Rhodium-Catalyzed Oxidative Annulation of (2-Arylphenyl)boronic Acids with Alkynes: Selective Synthesis of Phenanthrene Derivatives

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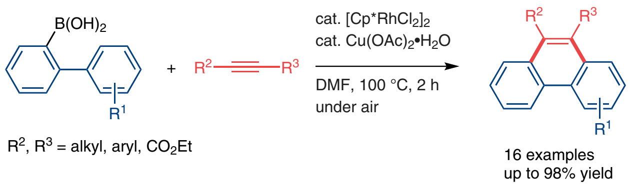


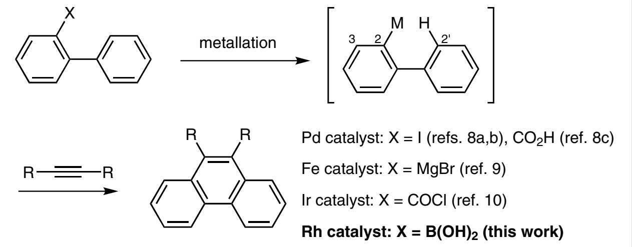
Received: 29.01.2016
Accepted after revision: 28.02.2016
Published online: 24.03.2016
DOI: 10.1055/s-0035-1561940; Art ID: st-2016-u0061-l

Abstract A rhodium-catalyzed annulative coupling of (2-arylphenyl)boronic acids with alkynes has been developed for the facile construction of phenanthrene frameworks. The reaction proceeded without external bases, and dioxygen worked as a terminal oxidant. Deuterium-labeling experiments indicated the involvement of five-membered rhodacycle intermediates.

Key words alkynes, arylboronic acids, phenanthrenes, rhodium, oxidative coupling, C–H functionalization

The chemistry of polycyclic aromatic hydrocarbons (PAHs) has attracted much interest because of their increasing importance in organic materials chemistry.[1] Despite their plain chemical compositions, PAHs exhibit diverse chemical and physical properties based on the molecular architectures, ranging from simple acene and phenacene derivatives to elaborate three-dimensional compounds such as fullerenes[2] and carbon nanotubes.[3]

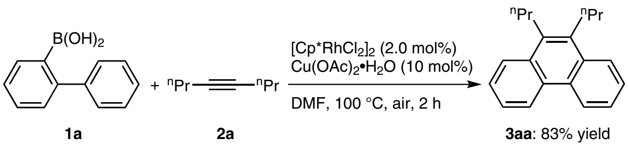
Phenanthrenes are one of the most simple and stable compound classes among PAHs,[4] so that it would be rather easy to modify their properties by the installation of functional groups. In fact, various phenanthrene derivatives have been synthesized focusing on their excellent optical and electric properties[5] as well as interesting biological activities.[6] It is a growing tendency to apply transition-metal-catalyzed C–H bond transformations to the synthesis of aromatic functional molecules from the viewpoint of step- and atom-efficiency.[7] For the construction of phenanthrene frameworks, the annulative coupling reactions of appropriate C2-functionalized 1,1′-biphenyls with alkynes have emerged as promising methods under palladium,[8] iron,[9] and iridium[10] catalysis (Scheme 1). All these reactions involve a mechanism involving C2 metalation, which occurs by substituting C2-functional group (X in Scheme 1), and subsequent C2′–H bond cleavage prior to or posterior to alkyne insertion.



Scheme 1 Phenanthrene synthesis via annulative coupling with alkynes

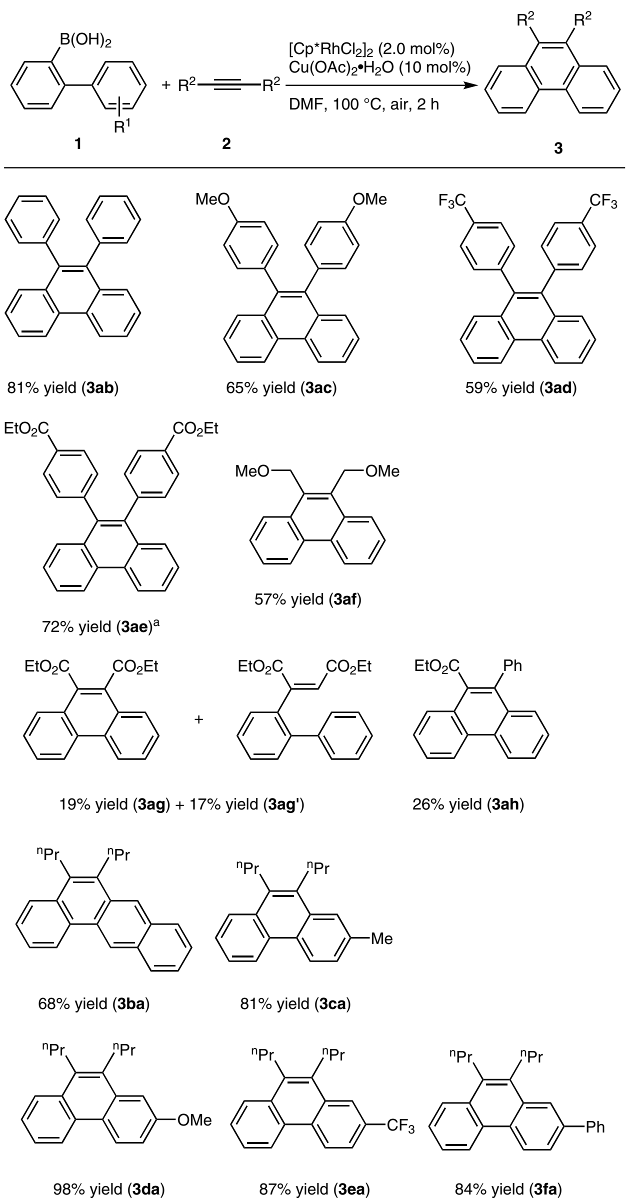
We previously reported the rhodium-catalyzed oxidative 1:2 coupling reaction of arylboronic acids with alkynes to produce linearly fused aromatic molecules such as naphthalene and anthracene derivatives.[11] On the basis of these findings, it may be conceived that (2-arylphenyl)boronic acids can be converted into the corresponding phenanthrenes under a similar catalytic system. Indeed, we demonstrated a single example to construct 9,10-diphenylphenanthrene by the method.[11b] Subsequently, we report herein that the rhodium-catalyzed strategy allows to prepare variously substituted phenanthrene derivatives via the oxidative 1:1 coupling of the boronic acids and alkynes using dioxygen as a terminal oxidant. This catalytic system triggers a selective C2′–H scission over the formation of 1:2 coupling product via C3–H cleavage, and, additionally, 9,9′-biphenanthrenes are formed upon applying diynes into the present protocol. Preliminary mechanistic insights obtained from deuterium-labeling experiments are also described.

At the outset in the present work, we examined the test reaction of [1,1′-biphenyl]-2-ylboronic acid (**1a**) with 4-octyne (**2a**) as a typical aliphatic alkyne in the presence of $[Cp^*RhCl_2]_2$ (Cp* = pentamethylcyclopentadienyl) and $Cu(OAc)_2{\cdot}H_2O$ under air. Expectedly, the corresponding phenanthrene **3aa** was obtained selectively in 83% isolated yield under the optimal reaction conditions (Equation 1).[12] It was confirmed that the reaction did not proceed without adding either the rhodium catalyst or the copper co-catalyst.



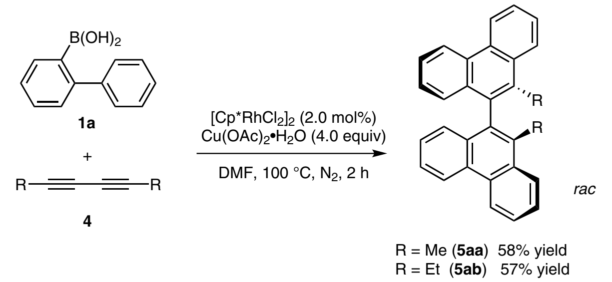
Equation 1 Rhodium-catalyzed oxidative annulation of [1,11′-biphenyl]-2-yl-boronic acid (**1a**) with 4-octyne (**2a**)

We thus investigated the substrate scope for alkynes and boronic acids under the conditions employed in Equation 1 (Scheme 2). The reaction of **1a** with diphenylacetylene (**2b**) successfully afforded the corresponding phenanthrene compound **3ab** in 81% yield. 4,4′-Dimethoxy- and 4,4′-bis(trifluoromethyl)-substituted diphenylacetylenes **2c** and **2d** also reacted to give **3ac** and **3ad** in good yields, whereas a stoichiometric amount of the copper salt was required to achieve a high yield for the production of ethoxycarbonyl-substituted **3ae**. Use of phenylacetylene as a terminal alkyne gave a poor result, giving only a ca. 5% yield of the product (not shown). 1,4-Dimethoxy-substituted 2-butyne **2f** was converted into **3af** in 57% yield. Diethyl acetylenedicarboxylate (**2g**) gave a mixture of annulation product **3ag** and hydroarylation product **3ag′**. On the other hand, acetylene-monoester **2h** gave phenanthrene **3ah** as a sole product, albeit with a low yield. Various 2-arylphenyl boronic acids **1b**–**f** smoothly underwent cyclization upon treatment with alkyne **2a** and the desired phenanthrenes **3ba**–**fa** were obtained in high to excellent yields. It is noted that the yields of compounds **3ba** and **3da** were significantly improved compared with the previous method using the corresponding acid chlorides under iridium catalysis.[10]



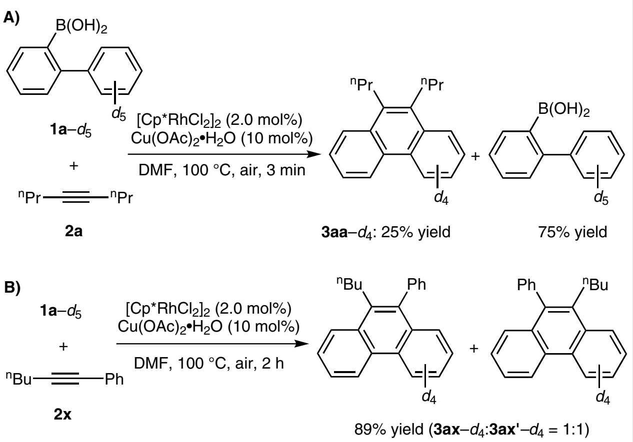
Scheme 2 Substrate scope for alkynes and boronic acids. [a] 2.0 equiv of $Cu(OAc)_2{\cdot}H_2O$ was used under N_2.

This annulation protocol was successfully expanded to the synthesis of 9,9′-biphenanthrenes using diynes as coupling partners (Equation 2).[9,13] Thus, 1,4-dialkylbuta-1,3-diynes **4a** and **4b** underwent twofold cyclization to give **5aa** and **5ab** upon treatment of boronic acid **1a** using a stoichiometric amount of the copper salt. This class of twisted aromatic molecules has recently attracted considerable interest for their unique redox and electric properties.[14]



Equation 2 Twofold annulation with diynes

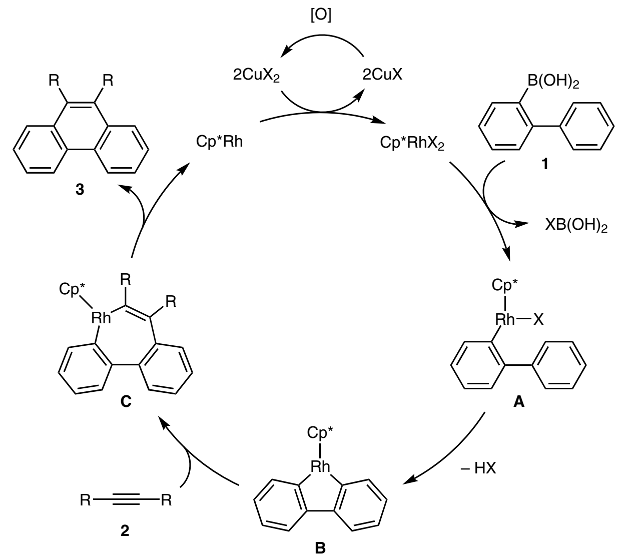
To gain some mechanistic insights into the present catalytic system, a number of deuterium-labeling experiments were conducted using **1a**-d_5 (Scheme 3). When **1a**-d_5 was treated with alkyne **2a** for three minutes under the catalytic conditions, **3aa**-d_4 was obtained in 25% yield along with recovered **1a**-d_5 without any loss of its deuterium content (Scheme 3, A). This result clearly indicated that the C2′–H cleavage should be irreversible. Additionally, KIE values for **1a** against **1a**-d_5 which were calculated from a set of parallel reactions and an intermolecular competition, 1.11 and 0.96, respectively, suggested that the C2′–H cleavage event is not involved in the rate-determining step (for details, see Supporting Information). The reaction of an asymmetric alkyne **2x** afforded a 1:1 mixture of isomers **3ax**-d_4 and **3ax′**-d_4 in 89% yield (Scheme 3, B). Because we previously observed that such an insertion of alkyl(aryl)alkynes into a Rh–C bond proceeded regioselectively,[11] this result strongly suggested the involvement of five-membered rhodacycle intermediates in the catalytic cycle (vide infra).



Scheme 3 Deuterium-labeling experiments

Based on these observations, a plausible mechanism for the annulative coupling is illustrated in Scheme 4. A rhodium(III) complex undergoes transmetalation with boronic acid **1** to afford intermediate **A**. Consequently, C2′–H cleavage takes place to generate the five-membered rhodacycle complex **B**, which is followed by insertion of alkyne **2** into one of two Rh–C bonds. Since this insertion proceeds with almost the same frequency in the Rh–C bonds of the complex **B**, use of the asymmetric alkyne **2x** resulted in the formation of 1:1 mixture of the regioisomers (Scheme 3, B). Thus, complex **C** produces the corresponding phenanthrene **3** by reductive elimination, and the catalytically active rhodium(III) species are regenerated by copper(II)-mediated oxidation to close the catalytic cycle.

In conclusion, we have described a rhodium-catalyzed oxidative annulation of (2-arylphenyl)boronic acids with alkynes that ensured the rapid access to a range of functionalized phenanthrene derivatives from readily available boronic acids. This catalytic system called for no external bases, and atmospheric dioxygen in air basically worked as terminal oxidant. Some twisted 9,9′-biphenanthrenes were also accessible upon applying diynes, so that the present protocol would be a practical synthetic tool for such a series of π-conjugated compounds.



Scheme 4 A plausible catalytic cycle for the rhodium-catalyzed annulative coupling

Acknowledgment

This work was supported by Grants-in-Aid for Scientific Research from the MEXT, JSPS, and JST (ACT-C) of Japan.

Supporting Information

Supporting information for this article is available online at http://dx.doi.org/10.1055/s-0035-1561940.

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(12) **General Procedure for Equation 1 and Scheme 2**

To a 20 mL two-necked flask were added arylboronic acid **1** (0.25 mmol), alkyne **2** (0.25 mmol), $[(Cp^*RhCl_2)_2]$ (0.005 mmol, 3 mg), $Cu(OAc)_2 \cdot H_2O$ (0.025 mmol, 5 mg), 1-methylnaphthalene (ca. 50 mg) as internal standard, and DMF (3 mL). The resulting mixture was stirred under air at 100 °C for 2 h. Then, the reaction mixture was cooled to room temperature and filtered through an alumina pad with CH_2Cl_2. After evaporating the solvents, product **3** was isolated by column chromatography on silica gel.

9,10-Dipropylphenanthrene (3aa) [CAS Reg. No. 19793-67-0][10]

Purified by column chromatography with hexane as eluent (54.2 mg, 83%); white solid. ^1H NMR (400 MHz, $CDCl_3$): $\delta = 1.19$ (t, $J = 7.3$ Hz, 6 H), 1.71–1.84 (m, 4 H), 3.11–3.22 (m, 4 H), 7.57–7.68 (m, 4 H), 8.08–8.17 (m, 2 H), 8.74 (dd, $J = 7.2, 2.4$ Hz, 2 H). ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 15.0$, 24.2, 31.7, 123.1, 124.9, 125.5, 126.7, 130.0, 131.5, 134.0. HRMS: m/z calcd for $C_{20}H_{23}$ $[M + H^+]$: 263.1794; found: 263.1771.

For other compounds, see the Supporting Information.

(13) **Procedure for Equation 2**

To a 20 mL two-necked flask were added arylboronic acid **1a** (1.0 mmol, 198 mg), alkyne **4** (0.25 mmol), $[(Cp^*RhCl_2)_2]$ (0.01 mmol, 6 mg), $Cu(OAc)_2 \cdot H_2O$ (1.0 mmol, 200 mg), 1-methylnaphthalene (ca. 50 mg) as internal standard, and DMF (3 mL). The resulting mixture was stirred under N_2 at 100 °C for 2 h. Then, the reaction mixture was cooled to room temperature and filtered through a Celite pad with CH_2Cl_2. After evaporating the solvents, product **5** was isolated by column chromatography on silica gel.

10,10′-Dimethyl-9,9′-biphenanthrene (5aa)

Purified by column chromatography with hexane–toluene (95:5, v/v) as eluent and then preparative GPC (55.6 mg, 58%); white solid; mp 268–269 °C. ^1H NMR (400 MHz, $CDCl_3$): $\delta = 2.37$ (s, 6 H), 7.22 (dd, $J = 8.2, 1.1$ Hz, 2 H), 7.29 (ddd, $J = 8.2, 6.8, 1.1$ Hz, 2 H), 7.58 (ddd, $J = 8.3, 6.8, 1.4$ Hz, 2 H), 7.70–7.80 (m, 4 H), 8.19–8.26 (m, 2 H), 8.81 (d, $J = 8.3$ Hz, 2 H), 8.85–8.92 (m, 2 H). ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 16.8$, 122.7, 123.2, 125.2, 126.0, 126.5, 127.0, 127.0, 127.2, 129.8, 130.4, 131.5, 132.0, 132.1, 134.8. HRMS: m/z calcd for $C_{30}H_{23}$ $[M + H^+]$: 383.1794; found: 383.1796.

10,10′-Diethyl-9,9′-biphenanthrene (5ab)

Purified by preparative GPC (58.1 mg, 57%); white solid; mp 260–261 °C. ^1H NMR (400 MHz, $CDCl_3$): $\delta = 1.03$ (t, $J = 7.5$ Hz, 6 H), 2.75–2.93 (m, 4 H), 7.21–7.30 (m, 4 H), 7.58 (ddd, $J = 8.3, 6.3, 1.9$ Hz, 2 H), 7.70–7.79 (m, 4 H), 8.20–8.27 (m, 2 H), 8.80 (d, $J = 8.3$ Hz, 2 H), 8.87–8.93 (m, 2 H). ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 14.3$, 24.4, 122.6, 123.4, 125.5, 126.1, 126.4, 126.7, 126.9, 127.9, 129.9, 130.9, 131.1, 132.2, 134.3, 136.7. HRMS: m/z calcd for $C_{32}H_{27}$ $[M + H^+]$: 411.2107; found: 411.2086.

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