

Palladium-Catalyzed Selenoacylation of Allenes Leading to the Regioselective Formation of Functionalized Allyl Selenides

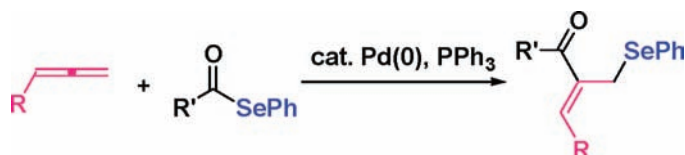
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ABSTRACT



Palladium-catalyzed regio- and stereoselective selenoacylation of allenes with selenol esters proceeded to produce functionalized allyl selenides with the acyl moiety at the inner carbon and the SePh group at the terminal carbon in high yields. A mechanism accounting for the observed regio- and stereoselectivities is proposed based on the results of DFT calculations.

During the past 20 years, allenes have been shown to be versatile building blocks in organic synthesis.¹ It is known that a variety of heteroatom compounds such as organotin, -borane, and -selenium species add to allenes in the presence of transition metal catalysts such that an allene double bond inserts into R₃Sn–H, R₃Si–BR′₂, and RSe–SeR′ bonds.² There are fewer known examples, however, of allene insertion into carbon–heteroatom bonds.^{3,4} Chatani and co-workers reported Ni or Pd catalyzed cyanosilylation of allenes with trimethylsilyl cyanide (NC–SiMe₃).^{3a} Hua and

Tanaka reported Rh catalyzed chloroesterification of allenes with chloro carbonates (ROC(O)–Cl).^{3b} Shirakawa, Hiyama, and co-workers described Ni catalyzed acylstannylation and alkynylstannylation of allenes with acyl stannanes and alkynyl stannanes (RC(O)–SnR′₃ and RC≡C–SnR′₃, respectively).^{3c–e} In these cases, vinylic heteroatom products like **1** were obtained as the major products rather than allylic compounds **2** (eq 1). Here, we disclose the first example of carbothioloation and carboselenation of allenes that proceeds with reverse regioselectivity leading to **2** (eq 2).

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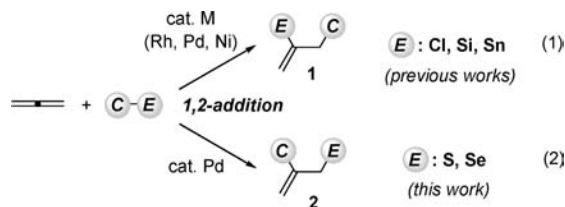
[‡] Osaka Dental University.

(1) For recent reviews, see: (a) Ma, S. *Chem. Rev.* **2005**, *105*, 2829. (b) Ma, S. *Acc. Chem. Res.* **2003**, *36*, 701. (c) *Modern Allene Chemistry*; Krause, N., Hashmi, A. S. K., Eds.; Wiley-VCH: Weinheim, 2004.

(2) For recent examples, see: (a) Kamiya, I.; Nishinaka, E.; Ogawa, A. *Tetrahedron Lett.* **2005**, *46*, 3649. (b) Kazmaier, U.; Lucas, S.; Klein, M. *J. Org. Chem.* **2006**, *71*, 2429. (c) Ohmura, T.; Suginome, M. *Org. Lett.* **2006**, *8*, 2503. (d) Ohmura, T.; Taniguchi, H.; Suginome, M. *J. Am. Chem. Soc.* **2006**, *128*, 13682. (e) Kodama, S.; Nishinaka, E.; Nomoto, A.; Sonoda, M.; Ogawa, A. *Tetrahedron Lett.* **2007**, *48*, 6312. (f) Abe, Y.; Kuramoto, K.; Ehara, M.; Nakatsuji, H.; Suginome, M.; Murakami, M.; Ito, Y. *Organometallics* **2008**, *27*, 1736. For others, see refs 1a and 1c.

(3) (a) Chatani, N.; Takeyasu, T.; Hanafusa, T. *Tetrahedron Lett.* **1986**, *27*, 1841. (b) Hua, R.; Tanaka, M. *Tetrahedron Lett.* **2004**, *45*, 2367. (c) Shirakawa, E.; Nakao, Y.; Hiyama, T. *Chem. Commun.* **2001**, 263. (d) Shirakawa, E.; Nakao, Y.; Tsuchimoto, T.; Hiyama, T. *Chem. Commun.* **2002**, 1962. (e) Nakao, Y.; Shirakawa, E.; Tsuchimoto, T.; Hiyama, T. *J. Organomet. Chem.* **2004**, *689*, 3701. (f) Saso, H.; Ando, W. *Chem. Lett.* **1988**, 1567. (g) Seyferth, D.; Shannon, M. L.; Vick, S. C.; Lim, T. F. O. *Organometallics* **1985**, *4*, 57.

(4) For recent radical reactions, see: (a) Tsuchii, K.; Imura, M.; Kamada, N.; Hirao, T.; Ogawa, A. *J. Org. Chem.* **2004**, *69*, 6658. (b) Mei, Y.-Q.; Liu, J.-T.; Liu, Z.-J. *Synthesis* **2007**, 739.



When a toluene solution (0.3 mL) containing selenol ester **4a** ($R' = n\text{Hex}$, 0.4 mmol), cyclohexyllallene **3a** ($R = c\text{Hex}$, 1.2 equiv), $\text{Pd}_2(\text{dba})_3\cdot\text{CHCl}_3$ (2.5 mol %), and PPh_3 (10 mol %) was heated at reflux for 12 h, selenoacylation product, allyl selenide **5a**⁵ (corresponds to **2** in eq 2), was obtained in 70% yield (Table 1, entry 1) with excellent regio- and stereoselectivity.⁶ In this reaction, the selenol ester adds to the terminal C–C double bond of the allene exclusively with the acyl moiety at the inner carbon and the SePh group at the terminal carbon to form an allyl selenide. Regioisomers such as vinyl selenide **1** or its stereoisomers were not detected by ¹H NMR analysis of the crude product.

Table 1 summarizes the results obtained using several selenol esters and allenes. When *n*-octyllallene **3b** was employed, allyl selenide **5b** was formed when $\text{Pd}(\text{PPh}_3)_4$ was used instead of $\text{Pd}_2(\text{dba})_3\cdot\text{CHCl}_3$ and PPh_3 as a catalyst (entry 2).⁶ Although the reaction of phenyllallene **3c** with **4a** gave allyl selenide **5c** in 90% yield (entry 3) in 5 h, a small amount of *E* isomer was also detected.⁷ Next, selenoacylation of allenes having an electron-donating or -withdrawing group was examined. For example, allene **3d** having a benzyloxy group can be subjected to selenoacylation using **4a** giving rise to allyl selenide **5d** in 87% yield (entry 4); however, when ethyl 2,3-butadienoate ($R = \text{CO}_2\text{Et}$) was employed under similar reaction conditions, almost all of **4a** was recovered and the expected allyl selenide was not obtained probably due to oligomerization of the allene.^{8,9} Selenol ester **4b** bearing a cyclohexyl group also underwent selenoacylation with **3c** to give **5e**; however, the stereoselectivity diminished in this case (entry 5). In all cases, no decarbonylative product was formed.¹⁰ Next, selenoesterification and

Table 1. Pd(0)-Catalyzed Selenoacylation of Allenes^a

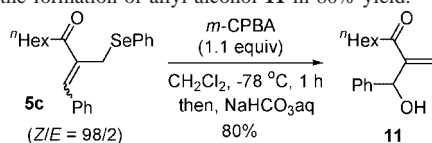
entry	3	4	time, h	5 , % ^b	Z/E ^c
1	3a ($R = c\text{Hex}$)	4a ($R' = n\text{Hex}$)	12	5a , 70 (71)	>98/2
2 ^d	3b ($R = n\text{Oct}$)	4a	22	5b , 55 (71)	>98/2
3	3c ($R = \text{Ph}$)	4a	5	5c , 90 (91)	98/2
4	3d ($R = \text{OBn}$)	4a	12	5d , 87	98/2
5	3c	4b ($R' = c\text{Hex}$)	5	5e , 69	91/9
6	3c	4c ($R' = O^n\text{Bu}$)	5	5f , 70 (80)	>98/2
7 ^d	3c	4d ($R' = \text{NMe}_2$)	3	5g , 83	21/79

^a Conditions: **4** (0.4 mmol), **3** (0.48 mmol), $\text{Pd}_2(\text{dba})_3\cdot\text{CHCl}_3$ (2.5 mol %), PPh_3 (10 mol %), toluene (0.3 mL), reflux. ^b Isolated yields (NMR yields). ^c Determined by ¹H NMR. “>98/2” means no minor isomer was detected by NMR. ^d 5 mol % of $\text{Pd}(\text{PPh}_3)_4$ was used as catalyst.

(5) For synthetic utilities of allyl selenides, see: (a) Tanaka, K.; Horiuchi, H.; Yoda, H. *J. Org. Chem.* **1989**, *54*, 63. (b) Krief, A.; Colaux, C.; Dumont, W. *Tetrahedron Lett.* **1997**, *38*, 3315. (c) Takada, H.; Oda, M.; Miyake, Y.; Ohe, K.; Uemura, S. *Chem. Commun.* **1998**, 1557. (d) Nishiyama, Y.; Kishimoto, Y.; Itoh, K.; Sonoda, N. *Synlett* **1999**, 611. (e) Bourland, T. C.; Carter, R. G.; Yokochi, A. F. T. *Org. Biomol. Chem.* **2004**, *2*, 1315. (f) Yamashita, K.; Takeda, H.; Kashiwabara, T.; Hua, R.; Shimada, S.; Tanaka, M. *Tetrahedron Lett.* **2007**, *48*, 6655. (g) Waetzig, S. R.; Tunge, J. A. *Chem. Commun.* **2008**, 3311. For recent total synthesis of natural products using transformation of allyl selenides, see: (h) Albert, B. J.; Sivaramakrishnan, A.; Naka, T.; Koide, K. *J. Am. Chem. Soc.* **2006**, *128*, 2792. (i) Albert, B. J.; Sivaramakrishnan, A.; Naka, T.; Czaicki, A.; Koide, K. *J. Am. Chem. Soc.* **2007**, *129*, 2648.

(6) For screening of phosphine ligands, see Supporting Information.

(7) Oxidation of isolated **5c** with *m*-CPBA followed by hydrolysis resulted in the formation of allyl alcohol **11** in 80% yield.



(8) Ethyl 2,3-butadienoate was reported to oligomerize in the presence of PPh_3 . See: Zhang, C.; Lu, X. *J. Org. Chem.* **1995**, *60*, 2906.

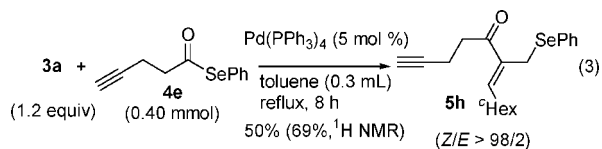
(9) Selenoacylation of α,α -disubstituted allenes such as vinylidenecyclohexane with **4a** did not proceed at all.

selenocarbonylation of allene precursors were examined. When the reaction of selenocarbonate **4c** with phenyllallene **3c** was carried out under similar conditions, the expected allyl selenide **5f** was obtained in high yield with perfect regio- and stereoselectivity (entry 6).¹¹ In contrast, although selenocarbonylation of **3c** with carbamoselenoate **4d** proceeded to give **5g** in high yield, the *E* isomer was formed predominantly (entry 7).¹² Existence of an alkyne unit did not affect the reaction. For example, the reaction of cyclohexyllallene **3a** with selenol ester **4e** bearing a terminal alkynyl group proceeded to give selenoacylation product **5h** selectively (eq 3).

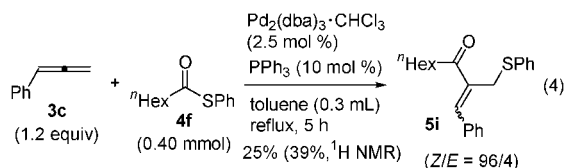
(10) Hirai, T.; Kuniyasu, H.; Kato, T.; Kurata, Y.; Kambe, N. *Org. Lett.* **2003**, *5*, 3871.

(11) Pd-catalyzed addition of thiocarbonate to alkynes was reported. Hua, R.; Takeda, H.; Onozawa, S.; Abe, Y.; Tanaka, M. *J. Am. Chem. Soc.* **2001**, *123*, 2899.

(12) Selenocarbonylation of 1-octyne with **4d** proceeded to give β -selenoacrylamide in 40% yield: Toyofuku, M.; Fujiwara, S.; Shin-ike, T.; Kuniyasu, H.; Kambe, N. *J. Am. Chem. Soc.* **2005**, *127*, 9706.

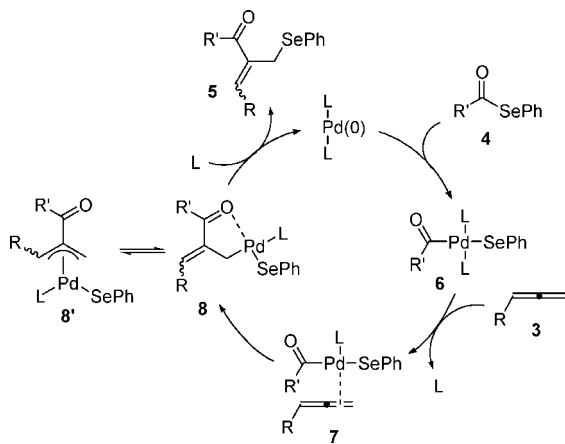


The reaction of a thiol ester **4f** with **3c** gave the thioacylation product **5i** with good regio- and stereoselectivity albeit in a low yield under similar conditions (eq 4).¹³



A plausible reaction pathway for allyl selenide formation involving a π -allylpalladium¹⁴ intermediate is shown in Scheme 1, which explains the regioselectivity of the products.

Scheme 1. Proposed Pathway Leading to Allyl Selenide **5**



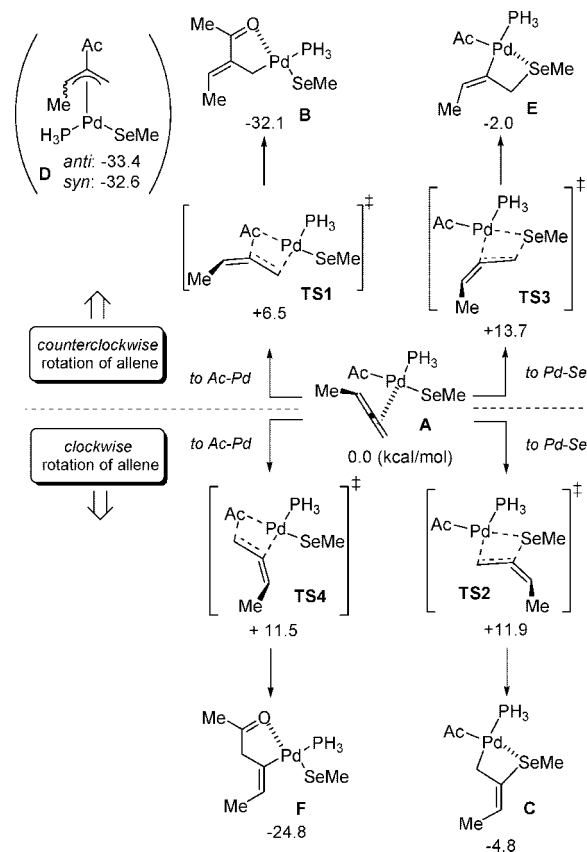
This catalytic process is initiated by oxidative addition of the *acyl*-*Se* bond of selenol ester **4** to Pd(0), affording the *acyl*-Pd-*Se* complex **6**. Insertion of the coordinated allene into the *acyl*-Pd bond generates σ -allylpalladium **8** (in equilibrium with π -allylpalladium **8'**) having an acyl group at the central carbon of the allene unit prior to reductive elimination which produces allyl selenide **5**.

To shed light on the mechanism of the reaction and on the regio- and stereoselectivity of the process, DFT calculations were performed with methylallene and MeC(O)SeMe as substrates and PH₃ as the ligand for the Pd. Complex **A** shown in Scheme 2 is the optimized model for the allene coordinated intermediate (corresponds to **7** in Scheme 1). It is noteworthy that the axis of the Pd-coordinated allene leans

(13) Although starting material **4f** remained, yield of **5i** was not improved when the reaction time was prolonged to 10 h.

(14) Carbopalladation of allene to form the π -allylpalladium intermediate is well known as a key step for various reactions using allene and Pd catalyst: Mandai, T. In *ref 1c*; pp 925–972.

Scheme 2. Computational Calculations for Allene Insertion



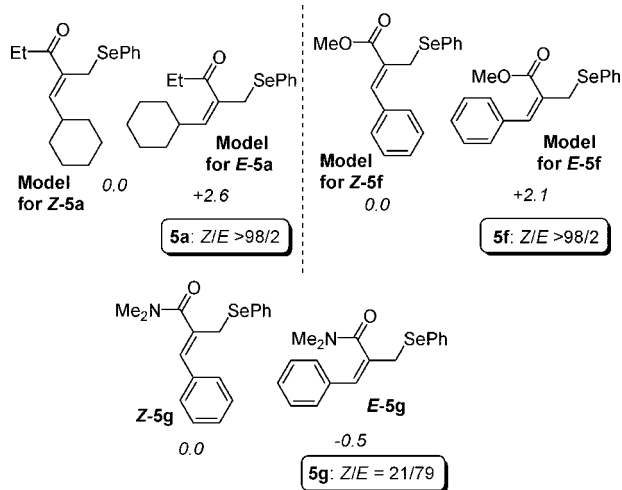
to the side of the acyl group in **A**.¹⁵ Subsequent allene insertion may occur in the *acyl*-Pd bond via counterclockwise rotation of the allene to give a σ -allylpalladium species **B**, which is the precursor of the π -allylpalladium intermediates **D**. Other possible pathways, i.e., formation of **C**, **E**, and **F** are unlikely since **TS2**, **TS3**, and **TS4** are less stable than **TS1** and **C**, **E**, and **F** are also less stable than **B**. Accordingly, formation of **B** via **TS1** will be both kinetically and thermodynamically the most favored pathway. In the formation of **B** and **F**, five-membered chelation by the intramolecular coordination of carbonyl oxygen to Pd could be important for structural stabilities (>20 kcal/mol more stable than **C** and **E**). In addition, the carbonyl group and the C=C unit are conjugated in **B** while not conjugated in **F**. These factors may be crucial for the predominant formation of the intermediate **B** in this system. Reductive elimination from **B** affords the allyl selenide products. In this step, the PPh₃ ligand may be essential based on Kurosawa's study of [Pd(π -allyl)(SPh)]₂ reactions with PPh₃.¹⁶ In fact, addition of **4a** to **3c** was sluggish (<5%) without the PPh₃ ligand (compare with entry 3 in Table 1).⁶

As for the stereoselectivity of the products, the (*Z*)-adduct of EtC(O)SePh to **3a** (model of (*Z*)-**5a**) is calculated to be

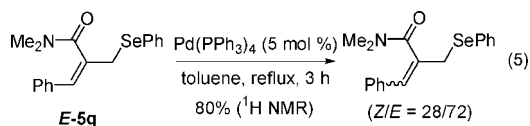
(15) It is proposed that insertion of coordinated olefins occurs via rotation of the C=C axis toward the coordination plane of the metal center. For examples, see: (a) Michalak, A.; Ziegler, T. *Organometallics* **1999**, *18*, 3998. (b) Lin, B.-L.; Liu, L.; Fu, Y.; Luo, S.-W.; Chen, Q.; Guo, Q.-X. *Organometallics* **2004**, *23*, 2114.

2.6 kcal/mol more stable than the corresponding (*E*)-adduct. Similarly, the (*Z*)-adduct of MeOC(O)SePh to **3a** (model of (*Z*)-**5f**) is calculated to be 2.1 kcal/mol more stable than the corresponding (*E*)-adduct. However, (*Z*)-**5g** is 0.5 kcal/mol less stable than (*E*)-**5g**.¹⁷ These results do not conflict with the observed stereoselectivities in entries 1, 6, and 7 (Scheme 3). In addition, when the isolated product (*E*)-**5g** was

Scheme 3. Computational Calculations for Stabilities of Products



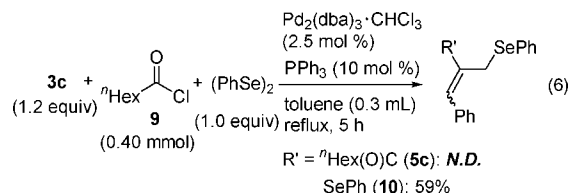
subjected to the same reaction conditions as in entry 7, isomerization ensued to give the *Z/E* (28/72) mixture of **5g**, while isomerization did not proceed in the presence of a catalytic amount of PPh₃ without Pd (eq 5).



These results suggest that the stereoselectivities observed reflect the relative thermodynamic stabilities of the products. Furthermore, the evidence that Pd(0) inserts into the C–Se bond of allyl selenides¹⁶ indicates that the last step of Scheme 1 (**8** to **5**) is reversible, and *Z/E* isomerization proceeds via the π -allylpalladium intermediates **8'**. Cheng and co-workers revealed that Pd-catalyzed three-component assembly of allenes, acyl chlorides, and bismetal reagents such as (BPin)₂

(16) Miyauchi, Y.; Watanabe, S.; Kuniyasu, H.; Kurosawa, H. *Organometallics* **1995**, *14*, 5450.

afforded allyl-metal species like **5**.¹⁸ The authors proposed transmetalation between bismetal reagents and the π -allylpalladium intermediate like **8'** prior to reductive elimination of the allyl-metal product. Thus, we examined the possibility of selenoacylation of allenes using diselenides as bismetal reagents. When the mixture of acyl chloride **9** (0.40 mmol), phenylallene **3c** (0.48 mmol), and (PhSe)₂ (0.40 mmol) was heated at reflux for 5 h with Pd(0)-PPh₃ catalyst, only biselenation product **10** was obtained,^{2a} and no selenoacylation product such as **5c** was detected probably due to faster oxidative addition of (PhSe)₂ to Pd(0) over that of acyl chloride **9** (eq 6).



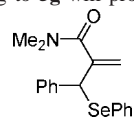
In summary, we report that 1,2-addition of selenol esters onto allenes proceeds with excellent regioselectivity and high stereoselectivity in the presence of Pd(0)-PPh₃ catalyst, producing functionalized allyl selenides. A reaction pathway accounting for the observed regio- and stereoselectivity is proposed based on the results of DFT calculations.

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Supporting Information Available: Experimental procedures and characterization data of new compounds. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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(17) Since the regioisomer of **5g** shown below is calculated to be ca. 5 kcal/mol less stable than (*Z*)-**5g**, formation of this isomer will be thermodynamically unfavored. In addition, reverse oxidative addition and reductive elimination leading to **5g** will proceed from the result of eq 5.



(18) Yang, F.-Y.; Shanmugasundaram, M.; Chuang, S.-Y.; Ku, P.-J.; Wu, M.-Y.; Cheng, C.-H. *J. Am. Chem. Soc.* **2003**, *125*, 12576.