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A novel palladium(0)-catalyzed addition of diphenyl disulfide to allenes leading to vicinal disulfides and its application to carbonylation with carbon monoxide

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Abstract—Tetrakis(triphenylphosphine)palladium(0) catalyzes a highly regioselective bisthiolation of terminal allenes with diphenyl disulfide to afford the corresponding 2-(phenylthio)-substituted allyl sulfides in good yields. In addition, this reaction system can be applied to the carbonylation under pressurized carbon monoxide.

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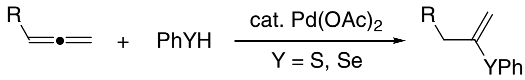
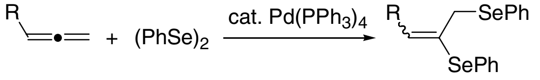
Heteroatom compounds can be employed as useful synthetic intermediates in organic synthesis. Hence, it is of great importance to develop atom-economically and environmentally superior routes to various heteroatom compounds. As one of the methods for realizing this purpose, transition-metal-catalyzed addition reactions of heteroatom compounds to carbon–carbon unsaturated bonds are promising. However, group 16 heteroatom compounds have been believed to work as catalyst poisons, and therefore, examples of transition-metal-catalyzed addition of group 16 heteroatom compounds to unsaturated bonds, especially carbon–carbon double bonds, are still rare.[1,2]

With the aim of extending the transition-metal-catalyzed reactions of group 16 heteroatom compounds, we reported the palladium acetate-catalyzed addition reactions of benzenethiol and benzeneselenol to allenes as activated double bond compounds, Eq. 1.[2a,b,3]



(1)

Furthermore, we have recently developed that the addition of diphenyl diselenide to allenes takes place regioselectively in the presence of tetrakis(triphenylphosphine)palladium catalyst, Eq. 2.[2g] Previously, we reported a similar bisselenation reaction of allenes with $(PhSe)_2$ proceeded with the same regioselectivity under the photoirradiated radical conditions, Eq. 3.[4]



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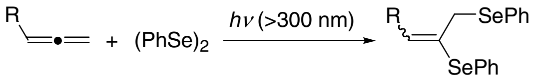
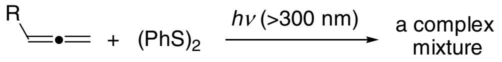


(3)

In contrast, the photoinduced reaction of diphenyl disulfide with allenes resulted in a complex mixture, because of the relatively lower carbon radical capturing ability of $(PhS)_2$ (compared with $(PhSe)_2$), Eq. 4.[4]



(4)

Accordingly, the development of transition-metal-catalyzed addition of disulfides to allenes is strongly desirable.[2f] Herein, we report a highly regioselective bisthiolation of allenes with diphenyl disulfide in the presence of tetrakis(triphenylphosphine)palladium(0) catalyst, Eq. 5.[5]

Keywords: Bisthiolation; Allenes; Diphenyl disulfide; Tetrakis(triphenylphosphine)palladium(0); Carbon monoxide.

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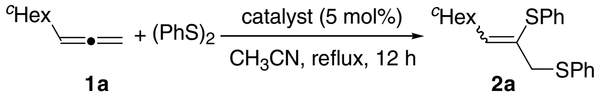
Table 1. Transition-metal-catalyzed bisthiolation of cyclohexylallene



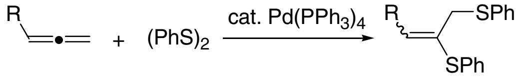
Entry	Catalyst	Yield[a] (%)	[*E*/*Z*]
1	$Pd(PPh_3)_4$	84[b]	[62/38]
2	$Pd(OAc)_2$	12	[62/38]
3	$PdCl_2(PPh_3)_2$	Trace	—
4	$RhCl(PPh_3)_3$	26	[38/62]
5	$Pt(PPh_3)_4$	No reaction	—
6[c]	$Pd(PPh_3)_4$	75	[87/13]
7	No catalyst	No reaction	—

Reaction conditions: catalyst (5 mol %), **1a** (0.6 mmol), CH_3CN (0.5 mL), $(PhS)_2$ (0.5 mmol), 12 h.

[a] Determined by ^1H NMR.

[b] Isolated yield.

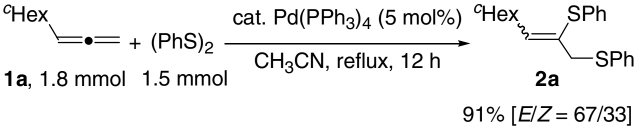
[c] Allene **1a** (0.5 mmol).



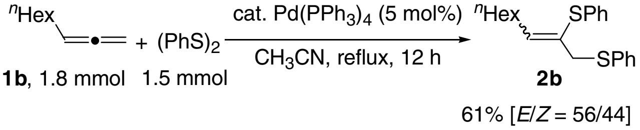
(5)

We first examined the addition reactions of diphenyl disulfide to cyclohexylallene by varying the catalysts (Table 1).

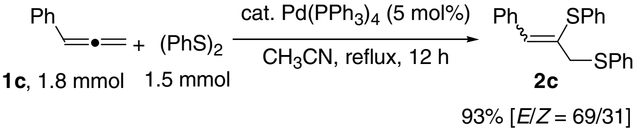
Among the catalysts employed, tetrakis(triphenylphosphine)palladium(0) exhibited the highest catalytic activity toward the desired addition reaction of $(PhS)_2$ to **1a** (entry 1). As for Pd(II) complexes, $Pd(OAc)_2$ also exhibited catalytic activity toward this bisthiolation, whereas $PdCl_2(PPh_3)_2$ was ineffective (entries 2 and 3). In addition, $RhCl(PPh_3)_3$ exhibited catalytic activity toward the bisthiolation (entry 4). $Pt(PPh_3)_4$ did not catalyze the reaction (entry 5). In the $Pd(PPh_3)_4$-catalyzed reaction, the use of slightly excess amounts of **1a** to $(PhS)_2$ is effective (entries 1 and 6). In the absence of the catalyst, no reaction took place (entry 7). These results clearly demonstrate that the present bisthiolation of allene **1a** proceeds as a catalytic reaction of several transition metal catalysts.[6]



(6)

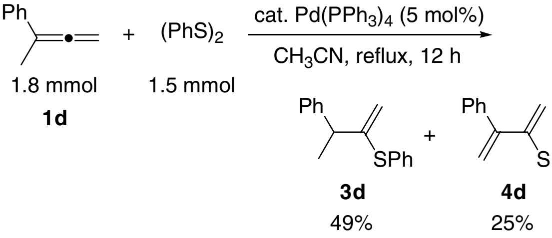


(7)



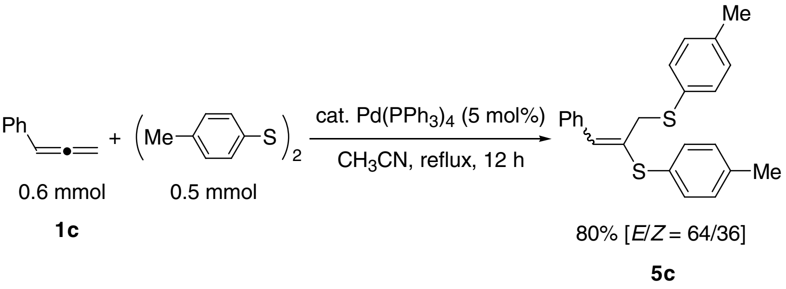
(8)

Next, we examined the $Pd(PPh_3)_4$-catalyzed addition of $(PhS)_2$ to several allenes.[7,8] Secondary alkyl substituted allene **1a** underwent regioselective bisthiolation with $(PhS)_2$ in high yield, Eq. 6.[9] Similar conditions could be employed with primary alkyl substituted allene **1b**, Eq. 7, whereas no reaction was observed with tertiary alkyl substituted allene such as *t*-butylallene. Phenylallene (**1c**) also underwent bisthiolation regioselectively in high yield, Eq. 8.



(9)

In the case of 1,1-disubstituted allene **1d**, however, the desired bisthiolation product was not obtained, and instead, vinylic sulfide **3d** and diene **4d** were obtained in 49% and 25% yields, respectively, Eq. 9.

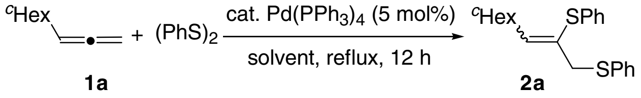


(10)

Table 2 summarizes the results of the palladium-catalyzed bisthiolation of **1a** in various solvents. Acetonitrile and 1,2-dichloroethane worked as excellent solvents, leading to the formation of **2a** in high yield (entries 4 and 5). In other solvents, such as benzene, THF, pyridine, and ethanol, **2a** was obtained in moderate yield (entries 1–3, 6).

The optimized conditions for the bisthiolation of allenes were employed for the bisthiolation of phenylallene (**1c**) with other disulfides such as *p*-tolyl disulfide and dibutyl disulfide. *p*-Tolyl disulfide could be used for the regioselective bisthiolation of phenylallene in high yield, Eq. 10, whereas no reaction was observed with dibutyl disulfide.

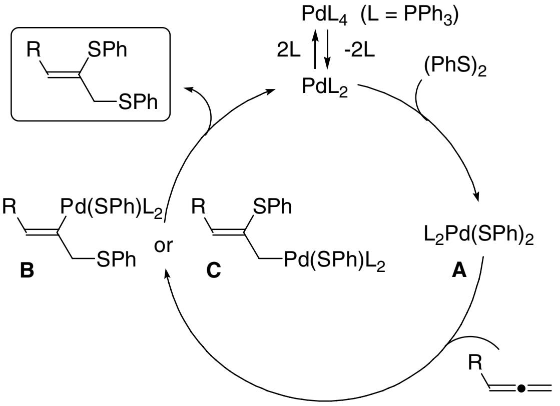
Table 2. Influence of solvents on the palladium-catalyzed bisthiolation



Entry	Solvent	Temperature (°C)	Yield[a] (%)	[*E*/*Z*]
1	Benzene	80	69	[67/33]
2	THF	69	46	[69/31]
3	Pyridine	115	62	[58/42]
4	$ClCH_2CH_2Cl$	83	88	[91/9]
5	CH_3CN	82	88	[97/3]
6	EtOH	78	55	[90/10]

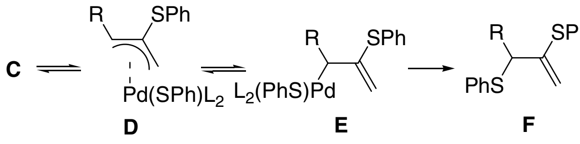
Reaction conditions: $Pd(PPh_3)_4$ (5 mol %), cyclohexylallene (0.6 mmol), solvent (0.5 mL), $(PhS)_2$ (0.5 mmol).

[a] Determined by ^1H NMR.



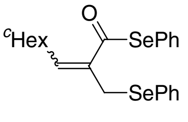
Scheme 1. A possible pathway for bisthiolation of allenes.

Scheme 1 shows a possible reaction pathway, which includes the following: (i) $(PhS)_2$ adds oxidatively to the low-valent palladium(0) complex, that is, $Pd(PPh_3)_2$, to generate an active catalyst **A**; (ii) allene coordinates to the palladium species **A** and then thiopalladation of allene takes place at the terminal carbon–carbon double bond to form either vinylpalladium intermediate **B** or σ-allylpalladium intermediate **C**; (iii) reductive elimination takes place to form the bisthiolation product with regeneration of the catalyst.

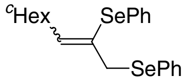


(11)

As shown in Eq. 11, if **C** is in equilibrium with π-allylpalladium intermediate **D**, **D** may generate σ-allylpalladium intermediate **E** to provide the corresponding regioisomeric bisthiolation product **F**. However, no formation of **F** was observed in the optimized conditions for the bisthiolation of allenes.[10] Thus, we estimate that the reductive elimination of bisthiolation product from σ-allylpalladium intermediate **C** is very fast, not generating π-allylpalladium intermediate **D**.



6a



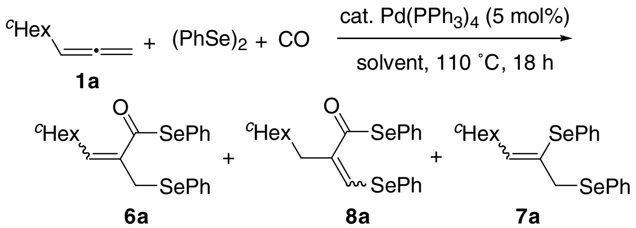
7a

In our previous paper concerning the palladium-catalyzed bisselenation of allenes with diphenyl diselenide, we reported a preliminary result of the selenative carbonylation of allenes in the presence of carbon monoxide (30 atm), in order to clarify the reaction pathway for the catalytic bisselenation of allenes. In this reaction in CH_3CN, the desired carbonylation product **6a** was obtained in a moderate yield (ca. 30%) along with bisselenation product **7a**. Therefore, we were interested in conducting the bisthiolation under the pressure of carbon monoxide.

Before examining the carbonylation of allenes with $(PhS)_2$ and CO, we examined the optimization of the selenative carbonylation of allenes with $(PhSe)_2$ and CO by varying the catalysts, solvents, and some other conditions (Tables 3 and 4). In the selenative carbonylation of cyclohexylallene (**1a**), increase in the molar ratio of allene/$(PhSe)_2$ and prolonged reaction time improved the yields of the carbonylation products **6a** and **8a**, although carbon–carbon double bond isomerization took place competitively (Table 3, entry 1). THF as a solvent was ineffective (entry 2). The use of toluene as the solvent suppressed the isomerization, affording the desired selenative carbonylation product **6a** in 70% yield (entry 3).

Table 4 indicates the results of the carbonylation in the presence of various transition metal catalysts. Tetrakis(triphenylphosphine)palladium(0) exhibited the highest catalytic activity toward the carbonylative bisselenation of **1a** (entry 3). The reaction did not finish for 9 h completely (entry 4). Under the higher pressure (60 atm) of carbon monoxide, the carbonylation pro-

Table 3. Influence of solvents on carbonylative addition of $(PhSe)_2$

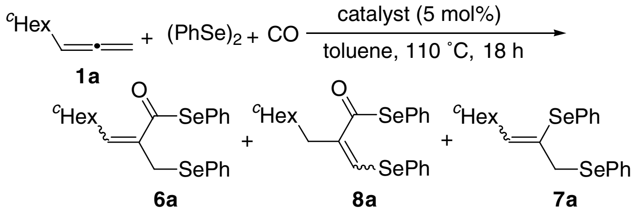


Entry	Solvent	Yield[a] (%) [*E*/*Z*]		
		6a	**8a**	**7a**
1	CH_3CN	39 [33/67]	34 [38/62]	21 [60/40]
2	THF	23 [30/70]	7 [1/99]	0
3	Toluene	70 [39/61]	16 [25/75]	8 [36/64]

Reaction conditions: $Pd(PPh_3)_4$ (5 mol %), cyclohexylallene (1.5 mmol), solvent (0.5 mL), $(PhSe)_2$ (1 mmol), CO (30 atm), 110 °C, 18 h.

[a] Determined by ^1H NMR.

Table 4. Transition-metal-catalyzed carbonylative addition of $(PhSe)_2$ to cyclohexylallene



Entry	CO (atm)	Catalyst	Yield[a] (%) [*E*/*Z*]		
			6a	**8a**	**7a**
1[b]	20	$PdCl_2(PPh_3)_2$	14 [43/57]	Trace	Trace
2	30	$PdCl_2(PhCN)_2$		No reaction	
3	30	$Pd(PPh_3)_4$	70 [39/61]	16 [25/75]	8 [36/64]
4[c]	30	$Pd(PPh_3)_4$	51 [37/63]	15 [31/69]	3 [30/70]
5	60	$Pd(PPh_3)_4$	51 [33/62]	36 [22/78]	Trace
6	30	$RhCl(PPh_3)_3$	0	0	12 [43/57]
7	30	$RhH(CO)(PPh_3)_3$		A complex mixture	
8	30	$Pt(PPh_3)_4$	0	0	18 [44/56]
9	30	No catalyst		No reaction	

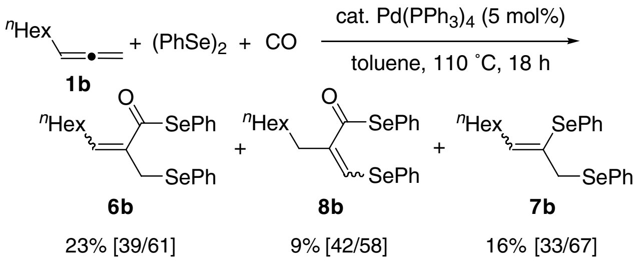
Reaction conditions: catalyst (5 mol %), cyclohexylallene (1–1.5 mmol), toluene (0.5 mL), $(PhSe)_2$ (1 mmol), CO (30 atm), 110 °C, 18 h.

[a] Determined by ^1H NMR.

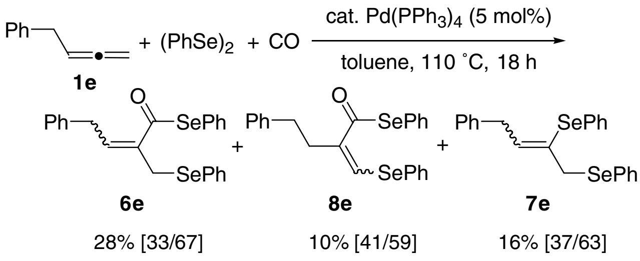
[b] Cyclohexylallene (1 mmol).

[c] 9 h.

ceeded efficiently, but the double bond isomerization took place competitively (entry 5). In the absence of the catalyst, no reaction took place; these results indicate that the present carbonylative bisselenation proceeds as a catalytic reaction by transition metal complexes (entry 9).

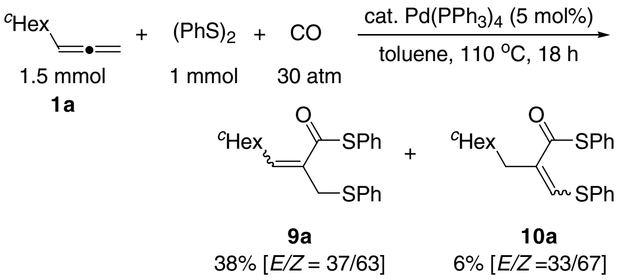


(12)



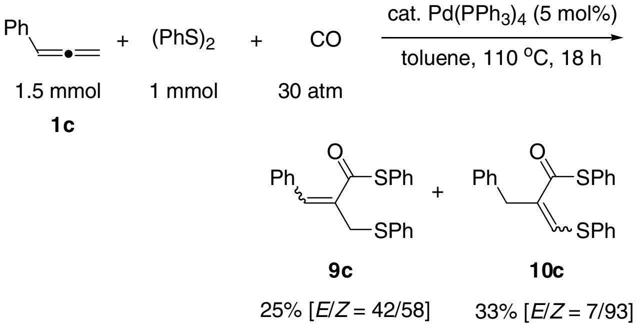
(13)

Next, we examined the $Pd(PPh_3)_4$-catalyzed selenative carbonylation of several allenes **1b** and **1e**. Both **1b** and **1e** underwent the carbonylative bisselenation, although the yields of the carbonylation products **6b** and **6e** were moderate, Eqs. 12 and 13.



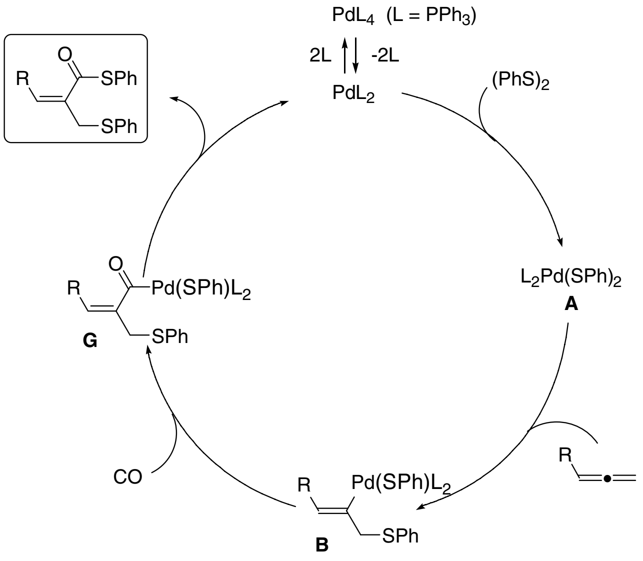
(14)

The optimized conditions for the selenative carbonylation were employed for the corresponding thiolative carbonylation of allenes with $(PhS)_2$ and CO. The desired thiolative carbonylation took place successfully, but the yields of the carbonylation products **9a** and **10a** are moderate, Eq. 14.



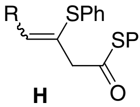
(15)

In addition, we examined the $Pd(PPh_3)_4$-catalyzed carbonylative addition of $(PhS)_2$ to other allenes. Benzylallene underwent carbonylative bisthiolation similarly to the reaction with cyclohexylallene (**1a**). In the case of phenylallene (**1c**), the double bond isomerised product **10c** was obtained as the major product, Eq. 15.[11]



Scheme 2. A possible pathway for carbonylative bisthiolation of allenes with (PhS)$_2$.

Scheme 2 shows a possible reaction pathway for this carbonylative bisthiolation, which includes the following: (i) After oxidative addition of (PhS)$_2$ to Pd(PPh$_3$)$_2$, thiopalladation of allene takes place at the terminal carbon–carbon double bond to form vinylpalladium intermediate **B**; (ii) carbon monoxide inserts into the Pd–C bond to form acylpalladium intermediate **G**; (iii) reductive elimination takes place to form the carbonylative bisthiolation product with regeneration of the catalyst. In this carbonylation, the product **H** derived from the carbonylation at the terminal carbon of allenes was not obtained at all. This result suggests that the thiopalladation of allenes takes place at the terminal carbon–carbon double bonds to form vinylpalladium intermediate **B**.



H

In summary, we have developed highly regioselective bisthiolation of allenes with diphenyl disulfide catalyzed by palladium(0) complex. Since radical addition of the disulfide to allenes affords a complex mixture, the present transition-metal-catalyzed reaction is useful for providing bisthiolated adducts. In addition, the carbonylative bisthiolation and bisselenation are investigated in detail. We believe that these reactions expand the utility of the transition-metal-catalyzed reactions of group 16 heteroatom compounds.

Acknowledgments

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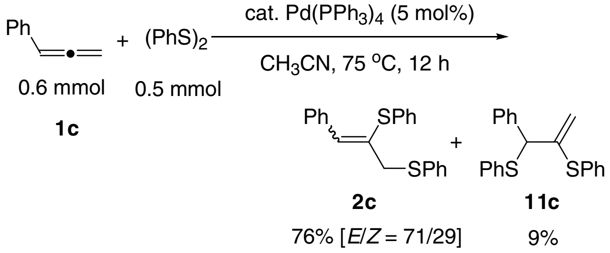
References and notes

1. For reviews concerning transition-metal-catalyzed addition reactions of group 16 heteroatom compounds to carbon–carbon unsaturated bonds, see: (a) Ogawa, A. In *Main Group Metals in Organic Synthesis*; Yamamoto, H., Oshima, K., Eds.; Wiley-VCH: Weinheim, 2004; Vol. 2, Chapter 15; (b) Beletskaya, I.; Moberg, C. *Chem. Rev.* **2006**, *106*, 2320–2354; (c) Alonso, F.; Beletskaya, I. P.; Yus, M. *Chem. Rev.* **2004**, *104*, 3079–3159; (d) Ogawa, A. In *Handbook of Organopalladium Chemistry for Organic Synthesis*; Negishi, E., Ed.; Wiley-Interscience: New York, 2002, Chapter VII.6; (e) El Ali, B.; Alper, H. In *Handbook of Organopalladium Chemistry for Organic Synthesis*; Negishi, E., Ed.; Wiley-Interscience: New York, 2002, Chapter VI.2.1.1.2; (f) Kuniyasu, H. In *Catalytic Heterofunctionalization*; Togni, A., Grützmacher, H., Eds.; Wiley-VCH: Weinheim, 2001, Chapter 7; (g) Kondo, T.; Mitsudo, T. *Chem. Rev.* **2000**, *100*, 3205–3220; (h) Ogawa, A. *J. Organomet. Chem.* **2000**, *611*, 463–474; (i) Beletskaya, I.; Moberg, C. *Chem. Rev.* **1999**, *99*, 3435–3461; (j) Han, L.-B.; Tanaka, M. *Chem. Commun.* **1999**, 395–402.
2. (a) Ogawa, A.; Kawakami, J.-i.; Sonoda, N.; Hirao, T. *J. Org. Chem.* **1996**, *61*, 4161–4163; (b) Ogawa, A.; Kudo, A.; Hirao, T. *Tetrahedron Lett.* **1998**, *39*, 5213–5216; (c) Xiao, W.-J.; Vasapollo, G.; Alper, H. *J. Org. Chem.* **1998**, *63*, 2609–2612; (d) Xiao, W.-J.; Alper, H. *J. Org. Chem.* **1999**, *64*, 9646–9652; (e) Kondo, T.; Uenoyama, S.; Fujita, K.; Mitsudo, T. *J. Am. Chem. Soc.* **1999**, *121*, 482–483; (f) Arisawa, M.; Suwa, A.; Fujimoto, K.; Yamaguchi, M. *Adv. Synth. Catal.* **2003**, *345*, 560–563; (g) Kamiya, I.; Nishinaka, E.; Ogawa, A. *Tetrahedron Lett.* **2005**, *46*, 3649–3652.
3. Transition-metal-catalyzed heterofunctionalization of allenes was reported. For reviews, see: (a) Yamamoto, Y.; Radhakrishnan, U. *Chem. Soc. Rev.* **1999**, *28*, 199–207; (b) Zimmer, R.; Dinesh, C. U.; Nandanan, E.; Khan, F. A. *Chem. Rev.* **2000**, *100*, 3067–3125; (c) Mandai, T. In *Modern Allene Chemistry*; Krause, N., Hashmi, A. S. K., Eds.; Wiley-VCH: Weinheim, 2004; Vol. 2, pp 925–972.
4. Ogawa, A.; Yokoyama, K.; Yokoyama, H.; Sekiguchi, M.; Kambe, N.; Sonoda, N. *Tetrahedron Lett.* **1990**, *31*, 5931–5934.
5. A stoichimetric reaction of a disulfide complex (Mo–Mn) with allenes has been reported, see: Adams, R. D.; Captain, B.; Kwon, O. S.; Miao, S. *Inorg. Chem.* **2003**, *42*, 3356–3365.
6. In addition, we conducted the Pd(PPh$_3$)$_4$-catalyzed addition of (PhS)$_2$ to **1a** in the presence of galvinoxyl to the reaction mixture. As a result, the bisthiolation of **1a** proceeded successfully.
7. General procedure for the Pd(PPh$_3$)$_4$-catalyzed bisthiolation of allenes: To a mixture of allene (0.5–1.8 mmol) and Pd(PPh$_3$)$_4$ (5 mol %) in solvent (0.5–1.5 mL) was added diphenyl disulide (0.5–1.5 mmol) under N_2 atmosphere. The resulting mixture was stirred magnetically for 12 h with heating at refluxing temperature (e.g., CH_3CN; 82 °C). After the reaction was complete, the reaction mixture was filtered through Celite, followed by washing with diethyl ether. The combined filtrate was concentrated under the reduced pressure. The products (**2**) were confirmed by ^{1}H NMR spectroscopy. The purification of the products was performed by preparative TLC on silica gel using hexane/AcOEt = 100:0–96:4 as an eluent.
8. The spectral and analytical data for the bisthiolation product, for example, **2a** is as follows: a yellow oil (obtained as a stereoisomeric mixture); ^{1}H NMR (400 MHz, $CDCl_3$) [*E*-isomer]: δ 1.02–1.13 (m, 5H), 1.14–1.42 (m, 3H), 1.50–1.62 (m, 2H), 1.98–2.10 (m,

1H), 3.64 (s, 2H), 5.81–5.85 (d, $J = 9.9$ Hz, 1H), 7.18–7.40 (m, 6H), 7.43–7.54 (m, 4H). [*Z*-isomer]: δ 1.02–1.13 (m, 5H), 1.14–1.42 (m, 3H), 1.50–1.62 (m, 2H), 2.59–2.70 (m, 1H), 3.54 (s, 2H), 5.73–5.77 (d, $J = 9.2$ Hz, 1H), 7.18–7.40 (m, 6H), 7.43–7.54 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) [*E*-isomer]: δ 25.6, 25.7, 32.7, 36.6, 38.9, 126.5, 126.7, 128.7, 129.0, 129.9, 131.7, 135.3, 147.0. [*Z*-isomer]: δ 25.6, 25.9, 32.5, 36.6, 38.9, 126.3, 126.9, 128.7, 128.8, 129.7, 131.5, 135.3, 145.6; IR (NaCl) 3059, 2922, 2849, 2318, 1583, 1506, 1475, 1437, 739, 691 cm^{-1}. Anal. Calcd for $C_{21}H_{24}S_2$: C, 74.06; H, 7.10; S, 18.83. Found: C, 73.78; H, 6.97; S, 18.54.

9. The $Pd(PPh_3)_4$-catalyzed bisthiolation of cyclohexylallene (**1a**) with $(PhS)_2$ in CD_3CN was monitored by taking ^{1}H NMR spectra: the *E*/*Z* ratio of **2a** (time) = 96/4 (4 h); 94/6 (10 h); 93/7 (20 h). However, the purification using preparative TLC on silica gel resulted in the formation of *Z*-isomer of **2a** (*E*/*Z* = 67/33).
10. The $Pd(PPh_3)_4$-catalyzed addition of $(PhS)_2$ to **1c** was conducted with heating at 75 °C, resulting in the formation of the regioisomer **11c** of **2c**, that is, the bisthiolation product at the inner carbon–carbon double bond of **1c** in 9% yield.



11. The *E*/*Z* ratios of **9c** and **10c** were tentatively determined by the comparison of the *E*/*Z* ratios of the selenative carbonylation products (**6** and **8**).