Synthesis of 1*H*-Inden-1-ol Derivatives via Rhodium-catalyzed Annulation of *o*-Acylphenylboronic Acids with Alkynes

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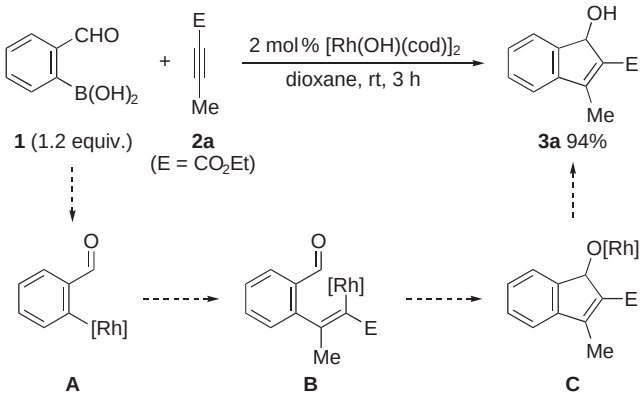
A rhodium-catalyzed annulation reaction of *o*-formylphenylboronic acid with alkynes occurred regioselectively at room temperature to give substituted 1*H*-inden-1-ol derivatives. *o*-Acetylphenylboronic acid also underwent the annulation reaction at 80 °C to afford 1-methyl-1*H*-inden-1-ols.

The rhodium-catalyzed addition reactions of organoboron compounds have rapidly emerged as a new protocol for the formation of carbon–carbon bonds.[1] An intermediate organorhodium(I) species can add to relatively polar unsaturated functionalities like carbonyl[2] and cyano[3] groups as well as carbon–carbon double[4] and triple[5] bonds. Recently, rhodium-catalyzed processes forming cyclic skeletons through consecutive additions to different unsaturated functionalities have been developed.[6] We now report a rhodium-catalyzed annulation reaction of *o*-acylphenylboronic acids with alkynes forming 1*H*-inden-1-ol derivatives.[7,8]

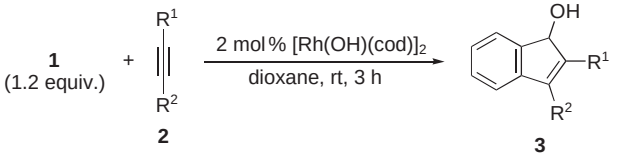
Commercially available *o*-formylphenylboronic acid (**1**, 1.2 equiv.) was allowed to react with methyl but-2-ynoate (**2a**, 1.0 equiv.) in the presence of $[Rh(OH)(cod)]_2$[9] (4 mol % Rh, cod = cycloocta-1,5-diene) in 1,4-dioxane at room temperature. After 3 h, 1*H*-inden-1-ol **3a** was obtained in 94% yield (Scheme 1).[10] The ester group was exclusively attached to the 2-position of the indenol skeleton. The annulation reaction is considered to consist of i) transmetalation between rhodium(I) and arylboronic acid **1** to form **A**, ii) highly regioselective (>98:2) 1,2-addition across the carbon–carbon triple bond of **2a** to form **B**, iii) intramolecular addition of the resulting β-styrylrhodium to the aldehydic carbonyl group to form **C**, and iv) protonolysis/transmetalation releasing **3a**. Neither benzaldehyde nor *o*-alkenylbenzaldehyde, which might arise from protonolysis of **A** or **B**, respectively, was found in the reaction mixture, indicating that the annulation sequence proceeded more facilely than protonolysis of the Rh–C(sp^2) linkages. Unlike the case with *o*-cyanophenylboronic acid,[7b] a seven-membered ring product through double insertion of **2a** was not found in the reaction mixture. Intermediate **B** once formed immediately underwent intramolecular addition to a formyl group, which should be considerably easier than the addition to a cyano group.

Examples of the rhodium-catalyzed annulation reaction of **1** with other alkynes **2b**–**2i** are shown in Table 1. 3-Trimethylsilyl acetylenic ester **2b** and ketone **2c** underwent the annulation reaction with **1** to give the corresponding products in high yield with excellent regioselectivity (Entries 1 and 2). Similar regioselectivity was achieved with 1-phenylprop-1-yne (**2d**) (Entry 3). The regioselectivity observed with **2d** was higher than those with simple phenylboronic acid (3:1)[5] and *o*-cyanophenylboronic acid (10:1),[7b] indicating effective coordination of the carbonyl



Scheme 1.

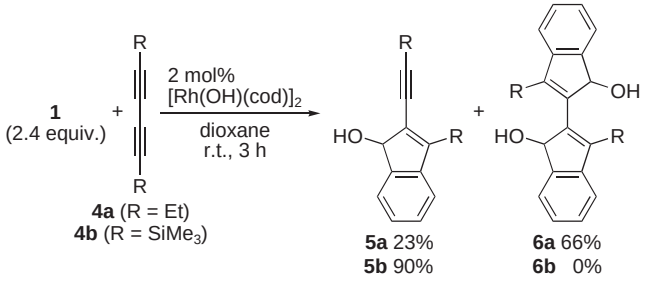
Table 1. Rhodium-catalyzed annulation of *o*-formylphenylboronic acid (**1**) with alkyne **2**[a]



Entry	**2** (R^1, R^2)	**3** (yield/%)[b]	Regioselectivity[c]
1	**2b** (CO_2Et, $SiMe_3$)	**3b** (95)	96:4
2	**2c** (COMe, $SiMe_3$)	**3c** (99)	96:4
3	**2d** (Ph, Me)	**3d** (94)	97:3
4	**2e** (Et, Et)	**3e** (98)	—
5	**2f** (CH_2OAc, CH_2OAc)	**3f** (73)	—
6[d]	**2g** (Ph, Ph)	**3g** (70)	—
7	**2h** (*i*-Bu, H)	**3h** (36)	88:12
8	**2i** (Ph, H)	**3i** (20)	>98:2

[a]Unless otherwise noted, all reactions were carried out with boronic acid **1** (0.48 mmol), alkyne **2** (0.40 mmol), and $[Rh(OH)(cod)]_2$ (8.0 μmol, 4 mol % Rh) in 1,4-dioxane (2.0 mL) for 3 h. [b]Isolated yield. [c]Determined by ^{1}H NMR. [d]10 h.

group of **1** as the directing group.[6d] Whereas the reaction of symmetrical alkynes, such as hex-3-yne (**2e**) and but-2-ynylene diacetate (**2f**), proceeded well (Entries 4 and 5), diphenylacetylene (**2g**) required a longer reaction time to attain good yield (Entry 6). Terminal alkynes could be used as the coupling partner but with far less efficiency (Entries 7 and 8). Oligomerization of terminal alkynes was unavoidable under the reaction conditions.[11] Dimethyl acetylene dicarboxylate and bis(trimethylsilyl)acetylene failed to give coupling products **3** in the presence of the rhodium catalyst. The reaction with alkenes such as ethyl



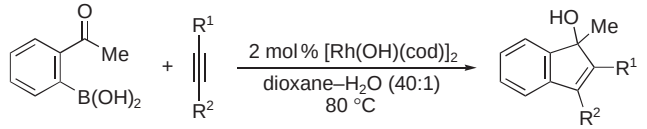
Scheme 2.

acrylate, phenyl vinyl ketone, and norborna-2,5-diene was also unsuccessful.

When octa-3,5-diyne (**4a**) was allowed to react with 2.4 equiv. of **1**, doubly annulated **6a** (66%, *dl*/*meso* = ca. 1:1) was furnished together with mono-annulated **5a** (23%) (Scheme 2). In the case of disilyl-capped diyne **4b**, the initial product **5b** was exclusively obtained in high yield. This may be attributed to severe steric congestion around the remaining C≡C bond of **5b**.

An analogous reaction of *o*-acetylphenylboronic acid (**7**) producing 1-methyl-1*H*-inden-1-ols **8** required more forcing conditions (Table 2). More than two equivalents of **7** was used at an elevated temperature.[12] Addition of a small amount of water was also noted to have a positive effect on the yield. Alkynoates **2a** and **2b** worked well to furnish **8a** and **8b**, respectively, in good yield with good regioselectivity, like the case of **1** (Entries 1 and 2). Whereas phenyl-substituted alkynes (**2d** and **2g**) gave the products (**8d** and **8g**) in acceptable yield (Entries 3 and 4), a lower yield was observed in the reaction of dialkylacetylene **2j** (Enrty 5).

Table 2. Rhodium-catalyzed annulation of *o*-acetylphenylboronic acid (**7**) with alkynes **2**[a]



7 **2** **8**

Entry	**7** (equiv.)	**2** (R^1, R^2)	Time/h	**8**/%yield[b]
1	2.4	**2a** (CO_2Et, Me)	3	**8a**[c] (80)
2	2.4	**2b** (CO_2Et, $SiMe_3$)	3	**8b**[c] (75)
3	4.0	**2d** (Ph, Me)	24	**8d**[c] (61)
4	4.0	**2g** (Ph, Ph)	24	**8g** (68)
5	4.0	**2j** (Pr, Pr)	24	**8j** (25)

[a]Boronic acid **7** (0.96 mmol or 1.60 mmol), alkyne **2** (0.40 mmol), $[Rh(OH)(cod)]_2$ (8.0 μmol, 4 mol % Rh), 1,4-dioxane (2.0 mL), and water (50 μL) were heated at 80 °C. [b]Isolated yield by preparative TLC. [c]Good regioselectivities (>95:5) were observed by ^{1}H NMR.

In summary, we developed a simple synthetic route to substituted 1*H*-inden-1-ol derivatives through rhodium-catalyzed annulation of *o*-acylphenylboronic acids with alkynes.[13]

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