C–C Coupling Reactions

Nickel-Catalyzed Tandem Carbostannylation of Alkynes and 1,2-Dienes with Alkynylstannanes**

Eiji Shirakawa, Youko Yamamoto, Yoshiaki Nakao, Shinichi Oda, Teruhisa Tsuchimoto, and Tamejiro Hiyama**

Carbometalation of carbon–carbon unsaturated bonds affords versatile synthetic reagents that have a newly formed carbon–carbon bond and a carbon–metal bond, which can be used for further construction of carbon frameworks.[1] In particular, a series of transition-metal-catalyzed carbostannylations[2] of alkynes,[3] 1,3-dienes[4] and 1,2-dienes[5] provides us with various substituted organostannanes, which are converted into a variety of conjugated and nonconjugated olefinic compounds through carbon–carbon bond forming reactions such as the Kosugi–Migita–Stille coupling.[6] The high chemoselectivity and mild reactivity of organostannanes make the sequence of carbostannylation and subsequent carbon–carbon bond-forming reactions an attractive synthetic strategy. Herein, we report an example of a tandem carbostannylation reaction,[7] namely, sequential insertion of two different carbon–carbon unsaturated bonds into a tin–alkynyl carbon bond.[8]

Treatment of trimethyl(phenylethynyl)tin (**1a**, 0.10 mmol) with 1-octyne (**2a**, 0.60 mmol) and 1,2-heptadiene (**3**, 0.30 mmol) in the presence of [Ni(cod)$_2$] (5.0 μmol) and [2-(dimethylamino)phenyl]diphenylphosphane (pn, 5.0 μmol; dibutyl ether, 50 °C, 24 h) gave rise to tandem alkynylstannylation to give a 98:2 mixture[9] of (3*Z*,6*Z*)-3-hexyl-1-phenyl-6-(trimethylstannyl)undeca-3,6-dien-1-yne (**4a**) and (3*Z*,6*E*)-

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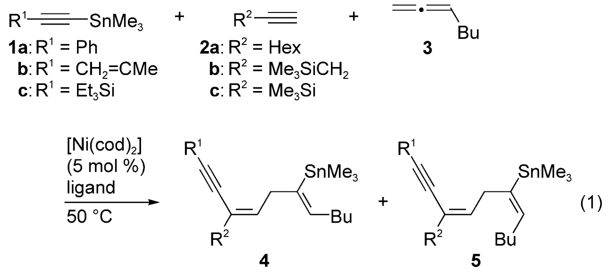
Table 1: Nickel-catalyzed tandem alkynylstannylation of alkynes and 1,2-heptadiene.[a]



Entry	R^1	R^2	Cond.[b]	*t* [h]	Yield [%][c]	**4**:**5**[c]	Product(s)
1	Ph (**1a**)	Hex (**2a**)	A	24	56	98:2	**4a**, **5a**
			B	24	73	4:96	**4a**, **5a**
			C	24	55	1:>99	**5a**
2[d]	Ph (**1'a**)	Hex (**2a**)	A	24	33	82:18	**4'a**, **5'a**
			B	24	49	1:>99	**5'a**
			C	49	12	1:>99	**5'a**
3	Ph (**1a**)	Me_3SiCH_2 (**2b**)	A	24	49	96:4	**4b**, **5b**
			B	24	59	12:88	**4b**, **5b**
			C	24	35	14:86	**4b**, **5b**
4	Ph (**1a**)	Me_3Si (**2c**)	A	6	5	>99:1	**4c**
			B	8	31	10:90	**4c**, **5c**
			C	6	31	7:93	**4c**, **5c**
5	$CH_2{=}CMe$ (**1b**)	Hex (**2a**)	A	4.5	44	>99:1	**4d**
			B	6	67	6:94	**4d**, **5d**
			C	24	31	9:91	**4d**, **5d**
6	Et_3Si (**1c**)	Hex (**2a**)	A	10	61	51:49	**4e**, **5e**
			B	9	60	5:95	**4e**, **5e**
			C	8	57	8:92	**4e**, **5e**

[a] The reaction was carried out in solvent (0.15 mL) with an alkynylstannane (0.10 mmol), an alkyne (0.60 mmol) and 1,2-heptadiene (0.30 mmol) in the presence of $[Ni(cod)_2]$ (5.0 μmol) and a ligand. [b] Ligand and solvent for Conditions A: pn (5.0 μmol), dibutyl ether; B: ttpp (10 μmol), toluene; C: dpp (5.0 μmol), THF. [c] Determined by ^{119}Sn NMR spectroscopy with Me_4Sn (Bu_4Sn for entry 2) as an internal standard. [d] Tributyl(phenylethynyl)tin was used instead of the trimethylstannyl analogue.

isomer **5a** in 56% yield [Eq. (1) and entry 1 of Table 1].[10] Screening of effective ligands led us to find that tris[*p*-(trifluoromethyl)phenyl]phosphane (ttpp) and 2-(diphenylphosphanyl)pyridine (dpp) gave the products in comparable yields[11] (entry 1 of Table 1) but in preference for **5a** over **4a** for conditions B and C (see Figure 1). Worthy of note is that **4a** or **5a** is generated in each case with selectivities higher than 96% out of 48 possible isomers.

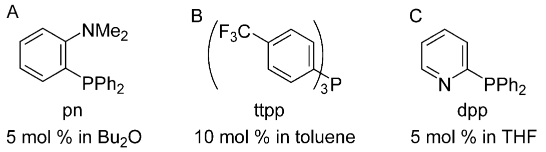
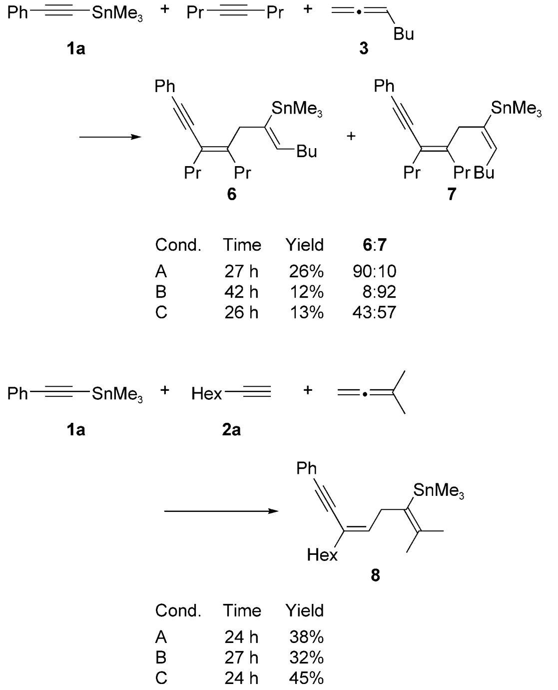


Figure 1. Ligands and solvents used in the tandem alkynylstannylation for conditions A, B, and C.

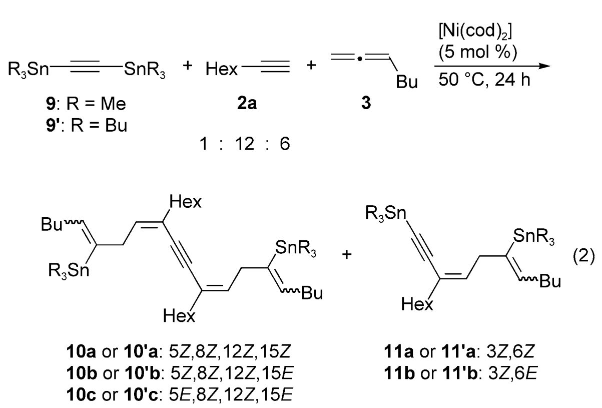
The tandem alkynylstannylation conditions A (pn in dibutyl ether), B (ttpp in toluene) or C (dpp in THF) were applied to various alkynylstannanes, alkynes and 1,2-heptadiene (entries 2–6 of Table 1). Tributylstannyl(phenyl)acetylene (**1'a**) also participated in the reaction (entry 2) but less efficiently. Similarly, stannyldienynes **4** and **5** that have a trimethylsilylmethyl or trimethylsilyl substituent were prepared (entries 3 and 4). Enynyl- and silylethynylstannanes also gave the corresponding trienynes and dienynes, respectively (entries 5 and 6). In addition to terminal alkynes and a monosubstituted allene, an internal alkyne and a 1,1-disubstituted allene reacted, albeit with much lower yields (Scheme 1).

Tandem alkynylstannylation of bis(trimethylstannyl)acetylene **9** with **2a** and **3** gave 1:2:2 adducts **10** predominantly, whereas bis(tributylstannyl) analogue **9'** gave a mixture of 1:1:1 adducts **11'** [Eq. (2)]. The stereochemical preferences change depending on whether conditions A or B are used, as before. Thus, the size of trialkylstannyl groups effectively controls the ratio of **10**:**11** or **10'**:**11'**.

Some pieces of evidence are available to contribute towards a discussion of the mechanism of the tandem reaction. An oxidative adduct of tributyl(phenylethynyl)tin (**1'a**) to a Ni^0–pn complex was observed by ^{31}P NMR and

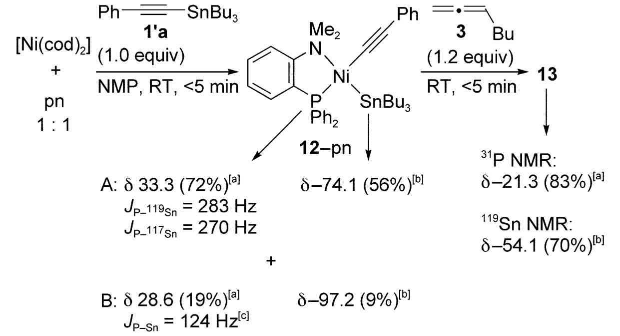


Scheme 1. Tandem alkynylstannylation by using an internal alkyne or a 1,1-disubstituted allene. Reagents and conditions are the same as those in Table 1.



R	Cond.	Yield	10a or 10'a	10b or 10'b	10c or 10'c	11a or 11'a	11b or 11'b
Me (9)	A	34%	84	16	<1	<1	<1
	B	58%	<1	6	56	4	34
Bu (9')	A	42%	11	11	<1	62	16
	B	58%	<1	<1	<1	<1	>99

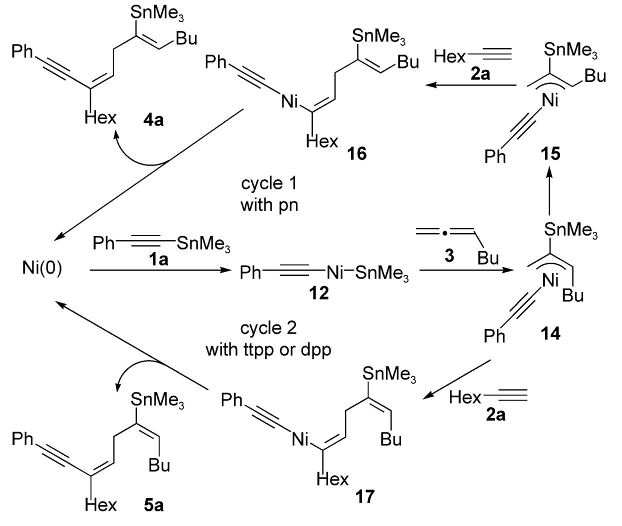
^{119}Sn NMR spectroscopies (Scheme 2),[12,13] while the reaction of [Ni(cod)$_2$]–pn with trimethylstannyl analogue **1a** gave a complex mixture. On treatment of **1′a** with [Ni(cod)$_2$] (1.0 equiv) and pn (1.0 equiv) in *N*-methylpyrrolidone (NMP)[14] in an NMR tube, two sets (**12**–pn A and **12**–pn B) of distinct signals were observed both in ^{31}P NMR and ^{119}Sn NMR spectra. Although the observed J_{P-Sn} values in both sets A and B indicate that a Sn–Ni σ bond is formed *cis* to the P atom,[15] thus suggesting structure **12**–pn shown in Scheme 2, we do not understand why two sets of peaks were observed. Both of these sets did not change on addition of alkyne **2a** (1.0 equiv) but did so smoothly with 1,2-diene **3** (1.2 equiv) to give **13**,[16] which lacks Sn–P coupling, thus showing that the insertion of **3** took place at the Ni–Sn bond of **12**–pn.[17] All attempts to obtain **4′a** or any other carbostannylation products by the reaction of **13** with **2a** were unsuccessful.



Scheme 2. Oxidative addition of an alkynylstannane to a nickel(0)–pn complex and the subsequent reactions traced by ^{31}P NMR and ^{119}Sn NMR spectroscopies: [a] Percentage of integral with respect to all of the observed peaks; [b] Yield based on **1′a** (determined by ^{119}Sn NMR spectroscopy with Bu$_4$Sn as an internal standard); [c] $J_{P-^{119}Sn}$ and $J_{P-^{117}Sn}$ were not resolved.

A survey of side products in the tandem alkynylstannylation of **1a**, **2a**, and **3** also provided information on the reaction order. Formation of any alkyne-alkynylstannylation product was not observed to any extent under conditions A, B, or C,[18] whereas a small amount of an allene-alkynylstannylation product was isolated under conditions A and B.[19] The results clearly show that 1,2-diene **3** rather than alkyne **2a** reacts with **12**–pn.

With the above data in hand, cycles 1 and 2 (see Scheme 3) may rationally explain the formation of tandem alkynylstannylation products **4a** and **5a** from the reaction of **1a** with **2a** and **3**. The catalytic cycles start with oxidative addition of **1a** to a nickel(0) complex. When oxidative adduct **12** undergoes insertion of **3** in a manner similar to acylstannane-nickel(0) oxidative adducts,[20] **3** should insert into the Ni–Sn bond of **12** in a direction such to avoid steric repulsion of the Bu substituent to give an (*E*)-σ-allylnickel complex,[21] which is prone to isomerize into the more stable *anti*-π-allyl complex **14**. Alkyne **2a** should then insert into the bond between the nickel atom and the nonsubstituted allyl carbon atom of **14** or the corresponding *syn*-isomer **15**.[22,23] The stereoselectivity of the tandem alkynylstannylation products should be determined by the relative rate of insertion of **2a** into the Ni–C bond of **14** and *anti–syn* isomerization from **14** to **15**, depending on ligand pn, ttpp or dpp. Reductive elimination from **16** or **17** should finally afford **4a** or **5a**, respectively.[24]



Scheme 3. Plausible catalytic cycles that start with oxidative addition of an alkynylstannane to a nickel(0) complex.

In conclusion, we have disclosed the first example of transition-metal-catalyzed tandem carbostannylation of two different carbon–carbon unsaturated bonds. Nickel catalysts assemble alkynylstannanes, alkynes and 1,2-dienes into alkenylstannanes having a dienyne structure that is otherwise hard to access by a direct route. Studies on the details of the mechanism as well as application of the reaction to other substrates are in progress.

Experimental Section

Tandem alkynylstannylation of alkynes and 1,2-dienes, general procedure: 1,2-Diene (0.30 mmol) and an alkyne (0.60 mmol) were added to a solution that contained an alkynylstannane (0.10 mmol), $[\mathrm{Ni(cod)_2}]$ (1.4 mg, 5.1 μmol) and a ligand (pn: 1.5 mg, 4.9 μmol; ttpp: 4.7 mg, 10 μmol; dpp: 1.3 mg, 4.9 μmol) in a solvent (dibutyl ether, toluene, or THF: 0.15 mL), and the resulting mixture was stirred at 50 °C. After the time specified (see Table 1 and Scheme 1 for specific details), the mixture was diluted with diethyl ether and filtered through a pad of florisil. The crude product was analyzed by ^{119}Sn NMR spectroscopy with $\mathrm{Me_4Sn}$ ($\mathrm{Bu_4Sn}$ for the reaction of tributyl(phenylethynyl)tin) as an internal standard.

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[2] For accounts, see: a) E. Shirakawa, T. Hiyama, *Bull. Chem. Soc. Jpn.* **2002**, *75*, 1435–1450; b) E. Shirakawa, T. Hiyama, *J. Organomet. Chem.* **2002**, *653*, 114–121.

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[7] We have already reported the dimerization–carbostannylation of alkynes, in which two molecules of alkynes insert into a carbon–tin bond: a) E. Shirakawa, H. Yoshida, Y. Nakao, T. Hiyama, *J. Am. Chem. Soc.* **1999**, *121*, 4290–4291; b) H. Yoshida, E. Shirakawa, Y. Nakao, Y. Honda, T. Hiyama, *Bull. Chem. Soc. Jpn.* **2001**, *74*, 637–647.

[8] For nickel-catalyzed multicomponent coupling reactions, see: a) J. Montgomery, *Acc. Chem. Res.* **2000**, *33*, 467–473; b) S. Ikeda, *Acc. Chem. Res.* **2000**, *33*, 511–519.

[9] Configuration of two double bonds in the tandem alkynylstannylation products was determined by NMR spectroscopic studies on coupling constants ($^3J_{\mathrm{Sn-H}}$ and $^3J_{\mathrm{Sn-C}}$) and NOE. For details, see Supporting Information.

[10] Unless otherwise noted, the yields and the ratio of isomers were determined by ^{119}Sn NMR spectroscopy with $\mathrm{Me_4Sn}$ or $\mathrm{Bu_4Sn}$ as an internal standard.

[11] The isolated yield of **4a** and **5a** after purification with reversed phase chromatography (octadecylsilyl, ODS) followed by gel-permeation chromatography (GPC) under conditions A or B (Figure 1) was 50% (88:12) or 63% (2:98), respectively, obtained from independent experiments from those shown in Table 1, entry 1.

[12] $[\mathrm{(Ph_3P)_2Ni(C{\equiv}CPh)(SnMe_3)}]$ is reportedly obtained, but in an analytically impure form, see: B. Cetinkaya, M. F. Lappert, J. McMeeking, D. E. Palmer, *J. Chem. Soc. Dalton Trans.* **1973**, 1202–1208.

[13] Density functional study shows that $\mathrm{HC{\equiv}CSnH_3}$ can oxidatively add to $[\mathrm{Ni(PH_3)_2}]$, see: T. Matsubara, K. Hirao, *Organometallics* **2002**, *21*, 4482–4489.

[14] Oxidative adduct **12**–pn was observed also in dibutyl ether, THF, $[\mathrm{D_6}]$benzene or DMF but in a purity less than 50%. NMP as a solvent for the Ni–pn-catalyzed reaction of **1a** with **2a** and **3** was found to be as efficient as dibutyl ether in the yield and stereoselectivity.

[15] The $J_{\mathrm{P-Sn}(cis)}$ of oxidative adduct of **1′a** to a palladium–iminophosphane or dppp complex is reported to be 21 or 29 Hz, respectively, whereas the $J_{\mathrm{P-Sn}(trans)}$ of the dppp complex is 1479/1411 Hz. See, E. Shirakawa, H. Yoshida, T. Hiyama, *Tetrahedron Lett.* **1997**, *38*, 5177–5180. The $J_{\mathrm{P-^{119}Sn}(cis)}$ and $J_{\mathrm{P-^{119}Sn}(trans)}$ of a similar complex, $[\mathrm{(dppe)Pd(SnMe_2Cl)(C{\equiv}CMe)}]$, prepared by successive transmetalation of the corresponding dichloro complex, are reported to be 183 and 2392 Hz. See, C. Stader, B. Wrackmeyer, *J. Organomet. Chem.* **1985**, *295*, C11–C15.

[16] Complex **12-pn** reacted with **3** also in the presence of **2a** (1.0 equiv) to give **13**.

[17] We could not obtain further information on the structure of complex **13**: its short lifetime and insufficient purity in addition to low availability of deuterated NMP do not allow us to gain meaningful ^{13}C and ^{1}H NMR spectra.

[18] The reaction of **1a** with **2a** in the absence of **3** under conditions A or B gave (*Z*)-2-hexyl-4-phenyl-1-trimethylstannylbut-1-en-3-yne in 13% or 6% yield, respectively. For the nickel-catalyzed alkynylstannylation of alkynes, see reference [3b].

[19] (*Z*)-4-Trimethylstannyl-1-phenylnon-4-en-1-yne or 3-butyl-5-phenyl-2-trimethylstannylpent-1-en-4-yne was generated in 6% yield under conditions A or B, respectively. For the nickel-catalyzed alkynylstannylation of 1,2-dienes, see reference [5b].

[20] In the nickel-catalyzed acylstannylation of 1,2-dienes, oxidative adducts of acylstannanes to nickel(0) complexes are considered to accept insertion of 1,2-dienes at the Ni–Sn bonds in the direction that affords σ-allylnickel complexes. See reference [5a].

[21] Intermediary σ-allylnickel complexes, which should be involved in cycle 1 and 2, are omitted from Scheme 3 for clarity.

[22] The regioselection should be reasonable, as terminal alkynes are considered to insert into a π-allylnickel complex at a less substituted carbon in the nickel-catalyzed three-component coupling of allyl chlorides, alkynes, and alkynylstannanes, see: a) S. Ikeda, D.-M. Cui, Y. Sato, *J. Org. Chem.* **1994**, *59*, 6877–6878; b) D.-M. Cui, T. Tsuzuki, K. Miyake, S. Ikeda, Y. Sato, *Tetrahedron* **1998**, *54*, 1063–1072.

[23] When allylnickel complexes fail to accept insertion of **2a**, alkynylstannylation products of **3** should be generated through reductive elimination.

[24] Oxidative cyclization of **2a** and **3** with a nickel(0) complex followed by the reaction with **1a** may be an alternative mechanism, but no evidence is currently available. See reference [7].