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A SeCSe−Pd(II) Pincer Complex as a Highly Efficient Catalyst for Allylation of Aldehydes with Allyltributyltin

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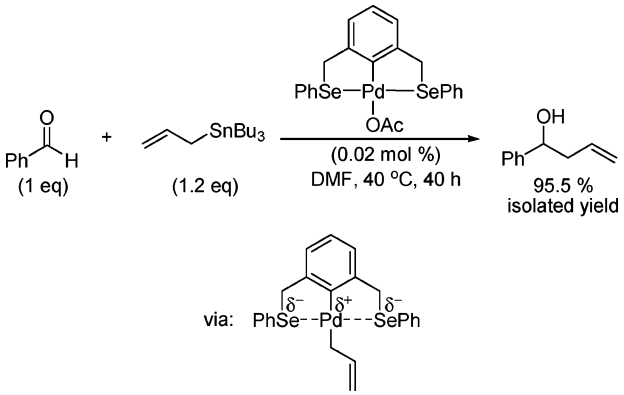
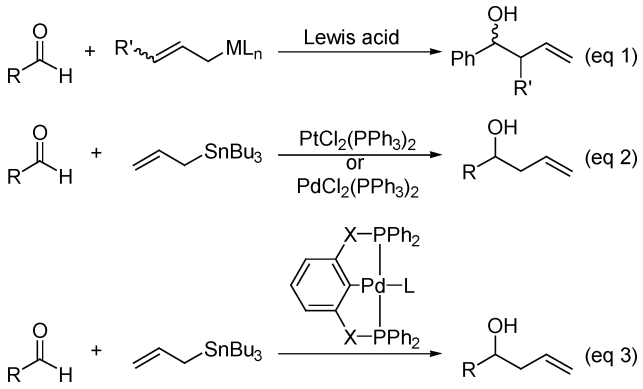


An air- and moisture-stable SeCSe−Pd(II) pincer complex was synthesized and found to catalyze the nucleophilic allylation of aldehydes with allyltributyltin. The allylation of a variety of aromatic and aliphatic aldehydes to give the corresponding homoallyl alcohols was performed at room temperature to 60 °C in yields ranging from 50% (for typical aliphatic aldehydes) to up to 97% (for aromatic aldehydes) using 5×10^{-3} to 1 mol % of the Pd catalyst. NMR spectroscopic study indicated that a σ-allylpalladium intermediate was formed and possibly functions as the nucleophilic species that undergoes addition to the aldehydes.

Nucleophilic addition of allylmetals to carbonyl compounds to give the corresponding homoallyl alcohols is a widely employed and versatile reaction in organic synthesis.[1] For stable allylmetals, such as allylsilanes and allylstannanes, activation of the carbonyl functionality is often necessary, with various Lewis acids, in either stoichiometric or catalytic amounts, being the most widely used promoters (Scheme 1, eq 1).[1,2] The past several years have witnessed an increased interest in the use of transition metals as catalysts for this powerful transformation. Several transition-metal-based catalysts have been reported,[3] particularly, in the context of catalytic enantioselective allylation of aldehydes and ketones.[4] Such transition-metal-based catalysts invariably function as a Lewis acid in promoting the allylation reactions. A lanthanide, cerium(III) chloride ($CeCl_3 \bullet 7H_2O$) in combination with NaI, has recently been introduced as a new, stoichiometric promoter for the allylation of various aldehydes with allyltributyltin.[5] Yamamoto and co-workers first reported the Pt- and Pd-catalyzed allylation of aldehydes and imines with allyltributyltin (Scheme 1, eq 2).[6] They demonstrated that a π-allyl-σ-allylpalladium complex in equilibrium with an isomeric bis-π-allylpalladium complex served as the nucleophilic allyl transfer species. Recently, pincer complexes[7] of Rh and Pd have been reported as efficient catalysts for this reaction (Scheme 1, eq 3).[8] While the NCN−Rh pincer complex used in Nishiyama's catalyst system[8a] was believed to function as a Lewis acid, results from the body of Szabó's work[8b−d] point to the likelihood of a nucleophilic allylpalladium intermediate formed by transmetalation with the tin reagent.[6,9,10]

SCHEME 1. Allylation of Aldehydes with Allylmetals



We have recently reported the synthesis of the first selenium-ligated palladium pincer complex **1** and the related Se-ligated

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(3) Selected recent examples. Ag-based catalysts: (a) Yanagisawa, A.; Nakashima, H.; Ishiba, A.; Yamamoto, H. *J. Am. Chem. Soc.* **1996**, *118*, 4723. (b) Yanagisawa, A.; Ishiba, A.; Nakashima, H.; Yamamoto, H. *Synlett* **1997**, 88. Zn-based catalysts: (c) Cozzi, P. G.; Orioli, P.; Tagliavini, E.; Umani-Ronchi, A. *Tetrahedron Lett.* **1997**, *38*, 145. (d) Imai, Y.; Zhang, W.; Kida, T.; Nakatsuji, Y.; Ikeda, I. *J. Org. Chem.* **2000**, *65*, 3326. (e) Kwong, H.-L.; Lau, K.-M.; Lee, W.-S.; Wong, W.-T. *New J. Chem.***1999**, *23*, 629. Zr-based catalysts: (f) Bedeschi, P.; Casolari, S.; Costa, A. L.; Tagliavini, E.; Umani-Ronchi, A. *Tetrahedron Lett.* **1995**, *36*, 7897. (g) Casolari, S.; Cozzi, P. G.; Orioli, P. A.; Tagliavini, E.; Umani-Ronchi, A. *Chem. Commun.* **1997**, 2123. (h) Kurosu, M.; Lorca, M. *Tetrahedron Lett.* **2002**, *43*, 1765. (i) Hanawa, H.; Kii, S.; Asao, N.; Maruoka, K. *Tetrahedron Lett.* **2000**, *41*, 5543.

(4) For an excellent recent review, see: Denmark, S. E.; Fu, J. *Chem. Rev.* **2003**, *103*, 2763.

(5) (a) Bartoli, G.; Bosco, M.; Giuliani, A.; Marcantoni, E.; Palmieri, A.; Petrini, M.; Sambri, L. *J. Org. Chem.* **2004**, *69*, 1290. (b) Bartoli, G.; Giuliani, A.; Marcantoni, E.; Massaccesi, M.; Melchiorre, P.; Lanari, S.; Sambri, L. *Adv. Synth. Catal.* **2005**, *347*, 1673.

(6) (a) Nakamura, H.; Asao, N.; Yamamoto, Y. *J. Chem. Soc., Chem. Commun.* **1995**, 1273. (b) Nakamura, H.; Iwama, H.; Yamamoto, Y. *J. Am. Chem. Soc.* **1996**, *118*, 6641. Simple Pd(II) or Pt(II) salts, such as $PdCl_2$ and $PtCl_2$, catalyze the allylation of aldehydes with allyltributyltin with only poor yield; see ref 3a.

(7) Leading recent reviews: (a) Albrecht, M.; van Koten, G. *Angew. Chem., Int. Ed.* **2001**, *40*, 3750. (b) Dupont, J.; Pfeffer, M. Spencer, M. *Eur. J. Inorg. Chem.* **2001**, 1917. (c) Bedford, R. B. *Chem. Commun.* **2003**, 1787. (d) Singleton, J. T. *Tetrahedron* **2003**, *59*, 1837. (e) van der Boom, M. E.; Milstein, D. *Chem. Rev.* **2003**, *103*, 1759. (f) Beletskaya, I. P.; Cheprakov, A. V. *J. Organomet. Chem.* **2004**, *689*, 4055. (g) Dupont, J.; Consorti, C. S.; Spencer, *J. Chem. Rev.* **2005**, *105*, 2527.

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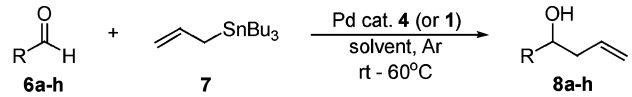
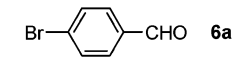
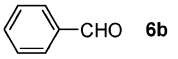
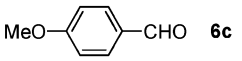
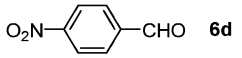
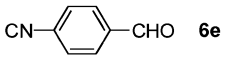
TABLE 1. Allylation of Aldehydes with Allyltributyltin 7 Using the SeCSe−Pd Pincer Complex 4 as Catalyst[a]



entry	aldehyde		mmol [M]	mol % **4**	Solvent	conditions	yield[b, c]
1		**6a**	0.5 [1.0]	**1**	**THF**	**rt (24h)**	**92.5**
2			0.5 [1.0]	1	THF	60 °C (18h)	64
3			0.5 [1.0]	1	DMF	rt (18h)	77
4			0.5 [1.0]	**1**	**DMF**	**40 °C (18h)**	**94**
5			0.5 [1.0]	1	DMF	60 °C (18h)	96
6			0.5 [1.0]	1	DMSO	rt (18h)	86.5
7			0.5 [1.0]	**1**	**DMSO**	**40 °C (18h)**	**96.5**
8			0.5 [1.0]	1	DMSO	60 °C (18h)	97
9		**6b**	1.0 [1.0]	1	DMF	rt (36h)	87.5
10			0.5 [1.0]	1	DMF	40 °C (18h)	92.5
11			2.0 [2.0]	0.25	DMF	40 °C (24h)	92
12			2.0 [2.0]	**0.02**	**DMF**	**40 °C (40h)**	**95.5**
13			1.0 [1.0]	1 (**1**)[d]	DMF	40 °C (18h)	54
14			1.0 [2.0]	none[e]	DMF	40 °C (18h)	<1[f]
15			1.0 [1.0]	1 (**2**)[g]	DMF	40 °C (18h)	74
16		**6c**	0.5 [1.0]	1	DMF	60 °C (18h)	58.5
17			2.0 [2.0]	1	DMA	60 °C (18h)	64.5
18		**6d**	1.0 [2.0]	1	DMF	rt (24h)	95
19			1.0 [2.0]	1	DMF	40 °C (6h)	95.5
20			2.0 [2.0]	**0.02**	**DMF**	**40 °C (24h)**	**95.5**
21			2.0 [1.0]	0.005	DMF	40 °C (96h)	79.5
22		**6e**	1.0 [2.0]	1	DMF	rt (24h)	94.5
23			4.0 [2.0]	0.1	DMF	40 °C (40h)	95.5
24	$PhCH_2CH_2CHO$	**6f**	1.0 [2.0]	1	DMF	40 °C (40h)	66.5
25	$CH_3(CH_2)_5CH_2CHO$	**6g**	2.0 [2.0]	1	DMF	60 °C (24h)	59

[a] All reactions were performed with 1 equiv of **6** and 1.2 equiv of **7** under conditions as indicated. [b] Referred to isolated yield after column chromatography on silica gel. [c] Average of two runs. [d] The SeCSe−Pd(II) pincer complex **1** was used. [e] This control reaction was performed in the absence of any catalyst. [f] Not detected by ^{1}H NMR. [g] The Se palladacycle **2** was used.

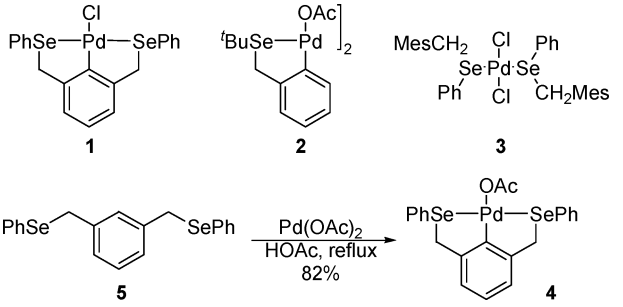


FIGURE 1. Se-ligated Pd complexes.

Pd(II) complexes **2** and **3** (Figure 1) and demonstrated their utility in catalysis.[11] These Se−Pd(II) complexes are highly active catalysts for the Heck reaction, outperforming analogous palladacycles derived from phosphorus-, sulfur-, and nitrogen-containing ligands. We now wish to report that the SeCSe−Pd(II) pincer complex **4** can be readily prepared and used as a highly reactive catalyst for the nucleophilic allylation of aldehydes with allyltributyltin.

Complex **4** can be conveniently assembled from the known bisselenide **5**[11] (Figure 1) and $Pd(OAc)_2$. It was isolated in 82% yield as an air-stable bright yellow crystalline solid and fully characterized by ^{1}H and ^{13}C NMR spectroscopy as well as elemental analysis. The catalytic activity of **4** in the reaction of aldehydes **6** and allyltributyltin (**7**) was initially examined using 4-bromobenzaldehyde (**6a**) as the test substrate in three common organic solvents: THF, DMF, and DMSO. We were pleased to find that the reaction proceeded smoothly in the presence of 1 mol % of **4** in THF at room temperature, affording homoallyl alcohol **8a** in high yield (Table 1, entry 1). However, performing the reaction at an elevated temperature gave diminished yields (entry 2). DMF and DMSO proved to be more suitable solvents for this reaction, allowing the reaction to be carried out at up to 60 °C (entries 3−8).

To test the activity scope of **4**, the reaction of a number of other representative aldehydes with **7** were examined in DMF with different catalyst loading and at different reaction temperature (Table 1). The benchmark benzaldehyde (**6b**) underwent allylation uneventfully in the presence of 1 mol % of **4** at either room temperature or 40 °C (entries 9 and 10). The reaction can also be performed with much reduced loading of the catalyst (entries 11 and 12). For example, use of as little as 0.02 mol % of **4** was found to be sufficient to achieve high conversion when the reaction was performed at 40 °C. It is interesting to note that the SeCSe−Pd(II) pincer complex **1**,[11] the chloride analogue of **4**, gave a much inferior result compared to **4** (entry 13). A control experiment established that no conversion was observed

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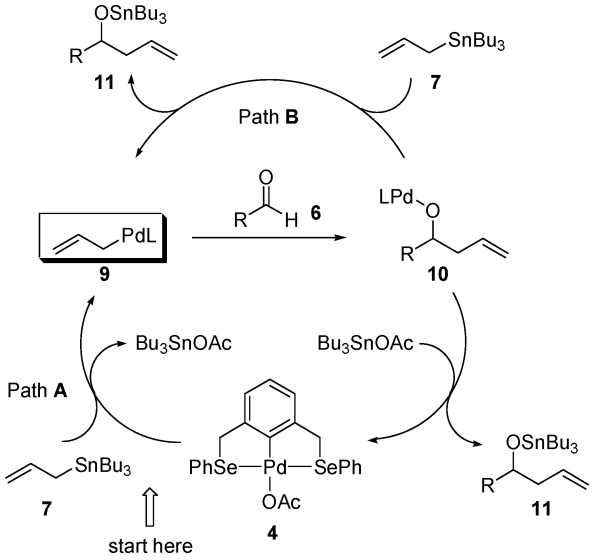
(11) Yao, Q.; Kinney, E. P.; Zheng, C. *Org. Lett.* **2004**, *6*, 2997.

SCHEME 2. Plausible Mechanistic Pathways for the Allylation of Aldehydes with Allyltributyltin 7 Catalyzed by the SeCSe−Pd(II) Pincer Complex 4



in the absence of **4** (entry 14). As expected, the electronically deactivated anisaldehyde (**6c**) required a higher reaction temperature to achieve a good yield, and the reaction gave slightly better yield in DMA (entry 17) than in DMF (entry 16). For activated aldehydes, such as **6d** and **6e**, the reaction went to completion after 24 h at room temperature (entries 18 and 22). When carried out at 40 °C, the reaction would go to completion with much shorter reaction times and lower catalyst loading (entries 19−21 and 23). In the case of aldehyde **6d**, use of 5.0 $\times$ 10^{-3} mol % of **4** still delivered the product in 80% yield (entry 21), corresponding to a turnover number (TON) of 15 900. This is, to the best of our knowledge, the highest TON for the allylation of aldehydes with an allylstannane promoted by any chemical catalyst. The allylation of aliphatic aldehydes, such as **6f** and **6g**, also worked, albeit in lower yields (entries 24 and 25).

Transmetalation to a more reactive allylic metal reagent from an allylstannane and subsequent nucleophilic addition to carbonyls is a well documented process.[1] However, examples of allylation with allylstannanes via *catalytic transmetalation* by a transition metal remain rare. Although the possibility that catalyst **4** functions simply as a *Lewis acid catalyst* (rather than a promoter[12]) in activating the aldehyde cannot be completely ruled out at this time, a mechanism involving transmetalation of the tin reagent **7** with **4** to form a nucleophilic σ-allylpalladium species[6b,8c,d] seems more reasonable. As outlined in Scheme 2, the catalytic cycle starts with the reaction of **4** and **7** (Path **A**) to generate the σ-allyl−Pd(II) intermediate **9**. This allyl−Pd species then undergoes nucleophilic addition to aldehyde **6**, probably via a cyclic transition state with the metal concurrently activating the carbonyl group. The resulting Pd(II)−alkoxide intermediate **10** undergoes an exchange reaction with tributylstannyl acetate to liberate the homoallyl alcohol product in the form of stannyl ether **11** and to regenerate catalyst **4**. Additionally or alternatively, transmetalation may occur at the stage of intermediate **10** (Path **B**). If Path **B** is operating, the difference in activity between catalyst **4** and its chloride analogue **1** may be attributed to a faster release of the more labile acetate ligand in **4** when entering into the catalytic cycle. The marked difference in the reactivity of the aldehyde substrates revealed by the data in Table 1 points to a relatively facile transmetalation for the formation of intermediate **9** and a rate-determining allyl transfer to aldehyde **6**. In this regard, analogues of **4** that would produce a σ-allylpalladium intermediate with enhanced nucleophilicity of the allyl moiety and/or increased Lewis acidity of the metal center could be expected to be even more reactive in catalyzing the allylation reaction.

We have performed a ^{1}H NMR experiment to probe the key step in the proposed mechanism, the reaction of catalyst **4** with allyltributyltin **7**. When a solution of **4** in deuterated THF was treated with an excess amount of **7**, a single allylpalladium species **9** (Figure 2) was formed in about 50% conversion after 20 min at 25 °C as monitored by 500 MHz ^{1}H NMR.[13] Careful NMR study using the proton decoupling and proton 2D COSY techniques established that this transmetalation product has the structure of a σ-allylpalladium species, denoted as **9**-η^1. Unlike the pincer complex **4** that exists as two diastereomeric isomers (*cis*- and *trans*-**4**), as revealed by the diastereotopic nature of the benzylic protons on the selenide ligand ($SeCH_2$) of each diastereomer, **9** exists as a single isomer and its $SeCH_2$ protons appear as a sharp singlet at δ 4.44 ppm (see Supporting Information for the ^{1}H NMR spectra of **4** and **9** in THF-d_8).[14] This suggests that the two phenylselenide groups are either free, spectator ligands or are only loosely associated with the Pd atom via electronic interaction, providing some electronic and/or steric stabilization around the metal center. If a tetracoordinated pincer σ-allyl−Pd complex, **9**-η^1-Se_2, were formed, one would expect the protons of the $SeCH_2$ groups to be diastereotopic. The release of the unbound phenylselenide ligands upon formation of the allylpalladium complex is also consistent with the observation of an upfield shift of the $-SeC_6H_6$ group relative to those found in **4**. The σ-allyl group on Pd is also well resolved. The α-protons (δ 3.33 ppm) in **9** are about 1.8 ppm downfield relative to those of **7**, whereas the β- and γ-protons of **9** are all shifted significantly upfield relative to those of **7**. This suggests that **9** possesses a more charge-delocalized anionic allyl group, and the γ-carbon of the allyl group in **9** is more nucleophilic than that of **7**. Furthermore, we have found no indication by ^{1}H NMR for the formation or involvement of any type of a π-allylpalladium complex, such as **9**-η^3-Se and **9**-η^3. Although a dynamic equilibration among these complexes may conceivably exist, it is clear that structure **9**-η^1 is the only species that could be observed by ^{1}H NMR spectroscopy.

The fact that the selenide ligands of the transmetalation product **9**-η^1 are not ligated with the metal center also suggests that the tridentate framework in the pincer complex **4** may not be a prerequisite for its catalytic activity. To test this hypothesis, a control experiment was carried out with the SeC palladacycle **2** for the reaction of **7** and benzaldehyde (**6b**). Interestingly, the allylation product was isolated in a respectable 74% yield (Table 1, entry 15), and catalyst **2** is even more reactive in this reaction than the pincer complex **1** (Table 1, entry 13).

In summary, we have shown that the new SeCSe−Pd(II) pincer complex **4** is a highly efficient catalyst for the allylation of aldehydes with allyltributyltin. Notable advantage of this catalyst includes its high stability,[15] straightforward synthesis, and superb catalytic activity compared to other transition catalysts developed

(12) For a clarification of Lewis acid-catalyzed and Lewis acid-promoted reactions of allylstannanes, see ref 6b.

(13) The reaction was found to be very slow when a stoichiometric mixture of **4** and **7** was used in this NMR experiment.

(14) The ^{1}H NMR assignment of **9** was based on the spectrum obtained in THF-d_8 at −5 °C after **4** reacted with **7** for 20 min at 25 °C. Details of this NMR study are given in the Supporting Information.

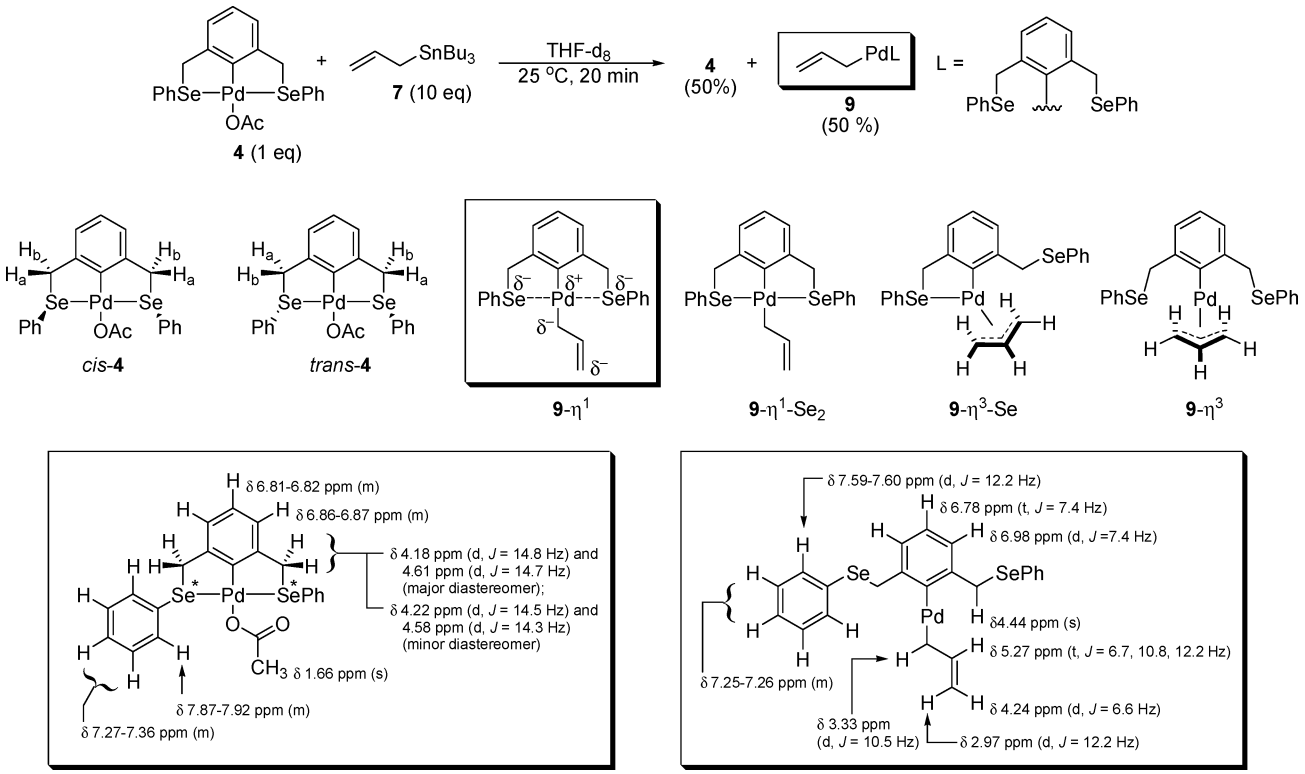


FIGURE 2. Formation and ^{1}H NMR data of the allyl−Pd(II) complex **9** from transmetalation between catalyst **4** and allyltributyltin **7**.

today for this reaction. The allylation reaction proceeded under mild and neutral reaction conditions in the presence of only 5.0×10^{-3} to 1 mol % of the catalyst. The results from this work further demonstrate the potential utility of organic selenides as alternative ligands in transition metal catalysis.[11]

Experimental Section

Synthesis of the SeCSe−Pd(II) Pincer Complex 4. An oven-dried flask was charged with bisselenide ligand **5**[11] (435 mg, 1.045 mmol) and 1 mL of glacial HOAc. Palladium acetate (236 mg, 1.05 mmol) was then added followed by an additional 1 mL of HOAc. The reaction mixture was heated to 116 °C and maintained at gentle reflux for 3 h. After the reaction was cooled to room temperature and HOAc was removed in vacuo, the crude reaction product was dissolved in dichloromethane (2 mL). Hexanes (10 mL) were then added, and the product was precipitated as a yellow crystalline solid. The precipitates were allowed to settle, and the solvent was decanted. This process was repeated three times, and the purified product was dried on vacuum line overnight to give pure **4** (498 mg, 82%) as a bright yellow solid, mp 185−188 °C. Spectroscopic analysis showed that this material exists as a diastereomeric mixture in a ratio of 3:2. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.98 (dd, J = 1.86 and 7.7 Hz, major diastereomer) and 7.91 (d, J = 7.2 Hz, minor diastereomer) (4 H in total), 7.33−7.41 (m, 6H), 6.87−6.94 (m, 3H), 4.573 (minor, d, J = 14.2 Hz) and 4.568 (d, J = 13.7 Hz, major diastereomer) (2 H in total), 4.32 (d, J = 13.7 Hz, major) and 4.21 (d, J = 14.1 Hz, minor diastereomer) (2 H in total), 1.84 (br s, minor diastereomer) and 1.71 (br s, major diastereomer) (3 H in total). ^{13}C NMR (125 Hz, $CDCl_3$): δ 177.2 (minor diastereomer) and 176.9 (major diastereomer), 152.7 (minor diastereomer) and 152.3 (major diastereomer), 150.7 (minor diastereomer) and 150.1 (major diastereomer), 133.3 (major diastereomer) and 133.2 (minor diastereomer), 130.0, 129.8, 129.59, 129.56, and 129.4 (isomeric peaks of 3 C), 124.5 (major diastereomer) and 124.3 (minor diastereomer), 123.7 (minor diastereomer) and 123.6 (major diastereomer), 43.0 (major diastereomer) and 42.4 (minor diastereomer), 23.6 (minor diastereomer) and 23.5 (major diastereomer). Anal. Calcd for $C_{22}H_{20}O_2PdSe_2$: C, 45.50; H, 3.47. Found: C, 45.45; H, 3.48.

Allylation of Aldehydes with Allyltributyltin in the Presence of the SeCSe−Pd(II) Pincer Catalyst 4. Representative Procedure: Allylation of 4-Bromobenzaldehyde (6a) with Allyltributyltin (7) in the Presence of 4 (Table 1, entry 6). A flame-dried Schlenk flask was charged with aldehyde **6a** (92.5 mg, 0.5 mmol), DMF (0.5 mL), and catalyst **4** (2.9 mg, 0.0050 mmol) under argon. Allyltributyltin (**7**) (186 μL, 199 mg, 0.6 mmol) was then added via syringe. The flask was sealed and heated to 40 °C (bath temperature) for 18 h. After cooling to room temperature, the reaction mixture was poured into water and extracted with ether. The combined extracts were stirred with aqueous KF (10%, w/v) overnight. The organic layer was then separated, washed with brine, dried (Na_2SO_4), and concentrated. The crude product was purified by flash column chromatography (hexanes/EtOAc 8:1) to give the known homoallyl alcohol **8a**[16] (106 mg, 93%) as a colorless oil. The reaction was repeated one more time, and the product was isolated in 95% yield.

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Supporting Information Available: Experimental details, including the NMR spectroscopic study on the reaction of **4** and **7**, spectroscopic data of catalyst **4** and all the products in Table 1. This material is available free of charge via the Internet at http://pubs.acs.org.

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(15) The isolation, purification, and handling of catalyst **4** are all performed in open vessels under ambient conditions without special precautions.

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