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Rhodium-Catalyzed Annulation Reactions of 2-Cyanophenylboronic Acid with Alkynes and Strained Alkenes

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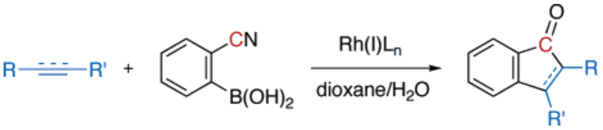
ABSTRACT

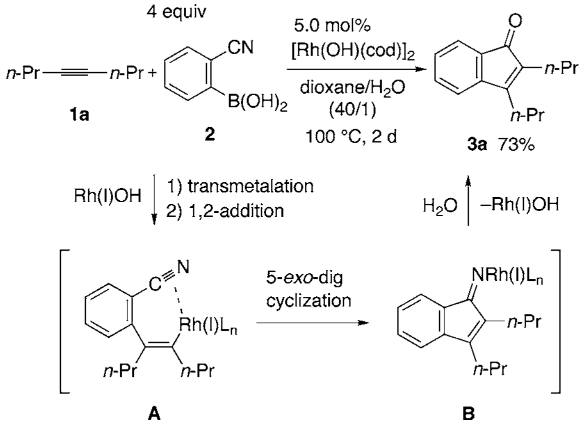


A new [3 + 2] annulation reaction was developed in which 2-cyanophenylboronic acid reacted as a three-carbon component with alkynes or alkenes to afford substituted indenones or indanones. The use of an alkynoate even produced benzotropone, a formal [3 + 2 + 2] adduct. The cyclic skeletons were constructed by intramolecular nucleophilic addition of an intermediate organorhodium(I) species to a cyano group.

Rhodium(I)-catalyzed carbon−carbon bond forming reactions using organoboron reagents have generated considerable interest in organic synthesis and have been extended even to asymmetric synthesis.[1] We have developed the rhodium-catalyzed cyclization reaction of cyano-substituted alkynes with arylboronic acids, in which the 1,2-addition of an arylrhodium(I) species across the carbon−carbon triple bond is followed by intramolecular addition onto the carbon−nitrogen triple bond of the cyano group.[2,3] 2-Cyanophenylboronic acid, a commercially available reagent, is attractive because it contains in one molecule both a potentially nucleophilic carbon−boron linkage that can be transmetalated to an organorhodium(I) species and an electrophilic cyano group that can act as an acceptor for an organorhodium(I) species.[4] In this report, we describe a new rhodium-catalyzed annulation reaction of 2-cyanophenylboronic acid with internal alkynes or strained alkenes.[5,6]

When 4-octyne (**1a**) was reacted with 2-cyanophenylboronic acid (**2**, 4.0 equiv) in the presence of $[Rh(OH)(cod)]_2$ (0.1 equiv in Rh) in dioxane/H_2O (40/1) at 100 °C under a nitrogen atmosphere, the 2,3-disubstituted indenone **3a** was obtained in 73% yield after chromatography (Scheme 1). Initially, (2-cyanophenyl)rhodium(I) is formed by transmetalation of 2-cyanophenylboronic acid (**2**) with hydroxorhod-

Scheme 1



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(1) For reviews on Rh-catalyzed carbon−carbon bond forming reactions, see: (a) Fagnou, K.; Lautens, M. *Chem. Rev.* **2003**, *103*, 169. (b) Hayashi, T.; Yamasaki, K. *Chem. Rev.* **2003**, *103*, 2829.

(2) Miura, T.; Nakazawa, H.; Murakami, M. *Chem. Commun.* **2005**, 2855.

(3) For examples of addition of organopalladium to a cyano group, see: (a) Yang, C.-C.; Sun, P.-J.; Fang, J.-M. *J. Chem. Soc., Chem. Commun.* **1994**, 2629. (b) Larock, R. C.; Tian, Q.; Pletnev, A. A. *J. Am. Chem. Soc.* **1999**, *121*, 3238. (c) Zhao, L.; Lu, X. *Angew. Chem., Int. Ed.* **2002**, *41*, 4343. (d) Zhou, C.; Larock, R. C. *J. Am. Chem. Soc.* **2004**, *126*, 2302 and references therein.

(4) Ueura, K.; Satoh, T.; Miura, M. *Org. Lett.* **2005**, *7*, 2229.

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ium(I). Then, 1,2-addition across the carbon−carbon triple bond occurs to give the alkenylrhodium(I) intermediate **A**.[7] Intramolecular nucleophilic addition to the cyano group in a 5-*exo-dig* mode follows to give intermediate **B**, which was hydrolyzed to **3a**, ammonia, and hydroxorhodium(I). Although similar indanone skeletons can be synthesized by a related [3 + 2] annulation reaction of 2-iodobenzonitrile with alkynes catalyzed by palladium, relatively low yields have been reported for internal alkynes other than diphenylacetylene.[6c]

The results of the [3 + 2] annulation reaction with other alkynes **1b**−**1f** are summarized in Table 1. Diphenylacetylene (**1b**) afforded 2,3-diphenylindenone (**3b**) in 76% yield (entry 1). Unsymmetrically disubstituted alkynes **1c**−**1f** gave moderate to good regioselectivities. Of note was that the major regioisomers obtained with **1e** and **1f** were opposite to those given by the related palladium-catalyzed reactions.[6a,c] Terminal alkynes, such as phenylacetylene and 1-octyne, failed to undergo the annulation reaction. Although ordinary alkenes did not react either, strained bicyclic alkenes **1g** and **1h** did participate in the [3 + 2] annulation reaction to afford the corresponding *exo*-adducts **3g** and **3h**, respectively. In addition, the use of chiral diene ligand **5**,[8] developed by Carreira et al., led to the formation of indanone **3h** in 80% ee (eq 1).

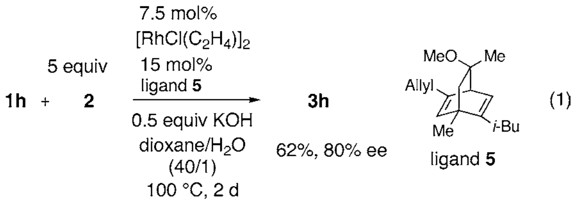
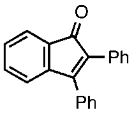
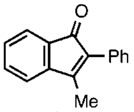
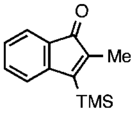
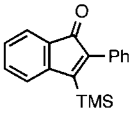
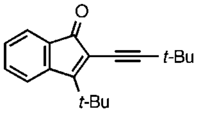
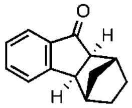
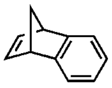
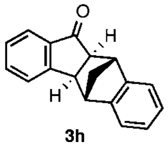
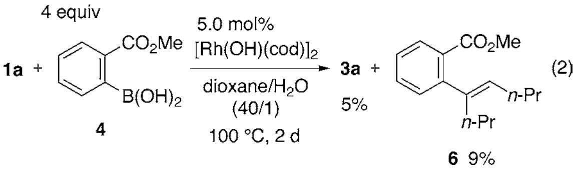


Table 1. Rhodium-Catalyzed Synthesis of Substituted Indenones or Indanones with 2-Cyanophenylboronic Acid (**2**)[a]

entry	substrate **1**	product **3**	yield (%)[b]
1	Ph—≡—Ph **1b**	 **3b**	76
2	Ph—≡—Me **1c**	 **3c**	83 (10:1)[c]
3	TMS—≡—Me **1d**	 **3d**	41 (3:1)[c]
4	Ph—≡—TMS **1e**	 **3e**	81 (3:1)[c]
5	*t*-Bu—≡—≡—*t*-Bu **1f**	 **3f**	91 (2:1)[c]
6	 **1g**	 **3g**	56
7	 **1h**	 **3h**	93

[a] The reaction was carried out with **1** (0.35 mmol) and **2** (1.40 mmol) in the presence of $[Rh(OH)(cod)]_2$ (0.035 mmol of Rh) at 100 °C in dioxane/H_2O (3.5 mL/88 μL) for 2 days. [b] Isolated yields. [c] Regioisomers ratio. The major isomer is designated.

To assess the reactivity of the cyano group relative to other electrophilic functional groups, 2-(methoxycarbonyl)phenylboronic acid (**4**) was examined under similar reaction conditions.[2] Direct hydrolysis of **4** to methyl benzoate mainly occurred, with only 5% of **3a** observed after 2 days along with a small amount of **6** (9%), likely resulting from hydrolysis of the initial 1,2-adduct (eq 2). In the case of



2-cyanophenylboronic acid (**2**), the product resulting from hydrolysis of **A** in Scheme 1 was not detected. The significantly different results obtained with **2** and **4** demonstrate the greatly increased reactivity of cyano groups relative to alkoxycarbonyl groups in intramolecular reactions with organorhodium(I) species.

Finally, ethyl 2-hexynoate (**7**) was reacted with **2** under similar reaction conditions. To our surprise, seven-membered ring benzotropone derivative **8** was obtained as the major product (64%) instead of the five-membered ring indenone derivative (Scheme 2).[9] The alkenylrhodium(I) intermediate

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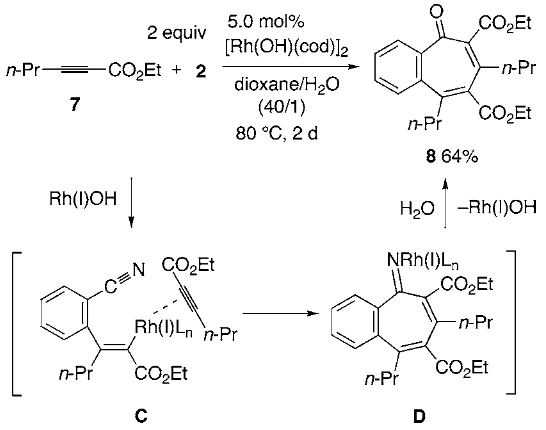
(5) For rhodium-catalyzed annulation using arylboronate esters bearing electron-deficient alkenes, see: (a) Lautens, M.; Mancuso, J. *J. Org. Chem.* **2004**, *69*, 3478. (b) Lautens, M.; Marquardt, T. *J. Org. Chem.* **2004**, *69*, 4607.

(6) For synthetic methods of 2,3-disubstiuted indenone from alkynes, see: (a) Larock, R. C.; Doty, M. J.; Cacchi, S. *J. Org. Chem.* **1993**, *58*, 4579. (b) Kokubo, K.; Matsumasa, K.; Miura, M.; Nomura, M. *J. Org. Chem.* **1996**, *61*, 6941. (c) Pletnev, A. A.; Tian, Q.; Larock, R. C. *J. Org. Chem.* **2002**, *67*, 9276. (d) Vicente, J.; Abad, J.-A.; López-Peláez, B.; Martínez-Viviente, E. *Organometallics* **2002**, *21*, 58.

(7) For 1,2-addition of arylrhodium(I) onto an internal alkyne, see: (a) Hayashi, T.; Inoue, K.; Taniguchi, N.; Ogasawara, M. *J. Am. Chem. Soc.* **2001**, *123*, 9918. (b) Lautens, M.; Yoshida, M. *Org. Lett.* **2002**, *4*, 123.

(8) Defieber, C.; Paquin, J.-F.; Serna, S.; Carreira, E. M. *Org. Lett.* **2004**, *6*, 3873. See also: Otomaru, Y.; Okamoto, K.; Shintani, R.; Hayashi. T. *J. Org. Chem.* **2005**, *70*, 2503 and references therein.

Scheme 2



C underwent the second intermolecular carborhodation onto the electron-deficient alkyne **7** rather than a 5-*exo-dig* cyclization. Then, 7-*exo-dig* ring closure to the cyano group followed to furnish **8** after hydrolysis.

In summary, we have developed a new [3 + 2] annulation reaction of 2-cyanophenylboronic acid (**2**) with internal alkynes or strained alkenes catalyzed by rhodium(I) complexes, which demonstrates that 2-cyanophenylboronic acid is a useful three-carbon scaffold. A benzotropone skeleton was also constructed through successive multiple carbon–carbon bond forming steps in a single operation.

Supporting Information Available: Experimental procedures and new compound characterization data for **3d**, **3f**, and **8**. This material is available free of charge via the Internet at http://pubs.acs.org.

OL051249U

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(9) For recent examples of synthetic methods for benzotropones, see: (a) Iwasawa, N.; Satoh, H. *J. Am. Chem. Soc.* **1999**, *121*, 7951. (b) Dastan, A.; Yildiz, Y. K.; Balci, M. *Synth. Commun.* **2001**, *31*, 3807. (c) Albrecht, U.; Nguyen, T. H. V.; Langer, P. *J. Org. Chem.* **2004**, *69*, 3417.