Palladium-catalyzed carboboration of alkynes using chloroborane and organozirconium reagents†

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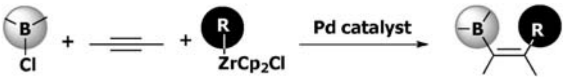
Three-component coupling of bis(dialkylamino)chloroborane, alkynes and organozirconium reagents proceeded in the presence of palladium catalysts, leading to the formation of stereo-defined alkenylborane derivatives *via cis*-carboboration of carbon–carbon triple bonds.

Organoboronic acid derivatives play important roles in synthetic organic chemistry.[1] Their high synthetic value primarily relies on the availability of a variety of organoboron-based transformation reactions, including Suzuki–Miyaura cross-coupling,[2] Rh-catalyzed conjugate addition,[3] the Petasis reaction,[4] *etc*. To take full advantage of the characteristic reactivity of the organoboronic acid derivatives, exploration of new methods for their synthesis is highly desirable.[5]

The transition metal-catalyzed borylation reaction is regarded as one of the most efficient and selective means for the synthesis of organoboronic acid derivatives. Besides the catalytic hydroboration,[6] additions of boron–element bonds across carbon–carbon multiple bonds, in which functional groups are selectively introduced in the close proximity of the boryl groups, have been developed.[7] Our effort has focused on the development of transition metal-catalyzed additions of element–boron bonds, such as a silicon–boron bond, to carbon–carbon unsaturated bonds.[8] These reactions provide new routes to highly functionalized organoboron compounds that are otherwise difficult to synthesize.

Our recent interest concerns catalytic carboborations, in which a B–C and a C–C bond are created simultaneously on unsaturated organic molecules. Uncatalyzed variants of the reaction[9] have been achieved only by using highly reactive triorganoboranes such as triallylborane[10] or unsaturated carbon compounds such as bisstannylethyne.[11] We have recently achieved a catalytic carboboration reaction through activation of the boron–carbon bond of cyanoboranes and alkynylboranes, which led to cyanoboration[12] and alkynylboration[13] of alkynes, respectively. We more recently established another mode of catalytic carboboration, in which the organic and the boryl groups are provided by organometallic reagents and chloroboranes, respectively.[14] In the previous reports, we used a two-component system in which the carbon–carbon triple bonds undergoing carboboration are tethered to a chloroborane moiety. Tethering the alkyne and the chloroborane moieties has significantly facilitated the reaction, although it narrows the substrate scope. Herein, we wish to report a three-component carboboration of alkynes, in which diaminochloroboranes and organozirconium reagents are used as the sources of the boron and organic substituents, respectively (Scheme 1).



Scheme 1 Palladium-catalyzed *cis*-carboboration of alkynes using chloroborane and organozirconium reagents.

As haloboranes employed in the optimization, we chose monohalobis(dialkylamino)borane derivatives **1a–e**, which showed much lower Lewis acidity than trihaloboranes, which have been used in uncatalyzed haloboration reactions.[15] In fact, the diaminohaloborane derivatives did not react at all with alkynes at 120 °C in toluene for 12 h either in the absence or presence of palladium catalysts. To pursue the optimum set of reagents, we initially carried out the reactions of 4-octyne and hexen-1-yldicyclopentadienylzirconium chloride with chloroboranes **1a–e** in the presence of palladium catalysts carrying several different phosphine ligands (Table 1). In the reactions of *N*,*N′*-dimethylethylenediamine-derived chloroborane **1a**, trimethylphosphine served as the best yielding ligand (entry 1). The reaction proceeded at 120 °C within 12 h, affording the alkenylboration product **4aaa** in 93% yield with high stereoselectivity for *cis*-addition. It is important to note that use of a smaller amount (3 equiv.) of 4-octyne resulted in a significant decrease in yield (entry 2). Use of more bulky phosphine ligands such as tricyclohexylphosphine and tri-*t*-butylphosphine gave lower yields of products (entries 3 and 4). Triphenylphosphine and bidentate phosphine ligands such as dppe and dppf afforded the corresponding product in moderate yields (entries 5–7). We then varied the diamine ligands of chloroboranes. By increasing the bulkiness of the alkyl groups on the nitrogen atoms of ethylenediamine, yields decreased significantly (entries 8 and 9). Bicyclic chloroboranes derived from 1,2-diaminocyclohexane and phenylenediamine afforded the alkenylboration products **4daa** and **4eaa** in moderate yields (entries 10 and 11). Although phenylboronic acid, phenyltrimethylsilane, and phenyltriisopropoxytitanium were tested in place of organozirconium reagent, no carboboration product was detectable in the reaction mixtures.

Under the optimized reaction conditions, other alkynes were reacted with hexen-1-ylzirconium reagent (Table 2). To

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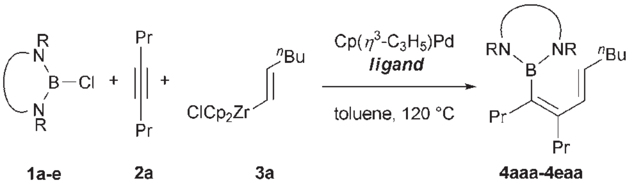
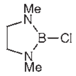
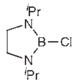
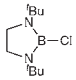
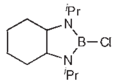
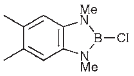
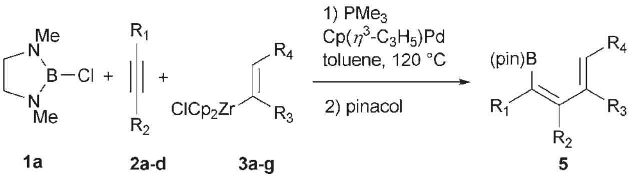
Table 1 Palladium-catalyzed intermolecular carboboration of 4-octyne with chloroboranes **1a–e** and hexenylzirconium **3a**[a]



Entry	Chloroborane **1**	Equiv. of **2a**	Ligand	% Yield[b] (product)
1	 (**1a**)	10	PMe_3	93 (**4aaa**)
2	**1a**	3	PMe_3	55 (**4aaa**)
3	**1a**	10	PCy_3	32 (**4aaa**)
4	**1a**	10	PBu^t_3	28 (**4aaa**)
5	**1a**	10	PPh_3	63 (**4aaa**)
6	**1a**	10	dppe	57 (**4aaa**)
7	**1a**	10	dppf	69 (**4aaa**)
8	 (**1b**)	10	PMe_3	78 (**4baa**)
9	 (**1c**)	10	PMe_3	16 (**4caa**)
10	 (**1d**)	10	PMe_3	40 (**4daa**)
11	 (**1e**)	10	PMe_3	55 (**4eaa**)

[a] A mixture of chloroborane (0.20 mmol), 4-octyne (amount indicated in the table), hexen-1-yldicyclopentadienylzirconium chloride (0.30 mmol), Cp(allyl)Pd (0.010 mmol), and a phosphine ligand (0.020 mmol for entries 1–5 and 8–11, 0.010 mmol for entries 6 and 7) in toluene was heated at 120 °C for 12 h under a nitrogen atmosphere. The alkenylzirconium reagent was prepared by the reaction of 1-hexyne with Cp_2ZrHCl and used after evaporation of the solvent without further purification. [b] NMR yield using an internal standard.

Table 2 Palladium-catalyzed intermolecular carboboration of alkynes **2a-d** with chloroborane **1a** and organozirconiums **3a–g**[a]



Entry	Alkyne (R^1, R^2)	Organozirconium (R^3, R^4)	% Yield[b] (product)
1	**2a** (Pr, Pr)	**3a** (H, Bu)	89 (93) (**5aaa**)
2	**2b** (H, Bu)	**3a**	75 (86) (**5aba**)
3	**2c** (H, *t*-Bu)	**3a**	51 (63) (**5aca**)
4	**2d** (Me, Ph)	**3a**	66 (77) (**5ada**)
5	**2b**	**3b** (H, Ph)	82 (91) (**5abb**)
6	**2b**	**3c** (H, *p*-$MeOC_6H_4$)	85 (92) (**5abc**)
7	**2b**	**3d** (H, *p*-$CF_3C_6H_4$)	76 (85) (**5abd**)
8	**2b**	**3e** (H, TMS)	68 (77) (**5abe**)
9	**2b**	**3f** (H, *t*-Bu)	64 (71) (**5abf**)
10	**2b**	**3g** (Pr, Pr)	73 (82) (**5abg**)

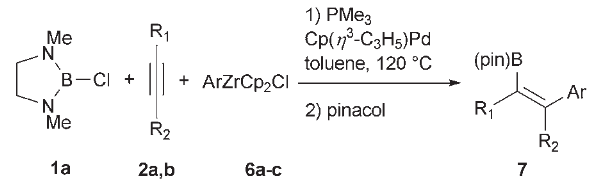
[a] A mixture of chloroborane **1a** (0.20 mmol), alkyne (2.0 mmol), alkenyldicyclopentadienylzirconium chloride (0.30 mmol), Cp(allyl)Pd (0.010 mmol), and PMe_3 (0.020 mmol) in toluene was heated at 120 °C for 12 h under a nitrogen atmosphere. After removal of the solvent *in vacuo*, pinacol (2.0 mmol) and TsOH (0.60 mmol) were added. [b] Isolated yield. NMR yield is in parentheses.

make the isolation easier, the diamine ligand on the boron atom was replaced with a pinacol ligand *in situ* after completion of the carboboration step. The adduct **5aaa** derived from 4-octyne and hexen-1-ylzirconium was isolated in 89% yield by silica gel column chromatography (entry 1).‡ Terminal alkynes (R^1 = H) such as 1-hexyne and *t*-butylacetylene afforded the corresponding carboboration products, in which the boron atom is attached to the terminal position, in high yields with high regio- and stereoselectivity (entries 2 and 3). 1-Phenylpropyne afforded the product in which the boryl group is attached selectively to the methyl-substituted carbon atom (entry 4). Various alkenylzirconium reagents could be used in the reactions with 1-hexyne. β-Styrylzirconium reagents with or without *p*-substituents (entries 5–7), β-silylethenyl (entry 8), β-*t*-butylvinyl (entry 9), and 4-octen-4-ylzirconium (entry 10) reagents afforded the corresponding dienylborane derivatives in good isolated yields.[16]

Further synthetic utility was demonstrated by an arylboration reaction using arylzirconium reagents **6** (Table 3). Phenylzirconium and its *p*-substituted derivatives afforded the corresponding arylboration products **7** in good yields with high stereoselectivity for *cis*-addition. Under the current reaction conditions, however, alkylzirconium compounds failed to take part in the carboboration reaction.

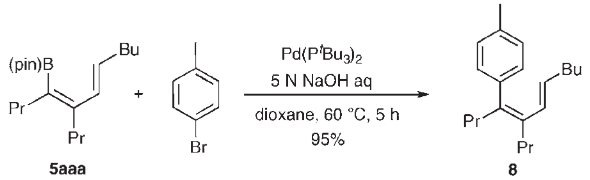
The carboboration product **5aaa** was successfully coupled with *p*-tolyl bromide under the Suzuki–Miyaura coupling

Table 3 Palladium-catalyzed intermolecular carboboration of alkynes **2a,b** with chloroborane **1a** and arylzirconiums **6a–c**[a]

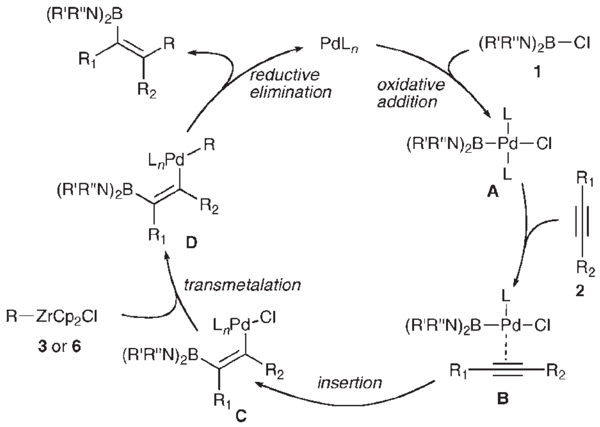


Entry	Alkyne (R^1, R^2)	Organozirconium (Ar)	% Yield[b] (product)
1	**2a** (Pr, Pr)	**6a** (Ph)	92 (97) (**7aaa**)
2	**2a**	**6b** (*p*-$MeOC_6H_4$)	89 (96) (**7aab**)
3	**2a**	**6c** (*p*-$CF_3C_6H_4$)	81 (89) (**7aac**)
4	**2b** (H, Bu)	**6a**	82 (90) (**7aba**)
5	**2b**	**6b**	82 (93) (**7abb**)
6	**2b**	**6c**	77 (87) (**7abc**)

[a] A mixture of chloroborane **1a** (0.20 mmol), alkyne (2.0 mmol), aryldicyclopentadienylzirconium chloride (0.30 mmol), Cp(allyl)Pd (0.010 mmol), and PMe_3 (0.020 mmol) in toluene was heated at 120 °C for 12 h under a nitrogen atmosphere. After removal of the solvent *in vacuo*, pinacol (2.0 mmol) and TsOH (0.60 mmol) were added. [b] Isolated yield. NMR yield is in parentheses.



Scheme 2 Suzuki–Miyaura coupling of **5aaa** with aryl halide.



Scheme 3 A possible mechanism for the palladium-catalyzed carboboration of alkynes using chloroborane and organozirconium reagents.

conditions using P(*t*-Bu)$_3$ as a ligand,[17] giving 1-aryl-1,3-diene **8** in high yield (Scheme 2).

The mechanism of the present carboboration reaction is postulated on the basis of the reported stoichiometric reaction of chloroboranes with palladium complexes (Scheme 3).[18,19] Oxidative addition of the B–Cl bond to palladium affords borylchlorobis(phosphine)palladium(II) intermediate **A**, which undergoes insertion of alkynes at the B–Pd bond, resulting in the formation of (β-borylalkenyl)chloropalladium(II) intermediate **C**. The alkenylpalladium intermediate **C** does not undergo reductive elimination, but reacts with organozirconium compounds, giving a diorganopalladium intermediate **D** from which the carboboration products are produced *via* reductive elimination.

In summary, we found a new palladium-catalyzed three-component coupling reaction of diaminochloroboranes, alkynes, and organozirconium reagents that afforded *cis*-carboboration products in good yields. Terminal alkynes and 1-phenylpropyne undergo the carboboration regioselectively, giving products in which the boryl group is attached to the less sterically hindered position. Further modifications to the reaction conditions and reagents are now being undertaken in our laboratory to expand the substrate scope and to reduce the amounts of alkynes needed.

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Notes and references

‡ General procedure for Pd-catalyzed intermolecular carboboration of alkynes with chloroboranes and organozirconiums: 1-Hexyne (25 mg, 0.30 mmol) was added to Cp$_2$ZrHCl (77 mg, 0.30 mmol) suspended in CH$_2$Cl$_2$ (0.3 mL) at room temperature. The mixture was stirred for 3 h at room temperature, and then the volatile material was removed *in vacuo*, leaving hexen-1-yldicyclopentadienylzirconium chloride **3a** as the residue. In another flask, Cp(π-allyl)Pd (0.010 mmol) and PMe$_3$ (0.020 mmol) were dissolved in toluene (0.05 mL). Chloroborane **1a** (0.20 mmol), 4-octyne **2a** (2.0 mmol), and a solution of **3a** (0.30 mmol) in toluene (0.05 mL) were added to the catalyst solution. The mixture was heated at 120 °C for 12 h under a nitrogen atmosphere. After removal of the solvent *in vacuo*, pinacol (2.0 mmol), THF (0.3 mL), and TsOH (0.60 mmol) were added, and the mixture was stirred for 3 h at room temperature. The mixture was passed through a pad of Florisil®, and the solvent was removed *in vacuo*. The residue was purified by silica gel column chromatography (hexane : EtOAc = 20 : 1), affording *cis*-alkenylboration product **5aaa** in 89% yield.

1 D. Hall, in *Boronic Acid*, ed. D. Hall, Wiley, Weinheim, 2005, p. 1.
2 (*a*) N. Miyaura, *Top. Curr. Chem.*, 2002, **219**, 11; (*b*) N. Miyaura and A. Suzuki, *Chem. Rev.*, 1995, **95**, 2457.
3 (*a*) M. Sakai, H. Hayashi and N. Miyaura, *Organometallics*, 1997, **16**, 4229. Reviews: ; (*b*) K. Fagnou and M. Lautens, *Chem. Rev.*, 2003, **103**, 169; (*c*) T. Hayashi and K. Yamasaki, *Chem. Rev.*, 2003, **103**, 2829.
4 (*a*) N. A. Petasis and I. Akritopoulou, *Tetrahedron Lett.*, 1993, **34**, 583; (*b*) N. A. Petasis and I. A. Zavialov, *J. Am. Chem. Soc.*, 1997, **119**, 445.
5 A. Suzuki and H. C. Brown, *Organic Synthesis via Boranes*, Aldrich, Milwaukee, WI, 2003, vol. 3.
6 Catalytic hydroborations: (*a*) H. Nöth and D. Männig, *Angew. Chem., Int. Ed. Engl.*, 1985, **24**, 878; For reviews, see: (*b*) K. Burgess and M. J. Ohlmeyer, *Chem. Rev.*, 1991, **91**, 1179; (*c*) I. Beletskaya and A. Pelter, *Tetrahedron*, 1997, **53**, 4957; (*d*) C. M. Crudden and D. Edwards, *Eur. J. Org. Chem.*, 2003, **24**, 4695.
7 Reviews on the catalytic boron–element addition: (*a*) T. B. Marder and N. C. Norman, *Top. Catal.*, 1998, **5**, 63; (*b*) T. Ishiyama and N. Miyaura, *J. Organomet. Chem.*, 2000, **611**, 392; (*c*) T. Ishiyama and N. Miyaura, *Chem. Rec.*, 2004, **3**, 271; (*d*) V. M. Dembitsky, H. Abu Ali and M. Srebnik, *Adv. Organomet. Chem.*, 2004, **51**, 193; (*e*) I. Beletskaya and C. Moberg, *Chem. Rev.*, 2006, **106**, 2320; (*f*) M. Suginome, T. Matsuda, T. Ohmura, A. Seki and M. Murakami, in *Comprehensive Organometallic Chemistry III*, ed. R. Crabtree, M. Mingos and I. Ojima, Elsevier, Oxford, 2007, vol. 10, p. 725.
8 (*a*) M. Suginome, H. Nakamura and Y. Ito, *Chem. Commun.*, 1996, 2777; (*b*) T. Ohmura, H. Taniguchi and M. Suginome, *J. Am. Chem. Soc.*, 2006, **128**, 13682; (*c*) T. Ohmura, H. Furukawa and M. Suginome, *J. Am. Chem. Soc.*, 2006, **128**, 13366; (*d*) T. Ohmura, H. Taniguchi, Y. Kondo and M. Suginome, *J. Am. Chem. Soc.*, 2007, **129**, 3518.
9 P. Knochel, in *Comprehensive Organic Synthesis*, ed. B. M. Trost, Pergamon Press, Oxford,1991, vol. 4, p. 865.
10 B. M. Mihailov and Y. N. Bubnov, *Tetrahedron Lett.*, 1971, 4597 and references therein.
11 B. Wrackmeyer and H. Nöth, *J. Organomet. Chem.*, 1976, **108**, C21.
12 (*a*) M. Suginome, A. Yamamoto and M. Murakami, *J. Am. Chem. Soc.*, 2003, **125**, 6358; (*b*) M. Suginome, A. Yamamoto and M. Murakami, *Angew. Chem., Int. Ed.*, 2005, **44**, 2380; (*c*) M. Suginome, A. Yamamoto, T. Sasaki and M. Murakami, *Organometallics*, 2006, **25**, 2911.
13 M. Suginome, M. Shirakura and A. Yamamoto, *J. Am. Chem. Soc.*, 2006, **128**, 14438.
14 (*a*) A. Yamamoto and M. Suginome, *J. Am. Chem. Soc.*, 2005, **127**, 15706; (*b*) M. Daini, A. Yamamoto and M. Suginome, *J. Am. Chem. Soc.*, 2008, **130**, 2918.
15 S. Hara, T. Kato, H. Shimizu and A. Suzuki, *Tetrahedron Lett.*, 1985, **26**, 1065.
16 For selected synthetic applications of dienylboranes, see: (*a*) P.-Y. Renard, Y. Six and J.-Y. Lallemand, *Tetrahedron Lett.*, 1997, **38**, 6589; (*b*) X. Gao and D. Hall, *Tetrahedron Lett.*, 2003, **44**, 2231; (*c*) G. Hilt, W. Hess and K. Harms, *Org. Lett.*, 2006, **8**, 3287; (*d*) M. Tortosa, N. A. Yakelis and W. R. Roush, *J. Am. Chem. Soc.*, 2008, **130**, 2722.
17 A. F. Littke, C. Dai and G. C. Fu, *J. Am. Chem. Soc.*, 2000, **122**, 4020.
18 S. Onozawa and M. Tanaka, *Organometallics*, 2001, **20**, 2956.
19 A catalytic reaction that involves oxidative addition of *in situ* generated B–I to palladium was reported. See: F.-Y. Yang and C.-H. Cheng, *J. Am. Chem. Soc.*, 2001, **123**, 761; K.-J. Chang, D. K. Rayabarapu, F.-Y. Yang and C.-H. Cheng, *J. Am. Chem. Soc.*, 2005, **127**, 126.