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Palladium-Catalyzed, Stereoselective, Cyclizative Alkenylboration of Carbon−Carbon Double Bonds through Activation of a Boron−Chlorine Bond

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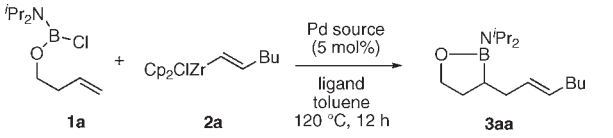
Supporting Information

ABSTRACT: Palladium-catalyzed alkenylboration of carbon−carbon double bonds has been achieved using the reaction of chloro(diisopropylamino)boryl ethers of homoallylic alcohols with alkenylzirconium reagents. The reaction may proceed through an initial oxidative addition of the B−Cl bond, intramolecular insertion of the C=C bond into the B−Pd bond, transmetalation from the alkenylzirconium reagent, and reductive elimination of the products. The cyclization proceeds with high diastereoselectivity for the formation of *cis*-3,5- or *trans*-3,4-disubstituted-1,2-oxaborolane products. Cross-coupling of the resultant products with aryl iodides proceeds with retention of configuration at the boron-bound secondary carbon atom.

Organoboronic acids and their ester derivatives have been utilized as a unique class of organometallic reagents in organic synthesis because they are isolable and purifiable yet reactive in a variety of transformation reactions.[1] In addition to conventional synthesis such as uncatalyzed hydroboration and transmetalation from other organometallic compounds, organoboronic acids have been efficiently prepared via transition-metal-catalyzed borylation reactions in recent years.[2] Such catalytic borylations even allow the introduction of additional functional groups into the organic framework, leading to the synthesis of highly elaborated organoboron compounds that are difficult to synthesize by other means.[3] Of particular interest are carboboration reactions, in which B−C and C−C bonds are created simultaneously.[4−7] Our recent study revealed that transmetalative carboboration, in which the catalytic cycle may be initiated with activation of the B−Cl bond, is widely applicable to the stereoselective synthesis of alkenylboronate derivatives.[6] It would be highly attractive if the strategy could be extended to carboboration of carbon−carbon double bonds, which would provide a new synthetic access to stereodefined alkylboronates. It should be noted that carbometalation of alkenes involving boron, silicon, and tin has had only limited success, including uncatalyzed carboboration with triallylborane[8] and catalytic carbostannation of norbornene and norbornadiene.[9] In this report, we describe our findings on palladium-catalyzed cyclizative carboboration of C=C bonds using organozirconium reagents as organic group donors.

Table 1. Palladium-Catalyzed Cyclizative Carboboration of 1a with Alkenylzirconium Reagent 2a[a]



1a 2a 3aa

entry	ligand	Pd source	Pd/P ratio	% yield (NMR)
1	none	PdCp(π-allyl)	−	trace
2	DPPE	PdCp(π-allyl)	1/2	27
3	DPPP	PdCp(π-allyl)	1/2	11
4	PPh_3	PdCp(π-allyl)	1/2	54
5	PCy_3	PdCp(π-allyl)	1/2	71
6	PCy_3	$Pd(dba)_2$	1/2	51
7	PCy_3	$Pd(OAc)_2$	1/2	60
8	$P(t\text{-}Bu)_3$	PdCp(π-allyl)	1/2	trace
9	PMe_3	PdCp(π-allyl)	1/1	58
10	PMe_3	PdCp(π-allyl)	1/2	86
11	PMe_3	PdCp(π-allyl)	1/3	74
12	PMe_3	PdCp(π-allyl)	1/4	65

[a] **1a** (0.20 mmol), **2a** (0.30 mmol), Pd complex (0.010 mmol), and triorganophosphine were heated in toluene (0.20 mL) at 120 °C (bath temperature) for 12 h.

We examined the reaction of chloroboranes **1** containing C=C bonds, on the basis of the success of alkyne carboborations using the same strategy.[5a,6a,6b] Chloroboryl ether **1a** derived from homoallylic alcohol was subjected to reaction with alkenylzirconium reagent **2a**, which was prepared in situ by the reaction of 1-hexyne with Cp_2ZrHCl (Table 1).[10] When the reactions were conducted at 120 °C in the presence of palladium/phosphine catalysts, cyclizative carboboration product **3aa** was formed in various yields via 5-exo cyclization. We observed a significant dependence of the reaction yield upon the phosphine ligand used in the reaction (Table 1). While only poor yields were obtained in the absence of the phosphine ligand or in the presence of bidentate ligands (entries 1−3), monodentate phosphines such as triphenylphosphine and tricyclohexylphosphine gave the

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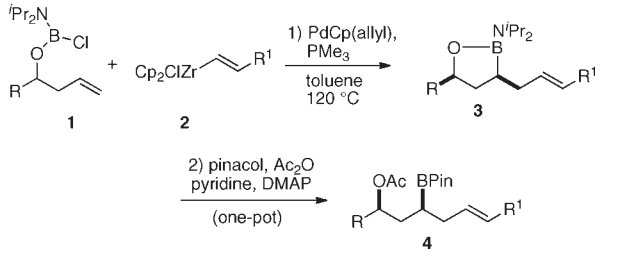
Table 2. Pd-Catalyzed Cyclizative Carboboration of the C═C Bond of 1 with Organozirconium Reagents 2[a]



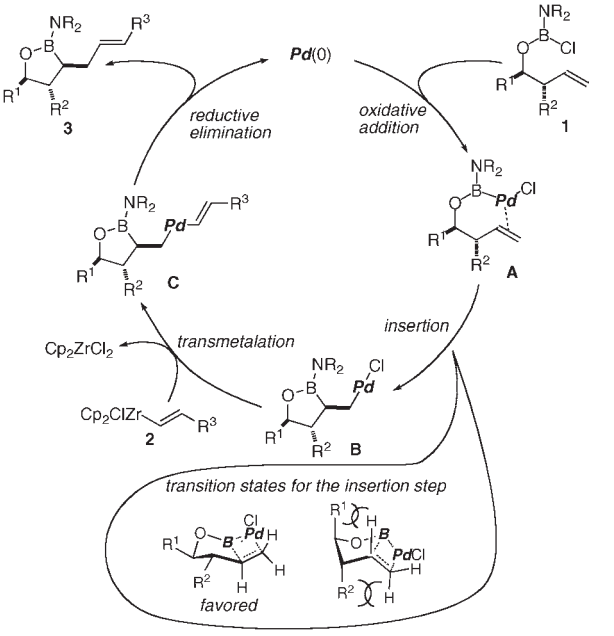
entry	1 (R)	2 (R^1)	product 4	% yield[b]
1	**1a** (H)	**2a** (Bu)	**aa**	72 (86)
2	**1b** (Me)	**2a**	**ba**	79 (86)
3	**1c** (*i*-Pr)	**2a**	**ca**	76 (86)
4	**1d** (Ph)	**2a**	**da**	81 (90)
5	**1b**	**2b** (Me_3Si)	**bb**	68 (79)
6	**1b**	**2c** (*t*-Bu)	**bc**	67 (76)
7	**1b**	**2d** (Ph)	**bd**	80 (88)
8[c]	**1b**	**2e** (H)	**be**	59 (69)

[a] Carboboration (the initial step): **1** (0.20 mmol), **2** (0.30 mmol), PdCp(π-allyl) (0.010 mmol), ligand (0.020 mmol), toluene (0.20 mL), 120 °C, 12 h. Conversion to **4** (the second step): pinacol (0.40 mmol), Ac_2O (0.51 mmol), pyridine (0.62 mmol), DMAP (0.027 mmol), 60 °C, 12 h. [b] Isolated yields of **4** (two steps); NMR yields of **3** are given in parentheses. [c] **2e** (0.40 mmol), 80 °C, 24 h.

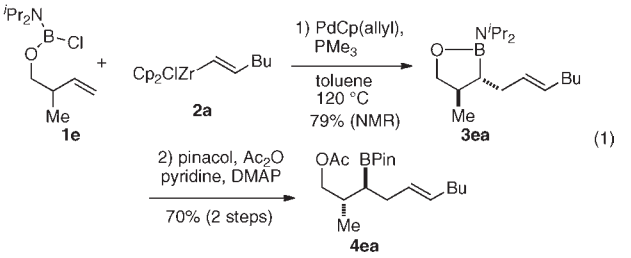
product in fair to good yields (entries 4 and 5). $Pd(dba)_2$ and $Pd(OAc)_2$ could also be used as the sources of palladium, although the reaction yields were slightly lower than that using a PdCp(π-allyl) complex (entries 6 and 7). No product formation was observed with tri-*tert*-butylphosphine as a ligand (entry 8). We finally found that trimethylphosphine served as an efficient ligand (entries 9−12). As for the Pd/ligand ratio, use of 2 equiv of PMe_3 gave the highest product yield (entry 10). The attempted use of some other organometallic compounds such as alkenylstannane and alkenylboronic acids did not afford the corresponding products under the same reaction conditions.

With PMe_3 as the ligand and PdCp(allyl) as the source of palladium (Pd:P = 1:2), reactions of chloroboryl ethers of various homoallylic alcohols were carried out (Table 2).[11] Chloroboryl ether **1a** afforded cyclization product **3aa** in 86% NMR yield, which was then converted into the hydrolytically stable ester **4aa** by treatment of the reaction mixture with acetic anhydride and pinacol (entry 1). Product **4aa** was isolated by column chromatography on silica gel in 72% yield from **1**. It should be remarked that reactions of **1b**−**d** bearing primary alkyl, secondary alkyl, and aryl groups α to the oxygen atoms all exclusively afforded the corresponding cis five-membered-ring products **3ba**−**da**, which were finally transformed to *syn*-**4ba**−**da** (entries 2−4). This high stereoselectivity held for the reactions with various alkenylzirconium reagents derived from TMS-, *t*-Bu-, and phenyl-substituted acetylenes (entries 5−7). Unsubstituted vinylzirconium successfully afforded the corresponding vinylboration product (entry 8). Substrate **1e** bearing an allylic substituent afforded anti product **4ea** derived from trans five-membered-ring product **3ea** (eq 1) with high stereoselectivity:

Scheme 1. Proposed Mechanism for the Palladium-catalyzed Alkenylboration.[a]



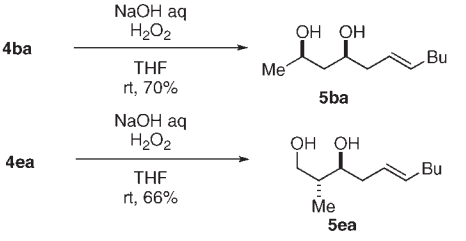
[a] ***Pd*** = PdL_n, ***B*** = BN^iPr_2



(1)

In sharp contrast to the carboboration of the C−C triple bond,[6b] arylzirconium and alkylzirconium reagents failed to take part in the reaction. Furthermore, substrates with homoallylic groups bearing 1,1-, (*E*)-1,2-, or (*Z*)-1,2-disubstituted C═C bonds failed to give the desired carboboration products. We should also note at this moment that substrates derived from allylic and bishomoallylic alcohols did not give the corresponding carboboration products.

The stereochemical assignments were made after the conversion of the products **4** into the corresponding diols **5** by hydrogen peroxide oxidation (eq 2):



(2)

The resultant diols were further converted into the corresponding acetonides, whose ^1H and ^{13}C NMR spectra clearly indicated the stereochemistry.[12]

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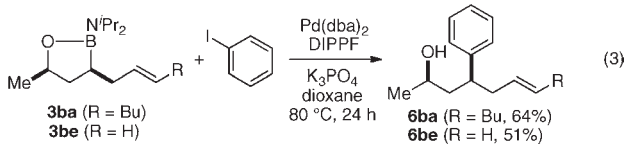
A possible mechanism for the cyclizative alkenylboration is depicted in Scheme 1. Following the initial oxidative addition of the boron−chlorine bond to the palladium(0) species generated from Cp(allyl)Pd, insertion of the carbon−carbon double bond in intermediate **A** into the B−Pd bond takes place. It should be noted that in the related cyclizative carboboration of carbon−carbon triple bonds, oxidative addition of the B−Cl bond to the Pd(0) species and subsequent facile insertion of the triple bond into B−Cl bond was elucidated by isolation of an intermediate corresponding to **B**.[6b,13] The chlorine atom is substituted by an alkenyl group in the transmetalation step, leading to the formation of **C**. Reductive elimination gives the alkenylboration product **3**. The observed stereoselectivities can be explained by chairlike transition states in the insertion step, in which the substituents preferentially occupy the equatorial positions. Similar stereoselectivities were observed in the palladium-catalyzed intramolecular bis-silylation of carbon−carbon double bonds.[14]

We attempted Suzuki−Miyaura cross-coupling of the carboboration products, which bear a boryl group at the stereogenic sp^3 carbon atom.[15] No coupling proceeded upon use of **4ba** with iodobenzene in the presence of a palladium catalyst bearing diisopropylphosphinoferrocene (DIPPF).[16] In contrast, the initial carboboration products **3ba** and **3be** afforded cross-coupling products **6**, in which the phenyl group was introduced with complete retention of configuration at the stereogenic carbon atom (eq 3):



(3)

Although the origin of the enhanced reactivity of **3** is not clear, intramolecular coordination of the oxygen atom may be the reason, on the basis of the recent discussion of the use of triolborate derivatives as highly reactive coupling reagents.[17] The stereochemical course of the Suzuki−Miyaura coupling at the stereogenic sp^3 carbon center has been discussed on the basis of the reactions of cyclic organoboranes, including cyclopropaneboronic acid derivatives,[18] a deuterated primary alkylborane derivative,[19] secondary benzylic organoboronates,[20] and α-aminobenzylboronic esters.[21] The present examples may be the first demonstration of retention of configuration with an acyclic, nonbenzylic *sec*-alkylboronate derivative.[22]

In summary, we have demonstrated the first catalytic carboboration of alkenes using alkenylzirconium reagents as donors of organic groups. The 5-exo cyclization mode and the high stereoselectivity are the key features of the carboboration reaction. Since the homoallylic alcohols used as starting materials are easily available in enantiomerically enriched forms, the present carboboration could be extended to the asymmetric synthesis of chiral molecules.[23] Cross-coupling of the product proceeds with retention of configuration at the stereogenic carbon atom carrying the boron atom. Modification of the reaction conditions for use of other organometallic reagents and internal alkenes as well as for more efficient cross-coupling reactions is now being undertaken in this laboratory.

■ ASSOCIATED CONTENT

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

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■ REFERENCES

(1) Hall, D. In *Boronic Acids: Preparation and Applications in Organic Synthesis and Medicine*; Hall, D., Ed.; Wiley-VCH: Weinheim, Germany, 2005; p 1.

(2) For reviews of catalyzed hydroborations, see: (a) Burgess, K.; Ohlmeyer, M. J. *Chem. Rev.* **1991**, *91*, 1179. (b) Beletskaya, I.; Pelter, A. *Tetrahedron* **1997**, *53*, 4957. (c) Crudden, C. M.; Edwards, D. *Eur. J. Org. Chem.* **2003**, 4695.

(3) For reviews of catalytic boron element additions, see: (a) Marder, T. B.; Norman, N. C. *Top. Catal.* **1998**, *5*, 63. (b) Ishiyama, T.; Miyaura, N. *J. Organomet. Chem.* **2000**, *611*, 392. (c) Ishiyama, T.; Miyaura, N. *Chem. Rec.* **2004**, *3*, 271. (d) Dembitsky, V. M.; Abu Ali, H.; Srebnik, M. *Adv. Organomet. Chem.* **2004**, *51*, 193. (e) Beletskaya, I.; Moberg, C. *Chem. Rev.* **2006**, *106*, 2320.(f) Suginome, M.; Matsuda, T.; Ohmura, T.; Seki, A.; Murakami, M. In *Comprehensive Organometallic Chemistry III*; Crabtree, R., Mingos, M., Ojima, I., Eds.; Elsevier: Oxford, 2007; Vol. 10, p 725. For recent accounts of silaborations, see: (g) Ohmura, T.; Suginome, M. *Bull. Chem. Soc. Jpn.* **2009**, *82*, 29.

(4) Acylboration of allenes was achieved by the Pd-catalyzed reaction of acyl halides with diboron. See: Yang, F.-Y.; Wu, M.-Y.; Cheng, C.-H. *J. Am. Chem. Soc.* **2000**, *122*, 7122.

(5) Cyanoboration: (a) Suginome, M.; Yamamoto, A.; Murakami, M. *J. Am. Chem. Soc.* **2003**, *125*, 6358. (b) Suginome, M.; Yamamoto, A.; Murakami, M. *Angew. Chem., Int. Ed.* **2005**, *44*, 2380. Alkynylboration: (c) Suginome, M.; Shirakura, M.; Yamamoto, A. *J. Am. Chem. Soc.* **2006**, *128*, 14438.

(6) For catalytic carboborations proceeding through activation of B−Cl bonds, see: (a) Suginome, M.; Yamamoto, A.; Murakami, M. *J. Am. Chem. Soc.* **2005**, *127*, 15706. (b) Daini, M.; Yamamoto, A.; Suginome, M. *J. Am. Chem. Soc.* **2008**, *130*, 2918. (c) Daini, M.; Suginome, M. *Chem. Commun.* **2008**, 5224.

(7) Suginome, M. *Chem. Rec.* **2010**, *10*, 348.

(8) For uncatalyzed allylboration of cyclopropenes, see: Bubnov, Y. N.; Nesmeyanova, O. A.; Rudashevakaya, T. Y.; Mikhailov, B. M.; Kazanaky, B. A. *Tetrahedron Lett.* **1971**, *12*, 2153.

(9) For Pd-catalyzed carbostannation of norbornene and norbornadiene, see: (a) Fugami, K.; Kawata, K.; Enokido, T.; Mishiba, Y.; Hagiwara, S.; Hirunuma, Y.; Koyama, D.; Kameyama, M.; Kosugi, M. *J. Organomet. Chem.* **2000**, *611*, 433. For a review, see:(b) Shirakawa, E. In *Tin Chemistry: Fundamentals, Frontiers, and Applications*; Davies, A., Gielen, M., Pannell, K. H., Tiekink, E. R. T., Eds.; Wiley: Chichester, U. K., 2008; p 640.

(10) Hart, D. W.; Blackburn, T. F.; Schwartz, J. *J. Am. Chem. Soc.* **1975**, *97*, 679.

(11) **1b**−**d** were prepared by reaction of the corresponding homoallylic alcohols with $Cl_2BN^iPr_2$ in the presence of Et_3N in THF (see the Supporting Information).

(12) Rychnovsky, S. D.; Skalitzky, D. J. *Tetrahedron Lett.* **1990**, *31*, 945.

(13) Onozawa, S.-y.; Tanaka, M. *Organometallics* **2001**, *20*, 2956.
(14) Murakami, M.; Suginome, M.; Fujimoto, K.; Nakamura, H.; Andersson, P. G.; Ito, Y. *J. Am. Chem. Soc.* **1993**, *115*, 6487.
(15) (a) Chemler, S. R.; Trauner, D.; Danishefsky, S. J. *Angew. Chem., Int. Ed.* **2001**, *40*, 4544. (b) Doucet, H. *Eur. J. Org. Chem.* **2008**, 2013.
(16) Lawrence, J. D.; Takahashi, M.; Bae, C.; Hartwig, J. F. *J. Am. Chem. Soc.* **2004**, *126*, 15334.
(17) Yamamoto, Y.; Takizawa, M.; Yu, X.-Q.; Miyaura, N. *Angew. Chem., Int. Ed.* **2008**, *47*, 928.
(18) For example, see: (a) Zhou, S.-M.; Deng, M.-Z.; Xia, L. J.; Tang, M.-H. *Angew. Chem., Int. Ed.* **1998**, *37*, 2845. For a review, see:Doucet, H. *Eur. J. Org. Chem.* **2008**, 2013.
(19) (a) Ridgway, B. H.; Woerpel, K. A. *J. Org. Chem.* **1998**, *63*, 458. (b) Matos, K.; Soderquist, J. A. *J. Org. Chem.* **1998**, *63*, 461.
(20) Imao, D.; Glasspoole, B. W.; Laberge, V. S.; Crudden, C. M. *J. Am. Chem. Soc.* **2009**, *131*, 5024.
(21) We recently reported highly stereospecific, invertive cross-coupling of α-aminobenzylboronates with aryl halides. See: Ohmura, T.; Awano, T.; Suginome, M. *J. Am. Chem. Soc.* **2010**, *132*, 13191.
(22) Stereoinversive cross-coupling of chiral alkyltrifluoroborate has been reported very recently. See: Sandrock, D. L.; Jean-Gérard, L.; Chen, C.-y.; Dreher, S. D.; Molander, G. A. *J. Am. Chem. Soc.* **2010**, *132*, 17108.
(23) Denmark, S. E.; Fu, J. *Chem. Rev.* **2003**, *103*, 2763.