J|A|C|S
COMMUNICATIONS

Published on Web 12/24/2003

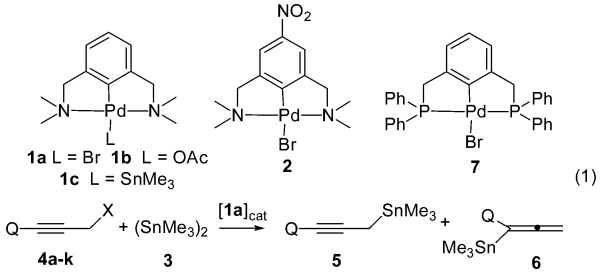
Palladium Pincer Complex-Catalyzed Trimethyltin Substitution of Functionalized Propargylic Substrates. An Efficient Route to Propargyl- and Allenyl-Stannanes

Johan Kjellgren, Henrik Sundén, and Kálmán J. Szabó*

Department of Organic Chemistry, Stockholm University, SE-106 91 Stockholm, Sweden

Received October 22, 2003; E-mail: kalman@organ.su.se

Palladium-catalyzed addition of hexaalkylditin to triple bonds is a widely applied, attractive synthetic route for preparation of difunctionalized olefins.[1,2] The usual application of this method involves oxidative addition of the palladium(0) catalyst to the Sn−Sn bond generating a bis-stannyl palladium(II) species, which subsequently adds to the triple bond of the alkyne substrate.[2] Our recent studies directed toward catalytic application of palladium pincer complexes in organo-stannane chemistry have indicated that restriction of the oxidation state of palladium to +2 and the limitation of the accessible coordination sites to a single one alters the catalytic reactivity of palladium.[3] We have now found (eq 1) that the pincer complex[4,5] (**1**,**2**)-catalyzed reaction of hexamethylditin (**3**) with propargylic substrates (**4**) leads to substitution reaction instead of bis-stannane addition, affording propargyl stannanes (**5a**−**e**) and allenyl stannanes (**6a**−**j**).



The catalytic reactions were conducted under mild conditions at rt or at 0 °C using 2.5 mol % catalyst in THF (Table 1). It was found that propargyl chloride derivatives react quickly with a high yield. Propargyl mesylate can also be used as a substrate (entry 4); however, **4b** reacts slower than the corresponding chloride analogue **4a**. The product distribution of the reaction was highly dependent on substituent Q. In the presence of electron-supplying functionalities (**4a**,**b**) such as phenyl (entries 1−4) and alkyl groups (entry 5), the main product is propargyl stannane (**5a**,**b**). However, in the case of carbethoxy- (**4e**) and hydroxymethylene-types of functionalities (**4f**−**h**) the only product is allenyl stannane. The substituent effects on the regioselectivity of the reaction were studied by employment of propargylic substrates with various aminomethylene-type functionalities (**4i**−**k**). The morpholino derivative **4i** (involving a trialkyl-substituted nitrogen atom) reacts with poor selectivity, affording **5c**/**6h** in a 2:3 ratio. However, in the presence of an electron-withdrawing acetyl (**4j**) or tosyl (**4k**) group on the nitrogen atom, the allenyl selectivity gradually increases (entries 12−13). Accordingly, electron-withdrawing groups direct the reaction to formation of allenyl stannane product, while with electron-supplying groups, the main product is a propargyl stannane. The only exception seems to be propargyl chloride (**4d**) lacking an electron-withdrawing functionality; nevertheless, its catalytic reaction with **3** gave allenyl stannane **6c**.

Table 1. Palladium-Catalyzed Substitution of Propargylic Substrates with Hexamethylditin[a]

Entry	Substrate	Cat.[b]	t[c]	Products	p.r.[d]	Yield[e]
1	Ph, Cl (**4a**)	**1a**	2	Ph, SnMe3 (**5a**) + Ph, Me3Sn (**6a**)	8:1	87
2	**4a**	**2**	8	**5a** + **6a**	7:1	86
3	**4a**	**7**	18			no reaction
4	Ph, OMs (**4b**)	**1a**	13	**5a** + **6a**	10:1	75
5	C5H11, Cl (**4c**)	**1a**	3	C5H11, SnMe3 (**5b**) + C5H11, Me3Sn (**6b**)	8:1	95
6	Cl (**4d**)	**1a**	2	Me3Sn (**6c**)		a.p. (87)[f]
7	EtOOC, Cl (**4e**)	**1a**	6	EtOOC, Me3Sn (**6d**)		a.p. 64
8	HO, Cl (**4f**)	**1a**	16	HO, Me3Sn (**6e**)		a.p. 81
9	AcO, Ph, Cl (**4g**)	**1a**	3	AcO, Ph, Me3Sn (**6f**)		a.p. 83
10	THPO, Ph, Cl (**4h**)	**1a**	2	THPO, Ph, Me3Sn (**6g**)		a.p. 87
11[g]	Mf, Cl (**4i**)	**1a**	4	Mf, SnMe3 (**5c**) + Mf, Me3Sn (**6h**)	2:3	80
12	PhNAc, Cl (**4j**)	**1a**	2	PhNAc, SnMe3 (**5d**) + PhNAc, Me3Sn (**6i**)	1:2	85
13	PhNTs, Cl (**4k**)	**1a**	4	PhNTs, SnMe3 (**5e**) + PhNTs, Me3Sn (**6j**)	1:6	85

[a] All reactions were conducted in THF using 2.5 mol % of catalyst at rt except entries 5 and 8, where 0 °C was employed. [b] Catalyst. [c] Reaction time in hours. [d] Propargyl/allenyl ratio; a.p. = only allene product. [e] Isolated yield unless otherwise stated. [f] Product was not isolated because of its volatility. The yield was determined by NMR spectroscopy. [g] Mf = morpholino group.

The functional group tolerance of the reaction is remarkably high, which can be ascribed to the mild and neutral reaction conditions. Carbethoxy (**4e**) and various propargylic functionalities including an unprotected OH group (**4f**−**k**) are tolerated. Furthermore, the propargylic acetate functionality (**4g**) does not undergo oxidative addition, since the oxidation state of catalyst **1a** is restricted to palladium(II) under the catalytic reaction (vide infra), and therefore undesired oxidative and reductive processes do not take place.

Complex **1a** proved to be the most efficient catalyst in the propargylic substitution reactions. In this NCN-type of pincer complex,[5a] palladium is electron-rich because of coordination to three σ-donor atoms. The high electron-density on palladium seems to be an important factor for obtaining high catalytic activity. In complex **2**, the electron density on palladium is reduced by the presence of a nitro group. This complex still catalyzes the

10.1021/ja0391715 CCC: $27.50

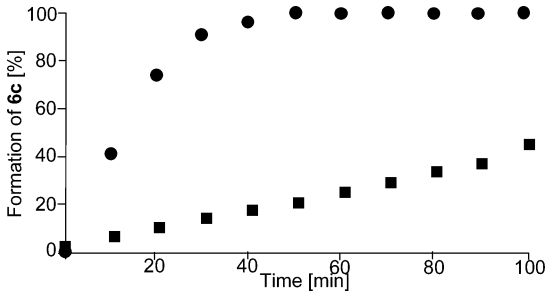


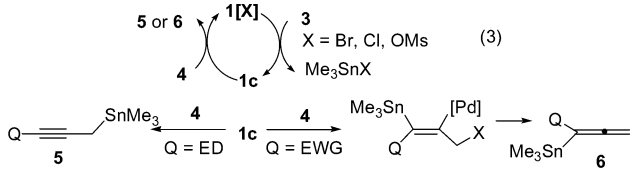
Figure 1. Formation of **6c** in the reaction of **4d** and **3** catalyzed by pincer complexes **1a** (●) and **2** (■).

substitution process; however, it shows a remarkably lower activity than the parent complex **1a** (cf. entries 1 and 2). The retarding effect of the nitro group was also clearly observed by monitoring the formation of **6c** in the reaction of **4d** and **3** with catalytic amounts of **1a** or **2** (Figure 1). Replacement of the σ-donor amino groups in **1a** with π-acceptor phosphines (**7**) leads to a complete loss of catalytic activity (entry 3). Commonly used catalysts such as $Pd(PPh_3)_4$ and $Li_2[PdCl_4]$ do not show any catalytic activity under the applied reaction conditions.

The mechanism of the catalytic substitution reaction of **4** with hexamethylditin (**3**) (eq 1) is obviously different from the addition reaction catalyzed by palladium(0) catalysts.[1,2] To study the mechanistic details of the transformation we carried out stoichiometric reactions with the catalytically active pincer complex and the substrates. In these studies we employed acetate complex **1b**, in which the counterion dissociates more easily than in **1a**. It was found that complex **1b** and propargylic derivative **4a** or **4d** do not react at all in THF-d_8 at room temperature (eq 2). However, the NMR spectrum of pincer complex **1b** gradually changed in the presence of hexamethylditin (**3**). This process was monitored by NMR spectroscopy at 25 °C using THF-d_8 as a solvent.[6] In the ^{1}H NMR spectrum of the reaction, two new peaks appeared at a high field: a sharp singlet at 0.05 ppm and a broad singlet at 0.5 ppm. The peak at 0.5 ppm was identified as the ^{1}H methyl resonance of Me_3Sn−OAc. The peaks of the ligand protons have also shifted somewhat, still reflecting a C_s symmetry, which is characteristic for the studied pincer complexes. The ^{119}Sn−NMR spectrum of the reaction was also monitored in regular time intervals. The sharp singlet of hexamethylditin (**3**) resonating at −109.0 ppm was slowly decreased, while about 15 min after starting the reaction, a new sharp singlet appeared at −0.2 ppm. This new peak did not arise from Me_3Sn−OAc, since it gives a broad singlet ^{119}Sn-resonance at 125.8 ppm.[7] Thus, we interpret the above ^{1}H and ^{119}Sn NMR results as formation of a new trimethyl-stannyl species **1c**. The observed ^{119}Sn NMR resonance of −0.2 ppm is in the range of the NMR values reported for other pallada−stannane complexes: $Pd(PMe_3)_2(SnMe_3)_2$ resonates at −28.0 ppm,[2d] while Pd(dppe)-(CON^{i}Pr)($SnMe_3$) resonates at 45.4 ppm.[2e]

$$\text{no reaction} \xleftarrow{\textbf{4a or 4d}} \textbf{1b} \xrightarrow{\textbf{3}} \textbf{1c} \qquad (2)$$

Considering the above results, the catalytic cycle (eq 3) is initiated by formation of (mono)stannane complex **1c** followed by the transfer of the trimethyltin functionality to the propargylic substrate and regeneration of the catalyst. In the case of alkyl and phenyl substituents, an S_N2-type of displacement of the leaving group (chloride or mesylate) takes place (eq 3). Alternatively, in the presence of electron-withdrawing substituents, addition of **1c** to the triple bond of the propargylic substrate followed by β-chloride elimination provides the allenyl stannane product.[8] A remarkable feature of this catalytic cycle is that redox processes do not occur, and thus palladium is kept in +2 oxidation state throughout the entire transformation. Accordingly, there are two crucial differences between the presented catalytic substitution reaction (eq 1) and the palladium(0)-catalyzed addition reaction:[1,2] (i) in the pincer complex-catalyzed processes, only a single trimethyltin group is coordinated to palladium (**1c**), which substitutes the propargylic chloride group, and (ii) application of pincer catalyst **1a** involves that a palladium(0) species does not form in the catalytic cycle, and therefore an initial oxidative addition to the propargylic chloride[9] (mesylate, acetate, etc.) functionality can be avoided. These features allow a highly selective novel transformation of functionalized propargyl chlorides.



In summary, we have devised a new pincer complex-catalyzed trimethyl-stannane substitution reaction of propargyl chlorides with hexamethylditin. The catalytic reaction proceeds under mild conditions tolerating many functional groups such as OH, OAc, COOEt, NR_3, and NR_2Ac. The outcome of the reaction can be controlled by the choice of the functionalities. Reaction of propargylic substrates with electron-donating groups gives propargyl stannanes, while substitution of propargyl chlorides with electron-withdrawing substituents gives allenyl stannanes. Due to the high level of functional group tolerance and the operational simplicity, this method provides an easy access to propargyl and allenyl stannanes, which are useful building blocks in coupling reactions and in natural product synthesis.[10]

Acknowledgment. This work was supported by the Swedish Research Council (VR).

Supporting Information Available: Experimental procedures as well as characterization and NMR spectra of the products. This material is available free of charge via the Internet at http://pubs.acs.org.

References

(1) Beletskaya, I.; Moberg, C. *Chem. Rev.* **1999**, *99*, 3435.
(2) (a) Mitchell, T. N.; Killing, A. A. H.; Rutschow, D. *J. Organomet. Chem.* **1986**, *304*, 257. (b) Piers, E.; Skrelj, R. T. *Chem. Soc., Chem. Commun.* **1986**, 626. (c) Mabon, R.; Richecoeur, A. M. E.; Sweeney, J. B. *J. Org. Chem.* **1999**, *64*, 328. (d) Tsuji, Y.; Nishiyama, K.; Hori, S.-i.; Ebihara, M.; Kawamura, T. *Organometallics* **1998**, *17*, 507. (e) Hua, R.; Onozawa, S.-y.; Tanaka, M. *Organometallics* **2000**, *19*, 3269. (f) Manusco, J.; Lautens, M. *Org. Lett.* **2003**, 1653.
(3) Solin, N.; Kjellgren, J.; Szabó, K. J. *Angew. Chem., Int. Ed.* **2003**, *42*, 3656.
(4) (a) Albrect, M.; van Koten, G. *Angew. Chem., Int. Ed.* **2001**, *40*, 3751. (b) Singleton, J. T. *Tetrahedron* **2003**, *59*, 1837.
(5) (a) Alsters, P. L.; Baesjou, P. J.; Janssen, M. D.; Kooijman, H.; Sicherer-Roetman, A.; Spek, A. L.; van Koten, G. *Organometallics* **1992**, *11*, 4124. (b) Rimml, H.; Venanzi, L. M. *J. Organomet. Chem.* **1983**, *259*, C6.
(6) ^{1}H and ^{119}Sn NMR experiments were performed using **1b** and 6.0 equiv of **3** in THF-d_8 at 25 °C.
(7) Due to line broadening, this ^{119}Sn NMR resonance can only be observed using a high concentration of Me_3Sn−OAc. Literature value for ^{119}Sn shift of Me_3Sn−OAc (in $CDCl_3$): 129.0 ppm. Wrackmeyer, B. *Annual Reports on NMR Spectroscopy*; Academic Press: London, 1985; Vol 16, p 73.
(8) Formation of the allenic product **6** in the presence of electron-withdrawing substituents can be ascribed to the polarization of the π-system of the triple bond. As a consequence, the carbon atom attached to the electron-withdrawing substituent is activated toward nucleophilic attack by the trimethyltin ligand of **1c**.
(9) (a) Tsuji, J.; Mandai, T. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 2589. (b) Elsevier, C. J.; Kleijn, H.; Boersma, J.; Vermeer, P. *Organometallics* **1986**, *5*, 716.
(10) (a) Marshall, J. A. *Chem. Rev.* **1996**, *96*, 31. (b) Marshall, J. A.; Wang, X.-j. *J. Org. Chem.* **1992**, *57*, 1242. (c) Ruitenberg, K.; Westmijze, H.; Meijer, C. J.; Elsevier, C. J.; Vermeer, P. J. *J. Organomet. Chem.* **1983**, *241*, 417.

JA0391715