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Palladium-Catalyzed Bismetallative Cyclization of Enynes

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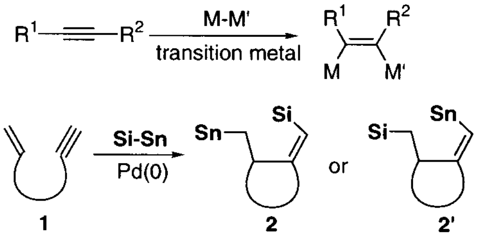
Summary: Enynes were reacted with $Me_3SiSnBu_3$ in the presence of $Pd_2dba_3{\cdot}CHCl_3$ or $Pd(OH)_2$ on charcoal to give cyclized products containing a vinylsilane moiety and a homoallyltin moiety in good yield.

The addition of a bimetallic reagent to a multiple bond is of interest because new metal−carbon bonds are formed. It may be expected that further insertion of various multiple bonds into these metal−carbon bonds could occur. We have investigated the reactivity of compounds having an Si−Sn[1a] bond or an Si−Zr bond.[1b] In this context, we investigated the palladium-catalyzed bismetallative cyclization of enynes with $Me_3SiSnBu_3$, **4**. If an enyne is treated with **4** in the presence of a palladium catalyst,[2] insertion of the alkyne part of **1** into the Si−Sn bond would be expected to occur to afford a cyclized compound, **2** or **2′**, which have Si−C and Sn−C bonds.[3] Such products could be converted to various compounds using reactions of the metal−carbon bonds.

Scheme 1. Bismetallative Cyclization of Enyne



Scheme 2. Reaction of Enyne 1a with 4 in the Presence of Pd(0)

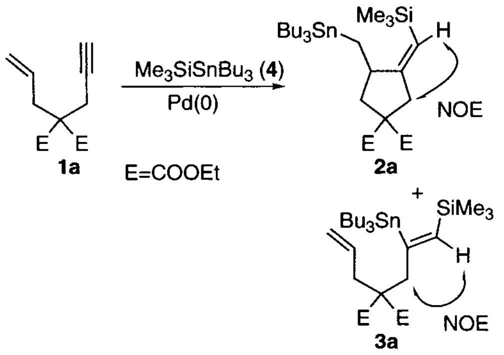


Table 1. Reaction of 1a with 4 in the Presence of Pd(0)[a]

					yield (%)		
run	catalyst	solvent	time (h)	temp	**2a**	**3a**	**1a**
1	$Pd(PPh_3)_4$	THF	4	50 °C	14	80	
2	$PdCl_2(PPh_3)_2$	THF	6	reflux	7	48	
3	$Pd(OAc)_2dppb$	THF	5	reflux	20	34	
4	$Pd(cod)Cl_2$	THF	16	rt	30		40
5	$PdCl_2$[b]	THF	45	rt	42		
6	$Pd_2(dba)_3$	THF	16	rt	63		
7	$Pd_2(dba)_3$	DMF	16	rt	10		15
8	$Pd_2(dba)_3$	toluene	16	rt	53		
9	Pd/C	THF	114	rt	86		10
10	$Pd(OH)_2/C$[c]	THF	42	rt	88		5
11	$Pd(OH)_2/C$[d]	THF	20	rt	90		2

[a] All reactions were carried out using 3 mol % of Pd catalyst and 1.1 equiv of **4**. [b] 6 mol % of $PdCl_2$ and 1.5 equiv of **4** were used. [c] 6 mol % of $Pd(OH)_2$ on charcoal and 1.1 equiv of **4** were used. [d] 10 mol % of $Pd(OH)_2$ on charcoal and 1.5 equiv of **4** were used.

When a THF solution containing equimolar quantities of enyne **1a** and $Me_3SiSnBu_3$ was stirred at 50 °C in the presence of a catalytic amount of $Pd(PPh_3)_4$ for 4 h, a small amount of cyclized product **2a** was obtained (14% yield) along with a bismetalated derivative of the alkyne, **3a**, in 80% yield after the usual workup (Table 1, run 1). The ^{119}Sn NMR spectra of **2a** and **3a** showed resonances at −15.7 and −53.2, respectively. Thus, **2a** contains an alkyltin moiety. An NOE experiment indicated that the *Z*-olefin had been formed (Scheme 2). To confirm the structure of **2a**, destannylation was carried out by treating it with HI in the presence of $[Bu_4N]I$ at 0 °C.[4] A three-membered ring compound, **5a**, was obtained in good yield (Scheme 3). Probably, protonation occurs at the α-position of vinylsilane, and then the

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(1) Mori, M.; Isono, N.; Wakamatsu, H. *Synlett*, **1999**, 269. (b) Mori, M.; Kuroda, S.; Dekura, F. *J. Am. Chem. Soc.* **1999**, *121*, 5591.

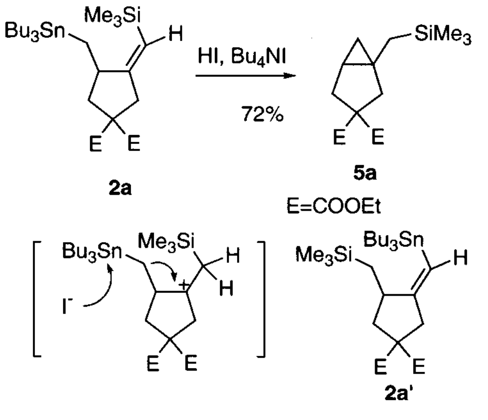
(2) Mitchell, T. N.; Killing, H.; Dicke, R.; Wickenkamp, R. *J. Chem. Soc., Chem. Commun*. **1985**, 354. (b) Chenard, B. L.; Laganis, E. D.; Davidson, F.; RajanBabu, T. V. *J. Org. Chem*. **1985**, *50*, 3667. (c) Chenard, B. L.; Van Zyl, C. M. *J. Org. Chem*. **1986**, *51*, 3561. (d) Mitchell, T. N.; Wickenkamp, R.; Amamria, A.; Dicke, R.; Schneider, U. *J. Org. Chem*. **1987**, *52*, 4868. (e) Murakami, M.; Morita, Y.; Ito, Y. *J. Chem. Soc., Chem. Commun*. **1990**, 428. (f) Tsuji, Y.; Obora, Y.; *J. Am. Chem. Soc.* **1991**, *113*, 9368. (g) Obora, Y.; Tsuji, Y.; Asayama, M.; Kawamura, T. *Organometallic* **1993**, *12*, 4697. (h) Obora, Y.; Tsuji, Y.; Kawamura, T. *J. Am. Chem. Soc.* **1995**, *117*, 9814. (i) Beletskaya, I.; Moberg, C. *Chem. Rev.* **1999**, *99*, 3435.

(3) Bismetallative cyclization: See: (a) Obora, Y.; Tsuji, Y. Kakehi, T.; Kobayashi, M.; Shinkai, Y.; Ebihara, M.; Kawamura, T. *J. Chem. Soc., Perkin Trans. 1* **1995**, 599. (b) Onozawa, S.-y.; Hatanaka, Y.; Tanaka, M. *Chem. Commun*. **1997**, 1229. (c) Onozawa, S.-y.; Hatanaka, Y.; Choi, N.; Tanaka, M. *Organometallics* **1997**, *16*, 5389. (d) Suginome, M.; Matsuda, T.; Ito, Y. *Organometallic* **1998**, *17*, 5233. (e) Suginome, M. Ito, Y. *Chem. Rev.* **2000**, *100*, 3221.

(4) Mori, M.; Watanabe, N.; Kaneta, N.; Shibasaki, M. *Chem. Lett.* **1991**, 1615.

10.1021/om000979x CCC: $20.00

Scheme 3. Confirmation of the Structure of 2a



iodide anion attacks at the tin atom to close the three-membered ring.[5] On the basis of these results, the structure of the cyclized compound is determined to be **2a**, not **2a′**.

The reaction was carried out under various conditions to improve the yield of the desired cyclized product **2a** (Table 1). It was found that the formation of the alkyne bismetalation product **3a** could be suppressed by using a palladium catalyst in the absence of a phosphine ligand (runs 1–6). THF was a suitable solvent, and toluene also can be used (runs 6–8). It is noteworthy that heterogeneous Pd catalysts, Pd/C or $Pd(OH)_2/C$,[6] also afforded the desired product **2a** in high yield, although the reaction time was longer (runs 9–11).

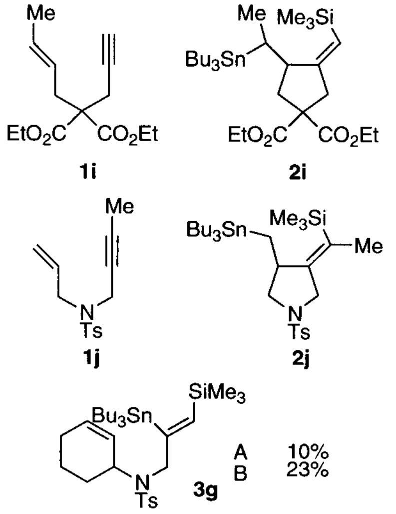
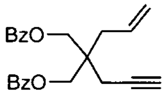
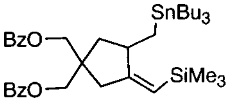
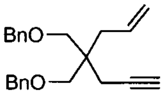
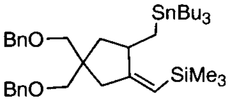
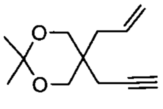
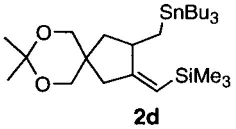
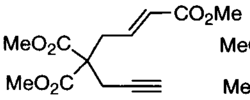
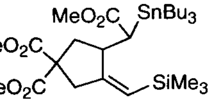
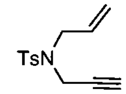
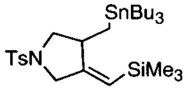
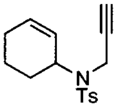
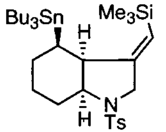
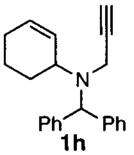
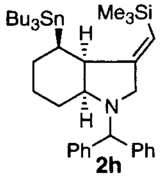


Figure 1.

Various enynes, **1b**–**1h**, were reacted with $Me_3SiSnBu_3$ in the presence of $Pd_2dba_3{\cdot}CHCl_3$ (method A) or $Pd(OH)_2/C$ (method B). The results are summarized in Table 2. In each case, the desired product **2** was obtained in moderate to good yield. The reaction of enyne **1e**, which has an electron-withdrawing substituent on the C=C bond, afforded the desired product **2e** in moderate yield, while the reaction of **1i** with a methyl substituent on the C=C bond (Figure 1) under similar conditions (method A) gave **2i**[7] in only 7% yield. Bicyclic heterocycle **2g** or **2h** was produced stereospecifically from the corresponding enyne **1g** or **1h**, respectively.

Table 2. Bismetallative Cyclization of Enyne 1

Substrate	Product	Method, Time (h)	Yield (%)
 **1b**	 **2b**	A 16 B 117	49 52
 **1c**	 **2c**	B 18	78
 **1d**	 **2d**	A 50 B 88	24 65
 **1e**	 **2e**	A 24 B 42	32 50
 **1f**	 **2f**	A 16 B 16	57 82
 **1g**	 **2g**	A 16 B 20	22 37
 **1h**	 **2h**	A 29 B 18	26 66

Method A.: The reaction was carried out in the presence of $Pd_2{\cdot}dba_3$ (3 mol %) and 1.1 equiv. of **4** at room temperature for 16 h. Method B: The reaction was carried out in the presence of 10 mol % of $Pd(OH)_2$ on charcol and 1.5 equiv. of **4** at room temperature.

However, in the reaction of **1g**, the alkyne bismetalation product **3g** was also obtained, which resulted in a lower yield of desired product **2g**. The reaction rate of enyne **1j** (Figure 1), which has a substituent on the alkyne, was relatively slow, and the cyclized product **2j** was obtained in only 5% yield. The starting material **1j** was recovered in 76% yield after 46 h (method A).

For the mechanism of this bismetallative cyclization, two possible pathways can be considered (Scheme 4). (1) The reaction proceeds by oxidative addition of $Me_3SiSnBu_3$ to Pd(0) to give $Me_3SiPdSnBu_3$ (**I**)[8] followed by insertion of the alkyne part of **1** into the Si–Pd bond to

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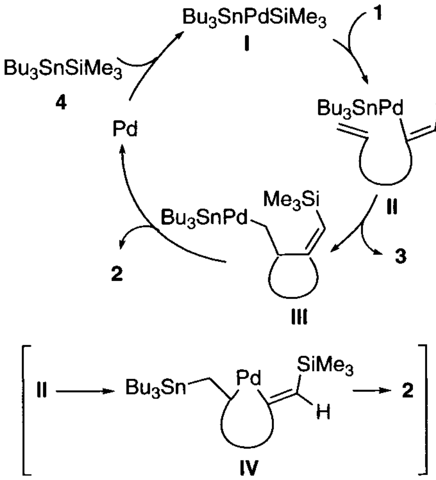
[5] Sugawara, M.; Yoshida, J. *Chem. Commun.* **1999**, 505.

[6] Lautens, M.; Kumanovic, S.; Meyer, C. *Angew. Chem., Int. Ed. Engl.* **1996**, *35*, 1329. (b) Lautens, M.; Ostrovsky, D.; Tao, B. *Tetrahedron Lett.* **1997**, *38*, 6343. (c) Lautens, M.; Smith, N. D.; Ostrovsky, D. *J. Org. Chem.* **1997**, *62*, 8970.

[7] The cyclized product **2e** was obtained as a single diastereomer, whose stereochemistry has not been determined yet.

Scheme 4. Possible Reaction Course



give complex **II**. Intramolecular insertion of the C=C bond into the C−Pd bond of **II** then occurs to give complex **III**, and reductive elimination finally affords cyclized product **2** and Pd(0) is regenerated. (2) On the other hand, the possibility of the formation of **IV**[3c] cannot be excluded in this mechanism. Thus, insertion of the C=C bond into the Sn−Pd bond in **II** could give complex **IV**. Reductive elimination from **IV** should afford the same cyclized product **2**. At present, it is not clear which pathway is followed in this reaction. Further studies are in progress.

Supporting Information Available: Typical procedure for bismetallative cyclization of enyne **1a**, spectral data for **2a**−**2h** and **5a**, and ^{1}H NMR spectrum of **2a**−**2h**. This material is available free of charge via the Internet at http://pubs.acs.org.

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(8) Ozawa, F.; Sakamoto, Y.; Sagawa, T.; Tanaka, R.; Katayama, H. *Chem. Lett.* **1999**, 1307. (b) Hada, M.; Tanaka, Y.; Ito, M.; Murakami, M.; Amii, H.; Ito, Y.; Nakatsuji, H. *J. Am. Chem. Soc.* **1994**, *116*, 8754.

(9) Very recently, Pd-catalyzed bismetallative cyclization of diynes with $Me_3SiSnBu_3$ has been reported, see: Gréau, S.; Radetich B.; RajanBabu, T. V. *J. Am. Chem. Soc.* **2000**, *122*, 8579.