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PALLADIUM-CATALYZED CROSS-COUPLING REACTIONS OF B-ALKYL-9-BBN OR TRIALKYLBORANES WITH ARYL AND 1-ALKENYL HALIDES

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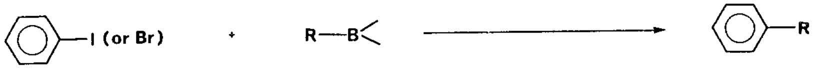
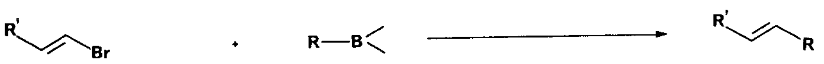
Abstract: The reactions of trialkylboranes or B-alkyl-9-BBN with aryl and 1-alkenyl halides take place readily in the presence of $PdCl_2(dppf)$ and sodium hydroxide or methoxide to afford alkylated arenes and alkenes in excellent yields.

The cross-coupling reaction of organic electrophiles with organometallic reagents in the presence of transition metals is a very mild and most straightforward method of forming carbon-carbon bonds.[1] Although organometallic reagents with methyl, 1-alkenyl, 1-alkynyl, and aryl groups have been successfully used for cross-coupling, those with alkyl groups having β-hydrogen have been severely limited due to the side reactions caused by β-hydride elimination, for example, from alkyl-Pd species generated in the catalytic cycle. Recently, Hayashi and coworkers found that such difficulties are readily overcome by Pd-catalyst having bis(diphenylphosphino)ferrocene ligand, $PdCl_2(dppf)$, and organomagnesiums and zincs containing primary- and secondary-alkyl groups become applicable for the coupling reactions.[2] Here, we wish to report the alkylation of 1-alkenyl and aryl halides with organoboranes such as trialkylboranes and B-alkyl-9-borabicyclo[3.3.1]nonanes (B-R-9-BBN) in the presence of $PdCl_2(dppf)$ and bases (eqs. 1 and 2).



(1)



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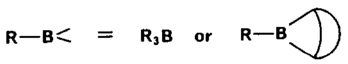


The optimum conditions for carrying out the reaction of eqs. 1 and 2 were studied by using phenyl or 2-phenylethenyl halides and B-octyl-9-BBN or trioctylborane in the presence of $PdCl_2(dppf)$ (3 mol%) and bases. The results are summarized in Table 1. It has been found that the coupling products can be obtained in high yields in the presence of NaOH or NaOMe without production of any noticeable quantities of by-products, and the reactions were failed in the absence of base or in the presence of weak bases such as sodium acetate.
It should be noted that a high yield of octylbenzene can be obtained when powdered NaOMe is

used, whereas 2M-NaOMe in MeOH which is employed in most cases of the cross-coupling reaction of 1-alkenylboronates,[3] gives only 18% yield (entries 1 and 2). Zn(acac)$_2$ successfully utilized for the carbonylative cross-coupling of organoboranes[4] also accelerates the reaction in the presence of HMPA and gives a moderate yield of octylbenzene (entry 5).

As an alkylborane, B-alkyl-9-BBN is rather favorable than trialkylborane, because only one of the three alkyl groups in the latter participates in the coupling reaction (entries 6 and 7) and the hydroboration of alkenes with 9-BBN is more regio- and stereoselective than borane.[6]

In Table 2, the representative results of the reaction of a variety of aryl and 1-alkenyl halides with B-alkyl-9-BBN are summarized. From these results, it is apparent that B-primary-alkyl-9-BBN with β-branched alkyl groups react with aryl iodides, bromides, and 1-alkenyl bromides[5] to give corresponding poducts in excellent yields. The retention of configuration of the starting (E)- and (Z)-1-alkenyl bromides in the coupling was observed (entries 9 and 10). On the other hand, no coupling was observed in the reaction of iodobenzene with sec-butylboranes (entrie 3 and 4).

Table 1. The Reactions of Octylboranes with Phenyl and 2-Phenyletheny halides[a]

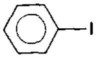
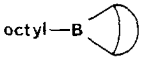
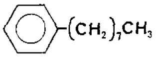
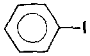
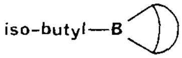
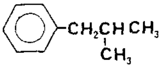
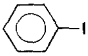
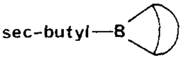
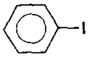
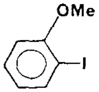
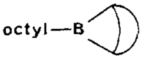
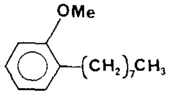
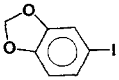
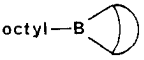
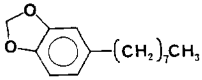
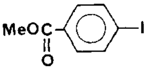
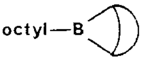
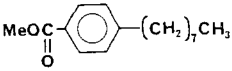
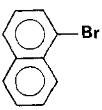
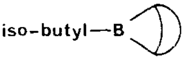
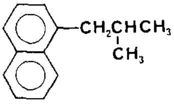
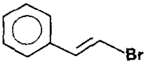
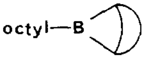
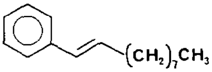
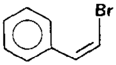
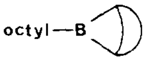
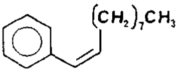
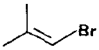
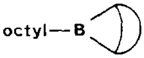
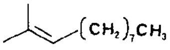
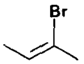
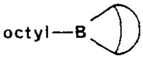
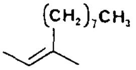
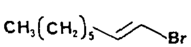
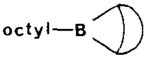
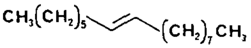
Entry	Halide	Borane	Base (equiv.)	Yield (%)[b]
1	PhI	B-Octyl-9-BBN	NaOMe (1.5)[c]	98
2	PhI	B-Octyl-9-BBN	2M-NaOMe in MeOH (1.5)	18
3	PhI	B-Octyl-9-BBN	3M-NaOH in H_2O (3)	99
4	PhI	B-Octyl-9-BBN	NaOAc (3)	8
5	PhI	B-Octyl-9-BBN	Zn(acac)$_2$[d]	51
6	PhI	(Octyl)$_3$B	NaOMe (1.5)[c]	98
7	PhI	(Octyl)$_3$B[e]	NaOMe (1.5)[c]	34
8	PhBr	B-Octyl-9-BBN	NaOMe (1.5)[c]	96
9	(E)-PhCH=CHBr	B-Octyl-9-BBN	NaOMe (1.5)[c]	61
10	(E)-PhCH=CHBr	B-Octyl-9-BBN	3M-NaOH in H_2O (3)	85
11	(E)-PhCH=CHBr	(Octyl)$_3$B	3M-NaOH in H_2O (3)	78

[a] All reactions were carried out at refluxing temperature of THF containing 3 mol% of PdCl$_2$(dppf) and bases for 16 h, using 10% excess of octylboranes, unless otherwise noted. [b] Glpc yields based on organic halides. [c] Powdered NaOMe was suspended in THF. [d] The reaction was conducted in THF-HMPA(4:1). [e] In this case, 0.33 equiv of borane was used.

A typical procedure is as follows. A dry 25ml-flask was charged with PdCl$_2$(dppf)[2] (22 mg, 0.03 mmol) and flushed with nitrogen. THF (5 ml), aqueous 3M-NaOH (1 ml), 1-bromonaphthalene (1.0 mmol) and B-iso-butyl-9-BBN[6] (1.1 ml of 1M solution, 1.1 mmol) in THF were added. After refluxing for 16 h, the reaction mixture was cooled down to room temperature and diluted with benzene (20 ml). The organic layer was separated, washed with brine and dried over MgSO$_4$. Column chromatography on silica gel with hexane gave 1-iso-butylnaphthalene in 88% yield.

The usefulness of the present method is demonstrated by the synthesis of an alkylbenzene with functional groups (**3**) and the extention of a side chain in a steroid (**4**) (eqs. 3 and 4). The hydroboration is tolerant of several functional groups such as cyano and ester groups and the organoboranes thus obtained also quite inert toward many functional groups. Thus, the reaction of organoborane (**1**) obtained via hydroboration of methyl 10-undecenoate

Table 2. The Cross-Coupling Reaction of Organoboranes with Organic Halides.[a]

Entry	halide	borane	base	Product	Yield(%)[b]
1			NaOMe (1.5)		98
2			NaOMe (1.5)		95
3			NaOMe (1.5)		0
4		(sec-butyl)$_3$B	NaOMe (1.5)		0
5			3M-NaOH (3)		90
6			3M-NaOH (3)		(78)
7			NaOMe (1.5)		82[c]
8			3M-NaOH (3)		(88)
9			3M-NaOH (3)		85[d]
10			3M-NaOH (3)		90[e]
11			3M-NaOH (3)		94
12			3M-NaOH (3)		98
13			NaOMe (1.5)		(75)

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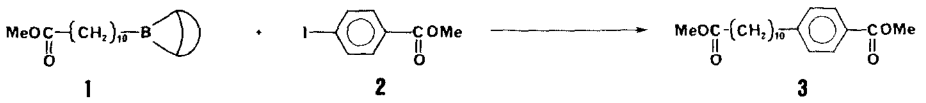
[a] All reactions were carried out under coditions described in the text, unless otherwise noted. [b] Glpc yields based on organic halides and isolated yields are in parentheses. [c] The reaction was conducted for 4 h at refluxing temperature of THF, and then the reaction mixture was treated with acetic anhydride (5 equiv.) for 30 min to prevent the ester group from hydrolysis. [d] β-Bromostyrene (E/Z=91/9) gave the decenylbenzene (E/Z=91/9). [e] The product has Z configuration (Z>97%).

with 9-BBN in THF, with methyl 4-iodobenzoate under the conditions shown in entry 7 in Table 2 gave **3** in 72% yield (eq. 3). The hydroboration of 20(21)-methylene steroid[7,8] with 9-BBN in THF, followed by cross-coupling with 2-methyl-1-propenyl bromide gave **6** in 77% yield (eq. 4).[9]



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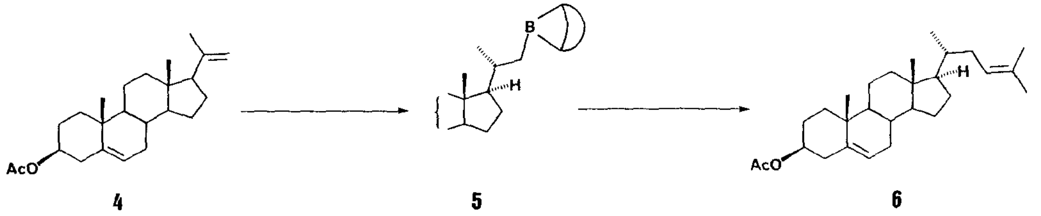

(4)

In a course of our study on the palladium-catalyzed reactions of organoboranes, we reported the reactions of 1-alkenylboronates[3] and phenylboronic acid[10] with organic halides. The present reaction can make it possible for saturated alkyl groups on boron to be used as organic groups of cross-coupling reactions, and extend the usefulness of such reactions in organic synthesis.

Reference and Notes

1 For reviews, see: (a) M. Kumada, Pure Appl. Chem., **52**, 669 (1980). (b) E. Negishi, Acc. Chem. Res., **15**, 340 (1982). (c) R. F. Heck, "Palladium Reagents in Organic Syntheses," Academic Press, London, 1985.

2 T. Hayashi, M. Konishi, Y. Kobori, M. Kumada, T. Higuchi and K. Hirotsu, J. Am. Chem. Soc., **106**, 158 (1984) and references cited therein.

3 (a) A. Suzuki and R. S. Dhillon, Topics in Current Chem., **130**, 25 (1985). (b) N. Miyaura, K. Yamada, H. Suginome and A. Suzuki, J. Am. Chem. Soc., **107**, 972 (1985). (c) M. Satoh, N. Miyaura and A. Suzuki, Chem. Lett., **1986**, 1329. (d) N. Miyaura, M. Satoh and A. Suzuki, Tetrahedron Lett., **27**, 3745 (1986).

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5 Extremely lower yields were observed with 1-alkenyl iodides.

6 9-BBN used is a commercial product from Aldrich Chem. Co. and for hydroboration of alkenes with 9-BBN, see: H. C. Brown, "Organic Syntheses via Boranes", John Wiley & Sons, N.Y., 1975.

7 Prepared from pregnelone acetate by the Sondheimer's method in 65% yield : F. Sondheimer and R. Mechoulam, J. Am. Chem. Soc., **80**, 3087 (1958).

8 Hydroboration gives predominantly 20R steroid (**5**) : J. Bottin and M. Fetizon, J. Chem. Soc., Chem. Commun., **1971**, 1087 ; M. M. Midland and Y. C. Kwon, J. Org. Chem., **46**, 229 (1981).

9 To a solution of **4** (0.56 mmol) in THF (4 ml) was added a solution of 9-BBN (0.59 mmol)[6] in THF at 0 °C, then stirred for 6 h at room temperature. $PdCl_2(dppf)$[2] (0.015 mmol), aqueous 3M-NaOH (0.6 ml) and 2-methyl-1-propenyl bromide (0.62 mmol) were added and refluxed for 16 h. After the usual work up, the crude product was reacetylated with acetic anhydride-pyridine, followed by purification by chromatography on silica gel. Recrystallization from MeOH gave 77% yield of **6**, mp. 127 °C.

10 N. Miyaura, T. Yanagi and A. Suzuki, Synth. Commun., **11**, 513 (1981)

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