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Palladium Pincer Complex-Catalyzed Allylic Stannylation with Hexaalkylditin Reagents

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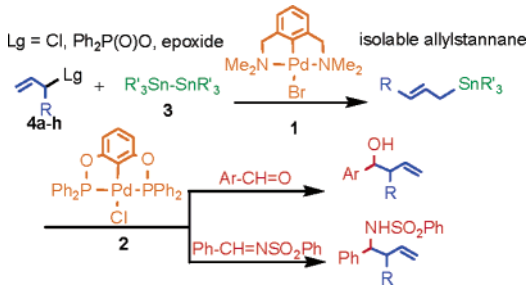
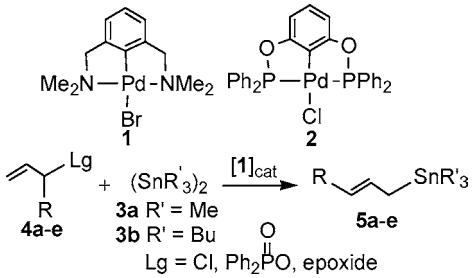
ABSTRACT



Palladium pincer complex (1)-catalyzed stannylation of allyl chloride, phosphonate, and epoxide substrates (4a–h) could be performed with hexaalkylditin reagents (3) under mild neutral reaction conditions. This catalytic reaction proceeds via palladium(II) intermediates without involvement of allyl–palladium complexes, and therefore the allylstannane product does not interfere with the palladium catalyst. Use of a combined catalytic system (1 + 2) allowed the development of an effective one-pot procedure for allylation of aldehyde and imine electrophiles.

Palladium pincer complexes are characterized by strong terdentate metal−ligand bonding leaving only a single coordination site available on the central atom.[1] Our recent studies[2] on catalytic applications of pincer complexes **1**[3a] and **2**[3b] in organo-stannane chemistry have shown that restriction of the oxidation state of palladium to +2 and limitation of the available coordination sites to a single site alters the catalytic reactivity of palladium. Recently, we have reported an efficient pincer complex-catalyzed substitution reaction of propargylic substrates with hexamethylditin (**3a**) affording propargyl- and allenyl-stannane products.[2a] We have now found that pincer complex **1** also catalyzes allylic substitution reactions in the presence of hexaalkylditin reagents. Thus, when allylic chloride, phosphonate, and epoxide substrates **4a**−**e** were reacted with hexaalkylditin reagents **3a**,**b** in the presence of catalytic amounts of pincer complex **1**, allyl-stannane products (**5a**−**e**) were obtained (Scheme 1).

Scheme 1



(1) (a) Albrect, M.; van Koten, G. *Angew. Chem., Int. Ed.* **2001**, *40*, 3751. (b) Singleton, J. T. *Tetrahedron* **2003**, *59*, 1837. (c) Slagt, M. Q.; Rodríguez, G.; Grutters, M. M. P.; Gebbink, R. J. M. K.; Klopper, W.; Jenneskens, L. W.; Lutz, M.; Spek, A. L.; van Koten, G. *Chem. Eur. J.* **2004**, *10*, 1331.

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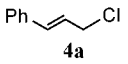
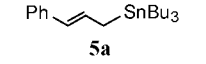
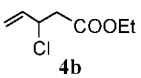
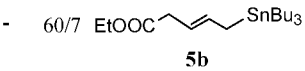
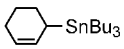
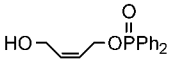
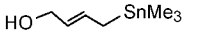
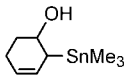
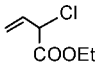
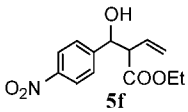
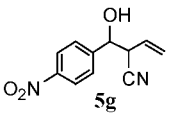
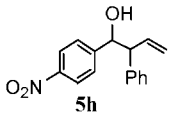
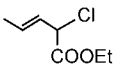
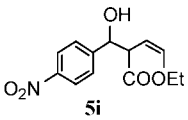
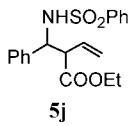
In a typical reaction, the corresponding allyl substrate **4** (0.25 mmol), **3** (0.25 mmol), and pincer complex **1** (2 mol %) were dissolved in THF (1.25 mL) under Ar. This reaction mixture was stirred at the indicated temperatures and times listed in Table 1. The products (**5**) were isolated by column chromatography.

Table 1. Pincer Complex-Catalyzed Transformation of Allylic Substrates **4a**−**h**[a]

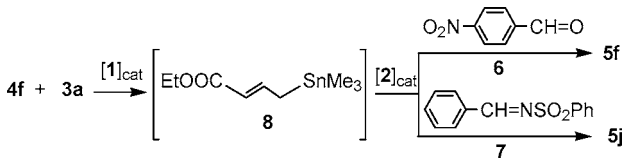
entry	allyl	ditin	E[b]	cond.[c]	product	d.r.[d]	yield[e]
1	 **4a**	**3b**	-	60/15	 **5a**	-	57
2	 **4b**	**3b**	-	60/7	 **5b**	-	62[f]
3	 **4c**	**3b**	-	60/15	 **5c**	-	72
4	 **4d**	**3a**	-	40/15	 **5d**	-	59[g]
5	 **4e**	**3a**	-	0/17	 **5e**	4:1	68[h]
6	 **4f**	**3a**	**6**	20/18	 **5f**	2:1	95
7	 **4g**	**3a**	**6**	20/18	 **5g**	1:1	96
8	**4a**	**3a**	**6**	40/18	 **5h**	10:1	96
9	 **4h**	**3a**	**6**	60/36	 **5i**	1:1	96[i]
10	**4f**	**3a**	**7**	40/18	 **5j**	1:4	56

[a] All reactions were conducted in THF using the following catalyst loadings: 2 mol % **1** in the stannylation reactions (entries 1−5); 1 mol % **1** and 2 mol % **2** in the rest of the reactions (entries 6−10). [b] Electrophile. [c] Reaction conditions: time [h]/temperature [°C]. [d] Diastereomer ratio determined by ^{1}H NMR spectroscopy. [e] Isolated yield after chromatography. [f] E/Z ratio = 9:1. [g] E/Z ratio = 5:3. [h] About 20% 1,4-substituted isomer was also formed. [i] E/Z ratio = 1:3.

The reactions usually could be carried out under mild, neutral conditions, and therefore many functionalities, including COOEt, CN, and unprotected OH, were tolerated. The best results were obtained with allyl chloride substrates (entries 1−3); however, phosphonate (entry 4) and epoxy (entry 5) leaving groups worked as well. The stannylation reaction with hexabutylditin **3b** required higher reaction temperatures (60 °C) than with hexamethylditin **3a** (typically 40 °C). Reaction products **5a**−**e** are sensitive to protonation, and therefore the isolated yields are somewhat lowered due to partial decomposition under silica gel chromatography. The regioselectivity of the stannylation reaction is high as both linear (**4a** and **4d**) and branched (**4b**) allyl chlorides gave solely linear allyl stannanes (**5a**,**b**,**d**). A somewhat lower regioselectivity was observed for opening of epoxide **4e**, which gave predominantly **5e** together with about 20% of the 1,4-substituted regioisomer.

We have also attempted to prepare allylstannanes bearing strongly electron-withdrawing groups in the allylic position. For example, carbethoxy-substituted allyl chloride **4f** was reacted with **3a** in the presence of **1** under the above mild reaction conditions. Monitoring the progress of the reaction with ^{1}H NMR spectroscopy clearly indicated the formation of allylstannane **8** (Scheme 2). However, our attempts to isolate **8** with an acceptable yield have failed. This compound rapidly decomposed under column chromatography, and in addition, it was also thermally unstable, probably because of polymerization. Nevertheless, we were able to combine the catalytic stannylation process with catalytic allylation of aldehyde (**6**) and imine (**7**) substrates using the in situ-formed allyl stannane **8** (Scheme 2). This reaction could be performed as a one-pot sequence by employment of catalysts **1** (1 mol %) and **2** (2 mol %) as well as the appropriate electrophile (**6** or **7**) in the presence of **3a**. As we reported recently,[2b] catalyst **1** is characterized by a very low activity in allylation of aldehydes and imines. In fact, this low reactivity allows the isolation of allylstannanes **5a**−**e** when using solely catalyst **1** (entries 1−5). Employment of catalyst **1** alone leads to a very slow allylation reaction with a low conversion and with a poor yield under the applied reaction conditions. On the other hand, PCP catalyst **2** facilitates the allylation of **6** and **7** without catalyzing the stannylation process.

Scheme 2



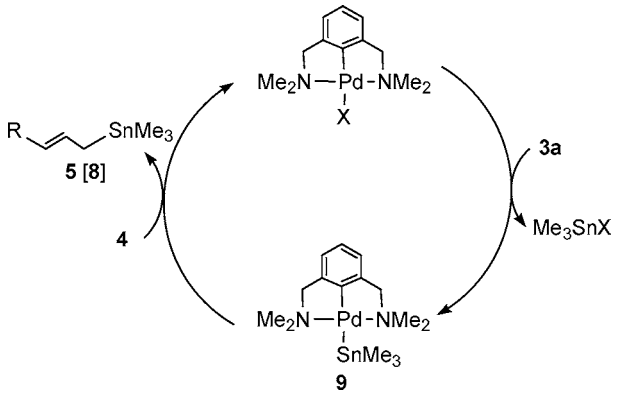
In particular, with aldehyde **6** the two pincer complex catalysts work perfectly together, affording an excellent yield for the overall process. The one-pot substitution reaction works smoothly also with substrates bearing cyano (**4g**) and phenyl (**4a**) substituents in the allylic position (entries 7, 8). The above one-pot substitution reaction (Scheme 2) proceeds with a high regioselectivity providing the branched allylic product (**5f**−**j**). This feature is maintained even for disub-

stituted substrate **4h**, where the substitution takes place at the bulky carbethoxy substituent affording **5i** as the only regioisomer. The stereoselectivity of the process is usually rather poor; the only exception is substitution of **4a**, providing predominantly the anti diastereomer of **5h**.

Mechanistic Aspects. Our previous studies[2a] revealed that hexamethylditin (**3a**) readily reacts with pincer complex **1** affording mono-stannyl complex **9**. Formation of complex **9** is probably also the introducing step of the allylic stannylation reaction (Scheme 1). The next step is a direct transfer of the trialkyl-stannyl group to the allylic substrate **4** affording allylstannane **5**. Since there is only a single coordination site available on palladium, the displacement of the allylic leaving group takes place via a metal-induced S_N2 (e.g., **4a** and **4d**) or S_N2' (e.g., **4b**) reaction affording linear products (**5a**,**b**,**d**) from functionalized substrates.[4]

There are two remarkable mechanistic features of this catalytic process (Scheme 3). The first is that allyl−palladium

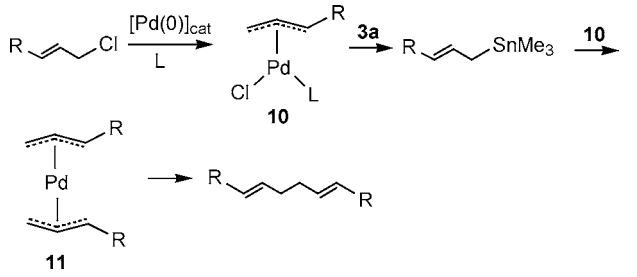
Scheme 3



complexes are not involved in formation of the allylstannanes because of the lack of free coordination sites on palladium. The other interesting feature is that the allylic substitution reaction does not involve change of the oxidation state of palladium, since it is restricted to +2 under the overall process.

Palladium(0)-catalyzed substitution of allyl chlorides and acetates using **3a** was also reported in the literature.[5a] However, this reaction usually proceeds with a low yield because of palladium-catalyzed homocoupling reaction of the allylstannane product (Scheme 4).[5a] This reactivity can be easily explained by formation of bis-allylpalladium complexes (**11**) from (η^3-allyl)palladium intermediates (**10**) and the allyl stannane products.[5b,c] Bis-allylpalladium complexes formed by transmetalation with allylstannanes are known to undergo allyl−allyl homocoupling reactions.[5d]

Scheme 4



A clear advantage of the pincer complex-catalyzed stannylation reaction is that formation of bis-allylpalladium complexes (such as **11**) is prohibited because of the firm terdentate coordination of the pincer ligand. The excellent yields obtained in the presented one-pot reactions (entries 6−9) clearly indicate that the pincer complex-catalyzed processes are more efficient than the corresponding reactions proceeding via bis-allylpalladium intermediates.[5b,c] Furthermore, under the applied reaction conditions, NCN complex **1** does not consume the allylstannane product,[2b] and therefore these products (**5a**−**e**) can be isolated in relatively good yield. On the other hand, PCP complexes (such as **2**) readily undergo transmetalation with allylstannanes and efficiently catalyze the electrophilic substitution of allyl stannanes.[2b,c] Accordingly, a combined catalytic system of **1** + **2** is suitable for electrophilic allylic substitution reaction of allyl chlorides (such as **4a**,**f**−**h**) via formation of unstable transient allyl stannanes (Scheme 2).

In summary, we have shown that allyl chloride, phosphonate, and epoxide substrates undergo palladium-catalyzed stannylation reaction with hexaalkylditin reagents affording allylstannanes. A particularly interesting feature of this process is that it proceeds solely via palladium(II) intermediates without formation of allylpalladium species. Furthermore, a combined catalytic system constructed from NCN complex **1** and PCP complex **2** is suitable for electrophilic substitution of allyl chlorides (Scheme 2) without isolation of unstable allyl stannanes (such as **8**).

Acknowledgment. This work was supported by the Swedish Research Council.

Supporting Information Available: Synthesis of PCP complex **2** and characterization and ^{13}C NMR spectra of products **5a**−**e**,**i**. This material is available free of charge via the Internet at http://pubs.acs.org.

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(4) Formation of the branched product is probably disfavored because of steric interactions between **9** and the allylic substituents in the TS of the reaction.

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