . Anal. Calcd for  $\text{C}_{20}\text{H}_{15}\text{SeBr}$ : C, 58.00; H, 3.65. Found: C, 57.61; H, 3.73.

#### 4.2.21. (*E*)-1-Bromo-2-phenylseleno-2-methylstyrene (**3x**)

$^1\text{H}$  NMR (270 MHz,  $\text{CDCl}_3$ )  $\delta$  7.48–7.43 (m, 2H), 7.39–7.12 (m, 8H), 2.22 (s, 3H);  $^{13}\text{C}$  NMR (67.5 MHz,  $\text{CDCl}_3$ )  $\delta$  141.4, 134.3, 133.5, 129.1, 129.0, 128.6, 128.2, 127.9, 127.7, 118.4, 26.3; IR (neat) 3055, 1576, 1475, 1438  $\text{cm}^{-1}$ . Anal. Calcd for  $\text{C}_{15}\text{H}_{13}\text{SeBr}$ : C, 51.16; H, 3.72. Found: C, 51.00; H, 3.82.

#### 4.2.22. (*E*)-1-Bromo-1-phenyl-2-phenylseleno-1-propenyl acetate (**3y**)

$^1\text{H}$  NMR (270 MHz,  $\text{CDCl}_3$ )  $\delta$  7.41–7.34 (m, 6H), 7.26–7.23 (m, 4H), 4.97 (s, 2H), 1.98 (s, 3H);  $^{13}\text{C}$  NMR (67.5 MHz,  $\text{CDCl}_3$ )  $\delta$  170.4, 138.9, 135.4, 133.7, 129.2, 129.1, 128.8, 128.1, 128.0, 124.7, 77.2, 64.8, 20.6; IR (neat) 3057, 1741, 1577, 1476, 1438  $\text{cm}^{-1}$ . Anal. Calcd for  $\text{C}_{17}\text{H}_{15}\text{O}_2\text{SeBr}$ : C, 49.78; H, 3.69. Found: C, 49.78; H, 3.79.

#### 4.2.23. (*E*)-2-Bromo-3-phenylseleno-2-butenyl acetate (**3z**)

$^1\text{H}$  NMR (270 MHz,  $\text{CDCl}_3$ )  $\delta$  7.49–7.40 (m, 2H), 7.32–7.26 (m, 3H), 4.91 (s, 2H), 2.66 (s, 3H), 1.95 (s, 3H);  $^{13}\text{C}$  NMR (67.5 MHz,  $\text{CDCl}_3$ )  $\delta$  170.4, 132.1, 129.9, 129.4, 129.3, 127.5, 123.6, 68.4, 29.9, 20.6; IR (neat) 3057, 1739, 1615, 1577, 1476, 1437  $\text{cm}^{-1}$ . Anal. Calcd for  $\text{C}_{12}\text{H}_{13}\text{O}_2\text{SeBr}$ : C, 41.40; H, 3.76. Found: C, 41.46; H, 3.80.

### 4.3. Debromination of $\beta$ -bromoalkenyl sulfides

To a mixture of  $\text{Pd}(\text{PPh}_3)_4$  (17.3 mg, 0.015 mmol) and MeONa (16.2 mg, 0.3 mmol) in DMF (0.5 mL) was added (*E*)-4-bromo-5-phenylthio-4-octene **3a** (44.9 mg, 0.15 mmol) under nitrogen atmosphere, and the mixture was stirred at 100 °C for 18 h. After the residue was dissolved in  $\text{Et}_2\text{O}$ , the solution was washed with  $\text{H}_2\text{O}$  and saturated sodium chloride and dried over anhydrous magnesium sulfate. Chromatography on silica gel (Hexane) gave (*Z*)-4-phenylthio-4-octene **5a** (30.3 mg, 92%).<sup>6b</sup>  $^1\text{H}$  NMR (270 MHz,  $\text{CDCl}_3$ )  $\delta$  7.29–7.11 (m, 5H), 5.90 (t,  $J=7.1$  Hz, 1H), 2.31 (q,  $J=7.2$  Hz, 2H), 2.14 (t,  $J=7.2$  Hz, 2H), 1.56–1.36 (m, 4H), 0.92 (t,  $J=7.2$  Hz, 3H), 0.82 (t,  $J=7.2$  Hz, 3H). The NOE was observed at two allyl positions ( $-\text{CH}_2-\text{CH}=\text{}$ , 15%) and ( $=\text{C}(\text{SPh})\text{CH}_2-$ , 11%) on irradiation at 5.90 ppm ( $=\text{CH}-$ );  $^{13}\text{C}$  NMR (67.5 MHz,  $\text{CDCl}_3$ )  $\delta$  136.7, 135.8, 133.0, 129.2, 128.7, 125.6, 39.6, 31.9, 22.7, 21.6, 13.8, 13.3; IR (neat) 2958, 1583, 1476  $\text{cm}^{-1}$ . Anal. Calcd for  $\text{C}_{14}\text{H}_{20}\text{S}$ : C, 76.30; H, 9.15. Found: C, 76.03; H, 8.92.

#### 4.3.1. (*Z*)-3-Phenylthio-3-hexene (**5b**)

$^1\text{H}$  NMR (270 MHz,  $\text{CDCl}_3$ )  $\delta$  7.27–7.12 (m, 5H), 5.91 (dt,  $J=7.3$  and 1.0 Hz, 1H), 2.33 (dq,  $J=7.4$  and 7.3 Hz, 2H), 2.18 (dq,  $J=7.4$  and 1.0 Hz, 2H), 1.04 (t,  $J=7.4$  Hz, 3H), 1.01 (t,  $J=7.4$  Hz, 3H). The NOE was observed at two allyl positions ( $-\text{CH}_2-\text{CH}=\text{}$ , 5%) and ( $=\text{C}(\text{SPh})\text{CH}_2-$ , 6%) on irradiation at 5.91 ppm ( $=\text{CH}-$ );  $^{13}\text{C}$  NMR (67.5 MHz,  $\text{CDCl}_3$ )  $\delta$  137.2, 135.8, 134.1, 129.1, 128.7, 125.6, 30.8, 23.3, 13.9, 13.5; IR (neat) 3072, 2965, 2930, 1583, 1476  $\text{cm}^{-1}$ . Anal. Calcd for  $\text{C}_{12}\text{H}_{16}\text{S}$ : C, 74.94; H, 8.39. Found: C, 74.98; H, 8.24.

#### 4.3.2. (*Z*)-2-Phenylthio-2-methylstyrene (**5c**)<sup>6b</sup>

$^1\text{H}$  NMR (270 MHz,  $\text{CDCl}_3$ )  $\delta$  7.54 (d,  $J=7.6$  Hz, 2H), 7.42–7.21 (m, 8H), 6.70 (s, 1H), 2.02 (d,  $J=1.3$  Hz, 3H). The NOE was observed at the phenyl (14%) and allyl positions ( $=\text{C}(\text{SPh})\text{CH}_2-$ , 15%) on

irradiation at 6.70 ppm ( $=\text{CH}-$ );  $^{13}\text{C}$  NMR (67.5 MHz,  $\text{CDCl}_3$ )  $\delta$  136.8, 133.6, 132.1, 131.7, 130.9, 129.0, 128.9, 128.0, 127.1, 126.9, 25.6; IR (neat) 3057, 3021, 2915, 1582, 1492, 1475  $\text{cm}^{-1}$ . Anal. Calcd for  $\text{C}_{15}\text{H}_{14}\text{S}$ : C, 79.60; H, 6.23. Found: C, 79.34; H, 6.31.

### 4.4. Copper-catalyzed synthesis of $\beta$ -chloro or thiocynoalkenyl chalcogenides (Table 3)

#### 4.4.1. (*E*)-4-Chloro-5-phenylseleno-4-octene (**7a**)

$^1\text{H}$  NMR (270 MHz,  $\text{CDCl}_3$ )  $\delta$  7.41–7.36 (m, 2H), 7.29–7.24 (m, 3H), 2.79 (t,  $J=7.4$  Hz, 2H), 2.41 (t,  $J=7.4$  Hz, 2H), 1.69–1.57 (m, 2H), 1.57–1.46 (m, 2H), 0.92 (t,  $J=7.4$  Hz, 3H), 0.86 (t,  $J=7.4$  Hz, 3H);  $^{13}\text{C}$  NMR (67.5 MHz,  $\text{CDCl}_3$ )  $\delta$  136.9, 131.9, 130.6, 129.2, 127.9, 126.9, 41.0, 37.7, 21.4, 21.3, 13.5, 13.2; IR (neat) 3057, 1746, 1576, 1488, 1476  $\text{cm}^{-1}$ . Anal. Calcd for  $\text{C}_{14}\text{H}_{19}\text{SeCl}$ : C, 55.73; H, 6.35. Found: C, 55.56; H, 6.21.

#### 4.4.2. (*E*)-3-Chloro-4-phenylthio-3-hexene (**7b**)

$^1\text{H}$  NMR (270 MHz,  $\text{CDCl}_3$ )  $\delta$  7.30–7.15 (m, 5H), 2.79 (q,  $J=7.4$  Hz, 2H), 2.39 (q,  $J=7.4$  Hz, 2H), 1.14 (t,  $J=7.4$  Hz, 3H), 1.05 (t,  $J=7.4$  Hz, 3H);  $^{13}\text{C}$  NMR (67.5 MHz,  $\text{CDCl}_3$ )  $\delta$  140.9, 135.5, 129.9, 128.9, 128.7, 126.1, 30.9, 27.8, 12.8, 12.1; IR (neat) 2971, 2934, 1582, 1477, 1457, 1439  $\text{cm}^{-1}$ . Anal. Calcd for  $\text{C}_{12}\text{H}_{15}\text{SCL}$ : C, 63.56; H, 6.67. Found: C, 63.58; H, 6.60.

#### 4.4.3. (*E*)-1-Chloro-1,2-diphenyl-2-(4-tolyl)thioethene (**7c**)

$^1\text{H}$  NMR (270 MHz,  $\text{CDCl}_3$ )  $\delta$  7.62–7.58 (m, 2H), 7.46–7.36 (m, 4H), 7.35–7.20 (m, 4H), 7.18 (d,  $J=6.0$  Hz, 2H), 7.01 (t,  $J=6.0$  Hz, 2H), 2.20 (s, 3H);  $^{13}\text{C}$  NMR (67.5 MHz,  $\text{CDCl}_3$ )  $\delta$  139.1, 138.1, 136.9, 133.7, 132.7, 131.3, 130.3, 129.8, 129.4, 128.8, 128.1, 127.8, 127.7, 127.6, 20.9; IR ( $\text{CHCl}_3$ ) 3018, 1583, 1491, 1443  $\text{cm}^{-1}$ . Anal. Calcd for  $\text{C}_{21}\text{H}_{17}\text{SCL}$ : C, 74.87; H, 5.09. Found: C, 74.49; H, 5.19.

#### 4.4.4. (*E*)-1-Chloro-2-phenylthio-2-methylstyrene (**7d**)

$^1\text{H}$  NMR (270 MHz,  $\text{CDCl}_3$ )  $\delta$  7.46–7.21 (m, 10H), 2.19 (s, 3H);  $^{13}\text{C}$  NMR (67.5 MHz,  $\text{CDCl}_3$ )  $\delta$  138.7, 134.6, 132.8, 130.2, 129.1, 129.0, 128.6, 128.0, 127.9, 126.8, 22.0; IR ( $\text{CHCl}_3$ ) 3019, 2157, 1475, 1441  $\text{cm}^{-1}$ . Anal. Calcd for  $\text{C}_{15}\text{H}_{13}\text{SCL}$ : C, 69.08; H, 5.02. Found: C, 68.72; H, 5.15.

#### 4.4.5. (*E*)-1-Chloro-2-phenylseleno-2-methylstyrene (**7e**)

$^1\text{H}$  NMR (270 MHz,  $\text{CDCl}_3$ )  $\delta$  7.46–7.24 (m, 10H), 2.21 (s, 3H);  $^{13}\text{C}$  NMR (67.5 MHz,  $\text{CDCl}_3$ )  $\delta$  139.7, 133.9, 131.5, 129.7, 129.1, 129.0, 128.7, 128.1, 127.8, 125.7, 23.4; IR (neat) 3056, 1577, 1475, 1438  $\text{cm}^{-1}$ . Anal. Calcd for  $\text{C}_{15}\text{H}_{13}\text{SeCl}$ : C, 58.56; H, 4.26. Found: C, 58.28; H, 4.34.

#### 4.4.6. (*E*)-1-Chloro-1-phenyl-2-phenylthio-1-propenyl acetate (**7f**)

$^1\text{H}$  NMR (270 MHz,  $\text{CDCl}_3$ )  $\delta$  7.47–7.44 (m, 2H), 7.37–7.22 (m, 8H), 4.96 (s, 2H), 1.99 (s, 3H);  $^{13}\text{C}$  NMR (67.5 MHz,  $\text{CDCl}_3$ )  $\delta$  170.5, 138.9, 137.8, 134.0, 130.1, 129.3, 129.1, 128.9, 128.1, 127.1, 127.0, 63.9, 20.6; IR (neat) 3058, 3020, 1743, 1583, 1477, 1441  $\text{cm}^{-1}$ . Anal. Calcd for  $\text{C}_{17}\text{H}_{15}\text{O}_2\text{SeCl}$ : C, 64.04; H, 4.74. Found: C, 63.90; H, 4.79.

#### 4.4.7. (*E*)-1-Chloro-1-phenyl-2-phenylthio-1-propenyl acetate (**7g**)

$^1\text{H}$  NMR (270 MHz,  $\text{CDCl}_3$ )  $\delta$  7.42–7.34 (m, 6H), 7.28–7.23 (m, 4H), 4.95 (s, 2H), 1.99 (s, 3H);  $^{13}\text{C}$  NMR (67.5 MHz,  $\text{CDCl}_3$ )  $\delta$  170.3, 138.9, 135.4, 133.7, 129.2, 129.1, 128.9, 128.8, 128.1, 128.0, 124.8, 64.9, 20.6; IR (neat) 2959, 1610, 1578, 1476, 1462, 1437  $\text{cm}^{-1}$ . Anal. Calcd for  $\text{C}_{17}\text{H}_{15}\text{O}_2\text{SeCl}$ : C, 55.83; H, 4.13. Found: C, 55.49; H, 4.20.

#### 4.4.8. (*E*)-4-Phenylthio-5-thiocyanato-4-octene (**7h**)

$^1\text{H}$  NMR (270 MHz,  $\text{CDCl}_3$ )  $\delta$  7.34–7.26 (m, 5H), 2.89 (t,  $J=7.4$  Hz, 2H), 2.33 (t,  $J=7.4$  Hz, 2H), 1.74–1.66 (m, 2H), 1.53–1.44 (m, 2H), 0.99 (t,  $J=7.4$  Hz, 3H), 0.81 (t,  $J=7.4$  Hz, 3H);  $^{13}\text{C}$  NMR (67.5 MHz,  $\text{CDCl}_3$ )

$\delta$  142.1, 133.0, 131.6, 129.2, 127.7, 126.2, 110.2, 37.2, 36.1, 21.8, 21.7, 13.4, 13.3; IR (neat) 2960, 2154, 1582, 1475, 1462, 1439  $\text{cm}^{-1}$ . Anal. Calcd for  $\text{C}_{15}\text{H}_{19}\text{S}_2\text{NCl}$ : C, 57.58; H, 6.12; N, 4.48. Found: C, 57.52; H, 5.96; N, 4.36.

#### 4.4.9. (*E*)-4-Phenylseleno-5-thiocyanato-4-octene (**7i**)

$^1\text{H}$  NMR (270 MHz,  $\text{CDCl}_3$ )  $\delta$  7.50–7.46 (m, 2H), 7.34–7.26 (m, 3H), 2.84 (t,  $J=7.4$  Hz, 2H), 2.36 (t,  $J=7.4$  Hz, 2H), 1.73–1.62 (m, 2H), 1.56–1.39 (m, 2H), 0.99 (t,  $J=7.4$  Hz, 3H), 0.78 (t,  $J=7.4$  Hz, 3H);  $^{13}\text{C}$  NMR (67.5 MHz,  $\text{CDCl}_3$ )  $\delta$  141.7, 134.4, 129.4, 128.5, 128.3, 123.6, 110.4, 39.2, 37.8, 22.1, 21.6, 13.3 (2C); IR (neat) 2960, 2152, 1577, 1476, 1462, 1438  $\text{cm}^{-1}$ . Anal. Calcd for  $\text{C}_{15}\text{H}_{19}\text{SeSN}$ : C, 55.55; H, 5.90; N, 4.32. Found: C, 55.52; H, 5.96; N, 4.36.

#### 4.4.10. (*E*)-3-Phenylthio-4-thiocyanato-3-hexene (**7j**)

$^1\text{H}$  NMR (270 MHz,  $\text{CDCl}_3$ )  $\delta$  7.31–7.24 (m, 5H), 2.90 (q,  $J=7.4$  Hz, 2H), 2.36 (q,  $J=7.4$  Hz, 2H), 1.23 (t,  $J=7.4$  Hz, 3H), 1.02 (t,  $J=7.4$  Hz, 3H);  $^{13}\text{C}$  NMR (67.5 MHz,  $\text{CDCl}_3$ )  $\delta$  142.9, 132.9, 131.5, 129.2, 127.7, 127.0, 110.2, 29.1, 27.9, 13.0 (2C); IR (neat) 2971, 2933, 2154, 1581, 1475, 1457, 1439  $\text{cm}^{-1}$ . Anal. Calcd for  $\text{C}_{13}\text{H}_{15}\text{S}_2\text{N}$ : C, 62.61; H, 6.06; N, 5.62. Found: C, 62.24; H, 6.07; N, 5.64.

### 4.5. Copper-catalyzed synthesis of $\beta$ -haloalkenyl sulfide using thiol (Table 4)

To a mixture of CuI (3.8 mg, 0.02 mmol), bpy (3.1 mg, 0.02 mmol), PhSH **4a** (26.4 mg, 0.24 mmol), and *n*-Bu<sub>4</sub>NBr (70.9 mg, 0.22 mmol) in AcOH (0.3 mL) was added 4-octyne **1a** (22.0 mg, 0.2 mmol), and the mixture was stirred at 100 °C for 18 h under oxygen atmosphere using a balloon. After the residue was dissolved in Et<sub>2</sub>O, the solution was washed with H<sub>2</sub>O and saturated sodium chloride and dried over anhydrous magnesium sulfate. Chromatography on silica gel (Hexane) gave (*E*)-4-bromo-5-phenylthio-4-octene **3a** (35.9 mg, 60%).

### 4.6. Synthesis of (*Z*)-tamoxifen

To a mixture of (*E*)-1-bromo-1,2-diphenyl-2-(4-tolyl)thioethene **3m** (178.3 mg, 0.47 mmol), Me<sub>2</sub>N(CH<sub>2</sub>)<sub>2</sub>OC<sub>6</sub>H<sub>4</sub>B(pin) (151.4 mg, 0.52 mmol), Pd(PPh<sub>3</sub>)<sub>4</sub> (46.2 mg, 0.04 mmol), and K<sub>2</sub>CO<sub>3</sub> (194.9 mg, 1.41 mmol) in dioxane (4 mL), and H<sub>2</sub>O (0.4 mL) was poured under nitrogen atmosphere, and the mixture was stirred at 100 °C for 24 h. After the residue was dissolved in Et<sub>2</sub>O, the solution was washed with H<sub>2</sub>O and saturated sodium chloride and dried over anhydrous magnesium sulfate. Chromatography on silica gel (5% methanol in ethyl acetate) gave (*E*)-1-(4-dimethylaminoethoxyphenyl)-1,2-diphenyl-2-(4-tolyl)thioethene **13** (156.4 mg, 72%).  $^1\text{H}$  NMR (270 MHz,  $\text{CDCl}_3$ )  $\delta$  7.30–7.29 (m, 7H), 7.07–7.00 (m, 5H), 6.89–6.83 (m, 4H), 6.59 (d,  $J=8.1$  Hz, 2H), 3.94 (t,  $J=5.4$  Hz, 2H), 2.65 (t,  $J=5.4$  Hz, 2H), 2.28 (s, 6H), 2.17 (s, 3H);  $^{13}\text{C}$  NMR (67.5 MHz,  $\text{CDCl}_3$ )  $\delta$  157.4, 145.7, 144.1, 139.5, 135.4, 134.9, 132.9, 132.2, 132.0, 131.0, 129.6, 129.5, 129.2, 128.0, 127.6, 127.1, 126.7, 113.6, 65.7, 58.2, 45.8, 20.9; IR (CHCl<sub>3</sub>) 2977, 2779, 1605, 1507  $\text{cm}^{-1}$ . Anal. Calcd for C<sub>31</sub>H<sub>31</sub>NOS: C, 79.96; H, 6.71, N, 3.01. Found: C, 79.91; H, 6.85, N, 2.92.

To a mixture of (*E*)-1-(4-dimethylaminoethoxyphenyl)-1,2-diphenyl-2-(4-tolyl)thioethene **13** (100 mg, 0.21 mmol), NiCl<sub>2</sub>(dppe) (9.0 mg, 0.017 mmol) in diethyl ether (2.0 mL) was added EtMgBr (2.0 mL, 0.5 M in diethyl ether) under nitrogen atmosphere, and the mixture was refluxed with stirring for 15 h. After H<sub>2</sub>O was added to the mixture, the residue was dissolved in Et<sub>2</sub>O, the solution was washed with H<sub>2</sub>O and saturated sodium chloride and dried over anhydrous magnesium sulfate. Chromatography on silica gel (5% methanol in ethyl acetate) gave tamoxifen **14** (60.1 mg, 75% *Z*/*E*=93/7).  $^1\text{H}$  NMR (270 MHz,  $\text{CDCl}_3$ )  $\delta$  7.34–7.10 (m, 10H), 6.77 (d,  $J=10.8$  Hz, 2H), 6.55 (d,  $J=10.8$  Hz, 2H), 3.92 (t,  $J=5.4$  Hz, 2H), 2.64

(t,  $J=5.4$  Hz, 2H), 2.45 (q,  $J=8.1$  Hz, 2H), 2.28 (s, 6H), 0.92 (t,  $J=8.1$  Hz, 3H);  $^{13}\text{C}$  NMR (67.5 MHz,  $\text{CDCl}_3$ )  $\delta$  150.7, 143.8, 142.4, 141.3, 138.2, 135.5, 131.8, 129.7, 129.4, 128.1, 126.4, 125.9, 113.4, 65.7, 58.3, 45.9, 28.9, 13.6; IR (CHCl<sub>3</sub>) 2971, 2823, 1606, 1508  $\text{cm}^{-1}$ . Anal. Calcd for C<sub>26</sub>H<sub>29</sub>NO: C, 84.06; H, 7.87; N, 3.77. Found: C, 83.60; H, 7.89; N, 3.62.

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