CHEMISTRY LETTERS, pp. 1405-1408, 1989.

Cross-Coupling Reaction of Alkyl- or Arylboronic Acid Esters with Organic Halides Induced by Thallium(I) Salts and Palladium-Catalyst

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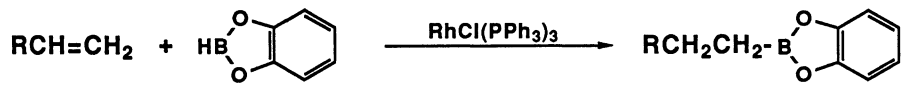
The cross-coupling reaction of alkylboronic acid esters with 1-alkenyl- or aryl halides is successfully catalyzed by $PdCl_2(dppf)$ or $Pd(PPh_3)_4$ in the presence of thallium(I) hydroxide or carbonate to give the corresponding alkenes or arenes in good yields. The coupling reaction of arylboronic acid esters with aryl halides under similar conditions to provide biaryls is also described.

In our recent papers,[1] we reported a synthesis of functionalized alkenes, arenes, or cycloalkenes by the palladium-catalyzed cross-coupling reaction between B-alkyl-9-BBN derivatives and 1-halo-1-alkenes or haloarenes. The major advantage of this coupling in synthesis is its ready availavility of a variety of functionalized B-alkyl-9-BBN via hydroboration of corresponding alkenes, and the coupling reaction takes place readily to give stereochemically pure alkenes and arenes under mild conditions. Although the reaction of B-alkyl-9-BBN proceeds readily, the use of boronic acid esters as coupling partners have been desired since many boronic esters have been prepared as useful reagents for organic synthesis. For example, the catalytic hydroboration[2] of alkenes with catecholborane proceeds under extremly mild conditions to give 2-alkyl-1,3,2-benzodioxaboroles (Eq. 1).



(1)

$$RCH{=}CH_2 + HBBr_2{\cdot}SMe_2 \xrightarrow{} \xrightarrow{R'OH} RCH_2CH_2B(OR')_2 \qquad (2)$$

$$RCH_2CH_2B< + ArX \xrightarrow[base]{Pd\text{-}catalyst} RCH_2CH_2Ar \qquad (3)$$

$$RCH_2CH_2B< + XCH{=}CHR' \xrightarrow[base]{Pd\text{-}catalyst} RCH_2CH_2CH{=}CHR' \qquad (4)$$

Hydroboration[3] of alkenes with dibromoborane-methylsulfide, followed by the alcoholysis provides a convenient procedure for boronic esters (Eq. 2). A variety of boronic esters including those with optically active alkyls were synthesized by Mattson's[4a,b] and Brown's[4c,d] groups. By utilizing tranformations via the cross-

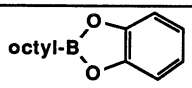
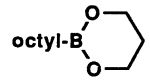
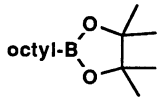
coupling, these esters can be converted into a multitude of products.

As reported previously, the base is essential for the success of the coupling reactions of 1-alkenylboronates[5] and alkylboranes.[1] However, the coupling reaction of boronic esters does not proceed smoothly in the presence of usual base such as sodium carbonate, hydroxide, and methoxide. This is probably due to the difficulty in transmetallation[1] between boronic ester and RPdX species because of the very low nucleophilicity of organic group on the boron. We have found that thallium(I) salts, successfully utilized by Kishi[6] for the coupling of 1-alkenylboronic acids, effectively promote the reaction of alkylboronic esters with 1-alkenyl or aryl halides in the presence of palladium-catalyst under very mild conditions.

In order to find the optimum conditions in the reaction of Eq. 3, we examined the reaction of iodobenzene with three types of esters of octylboronic acid. The results are summarized in Table 1. It is shown that the high yields of octylbenzene can be obtained in the reaction with catechol and trimethylene esters (I and II) in the presence of aqueous TlOH or powdered Tl_2CO_3 suspended in THF (entries 2-7). We also examined other metal reagents such as AgO, AgOAc, Tl(acac), TlOAc, and TlOEt, but TlOH and Tl_2CO_3 were proved to be effective bases. The use of pinacol ester resulted in an extremely slow reaction (entries 8 and 9), and no reaction occurred when the acid (IV) was used instead of esters (entry 10). The results indicate that the ester groups of the boronic acid give the promoting effect on the rate of transmetallation even under such aqueous conditions.

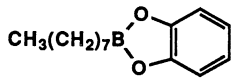
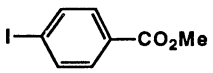
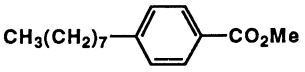
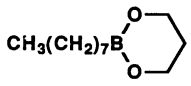
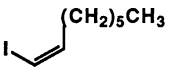
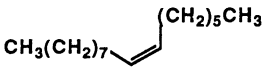
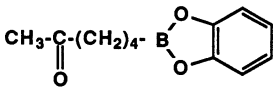
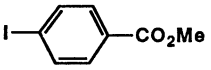
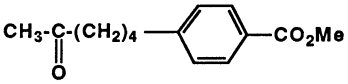
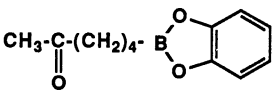
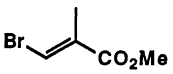
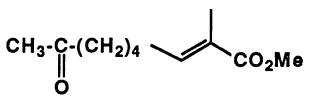
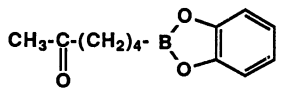
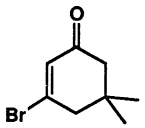
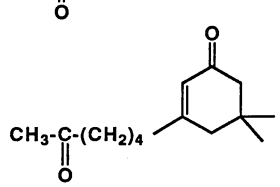
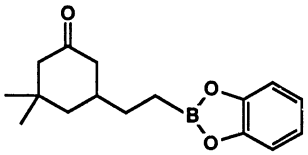
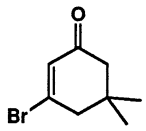
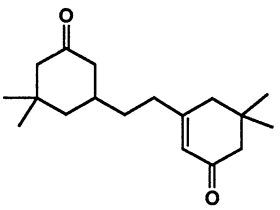
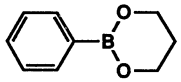
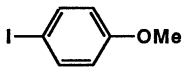
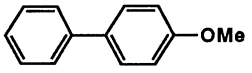
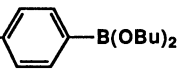
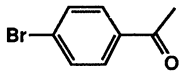
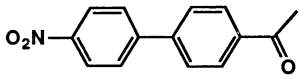
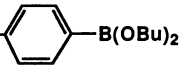
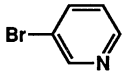
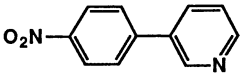
In Table 2, the results of the reaction of various 1-alkenyl and aryl halides with organoboronic esters are summarized. The conditions using Tl_2CO_3 and $PdCl_2(dppf)$ or $Pd(PPh_3)_4$ (entries 3 and 4, in Table 1) were found to work for the most of halides. For functionalized alkylboronic esters or organic halides, such

Table 1. Reaction Conditions for Coupling of Octylboronic Esters with Iodobenzene[a)]

Entry	Ester		Catalyst	Base (equiv.)	Solvent	Yield/%[b)]
1		(I)	$PdCl_2(dppf)$	KOH (3)	THF/H_2O	trace
2			$PdCl_2(dppf)$	TlOH (3)	THF/H_2O	41
3			$PdCl_2(dppf)$	Tl_2CO_3 (1.5)	THF	93
4			$Pd(PPh_3)_4$	Tl_2CO_3 (1.5)	benzene	84
5		(II)	$PdCl_2(dppf)$	TlOH (3)	THF/H_2O	75
6			$PdCl_2(dppf)$	Tl_2CO_3 (1.5)	THF	60
7			$PdCl_2(dppe)$	TlOH (3)	$benzene/H_2O$	93
8		(III)	$PdCl_2(dppf)$	TlOH (3)	THF/H_2O	34
9			$PdCl_2(dppf)$	Tl_2CO_3 (1.5)	THF	trace
10	octyl-$B(OH)_2$	(IV)	$PdCl_2(dppf)$	TlOH (3)	THF/H_2O	trace

a) Reactions were carried out at 50 °C for 16 h using 3 mol% of catalyst, base, octylbononic ester (1.1 mmol), iodobenzene (1 mmol), and 4 ml of solvent.
b) GLC yields based on iodobenzene.

Table 2. Cross-Coupling Reaction of Boronic Esters with Organic Halides

Run	Boronic Ester	Halide	Product	Procedure[a]	Yield/%[b]
1				A	88
2				C	77
3				A	15
4				B	72
5				A	62[c]
6				A	68[c]
7				A	66[c]
8				A	63[c]
9				B	82
10				C	(90)
11				C	(76)

a) The reactions were conducted using boronic esters (1.1 mmol) and halides (1 mmol) under the following conditions. Procedure A: $PdCl_2(dppf)$ (3 mol%) and Tl_2CO_3 (1.5 equiv.) in THF at 50 °C for 16 h. Procedure B: $PdCl_2(dppe)$ (3 mol%) and 0.5 M-TlOH (3 equiv.) in benzene at 50 °C for 15 h. Procedure C: $Pd(PPh_3)_4$ (3 mol%) and Tl_2CO_3 (1.5 equiv.) in benzene at 80 °C for 6 h (runs 2 and 10) or 12 h (run 11).

b) GLC yields are based on halides and isolated yields are in brackets.

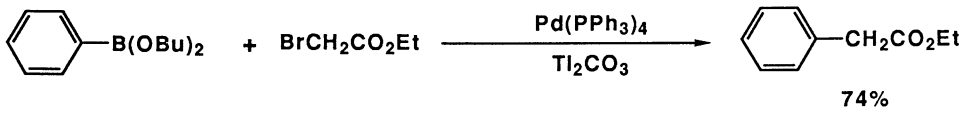
c) The 2-alkyl-1,3,2-benzodioxaboroles obtained by hydroboration[2] of olefinic ketones with catecholborane at 0 °C in the presence of $RhCl(PPh_3)_3$ (1 mol%) was directly used for the next coupling reaction.

nonaqeous conditions afford the advantage that the reaction can be carried out without protecting these groups.

The usefulness of the present method was demonstrated by the cross-coupling reaction of boronyl ketones and arylboronic esters. Although the hydroboration of alkenes can tolerate various functionalities such as cyano and alkoxycarbonyl groups, more reactive keto group must be protected. On the other hand, the catalytic hydroboration[2] of allyl acetone with catecholborane in the presence of 1 mole% of $RhCl(PPh_3)_3$ at 0 °C proceeds chemoselectively at the carbon-carbon double bond but not at the keto group. The boronyl ketones thus obtained were subjected to coupling with aryl and 1-alkenyl halides to give corresponding ketones in 62-69% yields (runs 5-8).

We reported[7] previously that phenylboronic acid undergoes the cross-coupling reaction with aryl halides in the presence of $Pd(PPh_3)_4$ and aqueous sodium carbonate. Thereafter, several articles[8] with respect to the application of this reaction have appeared, indicating that the conditions using aqueous sodium carbonate are available for a variety of arylboronic acids, boronic acids with electron-withdrawing groups such as nitro, susceptible to protonolysis[8a,b] under such aqueous conditions, which give lower yields of coupling products. By using Tl_2CO_3, the reaction can be carried out under nonaqueous conditios to afford biaryls in high yields (runs 10 and 11).

The reaction of phenylboronate with ethyl bromoacetate is an example which shows that even organic halides having sp^3 carbons undergo the cross-coupling at 50 °C in the presence of Tl_2CO_3 (1.5 equiv.) and $Pd(PPh_3)_4$ to provide the coupling product in a yield of 74%.



(5)

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(Received May 24, 1989)