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**Synthesis of Pinacol Allylic Boronic Esters *via* Olefin Cross-Metathesis between
Pinacol Allylboronate and Terminal or Internal Alkenes**

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Abstract: The ruthenium-catalyzed olefin cross-metathesis between pinacol allylboronate, $\text{CH}_2=\text{CHCH}_2\text{B}(\text{O}_2\text{C}_2\text{Me}_4)$, and $\text{RCH}=\text{CH}_2$ giving $\text{RCH}=\text{CHCH}_2\text{B}(\text{O}_2\text{C}_2\text{Me}_4)$ was carried out in refluxing CH_2Cl_2 in the presence of an alkylidene-ruthenium complex (3 mol%).

Key words: allylboron, olefin cross-metathesis, ruthenium catalyst

Reactions of allylboranes with aldehydes or ketones have proved to be very efficient for diastereoselective building of several adjacent chiral centers.¹ Allylboronic esters can be best synthesized by transmetalation between an allylmagnesium or -lithium reagent and $(\text{RO})_3\text{B}$.² A more general approach including synthesis of chiral allylboronates is to add an isomerically pure alkenylmetal to a (α -haloalkyl)boronic ester.³ These methods utilizing lithium or magnesium reagents are convenient for unfunctionalized derivatives, but they are limited by the lack of compatibility with functional groups. Herein, we report an alternative method for the synthesis of allylic boronic esters *via* olefin cross-metathesis⁴⁻⁶ between a pinacol allylboronate (**2**) and a terminal or internal alkene (Scheme 1). Grubbs's alkylidene-ruthenium complexes (**3**, **4**) in refluxing CH_2Cl_2 provided variously functionalized allylboronic esters (**5**) in high yields. Although the metathesis reaction has been used much less frequently for the preparation of organoboron compounds, synthesis of cyclic alkenylboronates *via* ring-closing metathesis has recently been demonstrated by Renaud and Ouellet.⁷

<<Scheme 1>>

Pinacol allylboronate **2** in CH_2Cl_2 was treated with an alkene (**1**, 2 equivs) in the presence of an alkylidene-ruthenium complex (**3** or **4**, 3 mol%). After being refluxed for 24 h, the reaction mixture was directly treated with benzaldehyde (2 equivs) to quantitatively convert pinacol allylboronate **5** to homoallyl alcohol **8/9**. The reaction was run in a flask equipped with an oil bubbler at the top of a condenser and at the reflux temperature of CH_2Cl_2 . The slow bubbling of argon into the CH_2Cl_2 solution to release ethylene generated by the metathesis or the reaction in benzene or 1,2-dichloroethane resulted in significantly low yields. Pinacol can be the best protecting group of allylboronic acid since the reaction failed for the corresponding 2,2-dimethyl-1,3-propanediol ester or 1,2-ethanediol ester.

The reaction of **2** with a stoichiometric amount of styrene giving the desired cross-metathesis product **5** (R=Ph, 40%) was accompanied by the formation of two homodimerization products **6** (20%) and **7** (R=Ph, trace). The product ratio was highly depended on the stoichiometry of added styrene. For example, homodimerization of **2** afforded a high yield of **6** (85%), whereas it was very slow for styrene (**7**: R=Ph, 37%). Thus, all reactions were carried out in the presence of a large excess of alkene, typically 2 equivalents of a terminal or internal alkene, to minimize the formation of **6**. Under these conditions, pinacol cinnamylboronate **5** (R=Ph) was selectively produced and was easily isolated by Kugelrohr distillation *in vacuo* (74%, *E/Z* = 91/9);

however, selective synthesis of **5** can be more difficult for aliphatic derivatives because the reactivity of aliphatic alkenes is comparable to that of **2**.

Due to the difficulty in isolating pure **5** in small-scale runs, the reaction mixture was directly trapped with benzaldehyde; however, the formation of **5** and their *cis/trans* ratios can be estimated from the yields and the diastereomeric ratios of **8/9**. *In situ* treatment of the reaction mixture of **2** and styrene, or the isolated **5** (R=Ph, *E/Z*=90/10), with benzaldehyde at room temperature overnight afforded 1,2-diphenyl-3-butenol **8/9** (R=Ph, 91/9). Thus, the correlation between the *E/Z* ratio of **5** and *anti/syn* selectivity (**8/9**) was consistent with the previous findings that *E-5* affords **8** and *Z-5* yields **9** in allylboration of aromatic and aliphatic aldehydes.^{3c}

The results of the olefin cross-metathesis between **2** and representative alkenes are summarized in Table 1. Aliphatic and terminal alkenes afforded the corresponding homoallyl alcohols in 55-94% yields with 52-96% *anti*-selectivities (entries 1-7). Among them, methyl 3-butenolate exhibited an exceptionally high *anti*-selectivity (*anti/syn*=96/4), thus suggesting a predominant formation of the *E*-allylboronic ester (entry 6), which in striking contrast to the corresponding molybdenum-catalyzed reaction of allyltrimethylsilane⁵ or allyltritylstanane⁶ that resulted in a mixture of *cis*- and *trans*-isomers. Such an effect of a neighboring group can be best explained by chelation of a carbonyl oxygen to the ruthenium metal center (**10**), as was suggested to occur in analogous metathesis reactions of unsaturated amides (**11** and **12**)^{8,9} (Scheme 2). Internal alkenes such as (*E*)- and (*Z*)-4-octene afforded comparable yields and selectivities to those of terminal alkenes (entries 8 and 9). The ruthenium catalyst **4** was used for the methallyl ester due to inefficiency of **3** for such 1,1-disubstituted alkenes (entry 10). High yields and high diastereoselectivities exceeding 90% were commonly achieved for styrene and its *para*-substituted derivatives (entries 11-13). The bulkiness of the aryl ring may serve to increase (*E*)-selectivity and to reduce homodimerization to 1,2-diarylethene. On the other hand, all attempts at metathesis of **2** with acrylonitrile, ethyl acrylate, or phenyl vinyl ether failed.

<<Table 1>> and <<Scheme 2>>

Finally, the utility of the protocol was demonstrated in the synthesis and reaction of a chiral allylboration reagent **14** (Scheme 3). Under conditions analogous to those used for the pinacol ester, cross-metathesis between tartrate ester **13** and methyl 3-butenolate was completed within 24 h. Allylboration of aldehydes at -78 °C for 5 h was followed by acid-catalyzed lactonization to provide **16a-c** (*syn/anti*=96/4). Although the enantioselectivities depended greatly upon the aldehydes employed, the reaction with 3-methyl-2-butenal achieved 82% ee.¹⁰

<<Scheme 3>>

Representative procedure: A 25-ml flask, connected through the condenser to a nitrogen source and an oil bubbler, was charged with a ruthenium catalyst (**3**, 0.03 mmol) and flushed with argon. Dry dichloromethane (5 ml), styrene (2 mmol), and pinacol allylboronate (**2**, 1 mmol) were added successively. After being refluxed for 24 h, benzaldehyde (2 mmol) was added and the mixture was then stirred at room temperature overnight. The product was extracted with ether, washed with brine, dried over MgSO₄, and finally chromatographed over silica gel with hexane/ether (2/1). **8** (R=Ph): ¹H NMR (400 MHz, CDCl₃) δ 7.04-7.38 (m, 10 H), 6.25 (ddd, 1 H, *J*=17.1, 10.2 and 8.9 Hz), 5.27 (d, 1 H, *J*=10.2 Hz), 5.23 (d, 1 H, *J*=17.1 Hz), 4.85 (dd, 1 H, *J*=7.8 and 2.4 Hz), 3.55 (dd, 1 H, *J*=8.3 and 8.3 Hz), 2.30 (d, 1 H, *J*=2.7 Hz); minor signals of **9** appeared at δ 5.90 (ddd, 1 H, *J*=17.2, 10.3 and 7.8 Hz), 4.91 (d, 1 H, *J*=8.3 Hz), 3.64 (dd, 1 H, *J*=8.1 and 8.1 Hz).

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10. **16c**: HPLC on Chiralcel OB-H (Dacel Co., Ltd) with hexane/2-propanol (99.5/0.5) showed 82% ee; $[\alpha]_D^{25} = +37.5$ (c 1.02, CHCl₃); ¹H NMR (400 MHz, CDCl₃) δ 5.73 (ddd, 1 H, *J*=17.1, 10.2 and 8.3 Hz), 5.11-5.29 (m, 4H), 3.24 (dddd, 1 H, *J*=7.6 Hz), 2.69 (dd, 1 H, *J*=17.3 and 8.0 Hz), 2.50 (dd, 1 H, *J*=17.3 and 7.6 Hz), 1.78 (s, 1 H), 1.71 (s, 1 H). Two percent of NOE was observed between two hydrogens at the carbon atoms attached to ethenyl and 2-methyl-1-propenyl group; ¹³C NMR (100 MHz, CDCl₃) δ 18.4, 25.8, 34.3, 43.7, 79.7, 117.7, 118.7, 134.3, 140.3, 176.2; exact mass calcd for C₁₀H₁₄O₂ 166.0994, found 166.0992

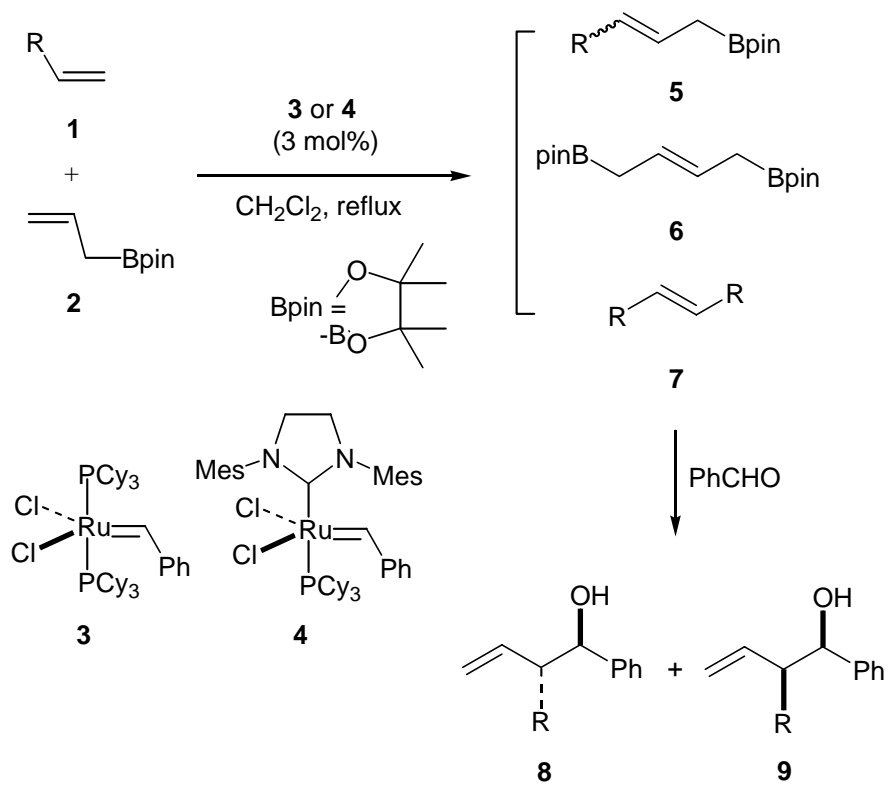
Table 1. Synthesis of Pinacol Allylic Boronates *via* Cross-Metathesis between **2** and Terminal or Internal Alkenes^a

entry	alkene	yield/% ^b
<i>anti/syn</i>		(8 / 9)
1	1-octene	62
2	PhCH ₂ CH=CH ₂	55
3	BrCH ₂ CH ₂ CH=CH ₂	69
4	BrCH ₂ CH ₂ CH ₂ CH=CH ₂	71
5	PhOCH ₂ CH=CH ₂	79
6	MeO ₂ CCH ₂ CH=CH ₂	94
7	MeCO ₂ CH ₂ CH=CH ₂	67
8	(<i>E</i>)-4-octene	55
9	(<i>Z</i>)-4-octene	57
10 ^c	PhCO ₂ CH ₂ C(CH ₃)=CH ₂	49
11	PhCH=CH ₂	88
12	4-MeOC ₆ H ₄ CH=CH ₂	87
13	4-ClC ₆ H ₄ CH=CH ₂	76

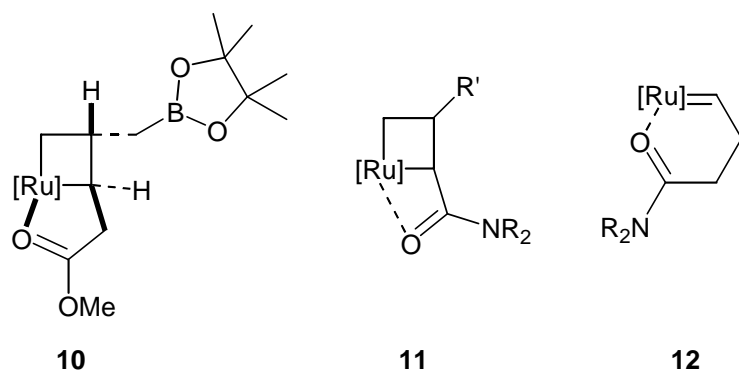
^aA mixture of pinacol allylboronate (**2**, 1 mmol), alkene (2 mmol) in CH₂Cl₂ was refluxed for 24 h in the presence of a ruthenium catalyst (**3**, 3 mol%). The reaction mixture was then treated with PhCHO (2 mmol) at room temperature for 24 h, unless otherwise noted.

^bIsolated yields.

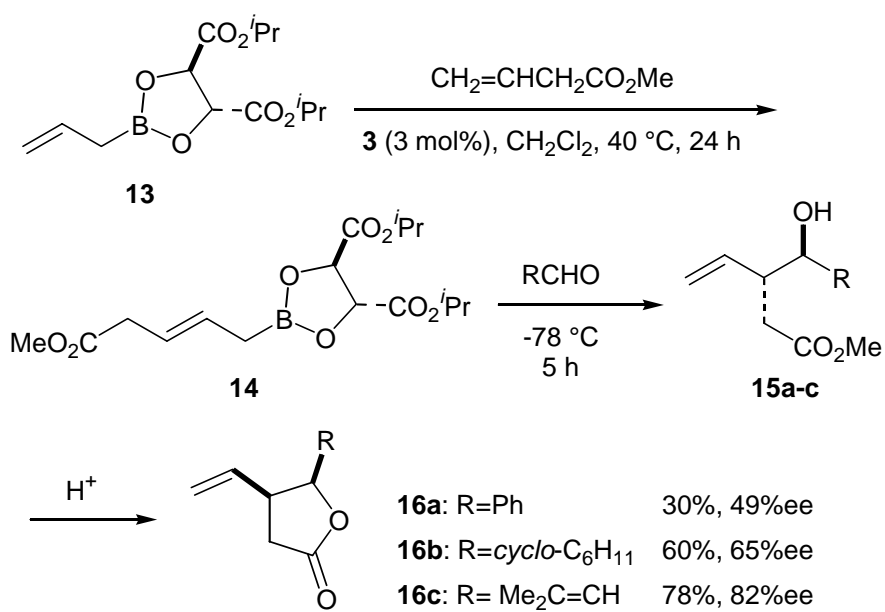
^cRuthenium catalyst (**4**, 3 mol%) was used.



Scheme 1. Olefin Cross-Metathesis for Synthesis of Allylboronates (5)



Scheme 2. Chelation Effect



Scheme 3. Synthesis of Chiral Allylboronates