Highly Regioselective Addition of Benzenethiol to Allenes Catalyzed by Palladium Acetate

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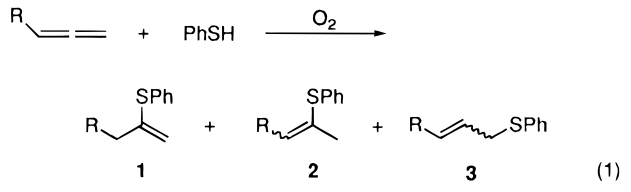
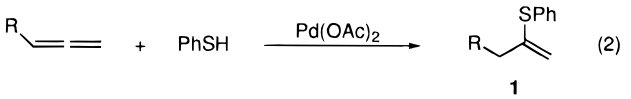
The addition reaction of thiols to allenes is one of the most straightforward routes to vinylic sulfides, which are well-known to be important synthetic intermediates.[1] It has been reported that thiols add to allenes by a free-radical mechanism.[2−5] However, thiyl radicals, as the key species in the radical addition, usually attack at both the center and terminal carbons of allenes, so the radical reaction results in the formation of a regioisomeric mixture of thiol adducts. For example, the radical addition of benzenethiol to monoalkyl-substituted allenes was reported to provide a regio- and stereoisomeric mixture of the adducts **1**, **2**, and **3**, with ratios of 38:37:25 (R = *t*-Bu)[5] and 2:81:17 (R = *n*-Bu)[5] (eq 1). These features make the radical reaction synthetically less useful. Contrary to this, we here report that palladium(II) acetate exhibits excellent catalytic activity toward the highly regioselective addition of thiols to allenes (eq 2).



1 **2** **3** (1)

R = *t*-Bu	38%	37%	25%
R = *n*-Bu	2%	81%	17%



1 (2)

The reaction of *tert*-butylallene (1 mmol) with benzenethiol (1 mmol) in the presence of 3 mol % of $Pd(OAc)_2$ at 67 °C for 2 h in THF (0.5−1.0 mL) led to high-yield formation of terminal vinylic sulfide **1a**, in which a phenylthio group is introduced at the center carbon of the allene, regioselectively (Table 1, entry 1). Similarly, *n*-butylallene and cyclohexylallene undergo regioselective addition of benzenethiol successfully to provide the corresponding terminal vinylic sulfides **1b** and **1c** in high yields (entries 2 and 3). With phenylallene as an aromatic allene, the addition also proceeded but gave a mixture of regioisomers (**1d** and **2d**) (entry 4). Although the double-bond isomerization of **1d** to **2d** under the reaction conditions may come to in mind, no conversion of **1d** to **2d** was observed in the experiment using **1d** as the substrate. Presumably, the formation of **2d** may be accounted for by the coordination of the terminal double bond of the allene to palladium(II) species, because the terminal double bond has higher electron density compared with that of the inner one (*vide post*).

Table 1. Pd(II)-Catalyzed Addition of PhSH to Monoalkylallenes[a]

entry	substrate	products	yield (%)[b]
1	*t*-Bu	SPh, *t*-Bu **1a**	85%
2	*n*-Bu	SPh, *n*-Bu **1b**	86%
3		SPh **1c**	76%
4	Ph	SPh, Ph **1d**	8%[c]
		SPh, Ph **2d**	36%[c] (*E*/*Z* = 50/50)[d]

[a]Condition: allene (1 mmol), PhSH (1 mmol), $Pd(OAc)_2$ (3 mol%), THF, 67 °C, 2h. [b]Isolated yield. [c]NMR yield. [d]Determined by ^{1}H NMR.

We have also investigated the palladium-catalyzed addition of 1,1-dimethylallene with benzenethiol in detail. The radical addition to 1,1-dimethylallene proceeded very rapidly and produced the thermodynamically more stable adduct **4** (96%), exclusively (Scheme 1).[4,5] In contrast, the $Pd(OAc)_2$-catalyzed addition to 1,1-dimethylallene provided its regioisomer (**5**, 67%) as a sole product. Accordingly, both methods are complementary to each other for the regioselective synthesis of vinylic sulfides from 1,1-dialkyl-substituted allenes. In the case of the $Pd(OAc)_2$-catalyzed addition, the amount of catalyst used is important to obtain the adduct **5** selectively. In the presence of 3 mol % of $Pd(OAc)_2$ both vinylic sulfides **5** (15%) and **4** (73%) were obtained. The use of 10 mol % of $Pd(OAc)_2$ resulted in the formation **5** (67%) and **4** (22%). Exclusive formation of the adduct **5** (67%) could be attained by using 15 mol % of $Pd(OAc)_2$.

To explore the mechanism of this palladium-catalyzed addition, the stoichiometric reaction of $Pd(OAc)_2$ with benzenethiol (2 equiv to $Pd(OAc)_2$) in THF at 15 °C for 0.5 h in the presence of 1,1-dimethylallene was examined. As a result, the reaction afforded AcOH and a brown solid. The elemental analysis of the brown solid suggested the formation of $[Pd(SPh)_2]_n$[6−8] (eq 3). Further-

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(4) Jacobs, T. L.; Illingworth, G. E., Jr. *J. Org. Chem.* **1963**, *28*, 2692.
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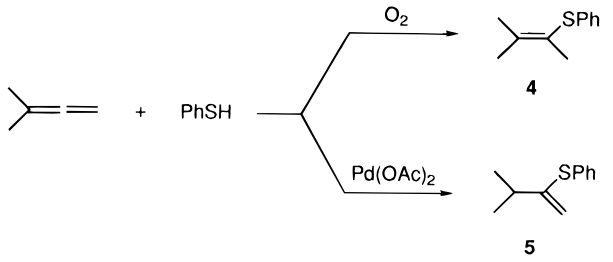
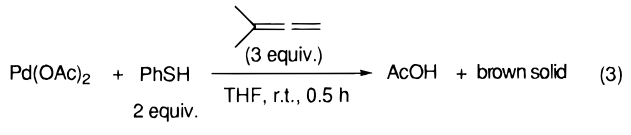
(6) The results of elemental analysis are in fair agreement with the calculated values of $[Pd(SPh)_2]_n$. Anal. Calcd for $[Pd(SPh)_2]_n$: C, 44.38; H, 3.10. Found: C, 44.67; H, 3.21.
(7) It is reported by Nyholm et al. that the reaction of $Pd(OAc)_2$ with pentafluorobenzenethiol at room temperature in THF for 0.5 h provided $Pd(SC_6F_5)_2$. Nyholm, R. S.; Skinner, J. F.; Stiddard, M. H. B. *J. Chem. Soc. A* **1968**, 38.

S0022-3263(95)02135-9 CCC: $12.00

Scheme 1



more, the attempted reaction of 1,1-dimethylallene by using the brown solid as a catalyst afforded **5** in 59% yield.[9]

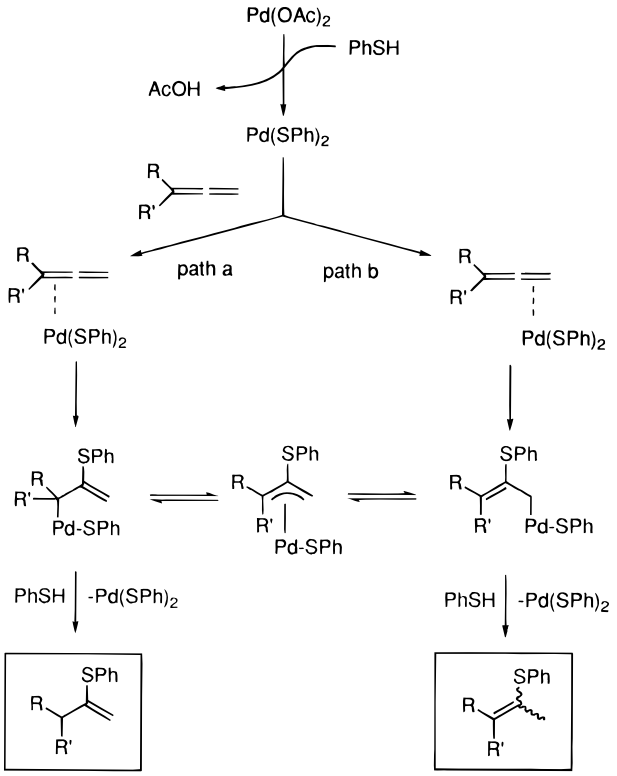


Anal. Calcd for $[Pd(SPh)_2]_n$: C, 44.38 ; H, 3.10.
Found : C, 44.67 ; H, 3.21.

Although the true reaction pathway is still unknown, a mechanistic proposal includes the following: (1) ligand exchange of the acetoxyl groups of $Pd(OAc)_2$ with PhS groups to give the palladium sulfide complex (as an active catalyst) with the concomitant formation of AcOH; (2) coordination of the allene double bond bearing higher electron density to the palladium species; (3) *syn*-thiopalladation[10] to form (σ-allyl)palladium; (4) immediate quenching of the (σ-allyl)palladium intermediate by PhSH,[11] without being changed into (π-allyl)palladium to give the desired adduct with regeneration of the catalyst. As shown in Scheme 2, the addition to alkyl-substituted allenes takes place selectively at the inner double bond of allenes, because the inner double bond is more electron-rich than the terminal one. Contrary to this, in the case of phenylallene, electron density of the terminal double bond is believed to be higher, so the thiopalladation seems to take place preferentially at the terminal double bond.

In summary, we have developed a palladium-catalyzed regioselective addition of benzenethiol to allenes. In general, organic sulfur compounds seem to be widely accepted as the catalyst poisons. On the contrary, the present reaction dose suggest the utility of transition-metal-catalyst in the reaction of sulfur compounds.[8,10,12] The clarification of precise mechanism of this reaction and the development of new transition-metal-catalyzed reactions of sulfur compounds is now under investigation.

Scheme 2



Experimental Section

General Comments. ^{1}H NMR spectra were recorded on a JEOL JNM-GSX-270 (270 MHz) spectrometer using $CDCl_3$ as the solvent with Me_4Si as the internal standard. ^{13}C NMR spectra were taken on a JEOL JNM-GSX-270 using $CDCl_3$ as the solvent. Chemical shifts in ^{13}C NMR were measured relative to $CDCl_3$ and converted to $\delta(Me_4Si)$ values by using $\delta(CDCl_3) = 76.9$ ppm. IR spectra were determined on a Perkin-Elmer Model 1600 spectrometer. Mass spectra were obtained on a JEOL JMS-DX303 in the analytical section of our department. Elemental analyses were also performed there.

General Procedure for the Synthesis of Terminal Vinylic Sulfide (1a). Representative procedure for the addition of allenes with thiols is as follows: In a two-necked flask equipped with a reflux condenser and a magnetic stirring bar under an argon atmosphere were placed $Pd(OAc)_2$ (3 mol %), THF (1 mL), *tert*-butylallene (1 mmol), and benzenethiol (1 mmol). The reaction was conducted with magnetic stirring for 2 h upon heating at 67 °C. After the reaction was complete, the resulting mixture was filtered through Celite and concentrated *in vacuo*. Purification by MPLC (silica gel, 25−40 μm, length 310 mm, i.d. 25 mm, eluent *n*-hexane:Et_2O = 4:1) provided 0.179 g (87%) of 3-*tert*-butyl-2-(phenylthio)-1-propene (**1a**).

3-*tert*-Butyl-2-(phenylthio)-1-propene (1a): ^{1}H NMR (270 MHz, $CDCl_3$) δ 1.00 (s, 9 H), 2.17 (s, 2 H), 4.82 (s, 1 H), 5.04 (s, 1 H), 7.31−7.34 (m, 3 H), 7.44 (d, J = 7.8 Hz, 2 H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 29.92, 31.53, 50.03, 114.28, 127.85, 129.14, 133.57, 133.72, 143.67; IR (NaCl) 3074, 2955, 2905, 2865, 1602, 1475, 1439, 1393, 1365, 1236, 1198, 1025, 859, 748, 707, 691 cm^{-1}; MS (EI), m/e = 206 (M^+, 41). Anal. Calcd for $C_{13}H_{18}S$: C, 75.67; H, 8.79. Found: C, 72.42; H, 8.95.

3-*n*-Butyl-2-(phenylthio)-1-propene (1b): ^{1}H NMR (270 MHz, $CDCl_3$) δ 0.88 (t, J = 6.8 Hz, 3 H), 1.28 (m, 4 H), 1.55 (quint, J = 7.3 Hz, 2 H), 2.23 (t, J = 7.6 Hz, 2 H), 4.87 (s, 1 H), 5.14 (s, 1 H), 7.25−7.35 (m, 3 H), 7.43 (d, J = 7.8 Hz, 2 H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 13.99, 22.41, 28.09, 31.10, 36.51, 112.42, 127.68, 129.04, 133.20, 133.26, 146.14; IR (NaCl) 3074, 2957, 2931, 2858, 1608, 1475, 1439, 1025, 857, 748, 706, 691 cm^{-1}; MS (EI), m/e = 206 (M^+, 11). Anal. Calcd for $C_{13}H_{18}S$: C, 75.67; H, 8.79. Found: C, 75.73; H, 8.84.

(8) Kuniyasu, H.; Ogawa, A.; Sato, K.; Ryu, I.; Kambe, N.; Sonoda, N. *J. Am. Chem. Soc.* **1992**, *114*, 5902.

(9) When the brown solid was used as the catalyst, **5** (59%) was formed accompanied by **4** (11%).

(10) Kuniyasu, H.; Ogawa, A.; Miyazaki, S.; Ryu, I.; Kambe, N.; Sonoda, N. *J. Am. Chem. Soc.* **1991**, *113*, 9796.

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3-Cyclohexyl-2-(phenylthio)-1-propene (1c): ^{1}H NMR (270 MHz, $CDCl_3$) δ 0.83−0.91 (m, 2 H), 1.10−1.28 (m, 3 H), 1.61−1.70 (m, 6 H), 2.11 (d, J = 6.8 Hz, 2 H), 4.81 (s, 1 H), 5.07 (s, 1 H), 7.30−7.35 (m, 3 H), 7.44 (d, J = 6.4 Hz, 2 H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 26.21, 26.53, 32.89, 36.10, 44.59, 112.89, 127.78, 129.06, 133.17, 133.46, 144.64; IR (NaCl) 3073, 2922, 2850, 1607, 1476, 1448, 1440, 748, 691 cm^{-1}; MS (EI), m/e = 232 (M^+, 31). Anal. Calcd for $C_{15}H_{20}S$: C, 77.53; H, 8.67. Found: C, 77.31; H, 8.85.

3,3-Dimethyl-2-(phenylthio)-1-propene (5): ^{1}H NMR (270 MHz, $CDCl_3$) δ 1.17 (d, J = 6.8 Hz, 6 H), 2.44 (septet, J = 6.8 Hz, 1 H), 4.80 (s, 1 H), 5.18 (s, 1 H), 7.24−7.34 (m, 3 H), 7.41−7.44 (m, 2 H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 22.28, 34.92, 110.25, 127.58, 129.07, 133.15, 133.67, 152.99; IR (NaCl) 3074, 2964, 2928, 2871, 1598, 1583, 1477, 1439, 1362, 1025, 860, 748, 691 cm^{-1}; MS (EI), m/e = 178 (M^+, 100); exact mass (M^+) calcd for $C_{11}H_{14}S$ 178.0817, found 178.0821.

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Supporting Information Available: Typical procedure and compound characterization data (5 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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