Palladium-Catalyzed Borylstannylative Carbocyclization of Diynes and an Enyne Compound

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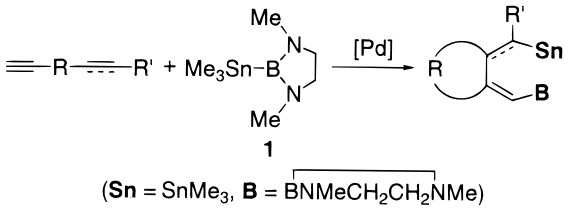
Summary: Highly regio- and stereoselective borylstannylative carbocyclization of diynes ***2a*****−****f** *with the borylstannane* ***1*** *are efficiently catalyzed at room temperature by a series of palladium complexes such as* $Cl_2Pd(PPh_3)_2$, $Cl_2Pd[P(o\text{-}tolyl)_3]_2$, $Pd(PPh_3)_4$, *and* $Pd(dba)_2$, *giving 1-(borylmethylidene)-2-(stannylmethylidene)cycloalkane derivatives* ***3a*****−****f** *in high yields. A 1,6-enyne (****2g****) also reacts similarly to afford a high yield of the corresponding cyclized product* ***3g****.*

The transition-metal-complex-catalyzed cyclizations of unsaturated organic compounds have received increasing attention as powerful tools for ring construction.[1] The addition−carbocyclization reactions of diynes,[2,3] enynes,[2,3a,4] or bis(dienes)[5] with reagents having inter-heteroatom bonds (E−E′ bonds: E, E′ = metals or heteroatoms) are particularly useful, because the resulting metal- or heteroatom-containing cyclic compounds allow numerous synthetic applications. However, such reactions are still very rare. Recently, we[2,6] and Ito's group[7] have reported palladium-catalyzed addition reactions of inter-heteroatom bonds such as B−Sn and B−Si bonds with alkynes. The high regio- and stereoselectivity of these reactions prompted us to study the reactivities of α,ω-diynes toward borylstannane **1**[8] (Scheme 1). We report herein that this reaction proceeds smoothly in the presence of a palladium catalyst under very mild conditions (room temperature, 1−5 h), affording good yields of 1-(borylmethylidene)-2-(stannylmethylidene)cycloalkanes with extremely high regio- and stereoselectivity.[9]

A representative procedure was as follows. To a benzene solution (3 mL) of $Cl_2Pd(PPh_3)_2$ (1 mol %) and decane (50 μL, an internal standard for GC analysis) in a Schlenk tube were added 1,3-dimethyl-2-(trimethylstannyl)-2-bora-1,3-diazacyclopentane (**1**; 0.582 mmol) and 1,6-heptadiyne (**2a**; 0.873 mmol) at 0 °C. The mixture was warmed to room temperature and stirred for 1 h. Analysis of the resulting reaction mixture by GC, GC−MS, and NMR indicated that the starting materials were completely consumed and that 1-[(*Z*)-(1,3-dimethyl-2-bora-1,3-diazacyclopent-2-yl)methylidene]-2-[(*Z*)-(trimethylstannyl)methylidene]cyclopentane (**3a**) was formed as the sole product in 98% ^{1}H NMR yield (Table 1, entry 1). Isolation of this product was very easy; evaporation of the solvent, addition of pentane (10 mL) to the residue, filtration, and bulb-to-bulb distillation of the concentrated filtrate afforded analytically pure **3a** in 79% yield.[10] Despite serious congestion, product **3a** (and other products also) adopts the *Z,Z*-configuration, as evidenced by the NOE experiments (see ref 11 and Chart 1). The configuration was further confirmed by X-ray crystallography in the case of **3d** (*vide infra*). With regard to the catalyst, besides $Cl_2Pd(PPh_3)_2$, a series of palladium complexes such as $Cl_2Pd[P(o\text{-}tolyl)_3]_2$, $Pd(PPh_3)_4$, and $Pd(dba)_2$ exhibited equally excellent catalytic activity; when they were applied to the reaction of **1** with **2a** under the same conditions, these palladium catalysts gave **3a** in nearly quantitative yields (determined by ^{1}H NMR).

Scheme 1



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(**Sn** = $SnMe_3$, **B** = $\overline{BNMeCH_2CH_2NMe}$)

The analogous borylsilylative carbocyclization reaction of diynes with a borylsilane usually gave a mixture of a desired cyclization product and another undesired product arising from simple addition of the borylsilane to one of the two acetylenic bonds of diynes.[2] Depending on the structure of the diynes, the undesired product could be the main product of the reaction. On the other hand, such a byproduct was not formed in the present

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(1) (a) Ojima, I.; Tzamarioudaki, M.; Li, Z.; Donovan, R. J. *Chem. Rev.* **1996**, *96*, 635. (b) Trost, B. M. *Acc. Chem. Res.* **1990**, *23*, 34. (c) Schore, N. E. *Chem. Rev.* **1988**, *88*, 1081. (d) Vollhardt, K. P. C. *Angew. Chem., Int. Ed. Engl.* **1984**, *23*, 539.

(2) Onozawa, S.-y.; Hatanaka, Y.; Tanaka, M. *Chem. Commun.* **1997**, 1229.

(3) (a) Chatani, N.; Morimoto, T.; Muto, T.; Murai, S. *J. Organomet. Chem.* **1994**, *473*, 335. (b) Tamao, K.; Kobayashi, K.; Ito, Y. *J. Am. Chem. Soc.* **1989**, *111*, 6478. (c) Chatani, N.; Takeyasu, T.; Horiuchi, N.; Hanafusa, T. *J. Org. Chem.* **1988**, *53*, 3539.

(4) Ojima, I.; Donovan, R. J.; Shay, W. R. *J. Am. Chem. Soc.* **1992**, *114*, 6580.

(5) Obora, Y.; Tsuji, Y.; Kakeshi, T.; Kobayashi, M.; Shinkai, Y.; Ebihara, M.; Kawamura, T. *J. Chem. Soc., Perkin Trans. 1* **1995**, 599.

(6) Onozawa, S.-y.; Hatanaka, Y.; Sakakura, T.; Shimada, S.; Tanaka, M. *Organometallics* **1996**, *15*, 5450.

(7) Suginome, M.; Nakamura, H.; Ito, Y. *Chem. Commun.* **1996**, 2777.

(8) Borylstannane **1** can be easily prepared according to the literature procedure. See: Niedenzu, K.; Rothgery, E. F. *Synth. Inorg. Met.-Org. Chem.* **1972**, *2*, 1.

(9) A part of this work was presented at the 43rd Symposium on Organometallic Chemistry, Osaka, Japan, Oct 31−Nov 1, 1996; Kinki Chemical Society: Osaka, Japan, 1996; Abstract PB231.

(10) **3a**: bp 110−115 °C/5.5 × 10^{-3} Torr; IR (neat) 766, 1253, 1291, 1350, 1404, 1439, 1500, 1632, 2792, 2848 cm^{-1}; ^{1}H NMR (C_6D_6) δ 0.17 (s, J_{H-Sn} = 55.0 Hz, 9H, $SnCH_3$), 1.53−1.64 (m, 2H, CH_2), 2.36−2.44 (m, 4H, CH_2), 2.52 (s, 6H, NCH_3), 3.04 (s, 4H, NCH_2), 5.35 (s, 1H, =CHB), 5.73 (s, J_{H-Sn} = 63.6 Hz, 1H, =CHSn); ^{13}C NMR (C_6D_6) δ −8.5 (J_{C-Sn} = 350 Hz, $SnCH_3$), 21.9, 35.0 (NCH_3), 36.7, 37.6, 52.0 (NCH_2), 116.9 (broad, =CHB), 123.5 (J_{C-Sn} = 485 Hz, =CHSn), 158.3 (C=), 160.3 (C=); ^{119}Sn NMR (C_6D_6) δ −51.4; ^{11}B NMR δ 29.7 (broad); GC−MS (70 eV, EI) *m/z* (relative intensity) 354 (M^+ for **3a** having ^{11}B and ^{120}Sn isotopes, 0.05; molecular peaks corresponding to other isotopes were also observed), 189 (100), 188 (28), 187 (15), 174 (84), 173 (38). Anal. Calcd for $C_{14}H_{27}BN_2Sn$: C, 47.65; H, 7.71; N, 7.94. Found: C, 48.00; H, 7.86; N, 8.04.

(11) The stereochemistry of the diene moiety was confirmed by NOE experiments, in which irradiation at allylic protons in the ring resulted in enhancement of vinylic proton (or allylic protons in the side chain for **3f**) signals, as shown in Chart 1.

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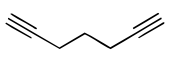
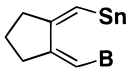
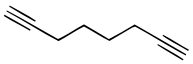
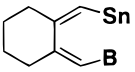
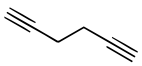
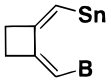
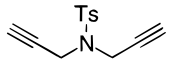
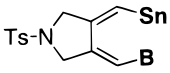
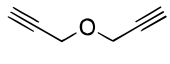
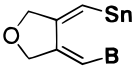
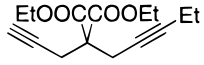
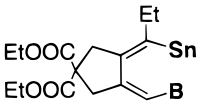
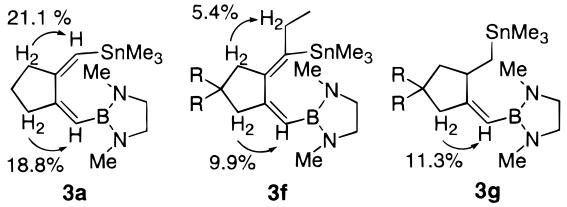
Table 1. Borylstannylative Carbocyclization of Diynes[a]

entry	substrate	time (h)	product[b]	yield (%)[c]
1	 **2a**	1	 **3a**	79 (92)
2	 **2b**	1	 **3b**	74 (84)
3	 **2c**	5	 **3c**	64 (97)
4	 **2d**	5	 **3d**	82[d]
5	 **2e**	3	 **3e**	83 (93)
6	 **2f**	1	 **3f**	86

[a] All reactions were carried out in benzene using **1** (1.0 equiv), **2** (1.5 equiv), and $Cl_2Pd(PPh_3)_2$ (1 mol %) at room temperature. [b] **Sn** = $SnMe_3$, **B** = $BNMeCH_2CH_2NMe$. [c] Isolated yields based on borylstannane **1**. Yields in parentheses were determined by GC (entries 1, 2, and 5) or ^1H NMR (entry 3). [d] Isolated by recrystallization from toluene/pentane.

Chart 1[a]



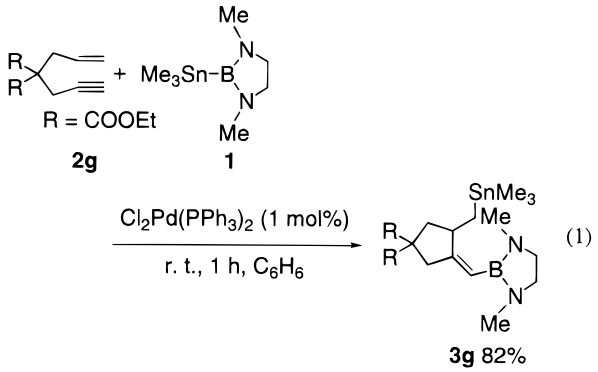
[a] R = COOEt.

reaction, indicating that the borylstannylative carbocyclization with **1** appears to be more general and selective. Accordingly, the reaction could be readily applicable to various diynes, as summarized in Table 1. The reaction of 1,7-octadiyne (**2b**) with **1** under the same conditions proceeded smoothly to give the corresponding 1,2-dimethylidenecyclohexane derivative **3b** in 74% yield (entry 2). Surprisingly, even a strained four-membered ring could be readily formed; a similar procedure starting with 1,5-hexadiyne (**2c**) and **1** furnished the 1,2-dimethylidenecyclobutane derivative **3c** in 64% yield (entry 3).[12]

Nitrogen- and oxygen-containing 1,6-diynes also efficiently participated in the palladium-catalyzed borylstannylative carbocyclization, providing a facile route to 1,2-dimethylidene heterocyclic compounds. For instance, the reaction of *N*,*N*-dipropargyltosylamine (**2d**) with **1** afforded the 3,4-dimethylidenepyrrolidine derivative **3d**. Since recrystallization of crude **3d** from pentane−toluene afforded colorless parallelepipeds (82%, entry 4), the structure was unequivocally confirmed by X-ray crystallography.[13] As the ORTEP[14] drawing (Figure 1) shows, the structure of the diene moiety of **3d** is considerably distorted from planarity, the dihedral angle between the two π planes being 39°. This distortion is apparently due to the steric repulsion between the boryl and stannyl groups bound to the diene moiety. Dipropargyl ether (**2e**) also underwent borylstannylative carbocyclization to give the 3,4-dimethylidenetetrahydrofuran derivative **3e** in 83% yield (entry 5).

The versatility of the present method in the preparation of various types of dialkylidenecycloalkanes is further substantiated by the cyclization of the unsymmetrical diyne **2f** with **1** (entry 6). In this case, the boryl group was selectively introduced to the terminal acetylenic bond. The corresponding cyclized product **3f** was isolated in 86% yield without formation of other regio- and stereoisomers. ^1H and ^{13}C NMR spectra and NOE analysis[11] completely agreed with the structure of **3f**.

An enyne such as the hept-6-en-1-yne derivative **2g** also undergoes the borylstannylative carbocyclization with **1** in a completely regioselective fashion. Despite



(1)

the presence of both olefinic and acetylenic bonds in **2g**, the boryl group was introduced exclusively to the acetylenic bond to give isomerically pure **3g** in 82% yield. Its structure was confirmed by NOE analysis[11] as well as ^{13}C NMR spectroscopy, which displayed signals assignable to methylene and olefinic carbons bound to tin (18.4 ppm, J_{Sn-C} = 350 Hz) and boron (115.3 ppm, broad), respectively.[15]

The mechanism of the present reaction has not been investigated in detail; however, on the basis of the regio- and stereoselectivities observed, it appears reasonable to assume the catalytic cycle depicted in Scheme 2. The oxidative addition of the B−Sn bond to a palladium(0) species, generating the *cis*-boryl(stannyl)palladium(II) species **4**, was verified by us previously.[6] Coordination of a diyne (or an enyne) to **4** followed by *cis* insertion of an acetylenic moiety into the Pd−B bond affords **6**. The

(12) Distillation of **3c** at 105−110 °C (bath temperature)/3.2 × 10^{-3} Torr caused deterioration of the product, leading to a significant decrease of the isolated yield as compared with the ^1H NMR yield (97%).

(13) X-ray data for **3d**: $C_{20}H_{32}BN_2O_2SSn$, M_r = 508.10, colorless crystal, crystal size 0.55 × 0.40 × 0.20 mm^3, triclinic, a = 9.832(2) Å, b = 11.362(3) Å, c = 11.534(6) Å, α = 90.68(3)°, β = 103.04(2)°, γ = 102.19(2)°, V = 1224.6(7) $Å^3$, space group $P\bar{1}$, Z = 2, μ(Mo Kα) = 11.454 cm^{-1}, ρ_{calcd} = 1.38 g/cm^3. The 5627 independent reflections ($|F_o| > 3\sigma|F_o|$, $\theta < 27°$) were measured on a Mac Science MXC18 diffractometer using Mo Kα radiation and a $\omega-2\theta$ scan. The structure was solved by direct methods, and all non-hydrogen atoms were refined anisotropically by full-matrix least squares to R = 0.0582, R_w = 0.0820, and GOF = 0.856.

(14) Johnson, C. K. ORTEP, a FORTRAN Thermal-Ellipsoid Plot Program for Crystal Structure Illustrations; Report ORNL-3794; Oak Ridge National Laboratory: Oak Ridge, TN, 1970.

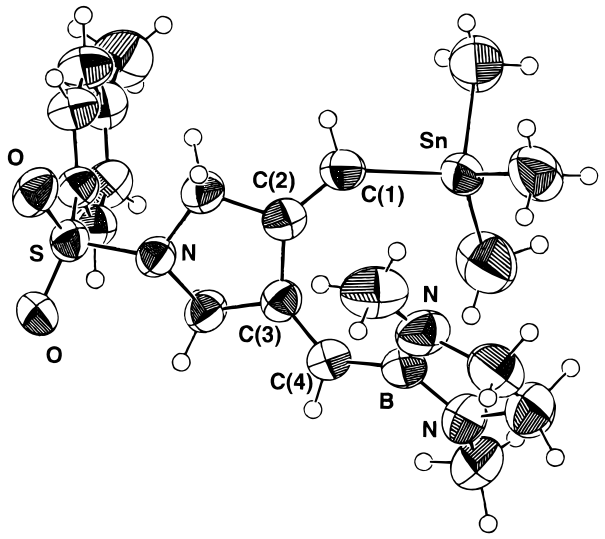
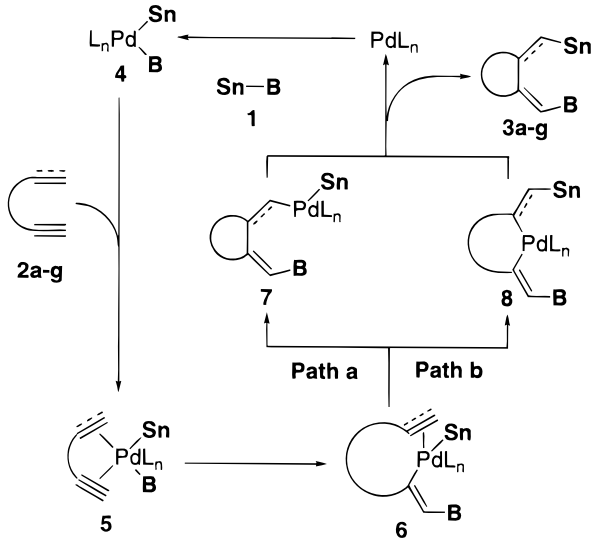


Figure 1. ORTEP drawing of **3d**. Selected bond distances (Å): C(1)−C(2), 1.332(8); C(2)−C(3), 1.472(7); C(3)−C(4), 1.348(8). Selected torsion angles (deg): Sn−C(1)−C(2)−C(3), 7.2(5); C(1)−C(2)−C(3)−C(4), 39.1(7); C(2)−C(3)−C(4)−B, 4.3(6).

preferential insertion into the Pd−B bond rather than the Pd−Sn bond is strongly supported by the regioselective introduction of the boryl group into the more reactive terminal acetylene in the reaction of unsymmetrical diyne **2f** and enyne **2g**. Subsequent *cis* insertion of the other acetylenic (or the olefinic) moiety into the resulting Pd−alkenyl bond and reductive elimination of **7** give the cyclized product and regenerate the palladium(0) species (path a). An alternative mechanistic pathway (path b) involving the palladacycle intermediate **8** cannot be excluded at the moment.

(15) **3g**: bp 135 °C/3.7 × 10^{-3} Torr; IR (neat) 766, 1065, 1098, 1181, 1212, 1243, 1290, 1404, 1437, 1499, 1645, 1734, 2788, 2892, 2980 cm^{-1}; ^{1}H NMR (C_6D_6) δ 0.11 (s, J_{H-Sn} = 52.4 Hz, 9H, $SnCH_3$), 0.92 (t, J = 7.1 Hz, 3H, CH_3CH_2O), 0.93 (t, J = 7.1 Hz, 3H, CH_3CH_2O), 1.02 (dd, J = 10.8, 12.9 Hz, J_{H-Sn} = 56.4 Hz, 1H, CH_2Sn), 1.29 (dd, J = 3.2, 12.9 Hz, J_{H-Sn} = 56.4 Hz, 1H, CH_2Sn), 1.93 (dd, J = 9.3, 12.4 Hz, 1H, CH_2), 2.58 (s, 6H, NCH_3), 2.90−3.13 (m, 6H, NCH_2, CH, CH_2), 3.25 (d, J = 16.2 Hz, 1H, CH_2), 3.40 (d, J = 2.4, 16.2 Hz, 1H, CH_2), 3.92−4.00 (m, 4H, CH_3CH_2O), 5.48 (s, 1H, =CHB); ^{13}C NMR (C_6D_6) δ −9.6 (J_{C-Sn} = 318 Hz, $SnCH_3$), 14.0 (CH_3CH_2O), 18.4 (J_{C-Sn} = 350 Hz, CH_2Sn), 34.4 (NCH_3), 41.2 (J_{C-Sn} = 20 Hz, CH), 43.8 (J_{C-Sn} = 14 Hz, CH_2), 44.3 (CH_2), 51.8 (NCH_2), 59.2 ($C(CO)_2$), 61.2 (CH_3CH_2O), 115.3 (broad, =CHB), 160.4 (J_{C-Sn} = 56 Hz, C=), 171.6 (C=O); ^{119}Sn NMR (C_6D_6) δ −3.4; ^{11}B NMR δ 31.0 (broad). Anal. Calcd for $C_{20}H_{37}BN_2O_4Sn$: C, 48.14; H, 7.47; N, 5.61. Found C, 48.24; H, 7.67; N, 5.50.

Scheme 2



In conclusion, the palladium-catalyzed borylstannylative carbocyclization of diyne and enyne compounds provides a versatile method for synthesizing a variety of cyclic compounds with high selectivities. Stereo- and regiochemical control in transition-metal-complex-catalyzed carbocyclizations is apparently one of the most important subjects in organic synthesis. The chemistry presented here would give unique and elegant solutions to these problems. Further studies are under way to clarify the mechanistic aspects of the reactions of various inter-heteroatom bonds with unsaturated organic compounds and to develop new synthetic methodologies.

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Supporting Information Available: Text giving detailed experimental procedures and characterization data for 1-(borylmethylidene)-2-(stannylmethylidene)cycloalkanes **3a**−**f** and 1-(*Z*)-(borylmethylidene)-2-(stannylmethyl)cycloalkane **3g** and text and tables giving full details of the crystal structure analysis for **3d** (12 pages). Ordering information is given on any current masthead page.

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