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Mechanistic Aspects of Palladium-Catalyzed Allylstannylation of Alkynes

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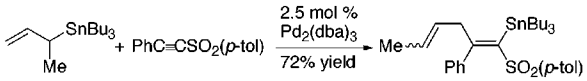
ABSTRACT

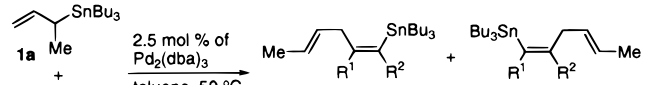


An α-methylallylstannane added to an alkyne in the presence of a palladium catalyst with perfect regioselectivity both in the allylic and alkynic moieties. Comparison of the reaction of isomeric butenylstannanes suggests two catalytic cycles, one of which includes a palladacyclopentene intermediate and *β*-tin elimination pathway.

Carbostannylation of alkynes has become a powerful synthetic tool,[1−3] because the resulting alkenylstannanes are versatile precursors for variously substituted ethenes.[4] Although carbostannylation of alkynes with allylstannanes has been reported to proceed in the presence of a Lewis acid,[2] a radical initiator,[3] or a nickel complex,[1c] little attention has been paid on the regiochemistry in allylstannanes. Here we report that a palladium complex catalyzes the addition of α-methylallylstannane highly selectively at a *γ*-carbon across alkynes with exclusive *syn*-selectivity, suggesting a novel catalytic cycle.

In our series of studies on carbostannylation of alkynes, we found that tris(dibenzylideneacetone)dipalladium, $Pd_2(dba)_3$, catalyzed the addition of 1-buten-3-yl(tributyl)tin (**1a**) to ethyl phenylpropiolate (**2a**) (50 °C, 38 h) to give ethyl (2*E*,5*E*)-3-phenyl-2-tributylstannyl-2,5-heptadienoate (**3a**) and its regioisomer, ethyl (1*E*,4*E*)-1-phenyl-1-tributylstannyl-1,4-hexadiene-2-carboxylate (**4a**), in a ratio of 90:10 in 74% yield (Scheme 1).[5] Noteworthy is that the *γ*-carbon of **1a** exclusively formed a bond with the alkyne carbon. The reaction of **1a** with *p*-tolyl phenylethynyl sulfone (**2b**) or dimethyl butynedioate (**2c**) also afforded the corresponding *γ*-adduct as a sole product.

Scheme 1. Palladium-Catalyzed Allylstannylation of Alkynes with 1-Buten-3-yl(tributyl)tin



alkyne	yield (time)	3 : 4
2a: R^1 = Ph, R^2 = CO_2Et	74% (38 h)	90 : 10
2b: R^1 = Ph, R^2 = SO_2(*p*-tol)	74% (17 h)	>99[a] : 1
2c: R^1 = R^2 = CO_2Me	72% (1 h)	—[b]

[a] *E*:*Z* = 76:24 [b] *E*:*Z* = 48:52

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(1) (a) Shirakawa, E.; Yoshida, H.; Kurahashi, T.; Nakao, Y.; Hiyama, T. *J. Am. Chem. Soc.* **1998**, *120*, 2975−2976. (b) Shirakawa, E.; Yoshida, H.; Nakao, Y.; Hiyama, T. *J. Am. Chem. Soc.* **1999**, *121*, 4290−4291. (c) Shirakawa, E.; Yamasaki, K.; Yoshida, H.; Hiyama, T. *J. Am. Chem. Soc.* **1999**, *121*, 10221−10222.

(2) (a) Asao, N.; Matsukawa, Y.; Yamamoto, Y. *Chem. Commun.* **1996**, 1513−1514. (b) Matsukawa, Y.; Asao, N.; Kitahara, H.; Yamamoto, Y. *Tetrahedron* **1999**, *55*, 3779−3790.

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(4) (a) Farina, V.; Krishnamurthy, V.; Scott, W. J. *Org. React.* **1997**, *50*, 1−652. (b) Davies, A. G. *Organotin Chemistry*; VCH: Weinheim, 1997. (c) Pereyre, M.; Quintard, J.-P.; Rahm, A. *Tin in Organic Synthesis*; Butterworth: London, 1987.

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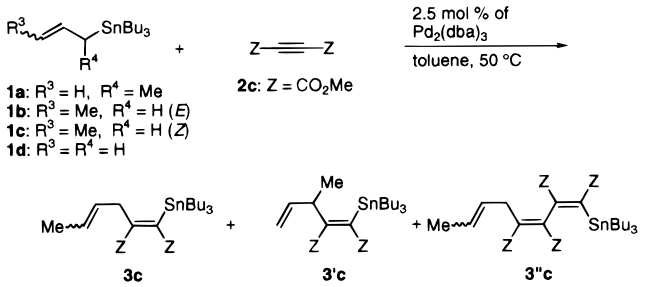
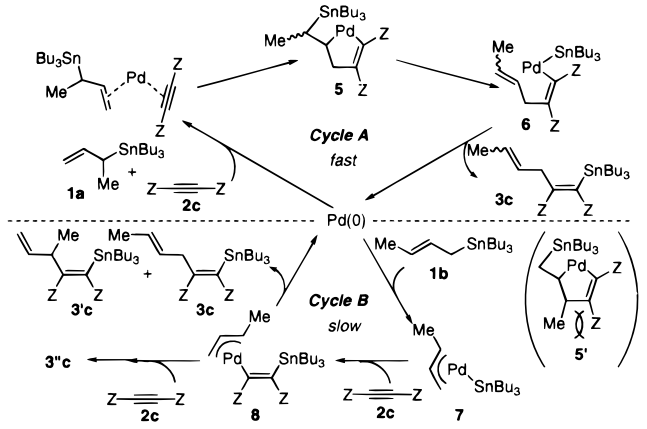
Regioisomers of **1a**, (*E*)-2-buten-1-yl(tributyl)tin (**1b**) and (*Z*)-2-buten-1-yl(tributyl)tin (**1c**), reacted with **2c** in a different manner and gave roughly equal amounts of α- and γ-adducts in addition to dimerization−carbostannylation product **3″c** (Scheme 2). It is noteworthy that the configu-

Scheme 2. Palladium-Catalyzed Allylstannylation of Dimethyl Butynedioate with Butenylstannanes



ration of the crotyl group in **1b** or **1c** is retained in **3c**, in contrast to the fact that **3c** derived from **1a** consisted of a mixture of stereoisomers. Allylstannanes **1a** and **1d**, both lacking the γ-methyl group, reacted much faster than **1b** or **1c**. All these observations are explained rationally by two catalytic cycles depicted in Scheme 3, although evidences

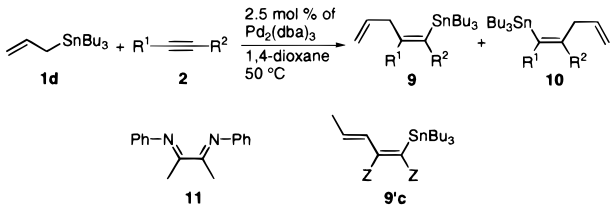
Scheme 3. Possible Catalytic Cycles of the Palladium-Catalyzed Allylstannylation of Alkynes



on the intermediates remain yet to be studied. Thus, **2c** and α-methylallylstannane **1a** might first undergo oxidative cyclization with a palladium(0) complex to afford palladacyclopentene **5** (cycle A). Oxidative cyclization of a terminal alkene and **2c** with a palladium(0) complex has a precedent.[6] β-Tin elimination from **5** would give **6**, whose reductive elimination affords allylstannylation products **3c** as a mixture of stereoisomers. Cycle A explains well the C−C bond formation at γ-carbon of allylstannanes.[7] Substitution at the γ-carbon reasonably retards the oxidative cyclization of crotylstannane **1b** (or **1c**), because steric repulsion between its γ-methyl and the ester moiety on **2c** should prevent the formation of palladacyclopentene **5′**. Thus, another pathway, cycle B, becomes plausible. Oxidative addition of **1b** to a palladium(0) might give **7**,[8] which undergoes insertion of alkyne **2c** to produce π-allylpalladium(II) complex **8**. Reductive elimination from **8** would provide dienylstannanes (*E*)-**3c** and **3′c**, whereas trienylstannane **3″c** is obtained by insertion of another **2c** to **8** and the consequent reductive elimination.[9−11]

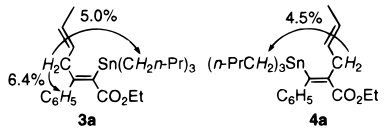
The allylstannylation of various alkynes with allyltributyltin (**1d**) utilizing $Pd_2(dba)_3$ catalyst was next examined (Scheme 4 and Table 1). We use 1,4-dioxane as a solvent

Scheme 4. Palladium-Catalyzed Allylstannylation of Alkynes



since the solvent was found to accelerate the reaction to a great extent. Internal alkynes having an electron-withdrawing group such as ester, trifluoromethyl, sulfonyl, or cyano reacted with **1d** in good to excellent yields. The regioselectivity was high with the alkynes where the electronic difference between R^1 and R^2 was large, and the predominant

(5) Configuration of the carbostannylation products was determined by NOEs in ^{1}H NMR of the alkenylstannanes and/or the alkenes obtained by protonolysis. For example, the configuration of **3a** and **4a** was determined on the basis of NOE (irradiation at a methylene peak) as shown below.



(6) Munz, C.; Stephan, C.; tom Dieck, H. *J. Organomet. Chem.* **1991**, *407*, 413−420.

(7) No reaction between **1d** and **2c** occurred in the absence of the palladium catalyst (50 °C, 1 h). This result excludes a metalloene reaction pathway, which is known to take place in the case of allylstannanes and carbonyl compounds; see ref 4b.

(8) Oxidative addition of allylstannanes to Pd(0) complexes has been suggested; see Shi, M.; Nicholas, K. M. *J. Am. Chem. Soc.* **1997**, *119*, 5057−5058. Franks, R. J.; Nicholas, K. M. *Organometallics* **2000**, *19*, 1458−1460.

(9) The retention of the double bond configuration in the reaction of **1b** or **1c** with **2c** to give *E*- or *Z*-**3c**/**3″c**, respectively, should imply that the isomerization between *syn*-**7**/**8** and *anti*-**7**/**8** does not take place under the reaction conditions.

(10) Trienylstannane **3″c** should not be formed through a palladacyclopentadiene because a stoichiometric reaction of 2,3,4,5-tetrakis(methoxycarbonyl)palladacyclopentadiene with crotylstannane **1b** (50 °C, 24 h, in toluene) did not afford the corresponding carbostannylation product. For a palladacyclopentadiene intermediate of the palladium-catalyzed dimerization−carbostannylation of alkynes, see ref 1b.

(11) Although the possibility that the reaction of **1a** proceeds also through cycle B, as noted by a referee, cannot be eliminated, it would be reasonable to consider that totally a different product distribution should be ascribed to different reaction mechanisms.

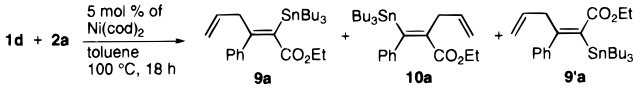
Table 1. Palladium-Catalyzed Allylstannylation of Alkynes[a]

	alkyne **2**				
entry	R^1	R^2	time (h)	yield (%)[b]	**9**:**10**[c]
1[d]	Bu	CN	72	63	>99:1
2	Ph	SO_2(*p*-tol)	1	73	92:8
3	Me	CO_2Et	50	37	86:14
4[e]	Me	CO_2Et	62	55	91:9
5	Ph	CO_2Et	43	100	79:21
6	Ph	CF_3	14	98	72:28
7[f]	CO_2Me	CO_2Me	0.5	80	—

[a] The reaction was carried out in 1,4-dioxane (3.0 mL) at 50 °C using allyl(tributyl)tin (0.33 mmol), an alkyne (0.99 mmol), and $Pd_2(dba)_3$ (8.2 μmol). [b] Isolated yield based on allyl(tributyl)tin. [c] Determined by ^{119}Sn NMR. [d] The reaction was carried out at 90 °C. [e] Diimine **11** (16.4 μmol) was used. [f] Conjugated dienylstannane **9′c** (8% yield) was also obtained.

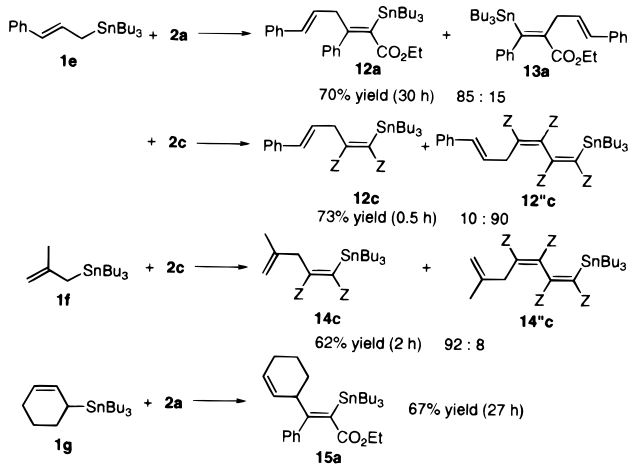
product had the stannyl group attached to the carbon substituted by a more electron-withdrawing group. Use of diimine **11** as a ligand increased the yield in the reaction of ethyl butynoate (entries 3 and 4). Although the reaction of a highly electron-deficient alkyne, dimethyl butynedioate (**2c**), proceeded smoothly, isomerization of the product to **9′c** took place during purification (entry 7). The palladium catalyst is better-suited for allylstannylation of these electron-deficient alkynes than is the previously reported nickel catalyst,[1c] showing much higher catalytic activity with higher stereo- and regioselectivities. For example, the reaction of **1d** with **2a** using a nickel catalyst proceeded at much higher temperature and gave the allylstannylation products as a mixture of three isomers including *anti*-adduct **9′a** (Scheme 5).

Scheme 5. Nickel-Catalyzed Allylstannylation of Ethyl Phenylpropiolate (**2a**) with Allyltributyltin (**1d**)



The reaction of other allylstannanes was examined with alkynes **2a** and **2c** (Scheme 6). Unlike crotylstannanes, cinnamylstannane **1e** added to **2a** and **2c** without any allylic

Scheme 6. Carbostannylation of **2a** and **2c** with **1e**−**1g**[a]



[a] Reagents: $Pd_2(dba)_3$ (2.5 mol %), 1,4-dioxane, 50 °C.

rearrangement, whereas **1e** reacted with **2c**, giving a dimerization−carbostannylation product as the major product. The addition of methallylstannane **1f** to **2c** was also accompanied by the dimerization of **2c**. The allylstannylation of **2a** using 2-cyclohexenylstannane **1g** proceeded in a highly regioselective manner to give a single isomer.

In conclusion, we have demonstrated that the palladium-catalyzed allylstannylation of alkynes proceeds in different pathways depending on the presence or absence of a γ-substituent in the allylstannanes. The reaction is applicable to various allylstannanes and electron-deficient alkynes. The results not only add new substrates to the family of the transition metal-catalyzed carbostannylation but also provide us with the novel mechanistic possibility of "β-tin elimination". Further studies on synthetic applications to various organostannanes and unsaturated compounds as well as on the development of new reactions utilizing "β-tin elimination" are in progress in our laboratories.

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

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