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Rhodium-Catalyzed Dehydrogenative Borylation of Cyclic Alkenes

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Abstract

A rhodium-catalyzed dehydrogenative borylation of cyclic alkenes is described. This reaction provides direct access to cyclic 1-alkenylboronic acid pinacol esters, useful intermediates in organic synthesis. Suzuki-Miyaura cross-coupling applications are also presented.

As they are versatile precursors in many C-C bond formation reactions including the Suzuki-Miyaura cross-coupling, 1-alkenylboron derivatives are an important class of compounds in organic synthesis.¹ Hydroboration of alkynes² is one of the most general methods for the preparation of 1-alkenylboron compounds. However, this method has inherent limitations. For example, cyclic 1-alkenylboron reagents generally are not synthesized by this method due to the need for the corresponding cyclic alkynes. Instead these compounds are often prepared by transmetalation of 1-alkenyllithium (or Grignard) reagents with trialkylborates,³ or via palladium-catalyzed cross-coupling between 1-alkenylhalides or -triflates with an appropriate organoboron reagent.⁴ However, these reactions generally require multistep preparation of the 1-alkenylmetal nucleophile and/or the 1-alkenylhalide electrophile.

Impressive advances in transition metal-catalyzed functionalization of arenes (replacement of aryl C-H with C-X, C-R, etc.) have been made in recent years, particularly in the preceding decade.⁵ In a similar vein, catalytic dehydrogenative borylation of alkenes would provide an attractive alternative for the synthesis of 1-alkenylboron compounds.^{6–9} Although several catalytic systems have been developed for this purpose, the substrates are mainly limited to: ethylene, styrene derivatives, and 1,1-disubstituted alkenes, i.e., a limited array of acyclic alkenes.⁶

Recently, Ishiyama and Miyaura reported vinylic C-H borylation of cyclic vinyl ethers with bis(pinacolato)diboron catalyzed by iridium-dtbp complex.⁸ In this reaction, the substrates are limited to five-membered or six-membered cyclic vinyl ethers. Szabó has also recently reported a tandem procedure consisting of an iridium-catalyzed, dehydrogenative borylation of an unactivated cyclic alkene and a subsequent palladium-catalyzed cross-coupling reaction.⁹

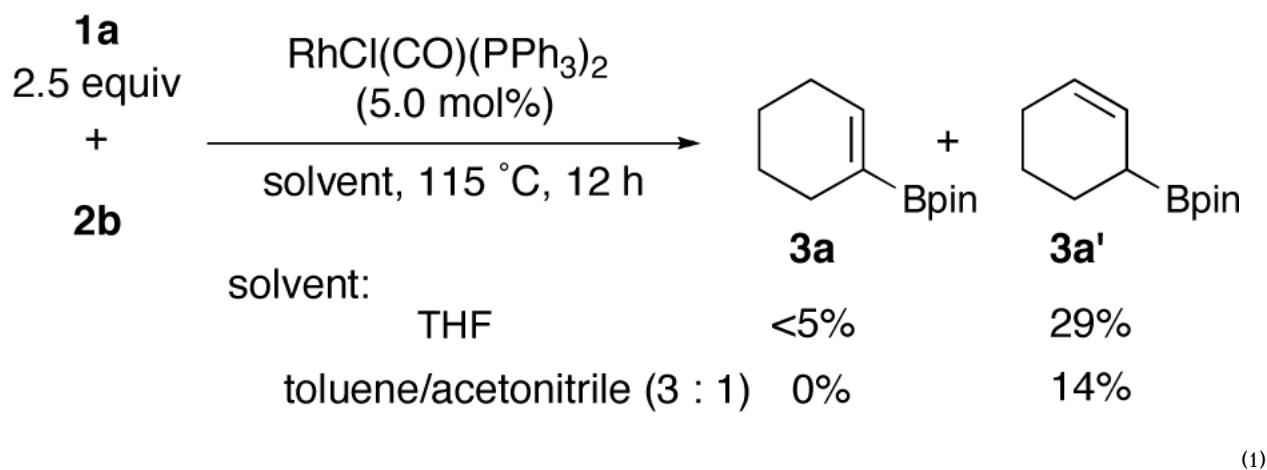
Herein, we describe a rhodium–Xantphos-catalyzed method for the dehydrogenative borylation of alkenes that may offer some advantages to these previously reported methods. In contrast to the Szabó method, which uses a large excess of alkene (as solvent), we have found that only a slight excess of alkene is required in this Rh-catalyzed procedure. Moreover, both of the boron atoms of bis(pinacolato)diboron (pinB)₂ can be employed in this C-H borylation reaction, whereas iridium catalysis incorporates only one of the Bpin groupings.

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[†]Electronic Supplementary Information (ESI) available: Experimental procedures. Data and spectra for new compounds (**3e**, **5d**). See DOI: 10.1039/b000000x/

Dehydrogenative borylation of alkenes catalyzed by rhodium complexes has been investigated extensively by Marder.^{6b} However, the reactions applied to cyclic alkenes are rare, and thus our investigations began with the evaluation of a variety of potential catalysts, i.e., combinations of phosphines and rhodium complexes. Treatment of pinacolborane (**2a**) with an excess of cyclohexene (**1a**) in the presence of catalytic amount of RhCl(PPh₃)₃ in THF at 115 °C afforded 1-alkenylboronate ester **3a** in 13% yield. Evaluation of other phosphines in conjunction with [RhCl(cod)]₂ (Table 1, entries 1–7) revealed that Xantphos and DPEphos (entries 6–7) were effective ligands and provided significant increases in yield. The use of bis(pinacolato)diboron (**2b**) as a boryl reagent instead of pinacolborane provided even better results (entry 8). Toluene and ethereal solvents except for 1,4-dioxane were suitable for this transformation (entries 9–14), but acetonitrile and 1,2-dichloroethane were not (entries 15–16). Heating at reflux or increasing in the amount of diboron reagent **2b** decreased the yield slightly (entries 17–18).

We also examined RhCl(CO)(PPh₃)₂ as a catalyst precursor, and this complex gave noticeably different results when (pinB)₂^{6b} was used (eq 1). Surprisingly, allylboronate ester **3a'** was obtained as the major product (29%), along with the desired 1-alkenylboronate ester (**3a**) as the minor product (<5%). In addition, 1-alkenyl product was not obtained in the toluene/acetonitrile mixtures, which were previously used for borylation of 1,1-disubstituted alkenes. The formation of the undesired allylboronate **3a'** could be suppressed (<2%) by using a catalyst derived from [RhCl(cod)]₂/Xantphos.



The substrate scope of this reaction is shown in Table 2. Several cyclic alkenes (**1a–e**) undergo dehydrogenative borylation to form the corresponding 1-alkenylboronate esters (**3a–e**) in good yields.¹⁰ In all cases, products of hydroboration **4a–e** are also obtained in varying amounts, and for this reason we also examined a two-stage application of this reaction (Scheme 1). After treatment of **1a**, **1c** and **1d** with **2b** under dehydrogenative borylation conditions, the resulting product mixtures were filtered through thin layer of silica and then subjected to Suzuki-Miyaura cross-coupling conditions.^{4c} The desired products (**5a–d**) were obtained in moderate-to-good yield.

At this stage of our investigations, the mechanism of this reaction is unclear, but we propose the sequence of events shown in Scheme 2. Initial oxidative addition of a Rh complex into the B-B bond would afford diboryl rhodium species **6**. Alkene insertion and β-hydride elimination would provide rhodium-allylboronate complex **8**. Isomerization to the major product likely would require dissociation, recomplexation, and hydrometalation to give **9**. Subsequent β-hydride elimination would then give the alkenylboronate ester product (**3**), along with a

rhodium hydride complex such as **10**. The catalytic cycle would be completed by σ -bond metathesis between **10** and **2a** or **2b**, regenerating Rh complex **6**.

This proposed mechanism also accounts for the observed byproducts. The allylboronate esters (**3a'** and **3c'**, see Table 2) would be furnished by the dissociation of complex **7**, and the reaction of rhodium hydride complex **10** with alkene **1** would lead to the hydroboration product **4**. In order to examine these hypotheses, allylboronate ester **3a'** was treated with a large excess of pinacolborane (**2a**) in the presence of the rhodium catalyst. In accord with the above prediction, isomerization of the double bond occurred to yield vinylboronate **3a**; **3a'** was completely consumed. Direct formation of **3** from intermediate **8** via selective deprotonation of the C-H bond α to the boronate ester is also conceivable, and formation of norbornyl derivative (**3e**) would be more easily explained by this pathway. Further investigation is required to evaluate these and other hypotheses.

In summary, the dehydrogenative borylation reaction of cyclic alkenes catalyzed by a rhodium/phosphine complex provides an easy access to cyclic 1-alkenyl boron compounds, a useful class of compounds.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

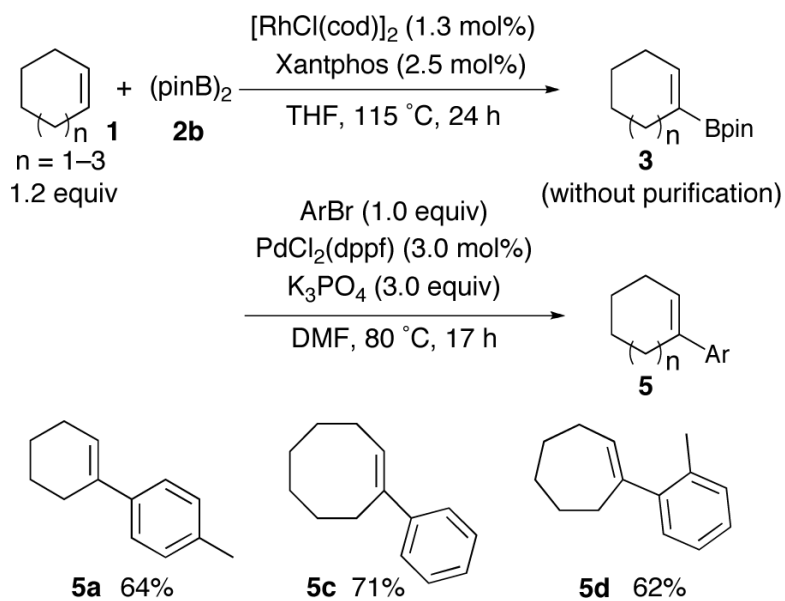
This work was supported in part by the National Institute of General Medical Sciences (GM-63755). We thank Li Li (MIT) for mass spectrometry data and the Japan Society for the Promotion of Science for fellowship support for A. K.

Notes and references

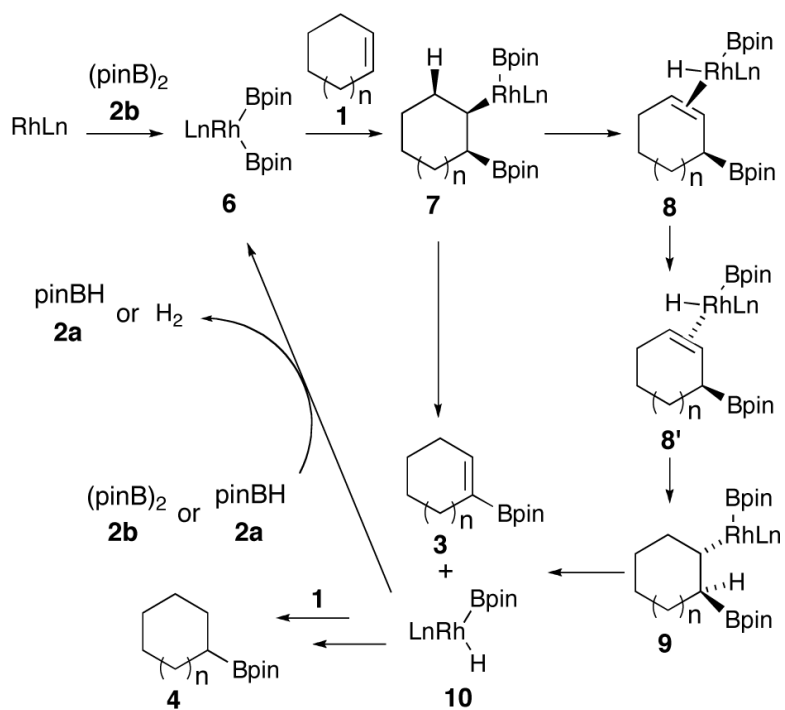
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10. Under the same reaction conditions, the acyclic internal alkenes *cis*-4-octene and *trans*-4-octene afforded a complex mixture of products.

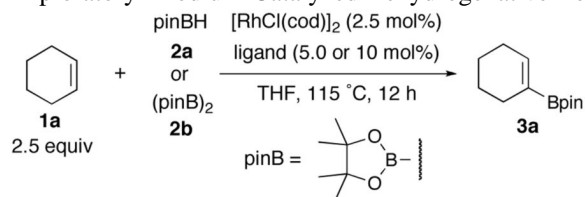


Scheme 1.
Suzuki-Miyaura Cross-Coupling Reaction

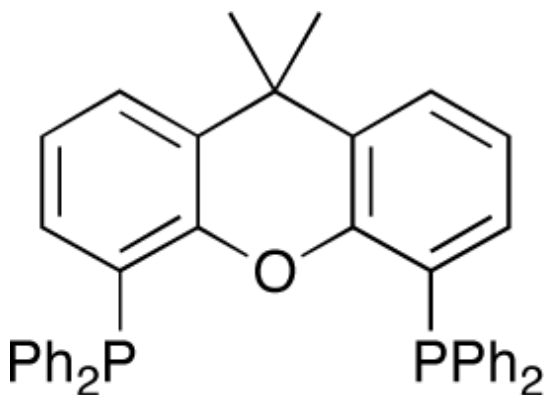


Scheme 2.
Proposed Reaction Mechanism

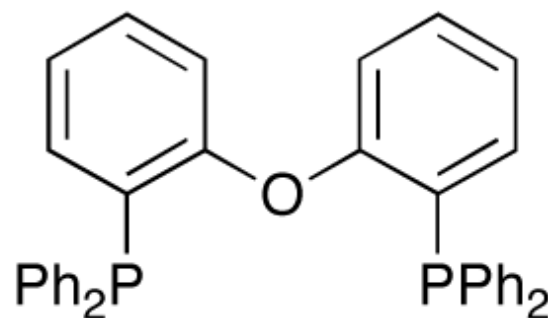
Table 1

Exploratory Rhodium-Catalyzed Dehydrogenative Borylation of Cyclic Alkenes^a

entry	2	ligand (mol%)	solvent	3a (%) ^b
1	2a	PPh ₃ (10)	THF	7
2	2a	PCy ₃ (10)	THF	2
3	2a	DPPB (5)	THF	6
4	2a	DPPF (5)	THF	21
5	2a	<i>rac</i> -BINAP (5)	THF	9
6	2a	Xantphos (5)	THF	41
7	2a	DPEphos (5)	THF	41
8	2b	Xantphos (5)	THF	54
9	2b	Xantphos (5)	<i>n</i> -Bu ₂ O	56
10	2b	Xantphos (5)	<i>c</i> -C ₅ H ₉ OMe	51
11	2b	Xantphos (5)	<i>t</i> -BuOMe	61
12	2b	Xantphos (5)	DME	55
13	2b	Xantphos (5)	1,4-dioxane	20
14	2b	Xantphos (5)	toluene	49
15	2b	Xantphos (5)	1,2-DCE	0
16	2b	Xantphos (5)	acetonitrile	0
17 ^c	2b	Xantphos (5)	THF	41
18 ^d	2b	Xantphos (5)	THF	48



Xantphos



DPEphos

^aConditions: **1a** (1.3 mmol), **2a** (0.50 mmol) or **2b** (0.25 mmol), [RhCl(cod)]₂ (0.013 mmol), THF (2.0 mL). Reactions were performed in a Schlenk tube unless otherwise noted.

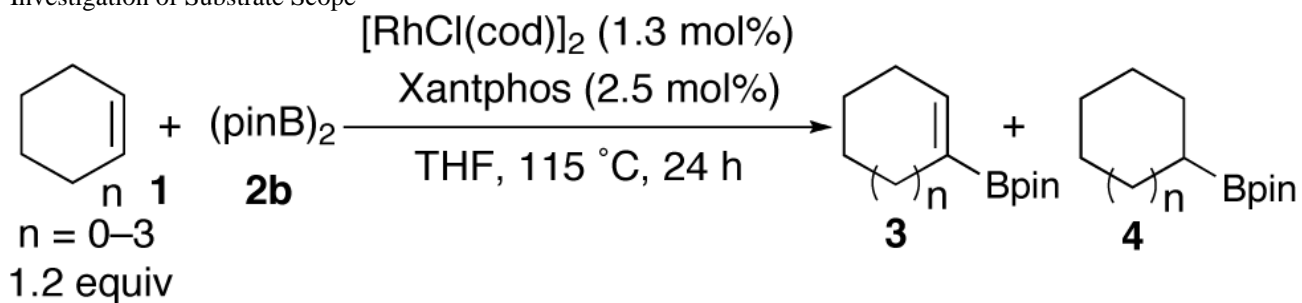
^bBased on ¹H NMR. Dibenzyl ether was used as an internal standard.

^cPerformed in a round bottom flask at reflux.

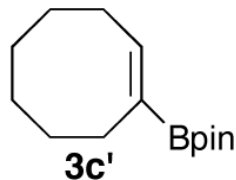
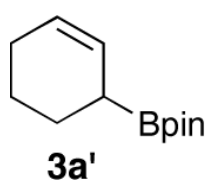
^dPerformed with 1.2 mmol of **1a** and 0.50 mmol of **2b**.

Table 2

Investigation of Substrate Scope



entry	Cycloalkene	3 (%) ^a	4 (%) ^a
1 ^b	cyclohexene (1a)	64	7
2	cyclopentene (1b)	54	9
3 ^c	cyclooctene (1c)	75	12
4	cycloheptene (1d)	63	8
5	norbornylene (1e)	61	21



^aYields were determined by ¹H NMR after column purification.

^b Allylboronate ester **3a'** was obtained in 2% yield.

^c Trace amount of allylboronate ester **3c'** was observed.