

Palladium-Catalyzed *trans*- and *cis*-Carboboration of Alkynes Tethered to Chloroborane with Organozirconium Reagents: Ligand-Dependent Complementary Stereoselectivity

Masaki Daini, Akihiko Yamamoto, and Michinori Suginome*

Department of Synthetic Chemistry and Biological Chemistry, Graduate School of Engineering, Kyoto University
Katsura, Nishikyo-ku, Kyoto 615-8510, Japan

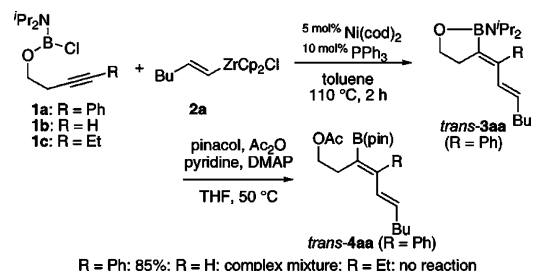
Received December 17, 2007; E-mail: suginome@sbchem.kyoto-u.ac.jp

There are increasing demands for organoboronic acid derivatives in synthetic organic chemistry because they exhibit remarkable reactivities upon appropriate activation, while being stable, storable, and nonpoisonous.¹ Their applications are spreading over the pharmaceutical and material sciences in recognition of the unique properties of organoboron compounds. Therefore, development of efficient methods for the synthesis of stereodefined, functionalized organoboronic acids is highly desirable.

Catalytic borylation reactions have gained much attention with respect to efficiency, selectivity, and functional group compatibility.^{2,3} Recent efforts have focused on the additions of boron–element bonds across carbon–carbon multiple bonds,⁴ such as diboration⁵ and silaboration.⁶ Our attention has been focused on the development of catalytic carboboration reactions, in which B–C and C–C bonds are formed concurrently. We have so far reported two distinctive classes of carboborations, i.e., direct⁷ and transmetalative⁸ carboborations. While direct carboboration involves the activation of B–C bonds of the boron reagents, transmetalative carboboration uses haloborane as the source of the boryl group, with organometallic reagents as the source of the organic group. As the first example of the latter class of carboboration, we recently established that a carbon–carbon triple bond tethered to chlorobound boron underwent nickel-catalyzed carboboration upon use of alkynylstannanes as the transmetalation reagents.⁸ In contrast to our mechanism-based assumption, the carboboration proceeded with a *trans*-addition mode. In this paper, we report a new carboboration system utilizing organozirconium reagents with palladium catalysts. The Pd/Zr system not only allows significant expansion of the substrate scope but also brings about highly stereoselective carboboration with either stereochemical course, which critically depends on the phosphine ligands.

After screening various alkenyl organometallics as the transmetalation reagents, we found that reaction of alkenylzirconium reagent **2a** with chloroborane **1a**, which was tethered to an aryl-substituted alkyne, gave the carboboration product *trans*-**3aa** in good yield in the presence of nickel catalysts (Scheme 1). The Ni/Zr system still gave a *trans*-addition product with high selectivity, as did the Ni/Sn system. However, no carboboration products were obtained in the reaction of terminal or alkyl-substituted alkynes **1b** or **1c**, even with the Ni/Zr system.

We then reexamined the transition metal catalysts for use with the organozirconium reagent. We found that palladium catalysts exhibited high catalytic activity. On using bulky trialkylphosphines such as P^tBu₃ or PCy₃ with palladium complexes such as PdCp(allyl) or Pd(acac)₂, the alkenylboration proceeded with high stereoselectivities for the *trans*-addition product, as observed in the Ni-catalyzed reaction (Table 1, entries 1 and 2).⁹ To our surprise, however, the stereochemical course was completely switched to favor *cis*-addition, when PMe₃ was used as a ligand in the reaction of **1a** with **2a** (entry 6). As shown in Table 1, a clear relationship

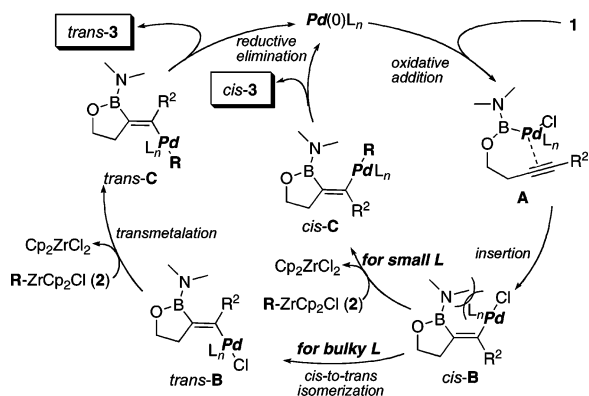
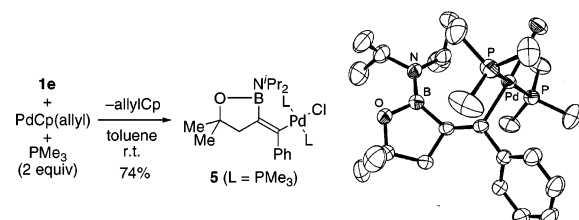
Scheme 1. Ni-Catalyzed Carboboration with a Zr Reagent**Table 1.** Ligand-Dependent Stereoselectivities in the Palladium-Catalyzed Reactions of **1a** with **2a**^a

entry	ligand	% yield (NMR)	<i>trans</i> / <i>cis</i> (NMR)
1	P ^t Bu ₃	86	96:4
2	PCy ₃	91	88:12
3	PPh ₃	80	71:29
4	PMePh ₂	77	41:59
5	PMe ₂ Ph	58	17:83
6	PMe ₃	75	6:94

^a **1a** (0.2 mmol) and **2a** (0.3 mmol) in toluene (0.25 mL) were heated at 110 °C in the presence of PdCp(π -allyl) (0.010 mmol) with a phosphine ligand (0.020 mmol).

between the stereoselectivities and the bulkiness of the phosphine ligands was observed.

The ligand-dependent stereoselectivity can be rationalized well by the reaction mechanism. As shown in Scheme 2, the catalysis is triggered by the oxidative addition of a B–Cl bond to a Pd(0) complex.^{10,11} Subsequent intramolecular insertion of the carbon–carbon triple bond into the B–Pd bond of **A** leads to the formation of β -borylalkenylpalladium intermediate *cis*-**B**. As proposed for the Ni/Sn system, the *trans*-addition pathway may involve isomerization of *cis*-**B** to *trans*-**B** before the transmetalation step. The isomerization pathway can be rationalized by the large steric repulsion between the L₂PdCl and the isopropyl groups on the nitrogen atom, which are inevitably coplanar with the boron-containing five-membered ring due to the double bond character of the B–N bond. On the other hand, with less bulky phosphine ligands such as PMe₃, transmetalation with the organozirconium reagent proceeds without isomerization, giving the *cis*-carbaboration products *cis*-**3** directly through *cis*-**C**. To support this assumption, palladium complex **5**, which corresponds to *cis*-**B** in Scheme 2, was isolated in high yield in the stoichiometric reaction of **1e** with PdCp(allyl) and PMe₃ (Scheme 3). The observed *cis* stereochemistry of the C=C bond in

Scheme 2. Proposed Mechanism for the Pd-Catalyzed *trans*- and *cis*-Carboboration**Scheme 3.** Formation and X-ray Crystal Structure of **5****Table 2.** Pd-Catalyzed *trans*- and *cis*-Carbaborations with **1** and Organozirconium Reagents **2**^a

entry	1	2	ligand	4 (%yield) ^b	trans/cis
1	a	a	P ^t Bu ₃	<i>trans</i> - 4aa (71)	96:4
2	b	a	PCy ₃	<i>trans</i> - 4ba (83)	>99:1
3	c	a	P ^t Bu ₃	<i>trans</i> - 4ca (75)	>99:1
4	d	a	PCy ₃	<i>trans</i> - 4da (71)	94:6
5	e	a	PCy ₃	<i>trans</i> - 4ea (70)	>99:1
6	f	a	P(2-furyl) ₃	<i>trans</i> - 4fa (69)	93:7
7	a	b	P ^t Bu ₃	<i>trans</i> - 4ab (86)	>99:1
8	a	c	P ^t Bu ₃	<i>trans</i> - 4ac (82)	>99:1
9	a	d	PCy ₃	<i>trans</i> - 4ad (87)	>99:1
10	a	e	PCy ₃	<i>trans</i> - 4ae (70)	>99:1
11	a	f	PCy ₃	<i>trans</i> - 4af (81)	>99:1
12	a	a	PMe ₃	<i>cis</i> - 4aa (67)	6:94
13	b	a	PMe ₃	<i>cis</i> - 4ba (71)	<1:99
14	c	a	PMe ₃	<i>cis</i> - 4ca (69)	<1:99
15	d	a	PMe ₃	<i>cis</i> - 4da (60)	<1:99
16	e	a	PMe ₃	<i>cis</i> - 4ea (63)	4:96
17	f	a	PMe ₃	<i>cis</i> - 4fa (44)	<1:99
18	a	d	PMe ₃	<i>cis</i> - 4ad (54)	4:96
19	a	e	PMe ₃	<i>cis</i> - 4ae (61)	<1:99

^a **1** (0.40 mmol), **2** (0.60 mmol), PdCp(π-allyl) (8.0 μmol), and a ligand (0.016 mmol) in toluene (0.50 mL) were heated at 110 °C unless otherwise noted. ^b Isolated yield.

5 is in sharp contrast to the *trans* stereochemistry for the corresponding Ni complex in a previous report.⁸

The Pd/Zr-based new carboboration system showed a remarkably wider substrate scope than the previous Ni/Sn or Ni/Zr system (Table 2). While the Ni/Sn and the Ni/Zr systems could utilize neither terminal nor alkyl-substituted alkynes, the Pd/Zr system allowed those types of alkynes to give the corresponding alkenylboration product in high yields (entries 2 and 3). In both cases, high selectivities for the *trans* addition were observed in the presence

of P^tBu₃ or PCy₃. Chloroborane **1d** tethered to a tertiary alcohol was similarly reactive to give the corresponding *trans* products selectively (entry 4). It was remarkable that the chloroboranes derived from propargylic alcohol (*n* = 0) and bishomopropargylic alcohols (*n* = 2) underwent the *trans*-carboboration selectively (entries 5 and 6). With respect to the organometallic reagents, not only a wide range of alkenylzirconium reagents (entries 7 and 8) but also arylzirconium (entry 9) and even alkylzirconium reagents (entries 10 and 11) took part in the reaction giving alkenyl-, aryl-, and alkylboration products in high yields. These groups could not be introduced by the previous carboboration using organostannanes as transmetalation reagents.

It should be remarked that the stereochemical complementarity held generally. Highly stereoselective *cis*-carboboration proceeded in the presence of PMe₃ as a ligand, regardless of the R¹, R², and R³ substituents of the reactants as well as the ring size formed (entries 12–19). In general, *trans*-carboboration using bulky phosphine ligands shows somewhat higher yields than the corresponding *cis*-carboboration using the PMe₃ ligand.

In summary, we report a new cyclizative carboboration system using alkynes tethered to chloroborane moieties, organozirconium reagents, and palladium catalysts. The Pd/Zr system shows a remarkably broad substrate scope, leading to alkenyl-, aryl-, and alkylborations of terminal and internal alkynes through four-, five-, and six-membered ring formations. Furthermore, the stereochemical course of the addition is successfully controlled by the phosphine ligand: *trans* addition is preferred with the bulky phosphines such as P^tBu₃, PCy₃, and PAr₃, while *cis* addition is favored with small phosphines such as PMe₃.

Acknowledgment. This work was supported by a Grant-in-Aid for Scientific Research on Priority Areas “Advanced Molecular Transformations of Carbon Resources” from MEXT.

Supporting Information Available: Experimental procedures and spectral data for the new compounds. This material is available free of charge via Internet at <http://pubs.acs.org>.

References

- Hall, D. In *Boronic Acid*; Hall, D., Ed.; Wiley: Weinheim, 2005; p 1.
- Catalytic hydroborations: (a) Nöth, H.; Männig, D. *Angew. Chem., Int. Ed. Engl.* **1985**, *24*, 878. For reviews, see: (b) Burgess, K.; Ohlmeyer, M. *J. Chem. Rev.* **1991**, *91*, 1179. (c) Beletskaya, I.; Pelter, A. *Tetrahedron* **1997**, *53*, 4957. (d) Crudden, C. M.; Edwards, D. *Eur. J. Org. Chem.* **2003**, 4695.
- Selected examples for catalytic C–H borylations: (a) Shimada, S.; Batsanov, A. S.; Howard, J. A. K.; Marder, T. B. *Angew. Chem., Int. Ed.* **2001**, *40*, 2168. (b) Cho, J.-Y.; Tse, M. K.; Holmes, D.; Maleczka, R. E., Jr.; Smith, M. R., III. *Science* **2002**, *295*, 305. (c) Ishiyama, T.; Takagi, J.; Ishida, K.; Miyaura, N.; Anastasi, N. R.; Hartwig, J. F. *J. Am. Chem. Soc.* **2002**, *124*, 390.
- Reviews on the catalytic boron-element addition: (a) Beletskaya, I.; Moberg, C. *Chem. Rev.* **2006**, *106*, 2320. (b) Sugimoto, M.; Matsuda, T.; Ohmura, T.; Seki, A.; Murakami, M. In *Comprehensive Organometallic Chemistry III*; Crabtree, R.; Mingos, D. M., Eds.; Ojima, I., Vol. Ed.; Elsevier, **2007**; Vol. 10, p 725.
- (a) Ishiyama, T.; Nishijima, K.-i.; Miyaura, N.; Suzuki, A. *J. Am. Chem. Soc.* **1993**, *115*, 7219. For reviews, see: (b) Marder, T. B.; Norman, N. C. *Top. Catal.* **1998**, *63*–73. (c) Ishiyama, T.; Miyaura, N. *J. Organomet. Chem.* **2000**, *611*, 392. (d) Ishiyama, T.; Miyaura, N. *Chem. Rec.* **2004**, *3*, 271–280.
- (a) Sugimoto, M.; Nakamura, H.; Ito, Y. *J. Chem. Soc., Chem. Commun.* **1996**, 2777. (b) Ohmura, T.; Taniguchi, H.; Sugimoto, M. *J. Am. Chem. Soc.* **2006**, *128*, 13682. (c) Ohmura, T.; Furukawa, H.; Sugimoto, M. *J. Am. Chem. Soc.* **2006**, *128*, 13366. (d) Ohmura, T.; Taniguchi, H.; Kondo, Y.; Sugimoto, M. *J. Am. Chem. Soc.* **2007**, *129*, 3518.
- (a) Sugimoto, M.; Yamamoto, A.; Murakami, M. *J. Am. Chem. Soc.* **2003**, *125*, 6358. (b) Sugimoto, M.; Yamamoto, A.; Murakami, M. *Angew. Chem., Int. Ed.* **2005**, *44*, 2380. (c) Sugimoto, M.; Yamamoto, A.; Sasaki, T.; Murakami, M. *Organometallics* **2006**, *25*, 2911. (d) Sugimoto, M.; Shirakura, M.; Yamamoto, A. *J. Am. Chem. Soc.* **2006**, *128*, 14438.
- Sugimoto, M.; Yamamoto, A.; Murakami, M. *J. Am. Chem. Soc.* **2005**, *127*, 15706.
- Use of Pd(acac)₂ instead of PdCp(allyl) with P^tBu₃ resulted in the formation of *trans*-**3aa** in 66% yield with the same stereoselectivity.
- Onozawa, S.-y.; Tanaka, M. *Organometallics* **2001**, *20*, 2956.
- For catalytic diboration and silaboration involving oxidative addition of B–I to palladium, see: Yang, F.-Y.; Cheng, C.-H. *J. Am. Chem. Soc.* **2001**, *123*, 761. Chang, K.-J.; Rayabarapu, D. K.; Yang, F.-Y.; Cheng, C.-H. *J. Am. Chem. Soc.* **2005**, *127*, 131.

JA711160H