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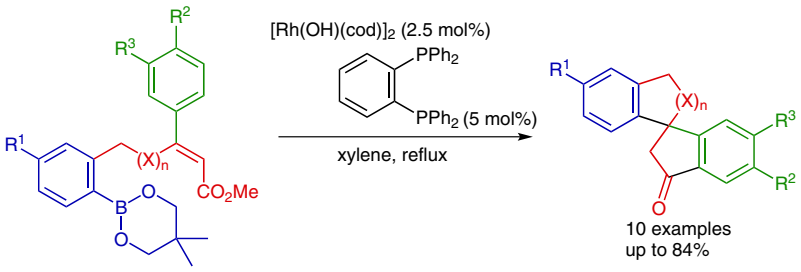
Rhodium-Catalyzed Addition–Spirocyclization of Arylboronic Esters Containing β-Aryl α,β-Unsaturated Ester Moiety

Takanori Matsuda*
Satoshi Yasuoka
Shoichi Watanuki
Keisuke Fukuhara

Department of Applied Chemistry, Tokyo University of Science, 1–3 Kagurazaka, Shinjuku-ku, Tokyo 162-8601, Japan
mtd@rs.tus.ac.jp



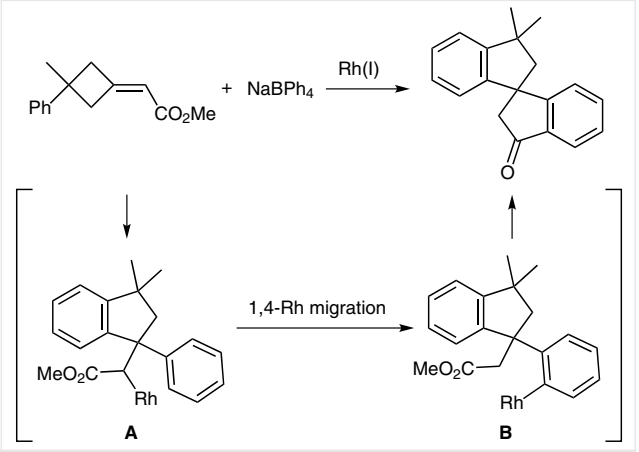
Received: 17.01.2015
Accepted after revision: 22.02.2015
Published online: 19.03.2015
DOI: 10.1055/s-0034-1378691; Art ID: st-2015-u0033-l

Abstract In this study, we developed a rhodium(I)-catalyzed spirocyclization. The reaction includes 1,4-rhodium migration and provides a route for forming spirocyclic 1-indanones.

Key words addition, boron, cyclization, rhodium, spiro compounds

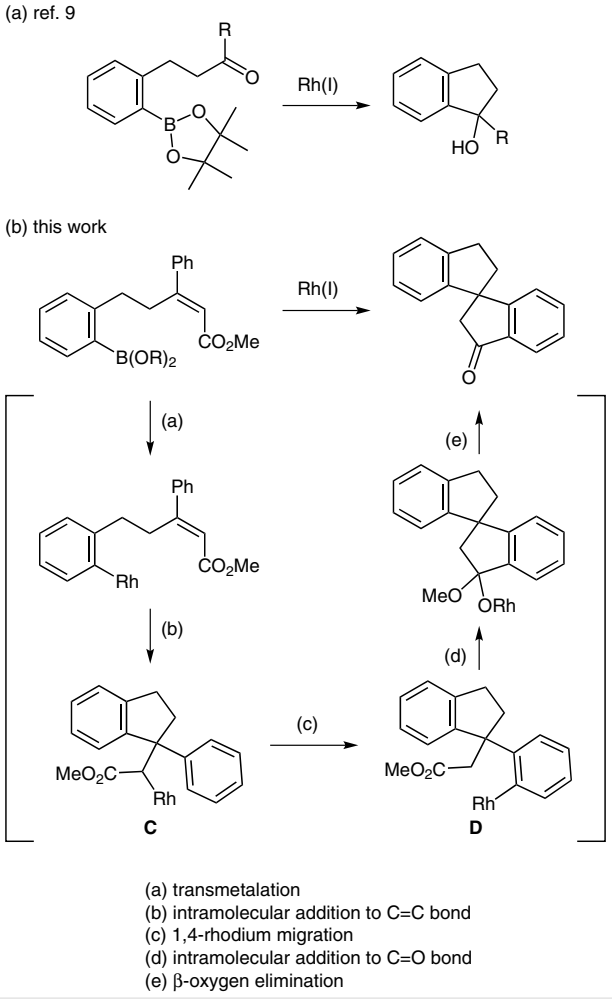
1,4-Rhodium migration is an effective intramolecular C–H bond-activation process,[1–5] which has been used in the formation of carbo- and heterocyclic frameworks.[3] Recently, we reported that 1,1′-spirobi[indan]-3-ones were synthesized using the rhodium-catalyzed addition–ring-expansion reaction of (3-arylcyclobutylidene)acetates involving successive 1,4-rhodium migration tandem (Scheme 1).[4] The second 1,4-rhodium migration in this reaction occurred with (1-phenylindan-1-ylmethyl)rhodium(I) species **A** to generate 2-(indan-1-yl)phenylrhodium(I) **B**, which subsequently reacted with the ester group to provide a spirocyclic structure.[6]

Rhodium(I)-catalyzed cyclization reactions of arylboronic acids and esters bearing electrophilic functionalities have been extensively studied.[7–9] In 2012, Sarpong et al. reported rhodium(I)-catalyzed asymmetric cyclization of arylboronic esters bearing a pendant ketone group (Scheme 2, a).[9] The reaction produced tertiary 1-indanols in good yields and enantioselectivities. We anticipated that the replacement of the ketone group with a β-aryl α,β-unsaturated ester group would cause spirocyclization through a mechanism analogous to our previous addition–ring-expansion of (3-arylcyclobutylidene)acetates (Scheme 2, b). Herein, we report rhodium(I)-catalyzed addition–spirocyclization of arylboronic esters containing a pendant β-aryl α,β-unsaturated ester moiety that produces 1,1′-spirobi[indan]-3-ones through 1,4-rhodium migration.



Scheme 1

Phenylboronic pinacol ester **1a**[10] bearing a β-phenyl α,β-unsaturated ester with *E* stereochemistry was heated in refluxing toluene in the presence of 5 mol% $[Rh(OH)(cod)]_2$ (cod = cycloocta-1,5-diene; Table 1, entry 1). Spirobiindanone **2a** was formed, as expected, in 52% yield, with an accompanying 24% yield of indanylacetate **3a**, derived from the protonation of organorhodium(I) species **C** or **D**. The addition of base was subsequently investigated to facilitate the conversion of the rather robust pinacol ester. After screening several organic and inorganic bases, higher conversion of (*E*)-**1a** was achieved when two equivalents of tetramethylethylenediamine (TMEDA) was added to the reaction, albeit with a worse **2a**/**3a** ratio (Table 1, entry 2). Further, we examined the effects of phosphine ligands on the



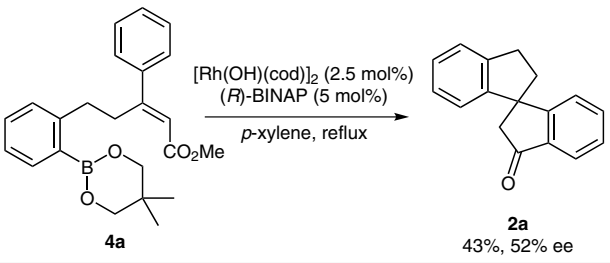
Scheme 2

rhodium-catalyzed cyclization of (*E*)-**1a**. The addition of DPPE [1,2-bis(diphenylphosphino)ethane] to the reaction improved the **2a**/**3a** ratio to 69:31 (Table 1, entry 3). The use of 2,2′-bis(diphenylphosphino)-1,1′-binaphthyl (BINAP) caused 76% total yield, with a **2a**/**3a** ratio of 59:41 (Table 1, entry 4). Among the diphosphine ligands investigated, 1,2-bis(diphenylphosphino)benzene (DPPBZ) exhibited superior activity in the reaction, producing **2a** in 63% yield (**2a**/**3a** = 70:30, Table 1, entry 5). In contrast, the reaction of (*Z*)-**1a** was significantly sluggish under the reaction conditions; **2a** was observed only in trace amounts in the crude reaction mixture (Table 1, entry 6). The unsatisfactory results with pinacol ester **1a** led us to utilize neopentyl glycol ester **4a**, since neopentyl glycol esters exhibit a greater reactivity relative to pinacol esters.[11] Although almost identical results were obtained when **4a** was subjected to the reaction conditions optimized for **1a** (Table 1, entry 7), the reaction of **4a** proceeded efficiently with a reduced amount of rhodium(I) catalyst without adding TMEDA, affording 78% yield of **2a** (**2a**/**3a** = 91:9, Table 1, entry 8). Gratifyingly, the suppression of the indane byproduct formation was finally possible when heated in refluxing xylene, providing 84% yield of **2a**, without any detectable formation of **3a** (Table 1, entry 9).[12]

Next, we examined the spirocyclization of various arylboronic neopentyl glycol esters **1** under the conditions with or without DPPBZ (Table 2). Phenylboronic ester **4b**–**d** containing 4-methylphenyl, 4-chlorophenyl and 4-methoxyphenyl groups at the β position of the α,β-unsaturated ester moiety produced spirobiindanones **2b**–**d** in good yields (Table 2, entries 1–3). The addition of DPPBZ as the ligand was found to be harmful to substrate **4e** having an aryl group with strong electron-withdrawing CF_3 substituent; trifluoromethyl-substituted products **2e** was obtained in 69% yield without using DPPBZ (Table 2, entry 4). For the reaction of 2-naphthyl derivative **4f**, 1,4-rhodium migration occurred selectively at the more sterically accessible site of the aromatic ring to provide the sole product **2f** in 65% yield (Table 2, entry 5), and 3-methoxyphenyl derivative **4g** similarly reacted to afford 6-methoxyspirobiindanone **2g** (Table 2, entry 6). The reaction of the 4-methoxyphenylboronic ester derivative **4h** produced an isomeric 5′-methoxyspirobiindanone **2h** in 74% yield (Table 2, entry 7). Substrates **4i** and **4j**, with one atom longer tethers, also participated in the spirocyclization, producing [5.6]-spirocyclic ketones **2i** and **2j** in modest yields (Table 2, entries 8 and 9).

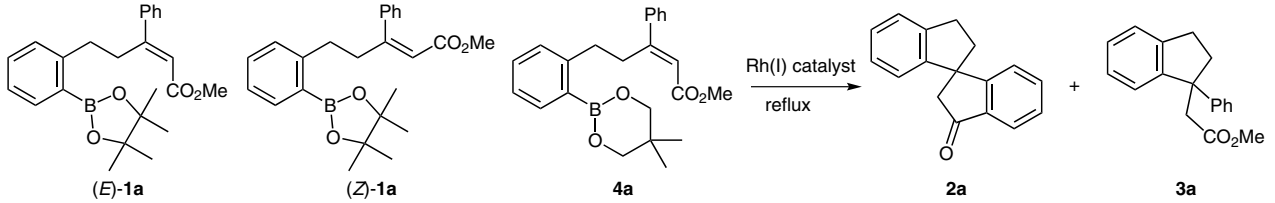
With successful demonstration of this new spiroannulation reaction, the asymmetric version of this process was examined (Scheme 3). The reaction of **4a** employing (*R*)-BINAP as the ligand afforded **2a** in 43% yield with 52% ee.[13]

In summary, a spirocyclization reaction synthesizing spirocyclic 1-indanones from phenylboronic esters, containing a pendant β-phenyl α,β-unsaturated ester moiety, was developed. The rhodium(I)-catalyzed reaction involved, in sequence, transmetalation, intramolecular addition to a C=C bond, 1,4-rhodium migration, intramolecular addition to a C=O bond, and β-oxygen elimination. We are currently focused on further exploration and exploitation of the migration of rhodium in synthesis toward complex cyclic structures.



Scheme 3

Table 1 Optimization of the Reaction Conditions for Rhodium-Catalyzed Addition–Spirocyclization[a]



(*E*)-**1a** (*Z*)-**1a** **4a** **2a** **3a**

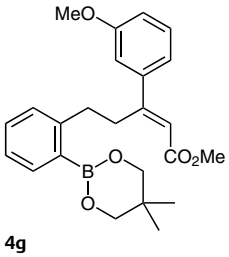
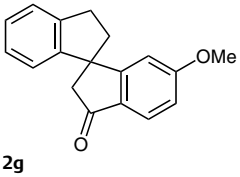
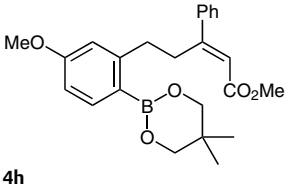
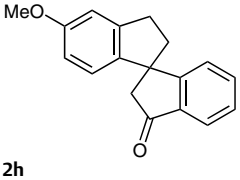
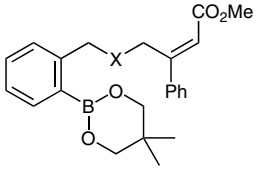
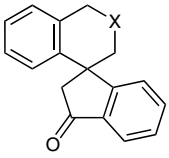
Entry	**1** or **4**	$[Rh(OH)(cod)]_2$ (mol%)	Phosphine ligand (mol%)	Additive (equiv)	Solvent	Yield of **2a** (%)[b]	Yield of **3a** (%)[c]
1	(*E*)-**1a**	5	none	none	toluene	52	24
2	(*E*)-**1a**	5	none	TMEDA (2)	toluene	46	50
3	(*E*)-**1a**	5	DPPE (10)	TMEDA (2)	toluene	60	27
4	(*E*)-**1a**	5	BINAP (10)	TMEDA (2)	toluene	45	31
5	(*E*)-**1a**	5	DPPBZ (10)	TMEDA (2)	toluene	63	27
6	(*Z*)-**1a**	5	DPPBZ (10)	TMEDA (2)	toluene	trace	–
7	**4a**	5	DPPBZ (10)	TMEDA (2)	toluene	63	30
8	**4a**	2.5	DPPBZ (5)	none	toluene	78	8
9	**4a**	2.5	DPPBZ (5)	none	xylene	84	–

[a] Conditions: **1a** or **4a** (0.10 mmol) was heated in toluene or xylene (1.0 mL) for 1–8 h in the presence of Rh catalyst.
[b] Isolated yield.
[c] Determined by ^{1}H NMR.

Table 2 Synthesis of Spirocyclic 1-Indanones through Rhodium-Catalyzed Addition–Spirocyclization of **4**[a]

Entry	**4**	**2**	Yield (%)[b] with DPPBZ	Yield (%)[b] without DPPBZ
1	**4b** R = Me	**2b**	76[c]	70
2	**4c** R = Cl	**2c**	68[d,e]	63
3	**4d** R = OMe	**2d**	73	71
4	**4e** R = CF_3	**2e**	(36)	69[d,e]
5	**4f**	**2f**	65	35

Table 2 (continued)

Entry	4	2	Yield (%)[b] with DPPBZ	Yield (%)[b] without DPPBZ
6	 **4g**	 **2g**	(44)	42
7	 **4h**	 **2h**	–[f]	74[g]
8	**4i** X = CH_2 	**2i** 	–[f]	42
9	**4j**[h] X = O	**2j**	–[f]	(40)[d]

[a] Arylboronic ester **4** was reacted in the presence of 5 mol% Rh catalyst in xylene (0.1 M) at 140 °C.
[b] Isolated yield. Yields in parentheses indicate yields determined by ^{1}H NMR spectroscopy.
[c] 44% yield with the corresponding pinacol ester [5 mol% $[Rh(OH)(cod)]_2$, toluene, reflux].
[d] The reaction produced mixtures of spirobiindanones **2** and indane byproducts **3** (**2c**/**3c** = 3:1, **2e**/**3e** = 5:1, **2j**/**3j** = 3:1).
[e] Pure products of **2** were obtained after the hydrolysis of esters **3** with a base.
[f] Not examined.
[g] 46% yield with the corresponding pinacol ester [5 mol% $[Rh(OH)(cod)]_2$, toluene, reflux].
[h] Used as a mixture of stereoisomers (*E*/*Z* = 78:22).

Acknowledgment

This work was supported by JSPS, Japan (Grant-in-Aid for Scientific Research (C) No. 25410054) and the Sumitomo Foundation.

Supporting Information

Supporting information for this article is available online at http://dx.doi.org/10.1055/s-0034-1378691.

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(12) **(*E*)-Methyl 5-[2-(5,5-dimethyl-1,3,2-dioxaborinan-2-yl)phenyl]-3-phenylpent-2-enoate (4a)**: White solid; mp 104–105 °C; ^{1}H NMR ($CDCl_3$, 301 MHz): δ = 0.98 (s, 6 H), 3.01–3.09 (m, 2 H), 3.31–3.40 (m, 2 H), 3.65 (s, 4 H), 3.78 (s, 3 H), 6.08 (s, 1 H), 7.15–7.22 (m, 1 H), 7.32–7.42 (m, 5 H), 7.51–7.57 (m, 2 H), 7.71–7.76 (m, 1 H). ^{13}C NMR ($CDCl_3$, 75.6 MHz): δ = 21.8, 31.5, 34.8, 35.2, 51.1, 72.0, 116.9, 125.1, 126.9, 128.4, 128.7, 129.9, 130.3, 134.8, 141.6, 147.6, 160.8, 166.7. HRMS (ESI) calcd for $C_{23}H_{27}BNaO_4$ $[M + Na]^+$ 401.1895; found: 401.1895. IR: 2960, 1712, 1301, 1161, 766 cm^{-1}.

General Procedure for Rhodium-Catalyzed Spirocyclization of Arylboronic Esters: To a Schlenk tube under nitrogen were added $[Rh(OH)(cod)]_2$ (1.2 mg, 2.6 μmol, 5 mol% Rh), 1,2-bis(diphenylphosphino)benzene (DPPBZ, 2.3 mg, 5.2 μmol), arylboronic ester 4 (0.100 mmol), and xylene (1.0 mL). The solution was stirred for 5 min. at rt, and the mixture was heated at 140 °C for 2 h. After cooling to r.t., the reaction mixture was filtered through a plug of Florisil® washing with hexane–EtOAc (3:1), and the filtrate was concentrated. The residue was purified by preparative TLC on silica gel (hexane–EtOAc) to afford **2**.

1,1′-Spirobi[indan]-3-one (2a): According to the general procedure, **4a** (37.9 mg, 0.100 mmol), $[Rh(OH)(cod)]_2$ (1.2 mg, 2.6 μmol), and DPPBZ (2.3 mg, 5.2 μmol) were treated in xylene (1.0 mL). Purification by preparative TLC on silica gel afforded **2a** (19.7 mg, 0.084 mmol, 84%) as a colorless oil. ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 2.37 (ddd, *J* = 12.7, 7.0, 5.5 Hz, 1 H), 2.52 (dt, *J* = 12.8, 8.2 Hz, 1 H), 2.85 (d, *J* = 18.9 Hz, 1 H), 3.00 (d, *J* = 18.9 Hz, 1 H), 3.10–3.20 (m, 2 H), 6.78 (d, *J* = 7.2 Hz, 1 H), 7.14 (dt, *J* = 0.8, 7.4 Hz, 1 H), 7.21 (dd, *J* = 7.3, 1.0 Hz, 1 H), 7.23–7.29 (m, 1 H), 7.32 (d, *J* = 7.2 Hz, 1 H), 7.37–7.46 (m, 1 H), 7.54– 7.62 (m, 1 H), 7.75–7.82 (m, 1 H); ^{13}C NMR ($CDCl_3$, 75.5 MHz): δ = 31.3, 42.9, 52.4, 54.5, 122.8, 123.1, 124.6, 125.1, 127.2, 127.3, 127.9, 135.4, 136.1, 143.3, 148.9, 161.5, 205.7. HRMS (ESI) calcd for $C_{17}H_{14}NaO$ $[M + Na]^+$ 257.0937; found: 257.0937. IR: 2948, 1716, 1602, 1236, 758 cm^{-1}.

(13) Asymmetric reaction: **4a** (37.8 mg, 0.100 mmol), $[Rh(OH)(cod)]_2$ (1.1 mg, 2.4 μmol), and (*R*)-BINAP (3.1 mg, 5.0 μmol) were reacted in xylene (1.0 mL) at 140 °C. Purification by preparative TLC on silica gel yielded **2a** (10.1 mg, 0.043 mmol, 43%); 52% ee determined by HPLC analysis (CHIRALCEL® OJ-H column, hexane–*i*-PrOH (90:10), 1.0 mL/min, t_{minor} = 7.7 min, t_{major} = 10.0 min).