

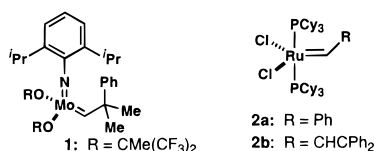
## Novel Synthesis of Cyclic Alkenylboronates via Ring-Closing Metathesis

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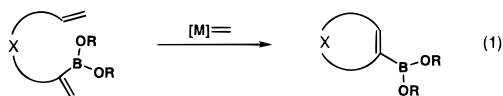
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The versatility and synthetic applicability of the ring-closing metathesis (RCM) reaction in the construction of functionalized carbocycles and heterocycles has recently been demonstrated by a number of groups.<sup>1,2</sup> The emergence of the well-defined transition metal catalysts **1**<sup>3</sup> and **2a,b**<sup>4,5</sup> has greatly expanded the



scope and utility of this method. Of distinct significance is the high tolerance of the alkylidene complexes **2a** and **2b** to commonly encountered functional groups. Various dienes, bearing substituents in the tether linking the olefins, have been shown to undergo metal alkylidene-catalyzed cyclizations.<sup>1</sup> Notably however, RCM has predominantly been exploited for the preparation of cyclic entities containing unsubstituted alkene moieties. In cases where the olefin is functionalized, substituents encountered are either carbon or oxygen.<sup>1,6–8</sup> We were intrigued by the possibility of employing such a strategy to access boron-substituted cyclic olefins (eq 1). Alkenylboronic esters and acids



are highly valuable synthetic intermediates, particularly with regards to carbon–carbon bond formation through palladium-catalyzed Suzuki coupling reactions.<sup>9</sup> Moreover, the propensity

(1) For recent reviews on olefin metathesis, see: (a) Grubbs, R. H.; Chang, S. *Tetrahedron* **1998**, *54*, 4413. (b) Armstrong, S. K. *J. Chem. Soc., Perkin Trans. 1* **1998**, 371. (c) Schuster, M.; Blechert, S. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 2037.

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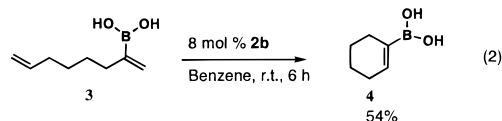
(6) Vinyl halides and diynes bearing substituents such as TMS, Cl, Br, I, and SnBu<sub>3</sub> at their alkyne terminus do not undergo RCM. See: (a) Kirkland, T. A.; Grubbs, R. H. *J. Org. Chem.* **1997**, *62*, 7310. (b) Kim, S.-H.; Zuercher, W. J.; Bowden, N. B.; Grubbs, R. H. *J. Org. Chem.* **1996**, *61*, 1073.

(7) Disubstituted cyclic vinylsilyl ethers, where the silyl group is embedded within the ring, were prepared through RCM catalyzed by **1**. See: Chang, S.; Grubbs, R. H. *Tetrahedron Lett.* **1997**, *38*, 4757.

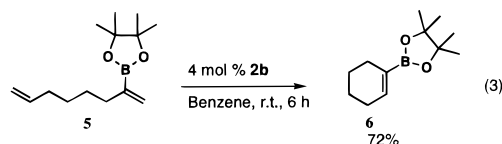
(8) For RCM of olefinic enol ethers, mediated by **1** see: (a) Clark, J. S.; Kettle, J. G. *Tetrahedron Lett.* **1997**, *38*, 123. (b) Fujimura, O.; Fu, G. C.; Grubbs, R. H. *J. Org. Chem.* **1994**, *59*, 4029. (c) Fu, G. C.; Grubbs, R. H. *J. Am. Chem. Soc.* **1993**, *115*, 3800.

of vinylboronates to undergo oxidation furnishes a route for the preparation of ketones.<sup>10</sup> In this communication, we disclose that five-, six-, and seven-membered carbocyclic and heterocyclic alkenylboronates are synthesized in high yield via metathesis of acyclic olefinic boronates.

Our initial attempts were directed toward the metathesis of dialkenylboronic acid **3** (eq 2). Much to our delight, upon



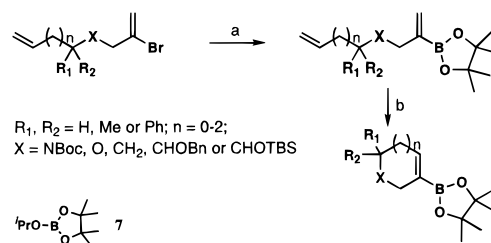
treatment of **3** with catalyst **2b** at room temperature in benzene (0.002 M), cyclization occurred smoothly to provide 1-cyclohexenylboronic acid (**4**) in 54% yield. In contrast, molybdenum catalyst **1** did not furnish the required material in significant quantity. Despite our effort to increase the efficiency of this cyclization reaction, the yield was not further improved. However, when the dialkenylboronic ester **5** was treated with catalyst **2b** (4 mol %), cycloalkene **6** was generated in 72% yield (eq 3).



The ease of isolation and handling of the dienyboronic esters compared to that of the corresponding acids directed our effort toward the utilization of the former substances in RCM reactions. Further investigations of the reaction conditions revealed that the transformation of **5** into **6** was also accomplished very efficiently in the presence of the commercially available catalyst [bis(tricyclohexylphosphine)benzylidene]ruthenium dichloride (**2a**). After purification of the crude material on neutral silica gel,<sup>11</sup> the desired cyclic vinylboronate **6** was obtained in an excellent 90% yield (Table 1, entry 1). These are the first examples of ruthenium-catalyzed RCM of substituted dienes into trisubstituted cyclic olefins bearing substituents other than carbon.

To establish the generality of this transformation, a series of carbon-, oxygen-, and nitrogen-containing acyclic dienyboronates was synthesized as summarized in Scheme 1. Reaction of

### Scheme 1. Synthesis and Ring-Closing Metathesis of Acyclic Dialkenylboronates<sup>a</sup>



<sup>a</sup> Reagents and conditions: (a) tBuLi, Et<sub>2</sub>O, –78 °C; 2-(isopropoxy)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (**7**), –78 °C to room temperature; H<sub>2</sub>O. (b) Grubbs' catalyst (**2a**), benzene, room temperature. Boc = *N*-(tert-butoxycarbonyl); Bn = CH<sub>2</sub>Ph; TBS = tBuMe<sub>2</sub>Si.

2-(isopropoxy)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (**7**)<sup>12</sup> with vinylolithium intermediates, generated from the corresponding

(9) Miyaura, N.; Suzuki, A. *Chem. Rev.* **1995**, *95*, 2457.

vinyl bromides<sup>13</sup> by lithium–halogen exchange, furnished the required dienyloboronate precursors. Subjection of these olefins to RCM conditions provided the corresponding borate-substituted carbocycles and heterocycles. The results of this study are listed in Table 1.

**Table 1.** Ring-Closing Metathesis of Acyclic Olefinic Boronates<sup>a</sup>

Entry	Diene	Product	Yields <sup>b</sup> Time
1			90% 15 h
2			84% 118 h
3			96% 6.5 h
4			85% 6 h
5			77% <sup>c</sup> 76 h
6			76% <sup>d</sup> 118 h
7			85% 5.25 h
8			66% 260 h
9			80% 159 h
10			84% 95 h

<sup>a</sup> Conditions: 5–10% catalyst **2a**, benzene, 0.004–0.05 M, room temperature. <sup>b</sup> Yields refer to isolated products. <sup>c</sup> 12% of dimeric material was also isolated. <sup>d</sup> 18% of dimeric material was also isolated. Boc = *N*-(*tert*-butoxycarbonyl); Bn = CH<sub>2</sub>Ph; TBS = <sup>t</sup>BuMe<sub>2</sub>Si.

Typically, metathesis reactions were carried out in benzene, in the presence of 5–10% ruthenium carbene **2a**, at concentrations ranging from 0.004 to 0.05 M. High-dilution conditions were

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employed to minimize the formation of dimer, resulting from cross-metathesis, when the reaction rates were slow. In the carbocyclic series, cyclization of the five-membered ring precursor cleanly furnished the cyclopenteneboronic ester in 84% yield after 118 h (entry 2). Under similar conditions, RCM of the six-membered ring diene precursors provided readily the cyclohexeneboronates, within 6–15 h, in excellent yields (entries 1, 3,

and 4). The seven-membered ring systems were synthesized in 77% and 76% yields, respectively (entries 5 and 6), but required prolonged reaction times (76 and 118 h). In each of the latter two reactions, dimeric products, resulting from intermolecular metathesis of the less substituted alkene, were also isolated. In the heterocyclic series, conversions of dialkenylboronates into five- and six-membered oxygen and nitrogen heterocycles bearing a vinylboronate moiety were achieved in yields ranging from 66% to 85% (entries 7–10). Interestingly, while the five-membered oxacycle formed in 5 h (entry 7), extended reaction times were required for the preparation of the remaining heterocyclic compounds. The reasons for the difference in reactivity of the various dienes are unclear. The slower rates of ring closure may result from the formation of intermediate ruthenium complexes, formed ruthenium carbene center.<sup>14</sup> It seems likely that the pinacolboronate oxygens are involved in the chelation since, in a few instances, related unsubstituted alkenes have been shown to undergo RCM much faster. Moreover, it appears that, in addition to the presence of the boronate functional group, a donor center (ether or benzyloxy oxygen) is required to reduce the rate of the reaction. Thus, the presence and the location of both functionalities within the diene and their interaction with the ruthenium alkylidene center may be responsible for the variations in the rates of cyclization. Alternatively, conformational bias of the diene could retard ring closure. Further studies to understand the origin of this phenomenon are underway.

In summary, we have demonstrated that the RCM reaction is a practical and reliable procedure for the synthesis of trisubstituted cyclic vinylboronates. The work presented in this communication has established a novel strategy for the assembly of hitherto unexplored frameworks through ruthenium carbene-promoted cyclization, and further broadens the scope and synthetic utility of this powerful reaction.

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**Supporting Information Available:** General experimental procedures and characterization data for acyclic and cyclic vinylboronates (22 pages, print/PDF). See any current masthead page for ordering information and Web access instructions.

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