

Synthesis of Cyclic 1-Alkenylboronates via Zr-Mediated Double Functionalization of Alkynylboronates and Sequential Ru-Catalyzed Ring-Closing Olefin Metathesis

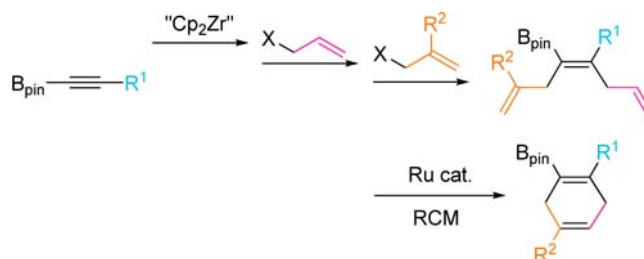
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ABSTRACT



Synthesis of novel cyclic 1-alkenylboronates is accomplished through the zirconium-mediated regio- and stereoselective double functionalization of 1-alkynylboronates and the subsequent ruthenium-catalyzed ring-closing metathesis (RCM). The obtained substituted cyclic 1-alkenylboronates are transformed into *o*-terphenyl and triphenylene derivatives.

Cyclic alkenylboron compounds are highly valuable synthetic intermediates, particularly with regards to C–C bond formation through Pd-catalyzed Suzuki–Miyaura cross-coupling reactions,¹ giving rise to useful organic compounds showing biological activity such as Manzamine A and its derivatives.² Several synthetic routes to cyclic 1-alkenylboronates have been realized through Diels–Alder reactions of 1,3-dienyl-2-boronates with

alkynes³ or of 1-alkynylboronates with dienes,⁴ halogen–boron exchange reactions,^{5,6} and transition-metal-catalyzed dehydrogenative borylations of cyclic alkenes.⁷ However, we often encounter difficulties in obtaining cyclic 1-alkenylboronates by utilizing transition-metal-catalyzed addition reactions of the boron-containing compounds to the internal alkynes⁸ due to the less common availability

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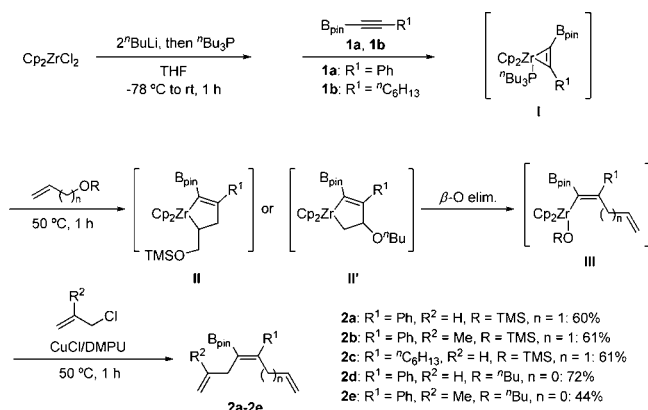
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of cyclic alkynes⁹ or benzyne¹⁰ as the precursors. On the other hand, the versatility and synthetic applicability of the ring-closing olefin metathesis (RCM) reaction in the construction of functionalized carbocycles and heterocycles has been thoroughly demonstrated.¹¹ Along this line, recent advances in the synthesis of cyclic 1-alkenylboronates using the Ru-catalyzed RCM of di-alkenylboronates provided cyclic 1-alkenylboronates with high versatility.¹² Recently, we have succeeded in the synthesis of various multisubstituted alkenylboronates regio- and stereoselectively, derived from alkynylboronates¹³ and a low-valent zirconocene complex.¹⁴ Herein, we disclose that the cyclic 1-alkenylboronates are synthesized in high yields via RCM of highly allylated alkenylboronates given by double functionalization of 1-alkynylboronates as the starting materials.

The tetrasubstituted alkenylboronates **2a–2e** were prepared in good to excellent yields by the reaction of the starting 1-alkynylboronates **1a** and **1b** with the low-valent zirconocene complex, followed by sequential introduction of various allyl and/or vinyl moieties.¹⁵ For instance, treatment of phenyl-substituted 1-alkynylboronate **1a** with $\text{Cp}_2\text{ZrCl}_2/2^\circ\text{BuLi}$ (Negishi's reagent)¹⁶ in the presence of $\text{P}^\text{n}\text{Bu}_3$ afforded the stabilized zirconacyclopentene **I**,¹⁷ which upon sequential double allylation generated **2a** in 60% yield with perfect stereoselectivity as shown in Scheme 1. To the best of our knowledge, zirconacyclopentenes as the intermediate species are believed to be fleeting and difficult to observe,¹⁸ although related complexes are known.¹⁹ Excellent selectivity forming **2** is attributed to the regioselective formation of zirconacyclopentene **II** (allyl) or **II'** (vinyl) bearing the boron moiety in the α -position, from which a smooth β -oxygen elimination gave rise to the alkenylzirconocene intermediate **III**.

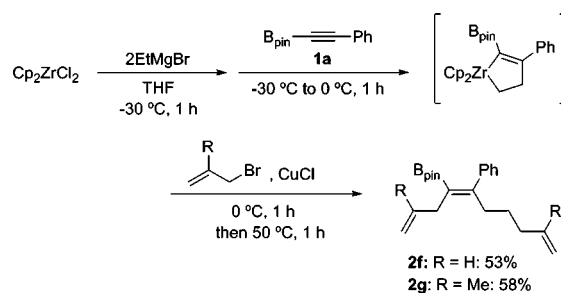
Similarly, analogous tetrasubstituted alkenylboronates **2b–2e** were obtained in moderate to high yields by double allylation or vinylation/allylation sequences. Perfect control of the stereochemistry of (*Z*)-alkenylboronates **2a–2e** is highly important for further cyclization reaction leading to the formation of the desired cyclic 1-alkenylboronates.

Scheme 1. Zirconocene-Mediated Synthesis of Tetrasubstituted Alkenylboronates **2a–2e**



Next our investigations focused on the regio- and stereoselective preparation of multisubstituted alkenylboronates through double allylation of zirconacyclopentenes (Scheme 2).²⁰ To our delight, upon treatment with $\text{Cp}_2\text{ZrCl}_2/2\text{EtMgBr}$ (Takahashi's reagent),²¹ 1-alkynylboronate **1a** afforded the zirconacyclopentene as an intermediate regioselectively, which was subjected to double allylation to give **2f** and **2g** in 53% and 58% yields, respectively. The obtained alkenylboronates **2a–2g** are fully characterized by GC-MS, ^1H , and $^{13}\text{C}\{^1\text{H}\}$ NMR spectra as well as elemental analyses.

Scheme 2. Synthesis of Tetrasubstituted Alkenylboronates **2f** and **2g** via Double Allylation of Zirconacyclopentene



With the doubly allylated alkenylboronate **2a** in hand, we next established the reaction conditions for RCM. The reactions were routinely carried out in the presence of 1–5 mol % of Grubbs second-generation catalyst **A**

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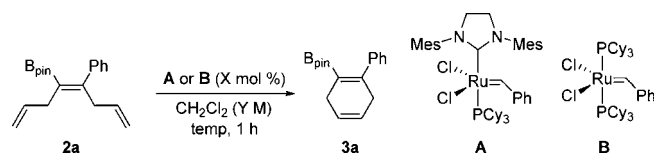
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(Mes = 2,4,6-Me₃C₆H₂)²² an efficient catalyst for RCM,²³ in CH₂Cl₂ at 25 or 40 °C. As shown in Table 1, the RCM catalyzed by Ru-complex **A** efficiently converted the substrate **2a** into the desired six-membered carbocyclic 1,4-cyclohexadienylboronate **3a** in 82% yield (Table 1, entry 1). Owing to a suppression of the intermolecular reaction, the diluted solution (0.01 M) of **2a** gave the better yield (Table 1, entry 2). A catalyst loading reduced to 1.0 mol % also generated **3a** in comparable yields (Table 1, entries 3 and 4). Finally, we found that the inexpensive first-generation Grubbs catalyst **B**²⁴ also furnished **3a** in 95% yield. This is the first example of the Ru-catalyzed RCM of tetrasubstituted alkenylboronates into cyclic 1-alkenylboronates bearing the substituents in the α-position of the boron functionality.

Table 1. Effect of Reaction Parameters on RCM of the Tetrasubstituted Alkenylboronate **2a**^a



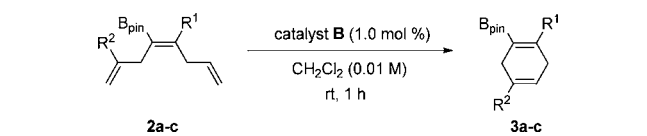
entry	catalyst	X (mol %)	Y (M)	temp (°C)	yield (%) ^b
1	A	5.0	0.10	40	82
2	A	5.0	0.01	40	94
3	A	1.0	0.01	40	92
4	A	1.0	0.01	25	99
5	B	1.0	0.01	25	95

^a All reactions employed alkenylboronate **2a** (0.1 mmol). ^b GC yields.

Under the optimized reaction conditions, a series of alkenylboronates **2a–c** were subjected to the Ru-catalyzed RCM. The results are summarized in Table 2. The six-membered cyclic 1-alkenylboronates **3a–c** were formed in excellent yields. Since an RCM forming five- to seven-membered rings has been known to proceed,¹¹ we attempted the RCM of the synthesized tetrasubstituted

alkenylboronate **2d** (for a five-membered ring) and **2f** (for an eight-membered ring). Unfortunately, however, no desired cyclic 1-alkenylboronates were isolated under the conditions described in Table 1. For example, when **2d** and **2f** were treated with catalyst **B**, the complete consumption of **2d** gave the complex mixture and the starting compound **2f** remained unreacted, respectively.

Table 2. Synthesis of Cyclic 1-Alkenylboronates **3a–c** via RCM of Alkenylboronates **2a–c**^a



entry	substrate	product	yield (%) ^b
1	2a	3a	95
2	2b	3b	94
3	2c	3c	94

^a All reactions employed alkenylboronates **2** (2.0 mmol) in CH₂Cl₂ (200 mL, 0.01 M) at rt. ^b Isolated yields.

The successful transformation of tetrasubstituted alkenylboronates **2** into six-membered cyclic ones **3** encouraged us to investigate the synthesis of 1,2-disubstituted 1,4-cyclohexadienes, *o*-terphenyls, and triphenylenes. In the field of organic materials science, the design and characterization of polycyclic aromatic hydrocarbons (PAHs), which exhibit superior electronic, optical, and/or self-assembling properties, have been studied intensively.²⁵ Hence, efficient synthetic methods leading to functionalized PAHs are expected to assist the rapid developments of PAH-based functional materials.²⁶ The Pd-catalyzed Suzuki–Miyaura cross-coupling reactions of **3a** with aryl iodides could be an efficient method for the formation of a wide variety of PAHs. The results of cross-couplings and the aromatization of **3a** are also summarized in Scheme 3. The resultant cyclic alkenylboronate **3a** was efficiently cross-coupled with various aryl iodides to give the corresponding 1,2-disubstituted 1,4-cyclohexadienes **4a–d** in excellent yields in the

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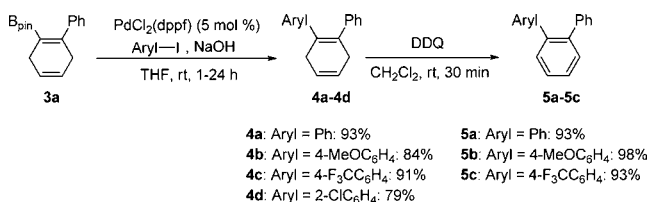
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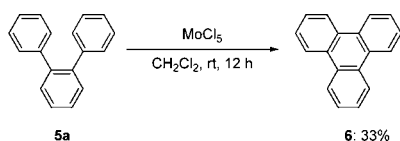
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Scheme 3. Synthesis of Symmetrical and Unsymmetrical 1,2-Diaryl-1,4-cyclohexadienes **4a–d** and *o*-Terphenyls **5a–c**



Scheme 4. Synthesis of Triphenylene (**6**) by Oxidative Cyclization of **5a**

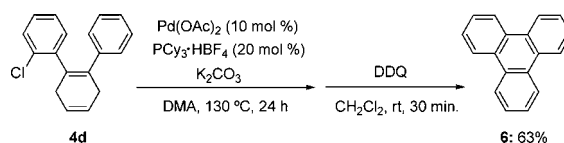


presence of a catalytic amount of PdCl₂(dppf) under the basic conditions. Furthermore, oxidation of the obtained **4a–c** with DDQ in CH₂Cl₂ furnished the *o*-terphenyls **5a–c** in 93, 98, and 93% yields, respectively.

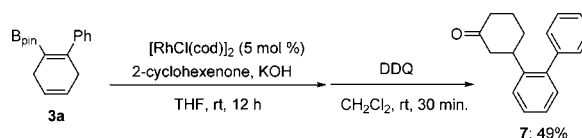
Triphenylene derivatives are known to be applied to several functional organic materials such as the discotic liquid crystals.^{27,28} When **5a** was treated with MoCl₅,²⁹ synthesis of triphenylene (**6**) was accomplished, albeit in 33% yield (Scheme 4).

Since a direct oxidative cyclization of *o*-terphenyl was known to give a complex mixture due to the severe reaction conditions and the presence of many C–H bonds in the molecule,²⁶ selective synthesis of triphenylene (**6**) was examined by the Pd-catalyzed C–H functionalization of **4d**. The once isolated **4d** was treated with a catalytic amount of Pd(OAc)₂ under basic conditions,³⁰ followed by DDQ oxidation to give the desired products **6** in 63% yield (Scheme 5).

Scheme 5. An Alternative Synthesis of Triphenylenes (**6**) by Pd-Catalyzed Annulation via C–H Functionalization of **4d**



Scheme 6. Rhodium-Catalyzed 1,4-Addition of Cyclic Alkenylboronate **3a**



In order to demonstrate the utility of the synthesized cyclic 1-alkenylboronates, conjugate addition of **3a** to 2-cyclohexenone catalyzed by Rh was conducted and the subsequent DDQ oxidation in CH₂Cl₂ afforded **7** in 49% yield (Scheme 6).³¹

In summary, we have developed the regio- and stereo-selective synthesis of tetrasubstituted alkenylboronates by a zirconocene-mediated stepwise allylation or vinylation of 1-alkynylboronates and zirconacyclopentene. The subsequent Ru-catalyzed RCM gave rise to the formation of six-membered cyclic 1-alkenylboronates that are not available by other methods. Current efforts to expand the scope of 1-alkynylboronates as well as to elucidate the application to the synthesis of various PAHs are in progress.

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Supporting Information Available. Copies of ¹H NMR and ¹³C{¹H} NMR spectra for all the new compounds, as well as details on experimental procedures and characterization data. This material is available free of charge via the Internet at <http://pubs.acs.org>.

The authors declare no competing financial interest.

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