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Copper-catalyzed synthesis of β-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 β-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 chalocogenides, 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.

1. Introduction

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

As a general rule, to synthesize alkenyl sulfides, disulfidations[5] or hydrosulfidations[6] 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.[7] However, a transition-metal-catalyzed preparation of *anti*-additive products has been rarely exploited.[8] Moreover, an employment of internal alkyne is very limited though various reactions using terminal alkynes are reported.[6]

Although β-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 sulfenyl halides to alkynes[9,10] or decarboxylative dehydrohalogenation of β-arylmercapto-α,β-dihalopropionic acids.[11] 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 β-haloalkenyl sulfides from internal alkynes are desired now.

To synthesize β-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 sulfenyl cation and reusing a metal-thiolate complex generated as an intermediates.[12] From various investigations, I found that a synthesis of β-haloalkenyl sulfides from disulfides with internal alkynes could carry out by a copper catalyst in air.[13] 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_4NBr was employed, the corresponding β-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_3P 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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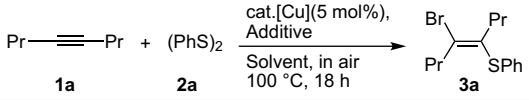
Table 1
Addition of bromide and sulfide-group to 4-octyne



1a 2a 3a

Entry	[Cu]–L	Additive	Solvent	**3a** (%)[a]
1	CuI–bpy	KBr	AcOH	38
2	CuI–bpy	$BrCH_2CH_2Br$	AcOH	Trace
3	CuI–bpy	*n*-Bu_4NBr	AcOH	81
4	CuI–none	*n*-Bu_4NBr	AcOH	44
5	CuI–Phen	*n*-Bu_4NBr	AcOH	65
6	CuI–TMEDA	*n*-Bu_4NBr	AcOH	21
7	CuI–Ph_3P	*n*-Bu_4NBr	AcOH	25
8	CuBr–bpy	*n*-Bu_4NBr	AcOH	77
9	CuCl–bpy	*n*-Bu_4NBr	AcOH	5
10	$CuBr_2$–bpy	*n*-Bu_4NBr	AcOH	15
11	$CuCl_2$–bpy	*n*-Bu_4NBr	AcOH	Trace
12	$Cu(OAc)_2$–bpy	*n*-Bu_4NBr	AcOH	Trace
13	CuI–bpy	*n*-Bu_4NBr	DMF	0
14	CuI–bpy	*n*-Bu_4NBr	DMSO	Trace
15	CuI–bpy	*n*-Bu_4NBr	Dioxane	Trace
16	CuI–bpy	*n*-Bu_4NBr	$PhCH_3$	0

[a] Isolated yields after silica gel chromatography.

used, the present reaction proceeded smoothly. But Cu(II) catalysts could not promote satisfactorily the reaction (entries 10–12). Other solvents (DMF, DMSO, dioxane, and $PhCH_3$) could not produce **3a** at all (entries 13–16).

Noteworthily, a combination of alkyne with thiol could afford β-bromoalkenyl sulfide **3a** in only 24% yield, and disulfide was obtained in 60% yield (Scheme 1). Thus, it has became apparent that the copper-catalyzed reaction of alkyne with disulfide could effectively promote the addition of halide and sulfide-groups.

Then, to clarify the stereochemistry of 4-bromo-5-phenythio-4-octene **3a**, a debromination of **3a** was carried out. When **3a** was reduced by cat. $Pd(PPh_3)_4$ and MeONa, 4-phenylthio-4-octene **5a** was obtained in 92% yield as a single isomer. The stereochemistry of **5a** was *Z*-isomer.[14] This result shows that the addition of bromide and phenylthio-group to internal alkynes is *anti*-selectively reaction.[13]

On the basis of my developed method, various copper-catalyzed syntheses of β-haloalkenyl sulfides using internal alkynes and disulfides were examined. As shown in Table 2, numerous combinations of diaryl or dialkyl disulfides and symmetrical internal alkynes could *anti*-selectively produced the corresponding β-bromo or iodoalkenyl sulfides in excellent yields (entries 1–13).[15] Regrettably, the case using *n*-Bu_4NCl or di(4-nitrophenyl)disulfide showed lower reactivity (entries 3 and 7), and the starting materials were recovered.

The present procedure could also employ unsymmetrical internal alkynes, and *regio*- and *anti*-selectively produced the corresponding β-bromo or iodoalkenyl sulfides (entries 14–18).[15,16] Although a reaction using 1-phenyl-1-propyne or 2-butyn-1-ol afforded good yields, the *anti*-selectivity decreased slightly (entries 14 and 18).[16] 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).

In this method, not only disulfides but also diselenides can participate (entries 21–26). The treatment of alkynes with diphenyl diselenide by CuI catalyst *regio*- or *anti*-selectively produced the corresponding β-bromoalkenyl selenides in excellent yields.

As shown in Table 2, the preparation of β-chloroalkenyl sulfide using *n*-Bu_4NCl was unsatisfactory results. To solve this problem, I examined an introducing condition of chloride (entry 3 in Table 2). From various experiments, I found that the employment of cesium chloride could form the β-chloroalkenyl sulfides or selenides in good yield (entries 1–8 in Table 3). In addition, the present procedure could introduce thiocyanide instead of halide by the use of potassium thiocyanate (entries 9–11 in Table 3).

Thus, β-haloalkenyl chalcogenides could *anti*- and *regio*-selectively synthesize from internal alkynes, dichalcogenides and tetrabutylammonium halides by the copper catalyst.

As an application of the present reaction, I then investigated β-halosulfenylations of alkynes using thiols. From previous experiments, it is evident that although the reaction using thiol can produce the desired alkenyl sulfide, the yield is very low. Therefore, to improve the yield, various conditions were researched. By various examinations, I found that a reaction under oxygen atmosphere could attain to the best result. When a mixture of 4-octyne **1a**, PhSH **4a**, and *n*-Bu_4NBr was treated by CuI–bpy (1:1, 10 mol %) under oxygen atmosphere, (*E*)-4-bromo-5-phenylthio-4-octene **3a** was obtained in 60% yield with diphenyl disulfide (entry 1 in Table 4).

On the basis of the above described condition, numerous additions of thiols to internal alkynes were carried out (Table 4). The present procedure could *regio*- and *anti*-selectively produce the (*E*)-β-haloalkenyl sulfides **3**, but the yields were decreased slightly.

Thus, I could also achieve the method using thiol under oxygen atmosphere.

To investigate the reaction process, we next researched both a reaction in the absence of oxygen and a reactivity of PhSCu(I).

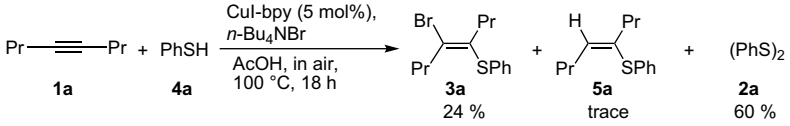
When the reaction of 4-octyne **1a** with diphenyl disulfide **2a** was carried out under nitrogen atmosphere, β-iodoalkenyl sulfide **3b** was obtained in only 22% yield with a recovery of disulfide (Scheme 2).

The reactivity of PhSCu(I) **8**[17] considered as an intermediate was also examined. The reaction of the complex **8** with 4-octyne **1a** in air could produce the expected alkenyl sulfide **3b** in 49% yield, but the reaction in the absence of oxygen gave in only 10% yield (Scheme 3). That is to say, the complex **8** cannot carry out sulfenylation of 4-octyne by itself.

Then, I examined changes of PhSCu(I) in various solvents (Table 5). When PhSCu(I) was treated in acetic acid, diphenyl disulfide **2a** was obtained in 92% yield. On the other hand, in other solvent such as DMSO or DMF, the formation of disulfide **2a** was inhibited. This fact suggests that PhSCu(I) undergo disproportionation in acetic acid.

From these results, oxygen is necessary for the promotion of the copper-catalyzed halosulfenylation of alkynes, and it is obvious that both disulfide and the copper catalyst can be reproduced from PhSCu(I) under acidic conditions in the presence of oxygen.

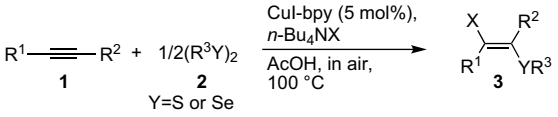
Therefore, a reaction mechanism is considered as follows (Fig. 1). After the Cu(I)-catalyst acted on the disulfide as the oxidant in air or Lewis acid,[13,18,19] a sulfenium ion **9** and $PhSCu(I)L_n$ **11** are

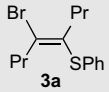
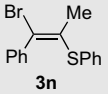
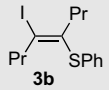
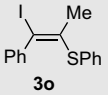
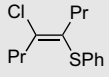
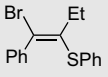
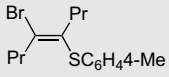
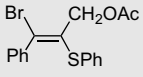
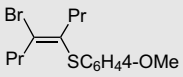
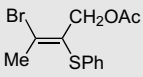
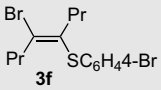
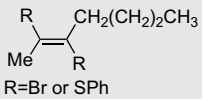
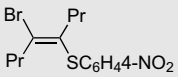
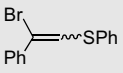
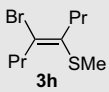
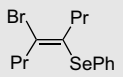
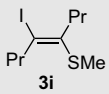
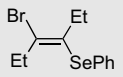
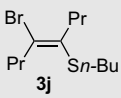
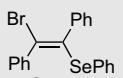
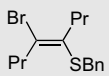
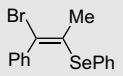
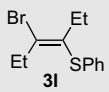
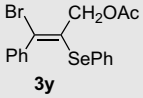
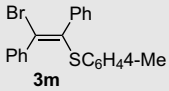
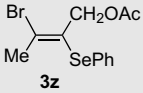


1a 4a **3a** 24 % **5a** trace **2a** 60 %

Scheme 1. Reaction of 4-octyne with benzenethiol.

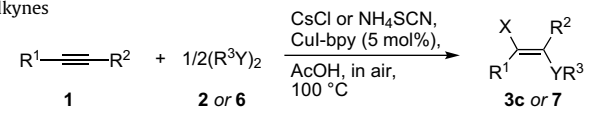
Table 2
Copper-catalyzed synthesis of β-haloalkenyl chalcogenides using dichalcogenides



Entry	3	Time (h)	3 (%)[a]	Entry	3	Time (h)	3 (%)[a] (*E*/*Z*)[c]
1	 **3a**	18	81	14	 **3n**	18	94 (98/2)[c,d]
2	 **3b**	18	80	15	 **3o**	18	66
3	 **3c**	18	42	16	 **3p**	18	86
4	 **3d**	18	85	17[f]	 **3q**	48	69
5	 **3e**	18	87	18[g]	 **3r**	36	85 (87/13)[c,d]
6	 **3f**	18	65	19	 R=Br or SPh **3s**	40	73[e]
7	 **3g**	24	45	20[b]	 **3t**	18	28 (65/35)[c]
8	 **3h**	18	74	21	 **3u**	18	94
9	 **3i**	18	77	22	 **3v**	18	80
10	 **3j**	18	76	23	 **3w**	40	81
11	 **3k**	18	81	24	 **3x**	18	80
12	 **3l**	18	71	25[b,f]	 **3y**	48	84
13	 **3m**	42	70	26[g]	 **3z**	48	87(87/13)[c,d]

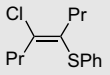
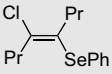
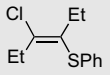
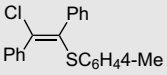
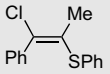
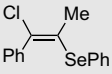
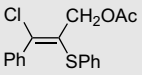
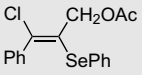
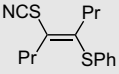
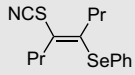
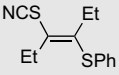
[a] Isolated yields after silica gel chromatography.
[b] CuI was used 10 mol %.
[c] Determined by ^{1}H NMR.
[d] These isomers can separate by silica gel chromatography.
[e] Regio-isomers were obtained in the ratio of 1:1.
[f] 3-Phenyl-2-propyn-1-ol was used as a starting material.
[g] 2-Butyn-1-ol was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

Table 3
Copper-catalyzed introduction of chloride or thiocyanide and chalcogenide-groups to alkynes



1 2 *or* 6 3c *or* 7

X = Cl or SCN

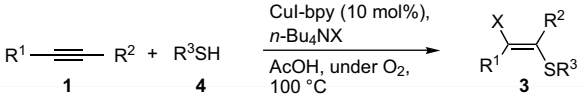
Entry	7	Time (h)	7 (%)[a]
1	 **3c**	40	76
2	 **7a**	42	86
3	 **7b**	43	67
4	 **7c**	40	75
5	 **7d**	42	75
6	 **7e**	42	78
7[b]	 **7f**	72	52
8[b]	 **7g**	72	70
9	 **7h**	18	90
10	 **7i**	18	63
11	 **7j**	18	66

[a] Isolated yields after silica gel chromatography.
[b] 3-Phenyl-2-propyn-1-ol was used as a starting material.

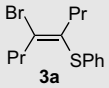
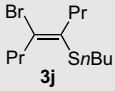
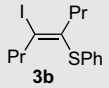
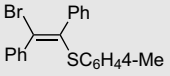
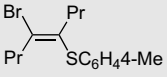
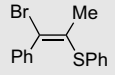
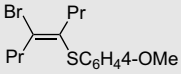
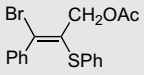
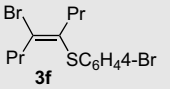
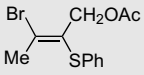
produced from intermediates **10** with alkyne **1**. Sequentially, β-haloalkenyl sulfides **3** are formed by a reaction of **9** with X^-.[19] On the other hand, the disproportionation of $PhSCu(I)L_n$ **11** under acidic conditions gave $(PhS)_2Cu(II)L_n$ **12** and $Cu(0)L_n$. Finally, the oxidation of the complex **12** produces disulfide **2a** and $Cu(I)IL_n$ again in air.[12,20]

Herein developed method can be carried out on a larger preparative scale. The copper-catalyzed bromosulfenylation of 4-octyne **1a** (1.1 g, 10 mmol) or 1-phenyl-1-propyne **1m** (1.2 g, 10 mmol) using $(PhS)_2$ **2a** (1.1 g, 5 mmol) and *n*-Bu_4NBr (3.5 g, 11 mmol) afforded (*E*)-4-bromo-5-phenylthio-4-octene **3a** (2.3 g)

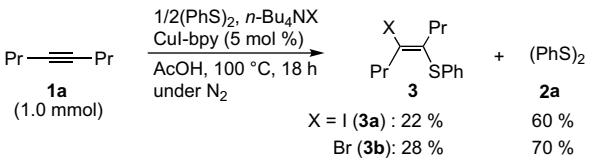
Table 4
Copper-catalyzed synthesis of β-haloalkenyl chalcogenides using thiol



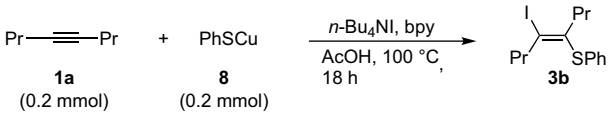
1 4 3

Entry	3	Time (h)	3 (%)[a]	Entry	3	Time (h)	3 (%)[a] (*E*/*Z*)[b]
1	 **3a**	18	60	6	 **3j**	18	45
2	 **3b**	18	24	7	 **3m**	24	77
4	 **3d**	18	57	8	 **3n**	18	90 (98/2)[b,c]
4	 **3e**	18	52	9[d]	 **3q**	46	74
5	 **3f**	18	60	10[e]	 **3r**	40	68 (91/9)[b,c]

[a] Isolated yields after silica gel chromatography.
[b] Determined by ^1H NMR.
[c] These isomers can separate by silica gel chromatography.
[d] 3-Phenyl-2-propyn-1-ol was used as a starting material.
[e] 2-Butyn-1-ol was used as a starting material.



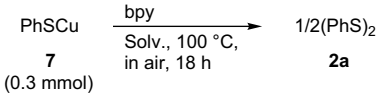
Scheme 2. Reaction in the absence of oxygen.



	3b (%)	$(PhS)_2$ (%)
in air	49	25
under N_2	10	46

Scheme 3. Reactivity of PhSCu.

Table 5
PhSCu(I) in various solvents



Entry	Solvent	2a (%)[a]
1	AcOH	92
2[b]		48
3[c]		57
4	DMF	43
5	DMSO	35

[a] Isolated yield after silica gel chromatography.
[b] bpy was not added.
[c] This reaction was carried out at room temperature.

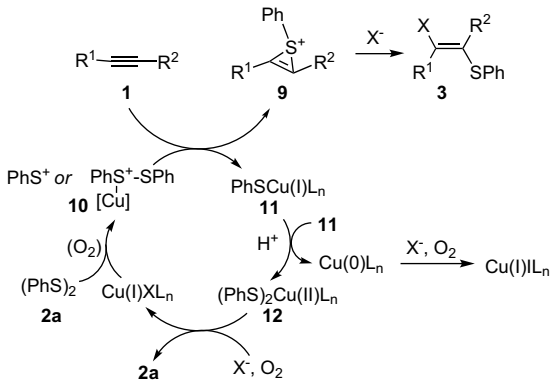
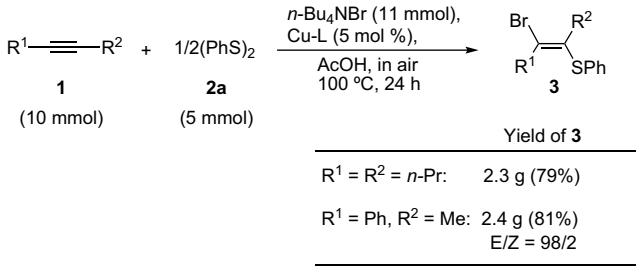


Figure 1. Plausible reaction mechanism.



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.[21] For example, (*Z*)-tamoxifen is known as an estrogen antagonist, and is effective for metastatic breast cancer.[22] Previous syntheses have been carried out by a classical synthesis using stoichiometric regents or a stereospecific synthesis by multi-steps.[23]

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 ^{1}H, 67.5 MHz for ^{13}C). Chemical shifts are reported in δ parts per million referenced to an internal tetramethylsilane standard for ^{1}H NMR and chloroform-*d* (δ 77.0) for ^{13}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)

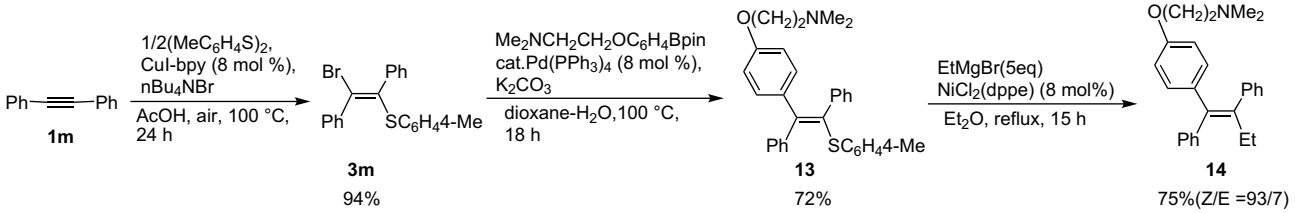
To a mixture of CuI (1.9 mg, 0.01 mmol), bpy (1.6 mg, 0.01 mmol), diphenyl disulfide **2a** (21.8 mg, 0.1 mmol), and *n*-Bu$_4$NBr (70.9 mg, 0.22 mmol) in AcOH (0.3 mL) was added 4-octyne **1a** (22.0 mg, 0.2 mmol), and the mixture was stirred at 100 °C for 18 h in air. After the residue was dissolved in Et$_2$O, the solution was washed with H$_2$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%). ^{1}H NMR (270 MHz, CDCl$_3$) 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); ^{13}C NMR (67.5 MHz, CDCl$_3$) 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^{-1}. Anal. Calcd for $C_{14}H_{19}SBr$: C, 56.19; H, 6.40. Found: C, 56.09; H, 6.27.

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

^{1}H NMR (270 MHz, CDCl$_3$) 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); ^{13}C NMR (67.5 MHz, CDCl$_3$) 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^{-1}. Anal. Calcd for $C_{14}H_{19}SI$: C, 48.56; H, 5.53. Found: C, 48.48; H, 5.47.

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

^{1}H NMR (270 MHz, CDCl$_3$) 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); ^{13}C NMR (67.5 MHz, CDCl$_3$) 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^{-1}. Anal. Calcd for $C_{14}H_{19}SCl$: 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}H NMR (270 MHz, $CDCl_3$) δ 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}C NMR (67.5 MHz, $CDCl_3$) δ 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 cm^{-1}. Anal. Calcd for $C_{15}H_{21}SBr$: 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}H NMR (270 MHz, $CDCl_3$) δ 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}C NMR (67.5 MHz, $CDCl_3$) δ 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 cm^{-1}. Anal. Calcd for $C_{15}H_{21}OSBr$: 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}H NMR (270 MHz, $CDCl_3$) δ 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}C NMR (67.5 MHz, $CDCl_3$) δ 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 cm^{-1}. Anal. Calcd for $C_{14}H_{18}SBr_2$: 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}H NMR (270 MHz, $CDCl_3$) δ 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}C NMR (67.5 MHz, $CDCl_3$) δ 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 cm^{-1}. Anal. Calcd for $C_{14}H_{18}NO_2SBr$: 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}H NMR (270 MHz, $CDCl_3$) δ 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}C NMR (67.5 MHz, $CDCl_3$) δ 133.4, 127.4, 40.8, 37.4, 21.7, 21.0, 16.4, 13.6, 12.9; IR (neat) 2960, 2928, 1602, 1459 cm^{-1}. Anal. Calcd for $C_9H_{17}SBr$: 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}H NMR (270 MHz, $CDCl_3$) δ 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}C NMR (67.5 MHz, $CDCl_3$) δ 137.2, 106.8, 44.8, 42.5, 22.5, 21.2, 16.7, 13.6, 12.8; IR (neat) 2958, 2926, 1455, 1462 cm^{-1}. Anal. Calcd for $C_9H_{17}SI$: 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}H NMR (270 MHz, $CDCl_3$) δ 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}C NMR (67.5 MHz, $CDCl_3$) δ 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 cm^{-1}. Anal. Calcd for $C_{12}H_{23}SBr$: 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}H NMR (270 MHz, $CDCl_3$) δ 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}C NMR (67.5 MHz, $CDCl_3$) δ 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 cm^{-1}. Anal. Calcd for $C_{15}H_{21}SBr$: 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}H NMR (270 MHz, $CDCl_3$) δ 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}C NMR (67.5 MHz, $CDCl_3$) δ 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 cm^{-1}. Anal. Calcd for $C_{12}H_{15}SBr$: 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 °C; ^{1}H NMR (270 MHz, $CDCl_3$) δ 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}C NMR (67.5 MHz, $CDCl_3$) δ 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 ($CHCl_3$) 3019, 1598, 1492 cm^{-1}. Anal. Calcd for $C_{21}H_{17}SBr$: 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}H NMR (270 MHz, $CDCl_3$) δ 7.41–7.24 (m, 10H), 2.21 (s, 3H); ^{13}C NMR (67.5 MHz, $CDCl_3$) δ 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 cm^{-1}. Anal. Calcd for $C_{15}H_{13}SBr$: 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}H NMR (270 MHz, $CDCl_3$) δ 7.33–7.22 (m, 10H), 2.27 (s, 3H); ^{13}C NMR (67.5 MHz, $CDCl_3$) δ 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 cm^{-1}. Anal. Calcd for $C_{15}H_{13}SI$: 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}H NMR (270 MHz, $CDCl_3$) δ 7.38–7.18 (m, 10H), 2.56 (q, J=7.4 Hz, 2H), 1.16 (t, J=7.4 Hz, 3H); ^{13}C NMR (67.5 MHz, $CDCl_3$) δ 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 cm^{-1}. Anal. Calcd for $C_{16}H_{15}SBr$: 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}H NMR (270 MHz, $CDCl_3$) δ 7.41–7.20 (m, 10H), 4.96 (s, 2H), 2.00 (s, 3H); ^{13}C NMR (67.5 MHz, $CDCl_3$) δ 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 cm^{-1}. Anal. Calcd for $C_{17}H_{15}O_2SBr$: 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}H NMR (270 MHz, $CDCl_3$) δ 7.32–7.21 (m, 5H), 4.87 (d, J=0.7 Hz, 2H), 2.67 (s, 3H), 1.95 (s, 3H); ^{13}C NMR (67.5 MHz, $CDCl_3$) δ 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 cm^{-1}. Anal. Calcd for $C_{12}H_{13}O_2SBr$: 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}H NMR (270 MHz, $CDCl_3$) δ 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}C NMR (67.5 MHz, $CDCl_3$) δ 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 cm^{-1}. Anal. Calcd for $C_{14}H_{19}SeBr$: 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}H NMR (270 MHz, $CDCl_3$) δ 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}C NMR (67.5 MHz, $CDCl_3$) δ 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 cm^{-1}. Anal. Calcd for $C_{12}H_{15}SeBr$: 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; ^1H NMR (270 MHz, $CDCl_3$) δ 7.55–7.40 (m, 2H), 7.38–7.34 (m, 4H), 7.21–6.97 (m, 9H); ^{13}C NMR (67.5 MHz, $CDCl_3$) δ 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 ($CHCl_3$) 3019, 1578, 1476, 1443 cm^{-1}. Anal. Calcd for $C_{20}H_{15}SeBr$: C, 58.00; H, 3.65. Found: C, 57.61; H, 3.73.

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

^1H NMR (270 MHz, $CDCl_3$) δ 7.48–7.43 (m, 2H), 7.39–7.12 (m, 8H), 2.22 (s, 3H); ^{13}C NMR (67.5 MHz, $CDCl_3$) δ 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 cm^{-1}. Anal. Calcd for $C_{15}H_{13}SeBr$: 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**)*

^1H NMR (270 MHz, $CDCl_3$) δ 7.41–7.34 (m, 6H), 7.26–7.23 (m, 4H), 4.97 (s, 2H), 1.98 (s, 3H); ^{13}C NMR (67.5 MHz, $CDCl_3$) δ 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 cm^{-1}. Anal. Calcd for $C_{17}H_{15}O_2SeBr$: 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**)*

^1H NMR (270 MHz, $CDCl_3$) δ 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}C NMR (67.5 MHz, $CDCl_3$) δ 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 cm^{-1}. Anal. Calcd for $C_{12}H_{13}O_2SeBr$: C, 41.40; H, 3.76. Found: C, 41.46; H, 3.80.

4.3. Debromination of β-bromoalkenyl sulfides

To a mixture of $Pd(PPh_3)_4$ (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 Et_2O, the solution was washed with H_2O 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%).[6b] ^1H NMR (270 MHz, $CDCl_3$) δ 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 (–C*H*$_2$–CH=, 15%) and (=C(SPh)C*H*$_2$–, 11%) on irradiation at 5.90 ppm (=CH–); ^{13}C NMR (67.5 MHz, $CDCl_3$) δ 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 cm^{-1}. Anal. Calcd for $C_{14}H_{20}S$: C, 76.30; H, 9.15. Found: C, 76.03; H, 8.92.

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

^1H NMR (270 MHz, $CDCl_3$) δ 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 (–C*H*$_2$–CH=, 5%) and (=C(SPh)C*H*$_2$–, 6%) on irradiation at 5.91 ppm (=CH–); ^{13}C NMR (67.5 MHz, $CDCl_3$) δ 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 cm^{-1}. Anal. Calcd for $C_{12}H_{16}S$: C, 74.94; H, 8.39. Found: C, 74.98; H, 8.24.

*4.3.2. (Z)-2-Phenylthio-2-methylstyrene (**5c**)*[6b]

^1H NMR (270 MHz, $CDCl_3$) δ 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 (=C(SPh)C*H*$_2$–, 15%) on irradiation at 6.70 ppm (=CH–); ^{13}C NMR (67.5 MHz, $CDCl_3$) δ 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 cm^{-1}. Anal. Calcd for $C_{15}H_{14}S$: C, 79.60; H, 6.23. Found: C, 79.34; H, 6.31.

4.4. Copper-catalyzed synthesis of β-chloro or thiocyanoalkenyl chalcogenides (Table 3)

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

^1H NMR (270 MHz, $CDCl_3$) δ 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}C NMR (67.5 MHz, $CDCl_3$) δ 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 cm^{-1}. Anal. Calcd for $C_{14}H_{19}SeCl$: C, 55.73; H, 6.35. Found: C, 55.56; H, 6.21.

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

^1H NMR (270 MHz, $CDCl_3$) δ 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}C NMR (67.5 MHz, $CDCl_3$) δ 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 cm^{-1}. Anal. Calcd for $C_{12}H_{15}SCl$: 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**)*

^1H NMR (270 MHz, $CDCl_3$) δ 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}C NMR (67.5 MHz, $CDCl_3$) δ 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 ($CHCl_3$) 3018, 1583, 1491, 1443 cm^{-1}. Anal. Calcd for $C_{21}H_{17}SCl$: C, 74.87; H, 5.09. Found: C, 74.49; H, 5.19.

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

^1H NMR (270 MHz, $CDCl_3$) δ 7.46–7.21 (m, 10H), 2.19 (s, 3H); ^{13}C NMR (67.5 MHz, $CDCl_3$) δ 138.7, 134.6, 132.8, 130.2, 129.1, 129.0, 128.6, 128.0, 127.9, 126.8, 22.0; IR ($CHCl_3$) 3019, 2157, 1475, 1441 cm^{-1}. Anal. Calcd for $C_{15}H_{13}SCl$: C, 69.08; H, 5.02. Found: C, 68.72; H, 5.15.

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

^1H NMR (270 MHz, $CDCl_3$) δ 7.46–7.24 (m, 10H), 2.21 (s, 3H); ^{13}C NMR (67.5 MHz, $CDCl_3$) δ 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 cm^{-1}. Anal. Calcd for $C_{15}H_{13}SeCl$: 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**)*

^1H NMR (270 MHz, $CDCl_3$) δ 7.47–7.44 (m, 2H), 7.37–7.22 (m, 8H), 4.96 (s, 2H), 1.99 (s, 3H); ^{13}C NMR (67.5 MHz, $CDCl_3$) δ 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 cm^{-1}. Anal. Calcd for $C_{17}H_{15}O_2SCl$: 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**)*

^1H NMR (270 MHz, $CDCl_3$) δ 7.42–7.34 (m, 6H), 7.28–7.23 (m, 4H), 4.95 (s, 2H), 1.99 (s, 3H); ^{13}C NMR (67.5 MHz, $CDCl_3$) δ 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 cm^{-1}. Anal. Calcd for $C_{17}H_{15}O_2SeCl$: C, 55.83; H, 4.13. Found: C, 55.49; H, 4.20.

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

^1H NMR (270 MHz, $CDCl_3$) δ 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}C NMR (67.5 MHz, $CDCl_3$)

δ 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 cm^{-1}. Anal. Calcd for $C_{15}H_{19}S_2NCl$: 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**)*

^1H NMR (270 MHz, $CDCl_3$) δ 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}C NMR (67.5 MHz, $CDCl_3$) δ 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 cm^{-1}. Anal. Calcd for $C_{15}H_{19}SeSN$: 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**)*

^1H NMR (270 MHz, $CDCl_3$) δ 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}C NMR (67.5 MHz, $CDCl_3$) δ 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 cm^{-1}. Anal. Calcd for $C_{13}H_{15}S_2N$: 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 β-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_4NBr (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 atomosphere using a balloon. After the residue was dissolved in Et_2O, the solution was washed with H_2O 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), $Me_2N(CH_2)_2OC_6H_4B(pin)$ (151.4 mg, 0.52 mmol), $Pd(PPh_3)_4$ (46.2 mg, 0.04 mmol), and K_2CO_3 (194.9 mg, 1.41 mmol) in dioxane (4 mL), and H_2O (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_2O, the solution was washed with H_2O 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%). ^1H NMR (270 MHz, $CDCl_3$) δ 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}C NMR (67.5 MHz, $CDCl_3$) δ 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 ($CHCl_3$) 2977, 2779, 1605, 1507 cm^{-1}. Anal. Calcd for $C_{31}H_{31}NOS$: 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), $NiCl_2$(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_2O was added to the mixture, the residue was dissolved in Et_2O, the solution was washed with H_2O 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). ^1H NMR (270 MHz, $CDCl_3$) δ 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}C NMR (67.5 MHz, $CDCl_3$) δ 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 ($CHCl_3$) 2971, 2823, 1606, 1508 cm^{-1}. Anal. Calcd for $C_{26}H_{29}NO$: C, 84.06; H, 7.87; N, 3.77. Found: C, 83.60; H, 7.89; N, 3.62.

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