A Synthesis of (*E*)-(1-Organo-1-alkenyl)boronates by the Palladium-Catalyzed Cross-Coupling Reaction of (*E*)-1,2-Bis(boryl)-1-alkenes with Organic Halides: A Formal Carboboration of Alkynes *via* the Diboration-Coupling Sequence

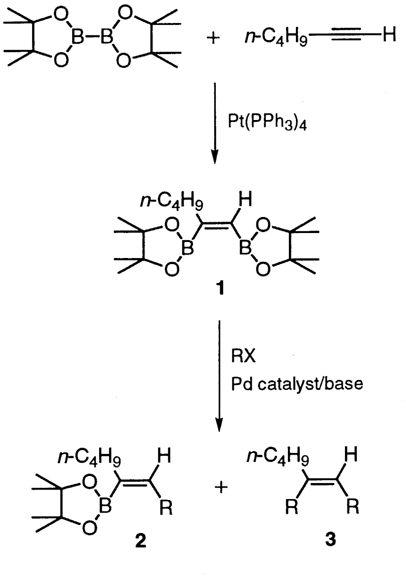
Tatsuo Ishiyama, Masafumi Yamamoto, and Norio Miyaura*
Division of Molecular Chemistry, Faculty of Engineering, Hokkaido University, Sapporo 060

(Received September 9, 1996)

(*E*)-1,2-Bis(boryl)-1-hexene, prepared by the platinum-catalyzed diboration of 1-hexyne with bis(pinacolato)diboron, regioselectively cross-coupled with aryl, 1-alkenyl, benzyl, and allyl halides in the presence of a palladium catalyst and a base to provide the corresponding pinacol esters of (*E*)-(1-butyl-1-alkenyl)boronic acid in good yields.

Numerous reactions reported in organoboron chemistry have shown 1-alkenylboron compounds to be a valuable reagent providing a route to reliable methods for the synthesis of stereodefined alkenes.[1] The regio- and stereoselective synthesis of 1-alkenylboron compounds has been conveniently achieved by the addition of the B-H,[2] B-halogen,[3] or B-S bond to alkynes;[4] however, there has been only limited use of the addition of the B-C bond (carboboration) to alkynes.[5] Recently, we reported a convenient route to *cis*-bis(boryl)alkenes *via* the platinum(0)-catalyzed diboration of internal and terminal alkynes with bis(pinacolato)diboron (Scheme 1).[6] Although the palladium-catalyzed cross-coupling reaction of 1,2-bis(boryl)-1-alkenes (**1**) with two equivs of iodoarene gave bis(aryl)alkenes in high yields,[6] monoalkylation of one of two C-B bonds may allow a regio- and stereoselective preparation of (*E*)-(1-organo-1-alkenyl)boronates, for example **2**. We have found the coupling with aryl, 1-alkenyl, benzyl, or allyl halides regioselectively occurs, indeed, at the terminal C-B bond in preference to the internal C-B bond, thus allowing a formal *cis*-carboboration of terminal alkynes *via* the diboration-coupling sequence.[7] Bis(boryl)alkenes derived from internal alkynes also exhibit some regioselectivity on the palladium-catalyzed cross-coupling, as was recently demonstrated by Armstrong and co-workers for the synthesis of tetrasubstituted alkenes.[8]

The representative results are summarized in Table 1. The steric, and probably also the electronic environment around the two boryl groups can differentiate the rate of transmetalation to the palladium(II) halide intermediates in the catalytic cycle. Indeed, the reaction resulted in perfect regioselection. Aryl halides (Runs 1-3) participated in the coupling with high regio- and stereoselectivity in the presence of $PdCl_2$(dppf) (dppf stands for 1,1'-bis(diphenylphosphino)ferrocene) and K_2CO_3 in DMF.[9] The GC analyses revealed the formation of **2** together with small amounts of **3** which are separable by chromatography over silica gel.[10] The ^1H NMR spectrum of **2** (R=4-MeC_6H_4) exhibited one singlet at 6.83 ppm (vinyl C-H) and large NOE enhancement (6.9%) between the vinyl proton and allylic protons at 2.28 ppm, thus suggesting that the coupling proceeded with complete retention of the configuration of the double bond. The selective coupling at the terminal carbon was confirmed by the oxidation[11] of the reaction mixture with trimethylamine *N*-oxide giving 1-(4-methylphenyl)-2-hexanone as the sole product.



Scheme 1.

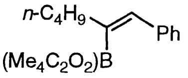
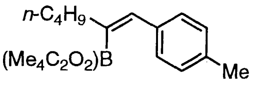
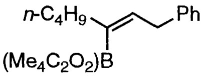
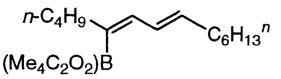
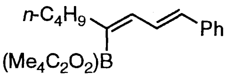
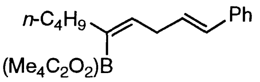
The ratio of **2** and **3** was considerably affected by the bases. The best yield (79%) and the best selectivity (**2**/**3** = 79/7) were obtained by the use of K_2CO_3 (Run 3). Strong bases such as KOH and K_3PO_4 accelerated the second coupling giving **3** (15-25%) while the reaction was very slow with KOAc (7%). As for the catalyst, $PdCl_2$(dppf) gave the best results. $PdCl_2(PPh_3)_2$ also exhibited high catalytic activity (70%), but the product was unexpectedly contaminated with ca. 10% of **2** (R=Ph) resulting from the coupling with a phenyl group on triphenylphosphine.[12]

Under similar reaction conditions used for the aryl halides, benzyl chloride afforded an 82% of the coupling product. Benzyl chlorides gave better results than the corresponding bromides (For example, runs 4 and 5).

The cross-coupling reaction of 1-halo-1-alkenes with **1** can provide 1,3-alkadienylboronates which serve as a valuable reagent for the synthesis of conjugated polyenes through the cross-coupling. Although the above conditions optimized by the reaction with aryl halides did not give satisfactory results for 1-iodo-1-octene and β-bromostyrene, good yields were readily obtained under the conditions which have been used for the vinyl-vinyl coupling (KOH and $Pd(PPh_3)_4$) (Runs 6 and 7).[13] The stereochemistry of both double bonds were retained completely during the coupling (>99%).

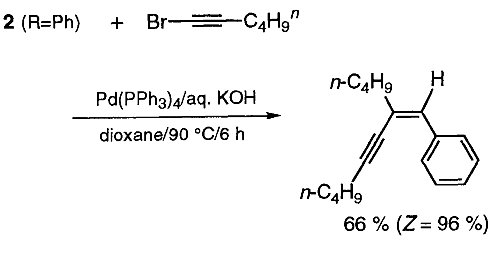
Finally, the cross-coupling of **1** with allyl electrophiles afforded 1,4-alkadienylboronates. For example, the reaction with cinnamyl halides or acetate provided the corresponding coupling product in moderate yields when using $PdCl_2$(dppf) and K_3PO_4 in dioxane (Runs 8-10).

Table 1. Synthesis of **2** (Scheme 1)[a]

Run	RX	Catalyst/Base/Solvent/Temp	Product (**2**)	Yield/%[b]
1	BrPh	$PdCl_2$(dppf)/K_2CO_3/DMF/80 °C		79[c]
2	IPh	$PdCl_2$(dppf)/K_2CO_3/DMF/80 °C		65[d]
3	4-BrC_6H_4Me	$PdCl_2$(dppf)/K_2CO_3/DMF/80 °C		(79)[e]
4	$ClCH_2Ph$	$PdCl_2$(dppf)/K_2CO_3/DMF/80 °C		82
5	$BrCH_2Ph$	$PdCl_2$(dppf)/K_2CO_3/DMF/80 °C		32
6	(*E*)-$ICH=CHC_6H_{13}{}^n$	$Pd(PPh_3)_4$/aq. KOH/DME/70 °C		63[f]
7	(*E*)-$BrCH=CHPh$	$Pd(PPh_3)_4$/aq. KOH/DME/70 °C		72[f]
8	(*E*)-$ClCH_2CH=CHPh$	$PdCl_2$(dppf)/K_3PO_4/dioxane/80 °C		(67)
9	(*E*)-$BrCH_2CH=CHPh$	$PdCl_2$(dppf)/K_3PO_4/dioxane/80 °C		(56)
10	(*E*)-$AcOCH_2CH=CHPh$	$PdCl_2$(dppf)/K_3PO_4/dioxane/80 °C		(62)

[a] The reactions were carried out for 16 h in the presence of **1** (1.1 mmol), RX (1.0 mmol), palladium catalyst (0.03 mmol) and base (3 mmol).
[b] Isolated yields by chromatography and GC yields are in the parentheses. [c] 6% of **3**. [d] 5% of **3**. [e] 7% of **3**. [f] 1-2% of **3**.

The ready availability of various **2** from terminal alkynes and organic halides may now offer a simple route to trisubstituted alkenes. For example, the reaction of **2** (R=Ph) (1.1 mmol) with 1-bromo-1-hexyne (1.0 mmol) at 90 °C for 6 h in the presence of $Pd(PPh_3)_4$ (0.03 mmol) and aqueous KOH (3 mmol) in dioxane (6 ml) afforded 66% yield of (*Z*)-2-butyl-1-phenyl-1-octen-3-yne with 96% isomeric purity (Scheme 2). The coupling with other organic halides may also provide access to a variety of trisubstituted alkenes through the diboration-coupling sequence.



Scheme 2.

References and Notes

1 D. S. Matteson, Stereodirected Synthesis with Organoboranes, Springer, New York (1995).
2 H. C. Brown, Organic Syntheses *via* Boranes, John Wiley & Sons, New York (1975).
3 A. Suzuki, *Pure & Appl. Chem.*, **58**, 629 (1986).
4 T. Ishiyama, K.-i. Nishijima, N. Miyaura, and A. Suzuki, *J. Am. Chem. Soc.*, **115**, 7219 (1993).
5 B. M. Mikhailov, *Pure & Appl. Chem.*, **39**, 505 (1974).
6 T. Ishiyama, N. Matsuda, N. Miyaura, and A. Suzuki, *J. Am. Chem. Soc.*, **115**, 11018 (1993).
T. Ishiyama, N. Matsuda, M. Murata, F. Ozawa, A. Suzuki, and N. Miyaura, *Organometallics*, **15**, 713 (1996).
7 Part of this study was presented at Symposium: Transition Metal-Catalyzed Cross Coupling Reactions. Mechanism, Structure, and Synthesis on the 209th ACS meeting in Anaheim, April, 1995.
8 S. D. Brown and R. W. Armstrong, *J. Am. Chem. Soc.*, **118**, 6331 (1996).
9 A representative procedure: To a mixture of PdCl2(dppf) (0.03 mmol) and K2CO3 (3 mmol) in DMF (6 ml) were successively added **1** (1.1 mmol) and 4-bromotoluene (1.0 mmol), and the resulting mixture was then stirred at 80 °C for 16 h. Chromatography over silica gel gave **2** (R= 4-MeC6H4): ^{1}H NMR (400 MHz, CDCl3): δ 0.91 (t, 3H, *J* = 7.3 Hz), 1.26 (s, 12H), 1.3-1.4 (m, 2H), 1.4-1.5 (m, 2H), 2.28 (t, 2H, *J* = 7.6 Hz), 2.31 (s, 3H), 6.83 (s, 1H), 7.05 (d, 2H, *J* = 7.8 Hz), 7.23 (d, 2H, *J* = 7.8 Hz).
10 Similar regioselective cross-coupling at the terminal C-B bond was recently reported; G. Desurmont, R. Klein, S. Uhlenbrock, E. Laloë , L. Deloux, D. M. Giolando, Y. W. Kim, S. Pereira, and M. Srebnik, *Organometallics*, **15**, 3323 (1996).
11 R. W. Hoffmann, K. Ditrich, and S. Fröch, *Liebigs Ann. Chem.*, **1987**, 977.
12 B. E. Segelstein, T. W. Butler, and B. L. Chenard, *J. Org. Chem.*, **60**, 12 (1995).
13 N. Miyaura and A. Suzuki, *Chem. Rev.*, **95**, 2457 (1995).