It is now clear that the chemoselectivities in the Lewis acid promoted reactions of certain aldehydes and ketones are opposite to those in the reactions in the absence of Lewis acid. By proper choice of the reaction conditions, either by carrying out the reaction in the presence or in the absence of Lewis acids, secondary and primary alcohols, homoallylic alcohols, and Diels–Alder adducts can be synthesized chemoselectively. A further extension of the above concept is being investigated in our laboratories.

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The Fate of Bis(η^3-allyl)palladium Complexes in the Presence of Aldehydes (or Imines) and Allylic Chlorides: Stille Coupling versus Allylation of Aldehydes (or Imines)

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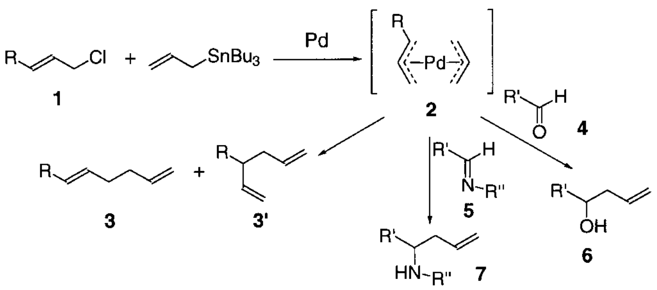
Yoshinori Yamamoto*

Palladium-catalyzed Stille coupling between allylic chlorides **1** and allyltributyltin proceeds through bis(η^3-allyl)palladium intermediates **2** to give the allylic–allylic 1,5-hexadiene coupling products **3** and **3′** in moderate to high yields (Scheme 1).[1] Recently, we found that **2** (R = H), generated from allyl chloride and allyltributyltin in the presence of a palladium catalyst, reacts with aldehydes **4** and imines **5** to produce the corresponding homoallyl alcohols **6** and amines **7**, respectively, in high yields.[2, 3] Also, we found that unsymmetrical bis(η^3-allyl)palladium complexes **2** can selectively transfer the unsubstituted allyl group to aldehydes and imines.[4] Important questions are what factors control the reaction pathways of bis(η^3-allyl)palladium intermediates **2**, and why does the Stille coupling of **2** cease in the presence of aldehydes **4** or imines **5**?



Scheme 1. Different reaction pathways of bis(η^3-allyl)palladium intermediates **2**.

We now report that phosphine ligands play a key role in this process; the Stille coupling reaction takes place in the presence of triphenylphosphine,[5] even if aldehydes **4** and imines **5** are present, whereas the allylation of aldehydes and imines occurs in the absence of the phosphine, even in the presence of allylic chlorides **1** (Scheme 2).

The palladium-catalyzed reactions of various aldehydes **4** and imines **5** with allylic chlorides were investigated in the presence or absence of PPh$_3$ (Table 1). In the absence of a phosphine ligand, the reaction of **1a** and allyltributyltin with benzaldehyde (**4a**) gave the homoallyl alcohol **6a** in 94% yield, and cinnamyl chloride **1a** was recovered in essentially

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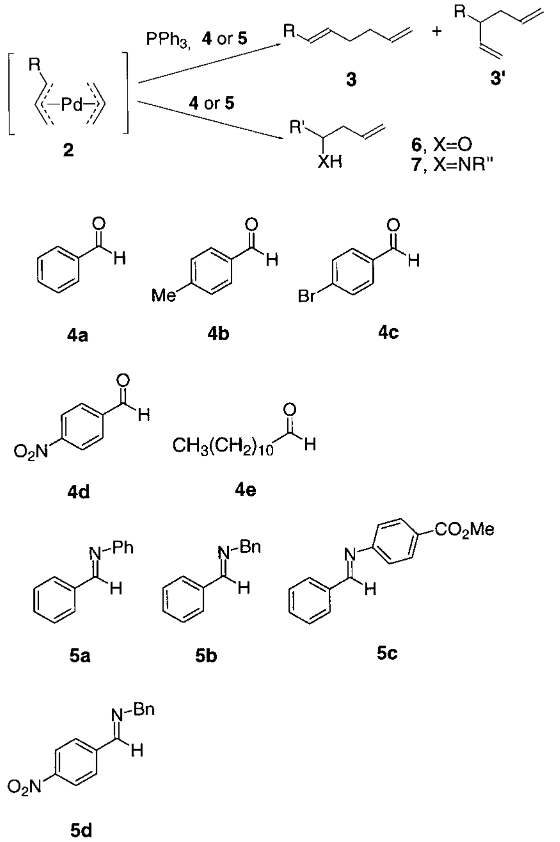


Scheme 2. The chemoselectivities of bis(η^3-allyl)palladium complexes in the presence of aldehydes (or imines) and allylic chlorides. **4a**–**4e** and **5a**–**5d** were used for the reactions shown in Table 1.

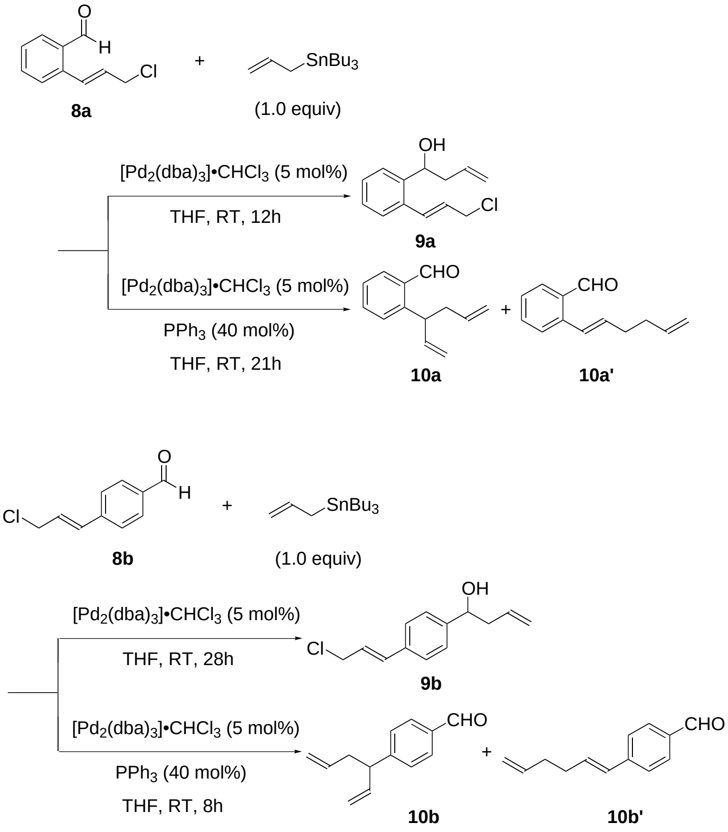
Table 1. Palladium-catalyzed reaction of allylic chlorides **1** and allyltributyltin with aldehydes **4** or imines **5** in the presence or absence of PPh_3.[a]

Entry	**1**, R	**4** or **5**	Ligand/ time [h]	Yield [%] of **6** or **7**[b]	Yield [%] of **3** + **3′** (**3**/**3′**)[b,c]
1	**1a**, Ph	**4a**	none/11	94	–
			PPh_3/19	–	90 (92/8)
2	**1b**, *p*-MeC_6H_4	**4b**	none/37	83	–
			PPh_3/13	–	78 (100/0)
3	**1c**, *p*-BrC_6H_4	**4c**	none/22	98	–
			PPh_3/22	–	80 (83/17)
4	**1a**, Ph	**4d**	none/26	93	–
			PPh_3/22	–	88 (92/8)
5	**1d**, $CH_3(CH_2)_{10}$	**4e**	none/29	71	–
			PPh_3/17	–	–[c]
6	**1a**, Ph	**5a**	none/2	82	–
			PPh_3/4	–	91 (92/8)
7	**1a**, Ph	**5b**	none/64	78	–
			PPh_3/4	–	82 (91/9)
8	**1a**, Ph	**5c**	none/132	92	–
			PPh_3/5	–	79 (91/9)
9	**1a**, Ph	**5d**	none/132	73	–
			PPh_3/21	–	80 (91/9)

[a] All reactions were carried out in the presence of 5 mol% of $[Pd_2(dba)_3]\cdot CHCl_3$ in THF at room temperature (dba = dibenzylideneacetonate). In the Stille coupling, 40 mol% of PPh_3 was added. The aldehydes **4** and imines **5** are shown in Scheme 2. [b] Yields of isolated products based on **1**, **4**, or **5**. [c] β-Elimination took place to give the diene product $CH_3(CH_2)_9CH{=}CHCH{=}CH_2$ (89%, *cis*/*trans* = 1/1).

quantitative yield (entry 1), whereas in the presence of one equivalent of PPh_3 (relative to Pd), the reaction gave a 2/1 mixture of **6a** and **3a** + **3a′**. When two equivalents of PPh_3 were used, the ratio of **6a** to **3a** + **3a′** became 1/1. With 3–5 equiv of PPh_3, only the Stille coupling reaction took place; using four equivalents of PPh_3 gave the best result: a 92/8 mixture of **3a** and **3a′** in 90% yield, and benzaldehyde was recovered quantitatively (entry 1).[6] Similar observations were made in the reactions of **1b**, **1c**, and **1a** (entries 2–4). β-Elimination took place with the aliphatic substrate **1d** in the presence of PPh_3 to give 1,3-tetradecadiene (entry 5).[7] A key role of PPh_3 in controlling the chemoselectivity was also observed in the reactions of the imines. In the absence of the phosphine ligand, the reaction of **1a**, allyltributyltin, and **5a** gave the allylation product **7a** in 82% yield, and **1a** was recovered, whereas in the presence of 4 equiv of PPh_3, a 92/8 mixture of **3a** and **3a′** was obtained in 91% yield, and the imine **5a** remained unchanged (entry 6). Similar results were obtained in the other cases (entries 7–9). Thus, highly chemoselective reactions can be accomplished by means of the presence or absence of PPh_3.

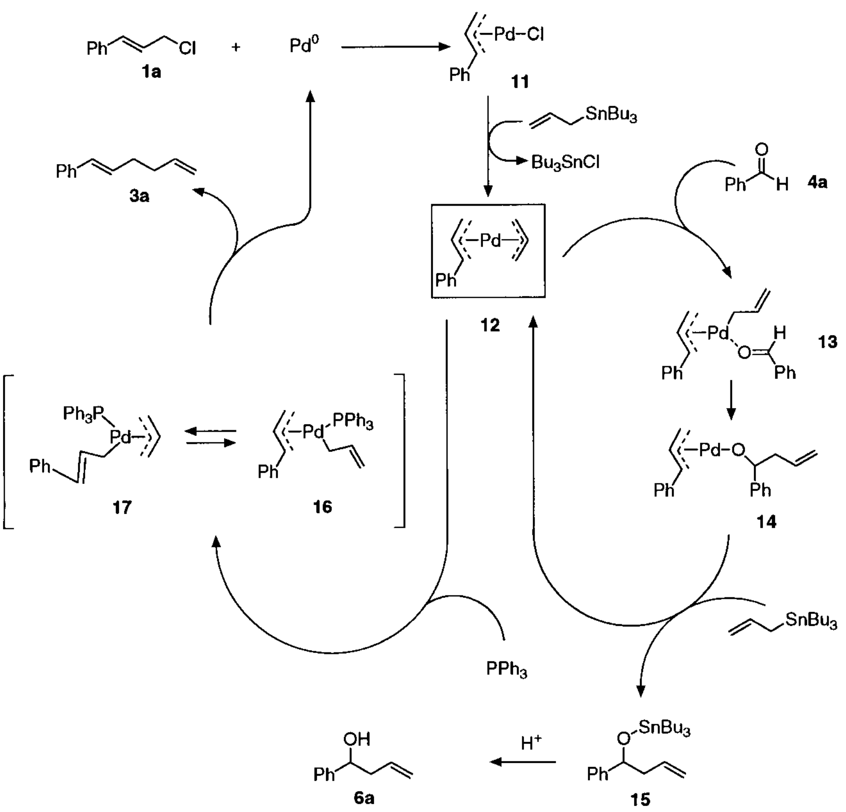
We investigated the chemoselectivity on substrates **8a** and **8b**, which contain an allyl chloride unit and an aldehyde group in the same molecule (Scheme 3). In the absence of the phosphine ligand, the *ortho* isomer **8a** reacted with allyltributyltin to give the allylation product **9a** in 88% yield, and the allyl chloride unit remained unchanged.



Scheme 3. Investigation of chemoselectivity on substrates **8a** and **8b**, which contain an allyl chloride unit and an aldehyde group in the same molecule.

However, in the presence of 4 equiv of PPh_3, only the Stille coupling reaction took place to give a 96/4 mixture of **10a** and **10a′** in 73% yield, and the aldehyde group remained unchanged. Similarly, the *para* isomer **8b** gave **9b** in 83% yield, whereas in the presence of PPh_3 a 90/10 mixture of **10b** and **10b′** was produced in 74% yield.

A plausible mechanism is shown in Scheme 4. Oxidative addition of **1a** to palladium(0) gives the η^3-allyl(chloro)palladium complex **11**, and transmetalation of **11** with allyltributyltin produces the bis(η^3-allyl)palladium complex **12**. In the absence of PPh_3, benzaldehyde (**4a**) coordinates to palladium(II) to produce the homoallyloxypalladium complex **14** via **13**. The transmetalation of **14** with allyltributyltin produces the corresponding homoallyloxytin compound **15** and regenerates the bis(η^3-allyl)palladium intermediate **12**. In the allylation reaction, the unsubstituted η^3-allyl group of **12** undergoes nucleophilic addition to benzaldehyde, while the phenyl-substituted allyl group acts as a nontransferable η^3-allyl ligand.[4b] Therefore, only catalytic amounts of cinnamyl chloride **1a** react initially with allyltributyltin to afford the bis(η^3-allyl)palladium intermediate **12**, and large amounts of **1a** remain in the reaction medium. However, in the presence of PPh_3, the phosphine ligand coordinates to **12** to give **16** and/or **17**.[8] Reductive elimination from **16** and/or **17** gives the Stille coupling product **3a** and regenerates the palladium(0) catalyst. Indeed, the Stille coupling reaction of allyltributyltin with the dimer of complex **11**, which was synthesized according to a literature procedure,[9] proceeded in the presence of PPh_3 (1 equiv) to give **3a**, whereas only a trace of **3a** was obtained in the absence of PPh_3. Therefore, the coordination of PPh_3 to the complex **12** in the reaction is essential for the Stille coupling process.



Scheme 4. Proposed mechanism for the chemoselective allylation in the presence of cinnamyl chloride **1a** and benzaldehyde **4a**.

In conclusion, the fate of bis(η^3-allyl)palladium complexes in the presence of aldehydes (or imines) and allylic chlorides has been clarified for the first time. The PPh_3 ligand plays a key role in controlling the chemoselectivity. Now, we can perform chemoselective allylation of allylic halides and aldehydes (imines).

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