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Palladium Pincer Complex Catalyzed Stannyl and Silyl Transfer to Propargylic Substrates: Synthetic Scope and Mechanism

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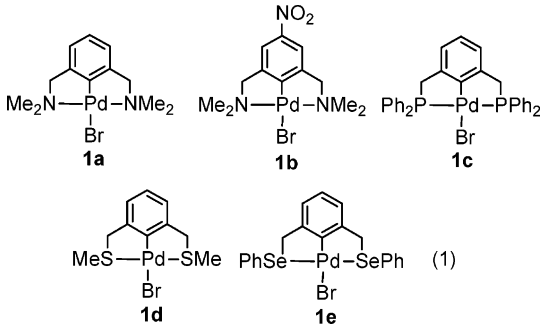
Abstract: Pincer complex catalyzed substitution of various propargylic substrates could be achieved using tin- and silicon-based dimetallic reagents to obtain propargyl- and allenylstannanes and silanes. These reactions involving chloride, mesylate, and epoxide substrates could be carried out under mild conditions, and therefore many functionalities (such as COOEt, OR, OH, NR, and NAc) are tolerated. It was shown that pincer catalysts with electron-supplying ligands, such as NCN, SCS, and SeCSe complexes, display the highest catalytic activity. The catalytic substitution of secondary propargyl chlorides and primary propargyl chlorides with electron-withdrawing substituents proceeds with high regioselectivity providing the allenyl product. Opening of the propargyl epoxides takes place with an excellent stereo- and regioselectivity to give stereodefined allenylstannanes. Silylstannanes as dimetallic reagents undergo an exclusive silyl transfer to the propargylic substrate affording allenylsilanes with high regioselectivity. According to our mechanistic studies, the key intermediate of the reaction is an organostannane (or silane)-coordinated pincer complex, which is formed from the dimetallic reagent and the corresponding pincer complex catalyst. DFT modeling studies have shown that the trimethylstannyl functionality is transferred to the propargylic substrate in a single reaction step with high allenyl selectivity. Inspection of the TS structures reveals that the trimethylstannyl group transfer is initiated by the attack of the palladium−tin σ-bond electrons on the propargylic substrate. This is a novel mechanism in palladium chemistry, which is based on the unique topology of the pincer complex catalysts.

I. Introduction

Palladium catalysis offers an attractive approach for synthesis of unsaturated organometallic compounds from dimetallic reagents because of the high selectivity and functional group tolerance of the process.[1−6] Application of pincer complex catalysts,[7−12] such as **1a**−**e** (eq 1), instead of commonly used palladium sources opens new synthetic routes for selective synthesis of densely functionalized organometallic reagents due to three important features: (1) in these pincer complexes, there is a strong rigid bonding between the central atom and the terdentate ligand; (2) there is only a single coordination site, trans to the electron-rich palladium−carbon bond available on palladium for catalytic processes; and (3) the oxidation state of palladium is largely restricted to +2. Because of feature 2, the catalytic activity of pincer complexes and commonly used palladium salts is particularly different,[13−16] as usual palladium sources have at least two coordination sites available for the catalytic processes.



The palladium-catalyzed reactions of hexaalkylditin with alkynes represent an interesting example.[1,17−20] Application of

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(2) Marshall, J. A. *Chem. Rev.* **2000**, *100*, 3163.
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(12) Singleton, J. T. *Tetrahedron* **2003**, *59*, 1837.
(13) Solin, N.; Kjellgren, J.; Szabó, K. J. *Angew. Chem., Int. Ed.* **2003**, *42*, 3656.
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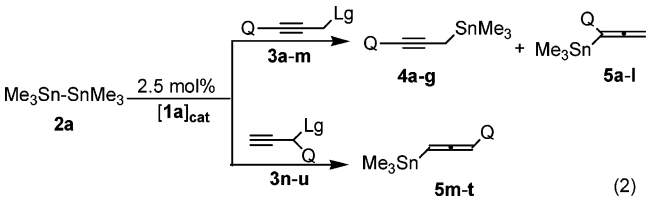
usual palladium(0) catalysts leads to oxidative addition of palladium to the tin−tin bond as long as propargylic leaving groups (such as halogenides, mesylate, epoxide, etc.) are not present in the substrate. This oxidative addition generates a bis-stannyl palladium(II) species,[19] which then adds to the triple bond providing a disubstituted olefin product. As only a single coordination site is available on palladium in a pincer complex catalyst, formation of a bis-stannyl reagent is unlikely, and therefore a completely different reactivity is expected. Indeed, we have found that using hexamethylditin (**2a**) with propargyl chloride or mesylate substrates (e.g., **3a**−**f**) and catalytic amounts (2.5 mol %) of pincer complex catalyst leads to displacement of the propargylic leaving group instead of addition of the trimethylstannane groups to the triple bond.[15] Thus, this reaction leads to formation of propargyl or allenylstannanes, depending on the steric and electronic effects of the substituents attached to the triple bond.



(2)

Recently, we have communicated our results involving primary propargyl chloride and mesylate substrates in these reactions.[15] In this paper, we give a full account of our results on pincer complex catalyzed substitution of propargylic substrates with dimetallic reagents. In addition, we present our new studies on the following synthetic (i−iii) and mechanistic (iv) aspects of this reaction:

(i) Possibilities to extend the synthetic scope to secondary propargylic substrates, including substitution of propargyl epoxides.

(ii) Application of unsymmetrical dimetal reagents, such as silylstannanes **2b**−**d**, for chemoselective silyl transfer reactions.

(iii) Possibilities to improve the catalytic activity of the applied pincer catalyst by varying the heteroatom in the ligand (cf. complexes **1d** and **1e**).

(iv) Modeling the transfer of the trimethylstannyl group from the pincer complex to the propargylic substrate using density functional theory (DFT).

2. Catalytic Trimethyltin Transfer to Propargylic Substrates

Primary Propargylic Substrates. As we communicated before,[15] NCN complex **1a** efficiently catalyzes the transfer of the trimethyltin group from hexamethylditin (**2a**) to primary propargyl chloride and mesylate substrates. The reactions are conducted under mild and neutral conditions at room temperature. Application of mild reaction conditions is essential to achieve high yields in these reactions since the functionalized propargyl and allenylstannane products have a limited thermal stability. Increase of the reaction temperature over 50 °C usually leads to substantial decomposition of these products giving poor yield. The neutral reaction conditions and the redox stability of the catalyst allow a wide variety of substrate functionalities, including COOEt, OR, OAc, NR, NAc, and even unprotected OH. The regioselectivity of the catalytic displacement reaction for primary propargyl chlorides is strongly dependent on the electronic effects of the propargylic substituents. For bulky electron-supplying substituents, such as phenyl (**3a**,**b**) and alkyl (**3c**) groups, the main product of the reaction is propargylstannane (entries 1−8). Propargyl chloride (**3d**) itself and substrates with electron-withdrawing substituents (e.g., **3e**, **3f**, **3i**, and **3j**) give exclusively allenyl products (entries 9−12, 16, and 17). Interestingly, even subtle electronic effects have a strong influence on the regioselectivity of the stannylation process. For example, the hydroxymethylene group in **3f** has a weak electron-withdrawing effect, which is sufficient to direct the reaction toward exclusive formation of the corresponding allenyl product **5e** (entry 12). However, benzyl protection (**3g**) of the hydroxy group slightly modifies the electronic properties of the substrate leading to an appearance of the corresponding propargyl product (**4c**) as a minor component in the reaction mixture (entry 13). Furthermore, insertion of a methylene unit renders the OBn functionality to the γ-position to the triple bond (**3h**), which leads to predominant formation of the propargyl product **4d** (entry 15). A similar trend is observed for an aminomethylene-type of substituents (entries 18−20). As one goes from electron-supplying (**3k**) to electron-withdrawing substituents (**3l** and **3m**) on nitrogen, the allenyl selectivity increases.

Secondary Propargylic Substrates. Our new studies on secondary propargyl chlorides (**3n**−**r**) show that NCN catalyst **1a** smoothly transforms these substrates to the corresponding allenylstannane products (entries 21−26). The reaction proceeds with an excellent regioselectivity for various propargylic substituents involving phenyl (**3n**), 2-naphthyl (**3o**), benzyl (**3p**), and N-Boc-aminomethylene (**3q**) groups to provide exclusively the corresponding allenyl product with good to excellent yield. Phenyl substitution of **3a** at the propargylic position (**3r**) leads to a complete reversal of the regioselectivity, as the catalytic stannylation of substrate **3r** gives exclusively the allenyl product **5q** (cf. entries 1 and 26).

We have found that propargyl epoxides (**3s**−**u**) can also be employed in place of propargyl chlorides. The epoxide opening takes place with an excellent regioselectivity providing exclusively the corresponding allenyl product (entries 27−29). When the reaction is conducted at 0 °C, the opening of cyclic epoxides **3t** and **3u** provides single diastereomers **5s** and **5t**, respectively (entries 28 and 29). Thus, the pincer complex catalyzed epoxide opening reaction proceeds with an excellent regio- and stereochemistry and, at least for **3t**, an excellent yield. Increasing the reaction temperature to r.t. leads to formation of small amounts the other diastereomeric form (up to 25%).

Attempts to Increase the Activity of the Pincer Complex Catalyst. The high electron density on palladium ensured by the σ-donor amino and phenyl ligands is essential to achieve a high catalytic activity by NCN complex **1a**. A slight decrease of the electron-donor properties of the phenyl group by nitro substitution (**1b**)[8] leads to lowering of the catalytic activity of the pincer complex (cf. entries 1 and 2). Commonly used catalysts, such as $Pd(PPh_3)_4$ (**6**) and $Li_2[PdCl_4]$, do not show any catalytic activity under the applied reaction conditions. Exchange of the amino groups in **1a** with less-efficient σ-donor

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(19) Tsuji, Y.; Nishiyama, K.; Hori, S.-i.; Ebihara, M.; Kawamura, T. *Organometallics* **1998**, *17*, 507.
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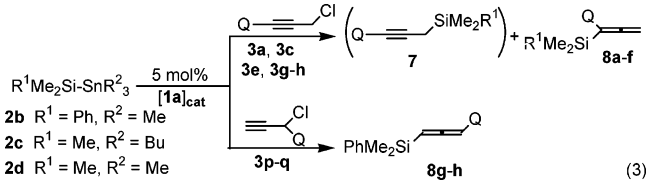
phosphines (**1c**)[21] also leads to a complete loss of the catalytic activity (entry 3). Therefore, we considered replacing the amino ligands of **1a** with strongly electron-supplying ligands, such as sulfur (**1d**)[22] and selenium-based ligands (**1e**).[23] The SCS complex **1d** displayed a high catalytic activity; however, the catalytic transformations using **1d** required longer reaction times and higher reaction temperatures than the corresponding processes with **1a** (cf. entries 1 and 4, as well as entries 7 and 8). On the other hand, SeCSe complex **1e**, reported very recently by Yao and co-workers,[23] displayed a catalytic activity higher than that of **1a**. Comparing the corresponding entries in Table 1 (entries 1 and 5, 10 and 11, 13 and 14, as well as 24 and 25) reveals that the stannylation reactions with SeCSe complex **1e** required typically 50% shorter reaction times than with **1a**. On the other hand, we obtained slightly lower regioselectivities (entries 5 and 14) and yields (entries 5 and 8) with **1e** than with **1a** as catalyst. These results indicate that in the presented trimethyltin transfer processes, NCN complex **1a** is a slightly more selective catalyst than SeCSe complex **1e**; on the other hand, slow catalytic transformations can be efficiently accelerated by employment of **1e** as catalyst.

3. Application of Unsymmetrical Dimetal Reagents 2b−d

Similar to **2a**, unsymmetrical dimetal reagents, such as silylstannanes (**2b**−**d**), are known to undergo addition to triple bonds in the presence of usual palladium catalysts (such as **6**) providing difunctionalized olefins.[1,4,24−26] In the above pincer complex catalyzed applications, symmetrical distannane **2a** was employed as reagent for the palladium pincer catalyzed trialkylmetal transfer process. However, when unsymmetrical reagents **2b**−**d** are employed, either the silyl or the stannyl group can be transferred to the propargyl substrates.



(3)

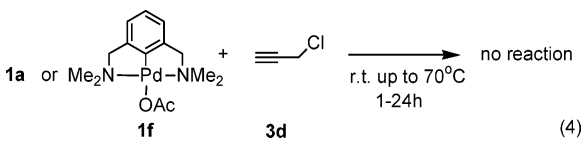
We have found that the pincer complex catalyzed substitution of propargyl chlorides can also be performed by employment of silylstannanes **2b** and **2c** (eq 3). A particularly important feature of this reaction is that exclusively the silyl functionality is transferred to the propargylic substrates, affording allenylsilanes in good yield (entries 30−37). These catalytic reactions were conducted at 40 °C with slow addition (over 5 h) of trimethylstannyl reagent **2b**, while a higher reaction temperature (60 °C) was required when tributylstannyl analogue **2c** was employed (entry 31). Since the allenylsilane products have a relatively poor thermal stability, the isolated yields of these products were usually higher with reagent **2b** (permitting a reaction temperature of 40 °C) than with **2c** (employed at 60 °C). A fast addition of **2b** usually leads to a partial decomposition of this dimetallic reagent, which caused lowering of the yields. Reagent **2d** could also be employed in the silylation reactions; however, this reagent undergoes extensive decomposition in the reaction mixture, even when it was added slowly to the reaction mixture. It was also found that addition of 4 Å molecular sieves leads to improved yields in the catalytic silylation reactions.

Since the substitution reactions with **2b** are still conducted under relatively mild and neutral conditions, many functionalities, including COOEt, OBn, CH_2Ph, and NHBoc, are tolerated. The regioselectivity of the reaction is excellent, as we obtained exclusively allenylsilane products (**8**). The only exception is the reaction of **3c** with **2b** affording predominantly the allenyl product **8c** together with 20% of propargylsilane **7** (entry 32). The high allenyl preference of the reaction with silylstannanes **2b**,**c** is in sharp contrast with the regioselectivity of the stannylation process with hexamethylditin (**2a**). For example, propargyl chloride **3a** reacts with **2a** in the presence of pincer complex catalyst **1a**, affording mainly the propargyl product **4a** and only traces of allenylstannane **5a** (entry 1). Conversely, the same catalytic reaction with silylstannanes **2b** and **2c** (entries 30 and 31) yields exclusively allenylsilanes **8a** and **8b**, respectively. As mentioned, the reaction with alkyl-substituted substrate **3c** gave the propargylic isomer as a minor product (entry 32). However, **3h** bearing a benzyloxy functionality at the γ-position gives again exclusively allenyl product **8f** (entry 35). This regioselectivity (entries 32 and 35) is also the opposite to the selectivity of the stannylation reactions (entries 7 and 15), which provide the corresponding propargylic isomers (**4b** and **4d**) as the major products.

The silylation reactions proceed smoothly in the presence of electron-withdrawing substituents at the α- or β-position to the triple bond (entries 33 and 34). Product **8e** proved to be particularly sensitive to thermal decomposition. When **3g** was treated with **2c** in place of **2b** at 60 °C, only traces of the corresponding allenylsilane product (**8e**) could be isolated from the reaction mixture. Secondary propargyl chloride derivatives **3p** and **3q** were also converted smoothly, affording the corresponding allenylsilanes **8g**,**h** (entries 36 and 37).

4. Mechanistic Considerations

The mechanistic aspects of the catalytic reactions were studied by performing stoichiometric reactions for the conceivable elementary steps of the catalytic cycle. These reactions were conducted in THF-d_8, and they were monitored by various NMR spectroscopy methods. It is well-known that palladium(0) complexes readily undergo oxidative addition to propargyl chlorides.[27−29] However, we found that NCN complex **1a** or its acetate analogue **1f** (in which the counterion dissociates easier than in **1a**) did not react with propargyl chloride **3d** at r.t. to 70 °C up to 24 h reaction time (eq 4).



(4)

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(22) Dupont, J.; Beydoun, N.; Pfeffer, M. *J. Chem. Soc., Dalton Trans.* **1989**, 1715.
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Table 1. Pincer Complex Catalyzed Silyl and Stannyl Transfer to Propargylic Substrates[a]

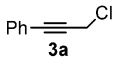
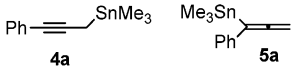
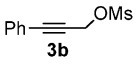
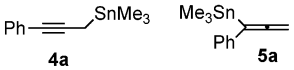
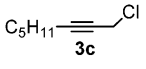
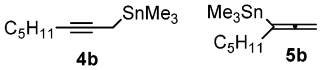
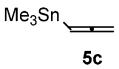
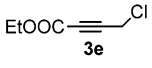
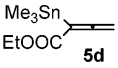
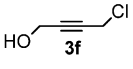
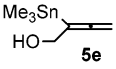
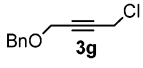
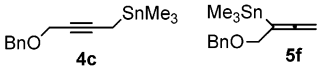
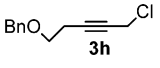
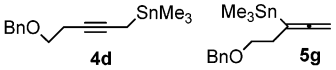
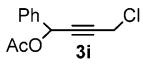
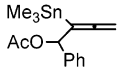
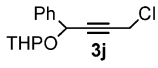
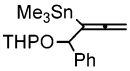
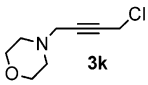
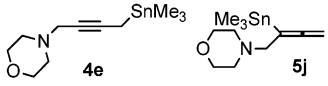
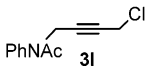
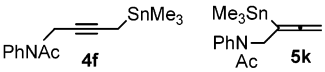
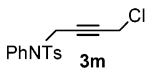
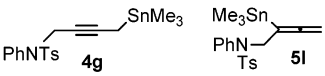
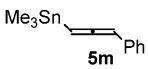
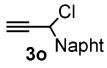
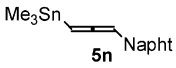
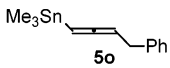
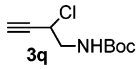
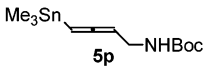
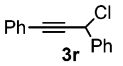
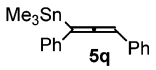
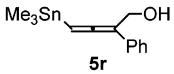
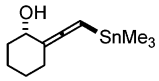
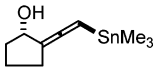
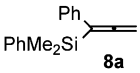
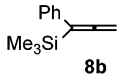
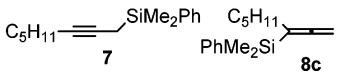
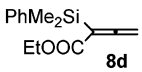
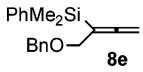
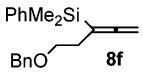
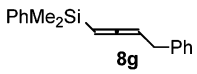
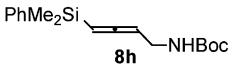
Entry	Substrate	Cat.[b]	Sn-M	Cond.[c]	Product	ratio[d]	Yield[e]
1	 **3a**	**1a**	**2a**	r.t / 2	 **4a** **5a**	8:1	87
2	**3a**	**1b**	**2a**	r.t. / 20	**4a** **5a**	7:1	86
3	**3a**	**1c**	**2a**	r.t. / 18		no reaction	
4	**3a**	**1d**	**2a**	r.t. / 5	**4a** **5a**	8:1	80
5	**3a**	**1e**	**2a**	r.t. / 1.5	**4a** **5a**	7:1	77
6	 **3b**	**1a**	**2a**	r.t / 13	 **4a** **5a**	10:1	75
7	 **3c**	**1a**	**2a**	0/ 3	 **4b** **5b**	8:1	95
8	**3c**	**1d**	**2a**	r.t. / 3	**4b** **5b**	8:1	91
9	 **3d**	**1a**	**2a**	r.t / 2	 **5c**	a.p.	(87)[f]
10	 **3e**	**1a**	**2a**	r.t. / 6	 **5d**	a.p.	64
11	**3e**	**1e**	**2a**	r.t. / 3	**5d**	a.p.	66
12	 **3f**	**1a**	**2a**	0 / 16	 **5e**	a.p.	81
13	 **3g**	**1a**	**2a**	r.t. / 16	 **4c** **5f**	1:5	95
14	**3g**	**1e**	**2a**	r.t. / 3	**4c** **5f**	1:4	95
15	 **3h**	**1a**	**2a**	r.t. / 6	 **4d** **5g**	8:1	95
16	 **3i**	**1a**	**2a**	r.t. / 3	 **5h**	a.p.	83
17	 **3j**	**1a**	**2a**	r.t. / 1.5	 **5i**	a.p.	87
18	 **3k**	**1a**	**2a**	r.t. / 4	 **4e** **5j**	2:3	74
19	 **3l**	**1a**	**2a**	r.t. / 3.5	 **4f** **5k**	1:2	85
20	 **3m**	**1a**	**2a**	r.t. / 3.5	 **4g** **5l**	1:6	67
21	 **3n**	**1a**	**2a**	r.t. / 4	 **5m**	a.p.	81
22	 **3o**	**1a**	**2a**	r.t. / 4	 **5n**	a.p.	70
23	 **3p**	**1a**	**2a**	r.t. / 4	 **5o**	a.p.	95

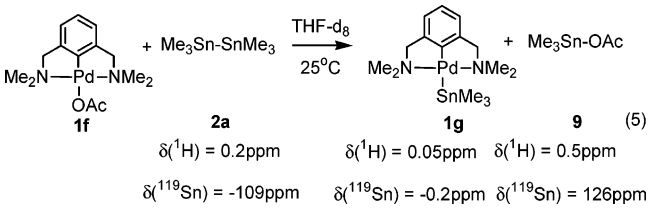
Table 1 (Continued)

Entry	Substrate	Cat.[b]	Sn-M	Cond.[c]	Product	ratio[d]	Yield[e]
24	 **3q**	**1a**	**2a**	r.t. / 5	 **5p**	a.p.	95
25	**3q**	**1e**	**2a**	r.t. / 2.5	**5p**	a.p.	95
26	 **3r**	**1a**	**2a**	r.t. / 6	 **5q**	a.p.	84
27	 **3s**	**1a**	**2a**	r.t. / 6	 **5r**	a.p.	83
28	 **3t**	**1a**	**2a**	0 / 16	 **5s**	a.p.	95
29	 **3u**	**1a**	**2a**	0 / 16	 **5t**	a.p.	64
30	**3a**	**1a**	**2b**	40/24	 **8a**	a.p.	74
31	**3a**	**1a**	**2c**	60/4	 **8b**	a.p.	66
32	**3c**	**1a**	**2b**	40/24	 **7** **8c**	1:4	78
33	**3e**	**1a**	**2b**	40/24	 **8d**	a.p.	71
34	**3g**	**1a**	**2b**	40/24	 **8e**	a.p.	63
35	**3h**	**1a**	**2b**	40/24	 **8f**	a.p.	64
36	**3p**	**1a**	**2b**	40/24	 **8g**	a.p.	80
37	**3q**	**1a**	**2b**	40/24	 **8h**	a.p.	70

[a] In the stannylation reactions, 2.5 mol % of pincer complex catalyst was applied (General Procedure A), while in the silylation processes, 5 mol % catalyst was applied and the silylstannane reagent (**2b**) was added in 5 h (General Procedure B). [b] Pincer complex catalyst. [c] Reaction conditions; reaction temperature [°C]/reaction time [h]; r.t. = room temperature. [d] Propargyl-to-allenyl ratio; a.p. = allenyl product only (indicating that the propargylic isomer was not detected in the crude and in the isolated product by ^{1}H NMR spectroscopy). [e] Isolated yield. [f] Product was not isolated because of its volatility. The yield was determined by NMR spectroscopy.

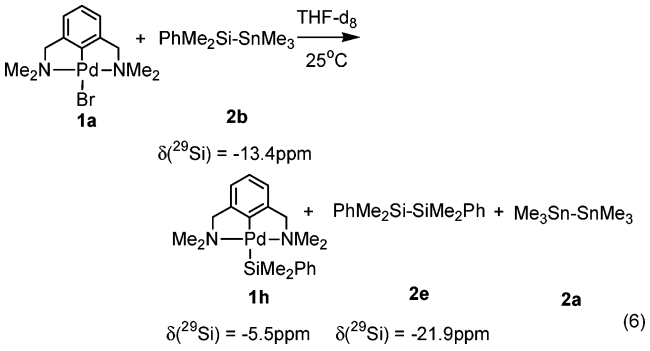
Stoichiometric Reactions with $(SnMe_3)_2$. In contrast to the above stoichiometric reaction (eq 4), complex **1f** reacted readily with **2a**. The progress of this reaction was clearly indicated by systematic changes of the ^{1}H and ^{119}Sn NMR spectrum of the reaction mixture. In the ^{1}H NMR spectrum of this stoichiometric reaction, the methyl peak of **2a** (0.2 ppm) gradually decreased, and at the same time, two new singlets appeared at 0.5 and 0.05 ppm (eq 5). The peak at 0.5 ppm belongs to the methyl resonance of **9**, while the appearance of the other singlet is indicative for the formation of a new trimethylstannyl species, **1g**. We could also observe a small (0.1 ppm) but significant upfield shift of the ^{1}H protons of the pincer complex. According to the time-averaged ^{1}H NMR spectrum, the newly formed species has a C_{2v} symmetry, indicating that the symmetrical pincer structure is maintained in the reaction of **1f** with **2a**. The above assumption for formation of **1g** is confirmed by the ^{119}Sn NMR spectrum of the reaction mixture. In the ^{119}Sn NMR spectrum, we observed a decrease of the resonance peak of **2a** (−109 ppm) and a simultaneous appearance of a new peak at −0.2 ppm. This latter peak we assigned to the ^{119}Sn NMR resonance of **1g**. This assignment is also in line with the ^{119}Sn NMR data published for similar palladium−

trimethylstannyl complexes, such as $Pd(PMe_3)_2(SnMe_3)_2$ [$\delta(^{119}Sn) = -28$ ppm][19] and Pddppe(CONiPr)($SnMe_3$) [$\delta(^{119}Sn) = 45.4$ ppm].[30] On the basis of the above results, we consider complex **1g** as the product of the introducing step of the catalytic process.



(5)

Stoichiometric Reactions with $PhMe_2Si-SnMe_3$. We have also briefly studied the stoichiometric reaction of complex **1a** with silylstannane **2b** (eq 6). Silylstannane **2b** in THF-d_8 was added slowly (over 5 h) to pincer complex **1a** dissolved in THF-d_8, then the resulting mixture was analyzed by ^{29}Si NMR. In this stoichiometric reaction, **2b** [δ (^{29}Si) = −13.4 ppm] was completely consumed, while two new peaks at −21.9 and −5.5 ppm appeared in the ^{29}Si NMR spectrum of the reaction mixture. The high field shift at −21.9 ppm arose from **2e** (lit.[31] = −21.7 ppm) formed by disproportionation of **2b** (eq 6). The other shift at −5.5 ppm could be easily distinguished from the resonance frequency of the possible hydrolysis product $(PhSiMe_2)_2O$ resonating at −1.2 ppm. The shift value at −5.5 ppm is close to the ^{29}Si NMR shift (−1.1 ppm) reported[32] for the $(dcpe)_2$-$PdHSiMe_2Ph$ complex also incorporating a palladium(II)−$SiMe_2Ph$ bond. Accordingly, we assigned this shift value to pincer complex **1h** (eq 6), which is the silyl analogue of **1g** formed in the corresponding reaction with **2a** (eq 5).

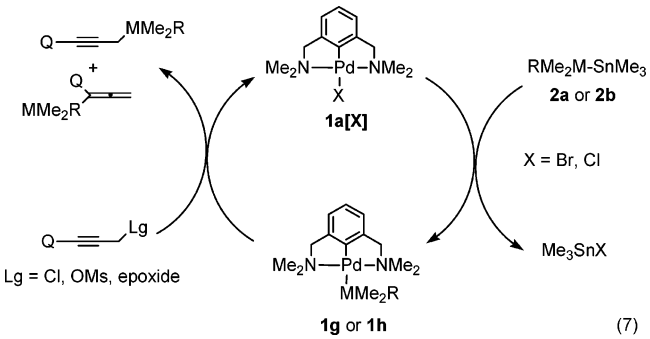


(6)

It was also observed that stoichiometric addition of **2b** to **1a** in one portion (instead of using slow addition) leads to an extensive disproportionation of **2b** yielding **2e** and **2a**. As mentioned above, fast addition of **2b** to the reaction mixture in the catalytic reactions (eq 3) usually leads to lowering of the yield, which can explained by disproportionation or other degradation processes of the unreacted **2b**.

Unfortunately, our efforts to isolate silicon− and tin−organic pincer complexes **1g** and **1h** were fruitless because of the poor stability of these species. This poor stability can probably be explained by the presence of a highly reactive tin/silicon−palladium σ-bond (vide infra) in these complexes.

The Catalytic Cycle. On the basis of the above stoichiometric reactions, we consider the transfer of the corresponding metal functionality from the dimetal reagent to the pincer complex (eq 7) as the introducing step of the catalytic cycle. This transmetalation process involves cleavage of the corresponding Sn−M bond. In the case of symmetrical dimetal reagent **2a**, this reaction leads to transfer of the trimethylstannyl group to palladium. However, for unsymmetrical reagent **2b**, either the silyl or the stannyl functionality can be transferred to palladium. Nevertheless, according to the experimental results (entries 30−37) and the results of the stoichiometric reactions (eq 6), it can be concluded that preferentially the silyl functionality is transferred to palladium. The predominant formation of **1h** instead of **1g** probably arises from the higher electronegativity of silicon in **2b**. The heterolytic cleavage of the Si−Sn bond leads to accumulation of the negative charge on the silicon atom and charge depletion on the more electropositive tin atom. Thus, in the transmetalation step, the halogenide counterion on palladium will be replaced by a negatively charged silyl group instead of a positively charged stannyl functionality.



(7)

The final step of the catalytic process is the transfer of the organometallic functionality (MMe_2R) from palladium to the propargylic substrate. Considering the fact that there is no accessible coordination site on palladium in **1g** (or **1h**), this process is expected to be the most unique reaction step in the above pincer complex catalyzed metalation process. Thus, to explore the mechanistic details of this step, we carried out DFT modeling studies. In these studies, we investigated the mechanistic aspects of the transfer of trimethylstannyl group from complex **1g** to propargyl chloride **3d**.

DFT Modeling of the Transfer of the Trimethylstannyl Group. The DFT studies were focused on the exploration of the potential energy surface (PES) of the trimethylstannyl transfer process (Figures 1 and 2). Study of the factors determining the regiochemistry of the reaction was of particular interest. Therefore, we studied various possible pathways leading to formation of the allenyl (**5c**) and propargyl (**11**) stannanes from **1g** and **3d**.

All geometries were fully optimized employing a Becke-type[33] three-parameter functional B3PW91 using a double-ζ-(DZ)+P basis constructed from the LANL2DZ basis[34−36] by adding one set of polarization functions to the heavy atoms (exponents: C, 0.63; N, 0.864; Cl, 0.514; Sn, 0.183) and one set of diffuse functions on palladium (exponent: 0.0628).

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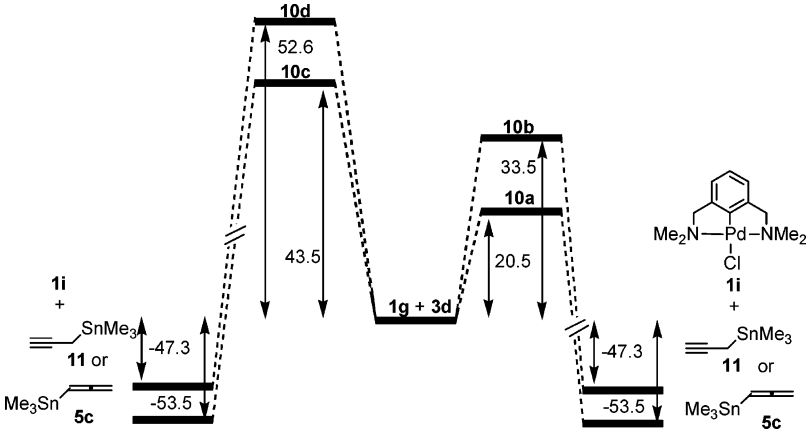

Figure 1. Reaction profiles for the trimethylstannyl transfer reactions from palladium (**1g**) to propargyl chloride (**3d**) giving allenyl (**5c**) or propargyl product (**11**). The TS structures (**10a**−**d**) are given in Figure 2. All energies are given in kcal mol^{-1}.

According to the vibrational analysis (performed at the optimization level), **10a**−**d** were characterized as transition-state structures, while the rest of the structures were characterized as minima on the PES. All calculations were carried out by employing the Gaussian 03 package.[37]

The calculated structure of **1g** was characterized by a relatively long palladium−tin bond (2.749 Å) and with a tight coordination by the nitrogen and carbon atoms of the pincer ligand. We considered two distinct pathways for the trimethyltin transfer reaction. (a) The first pathway involves interaction between the palladium atom and propargylic substrate. (b) The other one is performed without involvement of the palladium atom. An interesting feature of both pathways is that the formation of allenyl (**5c**) or propargyl stannane (**11**) from **1g** and **3d** takes place in a single reaction step. This means that the trimethylstannyl transfer from **1g** to **3d** involves a simultaneous formation of the carbon−tin bond and cleavage of the carbon−chlorine bond.

The lowest energy path on the PES leads to formation of allenylstannane via TS **10a** requiring a relatively low activation energy of 20.5 kcal mol^{-1} (Figure 1). In TS **10a**, the distances of the attacked propargylic carbon to the palladium (2.638 Å) and to the tin (2.664 Å) atoms (Figure 2) are about equal. The carbon−chlorine bond (1.952 Å) is much longer than the C−Cl bond length in **3d** (1.810 Å), indicating that a bond-breaking process also takes place in the TS. Formation of propargyl stannane (**11**) proceeds through TS structure **10b** requiring 13 kcal mol^{-1} higher activation energy (33.5 kcal mol^{-1}) than that required for formation of the allenyl analogue **5c**. The geometry of the reaction center in **10b** is similar to that in **10a**, as the attacked propargylic carbon interacts with both the palladium (2.961 Å) and the tin (2.773 Å) atoms accompanied by the cleavage of the carbon−chlorine bond (2.502 Å). We have also localized two other TS structures, **10c** and **10d**, in which the palladium atom is not directly involved in the trimethyltin transfer process. In these processes, however, the activation barrier is unrealistically high (43.5 and 52.6 kcal mol^{-1}), and therefore it is unlikely that the stannylation reaction would proceed through these TS structures.

A closer inspection of TS structures **10a** and **10b** reveals that the geometry of the reaction center is similar to that of the classical S_N2' and S_N2 reactions, in which the formation of the new bond and cleavage of the leaving group take place simultaneously. There is, however, a clear difference between the geometry of the TS of the classical nucleophilic substitution reactions and that of the presented processes (**10a**,**b**). In a classical S_N2 reaction, the attacking nucleophile is aligned with the reaction center and the leaving group closing an angle of 180°. However, the corresponding Sn−C−Cl angle in **10b** is 132°, and furthermore, the palladium atom is also involved in the displacement of the leaving group. On the other hand, the middle point of the palladium−tin bond, the attacked propargylic carbon, and the carbon−chloride bond do form an angle close to 180° in the TS structures. This suggests that the electron pair of the palladium−carbon σ-bond exerts a nucleophilic attack on the propargylic carbon, cleaving the carbon−chloride bond. This hypothesis can also be confirmed by inspection of the high-energy (−4.5 eV) HOMO orbital of complex **1g** (Figure 3), which is largely localized to the palladium−tin σ-bond. Thus, the electron pair of the palladium−tin σ-bond is readily available for electrophiles, such as **3d**. It is particularly interesting to compare the HOMO of **1g** to the corresponding HOMO of hexamethylditin (**2a**). The HOMO in **2a** has also a clear metal−metal σ-bond character; however, the HOMO energy (−6.3 eV) is considerably lower in **2a** than in **1g**. Because of this low HOMO energy, **2a** is not able to perform the nucleophilic displacement of the chloride of **3d**. On the other hand, palladium pincer complex **1g** has a high energy HOMO, and therefore this complex is more nucleophilic than **2a**, which leads to a successful trimethyltin transfer to the propargylic substrate **3d**. This can also be considered as the main reason for employment of palladium pincer complex catalysis in the above reaction.

As far as we know, the above-described palladium−metal σ-electron transfer-initiated single-step displacement of the

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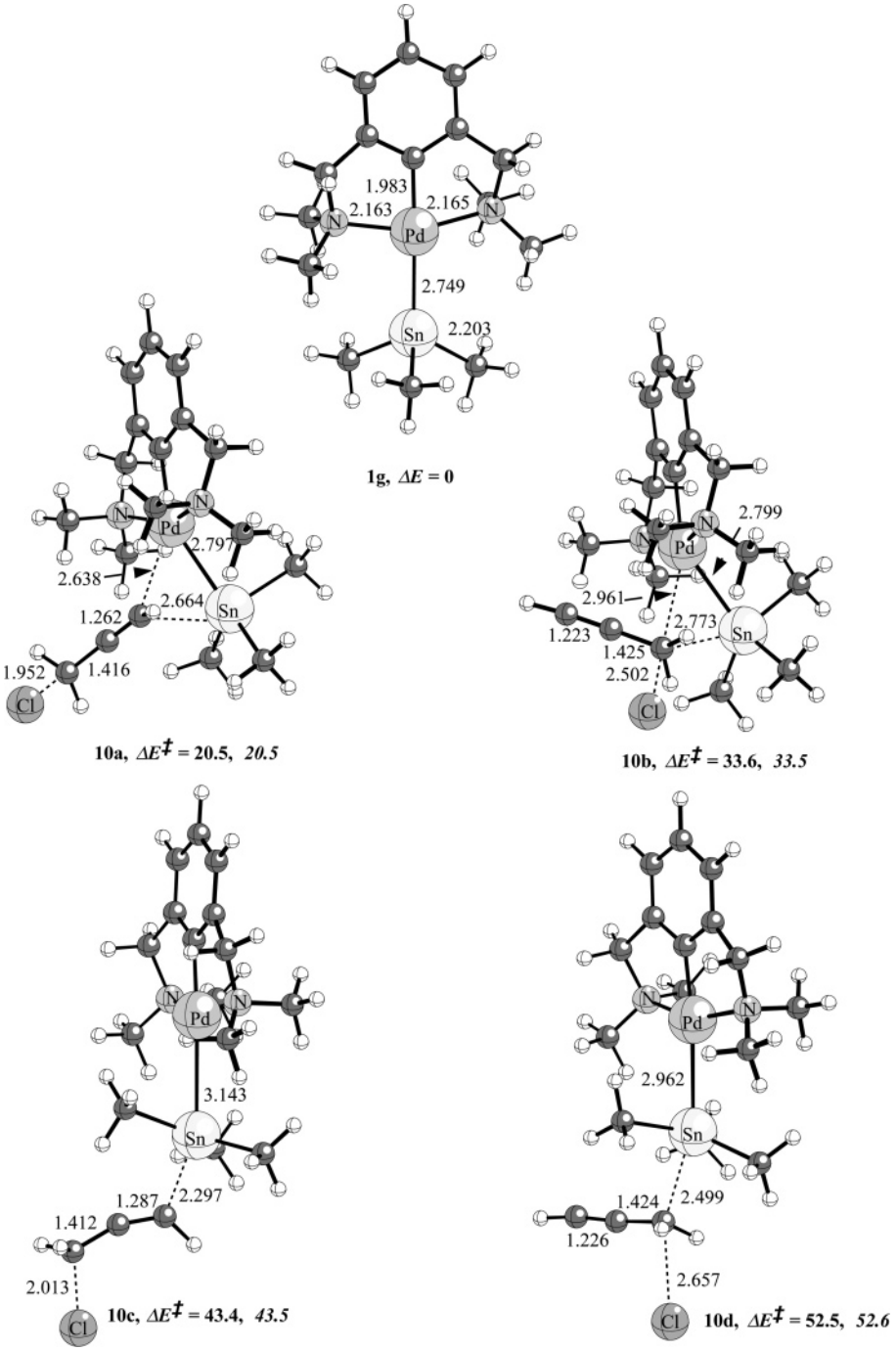

Figure 2. Calculated geometries for **1g** and the TS's of the trimethylstannane transfer reaction. The ZPV-corrected energies are given in italics. Energies in kcal mol^{-1} and bond lengths in Å.

leaving group is a unique process in palladium chemistry. This can be explained by the special topology of the pincer complex catalyst. In a typical reactive pincer complex intermediate, such as in **1g**, the high-energy palladium−tin and palladium−carbon σ-bonds are forced to a trans geometry. This topology does not permit a reductive elimination involving the Pd−Sn and Pd−C bonds. Thus, the high-energy Pd−Sn bond becomes available for reactive external electrophiles, such as **3d** (cf. **10a**,**b**). On the other hand, commonly occurring organopalladium intermediates have a considerably more flexible structure than pincer complexes, and therefore the high-energy Pd−Sn and Pd−C bonds may easily isomerize to a cis geometry, permitting a facile intramolecular reductive elimination reaction.[38]

Formation of the allenyl (**5c**) and propargyl (**11**) stannane products is a highly exothermic process (−47.3 and −53.5 kcal mol^{-1}), indicating that the trimethyltin transfer from the palladium atom of **1g** to **3d** is an irreversible process. The formation of allenylstannane **5c** is both kinetically and thermodynamically more favored than formation of propargyl stannane **11**, at least from the parent compound **3d** (entry 9). However,

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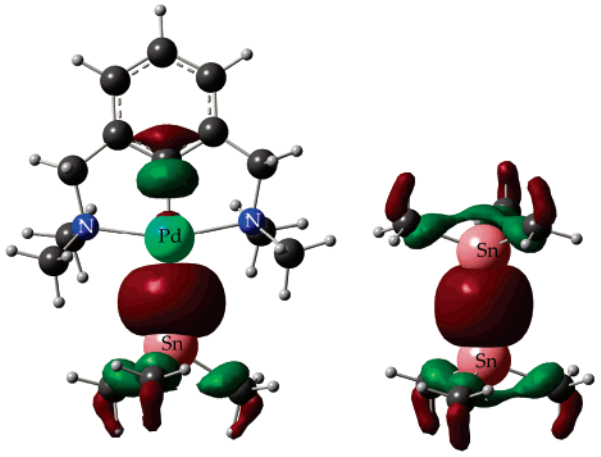
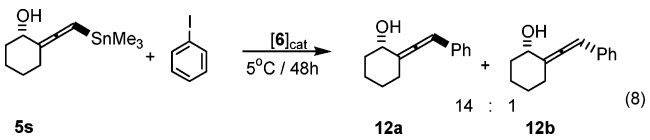


Figure 3. HOMO orbital of complex **1g** ($\epsilon_{HOMO} = -4.5$ eV) and hexamethylditin **2a** ($\epsilon_{HOMO} = -6.3$ eV).

substituent effects obviously influence the regioselectivity. For example, the presence of bulky phenyl (**3a**) or alkyl (**3c**) substituents at the attacked carbon in **10a** leads to unfavorable steric interactions with the pincer complex. This explains the predominant formation of the propargylic product via **10b**-type TS from **3a**,**b** (entries 1−8). On the other hand, electron-withdrawing substituents (e.g.**, 3e**, **3f**, **3i**, and **3j**) increase the electrophilicity of the unsaturated carbon, promoting the formation of the allenyl product via **10a**-type TS. The final allenyl-to-propargyl ratio of the reaction is determined by the counteracting electronic and steric effects. From secondary propargylic substrates (**3n**−**u**), allenyl products are formed (entries 21−29) because of the strongly destabilizing steric interactions in the TS structure of the S_N2-type process (cf. **10b**).

5. Synthetic Utility of the Products

Allenylstannanes and silanes are versatile building blocks in advanced organic synthesis and in natural product synthesis.[39−46] Although many excellent procedures for selective synthesis of these organometallic compounds are already available in the literature,[39−46] there is a considerable need to broaden the variety of available functionalized species. Allenylstannanes and silanes undergo highly stereoselective reactions with various aldehydes in the presence of Lewis acid catalysts to afford homopropargyl alcohol products.[39] Allenylstannanes can also be utilized in palladium-catalyzed coupling reactions, such as in Stille-type coupling[47,48] with aromatic halogenides to provide substituted allenes.[49] The palladium pincer catalysts **1a**−**e** do not react with allenylstannanes under the employed reaction conditions, which is a prerequisite of the high yields obtained in the catalytic transformations. On the other hand, commonly used palladium sources, such as $Pd(PPh_3)_4$ (**6**), readily catalyze the coupling reactions of allenylstannanes and aryl iodides. To demonstrate the synthetic utility of this reaction, we reacted compound **5s**, obtained from stannylation of **3t**, as a single diastereomer (entry 28) with phenyl iodide in the presence of catalytic amounts of **6** (eq 8). This procedure gave mainly trans-substituted allene **12a**[50,51] and only traces of its syn-substituted counterpart **12b**.[51] Since it is known that the analogue Stille-coupling reactions proceed with retention of the geometry of the vinyl−tin bond,[52,53] this reaction also helped us to assign the stereochemistry of **5s**. Thus, as the major product of the coupling reaction (**12a**) is the anti form, we conclude the same stereochemistry for **5s**.



A further, synthetically interesting feature of the products of the above-described pincer complex catalyzed reactions (eq 2) is that these compounds comprise a trimethylstannyl group instead of the more commonly used tributylstannyl functionality. Since the trimethylstannyl group is less bulky than its tributylstannyl counterpart, the presented allenylstannanes are expected to be more reactive in electrophilic substitution and coupling reactions than their tributylstannyl analogues.

6. Conclusions

Pincer complex catalysis can be employed for regioselective transfer of the stannyl and silyl functionality to propargylic substrates. The reactions proceed under mild and neutral conditions, and therefore many functionalities are tolerated. The catalytic activity of the employed catalyst strongly depends on the electronic effects of the employed pincer ligand. Pincer complexes with electron-supplying ligands, such as NCN, SCS, and SeCSe complexes, display a very high catalytic activity. The regioselectivity of the stannylation reaction of primary propargylic substrates depends on the steric and electronic effects of the substituents on the triple bond. Catalytic reactions involving secondary propargylic substrates provide exclusively the allenyl product. The epoxide opening via stannylation of the corresponding propargylic substrates takes place with an excellent regio- and stereochemistry. The silylation reactions proceed with higher allenyl selectivity than the corresponding stannylation processes. Interestingly, under the applied catalytic conditions, exclusively the silyl functionality is transferred from silylstannanes **2b**,**c** to the propargylic substrates. Mechanistic studies have shown that the active intermediate of the catalytic reactions is an organostannyl- or silyl ligand-coordinated pincer complex. According to DFT modeling, the stannyl group transfer from palladium to propargyl chloride is a single-step process. The displacement of the chloride is initiated by nucleophilic attack of the palladium−tin σ-bond electrons on the propargylic substrate. Since the above-described pincer complex catalyzed process is characterized by mild reaction conditions, a high level of selectivity, and operational simplicity, this transformation

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provides an attractive new route for preparation of functionalized allenylstannanes and silanes.

7. Experimental Section[54]

Catalytic Stannylation with 2a. General Procedure A. The corresponding propargylic substrates **3a**−**u** (0.16 mmol) and catalyst **1** (0.004 mmol, 2.5 mol %) were dissolved in THF (0.25 mL). To this mixture was added hexamethylditin **2a** (0.168 mmol), resulting in a dark-yellow solution. This reaction mixture was then stirred for the allotted temperatures and times given in Table 1. The solvent was evaporated, and the products were purified by column chromatography. To avoid decomposition of the allenyl and propargylstannane products, a rapid chromatography procedure was applied.

Catalytic Silylation with 2b. General Procedure B. The corresponding propargylic substrate (0.16 mmol), catalyst **1a** (0.008 mmol, 5 mol %), and 4 Å molecular sieves in THF (0.20 mL) were heated to 40 °C. To this mixture was added (dimethylphenylsilyl)trimethylstannane **2b** (0.24 mmol) in THF (0.25 mL) via a syringe-pump over 5 h at 40 °C, and the reaction mixture was stirred for an additional 19 h at 40 °C. Then the solvent was evaporated, and the products were purified by column chromatography. To avoid decomposition of the allenylsilane products, a rapid chromatography was applied (see General Procedure A). The same procedure was employed for silylation with (trimethylsilyl)tributylstannane (**2c**), except that this reagent was added in one portion and the reaction was conducted for 4 h at 60 °C.

Reaction of Complex 1b with 2a Monitored by NMR. The chloride counterion of **1a** was exchanged to acetate (forming **1f**) by using the following procedure. Complex **1a** (12 mg, 0.032 mmol) was added to AgOAc (8 mg, 0.048 mmol) suspended in $CHCl_3$ at 0 °C. This mixture was stirred 1 h at 0 °C and then an additional hour at 25 °C in a dark reaction vessel. The AgBr precipitation was separated by centrifugation, and the solvent was evaporated to yield **1f**. Complex **1f** was dissolved in 0.7 mL of THF-d_8, and then hexamethylditin (63 mg, 0.192 mmol) was added to the solution. The progress of the reaction was monitored by using ^{1}H and ^{119}Sn NMR spectroscopy. Under the above conditions, about 50% of **1f** was converted to tin complex **1g** according to the ^{1}H NMR spectrum of the reaction mixture. NMR data (ppm) for complex **1g** (determined from the obtained reaction mixture): ^{1}H NMR δ 0.05 (s, 9H), 2.87 (s, 12H), 3.98 (s, 4H), 6.64 (d, ^3J(H−H) = 7.9 Hz, 2H), 6.71 (t, ^3J(H−H) = 7.9 Hz, 1H); ^{119}Sn NMR δ −0.2 ppm.

Reaction of Complex 1a with Silylstannane 2b Monitored by NMR. To complex **1a** (12 mg, 0.032 mmol) in THF-d_8 (0.20 mL) was added silylstannane **2b** (29 mg, 0.096 mmol, 3 equiv) in THF-d_8 (0.25 mL) over 5 h via a syringe-pump at room temperature. Then, the reaction mixture was analyzed by ^{1}H and ^{29}Si NMR spectroscopy. According to ^{1}H NMR spectroscopy under these reaction conditions, **1a** was fully converted to silicon complex **1h**. NMR data (ppm) for complex **1h** (determined from the obtained reaction mixture): ^{1}H NMR δ 0.18 (s, 6H), 2.91 (s, 12H), 3.92 (s, 4H), 6.73 (d, ^3J(H−H) = 8.4 Hz, 2H), 6.89 (t, ^3J(H−H) = 8.4 Hz, 1H), 7.27−7.41 (m, 5H); ^{29}Si NMR δ −5.5 ppm.

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Supporting Information Available: Detailed experimental procedures, characterization and ^{13}C NMR spectra of the prepared allenyl and propargyl silanes and stannanes, ^{119}Sn and ^{29}Si NMR spectra of the stoichiometric reactions with pincer complexes and dimetal reagents, and computational details of the DFT studies. This material is available free of charge via the Internet at http://pubs.acs.org.

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(54) General experimental conditions, detailed experimental procedures and characterization of the products are given in the Supporting Information.