JOC Article

Rhodium-Catalyzed Vinylcyclopropanation/Cyclopentenation of Strained Alkenes via a Sequential Carborhodation Process

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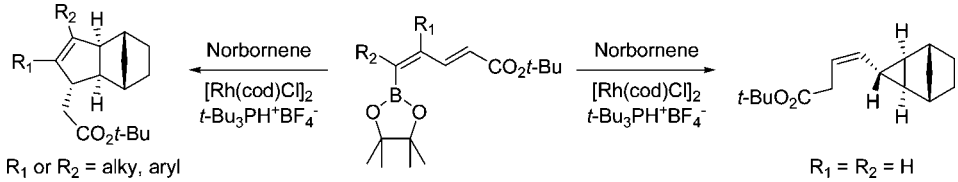
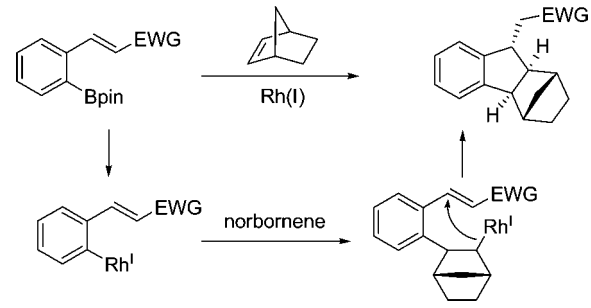


A rhodium-catalyzed reaction of dienylboronate esters with alkenes is described. Strained bicyclic alkenes show the highest reactivity toward the rhodium-catalyzed addition of the dienylboronate esters. Depending on the substitution pattern of dienylboronate esters, an intramolecular 1,6- or 1,4-addition mechanism may be operative, affording carbocycles containing a vinylcyclopropane or cyclopentene moiety.

Introduction

The development of the rhodium-catalyzed addition of organoboron reagents to unsaturated molecules has attracted a significant amount of attention in the past decade.[1] It has been demonstrated to be a powerful method to construct structurally complex molecules. In addition, this method has been extended toward the formation of carbocycles via a sequential carborhodation process, which provides a rapid and efficient synthetic route from simple starting materials.[2] We have previously employed this strategy with *ortho*-functionalized arylboronate esters for the synthesis of indanes[3] and indenes.[4] This process is triggered by the addition of an arylrhodium intermediate to alkene or alkyne coupling partners. The annulated products were obtained after intramolecular carborhodation of the organorhodium intermediate to the tethered Michael acceptor (Scheme 1). This approach has also been extended to a wide variety of the functional groups to form different carbocycles as demonstrated by other research groups.[3]

SCHEME 1. Rhodium-Catalyzed Cascade Addition/Cyclization Process



Our interest in using the dienylboronate ester **1** for the cascade addition/cyclization reaction arose from our previous studies.[3,4] The initial goal was to replace the aromatic system with a simple olefin group in the boronate ester starting material to give the corresponding carbocycles containing substituted cyclopentene moieties. However, when we subjected the dienylboronate ester **1** to previously reported conditions, an unexpected vinylcyclopropane product was obtained,[5] presumably via a rare 1,6-addition of an organorhodium species.[7] Further studies revealed that this reaction is a substrate-controlled process, as substituted dienylboronate esters afforded cyclopenetene products under the same reaction conditions. Herein, we disclose our full results on the scope of this rhodium-catalyzed addition of dienylboronate esters to bicyclic alkenes, as well as our latest insights into the reaction mechanism.

(1) (a) Hayashi, T. *Synlett* **2001**, *879*. (b) Fagnou, K.; Lautens, M. *Chem. Rev.* **2003**, *103*, 169. (c) Hayashi, T.; Yamasaki, K. *Chem. Rev.* **2003**, *103*, 2829. (d) Hayashi, T. *Bull. Chem. Soc. Jpn.* **2004**, *77*, 13. (e) *Modern Rhodium-Catalyzed Organic Reactions*; Evans, P. A., Ed.; Wiley-VCH: Weinheim, Germany, 2005.

(2) For a recent review, see: Miura, T.; Murakami, M. *Chem. Commun.* **2007**, 217.

(3) (a) Lautens, M.; Mancuso, J. *Org. Lett.* **2002**, *4*, 2105. (b) Lautens, M.; Mancuso, J. *J. Org. Chem.* **2004**, *69*, 3478.

(4) Lautens, M.; Marquardt, T. *J. Org. Chem.* **2004**, *69*, 4607.

(5) Tseng, N. W.; Mancuso, J.; Lautens, M. *J. Am. Chem. Soc.* **2006**, *128*, 5338.

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SCHEME 2. Synthesis of Dienylboronate Ester 1

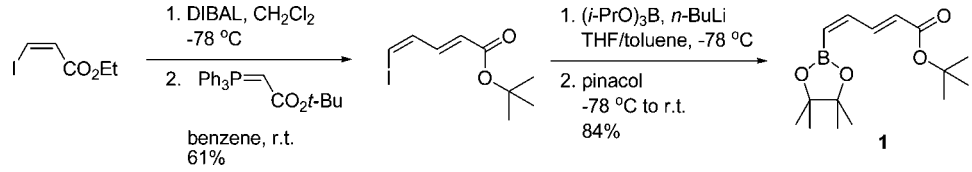
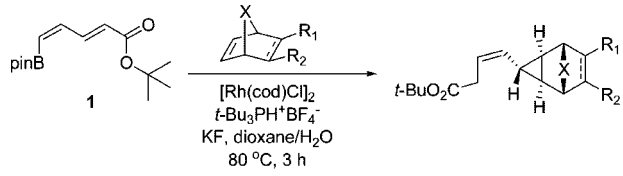


TABLE 1. Reaction with Norbornene Derivatives[a]



entry	alkene	product	yield (%)[b]
1	**2**	**3**	84
2	**4**	**5**	39 (51)[c]
3	**6**	**7**	74
4	**8**	**9**	63
5	**10**	**11**	15

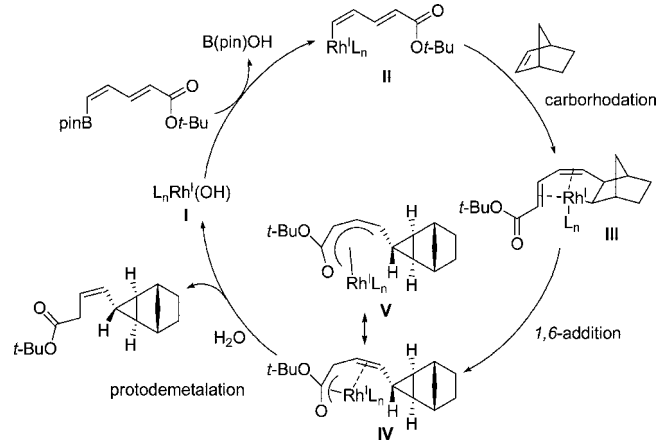
[a] All reactions were run under the following conditions: **1** (0.20 mmol, 1 equiv), alkene (0.20−0.22 mmol, 1.0−1.1 equiv), $[Rh(cod)Cl]_2$ (0.006 mmol, 3 mol %), t-$Bu_3PH^+BF_4^-$ (0.012 mmol, 6 mol %), and KF (0.40 mmol, 2 equiv) in 3.0 mL of dioxane and 0.3 mL of H_2O. [b] Isolated by column chromatography. [c] Yield obtained by using $[Rh(cod)Cl]_2$ (0.012 mmol, 6 mol %) and t-$Bu_3PH^+BF_4^-$ (0.024 mmol, 12 mol %).

Results and Discussions

Dienylboronate ester **1** was synthesized from readily available ethyl (*Z*)-β-iodoacrylate,[8] which was reduced with DIBAL, followed by Wittig olefination to generate the dienyl iodide. Conversion of the iodide to boronate ester **1** was accomplished via an in situ trapping of the vinyllithium intermediate with triisopropylborate,[9] which was then esterified with pinacol.

We initiated the investigations on this rhodium-catalyzed vinylcyclopropanation reaction by screening for optimal reaction conditions. The phosphine ligand was found to play a crucial role for this transformation as monodentate bulky phosphine ligands showed superior reactivity over bidentate phosphine ligands. Optimal reaction conditions were found using $[Rh(cod)Cl]_2$ as the rhodium source with t-$Bu_3PH^+BF_4^-$,[10] potassium fluoride as base,[11] with heating at 80 °C in dioxane/H_2O[12] for 3 h. With norbornene as a coupling partner, product **3** was obtained in 84% yield (Table 1, entry 1). The structures of the products **3** and **15** were determined unambiguously by X-ray crystallography, which also confirmed the *Z*-olefin geometry.[5]

SCHEME 3. Proposed Reaction Mechanism



We believe this unexpected rhodium-catalyzed vinylcyclopropanation reaction follows the mechanism proposed in Scheme 3. The active catalyst $L_nRh(I)OH$ **I**,[13] formed in situ, trans-

(6) For examples using aldehydes, ketones and esters, see: (a) Shintani, R.; Okamoto, K.; Hayashi, T. *Chem. Lett.* **2005**, *34*, 1294. (b) Matsuda, T.; Makino, M.; Murakami, M. *Chem. Lett.* **2005**, *34*, 1416. (c) Matsuda, T.; Shigeno, M.; Makino, M.; Murakami, M. *Org. Lett.* **2006**, *8*, 3379. (d) Shintani, R.; Okamoto, K.; Otomaru, Y.; Ueyama, K.; Hayashi, T. *J. Am. Chem. Soc.* **2005**, *127*, 54. (e) Miura, T.; Shimada, M.; Murakami, M. *Synlett* **2005**, 667. (f) Miura, T.; Shimada, M.; Murakami, M. *Angew. Chem., Int. Ed.* **2005**, *44*, 7598. (g) Miura, T.; Shimada, M.; Murakami, M. *Tetrahedron* **2007**, *63*, 6131. (h) Miura, T.; Sasaki, T.; Nakazawa, H.; Murakami, M. *J. Am. Chem. Soc.* **2005**, *127*, 1390. For nitriles, see: (i) Miura, T.; Nakazawa, H.; Murakami, M. *Chem. Commun.* **2005**, 2855. (j) Miura, T.; Murakami, M. *Org. Lett.* **2005**, *7*, 3339. For α,β-unsaturated carbonyl compounds, see: (k) Shintani, R.; Tsurusaki, A.; Okamoto, K.; Hayashi, T. *Angew. Chem., Int. Ed.* **2005**, *44*, 3909. (l) Kurahashi, T.; Shinokubo, H.; Osuka, A. *Angew. Chem., Int. Ed.* **2006**, *45*, 6336. For ethers, see: (m) Miura, T.; Shimada, M.; Murakami, M. *J. Am. Chem. Soc.* **2005**, *127*, 1094. (n) Miura, T.; Sasaki, T.; Harumashi, T.; Murakami, M. *J. Am. Chem. Soc.* **2006**, *128*, 2516. For bromides, see: (o) Harada, Y.; Nakanishi, J.; Fujihara, H.; Tobisu, M.; Fukumoto, Y.; Chatani, N. *J. Am. Chem. Soc.* **2007**, *129*, 5766. For iodides, see: (p) Shintani, R.; Yamagami, T.; Hayashi, T. *Org. Lett.* **2006**, *8*, 4799. For isocynates, see: (q) Miura, T.; Takahashi, Y.; Murakami, M. *Org. Lett.* **2007**, *9*, 5075. For benzyl chlorides, see: (r) Miyamoto, M.; Harada, Y.; Tobisu, M.; Chatani, N. *Org. Lett.* **2008**, *10*, 2975 For allenes, see: (s) Miura, T.; Ueda, K.; Takahashi, Y.; Murakami, M. *Chem. Commun.* **2008**, 5366.

(7) (a) de la Herran, G.; Murcia, C.; Csaky, A. G. *Org. Lett.* **2005**, *7*, 5629. (b) Hayashi, T.; Tokunaga, N.; Inoue, K. *Org. Lett.* **2004**, *6*, 305. (c) Hayashi, T.; Yamamoto, S.; Tokunaga, N. *Angew. Chem., Int. Ed.* **2005**, *44*, 4224. For a similar 1,6-addition using iridium catalyst, see: (d) Nishimura, T.; Yasuhara, Y.; Hayashi, T. *Angew. Chem., Int. Ed.* **2006**, *45*, 5164.

(8) (a) Piers, E.; Wong, T.; Coish, P. D.; Rogers, C. *Can. J. Chem.* **1994**, *72*, 1816. (b) Marek, I.; Meyer, C.; Normant, J.-F. *Org. Synth.* **1997**, *74*, 194.

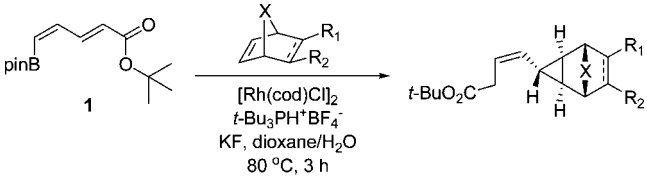
(9) Li, W.; Nelson, D. P.; Jensen, M. S.; Hoerrner, R. S.; Cai, D.; Larsen, R. D.; Reider, P. J. *J. Org. Chem.* **2002**, *67*, 5394.

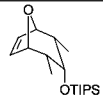
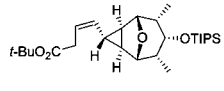
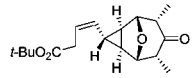
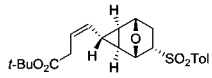
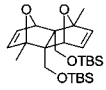
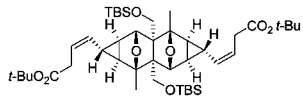
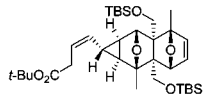
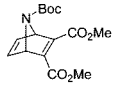
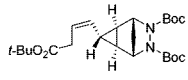
(10) Netherton, M. R.; Fu, G. C. *Org. Lett.* **2001**, *3*, 4295.

(11) Wright, S. W.; Hageman, D. L.; McClure, L. D. *J. Org. Chem.* **1994**, *59*, 6095.

(12) For recent reviews on organic reactions in aqueous media, see: (a) Li, C.-J. *Chem. Rev.* **2005**, *105*, 3095. (b) Li, C.-J.; Chen, L. *Chem. Soc. Rev.* **2006**, *35*, 68.

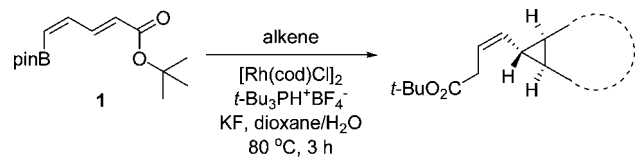
TABLE 2. Reaction with Aza- and Oxabicyclic Alkenes[a]

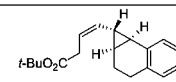
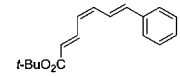
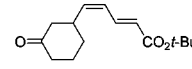


entry	alkene	product	yield (%)[b]
1	 **12**	 **13**	79
2	 **14**	 **15**	97
3	 **16**	 **17**	31
4	 **18**	---	N.R.
5	 **19**	 **20**	78[c]
6	**19**	 **21**	55[d] + **20**, 19
7	 **22**	---	N.R.
8	 **23**	---	N.R.
9	 **24**	 **25**	32

[a] All reactions were run under the following conditions: **1** (0.20 mmol, 1 equiv), alkene (0.08−0.22 mmol, 0.40−1.10 equiv), $[Rh(cod)Cl]_2$ (0.006 mmol, 3 mol %), t-$Bu_3PH^+BF_4^-$ (0.012 mmol, 6 mol %), and KF (0.40 mmol, 2 equiv) in 3.0 mL of dioxane and 0.3 mL of H_2O. [b] Isolated by column chromatography. [c] Yield obtained by using oxabicyclic alkene (0.08 mmol, 0.40 equiv). [d] Yield obtained by using oxabicyclic alkene (0.21 mmol, 1.05 equiv).

TABLE 3. Reaction with Nonbicyclic Alkenes[a]



entry	alkene	product	yield (%)[b]
1	 **26**	 **27**	20
2	 **28**	---	N.R.
3	 **29**	 **30**	15
4	 **31**	 **32**	69
5	 **33**	---	N.R.
6	 **34**	---	N.R.

[a] All reactions were run under the following conditions: **1** (0.20 mmol, 1 equiv), alkene (0.21−0.24 mmol, 1.05−1.20 equiv), $[Rh(cod)Cl]_2$ (0.006 mmol, 3 mol %), t-$Bu_3PH^+BF_4^-$ (0.012 mmol, 6 mol %), and KF (0.40 mmol, 2 equiv) in 3.0 mL of dioxane and 0.3 mL of H_2O. [b] Isolated by column chromatography.

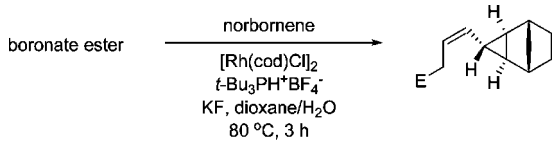
metalates with the boronate ester to give the dienylrhodium(I) intermediate **II** and B(pin)OH. Subsequent carborhodation at the *exo* face of norbornene affords the organorhodium(I) complex **III**,[14] which preferentially undergoes intramolecular 1,6-addition, presumably due to the close proximity of the δ carbon to the rhodium catalyst. Protodemetalation of the resulting oxo-π-allylrhodium(I) **IV** gives the vinylcyclopropane product and regenerates the catalyst $L_nRh(I)OH$ **I**. The Z-olefin geometry in the product is believed to be formed as a consequence of internal coordination of the carbonyl group in oxo-π-allylrhodium(I) **IV**. The presence of the oxo-π-allylrhodium(I) complex **IV** is supported by deuterium studies, which shows >95% deuterium incorporation at the α carbon.[5]

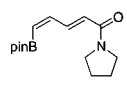
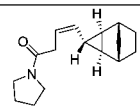
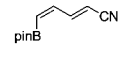
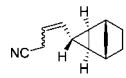
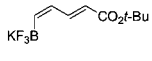
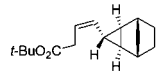
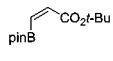
We set out to explore the scope of this vinylcyclopropanation reaction with a variety of alkenes. In general, norbornene and norbornene derivatives gave the desired product in moderate to good yield. Benzonorbornene **4** shows lower reactivity toward this process; even after doubling the amount of the catalyst loading, the corresponding product **5** was obtained in only 51% yield (Table 1, entry 2). Norbornene derivatives **6** and **8**

(13) (a) Brune, H.-A.; Unsin, J.; Hemmer, R.; Reichhardt, M. *J. Organomet. Chem.* **1989**, *369*, 335. (b) Grushin, V. V.; Kuznetsov, V. F.; Bensimon, C.; Alper, H. *Organometallics* **1995**, *14*, 3927. (c) Joó, F.; Kovács, J.; Bényei, A. C.; Nádasdi, L.; Laurenczy, G. *Chem.−Eur. J.* **2001**, *7*, 193. (d) Hayashi, T.; Takahashi, M.; Takaya, Y.; Ogasawara, M. *J. Am. Chem. Soc.* **2002**, *124*, 5052.

(14) Oguma, K.; Miura, M.; Satoh, T.; Nomura, M. *J. Am. Chem. Soc.* **2000**, *122*, 10464.

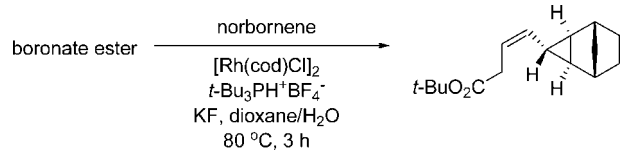
TABLE 4. Reaction with Different Boronate Esters[a]

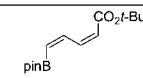
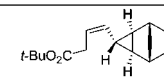
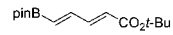
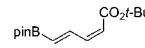


entry	boronate ester	product	yield (%)[b]
1	 **35**	 **36**	32
2	 **37**	 **38**, $Z:E = 3.3:1$	59
3	 **39**	 **3**	35
4	 **40**	---	N.R.

[a] All reactions were run under the following conditions: organoboron reagent (0.20 mmol, 1 equiv), norbornene (0.22 mmol, 1.1 equiv), $[Rh(cod)Cl]_2$ (0.006 mmol, 3 mol %), t-$Bu_3PH^+BF_4^-$ (0.012 mmol, 6 mol %), and KF (0.40 mmol, 2 equiv) in 3.0 mL of dioxane and 0.3 mL of H_2O. [b] Isolated by column chromatography.

TABLE 5. Reaction with Isomeric Dienylboronate Esters[a]



entry	boronate ester	product	yield (%)[b]
1	 **41**	 **3**	54
2	 **42**	**3**	48
3	 **43**	**3**	50

[a] All reactions were run under the following conditions: boronate ester (0.20 mmol, 1 equiv), norbornene (0.22 mmol, 1.1 equiv), $[Rh(cod)Cl]_2$ (0.006 mmol, 3 mol %), t-$Bu_3PH^+BF_4^-$ (0.012 mmol, 6 mol %), and KF (0.40 mmol, 2 equiv) in 3.0 mL of dioxane and 0.3 mL of H_2O. [b] Isolated by column chromatography.

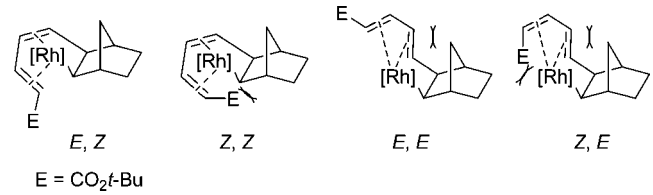


FIGURE 1. Proposed conformation of intermediate **III** with bronoate esters **1** and **41**−**43**.

demonstrated the chemoselectivity of this transformation, as vinylcyclopropanation occurred only at the strained and more electron-rich olefins, giving the products in moderate to good yields (entries 3 and 4). Reaction of bicyclo[2.2.2]oct-2-ene **10** gave the product **11** in low yield, suggesting that the reduced strain energy of this substrate led to the lower reactivity of this process (entry 5).

Aza- and oxabicyclic alkenes, which have been previously used in transition metal catalyzed ring-opening reactions, were also examined. Reacting with [3.2.1] oxabicyclic alkenes such as **12** and **14** gave the desired product in good to excellent yield (Table 2, entries 1 and 2). These results showed that ketone and silyl ether groups are compatible under the reaction conditions, as no 1,2-addition or desilylation were observed. Surprisingly, [2.2.1] oxabicyclic alkene **16** gave **17** in low yield, perhaps due to an interaction of the sulfone group with rhodium catalyst (entry 3). Oxabicyclic alkene **18** did not give the corresponding product, presumably due to a competitive acylation reaction of an organorhodium intermediate with anhydride functional groups, as previously reported by Frost and coworkers (entry 4).[15] Using less than 0.5 equiv of bisoxabicyclic alkene **19** gave the double vinylcyclopropanation product in good yield (entry 5). The monocyclized product could also be obtained in moderate yield by controlling the amount of boronate ester (entry 6). Extension of this method to nitrogen-containing alkenes such as **22** and **23** proved to be problematic and gave no desired product (entries 7 and 8). It is speculated that the bridging nitrogen atom might strongly coordinate to the catalyst and impede the catalytic cycle. However, we found that by employing an azabicyclic alkene with the nitrogen atoms further away from the alkene moiety, such as **24**, affording an interesting diamine product in low yield (entry 9).

We also screened a variety of nonbicyclic alkenes under the optimal reaction conditions. The unstrained 1,2-dihydronaphthalene **26** was found to undergo cyclopropanation, albeit in low yield (Table 3, entry 1). Extension to an analogous alkene, such as indene **28**, did not afford any product (entry 2). Using styrene **29** gave only the Heck-type product in low yield (entry 3).[16] Reacting with 1-cyclohexenone **31** only afford the 1,4-addition product in moderate yield (entry 4).[17] Using other strained alkenes, such as methylenecyclopropane **33** and cyclopropene **34**,[18] did not give any of the desired products (entries 5 and 6).

We next screened several boronate esters containing a similar diene framework, but with different electron-withdrawing groups and different groups on boron. Changing the *tert*-butyl ester to tertiary amide gave **36** in low yield (Table 4, entry 1). Reacting with boronate ester bearing a nitrile functional group afforded the desired product **38** in moderate yield as a mixture of *E*/*Z* isomers (entry 2). We speculate that the linear geometry of the

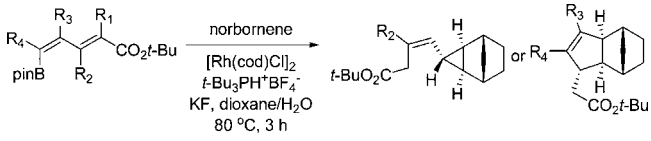
(15) Frost, C. G.; Wadsworth, K. J. *Chem. Commun.* **2001**, 2316.

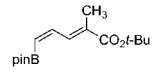
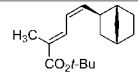
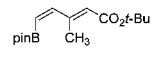
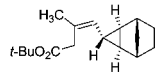
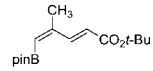
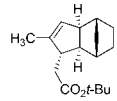
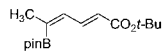
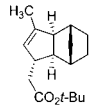
(16) Lautens, M.; Roy, A.; Fukuoka, K.; Fagnou, K.; Martin-Matute, B. *J. Am. Chem. Soc.* **2001**, *123*, 5358.

(17) Sakai, M.; Hayashi, H.; Miyaura, N. *Organometallics* **1997**, *16*, 4229.

(18) Leong, P. Ph. D. thesis, University of Toronto (Canada), 2007.

TABLE 6. Reaction with Substituted Boronate Esters[a]



entry	boronate ester	product	yield (%)[b]
1	 **44**	 **45**	5-10
2	 **46**	 **47**	36
3	 **48**	 **49**	66[c]
4	 **50**	 **51**	70

[a] All reactions were run under the following conditions: boronate ester (0.20 mmol, 1 equiv), norbornene (0.22 mmol, 1.1 equiv), $[Rh(cod)Cl]_2$ (0.006 mmol, 3 mol %), t-$Bu_3PH^+BF_4^-$ (0.012 mmol, 6 mol %), and KF (0.40 mmol, 2 equiv) in 3.0 mL of dioxane and 0.3 mL of H_2O. [b] Isolated by column chromatography. [c] Yield obtained by using boronate ester **48** (1.00 mmol, 1 equiv), norbornene (1.10 mmol, 1.1 equiv), $[Rh(cod)Cl]_2$ (0.03 mmol, 3 mol %), t-$Bu_3PH^+BF_4^-$ (0.06 mmol, 6 mol %), and KF (2.00 mmol, 2 equiv) in 10 mL of dioxane and 1 mL of H_2O.

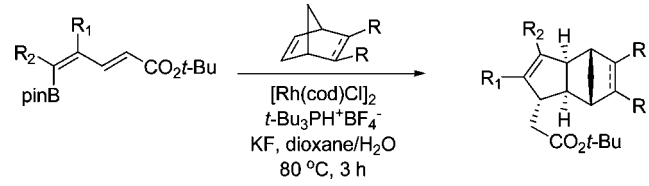
nitrile group has a weaker internal coordination as proposed in intermediate **IV**, leading to a mixture of olefins. Changing the pinacol boronate ester to potassium trifluoroborate **39**[19] gave the corresponding product in lower yield (entry 3). Using boronate ester **40**, containing only one olefin group, did not afford any product (entry 4), presumably due to the inability of this substrate to form the double coordinated intermediate **III**. This result indicates that the diene framework plays a crucial role in the vinylcyclopropanation process.

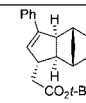
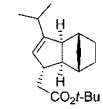
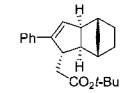
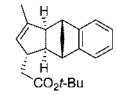
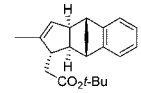
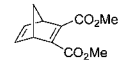
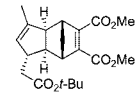
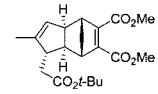
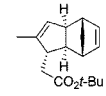
To probe the influence of olefin geometry on this vinylcyclopropanation reaction, various *E*,*Z* isomeric boronate esters were tested. To our surprise, all olefin isomers gave the same product as we obtained using **1**, though in lower yield (Table 5, entries 1−3). The boronate ester **1**, which has *E*,*Z* configuration, gave the highest yield, presumably due to a more favorable conformation in intermediate **III** compared to the other isomers (Figure 1). In addition, the Z-olefin geometry in the product was retained from different isomeric boronate esters, which suggests the reaction mechanism must involve an olefin isomerization step, possibly due to the presence of an equilibrium between (oxo-π-allyl)rhodium(I) **IV** and (oxo-π-pentadienyl)rhodium(I) **V**.

We then examined substituent effects on the dienyl fragment. When methyl-substituted boronate ester **44** was used, the

(19) For examples on rhodium-catalyzed 1,4-addition using potassium organotrifluoroborates, see: (a) Batey, R. A.; Thadani, A. N.; Smil, D. V. *Org. Lett.* **1999**, *1*, 1683. (b) Pucheault, M.; Darses, S.; Genêt, J.-P. *Eur. J. Org. Chem.* **2002**, *2002*, 3552.

TABLE 7. Reaction with Substituted Boronate Esters with Different Alkenes[a]



entry	alkene	R_1	R_2	product	yield (%)[b]
1	 **2**	H	Ph	 **52**	84
2	**2**	H	^{i}Pr	 **53**	84
3	**2**	Ph	H	 **54**	58
4	 **4**	H	CH_3	 **55**	69
5	**4**	CH_3	H	 **56**	68
6	 **6**	H	CH_3	 **57**	64
7	**6**	CH_3	H	 **58**	52
8	 **59**	H	CH_3	 **60**	46
9	**59**	CH_3	H	 **61**	44

[a] All reactions were run under the following conditions: boronate ester (0.20 mmol, 1 equiv), alkene (0.22−0.24 mmol, 1.1−1.2 equiv), $[Rh(cod)Cl]_2$ (0.006 mmol, 3 mol %), t-$Bu_3PH^+BF_4^-$ (0.012 mmol, 6 mol %), and KF (0.40 mmol, 2 equiv) in 3.0 mL of dioxane and 0.3 mL of H_2O. [b] Isolated by column chromatography.

reductive Heck product **45** was obtained in low yield (Table 6, entry 1). Reacting boronate ester **46** bearing a methyl substituent β to the ester group gave the vinylcyclopropane product, though in low yield (entry 2). In contrast, methyl-substituted boronate ester **48** and **50** afforded the cyclopentene products in moderate yield (entries 3 and 4). These results suggest that the rate of intramolecular 1,4- versus 1,6-addition was strongly influenced by the presence of substituents at δ or γ position. The structure of the cyclopentene **49** was further confirmed by X-ray crystallography of a derivative.[20]

We wanted to test the generality of this cyclopentenation reaction by varying the substituents on the boronate esters and the acceptor alkene. Reacting with boronate esters bearing phenyl or isopropyl groups afforded the corresponding cyclopentene products in moderate to good yield (Table 7, entries 1−3). Benzonorbornene and norbornene derivative gave the products in moderate yield with methyl substituted boronate esters (entries 4−7). More interestingly, using norbornadiene as coupling partner only gave the monocyclized product, albeit in unsatisfactory yield (entries 8 and 9).

In summary, we have developed a vinylcyclopropane-forming reaction via a rhodium-catalyzed cascade addition/cyclization sequence. This process works best when strained bicyclic alkenes were used. We also discovered that by using alkyl or aryl substituted dienylboronate esters, the reaction will undergo a different pathway to afford cyclopentene products. A wide variety of polycyclic molecules containing vinylcyclopropane or cyclopentene moieties can be synthesized via this convergent rhodium-catalyzed, substrate-controlled process.

Experimental Section

General Procedure for the Rhodium-Catalyzed Cascade Addition/Cyclization Reactions. A solution of 0.3 mL of water and 3 mL of dioxane in a 5-mL two-neck round-bottom flask was purged with argon and stirred for 10 min at 25 °C. $[Rh(cod)Cl]_2$ (3.0 mg, 0.006 mmol), tri-*tert*-butylphosphonium tetrafluoroborate (3.5 mg, 0.012 mmol), and potassium fluoride (23.3 mg, 0.40 mmol) were added to the solution, which was stirred at 25 °C for 10 min. To the bright yellow solution was added the alkene (0.09−0.24 mmol), followed by addition of the boronate ester (0.20 mmol), and the reaction mixture was stirred at 80 °C for 3 h. The reaction was quenched with brine, and the aqueous layer was extracted with Et_2O (× 3). The combined organic layers were dried with $MgSO_4$, filtrated, and concentrated in vacuo. The crude material was then purified by column chromatography on silica gel.

Vinylcyclopropane 3. (Table 1, entry 1) Yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.41 (dtd, J = 10.6, 7.1, 0.7 Hz, 1H), 4.86 (dddd, J = 10.5, 9.8, 1.6, 1.6 Hz, 1H), 3.09 (dd, J = 7.1, 1.6 Hz, 2H), 2.32 (s, 2H), 1.46 (s, 9H), 1.45−1.41 (m, 3H), 1.27−1.21 (m, 2H), 1.03−0.97 (m, 1H), 0.75 (d, J = 2.2 Hz, 2H), 0.66 (d, J = 10.6 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.5, 134.5, 119.3, 80.4, 35.9, 34.7, 29.4, 28.4, 28.1, 24.6, 12.9; IR (neat): 2954, 2870, 1735, 1458, 1392, 1367, 1328, 1256, 1146, 1113, 956, 833, 702 cm^{-1}. HRMS (ESI) calcd for $C_{16}H_{24}NaO_2$ [M + Na$^+$] 271.1668, found 271.1672.

Cyclopentene 49. (Table 6, entry 3) Yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.12 (d, J = 1.6 Hz, 1H), 2.50−2.46 (m, 1H), 2.47 (dd, J = 14.1, 4.3 Hz, 1H), 2.42−2.36 (m, 1H), 2.02−1.99 (m, 1H), 1.94−1.91 (m, 1H), 1.82 (dd, J = 7.0, 3.1 Hz, 1H), 1.62 (dd, J = 2.7, 1.6 Hz, 3H), 1.49−1.41 (m, 2H), 1.46 (s, 9H), 1.32−1.26 (m, 1H), 1.20−1.07 (m, 2H), 0.97−0.92 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 172.5, 142.9, 128.2, 80.1, 54.5, 52.2, 51.8, 42.9, 40.9, 40.4, 32.2, 29.0, 28.7, 28.1, 14.5; IR (neat): 2949, 2870, 1732, 1475, 1455, 1392, 1367, 1332, 1291, 1256, 1153, 1049, 954, 912, 867, 847, 830, 757 cm^{-1}. HRMS (EI) calcd for $C_{17}H_{26}O_2$ [M$^+$] 262.1933, found 262.1931.

Acknowledgment. We gratefully acknowledge the financial support of the Natural Sciences and Engineering Research Council (NSERC) of Canada, the Merck Frosst Centre for Therapeutic Research for an Industrial Research Chair, and the University of Toronto. We also thank Dr. Alan J. Lough for acquisition of X-ray crystallographic data.

Supporting Information Available: Experimental procedures and crystallographic and spectroscopic characterization data of all new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

JO900039G

(20) See Supporting Information.