

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

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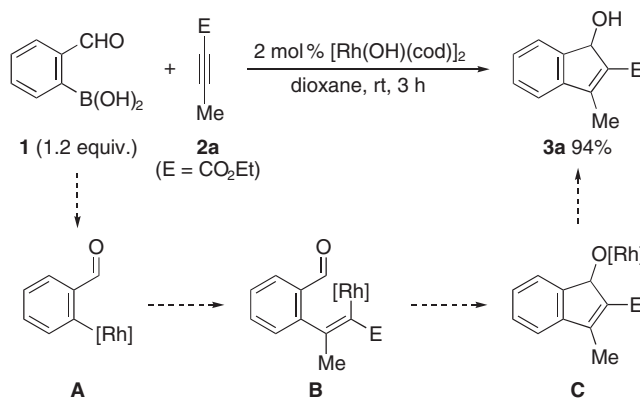
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A rhodium-catalyzed annulation reaction of *o*-formylphenylboronic acid with alkynes occurred regioselectively at room temperature to give substituted 1*H*-inden-1-ol derivatives. *o*-Acetylphenylboronic acid also underwent the annulation reaction 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 carbonyl² and cyano³ groups as well as carbon–carbon double⁴ and triple⁵ 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)]₂⁹ (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(sp²) 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.

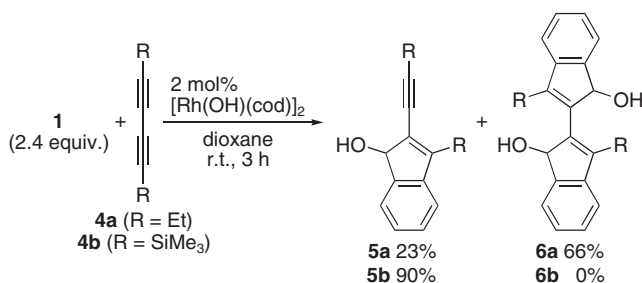
Table 1. Rhodium-catalyzed annulation of *o*-formylphenylboronic acid (**1**) with alkyne **2a**

Entry	2 (R ¹ , R ²)	3 (yield/%) ^b	Regioselectivity ^c
1	2b (CO ₂ Et, 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 ₂ OAc, CH ₂ OAc)	3f (73)	—
6 ^d	2g (Ph, Ph)	3g (70)	—
7	2h (<i>i</i> -Bu, H)	3h (36)	88:12
8	2i (Ph, H)	3i (20)	>98:2

^aUnless 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 μ mol, 4 mol % Rh) in 1,4-dioxane (2.0 mL) for 3 h.

^bIsolated yield. ^cDetermined by ¹H NMR. ^d10 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 dialkyl-acetylene **2j** (Entry 5).

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

Entry	7 (equiv.)	2 (R ¹ , R ²)	Time/h	8 /yield ^b
1	2.4	2a (CO ₂ Et, Me)	3	8a ^c (80)
2	2.4	2b (CO ₂ Et, 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)

^aBoronic 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. ^bIsolated yield by preparative TLC. ^cGood regioselectivities (>95:5) were observed by ¹H NMR.

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

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- A representative procedure for the rhodium-catalyzed reaction of **1** and **2a** (Scheme 1): To a mixture of boronic acid **1** (74.0 mg, 0.49 mmol) and [Rh(OH)(cod)]₂ (3.6 mg, 8.0 μmol) were added successively 1,4-dioxane (2.0 mL) and alkyne **2a** (46.7 mg, 0.42 mmol). After stirring the reaction mixture at room temperature for 3 h, hexane was added. The mixture was passed through a pad of Florisil® (hexane:AcOEt = 4:1). Removal of the volatile materials under reduced pressure gave **3a** (85.2 mg, 94%). **3a**: ¹H NMR (CDCl₃, 300 MHz) δ 1.40 (t, *J* = 7.2 Hz, 3H), 2.49 (d, *J* = 1.8 Hz, 3H), 3.30 (d, *J* = 2.4 Hz, 1H), 4.35 (q, *J* = 7.2 Hz, 2H), 5.40 (s, 1H), 7.35–7.44 (m, 3H), 7.55–7.62 (m, 1H); ¹³C NMR (CDCl₃, 75 MHz) δ 12.5, 14.4, 60.4, 75.8, 121.4, 123.9, 128.7, 129.0, 132.3, 142.5, 144.6, 152.7, 165.7. Anal. Calcd for C₁₃H₁₄O₃: C, 71.54; H, 6.47%. Found: C, 71.69; H, 6.53%.
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