THE DEVELOPMENT OF TRANSITION METAL-CATALYZED REACTIONS USING ORGANIC SULFIDES AND SELENIDES

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Contents

General Introduction

Recently, transition-metal-catalyzed synthetic reactions utilizing the characteristics of heteroatoms such as silicon,[1] tin,[2] and boron[3] have been well-developed to realize the fascinating transformations. On the contrary, the 16 group heteroatom compounds like sulfides and selenides have not been attracted much attention as the subject of study on the transition-metal-catalyzed reactions, partly because a lot of chalcogen compounds coordinating to transition-metals are widely believed to be too inert to construct catalytic reactions. The author was occupied with the clarification of the properties of organic chalcogen ligands and succeeded in developing several novel transition-metal-catalyzed reactions using organic sulfides and selenides as substrates.

This thesis consists of four chapters. Chapter **1** deals with the palladium-catalyzed addition of disulfides and diselenides to acetylenes. Chapter **2** deals with the palladium-catalyzed carbonylative addition of disulfides and diselenides to acetylenes and one-pot synthesis of lactones from propargyl alcohols. Chapter **3** deals with the palladium-catalyzed reduction of the compounds synthesized by the carbonylative addition revealed in chapter **2** using tin hydride as reducing reagent. Chapter **4** deals with the transition-metal-catalyzed addition of thiols and their derivatives.

References

(1) Ojima, I. In *The Chemistry of Organic Silicon Compounds*;. Patai, S., Rappoport, Z., Eds.; Wiley-Interscience: Chichester, 1989; Chapter. 25.

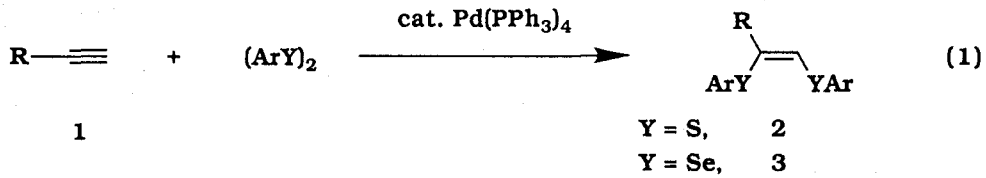
(2) Pereyre, M.; Quintard, J.-P.; Rahm, A. *Tin in Organic Synthesis*; Butterworths: London, 1987.

(3) (a) Miyaura, N.; Ishiyama, T.; Sasaki, H.; Ishikawa, M.; Satoh, M.; Suzuki, A. *J. Am. Chem. Soc.* **1989**, *111*, 314. (b) Burgess, K.; Donk, W. A.; Westcott, S. A.; Marder, T. B.; Baker, R. T.; Calabrese, J. C. *J. Am. Chem. Soc.* **1992**, *114*, 9350.

Chapter 1. Palladium-Catalyzed Addition of Disulfides and Diselenides to Acetylenes

1-1. Introduction

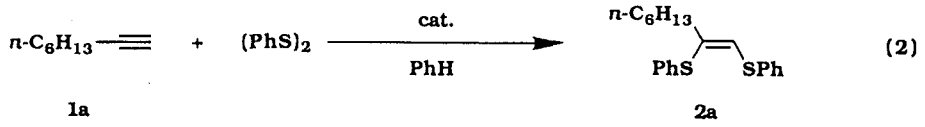
Although the oxidative additions of organic disulfides and diselenides to low-valent transition-metal complexes have been well-known,[1] the transition-metal-catalyzed reactions using dichalcogenides as substrates have been scarcely reported.[2,3] To develope a novel transition-metal-catalyzed reaction using chalcogenides as substrates, the author was interested in the oxidative additions of diaryl disulfides and diselenides to low-valent palladium complexes. After a close study on the elucidation of the properties of the coordinated chalcogenides to palladium, the author ultimately discovered that tetrakis(triphenylphosphine)palladium(0) [$Pd(PPh_3)_4$] successfully catalyzes the addition of diaryl disulfides and diselenides to terminal acetylenes **1**, which leads to the stereoselective formation of (*Z*)-1,2-bis(arylthio)-1-alkenes **2** and (*Z*)-1,2-bis(arylseleno)-1-alkenes **3**, respectively (eq 1).[4,5]



(1)

1-2. Results and Discussion

Reaction Conditions for the Addition of Disulfides and Diselenides to 1-Octyne (1a): The reaction of diphenyl disulfide (1.0 mmol) with 1-octyne (**1a**) (1.2 mmol) was examined in the presence of several transition-metal catalysts (5 mol%) (eq 2), and the results are summarized in Table I. The addition of $(PhS)_2$ to **1a** proceeded most effectively by use of $Pd(PPh_3)_4$ to give (*Z*)-1,2-bis(phenylthio)-1-octene (**2a**) in 77% yield stereoselectively (entry 4). $Pt(PPh_3)_4$ and $Rh(PPh_3)_3Cl$ also exhibited the catalytic activity for this addition (entries 6 and 7). Other transition-metal complexes, such as Pd(II) complexes, $Ni(PPh_3)_2Cl_2$, and $Ru(PPh_3)_3Cl_2$ did not catalyze the reaction (entries 1, 2, 3, 5, and 8).



1a 2a (2)

Table I. Addition of $(PhS)_2$ to 1-Octyne (1a) in the Presence of Several Transition-Metal Catalysts[a]

entry	catalyst	yield of 2a (%)[b,c]	entry	catalyst	yield of 2a (%)[b,c]
1	$Pd(PPh_3)_2Cl_2$	0	5	$Ni(PPh_3)_2Cl_2$	0
2	$Pd(PhCN)_2Cl_2$	0	6	$Pt(PPh_3)_4$	21
3	$Pd(OAc)_2$	0	7	$Rh(PPh_3)_3Cl$	24
4	$Pd(PPh_3)_4$	77	8	$Ru(PPh_3)_3Cl_2$	0

[a]All reactions were performed using 1.2 mmol of **1a**, 1.0 mmol of $(PhS)_2$, and 5 mol% of catalyst in PhH (2 mL) at 80 °C for 12 h. [b]Only Z isomer. [c]Determined by ^1H NMR.

Table II indicates some results of the effects of varying the reaction conditions. Increasing the concentration of the substrates (>2 M) could reduce the amounts of the catalyst (entries 1, 2, and 4). Reaction at 40 °C proceeded very slowly and was not complete within 12 h (entry 6). The best result was obtained when the reaction was conducted at 80 °C for 12 h using 1 mol% of $Pd(PPh_3)_4$ and 0.5 mL of benzene (entry 3).

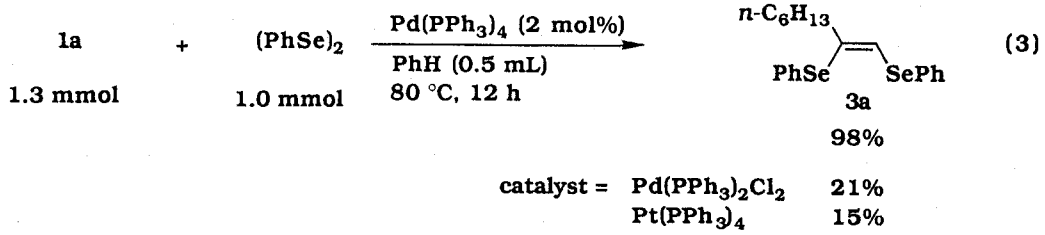
Table II. Palladium(0)-Catalyzed Addition of $(PhS)_2$ to 1a[a]

entry	$Pd(PPh_3)_4$ (mol%)	PhH (mL)	temp (°C)	time (h)	yield of 2a (%)[b,c]
1	5	2	80	12	77
2	1	2	80	12	78
3	1	0.5	80	12	100 (91)
4	0.1	0.5	80	12	86
5	1	0.5	80	3	85
6	1	0.5	40	12	15

[a]Reaction of 1.0 mmol of **1a**, 1.0 mmol of $(PhS)_2$ in the presence of $Pd(PPh_3)_4$. [b]Only Z isomer. [c]NMR yield (Isolated yield).

Next, the addition of diphenyl diselenide to 1-octyne (**1a**) was examined under similar conditions as described in the case of the addition of diphenyl disulfide. Diphenyl diselenide also

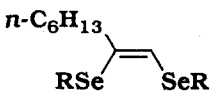
added to **1a** exclusively to give (Z)-1,2-bis(phenylseleno)-1-octene (**3a**) in an excellent yield (eq 3).



(3)

Noteworthy is the fact that $Pd(PPh_3)_2Cl_2$ also exhibited the catalytic activity for the addition of $(PhSe)_2$, though the yield of adduct was not satisfactory. The addition also proceeded smoothly in THF (67 °C: 98%), CH_3CN (82 °C: 93%) and $CH_3C_6H_5$ (80 °C: 95%). Similar additions of some other diselenides to **1a** were also performed (Table III). Diaryl diselenides produced high yields of the corresponding 1,2-adducts (entries 1, 2, and 3), whereas the addition of dialkyl diselenides such as dibutyl diselenide resulted in a low yield of the desired 1,2-adduct (entry 4).[6] Dibenzyl diselenide did not add to **1a** (entry 5).

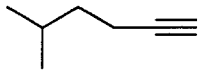
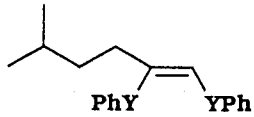
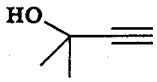
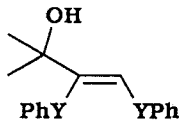
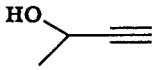
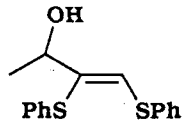
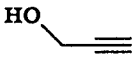
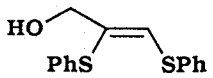
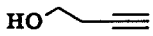
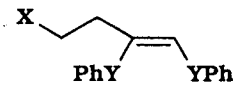
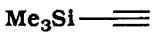
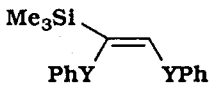
Table III. Palladium-Catalyzed Addition of $(RSe)_2$ to 1a[a]

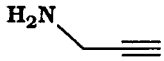
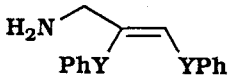
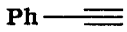
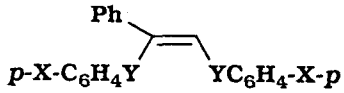
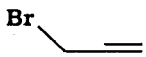
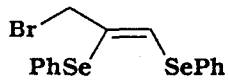
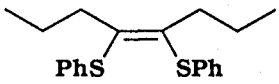
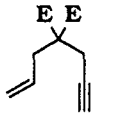
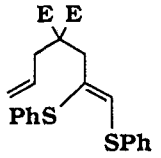
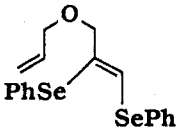
entry	$(RSe)_2$	yield (%)[b] (E/Z)[c]
		
1	$(PhSe)_2$	82 (0/100)
2	$(p\text{-}MeC_6H_4Se)_2$	76 (0/100)
3	$(p\text{-}CF_3C_6H_4Se)_2$	98 (0/100)
4	$(n\text{-}BuSe)_2$	24 (25/75)
5	$(PhCH_2Se)_2$	0

[a]Reactions were conducted under the conditions of 1.0 mmol of **1a** and 1.0 mmol of $(RSe)_2$ in the presence of 2 mol% of $Pd(PPh_3)_4$ for 12 h at 80 °C in PhH (0.5 mL). [b]Isolated yield. [c]Determined by ^1H NMR.

Addition of Diphenyl Disulfide and Diphenyl Diselenide to Various Acetylenes: The scope and limitations of the palladium-catalyzed addition of disulfides and diselenides to acetylenes are summarized in Table IV. In most cases, the reactions were clean and no by-products were formed. Some functional groups such as hydroxy (entries 3-8), trimethylsilyl (entries 9, 10), and amino (entries 11, 12) groups did not affect the addition of $(PhS)_2$ and

Table IV. Palladium-Catalyzed Addition of $(ArY)_2$ (Y = S, Se) to Various Acetylenes[a]

entry	acetylene 1	$(ArY)_2$		yield of 2 or 3 (%)[b]	(E/Z)[c]
					
1		$(PhS)_2$		Y = S	98 (0/100)
2		$(PhSe)_2$		Y = Se	79 (0/100)
					
3		$(PhS)_2$		Y = S	89 (0/100)
4		$(PhSe)_2$		Y = Se	96 (0/100)
5		$(PhS)_2$			87 (0/100)
6		$(PhS)_2$			79 (0/100)
					
7		$(PhS)_2$	Y = S	X = OH	80 (0/100)
				X = SPh	5[d] (0/100)
8		$(PhSe)_2$	Y = Se	X = OH	84 (0/100)
					
9[e]		$(PhS)_2$		Y = S	54 (1/99)
10[e]		$(PhSe)_2$		Y = Se	66 (0/100)

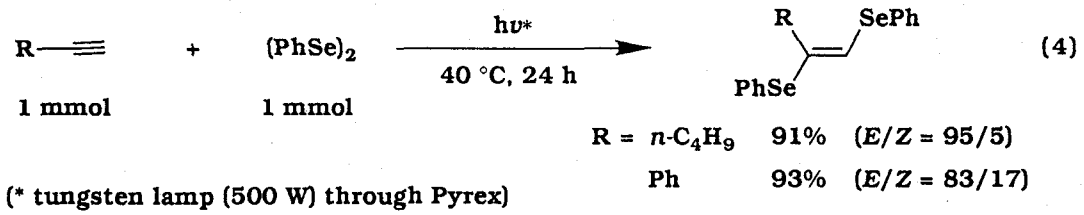
11		$(PhS)_2$		 Y = S	66 (94)[f] (0/100)
12		$(PhSe)_2$		Y = Se	90 (0/100)
13		$(PhS)_2$	X = H	 Y = S	85 (0/100)
14		$(p\text{-}MeC_6H_4Se)_2$	X = Me	Y = Se	85 (15/85)[g]
15		$(PhSe)_2$			0
16[h]		$(PhS)_2$			5[c]
17	 E = CO_2Et	$(PhS)_2$			55 (0/100)
18		$(PhSe)_2$			58 (0/100)

[a]Reaction were conducted under the conditions of 1.0 mmol of acetylene **1** and 1.0 mmol of $(ArY)_2$ in the presence of $Pd(PPh_3)_4$ (1-2 mol%) for 12-20 h at 80 °C in PhH (0.5 mL). Reaction times were unoptimized. [b]Isolated yield. [c]Determined by ^1H NMR. [d]See, reference 7. [e]The reaction was carried out without solvent at 70 °C in a sealed tube. [f]NMR yield. [g]See, reference 10. [h]5 mol% of $Pd(PPh_3)_4$, toluene reflux for 70 h.

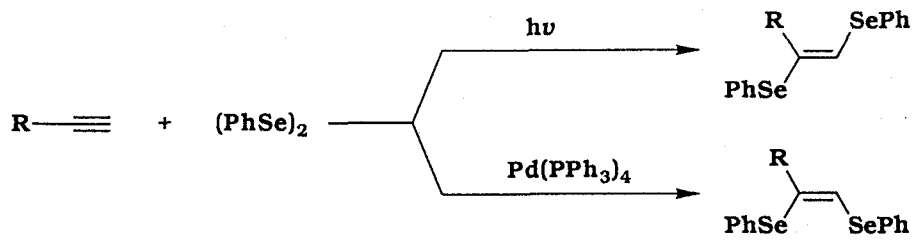
$(PhSe)_2$. The addition proceeded stereoselectively to give the corresponding *Z* isomers almost exclusively.[8,9] The addition of bis(*p*-methylphenyl) diselenide to phenylacetylene was the only

exception, giving a mixture of stereoisomers (*E*/*Z* = 15/85) (entry 14). Even in the thermal reaction without palladium catalyst, phenylacetylene underwent the addition of $(p\text{-}MeC_6H_4Se)_2$ under similar conditions, and the *E*/*Z* ratio of the adducts was 83/17 (76% yield). Thus, the *E* isomer of reaction in the presence of palladium catalyst would be generated by this competitive thermal addition.[10] In the case of the acetylenes bearing a carbon-carbon double bond, the addition took place chemoselectively to the triple bond, and no cyclization product was obtained (entries 17, 18). In contrast to terminal acetylenes as described above, the addition of disulfides and diselenides to the internal acetylenes like 4-octyne hardly proceeded (entry 16). On the other hand, the addition to propargyl bromide gave unidentified insoluble solids with recovery of $(PhSe)_2$ (entry 15).

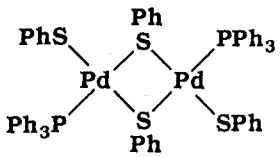
As to the synthesis of 1,2-bis(phenylseleno)-1-alkenes, we have already developed the methodology of the addition of diphenyl diselenide to acetylenes *via* a photo-initiated free radical mechanism.[11] As can be seen from the representative examples in eq 4, this radical reaction provided (*E*)-1,2-bis(phenylseleno)-1-alkenes, preferentially. Thus, the complementary methods, i. e., the palladium-catalyzed addition and the photo-initiated addition, present the routes to the stereoselective synthesis of (*Z*)- or (*E*)-1,2-bis(phenylseleno)-1-alkenes (Scheme I).



Scheme I



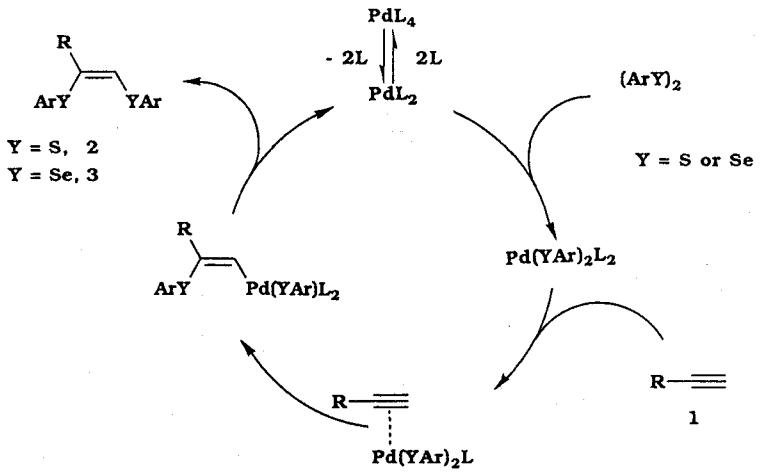
Stoichiometric Reaction and Proposed Reaction Path: Graziani et al. have already reported that the stoichiometric reaction of diphenyl disulfide with $Pd(PPh_3)_4$ gave the complex A formulated as a dimer having both terminal and bridged sulfide groups.[1e] The reaction of A[12] generated *in situ* with an equimolar amount of **1a** for 15 h at 65 °C afforded (*Z*)-1,2-bis(phenylthio)-1-octene (**2a**) in 65% yield (determined by ^1H NMR in C_6D_6).



A

This fact does not contradict the hypothesis that the palladium-catalyzed addition of disulfide to acetylene proceeded *via* the oxidative addition of disulfide to Pd(0). A proposed reaction path includes the stereoselective insertion of acetylenes into Pd-S bond to form *cis*-vinylpalladium, and the subsequent reductive elimination of the product with retention of the stereochemistry (Scheme II).

Scheme II. A Proposed Reaction Path for the Palladium-Catalyzed Addition of $(ArY)_2$ (Y = S, Se) to Acetylene



The oxidative addition of diaryl ditellurides to $Pd(PPh_3)_4$ has been also reported to proceed readily,[13] the corresponding palladium-catalyzed addition of diphenyl ditelluride to **1a** did not occur. At present, the reason why this reaction cannot apply to ditelluride is not clear.

Conclusion: $Pd(PPh_3)_4$ did effectively catalyze the addition of diaryl disulfides to various terminal acetylenes to give the high yields of *Z* adducts. While $Pt(PPh_3)_4$ and $Rh(PPh_3)_3Cl$ catalysts could be employed with varying degrees of success, $Pd(PPh_3)_4$ appeared to be superior. The addition of diaryl diselenides to terminal acetylenes was also successfully catalyzed by palladium complex. However, dibutyl diselenide gave poor yield of product, and dibenzyl diselenide did not add at all. An internal acetylene such as 4-octyne hardly undergoes the addition in this palladium-catalyzed addition.

These findings encouraged us to develope the transition-metal-catalyzed reactions using organic sulfides and selenides actively.

1-3. Experimental Section

Unless otherwise noted, acetylenes and catalysts were obtained commercially and the former were purified for use by distillation. Diaryl disulfides were purified by recrystallization from EtOH or *n*-hexane, were dried in *vacuo*. Diphenyl diselenide was prepared according to the literature,[14] and was recrystallized from *n*-hexane. The same procedure was employed for the syntheses of bis(*p*-methylphenyl) diselenide and bis(*p*-trifluoromethylphenyl) diselenide. Dibenzyl diselenide and dibutyl diselenide were prepared according to the procedures which we have recently developed,[15] and were purified by distillation or flash chromatography on silica gel (*n*-hexane). Enynes were prepared according to the literature methods.[16] Benzene and toluene were purified by distillation from potassium(>8%)-lead alloy before use.

^1H NMR spectra of $CDCl_3$ solutions were recorded with a JEOL JNM-GSX-270 (270 MHz) spectrometer. Me_4Si served as the internal standard. ^{13}C NMR spectra of $CDCl_3$ solutions were recorded with a JEOL JNM-GSX-270 (68 MHz) spectrometer. Chemical shifts in the ^{13}C NMR spectra were determined relative to Me_4Si. IR spectra were recorded with a Perkin Elmer Model 1600 spectrometer. Mass spectra were recorded with a JEOL JMS-DX303. High-resolution mass spectra (exact mass) and combustion analyses were performed in the Instrumental Analysis Center of the Faculty of Engineering, Osaka University. Unless otherwise noted in the following chapters, the reagents were obtained by the same procedure, and spectroscopic data were recorded with the same apparatus and similar methods described in this chapter.

Palladium-Catalyzed Addition: General Procedure (Tables II, III and IV). (Z)-1,2-

Bis(phenylthio)-1-octene (2a) (Table II, Entry 3): To a two-necked flask equipped with a reflux condenser and a magnetic stirring bar were placed tetrakis(triphenylphosphine)palladium (12 mg, 0.01 mmol), diphenyl disulfide (218 mg, 1.0 mmol), 1-octyne (**1a**) (110 mg, 1.0 mmol), and benzene (0.5 mL) under an argon atmosphere. The color of the solution turned rapidly from yellow to dark brown. The mixture was refluxed with stirring for 12 h. After the reaction was complete, the resulting catalyst was removed by filtration through Celite, and the filtrate was evaporated under reduced pressure. The residual mixture was purified by medium-pressure liquid chromatography (MPLC) and preparative TLC (PTLC) to give 300 mg (91%) of (*Z*)-1,2-bis(phenylthio)-1-octene as a clear oil. MPLC of reaction mixture were performed with Merck 25-40 um mesh silica gel (Art 9390). PTLC was carried out using Wakogel B-5F silica gel.

^{1}H NMR (270 MHz, $CDCl_3$) δ 0.84 (t, *J* = 6.6 Hz, 3 H), 1.20 (m, 6 H), 1.49 (m, 2 H), 2.24 (t, *J* = 7.5 Hz, 2 H), 6.56 (s, 1 H), 7.12-7.43 (m, 10 H). NOE experiment: Irradiation of the C-3 methylene triplet at δ 2.24 resulted in a 7% enhancement of the signal at δ 6.56 (vinyl singlet); ^{13}C NMR (68 MHz, $CDCl_3$) δ 14.05, 22.53, 28.47, 31.51, 37.10, 126.73, 126.82, 128.94, 129.04, 129.08, 129.69, 130.48, 133.81, 134.40, 135.87; IR (NaCl) 3071, 3057, 2953, 2926, 1582, 1477, 739, 690 cm^{-1}; mass spectrum (EI) m/e 328 (M^+, 100); Anal. Calcd for $C_{20}H_{24}S_2$: C, 73.12; H, 7.36; S, 19.52. Found: C, 73.28; H, 7.42; S, 19.44.

The solvent (hexane-Et_2O) was used as eluent in the following ratios: 10: 0 (entries 1-4 in Table III and entries 1-2, 9-10, 13-14 in Table IV), 1.5:1 (entries 3-8), 4:1 (entries 17-18), 2:1 containing Et_3N (entries 11, 12). Reactions were carried out for 12-20 h. Reaction times were unoptimized. Dichalcogen compounds and yields were listed in Tables III and IV. The following compounds were prepared according to the general procedure.

(*Z*)-1,2-Bis(phenylseleno)-1-octene (3a) (Table III, Entry 1): oil; ^{1}H NMR (270 MHz, $CDCl_3$) δ 0.86 (t, *J* = 6.7 Hz, 3 H), 1.24 (m, 6 H), 1.47 (m, 2 H), 2.29 (t, *J* = 8.1 Hz, 2 H), 6.95 (s, 1 H), 7.12-7.64 (m, 10 H). NOE experiment: Irradiation of the C-3 methylene triplet at δ 2.29 resulted in a 10% enhancement of the signal at δ 6.95 (vinyl singlet); ^{13}C NMR (68 MHz, $CDCl_3$) δ 13.95, 22.40, 28.27, 28.75, 31.37, 39.78, 127.12, 127.18, 127.73, 129.01, 129.10, 129.36, 131.10, 132.43, 132.74, 136.24; IR (NaCl) 3068, 2925, 1577, 1475, 1437, 1024, 734, 690 cm^{-1}; mass spectrum (EI), m/e 424 (M^+, 100); Anal. Calcd for $C_{20}H_{24}Se_2$: C, 56.88; H, 5.73. Found: C, 57.03; H, 5.78.

(Z)-1,2-Bis(*p*-methylphenylseleno)-1-octene (Table III, Entry 2): oil; ^{1}H NMR (270 MHz, $CDCl_3$) δ 0.84 (t, J = 6.8 Hz, 3 H), 1.15-1.27 (m, 6 H), 1.45 (quint, J = 7.6 Hz, 2 H), 2.23 (t, J = 7.6 Hz, 2 H), 2.32 (s, 6 H), 6.83 (s, 1 H), 7.06-7.11 (m, 4 H), 7.40-7.47 (m, 4 H). NOE experiment: Irradiation of the methylene triplet at δ 2.23 resulted in an 18% enhancement of the signal at δ 6.83 (vinyl singlet); ^{13}C NMR (68 MHz, $CDCl_3$) δ 14.06, 21.10, 22.53, 28.40, 28.84, 31.51, 39.65, 125.67, 127.18, 127.54, 129.94, 130.02, 132.89 (J_{Se-C} = 11.0 Hz), 133.42 (J_{Se-C} = 11.0 Hz), 136.37, 137.32; IR (NaCl) 3017, 2954, 2925, 2855, 1489, 1456, 1016, 802 cm^{-1}; mass spectrum (EI), m/e 452 (M^+, 100); Anal. Calcd for $C_{22}H_{28}Se_2$: C, 58.67; H, 6.62. Found: C, 58.49; H, 6.61.

(Z)-1,2-Bis(*p*-trifluoromethylphenylseleno)-1-octene (Table III, Entry 3): oil; ^{1}H NMR (270 MHz, $CDCl_3$) δ 0.85 (t, J = 6.3 Hz, 3 H), 1.18-1.33 (m, 6 H), 1.52 (m, 2 H), 2.36 (t, J = 7.5 Hz, 2 H), 7.07 (s, 1 H, J_{Se-H} = 18.9 Hz), 7.52 (d, J = 8.8 Hz, 2 H), 7.55 (d, J = 8.8 Hz, 2 H), 7.58 (d, J = 8.8 Hz, 2 H), 7.64 (d, J = 8.8 Hz, 2 H). NOE experiment: Irradiation of the C-3 methylene triplet at δ 2.36 resulted in a 15% enhancement of the signal at δ 7.07 (vinyl singlet); ^{13}C NMR (68 MHz, $CDCl_3$) δ 14.04, 22.60, 28.50, 28.99, 31.56, 40.57, 124.10 (q, J = 272.2 Hz), 124.16 (q, J = 271.6 Hz), 126.04 (q, J = 3.7 Hz), 126.10 (q, J = 3.7 Hz), 129.23, 129.36 (q, J = 32.6 Hz), 129.65 (q, J = 32.8 Hz), 131.84 (J_{Se-C} = 11.6 Hz), 132.18 (J_{Se-C} = 11.6 Hz), 134.87, 136.14, 136.78; IR (NaCl) 2929, 1602, 1398, 1326, 1165, 1127, 1077, 827 cm^{-1}; mass spectrum (EI), m/e 560 (M^+, 100); exact mass (M^+) calcd for $C_{22}H_{22}F_6Se_2$ 559.9955, found 559.9937.

1,2-Bis(*n*-butylseleno)-1-octene (Table III, Entry 4). *Z* isomer: oil; ^{1}H NMR (270 MHz, $CDCl_3$) δ 0.86-0.95 (m, 9 H), 1.24-1.34 (m, 6 H), 1.38-1.57 (m, 6 H), 1.66 (quintet, J = 7.8 Hz, 2 H), 1.70 (quintet, J = 7.8 Hz, 2 H), 2.30 (t, J = 7.3 Hz, 2 H), 2.70 (t, J = 7.8 Hz, 2 H), 2.73 (t, J = 7.8 Hz, 2 H), 6.55 (s, 1 H, J_{Se-H} = 14 Hz). NOE experiment: Irradiation of the C-3 methylene triplet at δ 2.30 resulted in a 17% enhancement of the signal at δ 6.55 (vinyl singlet); ^{13}C NMR (68 MHz, $CDCl_3$) δ 13.61, 13.62, 14.10, 22.64, 22.86, 23.03, 25.24, 26.51, 28.71, 28.97, 31.68, 32.69, 33.08, 39.98, 124.44, 133.79; IR (NaCl) 2956, 2927, 2856, 1574, 1464, 1478, 1257, 1196, 735 cm^{-1}; mass spectrum (EI), m/e 384 (M^+, 100); mass spectrum (EI), m/e 384 (M^+, 100); exact mass (M^+) calcd for $C_{16}H_{32}Se_2$ 384.0834, found 384.0846. *E* isomer: oil; ^{1}H NMR (270 MHz, $CDCl_3$) δ 0.85-0.94 (m, 9 H), 1.30-1.55 (m, 12 H), 1.66 (quintet, J = 7.8 Hz, 2 H), 1.68 (quintet, J = 7.8 Hz, 2 H), 2.35 (t, J = 7.3 Hz, 2 H), 2.70 (t, J = 7.8 Hz, 2 H), 2.73

(t, J = 7.8 Hz, 2 H), 6.37 (s, 1 H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 13.58, 13.61, 14.10, 22.61, 22.80, 23.03, 26.02, 27.02, 28.38, 28.82, 31.62, 32.11, 32.97, 37.01, 118.80, 131.95; IR (NaCl) 2957, 2927, 2856, 1574, 1464, 1258, 1199, 1118 cm^{-1}; mass spectrum (EI), m/e 384 (M^+, 100); Anal. Calcd for $C_{16}H_{32}Se_2$: C, 50.26; H, 8.44. Found: C, 50.64; H, 8.50.

(Z)-1,2-Bis(phenylthio)-5-methyl-1-hexene (Table IV, Entry 1): oil; ^{1}H NMR (270 MHz, $CDCl_3$) δ 0.80 (d, J = 6.4 Hz, 6 H), 1.36-1.49 (m, 3 H), 2.25 (t, J = 7.3 Hz, 2 H), 6.56 (s, 1 H), 7.20-7.43 (m, 10 H). NOE experiment: Irradiation of the methylene triplet at δ 2.25 resulted in a 16% enhancement of the signal at δ 6.56 (vinyl singlet); ^{13}C NMR (68 MHz, $CDCl_3$) δ 22.37, 27.35, 30.91, 35.04, 37.83, 126.79, 128.64, 128.93, 129.08, 129.68, 130.63, 133.73, 134.80, 135.88; IR (NaCl) 3058, 2954, 2854, 2867, 1582, 1478, 1438, 740, 690 cm^{-1}; mass spectrum (EI), m/e 314 (M^+, 73); Anal. Calcd for $C_{19}H_{22}S_2$: C, 72.56; H, 7.05; S, 20.39. Found: C, 72.26; H, 6.92; S, 20.14.

(Z)-1,2-Bis(phenylseleno)-5-methyl-1-hexene (Table IV, Entry 2): oil; ^{1}H NMR (270 MHz, $CDCl_3$) δ 0.78 (d, J = 6.1 Hz, 6 H), 1.34-1.48 (m, 3 H), 2.28 (t, J = 7.5 Hz, 2 H), 6.93 (s, 1 H), 7.26-7.30 (m, 6 H), 7.52-7.57 (m, 4 H). NOE experiment: Irradiation of the methylene triplet at δ 2.28 resulted in a 6% enhancement of the signal at δ 6.93 (vinyl singlet); ^{13}C NMR (68 MHz, $CDCl_3$) δ 22.38, 27.33, 37.88, 38.23, 127.29, 127.35, 129.16, 129.26, 129.49, 131.28, 132.60, 133.11, 136.89; IR (NaCl) 3070, 3056, 2954, 1578, 1476, 1438, 1022, 736, 690 cm^{-1}; mass spectrum (EI), m/e 410 (M^+, 18); Anal. Calcd for $C_{19}H_{22}Se_2$: C, 55.89; H, 5.43. Found: C, 55.76; H, 5.53.

(Z)-1,2-Bis(phenylthio)-3-hydroxy-3-methyl-1-butene (Table IV, Entry 3): oil; ^{1}H NMR (270 MHz, $CDCl_3$) δ 1.44 (s, 6 H), 2.30 (br s, 1 H), 7.11-7.41 (m, 11 H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 29.29, 75.07, 125.63, 126.95, 127.47, 128.98, 129.16, 130.60, 134.86, 134.91, 137.84; IR (NaCl) 3399, 2976, 1581, 1478, 1439, 738, 690 cm^{-1}; mass spectrum (EI), m/e 302 (M^+, 6); Anal. Calcd for $C_{17}H_{18}OS_2$: C, 67.51; H, 5.60; S 21.20. Found: C, 67.26; H, 5.98; S, 21.32.

(Z)-1,2-Bis(phenylseleno)-3-hydroxy-3-methyl-1-butene (Table IV, Entry 4): oil; ^{1}H NMR (270 MHz, $CDCl_3$) δ 1.45 (s, 6 H), 2.14 (br s, 1 H), 7.14-7.31 (m, 6 H), 7.47-7.56 (m, 4 H), 7.61 (s, 1 H, J_{Se-H} = 10.7 Hz). NOE experiment (in benzene-d_6): Irradiation of the methyl

singlet at δ 1.63 (which corresponds to the singlet at δ 1.45 in $CDCl_3$) resulted in an 8% enhancement of the signal at δ 8.09 (δ 7.61 in $CDCl_3$) (vinyl singlet); ^{13}C NMR (68 MHz, $CDCl_3$) δ 29.37, 75.82, 126.52, 127.77, 129.26, 129.29, 129.88 (J_{Se-C} = 12.0 Hz), 130.33, 130.67, 133.24 (J_{Se-C} = 10.0 Hz), 136.79, 139.01; IR (NaCl) 3428, 3056, 2974, 1577, 1476, 1438, 736, 690 cm^{-1}; mass spectrum (CI), m/e 381 (M^+-(H_2O)+1, 100); Anal. Calcd for $C_{17}H_{18}OSe_2$: C, 51.52; H, 4.57. Found: C, 51.33; H, 4.81.

(Z)-1,2-Bis(phenylthio)-3-hydroxy-1-butene (Table IV, Entry 5): oil; ^1H NMR (270 MHz, $CDCl_3$) δ 1.36 (d, *J* = 6.1 Hz, 3 H), 2.28 (d, *J* = 4.3 Hz, 1 H), 4.36 (quintet, *J* = 4.3, 6.1 Hz, 1 H), 7.15-7.49 (m, 11 H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 22.76, 71.07, 126.39, 127.50, 128.62, 129.14, 129.21, 130.57, 133.15, 134.10, 134.85, 136.12; IR (NaCl) 3372, 3057, 2974, 1581, 1478, 1439, 1024, 741, 690 cm^{-1}; mass spectrum (EI) m/e 288 (M^+, 4); Anal. Calcd for $C_{16}H_{16}OS_2$: C, 66.63; H, 5.59. Found: C, 66.64; H, 5.65.

(Z)-1,2-Bis(phenylthio)-3-hydroxy-1-propene (Table IV, Entry 6): oil; NMR (270 MHz, $CDCl_3$) δ 1.89 (t, *J* = 6.0 Hz, 1 H), 4.16 (d, *J* = 6.0 Hz, 2 H), 7.03 (s, 1 H), 7.20-7.47 (m, 10 H). NOE experiment: Irradiation at methylene doublet at δ 4.16 resulted in an 18% enhancement at δ 7.03 (vinyl singlet); ^{13}C NMR (68 MHz, $CDCl_3$) δ 65.45, 126.97, 127.47, 129.19, 129.22, 129.77, 129.83, 130.48, 133.07, 134.74, 134.87; IR (NaCl) 3369, 3058, 2914, 1580, 1478, 1438, 740, 689 cm^{-1}; mass spectrum (EI), m/e 274 (M^+, 100); Anal. Calcd for $C_{15}H_{14}OS_2$: C, 65.66; H, 5.14. Found: C, 65.54; H, 5.23.

(Z)-1,2-Bis(phenylthio)-4-hydroxy-1-butene (Table IV, Entry 7): oil; ^1H NMR (270 MHz, $CDCl_3$) δ 1.68 (br s, 1 H), 2.49 (t, *J* = 6.2 Hz, 2 H), 3.71 (t, *J* = 6.2 Hz, 2 H), 6.72 (s, 1 H), 7.21-7.46 (m, 10 H). NOE experiment: Irradiation at methylene triplet at δ 2.49 resulted in an 18% enhancement at δ 6.72 (vinyl singlet); ^{13}C NMR (68 MHz, $CDCl_3$) δ 40.08, 60.84, 127.02, 127.17, 129.10, 129.16, 129.19, 130.05, 130.38, 132.95, 133.38, 135.26; IR (NaCl) 3354, 3056, 2932, 1582, 1478, 1439, 1024, 741 cm^{-1}; mass spectrum (EI) m/e 288 (M^+, 34); Anal. Calcd for $C_{16}H_{16}OS_2$: C, 66.63, H, 5.59; S, 22.23. Found: C, 66.58; H, 5.64; S, 22.05.

(Z)-1,2,4-Tris(phenylthio)-1-butene (Table IV, Entry 7): oil; ^1H NMR (270 MHz, $CDCl_3$) δ 2.56 (t, *J* = 7.3 Hz, 2 H), 3.07 (t, *J* = 7.3 Hz, 2 H), 6.65 (s, 1 H), 7.11-7.44 (m, 15 H). NOE experiment: Irradiation at methylene triplet at δ 2.56 resulted in a 22% enhancement at δ

6.65 (vinyl singlet); ^{13}C NMR (68 MHz, $CDCl_3$) δ 31.46, 35.78, 124.90, 125.98, 126.12, 127.88, 128.05, 128.12, 128.15, 129.04, 129.36, 129.73, 131.51, 132.32, 134.33, 134.91; IR (NaCl) 3057, 2922, 1582, 1479, 1438, 739, 690 cm^{-1}; mass spectrum (EI) m/e 380 (M^+, 9); Anal. Calcd for $C_{22}H_{20}S_3$: C, 69.43; H, 5.29; S, 25.27. Found: C, 69.11; H, 5.29; S, 24.91.

(*Z*)-1,2-Bis(phenylseleno)-4-hydroxy-1-butene (Table IV, Entry 8): oil; ^1H NMR (270 MHz, $CDCl_3$) δ 1.77 (t, J = 5.8 Hz, 1 H), 2.52 (t, J = 5.6 Hz, 2 H), 3.69 (q, J = 5.6, 5.8 Hz, 2 H), 7.09 (s, 1 H, J_{Se-H} = 16.9 Hz), 7.26-7.34 (m, 6 H), 7.51-7.59 (m, 4 H). NOE experiment: Irradiation of methylene triplet at δ 2.52 resulted in a 5% enhancement at δ 7.09 (vinyl singlet); ^{13}C NMR (68 MHz, $CDCl_3$) δ 42.83, 61.08, 127.56, 127.61, 129.14, 129.34, 129.37, 130.77, 131.18, 131.81 (J_{Se-C} = 17 Hz), 132.85 (J_{Se-C} = 10 Hz); IR (NaCl) 3354, 3055, 2933, 1577, 1476, 1438, 1066, 1046, 1022, 737, 691 cm^{-1}; mass spectrum (EI), m/e 384 (M^+, 26); Anal. Calcd for $C_{16}H_{16}OSe_2$: C, 50.28; H, 4.22. Found: C, 49.97; H, 4.49.

(*Z*)-1,2-Bis(phenylthio)-1-(trimethylsilyl)ethene (Table IV, Entry 9): oil; ^1H NMR (270 MHz, $CDCl_3$) δ 0.08 (s, 9 H), 7.12-7.51 (m, 11 H); ^{13}C NMR (68 MHz, $CDCl_3$) δ -1.17, 125.68, 127.48, 128.34, 128.66, 129.16, 130.00, 130.72, 135.18, 135.80, 148.66; IR (NaCl) 3058, 2954, 1582, 1510, 1478, 1439, 1248, 929, 837, 739 cm^{-1}; mass spectrum (EI), m/e 316 (M^+, 100); Anal. Calcd for $C_{17}H_{20}S_2Si$: C, 64.50; H, 6.37; S, 20.26. Found: C, 64.50; H, 6.42; S, 19.97.

(*Z*)-1,2-Bis(phenylseleno)-1-(trimethylsilyl)ethene (Table IV, Entry 10): oil; ^1H NMR (270 MHz, $CDCl_3$, 1,4-dioxane (δ 3.69) as the internal standard) δ 0.05 (s, 9 H), 7.19-7.24 (m, 3 H), 7.31-7.33 (m, 3 H), 7.45-7.47 (m, 2 H), 7.58-7.60 (m, 2 H), 7.87 (s, 1 H); ^{13}C NMR (68 MHz, $CDCl_3$, $CDCl_3$ (δ 77.02) as the internal standard) δ -1.13, 126.48, 127.76, 128.99, 129.33, 130.89, 130.99, 131.08, 133.40 (J_{Se-C} = 12.0 Hz), 149.27 (J_{Se-C} = 12.0 Hz); IR (NaCl) 2954, 1578, 1520, 1476, 1438, 1247, 888, 840, 753, 690 cm^{-1}; mass spectrum (EI), m/e 412 (M^+, 3); Anal. Calcd for $C_{17}H_{20}Se_2Si$: C, 49.76; H, 4.91. Found: C, 49.48; H, 5.01.

(*Z*)-1,2-Bis(phenylthio)-3-amino-1-propene (Table IV. Entry 11): oil; ^1H NMR (270 MHz, $CDCl_3$) δ 1.40 (s, 2 H), 3.38 (s, 2 H), 6.86 (s, 1 H), 7.23-7.46 (m, 10 H). NOE experiment: Irradiation of the methylene singlet at δ 3.38 resulted in a 7% enhancement of the signal at δ 6.86 (vinyl singlet); ^{13}C NMR (68 MHz, $CDCl_3$) δ 47.71, 126.87, 127.30, 129.16,

129.18, 129.96, 130.31, 132.08, 133.27, 133.73, 135.10; IR (NaCl) 3375, 3056, 2912, 1654, 1581, 1477, 1438, 1024, 816, 744, 690 cm^{-1}; mass spectrum (EI), m/e 273 (M^+, 272); Anal. Calcd for $C_{15}H_{15}NS_2$: C, 65.89; H, 5.53; N, 5.12. Found: C, 65.53; H, 5.71; N 4.73.

(*Z*)-1,2-Bis(phenylseleno)-3-amino-1-propene (Table IV, Entry 12): oil; ^1H NMR (270 MHz, $CDCl_3$) δ 1.43 (br s, 2 H), 3.38 (br s 2 H), 7.22 (s, 1 H), 7.26-7.33 (m, 6 H), 7.51-7.61 (m, 4 H). NOE experiment (in benzene-d_6): Irradiation of the methylene singlet at δ 3.18 (which corresponds to the singlet at δ 3.38 in $CDCl_3$) resulted in a 14% enhancement of the signal at δ 7.12 (δ 7.22 in $CDCl_3$) (vinyl singlet); ^{13}C NMR (68 MHz, $CDCl_3$) δ 50.24, 127.46, 127.73, 128.88, 129.36, 129.39, 130.60, 130.81, 132.51 (J_{Se-C} = 12.0 Hz), 133.12 (J_{Se-C} = 12.0 Hz); IR (NaCl) 3369, 3054, 2360, 1577, 1416, 1437, 1021, 841, 736 cm^{-1}; mass spectrum (EI) m/e 369 (M^+, 9); Anal. Calcd for $C_{15}H_{15}NSe_2$: C, 49.06; H, 4.12; N, 3.81. Found: C, 49.43; H, 4.43; N, 3.93.

(*Z*)-1,2-Bis(phenylthio)styrene (Table IV, Entry 13): oil; ^1H NMR (270 MHz, $CDCl_3$) δ 7.06-7.56 (m, 16 H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 125.82, 126.68, 127.50, 127.55, 128.13, 128.35, 128.81, 129.24, 129.31, 130.40, 134.64, 135.13, 136.50, 138.66; IR (NaCl) 3054, 1580, 754, 739, 689 cm^{-1}; mass spectrum (EI), m/e 320 (M^+, 100); Anal. Calcd for $C_{20}H_{16}S_2$: C, 74.96; H, 5.03. Found: C, 75.12; H, 5.26.

(*Z*)-1,2-Bis(*p*-methylphenylseleno)styrene (Table IV, Entry 14). containing 15% of *E* isomer: oil; ^1H NMR (270 MHz, $CDCl_3$) *Z* isomer: δ 2.23 (s, 3 H), 2.34 (s, 3 H), 6.95-7.52 (m, 14 H). *E* isomer: δ 2.27 (s, 3 H), 2.30 (s, 3 H), 6.95-7.52 (m, 14 H); ^{13}C NMR (68 MHz, $CDCl_3$) *Z* isomer: δ 21.02, 21.14, 126.54, 127.28, 127.33, 128.20, 129.91, 130.16, 131.18, 131.39, 132.32, 133.48, 136.20, 136.54, 137.91, 140.66; IR (NaCl) 3013, 2966, 2916, 1591, 1487, 1440, 1264, 1014, 801; mass spectrum (EI), m/e 444 (M^+, 95); Anal. Calcd for $C_{22}H_{20}Se_2$: C, 59.74; H, 4.56. Found: C, 59.99; H, 4.71.

(*Z*)-1,2-Bis(phenylthio)-4,4-bis(carboethoxy)-hepta-1,6-diene (Table IV, Entry 17): oil; ^1H NMR (270 MHz, $CDCl_3$) δ 1.16 (t, *J* = 7.2 Hz, 6 H), 2.78 (d, *J* = 7.2 Hz, 2 H), 2.98 (s, 2 H), 4.01-4.02 (m, 4 H), 5.02-5.09 (m, 2 H), 5.55-5.56 (m, 1 H), 6.87 (s, 1 H), 7.19-7.43 (m, 10 H). NOE experiment: Irradiation of the methylene singlet at δ 2.98 resulted in an 19% enhancement of the signal at δ 6.87 (vinyl singlet); ^{13}C NMR (68 MHz, $CDCl_3$) δ 13.91, 36.62, 38.63, 57.60,

61.39, 119.18, 124.48, 126.24, 127.38, 128.42, 129.09, 129.19, 130.32, 132.47, 134.13, 134.97, 140.10, 170.48; IR (NaCl) 3075, 2981, 1732, 1583, 1479, 1440, 742, 692 cm^{-1}; mass spectrum (EI) m/e 456 (M^+, 99); Anal. Calcd for $C_{25}H_{28}O_4S_2$: C, 65.76; H, 6.18; S, 14.04. Found: C, 65.69; H, 6.21; S, 13.78.

(*Z*)-2,3-Bis(phenylseleno)-2-propenyl 2-propenyl ether (Table IV, Entry 18): oil; ^1H NMR (270 MHz, $CDCl_3$) δ 3.92 (d, J = 5.4 Hz, 2 H), 4.03 (s, 2 H), 5.13 (d, J = 10.3 Hz, 1 H), 5.20 (d, J = 17.0 Hz, 1 H), 5.83 (octet, J = 5.4, 10.3, 17.0 Hz, 1 H), 7.26-7.31 (m, 6 H), 7.40 (s, 1 H), 7.55-7.60 (m, 4 H). NOE experiment: Irradiation of the methylene singlet at δ 4.03 resulted in a 13% enhancement of the signal at δ 7.40 (vinyl singlet); ^{13}C NMR (68 MHz, $CDCl_3$) δ 70.96, 74.16, 117.08, 127.33, 127.57, 128.88, 129.15, 129.23, 130.51, 132.55 (J_{Se-C} = 12.0 Hz), 132.87 (J_{Se-C} = 12.0 Hz), 133.05, 134.30; IR (NaCl) 3056, 2846, 1577, 1476, 1438, 1099, 1022, 736, 690 cm^{-1}; mass spectrum (EI) m/e 410 (M^+, 26); Anal. Calcd for $C_{18}H_{18}OSe_2$: C, 52.96; H, 4.44. Found: C, 52.90; H, 4.72.

Reaction of A with 1-Octyne (1a): In a Pyrex NMR glass tube were placed $Pd(PPh_3)_4$ (23 mg, 0.02 mmol) and $(PhS)_2$ (4.4 mg, 0.02 mmol), and C_6D_6 (0.6 mL). When the mixture was heated at 65 °C for 2 h, the complete disappearance of $(PhS)_2$ was confirmed by ^{13}C NMR spectroscopy. Then 1-octyne (**1a**) (3.0 mg, 0.027 mmol) was added into this reaction mixture and the mixture was heated at 65 °C. After 15 h, the formation of (*Z*)-1,2-bis(phenylseleno)-1-octene (**3a**) was confirmed in 65% yield by ^1H NMR spectroscopy.

1-4. References and Notes

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(2) For the transition-metal-catalyzed reactions using disulfides and diselenides, see: (a) Fukuzawa, S.; Fujinami, T.; Sakai, S. *Chem. Lett.* **1990**, 927. (b) Takahashi, H.; Ohe, K.; Uemura, S.; Sugita, N. *J. Organomet. Chem.* **1987**, *334*, C43. (c) Kano, K.; Takeuchi, M.; Hashimoto, S.; Yoshida, Z. *Chem. Lett.* **1990**, 1381. (d) Antebi, S.; Alper, H. *Tetrahedron Lett.* **1985**, *26*, 2609.

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(4) For the synthetic utility of vinyl sulfides and selenides, see: (a) Trost, B. M.; Lavoie, A. C. *J. Am. Chem. Soc.* **1983**, *105*, 5075. (b) Magnus, P.; Quagliato, D. *J. Org. Chem.* **1985**, *50*, 1621. (c) Comasseto, J. V. *J. Organomet. Chem.* **1983**, *253*, 131 and references therein.

(5) During the course of our study, Dzhemilev, et al. have been reported the addition of $(PhS)_2$ to 1, 3-diene catalyzed by Ni complex to give the complicated mixture of adducts, see: Dzhemilev, U. M.; Kunakova, R. V.; Baibulatova, N. Z.; Mustafina, E. M.; Galkin, E. G.; Tolstikov, G. A. *Izv. Akad. Nauk SSSR, Ser. Khim.* **1989**, *3*, 747.

(6) The reaction of dibutyl disulfide with 1-octyne (**1a**) in the presence of $Pd(PPh_3)_4$ at 80 °C for 16 h gave the corresponding (Z)-1,2-adduct only in 9% yield (determined by ^1H NMR).

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(8) The photo-initiated radical addition of disulfides to acetylenes has been reported to proceed in a less stereoselective manner, see: Heiba, E. I.; Dessau, R. M. *J. Org. Chem.* **1967**, *32*, 3837.

(9) The stereochemistry and the ratios of the products were determined by NOE experiments and ^1H NMR spectroscopy, respectively.

(10) (p-$MeC_6H_4Se)_2$ was used to simplify the determination of the ratio of *E*/*Z* by ^1H NMR. Considering the results of the reactions in the presence and absence of catalyst, the palladium catalyst would suppress the thermal addition.

(11) For the photo-initiated addition, see: (a) Ogawa, A.; Yokoyama, H.; Yokoyama, K.; Masawaki, T.; Kambe, N.; Sonoda, N. *J. Org. Chem.* **1991**, *56*, 5721. (b) Back, T. G.; Krishna, M. V. *J. Org. Chem.* **1988**, *53*, 2533. For the thermal addition, see: Ogawa, A.; Takami, N.; Sekiguchi, M.; Yokoyama, H.; Kuniyasu, H.; Ryu, I.; Sonoda, N. *Chem. Lett.* **1991**, 2241.

(12) The structure of this complex in solution is still undetermined. The palladium complexes having benzenethiolate ligands often form the polymeric complexes, see: (a) Rauchfuss, T. B.; Shu, J. S.; Roundhill, D. M. *Inorg. Chem.* **1976**, *15*, 2096. (b) Schott, H.; Wilke, G. *Angew. Chem., Int. Ed. Engl.* **1969**, *8*, 877. (c) Woodward, P.; Dahl, L. F.; Abel, E. W.; Crosse, B. C. *J. Am. Chem. Soc.* **1965**, *87*, 5251.

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(15) (a) Nishiyama, Y.; Katsuura, A.; Negoro, A.; Hamanaka, S.; Miyoshi, N.; Yamana, Y.; Ogawa, A.; Sonoda, N. *J. Org. Chem.* **1991**, *56*, 3776. (b) Sekiguchi, M.; Tanaka, H.; Takami, N.; Ogawa, A.; Ryu, I.; Sonoda, N. *Heteroatom Chem.* **1991**, *2*, 427.

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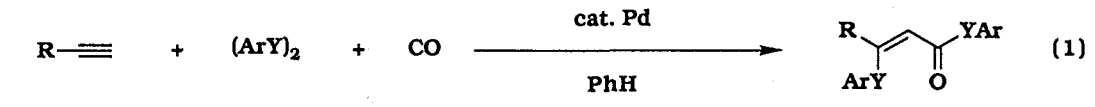
Chapter 2. Palladium-Catalyzed Carbonylative Addition of Disulfides and Diselenides to Acetylenes

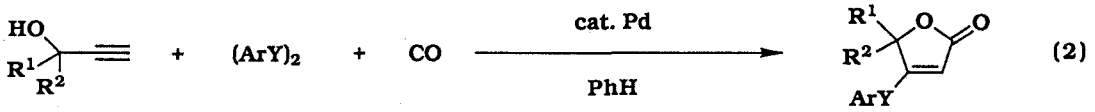
2-1. Regio- and Stereoselective Carbonylative Double Thiolation and Selenation of Terminal Acetylenes

2-1-1. Introduction

The transition-metal-catalyzed carbonylation using carbon monoxide is one of the most important and fundamental subjects for one carbon homologation.[1] In most cases the insertion of carbon monoxide into carbon-metal bond is proposed to be a crucial process in these transformations. When the palladium-catalyzed addition of disulfides and diselenides to acetylenes developed in chapter **1** is carried out in the presence of carbon monoxide, a carbonylation is prospected *via* insertion of carbon monoxide into a vinylic carbon-palladium bond which would be generated in the catalytic cycle of the reaction mechanism. This chapter deals with the palladium-catalyzed carbonylative double thiolation and selenation of terminal acetylenes (eq 1)[2] and one-pot lactonization of propargyl alcohols *via* the carbonylative addition (eq 2).



(1)



(2)

2-1-2. Results and Discussion

Reaction Conditions for the Carbonylative Addition of Diphenyl of Diphenyl Diselenide to 1-Octyne (1a): The reaction of 1-octyne (**1a**) (1.0 mmol) with diphenyl

diselenide (1.0 mmol) was attempted in the presence of 2 mol% of $Pd(PPh_3)_4$ under an atmosphere of carbon monoxide in toluene (2 mL) at 80 °C for 19 h. As we envisioned, the reaction gave the carbonylated product (*Z*)-1,3-(phenylseleno)-2-nonen-1-one (**5a**)[3] (29%) together with the direct 1,2-adduct of diselenide **3a** (29%) (eq 3).

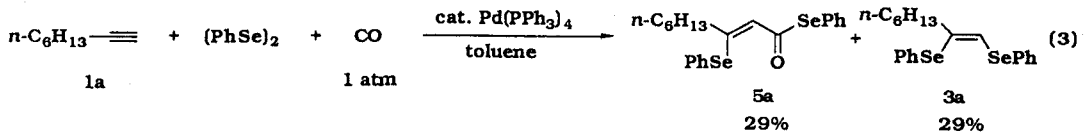


Table I summarized the results of the carbonylative addition of diphenyl diselenide to **1a** with the aid of palladium catalysts under various pressures of carbon monoxide.

Table I. The Effects of the Pressure of CO on the Carbonylative Addition of $(PhSe)_2$ to 1a[a]

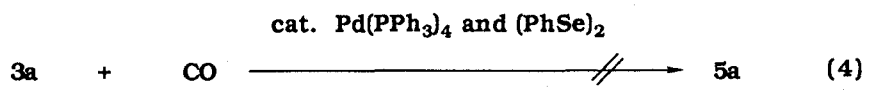
entry	CO (kg/cm^2)	conversion (%)	yield[b] of 5a (%) (E/Z)[c]	yield[b] of 3a (%)[d]
1	5	100	77 (0/100)	16
2	15	100	87 (1/99)	7
3[e]	15	88	75 (0/100)	9
4	30	94	86 (0/100)	6
5	60	63	53 (1/99)	3
6[f]	4	78	78 (0/100)	0

[a]Reactions were carried out using 1.2 mmol of **1a**, 1.0 mmol of $(PhSe)_2$, 2 mol% of $Pd(PPh_3)_4$, and PhH (0.5 mL) at 80 °C for 15 h. [b]Isolated yield. [c]Determined by ^1H NMR. [d]Only *Z* isomer. [e]Toluene (0.5 mL) was used as a solvent. [f]Cat. $Pd(PPh_3)_2Cl_2$, 30 h.

The reaction under pressurized carbon monoxide substantially suppressed the generation of **3a** and improved the yield of **5a** (entries 1, 2). Under the pressure of 60 kg/cm^2, however, the reaction was retarded and was not complete within 15 h (entry 5). Among the other transition-metal catalysts examined [$Pd(dppe)_2$, $PdCl_2$, $Pd(PPh_3)_2Cl_2$, $Pd(PhCN)_2Cl_2$, $Pd(OAc)_2$, $Ni(PPh_3)_2Cl_2$, $Rh(PPh_3)_3Cl$, $Co_2(CO)_8$,[4] $Cr(CO)_6$], $Pd(PPh_3)_2Cl_2$ and $Pd(PhCN)_2Cl_2$ also catalyzed the carbonylation. It should be noted that, in the case of $Pd(PPh_3)_2Cl_2$, the carbonylative addition proceeded smoothly and the formation of the direct adduct **3a** was suppressed despite the reaction being run under a relatively lower pressure of CO (4 kg/cm^2) (entry 6 vs eq 3 in chapter **1**).[5]

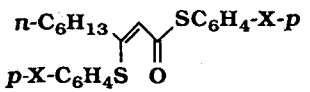
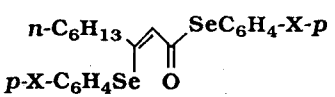
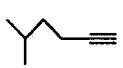
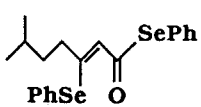
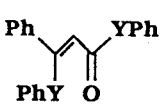
Carbonylative Addition of Diaryl Disulfides and Diaryl Diselenides to Various Acetylenes: The procedure for the carbonylative addition with carbon monoxide was also applicable to the diphenyl disulfide/acetylene reaction system. The reaction of $(PhS)_2$ with 1 equiv of **1a** in the presence of 2 mol% of $Pd(PPh_3)_4$ under the pressure of CO (15 kg/cm^2) provided the desired carbonylated product **4a** in 56% yield with 27% of the direct adduct of disulfide **2a**. Again, the excellent stereo- and regioselectivity of the introduction of carbon monoxide were achieved in this reaction. Higher pressure (60 kg/cm^2), compared with the case of diselenides, was indispensable for the suppression of the generation of **2a** when $Pd(PPh_3)_4$ was used as a catalyst (entries 1, 2 in Table II vs entry 2 in Table I). $Pd(PPh_3)_2Cl_2$ catalyzed the carbonylative addition even under a low pressure of CO, while the reaction was accompanied by the formation of a slight yield of *E* isomer (entry 3). Table II summarizes the results of the carbonylative addition of disulfides and diselenides to various acetylenes. This carbonylation was regioselective and highly stereoselective; the carbonyl group was introduced only at the terminal carbon of acetylenes, and *Z* isomers were obtained. The $Pd(PPh_3)_4$-catalyzed reaction of phenylacetylene gave the direct adducts as the major product (not shown). When $Pd(PPh_3)_2Cl_2$ was used, however, the carbonylation proceeded with a preference for the direct 1,2-addition (entries 8, 9). Acetylenes bearing a carbon-carbon double bond reacted chemoselectively at the triple bond (entry 10).[6] The hydroxy group at γ position of triple bond did not interfere with the carbonylative addition (entry 11).[7] In contrast, propargylamine afforded a complicated mixture of undetermined products, though the 1,2-addition of $(PhSe)_2$ to this substrate took place efficiently in the absence of CO (entry 13 in Table II vs entry 12 in Table IV of Chapter **1**). The carbonylation of (trimethylsilyl)acetylene scarcely proceeded (entry 12 in Table II vs entry 10 in Table IV of Chapter **1**).

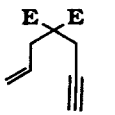
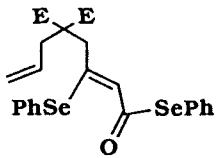
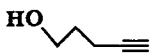
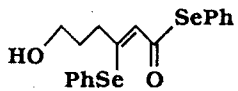
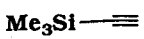
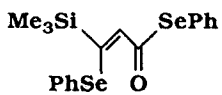
Proposed Reaction Path: When the reaction of (*Z*)-1,2-bis(phenylseleno)-1-octene (**3a**) with carbon monoxide was conducted in the presence of $Pd(PPh_3)_4$ under similar conditions, no CO-incorporated products were formed (eq 4).



(4)

Table II. Palladium-Catalyzed Carbonylative Addition of Diaryl Disulfides and Diaryl Diselenides to Acetylenes in the Presence of CO[a]

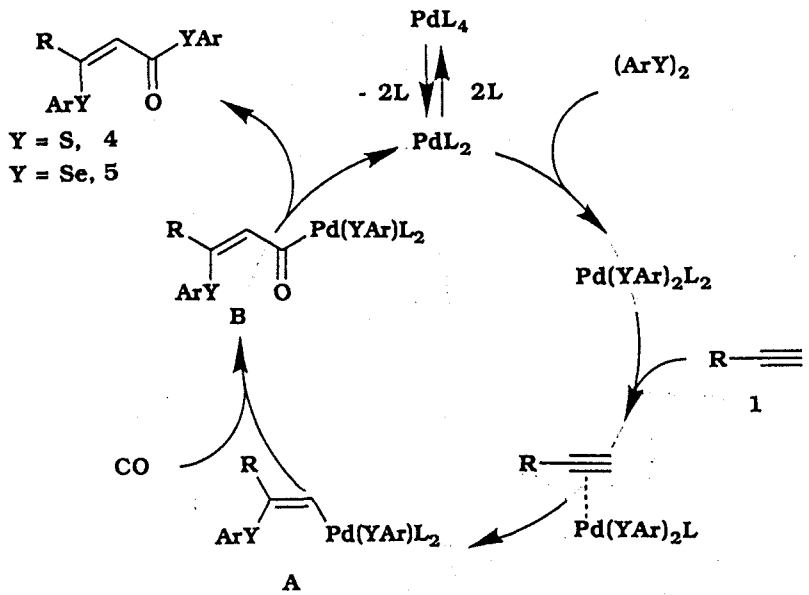
entry	acetylene	$(ArY)_2$	catalyst	CO (kg/cm^2)	time (h)	yield(%) 4 or 5 (E/Z)	2 or 3
	n-C_6H_{13}—≡						
1		$(PhS)_2$	$Pd(PPh_3)_4$	15	15	X = H 56 (0/100)	27
2				60	39	X = H 84 (0/100)	5
3			$Pd(PPh_3)_2Cl_2$	15	26	X = H 75 (6/94)	0
4		$(p$-$MeC_6H_4S)_2$	$Pd(PPh_3)_4$	60	26	X = Me 86 (0/100)	7
							
5		$(p$-$MeC_6H_4Se)_2$		15	18	X = Me 80 (0/100)	7
6		$(p$-$CF_3C_6H_4Se)_2$		15	18	X = CF_3 89 (2/98)	8
							
7		$(PhSe)_2$		15	15	76 (0/100)	6
	Ph—≡						
8		$(PhSe)_2$	$Pd(PPh_3)_2Cl_2$[b]	15	30	Y = Se 86 (3/97)	12
9		$(PhS)_2$	$Pd(PPh_3)_2Cl_2$[b]	15	44	Y = S 29 (3/97)	0

	 E = CO_2Et						
10[c]		$(PhSe)_2$	$Pd(PPh_3)_2Cl_2$	10	16	60 (0/100)	0
							
11		$(PhSe)_2$	$Pd(PPh_3)_4$	15	15	76 (8/92)	6
							
12		$(PhSe)_2$	$Pd(PPh_3)_2Cl_2$[b]	15	37	trace	0
13		$(PhSe)_2$	$Pd(PPh_3)_4$	30	19	a complicated mixture	

[a]Reactions were conducted under the condition of 1.0 mmol of acetylene, 1.0 mmol of $(ArY)_2$ and CO in the presence of 2.0 mol% of catalyst at 80 °C in 50 mL stainless steel autoclave in PhH (0.5-1.0 mL). [b]5 mol%. [c]110 °C.

This result indicates that **3** is not a precursor of the carbonylation.[5] Two different reaction paths can be proposed on the basis of the regio- and stereochemistry of this carbonylative addition. One involves the formation of vinylpalladium **A**, in which palladium bonds to the terminal position followed by the insertion of carbon monoxide (Scheme I). The other possibility is the initial formation of ArYCO-[Pd]-YAr **B** (Y = S or Se)[4, 8] species and subsequent insertion of the acetylene into C-Pd or Y-Pd bond, and reductive elimination of the product. Yet, it is not specified whether the carbonylation occurs *via* these pathways or occurs *via* a more complex sequence and we are now occupied in this problem.

Scheme I. A Proposed Reaction Path for the Carbonylative Addition of $(PhY)_2$ (Y = S, Se) to Acetylene



Conclusion: When the palladium-catalyzed addition of $(ArY)_2$ (Y = S, Se) to terminal acetylene was carried out in the presence of carbon monoxide, regio- and stereoselective carbonylative double thiolation and selenation occurred to give the (*Z*)-1,3-bis(arylthio)-2-alken-1-ones **4** and (*Z*)-1,3-bis(arylseleno)-2-alken-1-ones **5**, respectively. $Pd(PPh_3)_2Cl_2$ also effectively catalyzed the carbonylative addition even low pressure of carbon monoxide.

2-1-3. Experimental Section

Palladium-Catalyzed Carbonylative Addition of $(PhSe)_2$ to 1-Octyne (1a) in an Atmosphere of Carbon Monoxide (eq 3): To a two-necked 5 mL reaction vessel equipped with a magnetic stirring bar were placed the 1-octyne (**1a**) (110 mg, 1.0 mmol), diphenyl diselenide (314 mg, 1.0 mmol), $Pd(PPh_3)_4$ (24 mg, 0.02 mmol), and toluene (2.0 mL). The mixture was heated at 80 °C for 19 h under an atmosphere of carbon monoxide. The reaction mixture was filtered through Celite, and was evaporated in *vacuo*. The formation of (*Z*)-1,3-bis(phenylseleno)-2-nonen-1-one (**5a**) (29%) and (*Z*)-1,2-bis(phenylseleno)-1-octene (**3a**) (29%) was confirmed by ^1H NMR spectroscopy.

Palladium-Catalyzed Carbonylative Addition: General Procedure (Table I and II). 1,3-Bis(phenylthio)-2-nonen-1-one (4a) (Table II, Entry 2): In a 50 mL stainless steel autoclave were placed the 1-octyne (**1a**) (110 mg, 1.0 mmol), diphenyl disulfide (218 mg, 1.0 mmol), $Pd(PPh_3)_4$ (24 mg, 0.02 mmol), and benzene (0.5 mL). The mixture was heated at 80 °C for 15 h under the pressure of carbon monoxide (60 kg/cm^2) with magnetic stirring. The reaction mixture was filtered through Celite, and was evaporated in *vacuo*. The residual mixture was purified by MPLC and PTLC to provide 298 mg (85%) of (*Z*)-1,3-bis(phenylthio)-2-nonen-1-one (**4a**) as a clear oil.

Z isomer: oil; ^1H NMR (270 MHz, $CDCl_3$) δ 0.80 (t, J = 6.8 Hz, 3 H), 0.97-1.06 (m, 4 H), 1.15 (m, 2 H), 1.34 (m, 2 H), 2.09 (t, J = 5.4 Hz, 2 H), 6.25 (s, 1 H), 7.35-7.53 (m, 10 H). NOE experiment: Irradiation of the C-4 methylene triplet at δ 2.09 resulted in a 7% enhancement of the signal at δ 6.25 (vinyl singlet). The regiochemistry was determined from the result of the reduction of **4a** with an equimolar amount of *n*-Bu_3SnH in benzene-d_6 (The formyl doublet (J = 8.1 Hz) appeared at δ 10.15); ^{13}C NMR (68 MHz, $CDCl_3$) δ 13.90, 22.27, 28.43, 29.36, 31.12, 36.48, 116.93, 128.24, 128.97, 129.02, 129.07, 129.48, 130.31, 134.65, 135.79, 162.14, 184.96; IR (neat) 2926, 1671, 1548, 1476, 1439, 1085, 828, 745, 706, 690 cm^{-1}; mass spectrum (CI), m/e 357 (M^++1, 100); Anal. Calcd for $C_{21}H_{24}OS_2$: C, 70.74; H, 6.78. Found: C, 70.88; H, 6.78.

E isomer oil; ^1H NMR (270 MHz, $CDCl_3$) δ 0.86 (t, J = 6.7 Hz, 3 H), 1.20-1.42 (m, 6 H), 1.62 (quint, J = 7.6 Hz, 2 H), 2.77 (t, J = 7.8 Hz, 2 H), 5.47 (s, 1 H), 7.35 (m, 5 H), 7.47-7.52 (m, 5 H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 14.03, 22.54, 29.14, 29.80, 32.52, 34.49, 115.50, 128.56, 129.03, 129.09, 129.15, 129.87, 130.10, 134.59, 135.50, 165.64, 183.90; IR (neat) 3060, 2928, 1679, 1567, 1440, 1340, 1046, 841, 746, 708 cm^{-1}; mass spectrum (CI), m/e 357 (M^++1, 100).

The solvent (hexane-Et_2O) was used as eluent in the following ratios: 10:1 (entries 1-6, in Table I and entries 1-9 in Table II), 4:1 (entry 10), 1:1 (entry 11). Dichalcogen compounds, the pressure of carbon monoxide, catalyst, reaction time, and yields were listed in the Tables I and II. The following compounds were prepared according to the general procedure.

1,3-Bis(phenylseleno)-2-nonen-1-one (5a) (Table I): *Z* isomer: mp 35-39 °C (a light yellow crystal); ^{1}H NMR (270 MHz, $CDCl_3$) δ 0.81 (t, J = 7.2 Hz, 3 H), 1.01 (m, 4 H), 1.14 (m, 2 H), 1.31 (m, 2 H), 2.13 (t, J = 7.8 Hz, 2 H), 6.66 (s, 1 H, J_{Se-H} = 12.5 Hz), 7.31-7.44 (m, 6 H), 7.57-7.65 (m, 4 H). NOE experiment: Irradiation of the methylene triplet at δ 2.13 resulted in a 20% enhancement of the signal at δ 6.66 (vinyl singlet). The regiochemistry was determined from the result of the reduction of **5a** with an equimolar amount of *n*-Bu_3SnH in benzene-d_6 (The formyl doublet appeared at δ 9.88 (J = 3.8 Hz)); ^{13}C NMR (68 MHz, $CDCl_3$) δ 13.96, 22.32, 28.44, 29.78, 31.17, 37.77, 121.98, 126.70, 127.30, 128.81, 129.15, 129.29, 129.34, 135.83 (J_{Se-C} = 9.4 Hz), 137.32 (J_{Se-C} = 10.7 Hz), 163.13, 187.58; IR (KBr) 3081, 2928, 2855, 1671, 1539, 1438, 1092, 801, 738, 688 cm^{-1}; mass spectrum (CI), m/e 453 (M^++1, 68); Anal. Calcd for $C_{21}H_{24}OSe_2$: C, 56.00; H, 5.37. Found: C, 55.98; H,5.70.
E isomer: oil; ^{1}H NMR (270 MHz, $CDCl_3$) δ 0.85 (t, J = 6.6 Hz, 3 H), 1.19-1.38 (m, 6 H), 1.55 (m, 2 H), 2.76 (t, J = 7.8 Hz, 2 H), 5.82 (s, 1 H), 7.32-7.46 (m, 8 H), 7.57-7.60 (m, 2 H). The regiochemistry was determined from the result of the reduction of **5a** with an equimolar amount of *n*-Bu_3SnH in benzene-d_6 (The formyl doublet appeared at δ 9.74 (J = 7.6 Hz)); ^{13}C NMR (68 MHz, $CDCl_3$) δ 14.04, 22.53, 29.06, 29.90, 31.49, 35.89 (J_{Se-C} = 22.0 Hz), 122.41 (J_{Se-C} = 61.6 Hz), 126.29, 127.19, 128.69, 129.24, 129.77, 129.96, 135.71 (J_{Se-C} = 8.5 Hz), 136.74 (J_{Se-C} = 10.4 Hz), 164.50, 185.76; IR (NaCl) 3057, 2927, 1694, 1563, 1557, 1476, 1438, 1020, 736, 689 cm^{-1}; mass spectrum (CI) m/e 453 (M^++1, 44); Anal. Calcd for $C_{21}H_{24}OSe_2$: C, 56.00; H, 5.37. Fonud: C, 56.17; H, 5.66.

1,3-Bis(*p*-methylphenylthio)-2-nonen-1-one (Table VI, Entry 4). *Z* isomer: mp 49-49.5 °C (a white solid); ^{1}H NMR ($CDCl_3$, 270 MHz) δ 0.81 (t, J = 7.1 Hz, 3 H), 1.04 (m, 4 H), 1.16 (m, 2 H), 1.34 (m, 2 H), 2.09 (t, J = 7.6 Hz, 2 H), 2.36 (s, 6 H), 6.23 (s, 1 H), 7.14-7.22 (m, 4 H), 7.35-7.40 (m, 4 H). NOE experiment: Irradiation of the methylene triplet at δ 2.09 resulted in a 14% enhancement of the signal at δ 6.23 (vinyl singlet). The regiochemistry was determined from the result of the reduction with an equimolar amount of *n*-Bu_3SnH in benzene-d_6 (The two formyl doublets appeared at δ 9.79 (J = 7.0 Hz) and δ 10.43 (J = 7.0 Hz)); ^{13}C NMR (68 MHz,

$CDCl_3$) δ 13.92, 21.20, 21.25, 22.29, 28.43, 29.37, 31.16, 36.35, 116.72, 124.83, 126.87, 129.78, 129.78, 134.61, 135.70, 139.23, 139.69, 162.50, 185.34; IR (KBr) 2928, 1669, 1545, 1492, 1104, 1087, 831, 809, 796 cm^{-1}; mass spectrum (CI), m/e 385 (M^++1, 77); Anal. Calcd for $C_{23}H_{28}OS_2$: C, 71.82; H, 7.33; S, 16.67. Found: C, 71.78; H, 7.43; S, 16.71.

E isomer: This isomer was obtained by the reaction using $Pd(PPh_3)_2Cl_2$ as a catalyst (81%, *E/Z* = 5/95) (not shown in Table II): oil; ^1H NMR (270 MHz, $CDCl_3$) δ 0.87 (t, *J* = 6.8 Hz, 3 H), 1.26-1.37 (m, 6 H), 1.59-1.64 (m, 2 H), 2.35 (s, 3 H), 2.42 (s, 3 H), 2.76 (t, *J* = 7.8 Hz, 2 H), 5.47 (s, 1 H), 7.18 (d, *J* = 8.3 Hz, 2 H), 7.25 (d, *J* = 8.3 Hz, 2 H), 7.31 (d, *J* = 8.3 Hz, 2 H), 7.39 (d, *J* = 8.3 Hz, 2 H); ^{13}C NMR (68 MHz, $CDCl_3$), δ 14.08, 21.35, 21.44, 22,59, 29.21, 29.88, 31.58, 34.51, 115.29, 125.12, 125.64, 129.91, 130.68, 134.64, 135.44, 139.34, 140.45, 165.96, 184.40; IR (NaCl) 2955, 2926, 1679, 1568, 1493, 1044, 1018, 808, 688 cm^{-1}; mass spectrum (CI), m/e 385 (M^++1, 100); exact mass (M^+) calcd for $C_{23}H_{28}OS_2$ 384.1581, found 384.1593.

(Z)-1,3-Bis(*p*-methylphenylseleno)-2-nonen-1-one (Table II, Entry 5): oil; ^1H NMR (270 MHz, $CDCl_3$) δ 0.80 (t, *J* = 7.08 Hz, 3 H), 0.98-1.03 (m, 4 H), 1.14 (m, 2 H), 1.31 (quintet, *J* = 7.6 Hz, 2 H), 2.12 (t, *J* = 7.6 Hz, 2 H), 2.35 (s, 3 H), 2.36 (s, 3 H), 6.64 (s, 1 H, J_{Se-H} = 12.7 Hz), 7.13 (d, *J* = 7.8 Hz, 2 H), 7.19 (d, *J* = 8.3 Hz, 2 H), 7.45 (d, *J* = 8.3 Hz, 2 H), 7.49 (d, *J* = 7.8 Hz, 2 H). NOE experiment: Irradiation of the methylene triplet at δ 2.12 resulted in a 19% enhancement of the signal at δ 6.64 (vinyl singlet). The regiochemistry was determined from the result of the reduction with an equimolar amount of *n*-Bu_3SnH in benzene-d_6 (The formyl doublet appeared at δ 9.88 (*J* = 3.9 Hz)); ^{13}C NMR (68 MHz, $CDCl_3$) δ 14.00, 21.29, 21.32, 22.35, 28.45, 29.78, 31.21, 37.65, 121.92, 123.22, 123.85, 129.95, 130.15, 135.85 (J_{Se-C} = 9.5 Hz), 137.23 (J_{Se-C} = 9.5 Hz), 138.86, 139.46, 163.36, 187.91; IR (NaCl) 3018, 2954, 2926, 2857, 1667, 1538, 1489, 1090, 803 cm^{-1}; mass spectrum (CI), m/e 481 (M^++1, 21); Anal. Calcd for $C_{23}H_{28}OSe_2$: C, 57.74; H, 5.89. Found: C, 57.76; H, 6.11.

(Z)-1,3-Bis(*p*-trifluoromethylphenylseleno)-2-nonen-1-one (Table II, Entry 6): oil; ^1H NMR (270 MHz, $CDCl_3$) δ 0.80 (t, *J* = 7.1 Hz, 3 H), 1.02 (m, 4 H), 1.15 (m, 2 H), 1.34 (m, 2 H), 2.15 (t, *J* = 7.8 Hz, 2 H), 6.69 (s, 1 H, J_{Se-H} = 16 Hz), 7.61 (d, *J* = 7.8 Hz, 2 H), 7.64 (d, *J* = 7.8 Hz, 2 H), 7.71 (d, *J* = 7.8 Hz, 2 H), 7.78 (d, *J* = 7.8 Hz, 2 H). NOE experiment: Irradiation of the methylene triplet at δ 2.15 resulted in a 21% enhancement of the signal at δ 6.69 (vinyl singlet). The regiochemistry was determined from the result of the reduction with an equimolar amount of *n*-Bu_3SnH in benzene-d_6 (The formyl doublet appeared at δ 9.72 (*J* = 2.9 Hz)); ^{13}C

NMR (68 MHz, $CDCl_3$) δ 13.88, 22.33, 28.41, 29.76, 31.15, 37.97, 122.36, 123.78 (q, J = 272 Hz), 123.98 (q, J = 272 Hz), 125.99 (q, J = 2.9 Hz), 126.05 (q, J = 2.9 Hz), 130.93 (q, J = 33 Hz), 131.17, 131.69 (q, J = 33 Hz), 131.78, 135.86, 137.62, 162.52, 186.36; IR (NaCl) 2958, 2931, 2859, 1666, 1602, 1540, 1324, 1168, 1130, 1101, 1076, 1058, 1014, 832 cm^{-1}; mass spectrum (CI), m/e 589 (M^++1, 71); Anal. Calcd for $C_{23}H_{22}F_6OSe_2$: C, 47.11; H, 3.78. Found: C, 47.34; H, 3.86.

(*Z*)-1,3-Bis(phenylseleno)-6-methyl-2-hepten-1-one (Table II, Entry 7): mp 83-84 °C (a light yellow crystal); ^1H NMR (270 MHz, $CDCl_3$) δ 0.60 (d, J = 6.1 Hz, 6 H), 1.20-1.24 (m, 3 H), 2.15 (t, J = 7.6 Hz, 2 H), 6.66 (s, 1 H, J_{Se-H} = 14.0 Hz), 7.31-7.40 (m, 6 H), 7.57-7.65 (m, 4 H). NOE experiment: Irradiation of the methylene triplet at δ 2.15 resulted in a 10% enhancement of the signal at δ 6.66 (vinyl singlet). The regiochemistry was determined from the result of the reduction with an equimolar amount of *n*-Bu_3SnH in benzene-d_6 (The formyl doublet appeared at δ 9.84 (J = 3.5 Hz)); ^{13}C NMR (68 MHz, $CDCl_3$) δ 21.99, 27.66, 35.91, 39.07, 121.06, (J_{Se-C} = 58.0 Hz), 126.78, 127.35, 128.81, 129.18, 129.30, 129.40, 135.34 (J_{Se-C} = 9.0 Hz), 137.41 (J_{Se-C} = 10.0 Hz), 163.39, 187.49; IR (KBr) 3053, 2953, 2870, 1672, 1662, 1540, 1438, 1093, 804, 741, 690 cm^{-1}; mass spectrum (CI), m/e 439 (M^++1, 44); Anal. Calcd for $C_{20}H_{22}OSe_2$: C, 55.05; H, 5.08. Found: C, 55.15; H, 5.10.

1,3-Bis(phenylseleno)-3-phenyl-2-propen-1-one (Table II, Entry 8). *Z* isomer: mp 135-141 °C (a yellow crystal); ^1H NMR (270 MHz, $CDCl_3$) δ 6.80 (s, 1 H), 6.95-7.08 (m, 8 H), 7.19 (d, J = 6.8 Hz, 2 H), 7.40-7.42 (m, 3 H) 7.60-7.62 (m, 2 H). The regiochemistry was determined from the result of the reduction with an equimolar amount of *n*-Bu_3SnH in benzene-d_6 (The formyl doublet appeared at δ 10.06 (J = 4.9 Hz)); ^{13}C NMR (270 MHz, $CDCl_3$) δ 124.73, 126.66, 127.57, 128.09, 128.33, 128.45, 128.67, 128.93, 129.05, 129.37, 135.79, 136.05, 138.58, 159.57, 187.77; IR (KBr) 3057, 1658, 1531, 1486, 1476, 1437, 1227, 1042, 935, 760, 744, 696 cm^{-1}; mass spectrum (CI) m/e 445 (M^++1, 56); Anal. Calcd for $C_{21}H_{16}OSe_2$: C, 57.03; H, 3.64. Found: H, 3.64; C, 57.19.

E isomer: Pure *E* isomer could not be isolated, because it was formed in low yield.

1,3-Bis(phenylthio)-3-phenyl-2-propen-1-one (Table II, Entry 9). *Z* isomer: mp 135-139 °C (a yellow solid); ^1H NMR (270 MHz, $CDCl_3$) δ 6.45 (s, 1 H), 7.03-7.13 (m, 10 H), 7.43-7.44 (m, 3 H), 7.52-7.53 (m, 2 H). The regiochemistry was determined from the result of

the reduction with an equimolar amount of *n*-Bu_3SnH in benzene-d_6 (The two formyl doublets appeared at δ 9.50 (J = 8.1 Hz) and δ 10.47 (J = 6.5 Hz)); ^{13}C NMR (68 MHz, $CDCl_3$) δ 121.02, 127.83, 128.01, 128.11, 128.43, 128.66, 128.93, 129.14, 129.32, 132.06, 134.17, 134.67, 137.74, 158.63, 185.19; IR (KBr) 3059, 1661, 1537, 1078, 949, 791, 752, 705, 690, 671, 588 cm^{-1}; mass spectrum (CI) m/e 349 (M^++1, 100); Anal. Calcd for $C_{21}H_{16}OS_2$: C, 72.38; H, 4.62; S, 18.40. Found C, 72.37; H, 4.61; S, 18.32.

E isomer: Pure *E* isomer could not be isolated, because it was formed in low yield.

(Z)-1,3-Bis(phenylseleno)-5,5-bis(ethoxycarbonyl)-2,7-octadien-1-one (Table II, Entry 10): mp 66-68 °C (a light yellow crystal); ^1H NMR (270 MHz, $CDCl_3$) δ 1.22 (t, J = 7.1 Hz, 6 H), 2.54 (d, J = 8.3 Hz, 2 H), 2.80 (s, 2 H), 4.15 (q, J = 7.1 Hz, 4 H), 4.88 (d, J = 20.5 Hz, 1 H), 4.93 (d, J = 14.0 Hz, 1 H), 5.35 (octet, J = 8.3, 14.0, 20.5 Hz, 1 H), 6.74 (s, 1 H), 7.34-7.46 (m, 6 H), 7.55-7.60 (m, 4 H). NOE experiment: Irradiation of the methylene singlet at δ 2.80 resulted in an 11% enhancement of the signal at δ 6.74 (vinyl singlet). The regiochemistry was determined from the result of the reduction with an equimolar amount of *n*-Bu_3SnH in benzene-d_6 (The two formyl doublets appeared at δ 9.74 (J = 7.6 Hz) and δ 9.96 (J = 4.9 Hz)); ^{13}C NMR (68 MHz, $CDCl_3$) δ 14.07, 38.17, 38.60, 58.02, 61.76, 119.38, 124.52, 126.63, 127.75, 128.92, 129.37, 129.41, 129.50, 131.92, 135.76, 137.22, 155.35, 170.06, 187.45; IR (KBr) 3053, 2982, 1730, 1669, 1543, 1219, 1066, 793, 744, 693 cm^{-1}; mass spectrum (CI), m/e 581 (M^++1, 14); Anal. Calcd for $C_{26}H_{28}O_5Se_2$: C, 53.98; H, 4.87. Found: C, 54.23; H, 4.90.

1,3-Bis(phenylseleno)-6-hydroxy-2-hexen-1-one (Table II, Entry 11). *Z* isomer: mp 98-100 °C (a light yellow crystal); ^1H NMR (270 MHz, $CDCl_3$) δ 1.55 (quintet, J = 6.1, 7.6 Hz, 2 H), 1.70 (br s, 1 H), 2.26 (t, J = 7.6 Hz, 2 H), 3.29 (t, J = 6.1 Hz, 2 H), 6.71 (s, 1 H, $J_{Se\text{-}H}$ = 11.7 Hz), 7.30-7.65 (m, 10 H). NOE experiment: Irradiation of the methylene triplet at δ 2.26 resulted in a 21% enhancement of the signal at δ 6.71 (vinyl singlet). The regiochemistry was determined from the result of the reduction with an equimolar amount of *n*-Bu_3SnH in benzene-d_6 (The formyl doublet appeared at δ 9.81 (J = 3.9 Hz); ^{13}C NMR (68 MHz, $CDCl_3$) δ 32.35, 33.99, 61.06, 122.49, 126.58, 127.08, 128.83, 129.24, 129.29, 129.45, 135.74, 137.23, 161.95, 187.69; IR (KBr): 3326, 3055, 2937, 1664, 1546, 1532, 1085, 809, 742, 693 cm^{-1}; mass spectrum (CI), m/e 427 (M^++1, 8); Anal. Calcd for $C_{18}H_{18}O_2Se_2$: C, 4.27; H, 50.96. Found: C, 51.01; H. 4.34.

E isomer: oil; ^1H NMR (270 MHz, $CDCl_3$) δ 1.87 (quintet, J = 5.9, 7.3 Hz, 2 H), 2.07 (br s, 1

H), 2.88 (t, J = 7.3 Hz, 2 H), 3.62 (t, J = 5.9 Hz, 2 H), 5.94 (s, 1 H), 7.30-7.66 (m, 10 H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 31.69, 32.55, 61.09, 123.48, 126.03, 126.87, 128.88, 129.32, 129.94, 130.07, 135.69 (J_{Se-C} = 8.8 Hz), 136.72, 163.43, 187.74; IR (NaCl) 3368, 3056, 2942, 2874, 1693, 1564, 1557, 1476, 1438, 1338, 1038, 1020, 738, 690 cm^{-1}; mass spectrum (CI), m/e 427 (M^++1, 8).

2-1-4. References and Notes

(1) For a recent review, see: Colquhoun, H. M.; Thompson, D. J.; Twigg, M. V. *Carbonylation: Direct Synthesis of Carbonyl Compounds*; Plenum Press: New York, 1991.

(2) For the synthetic utility of thioesters, for example: (a) Masamune, S.; Hayase, Y.; Schilling, W.; Chan, W. K.; Bates, G. S. *J. Am. Chem. Soc.* **1977**, *99*, 6756. (b) Anderson, R. J.; Henrick, C. A.; Rosenblum, L. D. *J. Am. Chem. Soc.* **1974**, *96*, 3654. For the synthetic utility of selenolesters, see: (c) Ogawa, A.; Sonoda, N. *Comprehensive Organic Synthesis Vol 6*; Winterfeldt, E.,Ed.; Pergamon Press: Oxford, in press. (d) Boger, D. L.; Mathvink, R. J. *J. Am. Chem. Soc.* **1990**, *112*, 4003. (e) Crich, D.; Fortt. S. M. *Tetrahedron Lett.* **1987**, *28*, 2895.

(3) The stereochemistry of **5a** was confirmed by NOE experiment, and the regiochemistry was determined from the result of the reduction of **5a** with tri-*n*-butyltin hydride. The details are described in chapter **3**.

(4) It has been reported that the reaction of diaryl diselenides and disulfides with carbon monoxide in the presence of $Co_2(CO)_8$ gave the selenoesters and thioesters, see: Takahashi, H.; Ohe, K.; Uemura, S.; Sugita, N. *J. Organomet. Chem.* **1987**, *334*, C43. (b) Antebi, S.; Alper, H. *Tetrahedron Lett.* **1985**, *26*, 2609.

(5) This extent of pressure was necessarily to avoid the generation of by-products.

(6) In the case of the carbonylative addition of $(PhS)_2$ to this substrate, cyclization reaction also occurred. The details are now under investigation.

(7) Acetylenes having a hydroxy group at the α or β position to the carbon-carbon triple bond provided lactones. The details are described in the following section.

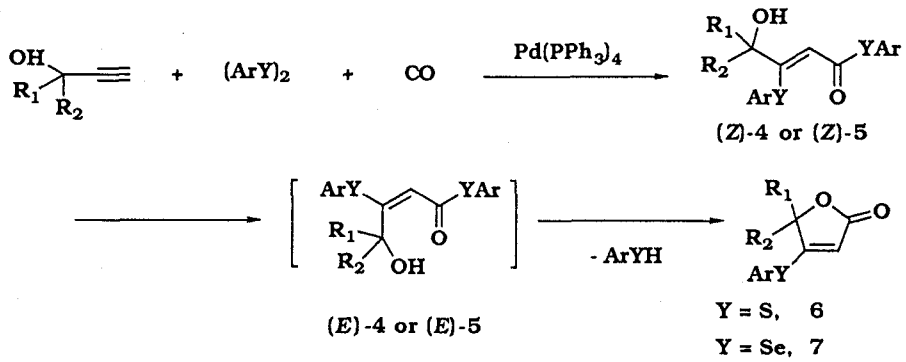
(8) Kim, Y. J.; Osakada, K.; Sugita, K.; Yamamoto, T.; Yamamoto, A. *Organometallics* **1988**, *7*, 2182.

2-2. One-Pot Lactonization of Propargyl Alcohols *via* Palladium-Catalyzed Carbonylative Addition

2-2-1. Introduction

Disclosed in this section is an extension of the reaction system of palladium-catalyzed carbonylative double thiolations and double selenations to propargyl alcohols as substrates. Contrary to our initial expectation, the products obtained by the carbonylative double addition (*Z*)-**4** and (*Z*)-**5**, which possess a hydroxy group at γ position for carbonyl group easily isomerized to *E* isomer, and subsequent intramolecular cyclization took place to give the butenolides **6** and **7** as the major products, respectively (Scheme I).[1] Some results of the insight into the reaction pathway of the cyclization from **4** to **6** is also described.

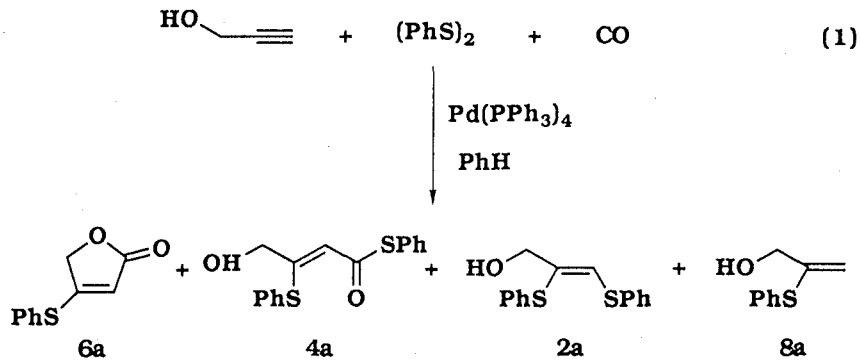
Scheme I



2-2-2. Results and Discussion

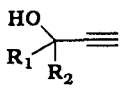
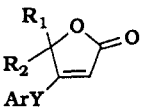
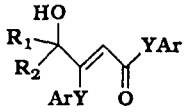
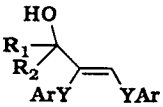
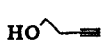
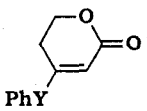
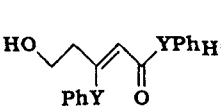
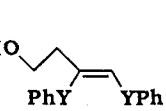
Typical Procedure for Converting the Propargyl Alcohols to Butenolides Bearing Arylthio Groups at 3-Position: In a 50 mL stainless steel autoclave were placed diphenyl disulfide [$(PhS)_2$] (1.0 mmol), 2-propyn-1-ol (**1a**) (1.0 mmol), $Pd(PPh_3)_4$ (0.02 mmol), and benzene (1 mL) with a magnetic stirring bar. Then the reaction mixture was pressurized at 60 kg/cm^2 with carbon monoxide. After the reaction mixture was stirred for 50 h at 100 °C, the carbon monoxide was purged and the precipitated palladium complex was removed through

Celite and the reaction mixture was concentrated in *vacuo*. The residue was separated by MPLC and HPLC to provide the 3-phenylthio-2-buten-4-olide (**6a**) (43%) and (*Z*)-1,2-bis(phenylthio)-3-hydroxy-1-propene (**2a**) (35%) together with a trace amount of 2-phenylthio-3-hydroxy-1-propene (**8a**).[2] Under this reaction condition, 1,3-bis(phenylthio)-4-hydroxy-2-buten-1-one (**4a**) was scarcely detected (eq 1 and entry 1 in Table I).



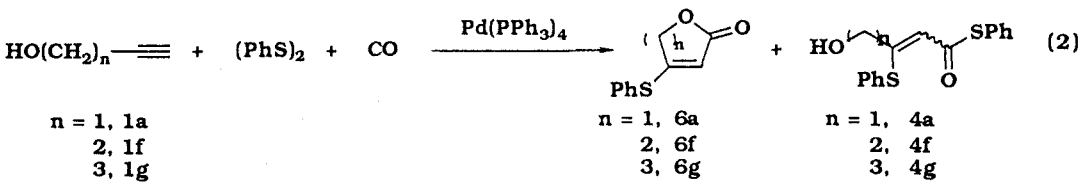
Generality of the One-Pot Lactonization (Table I): The structures of the lactones were characterized on the basis of analytical and spectral data. The reaction using diphenyl diselenide in lieu of diphenyl disulfide as a reagent also underwent a similar lactonization to provide the 3-phenylseleno-2-buten-4-olide (**7a**) in 36% yield (entry 4). $Pd(PPh_3)_2Cl_2$ also exhibited the catalytic ability for this transformation, although, in the case of $(PhS)_2$, the conversion was low compared with the case of $Pd(PPh_3)_4$-catalyzed reaction (entries 1, 2 vs entries 4, 5). Replacing the para substituent of the Ar group of diselenide with electron withdrawing group improved the yield of the butenolide (entry 7). When the reactions using propargyl tertiary alcohols were performed, desired butenolides were difficult to obtain in the case of using diphenyl disulfide. For instance, the reaction of 2-methyl-3-butyn-2-ol (**1c**) with $(PhS)_2$ and CO permitted the formation of (*Z*)-**4c** as a major product (entry 10). In the case of $(PhSe)_2$, however, the lactonization from **5** to **7** was not affected, even if two alkyl substituents were present at the position (entry 11). The palladium-catalyzed reaction of 1-ethynyl-1-cyclopentanol (**1d**) and 1-ethynyl-1-cyclohexanol (**1e**) with $(PhSe)_2$ and CO gave spirocyclic compounds in moderate yields (entries 13 and 14), although the corresponding sulfide was provided in a low yield (entry 12). A similar operation of $(PhY)_2$ (Y = S, Se) with 3-butyn-1-ol (**1f**) having a hydroxy group at the β position for acetylenic triple bond gave six-membered pentenolides in moderate yields (entries 15 and 16) .

Table I. Carbonylative Addition of Propargyl and Homopropargyl Alcohols with Diaryl Disulfides and Diselenides and CO Catalyzed by $Pd(PPh_3)_4$[a]

entry	substrate	$(ArY)_2$	yields of products		
			6 or 7 (%)[b]	4 or 5 (%)[c]	2 or 3 (%)[c]
					
1	R_1=R_2=H	$(PhS)_2$	43	<1	35
2[d]	1a	$(PhS)_2$	17[c]	10	-[f]
3		$(p\text{-}MeC_6H_5S)_2$	18	10 (only *Z*)	13
4		$(PhSe)_2$	36[e]	-[f]	12
5[d]		$(PhSe)_2$	53[c]	-[f]	-[f]
6		$(p\text{-}MeC_6H_4Se)_2$	56[g]	-[f]	16
7		$(p\text{-}CF_3C_6H_4Se)_2$	74	-[f]	14
8	R_1=Me, R_2=H	$(PhS)_2$	52	-[f]	37
9	1b	$(PhSe)_2$	54	-[f]	20
10	R_1=R_2=Me	$(PhS)_2$	16	38 (only *Z*)	16
11	1c	$(PhSe)_2$	57	-[f]	10
12	R_1, R_2=-$(CH_2)_4$-	$(PhS)_2$	14	58 (only *Z*)	-[h]
13	1d	$(PhSe)_2$	70	-[f]	5
14	R_1, R_2=-$(CH_2)_5$-	$(PhSe)_2$	62	-[f]	13
	1e				
	 1f				
15		$(PhS)_2$	64	-[f]	19
16		$(PhSe)_2$	66[i]	<1	4

[a]Conditions: Unless otherwise noted, the reactions of substrate (1.0 mmol), $(ArY)_2$, (1.0 mmol), $Pd(PPh_3)_4$ (2 mol%), and PhH (1 mL) in the 60 kg/cm^2 of carbon monoxide were carried out at 100 °C for 50 h. [b]Isolated yield. [c]NMR yield. [d]$Pd(PPh_3)_2Cl_2$ (2 mol%), CO (20 kg/cm^2). [e]3,3-Bis(phenylseleno)butan-4-olide (12%) was also obtained. [f]Not detected. [g]3,3-Bis(4-methylphenylseleno)butan-4-olide (13%) was also obtained. [h]1-[1,2-bis(phenylthio)-ethenyl]-cyclohexene was obtained in 6% yield. [i]3,3-bis(diphenylseleno)pentan-5-olide (10%) was also obtained.

Some Insights into the Reaction Pathway of this One-Pot Lactonization from Propargyl and Homopropargyl Alcohols (eq 2 and Table II):



(2)

n = 1, 1a
2, 1f
3, 1g

n = 1, 6a
2, 6f
3, 6g

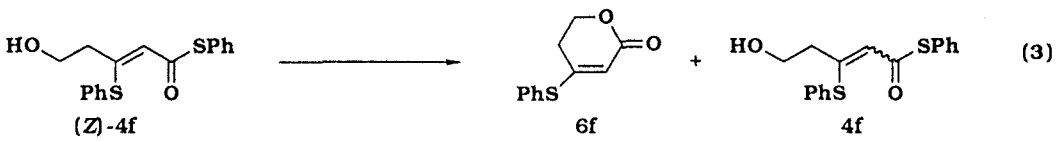
n = 1, 4a
2, 4f
3, 4g

Table II[a]

entry	$(PhS)_2$		condition	yield of 6 (%)[b]	yield of 4 (%)[b]
1	1 equiv	n = 2,	80 °C, 30 h	46	28 (*E*/*Z* = 47/53)
2	4 equiv	n = 1,	100 °C, 50 h	16	45 (only *Z*)
3	4 equiv	n = 2,	100 °C, 50 h	16	51 (*E*/*Z* = 2/98)
4	1 equiv	n = 3,	100 °C, 50 h	trace	41 (*E*/*Z* = 62/38)
5[c]	1 equiv	n = 3,	100 °C, 50 h	trace	56 (*E*/*Z* = 36/64)

[a]Conditions: **1** (1.0 mmol), $(PhS)_2$ (1.0 or 4.0 mmol), CO (60 kg/cm^2), and $Pd(PPh_3)_4$ (2 mol%). [b]Determined by ^{1}H NMR. [c]$(PhSe)_2$ was used in place of $(PhS)_2$.

When the reaction of **1f** and $(PhS)_2$ was carried out under more moderate reaction conditions (80 °C, 30 h), carbonylative double thiolation product **4f**, which is a precursor of pentenolide **6f** was also obtained in 28% yield (entry 1). Noteworthy is the fact that the formation of **6f** and (*E*)-**4f** were also confirmed even under this reaction conditions.[3] It markedly contrasts with the result of the carbonylative addition to acetylenes without hydroxy group as substrates under analogous reaction conditions.[4] This fact indicates that the presence of hydroxy group in **4** plays an important role for the C-C double bond isomerization. The reaction using 5-pentyn-1-ol (**1g**) having a hydroxy group at γ position for C-C triple bond scarcely gave the seven-membered lactone **6g**, and **4g** was obtained as the major product. It is also interesting that the stereoselectivity of **4g** was disappeared (entry 4). This tendency was also observed in the reaction using $(PhSe)_2$ (*E*/*Z* = 36/64) (entry 5).[5] These results also stand for the proposal that the presence of hydroxy groups in **4** (and **5**) is a crucial factor for the carbon-carbon double bond isomerization. On the other hand, when **1a** and **1f** with excess amount of $(PhS)_2$ (4 equiv) were subjected to the palladium-catalyzed reaction at 100 °C for 50 h, **4a** and **4f** were formed as the major products with the high preponderance of *Z* isomer, respectively (entries 2, 3 in Table II vs entries 1, 15 in Table I). Furthermore, to elucidate the role of the palladium catalyst and carbon monoxide, the reaction using isolated (*Z*)-**4f** was examined under the conditions listed in eq 3 and Table III.



(3)

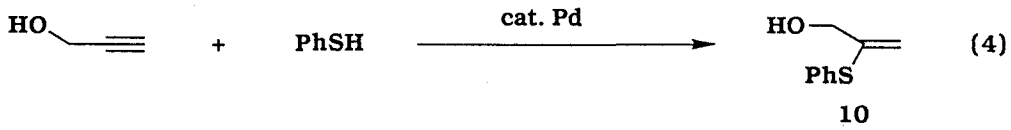
Table III. Effects of Pd complex on the Cyclization from 4f to 6f[a]

entry	CO	$Pd(PPh_3)_4$	$(PhY)_2$	yield of 6f (%)[b]	yield of 4f (%)[b]
1	60 kg/cm^2	3 mol%	0	19	75(E/Z = 5/95)
2	60 kg/cm^2	0	0	0	~100 (E/Z = 1/99)

[a]Conditions: **4f** (0.05 mmol), PhH (0.1 mL), 100 °C, 5 h. [b]Determined by ^{1}H NMR.

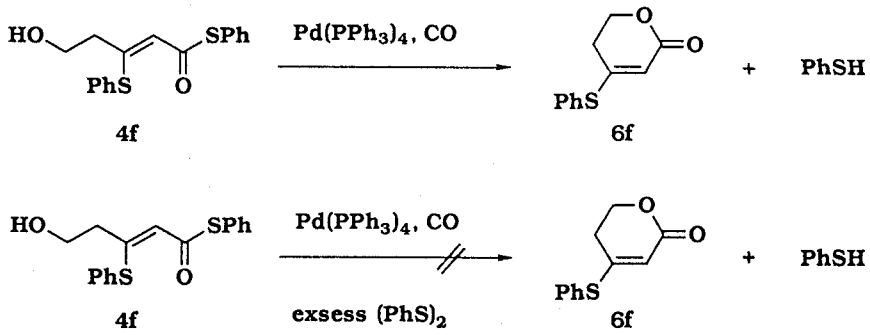
When the reaction of (Z)-**4f** with CO (60 kg/cm^2) was carried out in the presence of $Pd(PPh_3)_4$ at 100 °C for 5 h, **6f** was obtained in 19% yield (entry 1). On the other hand, the reaction without catalyst in the presence of CO (60 kg/cm^2) scarcely yielded **6f** (entry 2).

These facts suggest that the pathway from **4f** to **6f** was suppressed by the presence of excess amount of $(PhS)_2$ and promoted by palladium complex generated *in situ*.[6] At the beginning stage of the one-pot lactonization, the suppression by $(PhS)_2$ have an effect on decrease in the formation of **10**, which is competitively formed by palladium-catalyzed addition of aromatic thiol to acetylene (eq 4[2] and Scheme II).



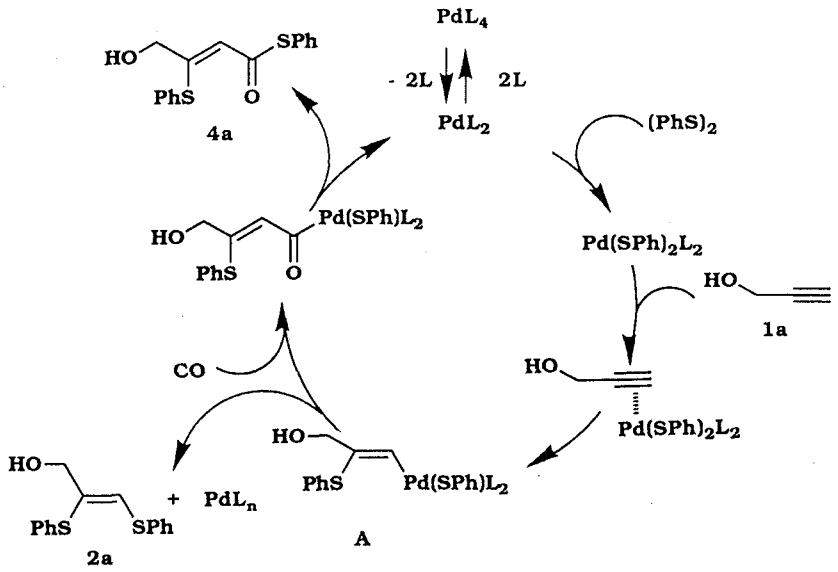
(4)

scheme II



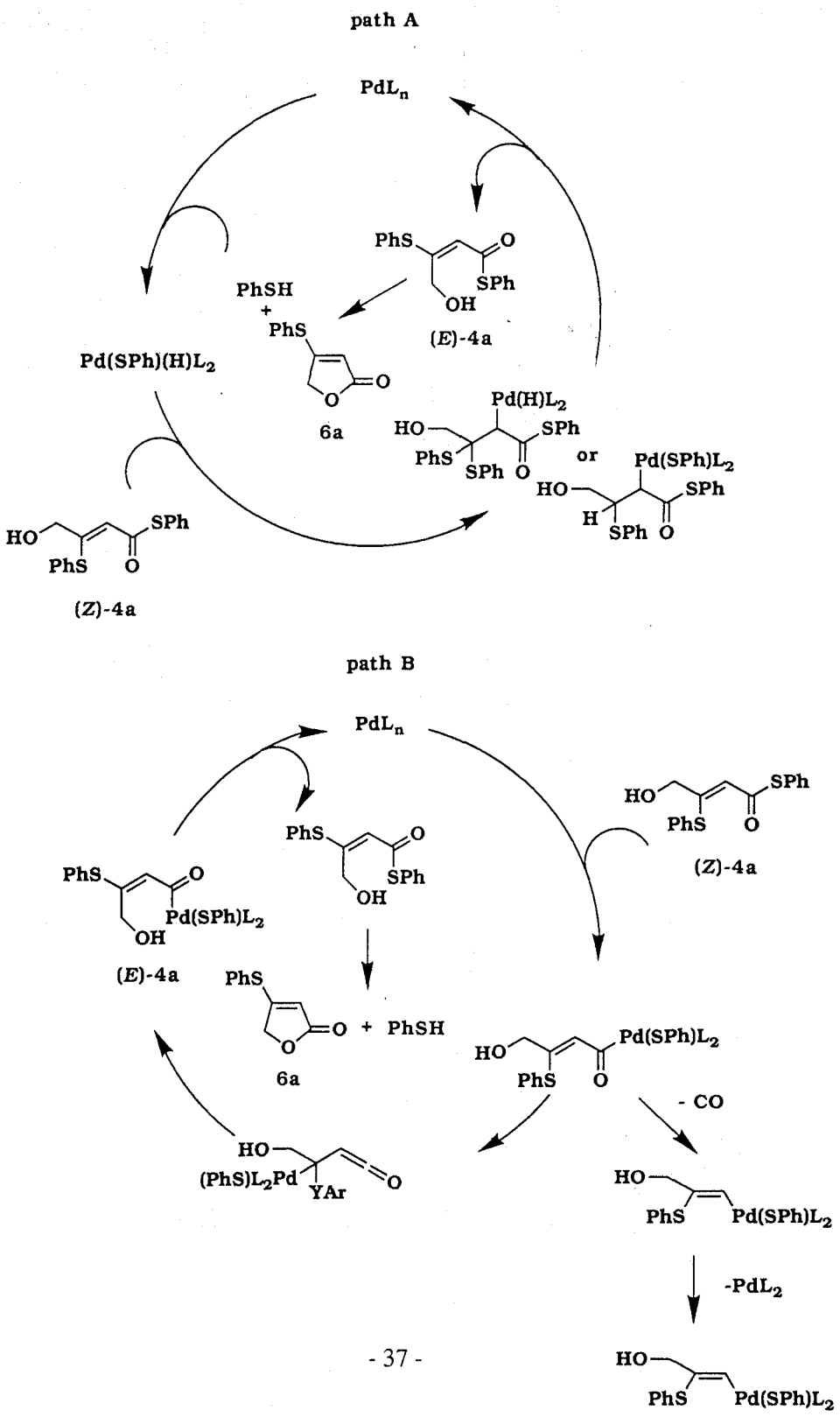
Proposed reaction pathways of this one-pot lactonization are shown in Scheme III and IV (illustrated for 2-propyn-1-ol (**1a**) and $(PhS)_2$ as substrates). Scheme III shows the pathway of the stereo- and regioselective carbonylative double thiolation, which involves the oxidative addition of $(PhS)_2$ to low-valent palladium complex,[7] coordination of **1a** to the palladium complex, and subsequent *cis* insertion of **1a** into Pd-S bond to form a vinylpalladium intermediate **A** in a regio- and stereoselective manner. The direct reductive elimination from **A** gives (*Z*)-**2a** with retention of the stereochemistry. When carbon monoxide is inserted into palladium-carbon bond of **A**, subsequent reductive elimination provides (*Z*)-**4a**.

Scheme III. A Proposed Reaction Pathway for the Palladium-Catalyzed Carbonylative Double Thiolation of 1a with $(PhS)_2$ and CO



Subsequently (*Z*)-**4a** isomerizes into *E* isomer and undergoes the intramolecular nucleophilic substituent to afford **6a** accompanied by the formation of PhSH as a by-product. Although the precise mechanism of the double bond isomerization remains unclear, the isomerization is promoted by palladium complex, in which the hydroxy groups and carbon monoxide may coordinate to it. We propose here two different pathways of this palladium-promoted isomerization as shown in Scheme IV. Path **A** is the addition-elimination mechanism of Pd-S bond or Pd-H bond generated *in situ* to (*Z*)-**4a**. As we disclose in Chapter **4**, isomerization of carbon-carbon double bond took place easily in the reaction system of acetylene, thiol (or selenol) and palladium catalyst.

Scheme IV. Possible Reaction Pathways from (Z)-4a to 6a



Path **B** is an alternative route *via* the oxidative addition of acyl-S bond of (*Z*)-**4a** bond to palladium complex, followed by reductive elimination to *E* isomer through ketene species, in which intramolecular hydrogen group would coordinate to the palladium. The presence of excess amount of $(PhS)_2$ for palladium catalyst probably suppresses these isomerization steps in any case, provably because the oxidative addition of PhSH (path **A**) or (*Z*)-**4a** (path **B**) to low-valent palladium (PdL_n) would be avoided by the excess presence of $(PhS)_2$.[7] After the isomerization takes place, (*E*)-**4a** undergoes facile cyclization to give **6a** and PhSH.

Conclusion: The palladium-catalyzed reactions of diaryl disulfide and selenides, carbon monoxide and propargyl alcohols and homopropargyl alcohols allow the preparation of butenolides and pentenolides possessing ArS and ArSe groups, which would be a clue to develope further transformations.[8] This study also demonstrates the utility of transition-metal catalysts in the synthetic reactions using chalcogen compounds.

2-2-3. Experimental Section

Palladium-Catalyzed One-Pot Carbonylative Lactonization. General Procedure (Table I, Entry 1): To a 50 mL stainless autoclave equipped with a magnetic stirring bar were placed diphenyl disulfide (1.0 mmol), 2-propyn-1-ol (**1a**) (1.0 mmol), tetrakis(triphenylphosphine)palladium [$Pd(PPh_3)_4$] (0.02 mmol), and benzene (1 mL). The mixture was heated with stirring for 50 h at 100 °C. After the reaction was complete, the brown precipitates were removed by filtration through Celite, and the filtrate was evaporated under reduced pressure. The crude mixture was analyzed by ^1H and ^{13}C NMR spectrum, and then it was separated by MPLC (silica gel, 25~40 mm, length 310 mm, i.d. 25 mm, *n*-hexane/ether as eluent) and/or HPLC (Japan Analytical Industry Co., Ltd. Model LC-908, JAIGEL-1H and -2H (GPC), length 600 mm, i.d. 20 mm, eluent $CHCl_3$) to provide 83 mg of 3-phenylthio-2-butene-4-olide (**6a**) (43%) as a light yellow oil.

6a (Table I, Entry 1): yellow oil; ^1H NMR (270 MHz, $CDCl_3$) δ 4.75 (s, 2 H), 5.50 (s, 1 H), 7.46-7.58 (m, 5 H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 71.74, 111.02, 127.13, 130.14, 130.51, 134.73, 168.54, 172.08; IR (NaCl) 3059, 1778, 1747, 1568, 1475, 1442, 1255, 1152, 1021, 887, 823, 752, 692 cm^{-1}; mass spectrum (EI), m/e 192 (M^+, 100); exact mass (M^+) calcd for $C_{10}H_8O_2S$ 192.02451, found 192.0273.

3-(4-Methylphenylthio)-2-buten-4-olide (Table I, Entry 3): yellow oil; ^{1}H NMR (270 MHz, $CDCl_3$) δ 2.41 (s, 3 H), 4.73 (s, 2 H), 5.50 (s, 1 H), 7.26 (d, J = 8.1 Hz, 2 H), 7.44 (d, J = 8.1 Hz, 2 H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 21.33, 71.74, 110.83, 123.55, 130.89, 134.62, 141.17, 169.06, 172.19; IR (NaCl) 3028, 2925, 1777, 1750, 1570, 1255, 1151, 1021, 886, 866, 812, 727, 699 cm^{-1}; mass spectrum (EI), m/e 206 (M^+, 100); Anal. Calcd for $C_{11}H_{10}O_2S$: C, 64.06; H, 4.89; S, 15.55. Found: C, 63.93; H, 4.94; S, 15.58.

3-Phenylseleno-2-buten-4-olide (Table I, Entry 4): yellow oil; ^{1}H NMR (270 MHz, $CDCl_3$) δ 4.72 (s, 2 H), 5.76 (s, 1 H), 7.39-7.48 (m, 3 H), 7.63-7.66 (m, 2 H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 73.51, 115.60, 123.32, 130.01, 130.10, 136.00, 164.50, 171.80; IR (NaCl) 3058, 2932, 1770, 1742, 1567, 1440, 1249, 1150, 1008, 884, 845, 744, 692 cm^{-1}; mass spectrum (EI) m/e 240 (M^+, 100); Anal. Calcd for $C_{10}H_8O_2Se$: C, 50.23; H, 3.37. Found: C, 49.98; H. 3.41.

3-(4-Methylphenylseleno)-2-buten-4-olide (Table I, Entry 6): yellow oil; ^{1}H NMR (270 MHz, $CDCl_3$) δ 2.39 (s, 3 H), 4.70 (d, J = 1.7 Hz, 2 H), 5.75 (t, J = 1.7 Hz, 1 H), 7.21 (d, J = 7.9 Hz, 2 H), 7.51 (d, J = 7.9 Hz, 2 H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 21.22, 73.61, 115.46, 119.73, 130.88, 136.05, 140.62, 165.09, 172.00; IR (NaCl) 3024, 2924, 1774, 1743, 1569, 1490, 1249, 1149, 1007, 883, 846, 807, 725, 697 cm^{-1}; mass spectrum (EI) m/e 254 (M^+, 100); Anal. Calcd for $C_{11}H_{10}O_2Se$: C, 52.19; H, 3.98. Found: C, 52.37; H, 4.08.

3,3-Bis(4-methylphenylseleno)butan-4-olide (Table I, Entry 6): yellow oil; ^{1}H NMR (270 MHz, $CDCl_3$) δ 2.38 (s, 6 H), 2.70 (s, 2 H), 4.26 (s, 2 H), 7.18 (d, J = 7.3 Hz, 4 H), 7.33 (d, J = 7.3 Hz, 4 H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 21.35, 41.42, 44.24, 76.25, 123.80, 130.38, 137.87, 140.47, 174.00; IR (NaCl) 3019, 2973, 2919, 1789, 1488, 1157, 1015, 843, 807 cm^{-1}; mass spectrum (EI) m/e 426 (M^+, 7); exact mass (M^+) calcd for $C_{18}H_{18}O_2Se_2$ 425.9637, found 425.9625.

3-(4-Trifluoromethylphenylseleno)-2-buten-4-olide (Table I, Entry 7): mp 48-49 °C (a white solid); ^{1}H NMR (270 MHz, $CDCl_3$) δ 4.78 (s, 2 H), 5.80 (s, 1 H), 7.69 (d, J = 7.7 Hz, 2 H), 7.82 (d, J = 7.7 Hz, 2 H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 73.52, 116.61, 123.43 (q, J = 273 Hz), 126.89 (q, J = 3.8 Hz), 128.06, 132.30 (q, J = 33 Hz), 136.31, 162.71, 171.45; IR (KBr) 3067, 2970, 1783, 1736, 1571, 1249, 1166, 1124, 1006, 834, 702, 596, 500, 438 cm^{-1}; mass

spectrum (EI) m/e 308 (M^+, 100); Anal. Calcd for $C_{11}H_7O_2F_3Se$: C, 43.02; H, 2.30. Found: C, 43.24; H, 2.43.

4-Methyl-3-phenylthio-2-buten-4-olide (Table I, Entry 8): yellow oil; ^1H NMR ($CDCl_3$, 270 MHz) δ 1.55 (d, J = 6.8 Hz, 3 H), 5.08 (q, J = 6.8 Hz, 1 H), 5.27 (s, 1 H), 7.46-7.58 (m, 5 H); ^{13}C NMR ($CDCl_3$, 68 MHz) δ 20.00, 79.20, 110.75, 127.86, 130.15, 130.48, 134.48, 170.95, 173.73; IR (NaCl) 3060, 2983, 1823, 1752, 1570, 1474, 1442, 1319, 1251, 1164, 1059, 940, 887, 828, 691 cm^{-1}; mass spectrum (EI), m/e 206 (M^+, 100); Anal. Calcd for $C_{11}H_{10}O_2S$: C, 64.06; H, 4.89; S,15.55. Found: C, 63.90; H, 4.85; S, 15.95.

4-Methyl-3-phenylseleno-2-buten-4-olide (Table I, Entry 9): yellow oil ^1H NMR (270 MHz, $CDCl_3$) δ 1.51 (d, J = 6.8 Hz, 3 H), 5.10 (q, J = 6.8 Hz, 1 H), 5.48 (s, 1 H), 7.39-7.48 (m, 3 H), 7.62-7.65 (m, 2 H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 20.23, 80.72, 115.70, 124.49, 130.11, 130.22, 135.91, 170.84; IR (NaCl) 3057, 2982, 2929, 1746, 1571, 1163, 1056, 931, 743, 692 cm^{-1}; mass spectrum (EI) m/e 254 (M^+, 100); Anal. Calcd for $C_{11}H_{10}O_2Se$: C, 52.19; H, 3.98. Found: C, 52.23; H, 4.02.

4,4-Dimethyl-3-phenylthio-2-buten-4-olide (Table I, Entry 10): yellow oil; ^1H NMR (270 MHz, $CDCl_3$) δ 1.60 (s, 6 H), 5.13 (s, 1 H), 7.46-7.57 (m, 5 H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 26.62, 86.30, 109.66, 128.02, 130.14, 130.46, 134.60, 170.02, 177.98; IR (NaCl) 3060, 2981, 2931, 1748, 1574, 1442, 1241, 1122, 979, 930, 829, 734, 691, 618 cm^{-1}; mass spectrum (EI) m/e 220 (M^+, 100); exact mass (M^+) cacld for $C_{12}H_{12}O_2S$ 220.0558, found 220.0567.

1,3-Bis(phenylthio)-4-methyl-4-hydroxy-2-penten-1-one (Table I, Entry 10): mp 103-104 °C (yellow solid); ^1H NMR (270 MHz, $CDCl_3$) δ 1.53 (s, 6 H), 2.27 (s, 1 H), 7.09-7.36 (m, 10 H) (NOE experiment: Irradiation of methyl singlet at δ 1.53 resulted in a 23% enhancement at δ 6.91 (vinyl singlet); ^{13}C NMR (68 MHz, $CDCl_3$) δ 29.19, 75.20, 125.56, 126.87, 127.67, 128.96, 129.04, 129.22, 130.10, 134.38, 134.90, 157.41, 186.57; IR (KBr) 3496, 2979, 1672, 1585, 1479, 1440, 1037, 762, 746, 689 cm^{-1}; Anal. Calcd for $C_{18}H_{18}O_2S_2$: C, 65.42; H, 5.49; S, 19.40. Found C, 65.05; H, 5.32; S, 19.32.

4,4-Dimethyl-3-phenylseleno-2-buten-4-olide (Table I, Entry 11): oil; ^1H NMR (270

MHz, $CDCl_3$) δ 1.57 (s, 6 H), 5.29 (s, 1 H), 7.41-7.47 (m, 3 H), 7.61-7.64 (m, 2 H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 26.89, 87.52, 114.46, 124.59, 130.06, 130.17, 135.98, 169.87, 176.02; IR (NaCl) 3058, 2980, 1749, 1573, 1240, 1117, 980, 923, 812, 835, 744, 691 cm^{-1}; mass spectra (CI), m/e 269 (M^++1, 100); Anal. Calcd for $C_{12}H_{12}O_2Se$: C, 53.94; H, 4.53; Found C, 53.76; H, 4.70.

2-Oxa-5-phenylthio-4-penten-3-onespiropentane (Table I, Entry 12): mp 59-61 °C (a white solid); ^1H NMR (270 MHz, $CDCl_3$) δ 1.79-2.38 (m, 8 H), 5.16 (s, 1 H), 7.46-7.57 (m, 5 H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 25.15, 38.66, 96.36, 128.12, 130.20, 130.40, 134.77, 170.31, 175.44; IR (KBr) 2966, 1754, 1572, 1472, 1440, 1270, 1148, 938, 832, 762, 598, 586 cm^{-1}; mass spectrum (EI) m/e 246 (M^+, 61); Anal. Calcd for $C_{14}H_{14}O_2S$: C, 68.27; H, 5.73; S, 13.02. Found: C, 68.33, H, 5.69; S, 12.96.

1,3-Bis(phenylthio)-3-(1'-hydroxycyclopenthyl)-2-buten-1-one (Table I, Entry 12): mp 87-88 °C (a light yellow solid); ^1H NMR (270 MHz, $CDCl_3$) δ 1.62-1.95 (m, 6 H), 2.04 (s, 1 H), 2.07-2.14 (m, 2 H), 6.96 (s, 1 H), 7.10-7.35 (m, 10 H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 24.16, 39.97, 85.80, 125.97, 126.81, 127.68, 128.95, 129.02, 129.18, 129.93, 134.36, 135.06, 155.81, 186.49; IR (KBr) 3489, 3055, 2949, 1669, 1582, 1478, 1440, 1043, 1008, 754, 702, 579, 487 cm^{-1}; mass spectrum (EI), m/e 247 (M^+-SPh, 67); Anal. Calcd for $C_{20}H_{20}O_2S_2$: C, 67.38; H, 5.65; S 17.99. Found: C, 67.67; H, 5.68; S, 17.93.

2-Oxa-5-phenylseleno-4-penten-3-onespiropentane (Table I, Entry 13): mp 85-89 °C (a white solid); ^1H NMR (270 MHz, $CDCl_3$) δ 1.82-2.18 (m, 8 H), 5.33 (s, 1 H), 7.42-7.50 (m, 3 H), 7.60-7.70 (m, 2 H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 25.09, 38.90, 97.61, 115.41, 124.67, 130.08, 130.22, 136.11, 170.14, 173.44; IR (KBr) 2966, 1736, 1564, 1442, 1246, 1149, 946, 922, 834, 752, 692, 578, 478 cm^{-1}; mass spectrum (EI), m/e 294 (M^+, 70); Anal. Calcd for $C_{14}H_{14}O_2Se$: C, 57.35; H, 4.81. Found: C, 57.18; H, 4.80.

Cyclohexanespiro-(3'-oxa-6'-phenylthio-5'-hexen-4'-one) (Table I, Entry 14): mp 101-106 °C (a white solid); ^1H NMR (270 MHz, $CDCl_3$) δ 1.65-2.05 (m, 10 H), 5.28 (s, 1 H), 7.35-7.51 (m, 3 H), 7.61-7.64 (m, 2 H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 22.06, 24.46, 36.21, 89.27, 114.36, 124.73, 130.08, 130.22, 136.11, 170.36, 176.22; IR (KBr) 3044, 2932, 1740, 1568, 1269, 1251, 1211, 931, 888, 835, 754, 694, 578, 478 cm^{-1}; mass spectrum (EI), m/e 308

(M^+, 100); Anal. Calcd for $C_{15}H_{16}O_2Se$: C, 58.64; H, 5.25. Found: C, 54.43; H, 5.36.

3-Phenylthio-2-penten-5-olide (Table I, Entry 15): mp 71-73 °C (yellow solid); ^1H NMR (270 MHz, $CDCl_3$) δ 2.59 (t, J = 6.1 Hz, 2 H), 4.39 (t, J = 6.1 Hz, 2 H), 5.32 (s, 1 H), 7.46-7.52 (m, 5 H); ^{13}C NMR ($CDCl_3$, 68 MHz) δ 28.67, 65.68, 110.15, 127.03, 130.03, 130.49, 135.37, 161.06, 163.18; IR (KBr) 3056, 2893, 1708, 1591, 1472, 1398, 1290, 1210, 1202, 1078, 1050, 746, 694, 631 cm^{-1}; mass spectrum (EI), m/e 206 (M^+, 100); Anal. Calcd for $C_{11}H_{10}O_2S$: C, 64.06; H, 4.89; S, 15.54. Found: C, 63.80; H, 5.03; S, 15.50.

3-Phenylseleno-2-penten-5-olide (Table I, Entry 16): yellow oil; ^1H NMR (270 MHz, $CDCl_3$) δ 2.61 (t, J = 6.1 Hz, 2 H), 4.37 (t, J = 6.1 Hz, 2 H), 5.64 (s, 1 H), 7.37-7.49 (m, 3 H), 7.58-7.61 (m, 2 H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 29.65, 65.88, 114.99, 124.18, 129.98, 129.98, 136.50, 159.02, 162.43; IR (NaCl) 3057, 2990, 2945, 2894, 1715, 1590, 1284, 1214, 1080, 1048, 1022, 856, 743 cm^{-1}; mass spectrum (EI) m/e 254 (M^+, 19); Anal. Calcd for $C_{11}H_{10}O_2Se$: C, 52.19; H, 3.98. Found C, 51.93; H, 4.12.

3,3-Bis(phenylseleno)pentan-5-olide (Table I, Entry 16): yellow oil; ^1H NMR (270 MHz, $CDCl_3$) δ 2.18 (t, J = 5.9 Hz, 2 H), 2.94 (s, 2 H), 4.43 (t, J = 5.9 Hz 2 H), 7.28-7.48 (m, 6 H), 7.69-7.72 (m, 4 H); ^{13}C NMR (270 MHz, $CDCl_3$) δ 35.04, 43.64, 66.44, 126.94, 129.36, 129.90, 130.11, 137.89, 168.08; IR (NaCl) 1738 cm^{-1}. Because this compound gradually decomposed into **7 f**, it was not able to be isolated in pure form.

(*Z*)-1,3-Bis(phenylthio)-5-hydroxy-2-penten-1-one (Table II, Entry 3): mp 110-112 °C (a white solid); ^1H NMR (270 MHz, $CDCl_3$) δ 1.46 (t, J = 5.4 Hz, 1 H), 2.41 (t, J = 6.4 Hz, 2 H), 3.58, (q, J(average) = 5.9 Hz, 2 H), 6.35 (s, 1 H), 7.34-7.55 (m, 10 H). NOE experiment: Irradiation at methylene triplet of δ 2.41 resulted in a 28% enhancement at δ 6.35 (vinyl singlet); IR (KBr) 3531, 2872, 1641, 1537, 1476, 1439, 1111, 1073, 1046, 842, 748, 706 cm^{-1}; mass spectrum (CI), m/e 317 (M^++1, 100); Anal. Calcd for $C_{17}H_{16}O_2S_2$: C, 64.53; H, 5.10; S, 20.26. Found: C, 64.46; H, 5.09; S, 20.12.

(*Z*)-1,3-Bis(phenylthio)-6-hydroxy-2-hexen-1-one (Table II, Entry 4): (This compound was prepared under more moderate reaction condition (80 °C, 24 h) than that of listed in Table II.) oil; ^1H NMR ($CDCl_3$, 270 MHz) δ 1.42 (br s, 1 H), 1.57 (quint, J = 7.6, 6.1

Hz, 2 H), 2.23 (t, J = 7.6 Hz, 2 H), 3.36 (t, J = 6.1 H, 2 H), 6.30 (s, 1 H), 7.36-7.53 (m, 10 H). NOE enhancement: Irradiation of methylene triplet at δ 2.23 resulted in a 25% experiment at δ 6.30 (vinyl singlet); ^{13}C NMR ($CDCl_3$, 68 MHz) δ 32.03, 32.76, 61.19, 117.47, 128.07, 129.00, 129.13, 129.13, 129.60, 130.13, 134.61, 135.71, 161.03, 185.06; IR (NaCl) 3398, 3057, 2943, 1667, 1548, 1477, 1440, 1111, 1078, 1023, 828, 748, 707, 690 cm^{-1}; mass spectrum (EI), m/e 330 (M^+, 2), 221 (M^+-SPh, 100); Anal. Calcd for $C_{18}H_{18}O_2S_2$: C, 65.42; H, 5.49; S, 19.40. Found: C, 65.21; H, 5.51; S, 19.12.

1,3-Bis(phenylseleno)-6-hydroxy-2-hexen-1-one (Table II, Entry 5). *Z* isomer: mp 98-100 °C (a light yellow solid); ^{1}H NMR (270 MHz, $CDCl_3$) δ 1.55 (quintet, J = 6.1 Hz, 7.6 Hz, 2 H), 1.70 (br s, 1 H), 2.26 (t, J = 7.6 Hz, 2 H), 3.29 (t, J = 6.1 Hz, 2 H), 6.71 (s, 1 H), 7.30-7.65 (m, 10 H). NOE experiment: Irradiation of the methylene triplet at δ 2.26 resulted in a 21% enhancement of the signal at δ 6.71 (vinyl singlet); ^{13}C NMR (68 MHz, $CDCl_3$) δ 32.35, 33.99, 61.06, 122.49, 126.58, 127.08, 128.83, 129.24, 129.29, 129.45, 135.74, 137.23, 161.95, 187.69; IR (KBr) 3326, 3055, 2937, 1664, 1546, 1532, 1085, 809, 742, 693 cm^{-1}; mass spectrum (CI), m/e 427 (M^++1, 8); Anal. Calcd for $C_{18}H_{18}O_2Se_2$: C, 50.96; H, 4.27. Found: C, 51.01; H. 4.34.

E isomer: ^{1}H NMR (270 MHz, $CDCl_3$) δ 1.87 (quintet, J = 5.9, 7.3 Hz, 2 H), 2.07 (br s, 1 H), 2.88 (t, J = 7.3 Hz, 2 H), 3.62 (t, J = 5.9 Hz, 2 H), 5.94 (s, 1 H), 7.30-7.66 (m, 10 H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 31.69, 32.55, 61.09, 123.48, 126.03, 126.87, 128.88, 129.32, 129.94, 130.07, 135.69, 136.72, 163.43, 187.74; IR (NaCl) 3368, 3056, 2942, 2874, 1693, 1564, 1557, 1476, 1438, 1338, 1038, 1020, 738, 690 cm^{-1}; mass spectrum (CI), m/e 427 (M^++1, 8).

2-2-4. References and Notes

(1) For notable examples of transition-metal-catalyzed carbonylative lactonization of olefinic or acetylenic alcohols, see: (a) Matsuda, I.; Ogiso, A.; Sato, S. *J. Am. Chem. Soc.* **1990**, *112*, 6120. (b) Matin, L. D.; Stille, J. K. *J. Org. Chem.* **1982**, *47*, 3630. (c) Cowell, A.; Stille, J, K. *J. Am. Chem. Soc.* **1980**, *102*, 4193. (d) Ali, B. E.; Alper, H. *J. Org. Chem.* **1991**, *56*, 5357. (e) Alper, H.; Leonard, D. *J. Chem. Soc. Chem. Commun.* **1985**, 511. (f) Murray, T. F.; Varma, V.; Norton, J. R. *J. Org. Chem.* **1978**, *43*, 353. (g) Murray, T. F.; Varma, V.; Norton, J. R. *J. Am. Chem. Soc.* **1977**, *99*, 8085.

(2) The addition of aromatic thiols to acetylenes is also catalyzed by a variety of transition-metal complexes. Details are described in chapter **4**.

(3) When the carbonylative double thiolation of propargyl alcohols such as **1c** was carried out under similar milder reaction conditions, the formation of **6c** and (*Z*)-**4c** were also confirmed. In this case, however, no *E* isomer was detected at all by ^{1}H NMR spectrometer, probably because the 5-membered cyclization from (*E*)-**4** to **6** rapidly proceeds after the C-C double bond isomerization from (*Z*)-**4** to (*E*)-**4**.

(4) The carbonylative double thiolation to acetylene without hydroxy group exhibited the high stereoselectivity. For example, the reaction of 1-octyne, $(PhS)_2$, and CO under similar reaction conditions (80 °C, 39 h) gave (*Z*)-1,3-bis(phenylthio)-2-nonen-1-one in 84% yield stereoselectively; see Chapter **2-1**.

(5) The carbonylative addition of 1-octyne with $(PhSe)_2$ under the similar reaction conditions (100 °C, 50 h) gave 1,3-bis(phenylseleno)-2-nonen-1-one in 57% yield (*E*/*Z* = 1/99) with the concomitant formation of some unidentified materials..

(6) In the absence of both carbon monoxide and disulfide in the presence of $Pd(PPh_3)_4$, palladium-catalyzed decarbonylation occurred competitively, see: Osakada, K.; Yamamoto, T.; Yamamoto, A. *Tetrahedron Lett.* **1987**, *28*, 6321.

(7) The oxidative addition of $(PhS)_2$ to $Pd(PPh_3)_4$ easily proceeds at room temperature. See: Zanella, R.; Ros, R.; Graziani, M. *Inorg. Chem.* **1973**, *12*, 2736.

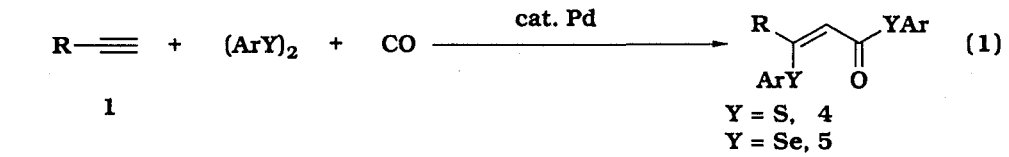
(8) (a) Tanikaga, R.; Yamasita, H.; Kaji, A. *Synthesis* **1986**, 416. (b) Barua, N. C.; Schmidt, R. R. *Synthesis* **1986**, 1067. (c) Trost, B. M.; Lavoie, A. C. *J. Am. Chem. Soc.* **1983**, *105*, 5075. (d) Magnus, P.; Quagliato, D. *J. Org. Chem.* **1985**, *50*, 1621. (e) Comasseto, J. V. *J. Organomet. Chem.* **1983**, *253*, 131. (f) Paulmier, C. *Selenium Reagents and Intermediates in Organic Synthesis*; Pergamom Press: Oxford, 1986.

Chapter 3. Palladium-Catalyzed Reduction of Thioesters and Selenoesters to Aldehydes with n-Bu_3SnH

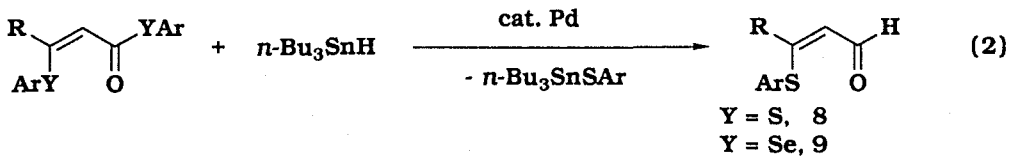
3-1. Chemoselective Conversion of (*Z*)-1,3-Bis(arylthio)-2-alken-1-ones to the Corresponding Enals

3-1-1. Introduction

Transformation of carboxylic acids to aldehydes has been the subject of intensive investigation among synthetic organic chemists. The most frequently employed procedure at the present time is reduction of acid or its derivatives followed by mild oxidation of the resultant alcohols. For the reduction of thioesters and selenoesters to the corresponding aldehydes, the general and convenient methods have been limited.[1,2] In this chapter, the author wish to disclose that the unprecedented access of aldehyde from thioester and selenoester: palladium-catalyzed chemoselective and site-selective reduction of (*Z*)-1,3-bis(arylthio)-2-alken-1-ones (**4**) and (*Z*)-1,3-bis(arylseleno)-2-alken-1-ones (**5**) (which can be easily prepared according to eq 1) with n-Bu_3SnH. Only the terminal ArS groups of **4** and **5** were selectively substituted for hydrogen to give the (*Z*)-3-(arylthio)-2-alkenals (**8**) and (*Z*)-3-(arylseleno)-2-alkenals (**9**) in good yields under moderate reaction conditions (eq 2).[3,4]



(1)

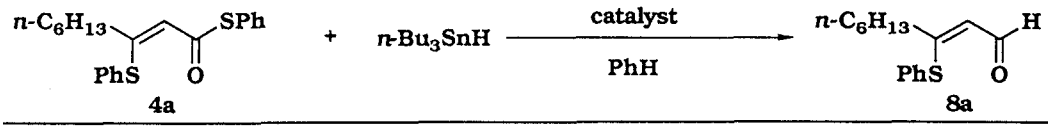


(2)

3-1-2. Results and discussion

Palladium-Catalyzed Reduction of Thioester: Table I summarizes the effects of catalysts on the reaction of (*Z*)-1,3-bis(phenylthio)-2-nonen-1-one (**4a**) with *n*-Bu_3SnH to give (Z)-3-(arylthio)-2-octenals (**8a**).

Table I. Reduction of 1a with *n*-Bu_3SnH in the Presence of Several Catalysts[a]



entry	catalyst	(mol%)	period of addition (min)	yield of 8a (%)[b]	(*E*/*Z*)[c]
1	$Pd(PPh_3)_4$	0.4	7	93[d]	(1/99)
2	$Pd(PPh_3)_4$	0.025	10	33	only Z
3[e]	$Pd(PPh_3)_4$	0.4	1	89	only Z
4	$Pd(PPh_3)_2Cl_2$	1.0	4	90	(7/93)
5	$Pd(OAc)_2$	1.0	11	26	(17/83)
6[f]	10% Pd on carbon	3.0	—	0[g]	
7[h]	$Pd(PPh_3)_4$	1.0	—	0[i]	
8[j]	AIBN	10	—	trace[k]	
9[l]	Et_3B	120		0[m]	

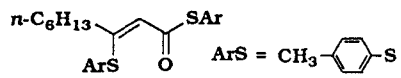
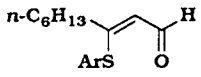
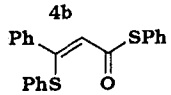
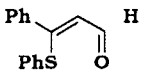
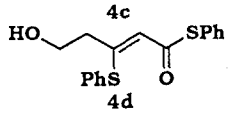
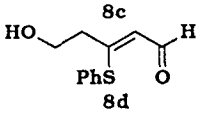
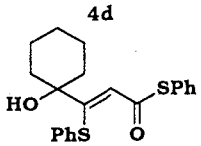
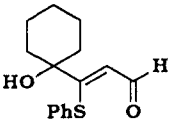
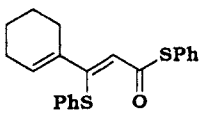
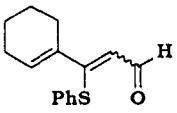
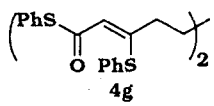
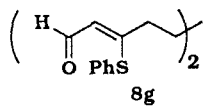
[a]A solution of *n*-Bu_3SnH (1.2 mmol in PhH 10 mL) was added to a solution of **4a** (1.0 mmol in PhH 20 mL) and catalyst at 25 °C. [b]NMR yield. [c]The *E*/*Z* ratio in crude reaction mixture. [d]Isolated yield (*E*/*Z* = 6/94). [e]3.1 equiv of *n*-Bu_3SnH was used. [f]The solution of Et_3SiH (2.3 mmol) and **4a** (1.0 mmol) with Pd/C in CH_2Cl_2 (1 mL) was stirred at 25 °C for 50 min, see ref 1b. [g]The *E*/*Z* ratio of recovered **4a** was 23/77. [h]Et_3SiH was used in lieu of *n*-Bu_3SnH. [i]No reaction. [j]*n*-Bu_3SnH (0.75 mmol) was added to a 5 mL of PhH solution of **4a** (0.5 mmol) and AIBN (0.05 mmol) at 70 °C over a period of 40 min. Then the mixture was refluxed for 4 h. [k]The *E*/*Z* ratio of recovered **4a** was 68/32. [l]*n*-Bu_3SnH (0.6 mmol) was added to a 10 mL of PhH solution of **4a** (0.5 mmol) and Et_3B over a period of 40 min. Then, the mixture was stirred at 25 °C for 16 h. [m]The *E*/*Z* ratio of recovered **4a** was 86/14.

Among the catalysts examined, $Pd(PPh_3)_4$ (0.4 mol% for **4a**) gave the best result (entry 1).[5] Further decrease in the amount of $Pd(PPh_3)_4$ caused the palladium-promoted decomposition of *n*-Bu_3SnH into hexabutyldistannane and gaseous hydrogen (entry 2). The overreduction from **8a** hardly occurred, even if the reaction was carried out with excess amount of *n*-Bu_3SnH (entry 3).[6] $Pd(PPh_3)_2Cl_2$ and $Pd(OAc)_2$ also exhibited the catalytic activities (entries 4 and 5), while $Ni(PPh_3)_2Cl_2$, $Pt(PPh_3)_4$, and $Rh(PPh_3)_3Cl$ did not catalyze this reduction. The reaction of **4a**

with Et_3SiH in the presence of Pd on carbon[1b] or $Pd(PPh_3)_4$ failed (entries 6 and 7). For the reductions of acid chlorides and selenoesters with *n*-Bu_3SnH, AIBN-initiated radical reactions have already been reported.[7,8] However, AIBN- and Et_3B-initiated reactions[9] of **4a** resulted in the double bond isomerization from (*Z*)-**4a** to (*E*)-**4a** (entries 8 and 9).

Reduction of Various Thioesters and Proposed Reaction Path: The results of the $Pd(PPh_3)_4$-catalyzed reduction of some (*Z*)-1,3-bis(arylthio)-2-alken-1-ones (**4**) with *n*-Bu_3SnH were listed in Table II. The reactions proceeded successfully to give the corresponding aldehydes (**8**) in good yields, although some double bond isomerization took place during the isolation of **8**. Hydroxy group and tethered olefinic unit did not affect the addition (entries 3, 4, and 5).

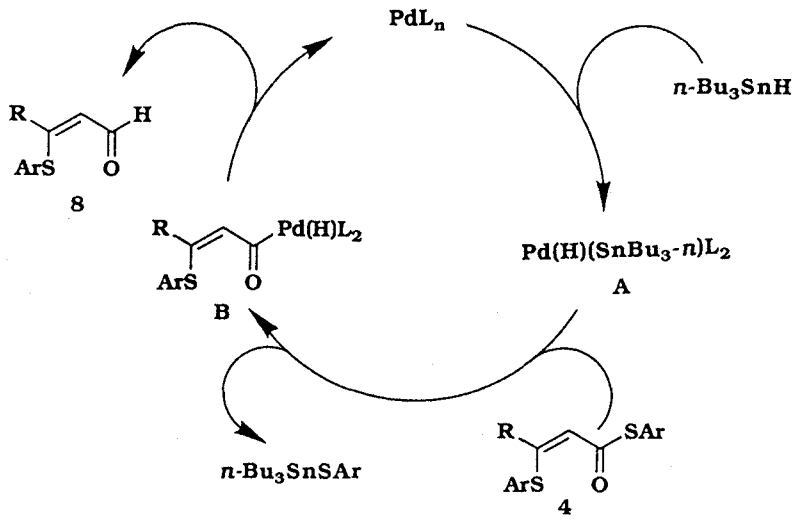
Table II. Palladium-Catalyzed Reduction of 4 with *n*-Bu_3SnH[a]

entry	substrate	product	yield (%)[b]	(*E*/*Z*)
1	 **4b**	 **8b**	98	(4/96)
2	 **4c**	 **8c**	89	(9/91)
3	 **4d**	 **8d**	91	(2/98)
4	 **4e**	 **8e**	94	(0/100)
5	 **4f**	 **8f**	98	(15/85) (0/100)[c]
6[d]	 **4g**	 **8g**	86	(Z,E/Z,Z = 2/98)

[a]Procedure: *n*-Bu_3SnH (1.1-1.3 mmol in PhH 10 mL) was added to a solution of **4** (1.0 mmol in PhH 20 mL) in the presence of 0.4 mol% of $Pd(PPh_3)_4$ over a period of 7-20 min at 25 °C. [b]Isolated yield. [c]The *E*/*Z* ratio in crude reaction mixture. [d]0.5 mmol of **4g** was used.

Scheme I illustrates one of the possible reaction paths for the present palladium-catalyzed reduction of **4** with *n*-Bu_3SnH. The reaction proceeds *via* the oxidative addition of *n*-Bu_3SnH to low-valent palladium complex to form Pd-H species **A**. The following ligand exchange with **4** generates the acylpalladium complex **B**, accompanied by the formation of *n*-Bu_3SnSAr. The subsequent reductive elimination from **B** affords **8** and regenerates the low-valent palladium catalyst.

Scheme I. A Possible Reaction Path for the Palladium-Catalyzed Reduction of 4 with *n*-Bu_3SnH



Conclusion: This study reveals the chemoselective and site-selective palladium-catalyzed reduction of (*Z*)-1,3-bis(arylthio)-2-alken-1-ones (**4**) to give (*Z*)-3-(arylthio)-2-alkenals (**8**). The carbonylative addition (eq 1) and subsequent reduction with tin hydride (eq 2) realizes the regio- and stereoselective thioformylation of terminal acetylenes (Scheme II). The present reduction system would be expected to provide a powerful strategy of ready access to aldehydes from the corresponding thioesters. Work is ongoing in efforts to further clarify the generality of this transformation and will be reported in due course.

3-1-3. Experimental Section

(Z)-1,3-Bis(arylthio)-2-alken-2-ones were prepared by the palladium-catalyzed carbonylative double thiolation of terminal acetylenes described in chapter **2-1**. Tri-*n*-butyltin hydride was prepared according to the literature methods (Mitchell, T. N. *J. Organomet. Chem.* **1973**, *59*, 189). All catalysts, triethylsilane, and triethylborane were obtained commercially. Benzene and dichloromethane was purified by distillation from sodium(>8%)-lead, and calcium hydride before use, respectively. The residual reaction mixture was separated by MPLC with Merck 25-40 mm mesh silica gel (Art 9390).

$Pd(PPh_3)_4$-Catalyzed Reduction of (*Z*)-1,3-Bis(phenylthio)-2-nonen-1-one (4a) with *n*-Bu_3SnH (Table I, Entry 1): General Procedure. Into a two-necked flask equipped with an additional funnel and a magnetic stirring bar were placed (*Z*)-1,3-bis(phenylthio)-2-nonen-1-one (**4a**) (356 mg, 1.0 mmol), $Pd(PPh_3)_4$ (4.6 mg, 0.004 mmol), and benzene (20 mL) under argon atmosphere. Then, a solution of *n*-Bu_3SnH (354 mg, 1.22 mmol) in benzene (10 mL) was added from the additional funnel at ambient temperature over a period of 7 min. After the resulting reaction mixture was concentrated under reduced pressure, the residual mixture was purified by MPLC to provide 217 mg of (*Z*)-3-(phenylthio)-2-nonen-1-one (*Z*-**8a**) (88%) and 14 mg of (*E*)-3-(phenylthio)-2-nonen-1-one (*E*-**8a**) (6%) as clear yellow oil, respectively.

Z isomer: oil; ^{1}H NMR (270 MHz, $CDCl_3$) δ 0.83 (t, *J* = 6.8 Hz, 3 H), 1.23-1.25 (m, 6 H), 1.46 (quint, *J* = 7.4 Hz, 2 H), 2.22 (t, *J* = 7.4 Hz, 2 H), 6.18 (d, *J* = 6.8 Hz, 1 H), 7.37-7.49 (m, 5 H), 10.15 (d, *J* = 6.8 Hz, 1 H). NOE experiment: Irradiation of methylene triplet at δ 2.22 resulted in a 5% enhancement of the vinyl doublet at δ 6.18; ^{13}C NMR (68 MHz, $CDCl_3$) δ 13.97, 22.39, 28.41, 28.63, 31.31, 37.12, 127.74, 129.04, 129.38, 130.66, 134.00, 164.38, 190.08; IR (NaCl) 2928, 2856, 1670, 1571, 1535, 1477, 1150, 749, 692 cm^{-1}; mass spectrum (EI), m/e 248 (M^+, 65); Anal. Calcd for $C_{15}H_{20}OS$: C, 72.54; H, 8.12; S, 12.91. Found: C, 72.61; H, 8.26; S, 12.91.

E isomer: oil; ^{1}H NMR (270 MHz, $CDCl_3$) δ 0.91 (t, *J* = 6.6 Hz, 3 H), 1.29-1.47 (m, 6 H), 1.75 (quint, *J* = 7.7 Hz, 2 H), 2.78 (t, *J* = 7.7 Hz, 2 H), 5.42 (d, *J* = 7.8 Hz, 1 H), 7.37-7.48 (m, 5 H), 9.78 (d, *J* = 7.8 Hz, 1 H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 14.01, 22.48, 28.89, 31.11, 31.42, 32.56, 121.89, 128.47, 129.93, 130.25, 135.59, 171.01, 186, 84; IR (NaCl) 3059, 2955, 2929, 2746, 1661, 1580, 1557, 1150, 751, 691 cm^{-1}; mass spectrum (EI), m/e 248 (M^+, 66). The following compounds were also prepared according to the general procedure.

3-(4-Methylphenylthio)-2-nonen-1-one (8b) (Table II, Entry 1). *Z* isomer: yellow oil; ^{1}H NMR (270 MHz, $CDCl_3$) δ 0.83 (t, *J* = 6.8 Hz, 3 H), 1.12-1.30 (m, 6 H), 1.44 (m, 2 H), 2.19 (t, *J* = 7.8 Hz, 2 H), 2.37 (s, 3 H), 6.14 (d, *J* = 6.8 Hz, 1 H), 7.18 (d, *J* = 7.8 Hz, 2 H), 7.32 (d, *J* = 7.8 Hz, 2 H), 10.14 (d, *J* = 6.8 Hz, 1 H). NOE experiment: Irradiation of methylene triplet at δ 2.19 resulted in a 14% enhancement of the vinyl doublet at δ 6.14; ^{13}C NMR (68 MHz, $CDCl_3$) δ 14.00, 21.22, 22.39, 28.41, 28.63, 31.32, 36.93, 126.79, 126.92, 130.15, 134.28, 139.46, 165.24, 189.84; IR (NaCl) 3023, 2955, 2928, 2858, 2734, 1671, 1575, 1537, 1492, 1456, 1381, 1150, 1090, 1018, 811, 725, 673 cm^{-1}; mass spectrum (EI), m/e 262 (M^+, 49). Anal. Calcd for $C_{16}H_{22}OS$: C, 73.23; H, 8.45, S, 12.22. Found: C, 73.14; H, 8.53; S, 12.09.
E isomer: Isolated as *E*/*Z* = 94/6 mixture; yellow oil; ^{1}H NMR (270 MHz, $CDCl_3$) δ 1.29-1.52 (m, 6 H), 1.75 (quint, *J* = 7.4 (average), 2 H), 2.45 (s, 3 H), 2.77 (t, *J* = 7.8 Hz, 2 H), 5.39 (d, *J* = 8.1 Hz, 1 H), 7.23 (d, *J* = 8.1 Hz, 2 H), 7.34 (d, *J* = 8.1 Hz, 2 H), 9.77 (d, *J* = 8.1 Hz, 1 H); mass spectrum (EI), m/e 262 (M^+, 50); exact mass (M^+) calcd for $C_{16}H_{22}OS$ 262.1391, found 262.1378.

3-(Phenylthio)-3-phenyl-2-propen-1-one (8c) (Table II, Entry 2). *Z* isomer: yellow oil; ^{1}H NMR (270 MHz, $CDCl_3$) δ 6.55 (d, *J* = 6.8 Hz, 1 H), 7.01-7.31 (m, 8 H), 7.50-7.54 (m, 2 H), 10.32, (d, *J* = 6.8 Hz, 1 H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 127.50, 128.44, 128.66, 128.98, 130.38, 131.25, 131.33, 132.45, 137.09, 159.05, 190.42; IR (NaCl) 3058, 2834, 1666, 1581, 1557, 1488, 1130, 765, 744, 691 cm^{-1}; mass spectrum (EI) m/e 240 (M^+, 100). Anal. Calcd for $C_{15}H_{12}OS$: C, 74.97; H, 5.03: S, 13.34. Found C, 74.74; H, 4.87; S, 13.39.
E isomer: yellow oil; ^{1}H NMR (270 MHz, $CDCl_3$) δ 5.67 (d, *J* = 7.8 Hz, 1 H), 7.47-7.58 (m, 10 H), 9.27 (d, *J* = 7.8 Hz, 1 H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 123.40, 128.58, 128.89, 129.53, 130.06, 130.34, 130.38, 134.69, 135.38, 169.06, 189.96.

(*Z*)-3-(Phenylthio)-5-hydroxy-2-penten-1-one (8d) (Table II, Entry 3): yellow oil; ^{1}H NMR (270 MHz, $CDCl_3$) δ 2.35 (br s, 1 H), 2.49 (t, *J* = 6.1 Hz, 2 H), 3.70 (t, *J* = 6.1 Hz, 2 H), 6.27 (d, *J* = 6.7 Hz, 1 H), 7.38-7.49 (m, 5 H), 10.13 (d, *J* = 6.7 Hz, 1 H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 39.91, 60.55, 129.15, 129.29, 129.52, 130.29, 133.74, 160.25, 190.00; IR (NaCl) 3420, 3056, 1667, 1571, 1533, 1477, 1440, 1384, 1275, 1146, 1080, 1047, 832, 751, 692 cm^{-1}; mass spectrum (EI) m/e 208 (M^+, 58); exact mass (M^+) calcd for $C_{11}H_{12}O_2S$ 208.0558, found 208.0545.

(Z)-3-(Phenylthio)-3-(1-hydroxy-cyclohexyl)-2-propen-1-one (8e) (Table II, Entry 4): yellow oil; ^{1}H NMR (270 MHz, $CDCl_3$) δ 1.20 (m, 1 H), 1.54-1.93 (m, 9 H), 2.46 (s, 1 H), 6.67 (d, *J* = 7.3 Hz, 1 H), 7.16-7.33 (m, 5 H), 9.97 (d, *J* = 7.3 Hz, 1 H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 21.47, 25.09, 35.76, 126.95, 128.46, 129.65, 130.74, 136.98, 166.44, 194.05; IR (NaCl) 3442, 3054, 2936, 2855, 1668, 1582, 1479, 1440, 1384, 1350, 1258, 1122, 1092, 985, 841, 742, 688, 666 cm^{-1}; mass spectrum (CI) 262 m/e (M^+, 35); exact mass (M^+) calcd for $C_{15}H_{18}O_2S$ 262.1027, found 262.1034.

3-(Phenylthio)-3-(1-cyclohexenyl)-2-propen-1-one (8f) (Table II, Entry 5). *Z* isomer: yellow oil; ^{1}H NMR (270 MHz, $CDCl_3$) δ 1.44-1.56 (m, 4 H), 2.05-2.07 (m, 2 H), 2.14-2.16 (m, 2 H), 6.36 (d, *J* = 7.3 Hz, 1 H), 6.60 (t, *J* = 3.9 Hz, 1 H), 7.17-7.30 (m, 5 H), 10.28 (d, *J* = 7.3 Hz, 1 H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 21.55, 22.31, 26.24, 27.28, 127.02, 129.02, 129.19, 129.86, 134.62, 135.14, 136.45, 159.00, 192.28; IR (NaCl) 3057, 2933, 2858, 1667, 1618, 1556, 1479, 1439, 1188, 1126, 835, 743, 690 cm^{-1}; mass spectrum (EI) 244 m/e (M^+, 100); Anal. Calcd for $C_{15}H_{16}OS$: C, 73.73; H, 6.60; S, 13.12. Found: C, 73.54; H, 6.65; S, 13.01.
E isomer: yellow oil; ^{1}H NMR (270 MHz, $CDCl_3$) δ 1.59-1.68 (m, 4 H), 2.15-2.20 (m, 2 H), 2.23-2.36 (m, 2 H), 5.53 (d, *J* = 7.8 Hz, 1 H), 5.98 (quint, *J* = 2.0 Hz, 1 H), 7.39-7.50 (m, 5 H), 9.55 (d, *J* = 7.8 Hz, 1 H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 21.50, 22.37, 25.43, 29.67, 123.00, 128.87, 129.77, 129.96, 133.16, 133.44, 135.32, 172.46, 189.61 cm^{-1}; IR (NaCl) 3404, 3056, 2932, 2859, 1660, 1652, 1557, 1564, 1440, 1147, 825, 749, 691 cm^{-1}.

(2Z,8Z)-3,8-Bis(phenylthio)-2,8-decadiendial (8g) (Table II, Entry 6): yellow, oil; ^{1}H NMR (270 MHz, $CDCl_3$) δ 1.32 (br s, 4 H), 2.11 (br s, 4 H), 6.09 (d, *J* = 6.3 Hz, 2 H), 7.38-7.43 (m, 10 H), 10.12 (d, *J* = 6.3 Hz, 2 H). NOE experiment: Irradiation of methylene at δ 2.11 resulted in a 12% enhancement of the vinyl doublet at δ 6.09; ^{13}C NMR (68 MHz, $CDCl_3$) δ 27.60, 36.52, 127.94, 129.18, 129.47, 130.32, 133.91, 163.11, 189.85; IR (NaCl) 3734, 2942, 1664, 1534, 1475, 1439, 1382, 1169, 1024, 750, 692 cm^{-1}; mass spectrum (EI) m/e 382 (M^+, 15); Anal. Calcd for $C_{22}H_{22}O_2S_2$: C, 69.08; H, 5.80; S, 16.76. Found: C, 68.92; H, 5.78; S, 16.55.

$Pd(PPh_3)_4$-Catalyzed Carbonylative Addition of Diaryl Disulfide to Terminal Acetylenes to 1,3-Bis(arylthio)-2-alken-1-one: General Procedure. In a 50 mL stainless steel autoclave were placed the 1-alkyne (10 mmol), diaryl disulfide (10 mmol),

$Pd(PPh_3)_4$ (240 mg, 0.2 mmol), and benzene (5 mL). The mixture was heated at 80 °C for 40 h under the pressurized of carbon monoxide (60 kg/cm^2) with magnetic stirring. The reaction mixture was filtered through Celite, and was evaporated in vacuo. The residual mixture was purified by MPLC with Merck 25-40 mm mesh silica gel (Art 9390). Then, 1,3-bis(arylthio)-2-alken-1-one was recrystallized from hexane or EtOH or toluene, if necessary.
The spectroscopic data of **4a**, **4b**, and **4c** were already listed in chapter **2**.

(*Z*)-1,3-Bis(phenylthio)-5-hydroxy-2-penten-1-one (4d) (Table II, Entry 3): This compound was prepared by the reaction of 3-butyn-1-ol with 4 equiv of $(PhS)_2$ in the presence of CO, see Table II of chapter **2-2**. mp 110-112 °C (light yellow crystal) ^{1}H NMR (270 MHz, $CDCl_3$) δ 1.46 (t, *J* = 5.4 Hz, 1 H), 2.41 (t, *J* = 6.4 Hz, 2 H), 3.58 (q, *J* = 5.9 Hz (average), 2 H), 6.35 (s, 1 H), 7.34-7.55 (m, 10 H). NOE experiment: Irradiation of methylene triplet at δ 2.41 resulted in a 28% enhancement of vinyl singlet at δ 6.35; IR (KBr) 3531, 2872, 1641, 1537, 1476, 1439, 1111, 1073, 1046, 842, 811, 748, 706 cm^{-1}; mass spectrum (CI) m/e 317 (M^++1, 100); Anal. Calcd for $C_{17}H_{16}O_2S_2$: C, 64.53; H, 5.10; S, 20.26. Found C, 64.46; H, 5.09; S, 20.12.

(*Z*)-1,3-Bis(phenylthio)-3-(1-hydroxy-cyclohexyl)-2-propen-1-one (4e) (Table II, Entry 4): mp 86-87 °C (yellow crystal) ^{1}H NMR (270 MHz, $CDCl_3$) δ 1.23 (m, 1 H), 1.53-1.77 (m, 7 H), 1.88-1.97 (m, 2 H), 2.21 (s, 1 H), 6.92 (s, 1 H), 7.04-7.08 (m, 2 H), 7.15-7.33 (m, 8 H). NOE experiment: Irradiation of vinyl singlet at δ 6.92 resulted in a 12% enhancement of hydroxy singlet at δ 2.21; ^{13}C NMR (68 MHz, $CDCl_3$) δ 21.58, 25.11, 35.76, 76.11, 125.97, 126.58, 127.71, 128.92, 128.96, 129.13, 129.79, 134.33, 135.36, 158.01, 186.51; IR (KBr) 3427, 3057, 2924, 1684, 1567, 1478, 1439, 1098, 1039, 1020, 883, 844, 735, 686, 581 cm^{-1}; mass spectrum (CI) 371 m/e (M^++1, 8); Anal. Calcd for $C_{21}H_{22}O_2S_2$: C, 68.07; H, 5.98; S, 17.31. Found C, 67.98; H, 5.97; S, 17.24.

(*Z*)-1,3-Bis(phenylthio)-3-(1-cyclohexenyl)-1-one (4f) (Table II, Entry 5): mp 95.5-96.5 °C (light yellow crystal); ^{1}H NMR (270 MHz, $CDCl_3$) δ 1.08-1.14 (m, 2 H), 1.23-1.27 (m, 2 H), 1.78 (m, 2 H), 1.83-1.92 (m, 2 H), 5.76 (m, 1 H), 6.29 (s, 1 H); ^{13}C NMR ($CDCl_3$, 68 MHz) δ 21.33, 21.88, 25.11, 28.89, 118.05, 128.31, 129.02, 129.15, 130.93, 132.51, 134.59, 134.63, 136.28, 161.92, 185.44; IR (KBr) 2934, 1662, 1542, 1474, 1438, 1184, 1039, 904, 748, 690, 616, 606, 528 cm^{-1}; mass spectrum (CI) m/e 353 (M^++1, 50); Anal. Calcd for $C_{21}H_{20}OS_2$:

C, 71.55; H, 5.72; S, 18.19. Found C, 71.59; H, 5.63, S, 18.09.

(2Z,8Z)-1,3,8,10-Tetrakis(phenylthio)-2,8-decadien-1,10-dione (4g) (Table II, Entry 6): 2.2 equiv of disulfide is used for preparation of this compound. mp 164-165 °C (light yellow crystal); ^{1}H NMR (270 MHz, $CDCl_3$) δ 1.10 (br s, 4 H), 1.91 (br s, 4 H), 6.14 (s, 2 H), 7.33-7.51 (m, 20 H). NOE experiment: Irradiation of broad singlet at δ 1.91 resulted in a 15 % enhancement of vinyl singlet at δ 6.14; ^{13}C NMR (68 MHz, $CDCl_3$) δ 28.50, 35.88, 117.44, 128.14, 129.08, 129.21, 129.21, 129.65, 130.18, 134.66, 135.72, 160.88, 184.93; IR (KBr) 3054, 1654, 1540, 1476, 1440, 1102, 1083, 1041, 972, 835, 815, 749, 708, 690, 625, 523 cm^{-1}; mass spectrum (CI) m/e 379 ($(M^{+}-(PhS)_2)+1$, 100); Anal. Calcd for $C_{34}H_{30}O_2S_4$: C, 68.19; H, 5.05; S, 21.41. Found C, 68.15; H, 5.01; S, 21.29.

3-1-4. References and Notes

(1) For the reduction of thioesters to aldehydes, see: (a) Mosettig, E. In *Organic Reactions*; Adams, R., Blatt, A. H., Cope, A. C., Curtin, D. Y., McGrew, F. C., Niemann, C., Eds.; Wiley: New York, 1954; Vol. VIII, P229. (b) Fukuyama, T.; Lin, S.; Li, L. *J. Am. Chem. Soc.* **1990**, *112*, 7050.

(2) For the reduction of selenoesters to aldehydes, see: Pfenninger, J.; Heuberger, C.; Graf, W. *Helv. Chim. Acta* **1980**, *63*, 2328.

(3) For an overview of the reductions with organotin reagents, see: Pereyre, M.; Quintard, J.-P.; Rahm, A. *Tin in Organic Synthesis*; Butterworths: London, 1987.

(4) For the palladium-catalyzed reduction of acid chlorides with tin hydride to give aldehydes, see: Four, P.; Guibe, F. *J. Org. Chem.* **1981**, *46*, 4439.

(5) The palladium-catalyzed decarbonylation did not occur at all. See: Osakada, K.; Yamamoto, T.; Yamamoto, A. *Tetrahedron Lett.* **1987**, *28*, 6321.

(6) In the case of the $Pd(PPh_3)_4$-catalyzed reaction of selenoester **5** with 2 equiv of *n*-Bu_3SnH, overreduction easily took place from the β-seleno-enals; see chapter **3-2.**

(7) Lusztyk, J.; Lusztyk, E.; Maillard, B.; Ingold, K. U. *J. Am. Chem. Soc.* **1984**, *106*, 2923 and references cited therein.

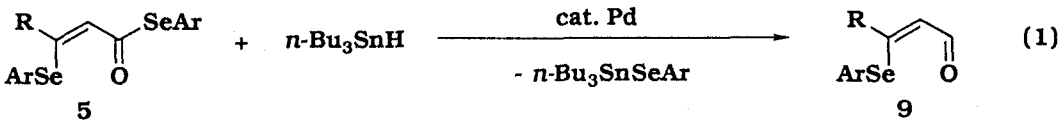
(8) Pfenninger, J.; Heuberger, C.; Graf, W. *Helv. Chim. Acta* **1980**, *63*, 2328.

(9) Nozaki, K.; Oshima, K.; Utimoto, K. *J. Am. Chem. Soc.* **1987**, *109*, 2547.

3-2. Chemoselective Conversion of (Z)-1,3-Bis(arylseleno)-2-alken-1-ones to the Corresponding Enals

3-2-1. Introduction

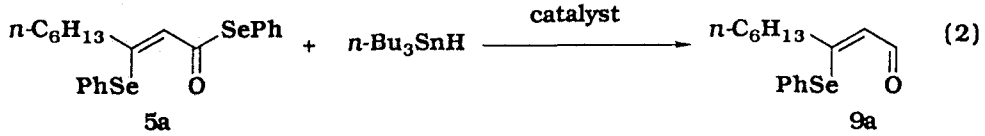
Described in this section is the palladium-catalyzed chemoselective and site-selective reduction of (*Z*)-1,3-bis(arylseleno)-2-alken-1-ones (**5**) with tri-*n*-butyltin hydride to provide the (*Z*)-3-arylseleno-2-alkenals (**9**) in high yields (eq 3).[1,2] This study would be expected to provide a quiet efficient method of selective reduction of selenoesters to the corresponding aldehydes under moderate reaction conditions.



(1)

3-2-2. Results and Discussion

Reaction Conditions for the Reduction of Selenoesters: To a benzene (20 mL) solution of (Z)-1,3-bis(phenylseleno)-2-nonen-1-one (**5a**) (1.0 mmol) and $Pd(PPh_3)_4$ (0.004 mmol) was added dropwise *n*-Bu_3SnH (0.1 M of benzene solution, 10 mL) over a period of 5 min at room temperature. Then, the reaction mixture was instantly evaporated and separated by MPLC (silica gel) to give (Z)-3-(phenylseleno)-2-nonenal (**9a**) in 91% yield (eq 2, Table I, entry 1).[3] The carbon-carbon double bond as well as the phenylseleno group attached to the vinylic carbon was scarcely reduced,[4] and neither decarbonylative product nor ester[5] was detected. Table I summarizes the results of the reaction of **5a** with *n*-Bu_3SnH under several reaction conditions.



(2)

Table I. Effects of Catalysts on the Reduction of 5a with *n*-Bu_3SnH[a]

entry	catalyst (mol%)		time of addition(min)	yield of 9a[b](%)	*E*/*Z*[b]
1	$Pd(PPh_3)_4$	0.4	5	91[c]	only *Z*
2	PPh_3	8.0	-	-[d]	
3	none		-	-[d]	
4	$Pd(PPh_3)_4$	0.01	25	94	2/98
5	$Pd(PPh_3)_4$	0.001	30	45	1/99
6	$Pd(PPh_3)_2Cl_2$	2.0	3	85	1/99
7	$Pd(OAc)_2$	5.0	3	45	1/99

[a] *n*-Bu_3SnH (1.0-1.4 equiv) was added to a benzene (or benzene-d_6) solution of **5a** (0.05-0.1 M) and catalyst at 25 °C. [b] Determined by ^1H NMR. [c] Isolated yield. [d] No reaction.

In the absence of catalyst or presence of 8 mol% of PPh_3, the reduction did not occur under similar reaction conditions (entries 2 and 3).[6] The amount of palladium catalyst can be lessened by 0.01 mol% for **5a** (entry 4). Further decrease of the catalyst (0.001 mol%) led to a low yield of **9a** (entry 5), because the competitive palladium-catalyzed decomposition of tri-*n*-butyltin hydride into hexabutyldistannane (eq 3) can not be suppressed.[7]

(3)

$Pd(PPh_3)_2Cl_2$ and $Pd(OAc)_2$ also catalyzed the reduction of **1a** to **2a** (entries 6 and 7).[8] For the reduction of selenoesters with *n*-Bu_3SnH to give aldehydes, an AIBN-initiated radical reaction has already been reported.[9] When the AIBN-initiated reaction system was applied to the reduction of **5a**, a similar chemoselective reduction also took place. However, the reaction proceeded very sluggishly, accompanied by the isomerization of the C-C double bond.[10]

Reduction of Various Selenoesters: Table II summarizes the results of palladium-catalyzed

reduction of some other (*Z*)-1,3-bis(arylseleno)-2-alken-1-ones (**5**) with *n*-Bu_3SnH. Electron-donating and -withdrawing substituents on the ArSe groups did not have significant effect on the yields of the products (entries 1 and 2).[11] The reduction of **5e**, which has olefinic and ester units, afforded the corresponding enal **9e** in 42% yield together with an undetermined complex mixture (entry 4). The reduction of **5'h** (synthesized from the reaction of the corresponding acid chloride with PhSeLi) also proceeded to give nonanal in moderate yield with the competitive decomposition of tri-*n*-butyltin hydride into hexabutyldistannane (entry 7). This result suggests the generality of this palladium-catalyzed reduction of selenoesters with tri-*n*-butyltin hydride to give aldehydes, although **5'h** is less reactive compared with (*Z*)-1,3-bis(arylseleno)-2-alken-1-ones (**5**).

Selenoformylation of Acetylene: The palladium-catalyzed carbonylative addition of terminal acetylene (chapter **2**) and the reduction of **5** by *n*-Bu_3SnH (eq 1) can be carried out successively without isolation of **5**. For example, after a reaction of 1-octyne (1.0 mmol) and $(PhSe)_2$ (1.0 mmol) in the presence of 2 mol% of $Pd(PPh_3)_4$ in benzene (1 mL) under the pressurized CO (20 kg/cm^2) was carried out at 80 °C for 15 h in a 50 mL stainless steel autoclave, the carbon monoxide was degassed and benzene (15 mL) was added to the resulting mixture. Then, *n*-Bu_3SnH (1.0 mmol) was added over a period of 5 min to provide **9a** in 86% yield (*E*/*Z* = 11/89). This one-pot transformation from acetylene to **9** is synthetically equivalent to regio- and stereoselective selenoformylation of acetylene (Scheme I).

Scheme I

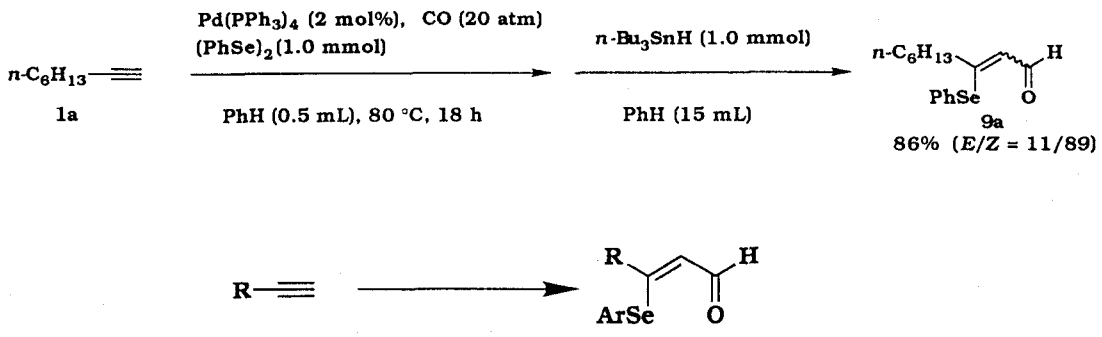
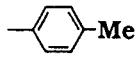
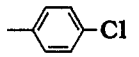
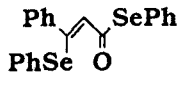
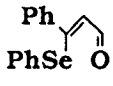
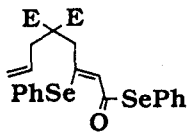
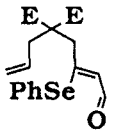
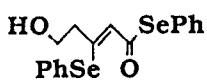
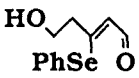
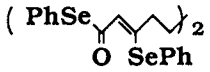
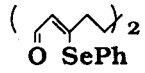
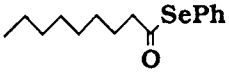
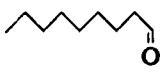


Table II. Palladium-Catalyzed Reduction of 5 with *n*-Bu_3SnH[a]

entry	substrate	product	yield(%)[b]	*E*/*Z*[c]
1	 5b Ar = 	 9b	90	2/98
2	5c Ar = 	9c	93	2/98
3	 5d	 9d	90	4/96
4	 5e E = CO_2Et	 9e	42[d]	8/92
5	 5f	 9f	87	0/100
6[e]	 5g	 9g	79	Z,E/Z,Z = 2/98
7[f]	 5'h	 9h	69[c]	

[a] *n*-Bu_3SnH (1.0 equiv) was added to a benzene solution of 5 and 0.4 mol% of $Pd(PPh_3)_4$ over a period of 3-17 min at 25 °C. [b] Isolated yield. [c] Determined by ^1H NMR. [d] Besides 9e, a complex mixture was formed. [e] n-Bu_3SnH (2.0 equiv) was added over a period of 50 min. [f] 2.4 equiv of *n*-Bu_3SnH was added to a benzene-d_6 solution of 5'h over a period of 10 min.

Conclusion: The present investigation provides the first example of transition-metal-catalyzed reduction of selenoesters with tin hydride to aldehydes: (*Z*)-1,3-bis(arylseleno)-2-alken-1-ones (**5**) are converted into (*Z*)-3-arylseleno-2-alkenals (**9**) with excellent chemoselectivity and site-selectivity in high yields under moderate reaction conditions. This study also reveals the utility of transition-metal catalysts in synthetic reactions using chalcogen compounds.

3-2-3. Experimental Section

(*Z*)-1,3-Bis(arylseleno)-2-alken-1-ones (**5**) were prepared by the palladium-catalyzed carbonylative addition of diaryl diselenides and carbon monoxide to terminal acetylenes described in chapter **2-1**. Tri-*n*-butyltin hydride was prepared according to the literature methods (Mitchell, T. N. *J. Organomet. Chem.* **1973**, *59*, 189). All catalysts were obtained commercially. Benzene was purified by distillation from sodium(>8%)-lead before use. The residual reaction mixture was separated by MPLC with Merck 25-40 mm mesh silica gel (Art 9390) and purified by recycling preparative HPLC (Japan Analytical Industry Co., Ltd. Model LC-908, JAIGEL-1H and -2H (GPC), length 600mm, i.d. 20 mm, eluent $CHCl_3$), if necessary.

$Pd(PPh_3)_4$-Catalyzed Reduction of (*Z*)-1,3-Bis(phenylseleno)-2-nonen-1-ones with *n*-Bu_3SnH (Table I, Entry 1): General Procedure. Into a two-necked flask equipped with an addition funnel and a magnetic stirring bar were placed, (*Z*)-1,3-bis(phenylseleno)-2-nonen-1-one (**5a**) (450 mg, 1.0 mmol), $Pd(PPh_3)_4$ (4.4 mg, 0.0038 mmol), and benzene (20 mL) under argon atmosphere. Then, a solution of *n*-Bu_3SnH (1.0 mmol in 10 mL of benzene) was added from the addition funnel over a period of 5 min. The reaction mixture was concentrated and subjected to MPLC (hexane/Et_2O as eluent) to give 270 mg (91%) of (*Z*)-3-phenylseleno-2-nonenal (**9a**) as a yellow oil.

(*Z*)-3-(Phenylseleno)-2-nonenal (9a): yellow oil; ^1H NMR (270 MHz, $CDCl_3$) δ 0.81 (t, J = 7.1 Hz, 3 H), 1.01-1.23 (m, 6 H), 1.40 (m, 2 H), 2.27 (t, J = 5.6 Hz, 2 H), 6.53 (d, J = 4.4 Hz, 1 H), 7.35-7.41 (m, 3 H), 7.62 (d, J = 6.8 Hz, 2 H), 9.87 (d, J = 4.4 Hz, 1 H). NOE experiment: Irradiation of the methylene triplet at δ 2.27 resulted in a 15% enhancement of the vinyl doublet at δ 6.53; ^{13}C NMR (68 MHz, $CDCl_3$) δ 13.96, 22.36, 28.41, 29.55, 31.27, 38.57, 125.05, 127.39, 129.13, 129.32, 136.39, 166.57, 189.80; IR (NaCl) 3056, 2955, 2928, 2856, 2742, 1671, 1534, 694, 742 cm^{-1}; mass spectrum (EI), m/e 296 (M^+, 97); Anal. Calcd for $C_{15}H_{20}OSe$:

C, 61.01; H, 6.83. Found: C, 60.96; H, 6.81. The following compounds were prepared according to the general procedure.

(Z)-3-(4-Methylphenylseleno)-2-nonenal (9b) (Table II, Entry 1): yellow oil; ^{1}H NMR (270 MHz, $CDCl_3$) δ 0.82 (t, J = 7.1 Hz, 3 H), 1.01-1.26 (m, 6 H), 1.30-1.48 (m, 2 H), 2.26 (t, J = 7.6 Hz, 2 H), 2.37 (s, 3 H), 6.51 (d, J = 3.9 Hz, 1 H), 7.15 (d, J = 8.0 Hz, 2 H), 7.49 (d, J = 8.0 Hz, 2 H), 9.86 (d, J = 3.9 Hz, 1 H). NOE experiment: Irradiation of methylene triplet at δ 2.26 resulted in a 21% enhancement of vinyl doublet at δ 6.51; ^{13}C NMR (68 MHz, $CDCl_3$) δ 14.00, 21.27, 22.39, 28.42, 29.57, 31.29, 38.40, 123.68, 124.71, 130.14, 136.46, 139.34, 167.25, 189.61; IR (NaCl) 3019, 2954, 2928, 2857, 2740, 1673, 1532, 1456, 1093, 1016, 806, 725 cm^{-1}; mass spectrum (EI), m/e 310 (M^+, 83); Anal. Calcd for $C_{16}H_{22}OSe$: C, 62.13; H, 7.17. Found: C, 62.02; H, 7.27.

(Z)-3-(4-Chlorophenylseleno)-2-nonenal (9c) (Table II, Entry 2): yellow oil; ^{1}H NMR (270 MHz, $CDCl_3$) δ 0.82 (t, J = 6.8 Hz, 3 H), 1.01-1.28 (m, 6 H), 1.39 (m, 2 H), 2.26 (t, J = 7.6 Hz, 2 H), 6.57 (d, J = 3.7 Hz, 1 H), 7.33 (d, J = 7.8 Hz, 2 H), 7.55 (d, J = 7.8 Hz, 2 H), 9.83 (d, J = 3.7 Hz, 1 H). NOE experiment: Irradiation of methylene triplet at δ 2.26 resulted in a 13% enhancement of vinyl doublet at δ 6.57; ^{13}C NMR (68 MHz, $CDCl_3$) δ 13.97, 22.37, 28.41, 29.52, 31.28, 38.43, 124.73, 125.72, 129.54, 135.70, 137.75, 165.79, 189.49; IR (NaCl) 2955, 2928, 2856, 2745, 1670, 1581, 1531, 1474, 1386, 1088, 1012, 818, 730 cm^{-1}; mass spectrum (EI), m/e 330 (M^+, 100); Anal. Calcd for $C_{15}H_{19}OClSe$: C, 54.51; H, 5.94. Found: C, 54.64; H, 5.81.

(Z)-3-(Phenylseleno)-3-phenyl-2-propenal (9d) (Table II, Entry 3): yellow oil; ^{1}H NMR (270 MHz) δ 6.70 (d, J = 5.8 Hz, 1 H), 7.06-7.37 (m, 10 H), 10.09 (d, J = 5.8 Hz, 1 H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 127.84, 128.09, 128.76, 128.91, 129.32, 129.63, 134.01, 138.63, 190.70; IR (NaCl) 3056, 2829, 1666, 1532, 1127, 762, 739, 691 cm^{-1}; mass spectrum (EI), m/e 288 (M^+, 79); Anal. Calcd for $C_{15}H_{12}OSe$: C, 62.73; H, 4.21. Found: C, 62.33; H, 4.31.

(Z)-3-(Phenylseleno)-5,5-bis(ethoxycarbonyl)-2,7-octadienal (9e) (Table II, Entry 4): yellow oil; ^{1}H NMR (270 MHz, $CDCl_3$) δ 1.21 (t, J = 7.1 Hz, 6 H), 2.68 (d, J = 7.3 Hz, 2 H), 3.02 (s, 2 H), 4.08-4.28 (m, 4 H), 5.00 (dd, J = 7.8, 1.5 Hz, 2 H), 5.04 (d, J = 1.5 Hz, 1 H), 5.51 (m, 1 H), 6.56 (d, J = 1.5 Hz, 1 H), 7.33-7.48 (m, 3 H), 7.52-7.63 (m, 2 H), 9.97 (d, J =

1.5 Hz, 1 H). NOE experiment: Irradiation of methylene triplet at δ 3.02 resulted in a 10% enhancement of vinyl doublet at δ 6.56; ^{13}C NMR (68 MHz, $CDCl_3$) δ 13.97, 37.30, 40.13, 57.77, 61.72, 119.69, 128.40, 128.83, 129.67, 129.67, 129.67, 131.82, 134.66, 156.39, 169.99, 191.11; IR (NaCl) 3076, 2981, 2838, 1732, 1674, 1535, 1298, 1211, 1140, 1096, 1065, 925, 859, 742, 693 cm^{-1}; mass spectrum (EI), m/e 424 (M^+, 15); Anal. Calcd for $C_{20}H_{24}O_5Se$: C, 56.74; H, 5.71. Found: C, 56.56; H, 5.73.

(Z)-3-(Phenylseleno)-5-hydroxy-2-pentenal (9f) (Table II, Entry 5): yellow oil; ^1H NMR (270 MHz, $CDCl_3$) δ 2.50 (br s, 1 H), 2.53 (t, J = 6.1 Hz, 2 H), 3.61 (q, J = 6.1 Hz, 2 H), 6.63 (d, J = 3.9 Hz, 1 H), 7.32-7.44 (m, 3 H), 7.59-7.62 (m, 2 H), 9.83 (d, J = 3.9 Hz, 1 H) NOE experiment: Irradiation of methylene triplet at δ 2.53 resulted in a 13% enhancement of vinyl doublet at δ 6.63; ^{13}C NMR (68 MHz, $CDCl_3$) δ 41.38, 61.04, 126.53, 127.16, 129.31, 129.54, 136.22, 162.10, 189.85; IR (NaCl) 3424, 3052, 2831, 1658, 1575, 1531, 1476, 1438, 1388, 1105, 1044, 1022, 743, 694 cm^{-1}; mass spectrum (EI), m/e 256 (M^+, 100); Anal. Calcd for $C_{11}H_{12}O_2Se$: C, 51.78; H, 4.74. Found: C, 51.81; H, 4.98.

(2Z,8Z)-3,8-Bis(phenylseleno)-2,8-decadiendial (9g) (Table II, Entry 6): yellow oil; ^1H NMR (270 MHz, $CDCl_3$) δ 1.19 (br s, 4 H), 2.10 (br s, 4 H), 6.42 (d, J = 4.1 Hz, 2 H), 7.31-7.45 (m, 6 H), 7.53-7.57 (m, 4 H), 9.84 (d, J = 4.1 Hz, 2 H). NOE experiment: Irradiation of broad singlet at δ 2.10 resulted in a 6% enhancement of vinyl doublet at δ 6.42; ^{13}C NMR (68 MHz, $CDCl_3$) δ 28.51, 37.86, 125.18, 127.15, 129.17, 129.35, 136.25, 165.20, 189.59; IR (NaCl) 3056, 2933, 2826, 2745, 1668, 1575, 1532, 1476, 1438, 1099, 1021, 1000, 742, 695 cm^{-1}; mass spectrum (EI), m/e 478 (M^+, 19); exact mass (M^+) calcd for $C_{22}H_{22}O_2Se_2$ 477.9947, found 477.9940.

Reduction of 5a with *n*-Bu_3SnH under Radical Conditions using AIBN as an Initiator: Into a two-necked flask equipped with a reflux condenser and a magnetic stirring bar were placed **5a** (90 mg, 0.2 mmol), AIBN (6.2 mg, 0.037 mmol) and benzene (8 mL), and then *n*-Bu_3SnH (0.3 mmol). The reaction mixture was refluxed and the reaction was followed by ^1H NMR spectrometer. After 5 h, the formation of **9a** was confirmed (67%, E/Z = 9/91).

One-Pot Synthesis of 9a without Isolation of 5a: In a 50 mL stainless autoclave were placed 1-octyne (1.0 mmol) (**1a**), $(PhSe)_2$ (1.0 mmol), $Pd(PPh_3)_4$ (23 mg, 0.02 mmol) and

benzene (0.5 mL). After stirring for 18 h at 80 °C under pressurized CO (20 kg/cm^2), CO was purged and benzene (15 mL) was added to the reaction mixture. Then *n*-Bu_3SnH (1.0 mmol) was added over a period of 5 min under flow of argon. The reaction mixture was filtered through Celite, and concentrated in vacuo. The formation of **9a** was confirmed by ^{1}H NMR spectroscopy (86%, *E*/*Z* = 11/89).

The spectroscopic data of **5a**, **5b**, **5d**, **5e** and **5f** were already listed in chapter **2**.

(*Z*)-1,3-Bis(4-chlorophenylseleno)-2-octen-1-one (5c) (Table II, Entry 2): yellow solid; mp 68-70 °C; ^{1}H NMR (270 MHz, $CDCl_3$) δ 0.82 (t, *J* = 7.1 Hz, 3 H), 1.01-1.12 (m, 4 H), 1.19 (m, 2 H), 1.32 (m, 2 H), 2.13 (t, *J* = 7.7 Hz, 2 H), 6.65 (s, 1 H), 7.32 (d, *J* = 8.5 Hz, 2 H), 7.36 (d, *J* = 8.5 Hz, 2 H), 7.50 (d, *J* = 8.5 Hz, 2 H), 7.56 (d, *J* = 8.5 Hz, 2 H). NOE experiment: Irradiation of methylene triplet at δ 2.13 resulted in a 44% enhancement of vinyl singlet at δ 6.65; ^{13}C NMR (68 MHz, $CDCl_3$) δ 13.98, 22.34, 28.44, 29.72, 31.20, 37.76, 122.03, 124.75, 125.42, 129.45, 129.54, 135.32, 136.05, 137.06, 138.57, 162.91, 186.98; IR (KBr) 2958, 2928, 2856, 1667, 1534, 1474, 1405, 1386, 1087, 1053, 1011, 815, 800, 730, 506, 490 cm^{-1}; mass spectrum (EI), m/e 329 (M^+-(ArSe)+1, 100). Anal. Calcd for $C_{21}H_{22}OCl_2Se$: C, 48.58; H, 4.27. Found: C, 49.00; H, 4.32.

(2*Z*,8*Z*)-1,3,8,10-Tetrakis(phenylseleno)-2,8-decadien-1,10-dione (5g) (Table II, Entry 6): yellow solid; mp 114-115 °C; ^{1}H NMR (270 MHz, $CDCl_3$) δ 1.02 (br s, 4 H), 1.91 (br s, 4 H), 6.52 (s, 2 H), 7.30-7.43 (m, 12 H), 7.54-7.60 (m, 8 H). NOE experiment: Irradiation of broad singlet at δ 1.91 resulted in a 20% enhancement of vinyl singlet at δ 6.52; ^{13}C NMR (68 MHz, $CDCl_3$) δ 28.74, 37.00, 122.33, 126.59, 127.12, 129.23, 129.31, 129.43, 135.76, 137.19, 161.75, 187.46; IR (KBr) 3056, 2953, 1664, 1541, 1477, 1438, 1093, 1070, 1020, 819, 793, 738, 685, 540, 489 cm^{-1}; mass spectrum (CI), m/e 631 (M^++1, 6); Anal. Calcd for $C_{34}H_{30}O_2Cl_2Se_2$: C, 51.93; H, 3.84. Found: C, 52.05; H, 3.82.

3-2-4. References and Notes

(1) For an overview of reductions with organotin reagents, see: Pereyre, M.; Quintard, J.-P.; Rahm, A. *Tin in Organic Synthesis*; Butterworths: London, 1987.

(2) For an example of the synthetic utility of **9**, see: Arrua, E. P.; Comasseto, J. V. *Synth.*

Commum. **1991**, *21*, 1663.

(3) For the palladium-catalyzed reduction of acid chloride with tin hydride, see: (a) Four, P.; Guibe, F. *J. Org. Chem.* **1981**, *46*, 4439. (b) Guibe, F.; Four, P.; Riviere, H. *J. Chem. Soc., Chem. Commun.* **1980**, 432.

(4) When 2 equiv of *n*-Bu_3SnH was added to a solution of **5a** and $Pd(PPh_3)_4$, overreduction from **9a** took place to produce (*E*)-2-nonenal and nonanal in 10% and 25% yields, respectively. This result clearly contrast with the reduction of thioester **4a**. See the chapter **3-1**. For the palladium-catalyzed reduction of α, β-unsaturated aldehydes, see: Keinan, E.; Gleize, P. A. *Tetrahedron Lett.* **1982**, *23*, 477.

(5) (a) Kuivila, H. G.; Walsh, E. J., Jr. *J. Am. Chem. Soc.* **1966**, *88*, 571. (b) Walsh, E. J., Jr.; Kuivila, H. G. *J. Am. Chem, Soc.* **1966**, *88*, 576.

(6) These reactions were carried out using benzene-d_6 as a solvent and analyzed by ^1H NMR spectroscopy directly without concentration of the reaction mixture, because the reduction of **5a** proceeded even in the absence of catalyst under higher concentrations. For example, the reduction of **5a** (1 M solution of benzene-d_6) with *n*-Bu_3SnH (1.1 equiv) took place at room temperature for 1 h to give **9a** in 39% yield, although the decomposition of *n*-Bu_3SnH into $(n\text{-}Bu_3Sn)_2$ competitively occurred. For a detailed investigation about the mechanism of the reduction of acid chloride with tin hydride under high concentration, see: (a) Lusztyk, J.; Lusztyk, E.; Maillard, B.; Lunazzi, L.; Ingold, K. U. *J. Am. Chem. Soc.* **1983**, *105*, 4475. (b) Lusztyk, J.; Lusztyk, E.; Maillard, B.; Ingold, K. U. *J. Am. Chem. Soc.* **1984**, *106*, 2923.

(7) Gas evolution was confirmed during the addition of *n*-Bu_3SnH.

(8) $Pt(PPh_3)_4$, $Ni(PPh_3)_2Cl_2$, $Rh(PPh_3)_3Cl$, and $Ru_3(CO)_{12}$ did not exhibit catalytic activity for the reduction of **1a** with *n*-Bu_3SnH.

(9) Pfenninger, J.; Heuberger, C.; Graf, W. *Helv. Chim. Acta* **1980**, *63*, 2328.

(10) After the benzene-d_6 solution of **5a** (0.025 M), *n*-Bu_3SnH (1.5 equiv), and AIBN (18 mol%) was refluxed for 5 h, the formation of **9a** (67%, *E*/*Z* = 9/91) was confirmed by ^1H NMR.

(11) The competitive reaction of **5b** (0.5 mmol) and **5c** (0.5 mmol) with 0.2 mmol of *n*-Bu_3SnH under otherwise identical conditions gave a mixture of **9b** and **9c** in the ratio, **9b**:**9c** = 0.34:1.

Chapter 4. Transition-Metal-Catalyzed Addition of Thiols, and their Derivatives

4-1. Transition-Metal-Catalyzed Hydrothiolation of Acetylenes

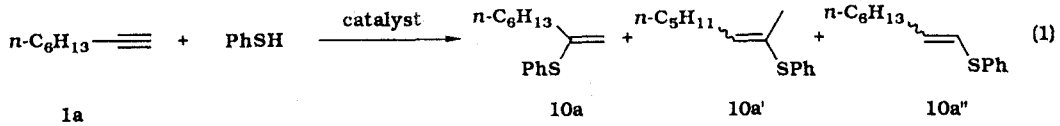
4-1-1. Introduction

While the properties of the complexes resulting from stoichiometric reactions of thiols with transition-metal complexes have been well-studied,[1] there are few reports of transition-metal-catalyzed synthetic reactions with thiols.[2] For instance, for transition-metal-catalyzed addition of thiols to carbon-carbon unsaturated compounds, there is only one example of addition to a 1,3-diene to the best of our knowledge.[2d] Perhaps widespread prejudice that thiols are catalyst poisons has precluded investigation in this area. In this chapter described is an interesting finding that many transition-metal catalysts indeed catalyze the addition of aromatic thiols to acetylenes to provide vinyl sulfides.[3]

4-1-2. Results and Discussion

Reaction Conditions for the Addition of Benzenethiol to 1-Octyne: Table I summarizes the results of the addition of benzenethiol to 1-octyne (**1a**) in the presence of various transition-metal catalysts. Among the catalysts examined, $Pd(OAc)_2$ exhibited excellent selectivity to afford the Markovnikov adduct **10a** (eq 1) in good yield (entries 1, 2, and 3).[4,5] In the absence of catalyst or presence of AcOH, **10a** was not obtained at all, and only anti-Markovnikov adduct **10a''** was produced (entries 4 and 5).[6] This may indicate that the palladium complex formed *in situ* also played an important role in suppression of the formation of **10a''**.[7] It has been well-established that the free radical additions of thiols to terminal acetylenes provide anti-Markovnikov adducts,[8] while the present $Pd(OAc)_2$-catalyzed addition afforded the Markovnikov adducts successfully. Thus, these methods presented the regiocomplementary approach to give vinyl sulfides (Scheme I).[9] When $Pt(PPh_3)_4$ was employed as a catalyst, **10a'** was produced as a major product (entry

9).



(1)

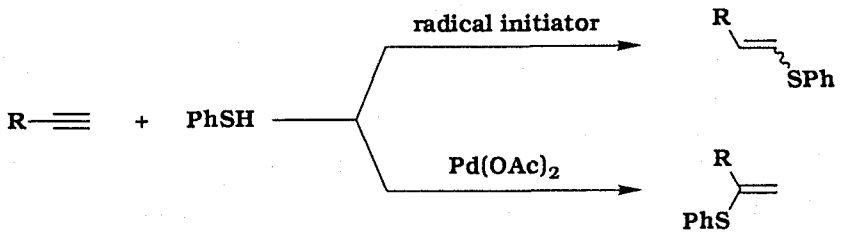
1a 10a 10a' 10a"

Table I. Effects of Catalysts on the Addition of PhSH to 1a[a]

entry	catalyst	condition[b]	yield (%)[c] 10a	10a'	10a"
1	$Pd(OAc)_2$	A	85[d]	<1	<1
2	$Pd(OAc)_2$	B	62	14	4
3[e]	$Pd(OAc)_2$	C	67	2	<1
4	none	A	0	0	47
5	AcOH	A	0	0	78
6	$Pd(PPh_3)_4$	B	4	10	2
7	$Pd(PPh_3)_4$	C	1	45	4
8	$Pd(PhCN)_2Cl_2$	C	2	73	0
9	$Pt(PPh_3)_4$	C	2	80	18
10	$Ni(PPh_3)_2Cl_2$	C	1	22	2
11	$Rh(PPh_3)_3Cl_2$	C	14	23	52[f]

[a] **1a** (1.0 mmol), catalyst (0.02 mmol), solvent (0.5 mL), and PhSH (1.0 mmol) for 16 h. [b] A: THF, 40 °C. B: THF, 67 °C. C: PhH, 80 °C. [c] Determined by GLC and ^1H NMR spectrometer. [d] Isolated yield. [e] 2,2-Bis(phenylthio)octane (5% based on **1a**) and $(PhS)_2$ (14%) were also produced. [f] *E/Z* = 98/2.

Scheme I



Considering that PhSH oxidatively adds to $Pt(PPh_3)_4$ to afford $PtH(PPh_3)_2(PhS)$,[1b,1c] similar species may be generated in this catalytic reaction system.[10] $Pd(PPh_3)_4$, $Pd(PhCN)_2Cl_2$, and $Ni(PPh_3)_2Cl_2$ also exhibited catalytic activity and similar selectivity of the products (entries 6, 7, 8, and 10), while the $Rh(PPh_3)_3Cl$-catalyzed reaction provided (*E*)-**10a''** as a major product with high stereoselectivity (entry 11).

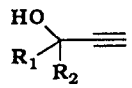
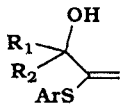
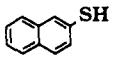
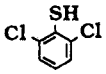
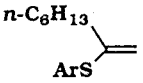
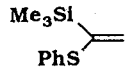
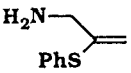
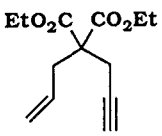
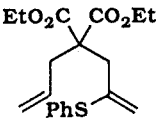
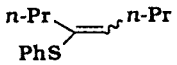
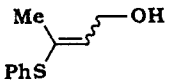
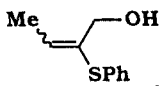
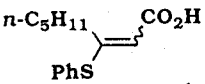
To ascertain the stereochemistry of the $Pd(OAc)_2$-catalyzed addition to give Markovnikov adduct **10a**, the reaction of PhSH with 1-octyne-1-*d* (containing >93% *d*) in THF-d_8 was followed by ^1H NMR spectroscopy. The *E*/*Z* ratio[11] of mono-deuterated adducts **10a** changed from 100/0 (6% conversion) after 15 min to 86/14 (81% conversion) after 8 h. Thus, the *E* isomer can be accepted as the kinetic product, which gradually isomerized to the *Z* isomer.[12] This clearly indicated that *cis* addition of PhSH to **1a** proceeded at least at the initial stage.

Addition of Aromatic Thiols to Various Acetylenes: The results of the $Pd(OAc)_2$-catalyzed addition of some aromatic thiols to acetylenes are shown in Table II. Hydroxy, trimethylsilyl, and amino groups may be present in the acetylenes (entries 1-3, 5, and 6). Among the aromatic thiols examined, 2,6-dichlorobenzenethiol and 2-naphthalenethiol also added to acetylenes (entries 3 and 4).[13] The acetylene bearing a tethered olefin unit underwent chemoselective addition to the triple bond (entry 7). The addition also proceeded smoothly with internal acetylenes like 4-octyne to give a mixture of stereoisomers, although the *cis* adduct (*E* isomer) was also predominantly formed at the beginning of the reaction (entry 8). The addition to 2-butyn-1-ol gave the slight regioselectivity (entry 9). Interestingly, the addition to 2-octynoic acid afforded the adducts with good stereo- and regioselectivity (entry 10).[14]

Stoichiometric Reaction and Proposed Reaction Path: To obtain some insight into active catalyst of the $Pd(OAc)_2$-catalyzed addition, the reaction of $Pd(OAc)_2$ with 3 equiv of PhSH[15] was carried out in THF-d_8. The mixture immediately deposited dark brown precipitates,[16] and the formation of ca. 2 equiv of AcOH was confirmed by ^1H NMR spectroscopy. Although actual reaction pathway of $Pd(OAc)_2$-catalyzed addition of ArSH to acetylenes is still unknown, a mechanistic proposal includes the following: (1) ligand exchange of AcO ligand with PhS group in the presence of acetylene[17,16] to give AcOH and active catalyst; (2) coordination of acetylene to palladium; (3) syn-thiopalladation[18] to acetylene to form *cis* vinylpalladium (the order of R' preferred: hydrogen > oxygen-containing group > alkyl group); and (4) trapping of the vinyl group by PhSH[19] or AcOH with retention of stereochemistry to give the Markovnikov

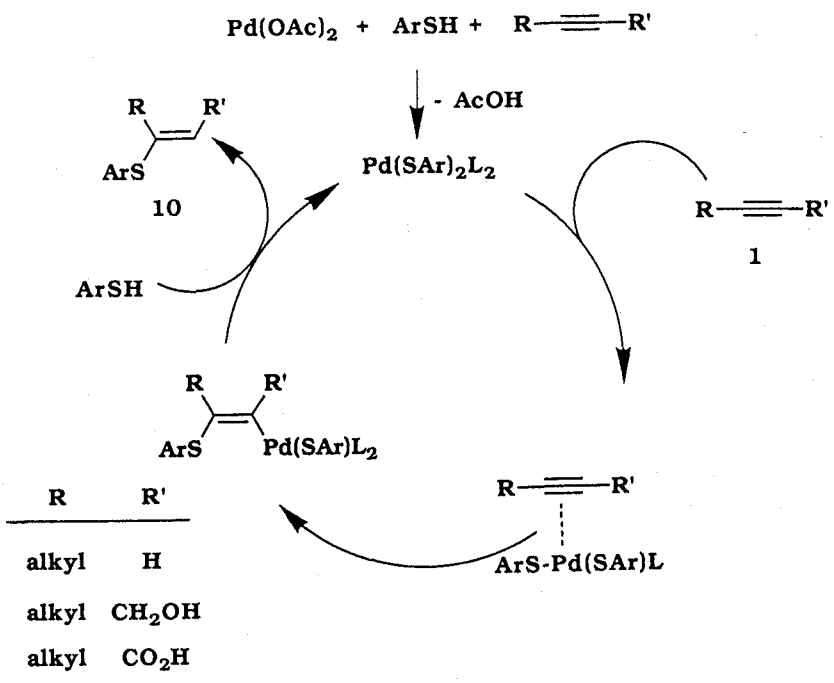
adduct with regeneration of the catalyst (Scheme II).

Table II. $Pd(OAc)_2$-Catalyzed Addition of ArSH to Acetylenes[a]

entry	acetylene	ArSH	product and yield (%)[b]	yield of regioisomers (%)[c]
				
1	$R_1=R_2=Me$	PhSH		86 0
2	$R_1,R_2=-(CH_2)_4-$	PhSH		63 0
3	$R_1=R_2=Me$			85 0
4	n-C_6H_{13}—≡			55 -[d]
5[e]	Me_3Si—≡	PhSH		56 5
6[f]		PhSH		65 (87)[g] 0
7		PhSH		70 -[d]
8	n-Pr—≡—n-Pr	PhSH	 72 (E/Z = 34/66)[c] (E/Z = 92/8)[c,h]	
9	Me—≡—OH	PhSH	 53(E/Z = 63/37)[c]	 29 (E/Z = 48/52)[c]
10	n-C_5H_{11}—≡—CO_2H	PhSH	 87(E/Z = 98/2)[i]	2

[a]Conditions: acetylene (1.0 mmol), $Pd(OAc)_2$ (0.02 mmol) and ArSH (1.0-1.3 mmol) in THF (0.5 mL) at 67 °C for 12-16 h. [b]Isolated yield. [c]Determined by ^1H NMR and GLC. [d]A complex mixture was produced as by-product. [e]Without solvent at 70 °C. [f]24 h. [g]NMR yield. [h]10 min. [i]See ref 14.

Scheme II. A Proposed Reaction Path for the $Pd(OAc)_2$-Catalyzed Addition of ArSH to Acetylenes



Conclusion: A variety of transition-metal complexes catalyzed the addition of aromatic thiols to acetylenes. Especially, $Pd(OAc)_2$-catalyzed addition exhibited high regioselectivity to give Markovnikov adducts in good yields. Further study is focusing on details of the mechanisms of this addition catalyzed by $Pd(OAc)_2$ and other catalysts. The present study presages the development of a new class of transition-metal-catalyzed reaction based on thiols.

4-1-3. Experimental Section

1-Octyne-1-*d* was prepared by the reaction of 1-octyne with *n*-BuLi followed by quenching with D_2O. Other acetylenes and thiols were obtained commercially and were purified by distillation before use if necessary. All catalysts were obtained commercially. Tetrahydrofuran and benzene were purified by distillation from sodium and sodium(>8%)-lead before use,

respectively. The residual mixture was purified by MPLC with Merck 25-40 mm mesh silica gel (Art 9390) and preparative TLC with Wakogel B-5F silica gel, or recycling preparative HPLC (Japan Analytical Industry Co., Ltd. Model LC-908, JAIGEL-1H and -2H (GPC), length 600mm, i.d. 20 mm, eluent $CHCl_3$).

$Pd(OAc)_2$-Catalyzed Addition of PhSH to 1-Octyne (1a) (Table I, Entry 1): To a two-necked flask equipped with a reflux condenser and a magnetic stirring bar were placed $Pd(OAc)_2$ (4.5 mg, 0.02 mmol), THF (0.5 mL), 1-octyne (**1a**) (110 mg, 1.0 mmol), and PhSH (110 mg, 1.0 mmol) under Ar atmosphere. The reaction mixture immediately deposited brown precipitates. The mixture was stirred at 40 °C for 16 h. After the reaction was complete, the resulting precipitates were removed by filtration through Celite, and the filtrate was evaporated under reduced pressure. The residual mixture was purified by MPLC and preparative TLC to provide 188 mg (85%) of 2-phenylthio-1-octene (**10a**) as a clear oil. The additions of ArSH to other acetylenes listed in Table II were performed in a similar manner at 67 °C.

$Pt(PPh_3)_4$-Catalyzed Addition of PhSH to 1-Octyne (Table I, Entry 9). To a two-necked flask equipped with a reflux condenser and a magnetic stirring bar were placed, under Ar atmosphere, $Pt(PPh_3)_4$ (25 mg, 0.02 mmol), PhH (0.5 mL), 1-octyne (**1a**) (110 mg, 1.0 mmol), and PhSH (110 mg, 1.0 mmol). This reaction system is homogeneous. The mixture was refluxed for 16 h. After the reaction was complete, the resulting precipitates was removed by filtration through Celite, and the filtrate was analyzed by GLC. $Pd(PhCN)_2Cl_2$, $Pd(PPh_3)_4$, $Ni(PPh_3)_2Cl_2$, and $Rh(PPh_3)_3Cl$-catalyzed additions listed in Table I were also performed in a similar procedure.

2-Phenylthio-1-octene (10a): oil; ^1H NMR (270 MHz, $CDCl_3$) δ 0.88 (t, J = 6.4 Hz, 3 H), 1.20-1.38 (m, 6 H), 1.53 (m, 2 H), 2.33 (t, J = 7.3 Hz, 2 H), 4.87 (s, 1 H), 5.14 (s, 1 H), 7.24-7.35 (m, 3 H), 7.43 (d, J = 6.8 Hz, 2 H). NOE experiment: Irradiation of methylene triplet at δ 2.33 resulted in an 8% enhancement of the δ 5.14, indicating this vinyl proton was *trans* for PhS group; ^{13}C NMR (68 MHz, $CDCl_3$) δ 14.06, 22.58, 28.40, 28.59, 31.61, 36.59, 112.44, 127.68, 129.06, 133.23, 133.34, 146.19; IR (NaCl) 3074, 3059, 2956, 2929, 2856, 1608, 1584, 1476, 1465, 1440, 748, 691 cm^{-1}; mass spectrum (EI), m/e 220 (M^+, 13); Anal. Calcd for $C_{14}H_{20}S$: C, 76.30; H, 9.14; S, 14.55. Found: C, 76.10; H, 9.27; S, 14.26.

3-Phenylthio-2-methyl-3-buten-2-ol (Table II, Entry 1): oil; ^{1}H NMR (270 MHz, $CDCl_3$) δ 1.51 (s, 6 H), 2.06 (br s, 1 H), 4.73 (s, 1 H), 5.47 (s, 1 H), 7.33 (m, 3 H), 7.47 (d, J = 7.3 Hz, 2 H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 29.68, 73.99, 110.83, 127.99, 129.29, 133.52, 133.71, 154.81; IR (NaCl) 3407, 3063, 2978, 1604, 1477, 1439, 1364, 1089, 882, 749, 691 cm^{-1}; mass spectrum (EI), m/e 194 (M^+, 27). Anal. Calcd for $C_{11}H_{14}OS$: C, 68.00; H, 7.26; S, 16.50. Found: C, 67.71; H, 7.34; S, 16.14.

1-(1'-phenylthio-ethenyl)-cyclopentanol (Table II, Entry 2): oil; ^{1}H NMR (270 MHz, $CDCl_3$) δ 1.75-2.03 (m, 9 H), 4.79 (s, 1 H), 5.54 (s, 1 H), 7.25-7.37 (m, 3 H), 7.45-7.49 (m, 2 H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 23.64, 39.62, 84.65, 111.57, 127.89, 129.25, 133.30, 133.73, 152.26; IR (NaCl) 3404, 3054, 2965, 1604, 1582, 1478, 1439, 1000, 749, 690 cm^{-1}; mass spectrum (EI), m/e 220 (M^+, 98); exact mass (M^+) calcd for $C_{13}H_{16}OS$ 220.0922, found 220.0923.

3-(2-Naphthylthio)-2-methyl-3-buten-2-ol (Table II, Entry 3): white solid; mp 78-79 °C; ^{1}H NMR (270 MHz, $CDCl_3$) δ 1.54 (s, 6 H), 2.23 (s, 1 H), 4.76 (s, 1 H), 5.48 (s, 1 H), 7.41-7.59 (m, 3 H), 7.71-7.89 (m, 3 H), 7.97 (s, 1 H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 29.67, 73.99, 110.99, 126.52, 126.55, 127.54, 127.69, 128.90, 130.37, 130.98, 132.71, 133.78, 154.71; IR (KBr) 3362, 3054, 2980, 1624, 1371, 1187, 1139, 1093, 966, 815, 655, 631, 593, 478 cm^{-1}; mass spectrum (EI), m/e 244 (M^+, 71); Anal Calcd for $C_{15}H_{16}OS$: C, 73.73; H, 6.60; S, 13.12. Found: C, 73.88; H, 6.76; S, 13.29.

2-(2',6'-Dichlorophenylthio)-1-octene (Table II, Entry 4): oil; ^{1}H NMR (270 MHz, $CDCl_3$) δ 0.86 (t, J = 6.8 Hz, 3 H), 1.21-1.45 (m, 6 H), 1.59 (quint, J = 7.6 Hz, 2 H), 2.23 (t, J = 7.6 Hz, 2 H), 4.42 (s, 1 H), 4.97 (s, 1 H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 14.07, 22.57, 28.33, 28.59, 31.58, 36.44, 107.83, 128.72, 130.77, 141.83, 143.60; IR (NaCl) 3077, 2929, 2857, 2364, 1611, 1555, 1425, 1402, 1187. 855, 778, 713 cm^{-1}; Anal Calcd for $C_{14}H_{18}Cl_2S$: C, 58.13; H, 6.27. Found: C, 57.85; H, 6.39.

1-Phenylthio-1-(trimethylsilyl)ethene (Table II, Entry 5): The reaction was performed without solvent at 70 °C in sealed tube. oil; ^{1}H NMR (270 MHz, $CDCl_3$, 1,4-Dioxane (δ 3.69) was used as the internal standard.) δ 0.19 (s, 9 H), 5.24 (s, 1 H), 5.49 (s, 1 H), 7.29-7.37 (m, 3 H), 7.43 (d, J = 7.8 Hz, 2 H); ^{13}C NMR (68 MHz, $CDCl_3$, $CDCl_3$ (δ 77.00) was used as the

internal standard.) δ -1.41, 120.43, 128.07, 129.14, 132.32, 134.46, 148.02; IR (NaCl) 3059, 2956, 2896, 1571, 1477, 1439, 1248, 1024, 855, 840, 742, 691, 630 cm^{-1}; mass spectrum (EI), m/e 208 (M^+, 32); exact mass (M^+) calcd for $C_{11}H_{16}SSi$ 208.0742, found 208.0717.

(*E*)-1-Phenylthio-2-(trimethylsilyl)ethene (Table II, Entry 5): oil; ^1H NMR (270 MHz, $CDCl_3$, 1,4-Dioxane (δ 3.69) was used as the internal standard.) δ 0.07 (s, 9 H), 5.89 (d, *J* = 18.1 Hz, 1 H), 6.66 (d, *J* = 18.1 Hz, 1 H), 7.25-7.41 (m, 5 H); IR (NaCl) 3059, 2955, 2896, 1546, 1480, 1440, 1248, 1025, 863, 839, 742, 691, 626 cm^{-1}; mass spectrum (EI), m/e 208 (M^+, 50); exact mass (M^+) calcd for $C_{11}H_{16}SSi$ 208.0742, found 208.0728.

2-Phenylthio-3-amino-1-propene (Table II, Entry 6): The reaction was carried out for 24 h. oil; ^1H NMR (270 MHz, $CDCl_3$) δ 1.97 (br s, 2 H), 3.36 (s, 2 H), 5.07 (s, 1 H), 5.39 (s, 1 H), 7.29-7.34 (m, 3 H), 7.42 (d, *J* = 6.8 Hz, 2 H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 47.13, 113.44, 127.73, 129.17, 132.63, 132.74, 147.47; IR (NaCl) 3375, 3059, 2914, 1610, 1583, 1476, 1440, 1068, 1024, 909, 863, 733, 692 cm^{-1}; mass spectrum (EI), m/e 165 (M^+, 66); Anal. Calcd for $C_9H_{11}NS$: C, 65.41; H, 6.71; N, 8.48; S, 19.40. Found: C, 65.18; H, 6.75; N, 8.65; S, 19.11.

2-Phenylthio-4,4-bis(carboethoxy)-hepta-1,6-diene (Table II, Entry 7): oil; ^1H NMR (270 MHz, $CDCl_3$) δ 1.24 (t, *J* = 7.1 Hz, 6 H), 2.82 (d, *J* = 7.3 Hz, 2 H), 2.94 (s, 2 H), 4.11-4.25 (m, 4 H), 4.92 (s, 1 H), 5.09 (d, *J* = 9.8 Hz, 1 H), 5.11 (d, *J* = 18.6 Hz, 1 H), 5.21 (s, 1 H), 5.69 (octet, *J* = 18.6, 9.8, 7.3 Hz, 1 H), 7.29-7.42 (m, 5 H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 14.00, 36.36, 38.23, 57.39, 61.37, 117.29, 119.25, 128.02, 129.27, 132.61, 132.90, 133.11, 140.61, 170.51; IR (NaCl) 3077, 2981, 2938, 2904, 1732, 1606, 1584, 1477, 1440, 1366, 1288, 1256, 1218, 1196, 1159, 1042, 923, 859, 750, 692 cm^{-1}; mass spectrum (EI), m/e 348 (M^+, 4); Anal. Calcd for $C_{19}H_{24}O_4S$: C, 65.49; H, 6.94; S, 9.20. Found: C, 65.77; H, 7.12; S, 9.41.

4-Phenylthio-4-octene (Table II, Entry 8). *Z* isomer: oil; ^1H NMR (270 MHz, $CDCl_3$) δ 0.82 (t, *J* = 7.3 Hz, 3 H), 0.92 (t, *J* = 7.3 Hz, 3 H), 1.39-1.53 (m, 4 H), 2.14 (t, *J* = 7.3 Hz, 2 H), 2.32 (q, *J* = 7.3 Hz, 2 H), 5.90 (t, *J* = 7.3 Hz, 1 H), 7.14-7.26 (m, 5 H). NOE experiment: Irradiation of methylene triplet at δ 2.14 resulted in a 19% enhancement of the signal at δ 5.90 (vinyl triplet); ^{13}C NMR (68 MHz, $CDCl_3$) δ 13.33, 13.82, 21.59, 22.69, 31.95, 39.62, 125.67, 128.75, 129.21, 133.07, 135.86, 136.76; IR (NaCl) 3073, 2958, 2930, 2870, 1582, 1477, 1458, 1437, 1024, 738, 690 cm^{-1}; mass spectrum (EI), m/e 220 (M^+, 100); Anal. Calcd for $C_{14}H_{20}S$:

C, 76.30; H, 9.15; S, 14.55. Found: C, 76.35; H, 9.35; S, 14.36.
E isomer: ^{1}H NMR (270 MHz, $CDCl_3$) δ 0.87 (t, *J* = 7.3 Hz, 3 H), 0.94 (t, *J* = 7.3 Hz, 3 H), 1.40-1.56 (m, 4 H), 2.11 (t, *J* = 7.3 Hz, 2 H), 2.16 (q, *J* = 7.3 Hz, 2 H), 5.87 (t, *J* = 7.3 Hz, 1 H), 7.15-7.32 (m, 5 H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 13.66, 13.83, 21.75, 22.69, 31.22, 33.10, 126.12, 128.82, 129.92, 133.62, 136.08, 137.27; mass spectrum (EI), m/e 220 (M^+, 100); Anal. Calcd for $C_{14}H_{20}S$: C, 76.30; H, 9.15; S, 14.55. Found: C, 76.53; H, 9.40; S, 14.14.

3-Phenylthio-2-buten-1-ol (Table II, Entry 9). isolated as *E*, *Z* mixture: ^{1}H NMR (270 MHz, $CDCl_3$) *Z* isomer: δ 1.61 (s, 1 H), 1.92 (d, *J* = 1.0 Hz, 3 H), 4.41 (d, *J* = 6.1 Hz, 2 H), 5.99(dd, *J* = 6.1, 1.0 Hz), 7.21-7.39 (m, 5 H). NOE experiment: Irradiation of doublet at δ 1.92 resulted in an 18% increase of the peak at δ 5.99. *E* isomer: δ 1.51 (br s, 1 H), 1.92 (d, *J* = 1.5 Hz, 3 H), 4.19 (d, *J* = 6.3 Hz, 2 H), 5.69 (dd, *J* = 6.6 Hz, 1 H), 7.12-7.42 (m, 5 H). Irradiation of doublet at δ 1.92 resulted in a 12% increase of the peak at δ 4.19; ^{13}C NMR (68 MHz, $CDCl_3$) *Z* isomer: δ 24.20, 60.49, 127.00, 127.95, 128.98, 131.21, 132.43, 133.16. *E* isomer: δ 17.89, 59.47, 127.74, 129.13, 131.21, 132.74, 133.52. IR (NaCl) 3342, 3058, 2918, 1584, 1478, 1439, 1079, 1003, 743, 692 cm^{-1}; mass spectrum (EI), *Z* isomer: m/e 180 (M^+, 26). *E* isomer: m/e 180 (M^+, 58); Anal. Calcd for $C_{10}H_{12}OS$: C, 66.63; H, 6.71. Found: C, 67.02; H, 6.66.

2-Phenylthio-2-buten-1-ol (Table II, Entry 9). *E* isomer: oil; ^{1}H NMR (270 MHz $CDCl_3$) δ 1.87 (d, *J* = 7.2 Hz, 3 H), 1.91 (t, *J* = 6.1 Hz, 1 H), 4.19 (d, *J* = 6.1 Hz, 2 H), 6.17 (q, *J* = 7.2 Hz, 1 H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 14.84, 59.26, 126.73, 129.08, 129.82, 134.77, 135.26; IR(NaCl) 3371, 3057, 2922, 1724, 1583, 1478, 1440, 1291, 1024, 983, 741, 691 cm^{-1}; mass spectrum (EI), m/e 180 (M^+, 100).
Z isomer: oil; ^{1}H NMR (270 MHz, $CDCl_3$) δ 1.93 (d, *J* = 6.4 Hz, 3 H), 2.23 (t, *J* = 5.5 Hz, 1 H), 4.07 (d, *J* = 5.5 Hz, 2 H), 6.34 (q, *J* = 6.4 Hz, 1 H), 7.16-7.27 (m, 5 H). NOE experiment: Irradiation of at δ 6.34 resulted in a 9% increase of at δ 2.23; ^{13}C NMR (68 MHz, $CDCl_3$) δ 15.31, 65.99, 126.15, 128.89, 129.02, 133.27, 134.63; mass spectrum (EI), m/e 180 (M^+, 99); Anal. Calcd for $C_{10}H_{12}OS$: C, 66.63; H, 6.71; S, 17.79. Found: C, 66.61; H, 6.73; S, 17.76.

3-Phenylthio-2-octenoic acid (Table II, Entry 10): isolated as *E*/*Z* (98/2) mixture: mp 108-111 °C; ^{1}H NMR (270 MHz, $CDCl_3$) *E* isomer: δ 1.12 (t, *J* = 7.1 Hz, 3 H), 1.52-1.61 (m, 4 H), 1.83-1.91 (m, 2 H), 3.03 (t, *J* = 7.8 Hz, 3 H), 5.34 (s, 1 H), 7.63-7.73 (m, 5 H), 11.0-12.0 (br s, 1 H). *Z* isomer: 2.11 (t, *J* = 8.1 Hz, 2 H), 5.85 (s, 1 H) Other peak was not able to be

assigned; ^{13}C NMR (68 MHz, $CDCl_3$) Z isomer: δ 12.93, 21.29, 28.57, 30.61, 32.58, 108.29, 128.40, 128.81, 128.96, 134.59, 168.09, 169.19; IR (KBr) 3062, 2956, 2928, 1680, 1591, 1246, 854, 750, 677 cm^{-1}; mass spectrum (CI), m/e 251 (M^++1, 100); Anal. Calcd for $C_{14}H_{18}O_2S$: C, 67.17; H, 7.25; S, 12.81. Found. C, 67.14; H, 7.33; S, 12.57.

The Isomerization of 10a to 10a' (Reference 10): In a NMR tube were added $Pt(PPh_3)_4$ (12.4 mg, 0.001 mmol), benzene-d_6 (0.5 mL), a mixture of **10a/10a'** (82/18) (44 mg, 0.02 mmol), diethyl acetylenedicarboxylate (16 mg, 0.1 mmol), and PhSH (11 mg, 0.1 mmol). After 12 h at 70 °C the ratio was changed to **10a/10a'** = 13/87 (determined by ^1H NMR spectroscopy).

$Pd(OAc)_2$-Catalyzed Addition of PhSH with 1-Octyne-1-*d*: In a NMR tube were added $Pd(OAc)_2$ (4.5 mg, 0.02 mmol), THF-d_8 (0.5 mL), 1-octyne-1-*d* ((containing >93% *d* determined by mass spectrum) 111 mg, 1.0 mmol), and PhSH (110 mg, 1.0 mmol) and the mixture was heated at 40 °C. The reaction was followed by the measurement of ^1H NMR spectroscopy. The reaction time, the ratio of the integration of the two vinyl protons (δ 4.87 vs δ 5.14), and conversion of PhSH were: 15 min, 94:6, 6%; 2 h, 90:10, 40%; 4 h, 84:16, 59%; 8 h, 81:19, 81%. The fragmentation of mass spectrum of the adduct indicated that the product containing two deuteriums was not formed.

Stoichiometric Reaction of PhSH with $Pd(OAc)_2$: In a NMR tube were added $Pd(OAc)_2$ (4.3 mg, 0.019 mmol), THF-d_8 (0.5 mL), PhSH (6.5 mg, 0.059 mmol), and 1,3,5-trioxane (1.3 mg, 0.014 mmol) as an internal standard. Immediately the brown precipitates was deposited. The formation of 0.037 mmol of AcOH was confirmed by ^1H NMR spectroscopy.

The Reaction of PhSH with 1-Octyne in the Presence of the Precipitates Prepared by PhSH with $Pd(OAc)_2$: To a solution of $Pd(OAc)_2$ (225 mg, 1.0 mmol) in THF (25 mL) was added the PhSH (275.5 mg, 2.5 mmol) under Ar at ambient temperature. Immediately the mixture deposited the dark brown precipitates. Then, after 30 min the solid was separated by filtration and washed with THF. This compound was scarcely soluble in THF. When this precipitates (10 mg) was used as a catalyst for the addition of PhSH (1.0 mmol) to 1-octyne (1.0 mmol) in THF (0.5 mL) at 40 °C for 16 h, the addition proceeded to give **10a** in 1% yield and 1-phenylthio-1-octene (**10a''**) in 41% yield.

The Reaction of PhSH with 1-Octyne in the Presence of the Precipitates Prepared by PhSH with $Pd(OAc)_2$ in the Presence of 1-Octyne: To a solution of $Pd(OAc)_2$ (225 mg, 1.0 mmol) in THF (25 mL) was added the 1-octyne (**1a**) (121 mg, 1.1 mmol) under Ar at ambient temperature. The color of the solution changed from brown to dark brown. After stirring at 10 min, PhSH (242 mg, 2.2 mmol) was added. Immediately the mixture deposited brown precipitates. After 30 min, the solid was separated by filtration and washed with THF to give dark brown solid. This compound was scarcely soluble in THF. The combustion analysis suggested that the formula of this compound was $[Pd(SPh)_2]_n$ (Anal. Calcd for $(C_{12}H_{10}S_2Pd)_n$:C, 44.38; H, 3.10; S, 19.53. Found: C, 44.22; H, 3.33; S, 19.53.). When this precipitates (10 mg) was used as a catalyst for the addition of PhSH (1.0 mmol) to 1-octyne (1.0 mmol) in THF (0.5 mL) at 40 °C for 16 h, the addition proceeded to give **10a** in 64% yield.

4-1-4. References and Notes

(1) For notable examples, see: (a) Kim, Y. J.; Osakada, K.; Sugita, K.; Yamamoto, T.; Yamamoto, A. *Organometallics* **1988**, *7*, 2182. (b) Keskinen, A. E.; Senoff, C. V. *J. Organomet. Chem.* **1972**, *37*, 201. (c) Ugo, R.; Monica, G. L.; Cenini, S. *J. Chem. Soc. A* **1971**, 522. (d) Nyholm, R. S.; Skinner, J. F.; Stiddard, M. H. B. *J. Chem. Soc. A* **1968**, 38. (e) Chatt, J.; Mann, F. G. *J. Chem. Soc.* **1938**, 1949. (f) Chatt, J.; Hart, F. A. *J. Chem. Soc.* **1960**, 2807. (g) Chatt, J.; Hart, F. A. *J. Chem. Soc.* **1953**, 2363. (h) Fenn, R. H.; Segrott, G. R. *J. Chem. Soc. Dalton Trans.* **1971**, 330. (i) Fenn, R. H.; Segrott, G. R. *J. Chem. Soc. A* **1970**, 3197. (j) Umakoshi, K.; Ichimura, A.; Kinoshita, I.; Ooi, S. *Inorg. Chem.* **1990**, *29*, 4005. (k) Gaylor, J. R.; Senoff, C. V. *Can. J. Chem.* **1972**, *50*, 1868. (l) Osakada, K.; Hayashi, H.; Maeda, M.; Yamamoto, T.; Yamamoto, A. *Chem. Lett.* **1986**, 597. (m) Gaines, T.; Roundhill, D.M. *Inorg. Chem.* **1974**, *13*, 2521. (n) Rakowski DuBois, M. *Chem. Rev.* **1989**, *89*, 1.

(2) (a) Antebi, S.; Alper, H. *Organometallics* **1986**, *5*, 596. (b) Shim, S. C.; Antebi, S.; Alper, H. *J. Org. Chem.* **1985**, *50*, 147. (c) Shim, S. C.; Antebi, S.; Alper, H. *Tetrahedron Lett.* **1985**, *26*, 1935. (d) Dzhemilev, U. M.; Kunakova, R. V.; Gaisin, R. L. *Izv. Akad. Nauk SSSR, Ser. Khim.* **1981**, *11*, 2655. (e) Talley, J. J.; Colley, A. M. *J. Organomet. Chem.* **1981**, *215*, C38. (f) McKervey, M. A.; Ratananukul, P. *Tetrahedron Lett.* **1982**, *23*, 2509. (g) Holmquist, H. E.; Carnahan, J. E. *J. Org. Chem.* **1960**, *25*, 2240. (h) Iqbal, J.; Pandey, A.; Shukla, A.; Srivastava, R. R.; Tripathi, S. *Tetrahedron* **1990**, *46*, 6423.

(3) For the synthetic utility of vinyl sulfides, see: (a) Trost, B. M.; Lavoie, A. C. *J. Am. Chem. Soc.* **1983**, *105*, 5075. (b) Magnus, P.; Quagliato, D. *J. Org. Chem.* **1985**, *50*, 1621.

(4) Procedure (entry 1): In a reaction vessel were placed $Pd(OAc)_2$ (0.02 mmol), THF (0.5 mL), **1a** (1.0 mmol), and then PhSH (1.0 mmol). After 16 h at 40 °C, the resulting catalyst was removed by filtration through Celite, and then the solvent was evaporated. The crude oil was subjected to MPLC (silica gel) to obtain **10a** (85%). Also isolated in smaller quantities were 2,2-bis(phenylthio)octane (3% based on **1a**), and diphenyl disulfide (6%).

(5) The additions to **1a** of some other thiols such as *n*-BuSH, C_6F_5SH, $MeOCOCH_2SH$, and 2-pyridinethiol were not catalyzed by $Pd(OAc)_2$ under similar reaction conditions.

(6) The addition proceeded probably *via* a free radical mechanism by an adventitious amount of oxygen.

(7) It has been reported that $Fe(CO)_5$ inhibited the radical addition of ArSH to phenylacetylene, see: Kandror, I. I.; Petrova, R. G.; Petrovskii, P. V.; Freidlina, R. Kh. *Izv. Akad. Nauk SSSR, Ser. Khim.* **1969**, *7*, 1621.

(8) (a) Peach, M. E. In *The Chemistry of the Thiol Group*; Patai, S., Ed.; Wiley: London, 1974; Vol. 2. (b) Ichinose, Y.; Wakamatu, K.; Nozaki, K.; Birbaum, J. L.; Oshima, K.; Utimoto, K. *Chem. Lett.* **1987**, 1647. (c) Griesbaum, K. *Angew. Chem., Int. Ed. Engl.* **1970**, *9*, 273.

(9) There are few examples of Markovnikov addition of thiols to acetylenes by nucleophilic attack of thiolate anion, but the relatively longer reaction time or more sever conditions are essential, see: (a) Truce, W. E.; Simms, J. A. *J. Am. Chem. Soc.* **1956**, *78*, 2756. (b) Borisova, A. I.; Filippova, A. K.; Voronov, V. K.; Shostakovski, M. F. *Izv. Akad. Nauk SSSR, Ser. Khim.* **1969**, 2498.

(10) The ratio of a mixture of isolated **10a/10a'** (82/18) changed to 13/87 in the presence of $Pt(PPh_3)_4$, PhSH and acetylene, suggesting that **10a** is a precursor of **10a'**; see experimental section.

(11) The assignment of the vinyl protons was confirmed by an NOE experiment of **10a**.

(12) The formation of the product containing two deuteriums was not observed judging from the fragmentation of the mass spectrum of the product. This fact may indicate that the isomerization of *E* to *Z* is promoted by addition and elimination of Pd-SPh (and/or PhS•) to the C-C double bond of **10a**.

(13) The substituents on aromatic thiol had drastic effects on the $Pd(OAc)_2$-catalyzed addition. For example, the addition of 4-chloro- or 4-hydroxybenzenethiol to **1a** gave bis-adducts as the main products. On the other hand, the addition of 4-methyl- or 4-methoxybenzenethiol to **1a**

was scarcely catalyzed by $Pd(OAc)_2$ under similar reaction conditions. The details are now under investigation.

(14) The assignment of stereochemistry was confirmed by ^1H NMR spectroscopy. The signal of the *cis* vinyl proton for the PhS group appeared upfield from that of *trans* vinyl proton by ca. 0.3-0.7 ppm. See experimental section.

(15) Nyholm et al. have already described that the reaction of $Pd(OAc)_2$ with PhSH gave a polymeric product; see ref 1d.

(16) This precipitate scarcely exhibited the catalytic activities for the addition of PhSH to **1a**. On the other hand, the precipitates prepared *in the presence of* ***1a*** had a moderate catalytic activity. Detailed results are provided in the experimental section.

(17) To obtain good yields of Markovnikov adducts in this $Pd(OAc)_2$-catalyzed addition, acetylenes must be added to $Pd(OAc)_2$ before the addition of PhSH; see ref 4.

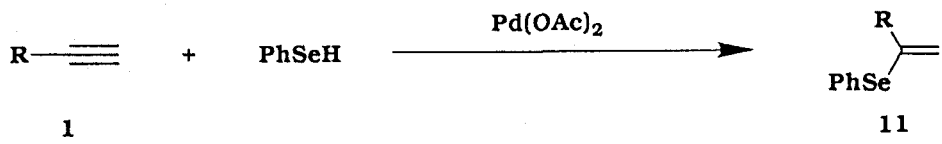
(18) We have already reported the $Pd(PPh_3)_4$-catalyzed addition of diphenyl disulfide to acetylenes, indicating the facile insertion of acetylene into the Pd-S bond; see: Kuniyasu, H.; Ogawa, A.; Miyazaki, S.; Ryu, I.; Kambe, N.; Sonoda, N. *J. Am. Chem. Soc.* **1991**, *113*, 9796 (chapter **1**).

(19) For the ability of thiol to cleave the alkyl-metal bond, see: Johnson, A.; Puddephatt, R. J. *J. Chem. Soc., Dalton Trans.* **1975**, 115.

4-2. Transition-Metal-Catalyzed Hydroselenation of Acetylenes

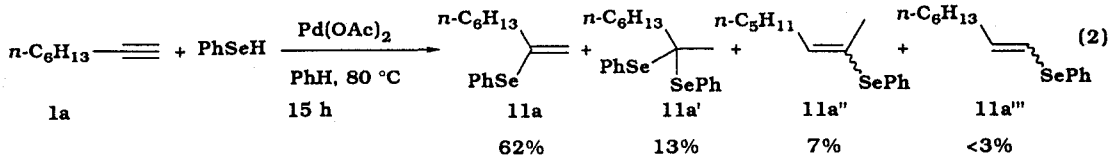
4-2-1. Introduction

Transition-metal-catalyzed Addition of heteroatom-hydrogen bonds to carbon-carbon multiple bonds is one of the most challenging subjects in organic chemistry. Along this line, the hydrosilylation,[1] hydrostannation,[2] and hydroboration[3] have been well-documented. However, there are few reports of a similar activation of heteroatom-hydrogen bond in which hydrogen is more electropositive than the heteroatom. In this section, we divulge the first example of transition-metal-catalyzed hydroselenation of acetylenes to give vinyl selenides[4] with high regioselectivity as shown in eq 1.



4-2-2. Results and Discussion

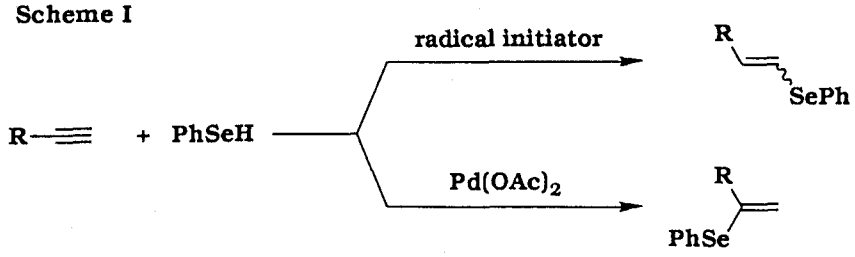
Addition of Benzeneselenol to Terminal Acetylenes: To a mixture of 1-octyne (**1a**) (1.0 mmol) and palladium acetate [$Pd(OAc)_2$] (0.02 mmol) in benzene (0.5 mL) was added benzeneselenol (1.0 mmol) under Ar atmosphere. Brown precipitates immediately deposited. After the mixture was heated at 80 °C for 15 h, the precipitated palladium complex was removed through Celite and the resultant mixture was purified by preparative TLC (silica gel) to give 2-phenylseleno-1-octene (**11a**) (62%) as the major product together with 2,2-bis(phenylseleno)octane (**11a'**) (13% based on **1a**), 2-phenylseleno-2-octene (**11a''**) (7%, *E*/*Z* = 30/70), and 1-phenylseleno-1-octene (**11a'''**) (<3%) (eq 2).

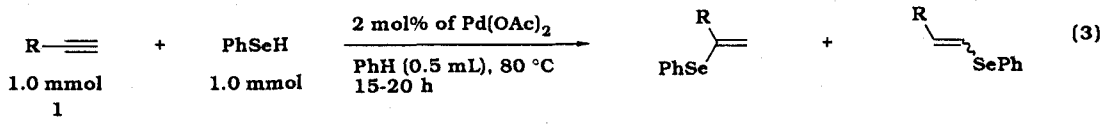


In the presence of AcOH (0.02 mmol) as a catalyst or in the absence of catalyst under otherwise identical conditions, the addition scarcely proceeded. While the free-radical addition of selenols to terminal acetylenes was reported to provide the anti-Markovnikov adducts,[5] the present $Pd(OAc)_2$-catalyzed reaction afforded the Markovnikov adducts as the major product. Accordingly, these methods are regiocomplementary for the synthesis of vinyl selenides from terminal acetylenes and benzeneselenol (Scheme I).

The results of the hydroselenation of some terminal acetylenes with benzeneselenol were shown in eq 3.

Scheme I

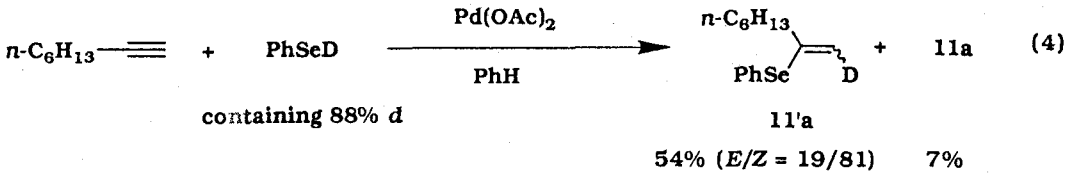




1a, R = n-C_6H_{13}	**11a**, 62%[a]	**11a'''**, <3%[b]
1b, R = $HO(CH_3)_2C$	**11b**, 72%[a]	**11b'''**, <1%[b]
1c, R = CH_2=$CHCH_2(CO_2Et)_2CCH_2$	**11c**, 73%[a]	**11c'''**, trace
1d, R = Ph	**11d**, 33%[b]	**11d'''**, 64%[b] (E/Z = 23/77)

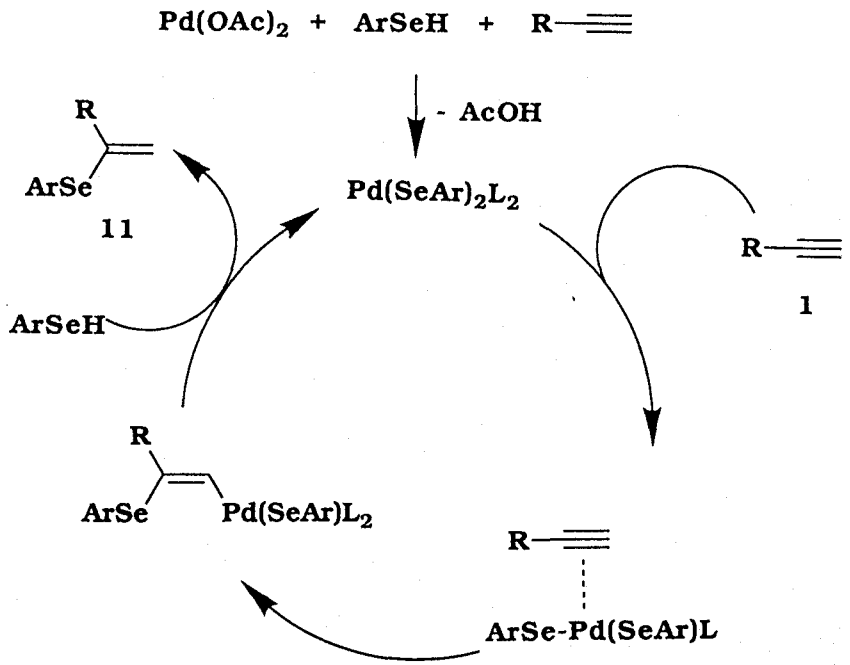
[a]Isolated yield. [b]NMR yield.

Both hydroxy and ester groups in acetylenes (**1b** and **1c**) did not affect the reaction. When the enyne **1c** was used as a substrate, the hydroselenation took place chemoselectively at the triple bond and the formation of cyclization products were not confirmed. The reaction of PhSeH to phenylacetylene (**1d**), however, permitted the formation of the regioisomer **11d'''** as the major product, probably because the free-radical addition to **1d** proceeded competitively in this reaction system.[6] To elucidate the stereochemistry of this $Pd(OAc)_2$-catalyzed hydroselenation, the reaction of PhSeD (containing 88% *d* determined by ^{1}H NMR spectrum) to 1-octyne (**1a**) was carried out at 80 °C for 15 h (eq 4). The *E*/*Z* ratio of **11'a** was tentatively determined as *E*/*Z* = 19/81 from the ratio of two vinyl protons of ^{1}H NMR spectroscopy.[7] This observed preponderance of *Z* isomer clearly indicates that the *cis* addition proceeded at least to a considerable extent.



Although it may be premature to discuss the reaction mechanism, a possible reaction path for this $Pd(OAc)_2$-catalyzed hydroselenation is envisioned in Scheme II. The reaction is initiated by the substitution of acetoxy ligands on palladium for PhSe group with generation of acetic acid, followed by coordination of acetylene to the palladium complex and regioselective insertion of the triple bond into Pd-Se bond. The resulting *cis* vinylpalladium intermediate is trapped by PhSeH[8] or AcOH with retention of the stereochemistry to produce the Markovnikov adduct with regeneration of the catalyst.

Scheme II. A Possible Reaction Path for the $Pd(OAc)_2$-Catalyzed Hydroselenation of Terminal Acetylene



Addition of Benzeneselenol to 1-Octyne Catalyzed by a Variety of Transition-Metal Complexes: Table I summarized the results of the hydroselenation of **1a** with PhSeH using other transition-metal catalysts. A variety of transition-metal catalysts, namely, platinum, palladium, rhodium, and nickel complexes, indeed exhibited the catalytic activities for this reaction. When $Pt(PPh_3)_4$ was employed as a catalyst, **11a''** was obtained in good yield. It has already reported that the stoichiometric reaction of PhSeH with $Pt(PPh_3)_4$ gave the $Pt(PPh_3)_2(SePh)(H)$.[9] Thus, when the reaction of a mixture of **11a** and **11a''** (**11a**:**11a''** = 80:20) with 2 mol% of $Pt(PPh_3)_4$ and 30 mol% of PhSeH was carried out at 80 °C for 15 h, the ratio was changed to **11a**:**11a''** = 7:93. This fact may suggest that **11a** is a kinetic product and isomerizes to **11a''** promoted by the Pt-H species in this reaction system.

Table I. Hydroselenation of 1-Octyne (1a) in the Presence of Several Transition-Metal Catalysts[a]

catalyst	11a	11a'	11a''	11a'''
$Pt(PPh_3)_4$	9%	-	81%	-
$Pd(PPh_3)_4$	2%	-	48%	-
$PdCl_2(PPh_3)_2$	3%	-	72%	-
$PdCl_2(PhCN)_2$	4%	-	68%	-

catalyst	11a	11a'	11a''	11a'''
$Rh(PPh_3)_3Cl_2$	15%	-	7%	15%
$Ni(PPh_3)_2Cl_2$	13%	-	-	-
$PdCl_2$	34%	16%	24%	-

[a]Reaction conditions: catalyst (0.02 mmol), **1a** (1.0 mmol), and PhSeH (1.0 mmol), PhH (0.5 mL), 80 °C, 14-16 h. Yields were determined by GLC or ^1H NMR.

Conclusion: Although organic selenide have been widely accepted as catalyst poisons,[10] this study clearly reveals that benzeneselenol also can be successfully employed in transition-metal-catalyzed reaction. Our efforts are continuing with emphases on the scope and mechanism of these catalytic transformations.

4-2-3. References and Notes

(1) Ojima, I. In *The Chemistry of Organic Silicon Compounds*; Patai, S., Rappoport, Z., Eds.; Wiley-Interscience: Chichester, 1989; Chapter 25.

(2) Zhang, H. X.; Guibe, F.; Balavoine, G. *J. Org. Chem.* **1990**, *55*, 1857 and references therein.

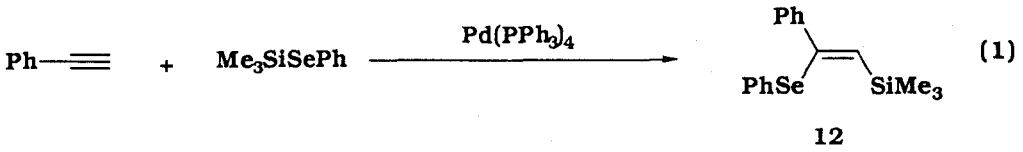
(3) (a) Mannig, D.; Noth, H. *Angew. Chem., Int. Ed. Engl.* **1985**, *24*, 878. (b) Burgess, K.; Donk, W. A.; Westcott, S. A.; Marder, T. B.; Baker, R. T.; Calabrese, J. C. *J. Am. Chem. Soc.* **1992**, *114*, 9350 and references therein.
(4) For the synthetic utility of vinyl selenides, see: (a) Comasseto, J. V. *J. Organomet. Chem.* **1983**, *253*, 131. (b) Paulmier, C. *Selenium Reagents and Intermediates in Organic Synthesis*; Pergamom Press: Oxford, 1986.
(5) For the addition of selenols to acetylenes, see: Comasseto, J. V.; Ferreira, J. T. B. *J. Organomet. Chem.* **1981**, *216*, 287 and references therein.
(6) Ogawa, A.; Obayashi, R.; Sekiguchi, M.; Masawaki, T.; Kambe, N.; Sonoda, N. *Tetrahedron Lett.* **1992**, *33*, 1329.
(7) It remains unclear whether the product containing two deuteriums is included or whether the deuterium isotope effect is observed in this reaction.
(8) Puddephatt, R. J.; Thompson, P. J. *J. Organomet. Chem.* **1976**, *117*, 395.
(9) Kawakami, K.; Ozaki, Y.; Tanaka, T. *J. Organomet. Chem.* **1974**, *69*, 151.
(10) For the stoichiometric reactions of selenium compounds with transition-metal complexes, see: Gysling, H. J. In *The Chemistry of Organic Selenium and Tellurium Compounds*; Patai, S., Rappoport, Z., Eds.; Wiley: New York, 1986; Vol. 1, P679.

4-3. Palladium-Catalysed Regio- and Stereoselective Silylselenation of Phenylacetylene

4-3-1. Introduction

Transition-metal-catalyzed addition of heteroatom-heteroatom and heteroatom-hydrogen bonds to carbon-carbon unsaturated bonds is an interesting and challenging subject in organic chemistry. Along this line, the additions to acetylenes of 14 group compounds like disilanes,[1] distannanes,[2] silylstannanes,[3] and hydrosilanes,[4] hydrostannanes[5] have been well-documented. On the other hand, the authors have found that the addition of 16 group compounds such as disulfides, diselenides (chapter **1**), thiols (chapter **4-1**), and selenols (chapter **4-2**), which have been believed to act as catalyst poison, were indeed catalyzed by transition-metal catalysts successfully.

The authors disclose here the first example of the palladium-catalyzed addition of silylselenide to phenylacetylene leading to alkene introduced vicinal silyl- and selenenyl-substituents with regio- and stereoselectivity according to eq 1.

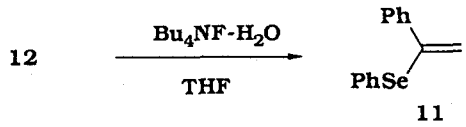


(1)

12

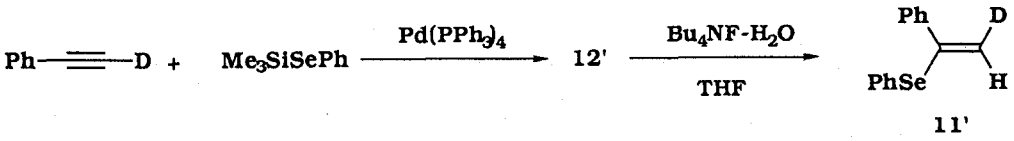
4-3-2. Results and discussion

We attempted the preliminary experiments of the reaction (neat, 120 °C, 24 h) of (trimethylsily)phenylselenide ($Me_3SiSePh$) (0.4 mmol) with phenylacetylene (0.6 mmol) in the presence of various transition-metal catalysts (5 mol%) at 120 °C for 24 h without solvent. Among the catalysts examined, $Pd(PPh_3)_4$ exhibited catalytic activity to give (Z)-1-phenyseleno-1-phenyl-2-(trimethylsilyl)-ethylene (**12**)[6] in 21% yield without formation of the stereo- or regioisomers of **12** and adducts of $(PhSe)_2$ or $(Me_3Si)_2$ to phenylacetylene. The assignment of regiochemistry of **12** was made by the result of protodesilylation of **12** with *n*-Bu_4NF (1N in THF-H_2O)[7], which afforded 1-phenyl-1-phenylselenoethene (**11**), not 1-phenyl-2-phenylselenoethene (eq 2). The stereochemistry of **12** was confirmed by the result of a similar protodesilylation of the adduct **12'** obtained by the reaction of phenylacetylene-1-*d* with $Me_3SiSePh$ (eq 3). The vinyl signals of the product **11'** after protodesilylation predominantly appeared uper field.[8] Considering that the protodesilylation of vinylsilanes proceeds with retention of stereochemistry[7], this observation unambiguously indicates that the stereochemistry of **11'** is *trans* and the stereochemistry of **12'** (also **12**) is *cis*.



11

(2)

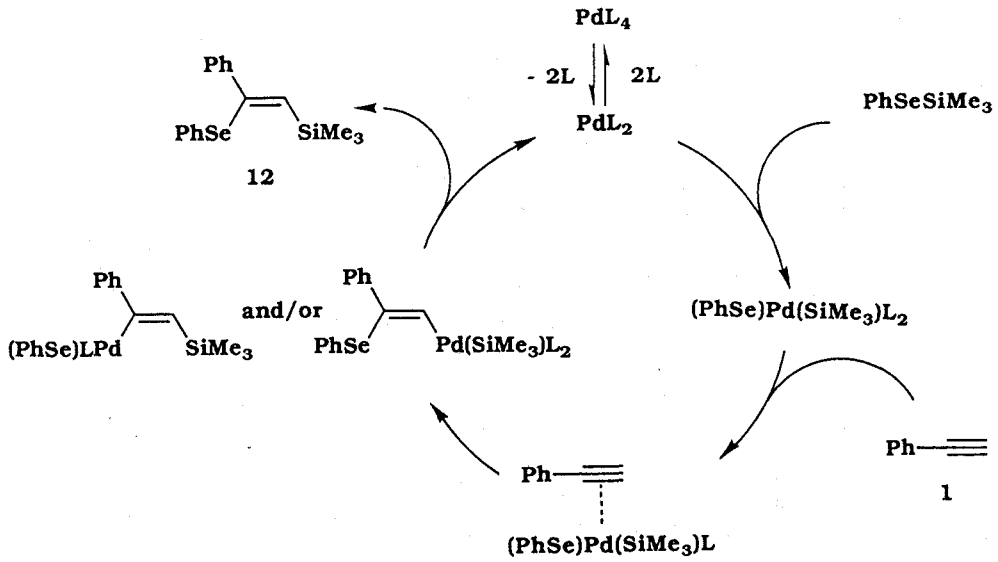


11'

(3)

Although it may be premature to discuss the reaction mechanism, a possible active species is PhSe[Pd]$SiMe_3$ which is generated by the oxidative addition of $Me_3SiSePh$ to low-valent palladium complex. The *cis*-insertion of phenylacetylene to Se-Pd or Si-Pd bond of this complex, followed by reductive elimination of the product **12** (Scheme I).

Scheme I. A Proposed Reaction Path for the $Pd(PPh_3)_4$-Catalyzed Addition of $Me_3SiSePh$ to Phenylacetylene



In conclusion, the palladium-catalyzed 1,2-silylselenation of phenylacetylene gave (Z)-1-phenylseleno-1-pheny-2-(trimethylsilyl)ethylene selectively. Since vinylsilanes[9] and vinyl selenides[10] are important synthetic intermediates in organic chemistry, the present reaction offers a very attractive methodology to provide vicinal silyl- and selenenyl-substituted alkene. Further studies on the scope and limitation of the transition-metal-catalyzed addition of 14-16 group element compounds to carbon-carbon unsaturated bonds are currently under investigation.[11]

4-3-3. References and Notes

(1) (a) Tamao, K.; Hayashi, T.; Kumada, M. *J. Organomet. Chem.* **1976**, *114*, C19. (b) Sakurai, H.; Kamiyama, Y.; Nakadaira, Y. *J. Am. Chem. Soc.* **1975**, *97*, 931. (c) Watanabe, H.; Kobayashi, M.; Higuchi, K.; Nagai, Y. *J. Organomet. Chem.* **1980**, *186*, 51.

(2) Mitchell,T. N.; Amamria, A.; Killing, H; Rutschow, D. *J. Organomet. Chem.* **1983**, *241*, C45.

(3) Mitchell, T. N.; Wickenkamp, R.; Amamria, A.; Dicke, R.; Schneider, U. *J. Org. Chem.* **1987**, *52*, 4868.

(4) Ojima, I. In *The Chemistry of Organic Silicon Compounds*; Patai, S., Rappoport, Z., Eds.; Wiley-Interscience: Chichester, 1989; Chapter 25.

(5) Zhang, H. X.; Guibe, F.; Balavoine, G. *J. Org. Chem.* **1990**, *55*, 1857.

(6) Spectroscopic data of **12**: oil; ^{1}H NMR (270 MHz, $CDCl_3$) δ 0.27 (s, 9 H), 6.68 (s, 1 H), 7.05-7.53 (m, 10 H); ^{13}C NMR (68 MHz, $CDCl_3$) δ -0.50, 126.27, 127.88, 127.88, 128.77, 131.41, 131.46, 140.69 ; mass spectrum (EI) m/e 332 (M^+, 1.4); Anal. Calcd for $C_{17}H_{20}SeSi$: C, 61.62; H, 6.08. Found: C, 61.89; H, 6.01.

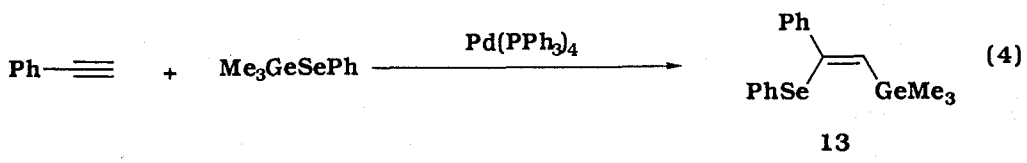
(7) Oda, H.; Sato, M.; Morizawa, Y.; Oshima, K.; Nozaki, H. *Tetrahedron* **1985**, *41*, 3257.

(8) The signal of the vinylic proton at the *cis* for PhSe group appeared upper field than that of *trans*, see chapter **4-2**.

(9) Weber, W. P. *Silicon Reagents in Organic Synthesis*, Springer-Verlag, Berlin, Heidelberg, New York, 1983.

(10) For the synthetic utility of vinyl selenides, see: (a) Comasseto, J. V. *J. Organomet. Chem.* **1983**, *253*, 131. (b) Paulmier, C. *Selenium Reagents and Intermediates in Organic Synthesis*; Pergamom Press: Oxford, 1986.

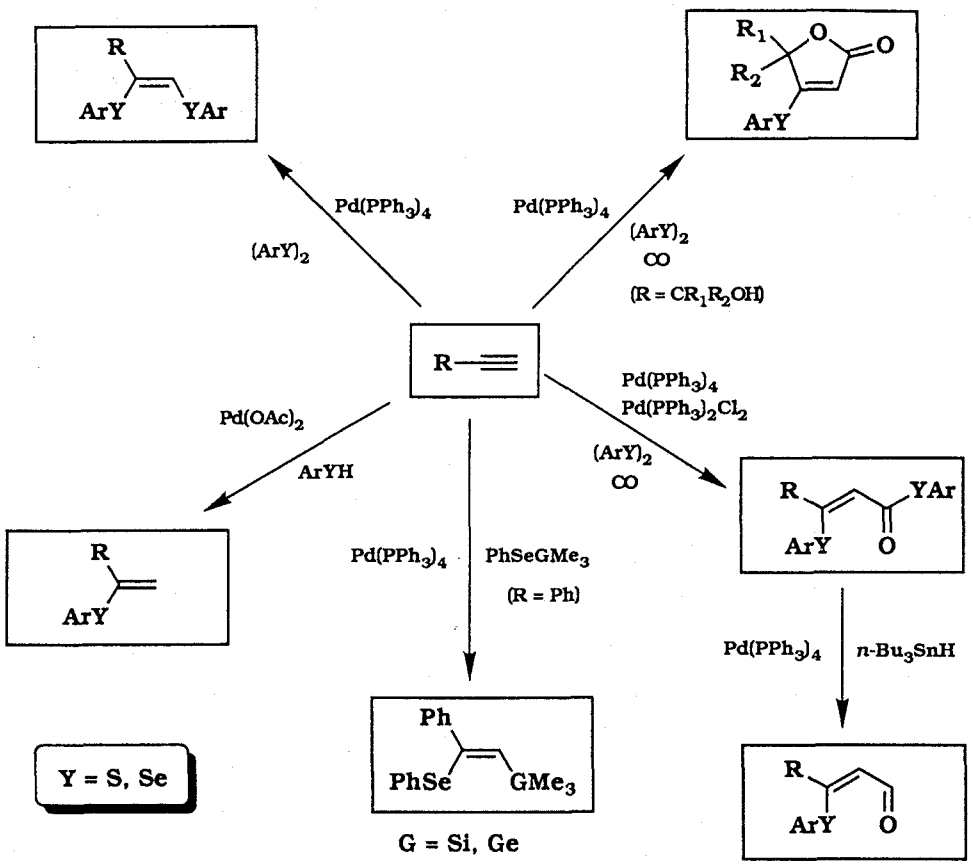
(11) For example, the addition of (trimethylgermyl)phenylselenide to phenylacetylene also catalyzed by $Pd(PPh_3)_4$ to give (Z)-1-phenyseleno-1-phenyl-2-(trimethylgermyl)ethylene (**13**) in 35% yield under similar reaction conditions (eq 4).



(4)

13

Conclusion



The transition-metal-catalyzed addition of heteroatom-heteroatom and heteroatom-hydrogen bonds to acetylenes is among the most interest subjects in organometallic chemistry. This thesis divulges the palladium-catalyzed stereoselective double thiolation and double selenation of acetylenes (chapter **1**), transition-metal-catalyzed regioselective hydrothiolation (chapter **4-1**) and hydroselenation (chapter **4-2**) of acetylenes, palladium-catalyzed regio- and stereoselective silyl- and germylselenation of phenylacetylene (chapter **4-3**). Furthermore the palladium-catalyzed regio- and stereoselective carbonylative double thiolation and double selenation to acetylene (chapter **2-1**) and palladium-catalyzed one-pot lactonization of propargyl alcohols *via* the carbonylative addition (chapter **2-2**) were also demonstrated. This study also developed a new

access to aldehydes from thioesters and selenoesters, namely, palladium-catalyzed reduction of the compounds obtained by the carbonylative addition reaction described in chapter **2-1** with *n*-Bu_3SnH as a reducing reagent. The thioester part (chapter **3-1**) and selenoester part (chapter **3-2**) were chemoselectively and site-selectively converted to formyl group under very moderate reaction conditions.

These reactions clearly disclose that the transition-metal catalysts are indeed available for the synthetic reactions of organic sulfides and selenides, which have been widely regarded as poisons for transition-metal catalyst. The author believes that this study will generate considerable significant advances in both the organic and the organometallic fields.

List of Publications

(1) Palladium-Catalyzed Addition and Carbonylative Addition of Diaryl Disulfides and Diselenides to Terminal Acetylenes (chapter **1** and **2-1**)
Kuniyasu, H.; Ogawa, A.; Miyazaki, S.; Ryu, I.; Kambe, N.; Sonoda, N. *J. Am. Chem. Soc.* **1991**, *113*, 9796.

(2) One-Pot Lactonization of Propargyl Alcohols *via* Palladium-Catalyzed Carbonylative Double Thiolation and Selenation (chapter **2-2**)
Kuniyasu, H.; Ogawa, A.; Sonoda, N., submitted to *J. Org. Chem.*

(3) Chemoselective Conversion of Thioesters to Aldehydes: Palladium-Catalyzed Reduction of (*Z*)-1,3-Bis(arylthio)-2-alken-1-ones with *n*-Bu_3SnH (chapter **3-1**)
Kuniyasu, H.; Ogawa, A.; Sonoda, N., submitted to *Tetrahedron Lett.*

(4) Palladium-Catalyzed Chemoselective and Site-Selective Reduction of (*Z*)-1,3-Bis(arylseleno)-2-alken-1-ones with *n*-Bu_3SnH (chapter **3-2**)
Kuniyasu, H.; Ogawa, A.; Higaki, K.; Sonoda, N. *Organometallics* **1992**, *11*, 3937.

(5) The First Example of Transition-Metal-Catalyzed Addition of Aromatic Thiols to Acetylenes (chapter **4-1**)
Kuniyasu, H.; Ogawa, A.; Sato, K.; Ryu, I.; Kambe, N.; Sonoda, N. *J. Am. Chem. Soc.* **1992**, *114*, 5902.

(6) The First Example of Transition-Metal-Catalyzed Hydroselenation of Acetylenes (chapter **4-2**)
Kuniyasu, H.; Ogawa, A.; Sato, K.; Ryu, I.; Sonoda, N. *Tetrahedron Lett.* **1992**, *33*, 5525.

(7) Palladium-Catalyzed Regio- and Stereoselective Addition of Silicon-Selenium Bond to Phenylacetylene (chapter **4-3**)
Kuniyasu, H.; Ogawa, A.; Takeba, M.; Kambe, N.; Sonoda, N., in preparation.

List of Other Publications

(1) Oxidation of 1,2-Bis(phenylseleno)-1-alkenes. A Novel Example of Selenoxide *anti*-Elimination
Ogawa, A.; Sekiguchi, M.; Shibuya, H.; Kuniyasu, H.; Takami, N.; Ryu, I.; Sonoda, N. *Chem. Lett.* **1991**, 1805.

(2) A Novel Thermal Addition of Diaryl Diselenides to Acetylenes
Ogawa, A.; Takami, N.; Sekiguchi, M.; Yokoyama, H.; Kuniyasu, H.; Ryu, I.; Sonoda, N.
Chem. Lett. **1991**, 2241.

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Finally the author would like to express his thanks to his parents for their understanding and encouragement.

Suita, Osaka
January, 1993

Hitoshi Kuniyasu