

Addition/Ring-Opening Reaction of Organoboronic Acids to Cyclobutanones Catalyzed by Rhodium(I)/P(*t*-Bu)$_3$ Complex

Takanori Matsuda, Masaomi Makino, and Masahiro Murakami*

Department of Synthetic Chemistry and Biological Chemistry, Graduate School of Engineering, Kyoto University, Katsura, Kyoto 615-8510

Received February 3, 2005; E-mail: murakami@sbchem.kyoto-u.ac.jp

An addition/ring-opening reaction of aryl- and alkenylboronic acids to cyclobutanones took place in 1,4-dioxane at 100 °C in the presence of a rhodium(I) catalyst bearing tri-*t*-butylphosphine, affording ring-opened ketones. Mechanistically, the reaction proceeded through the addition of an organorhodium species to the carbonyl group of a cyclobutanone and a subsequent ring-opening of the resulting rhodium cyclobutanolate through β-carbon elimination. A deuterium-labeling experiment revealed that an alkylrhodium species generated by the β-carbon elimination underwent successive β-hydride elimination/re-addition processes to form the η^3-oxaallylrhodium intermediate, which was readily protonated to afford the product.

Carbon–carbon bond forming reactions with organoboron compounds have gained considerable interest in synthetic organic chemistry because of the ease of accessibility, substantial stabilities, and low environmental impact of organoboron compounds compared with other conventional organometallics, like organolithium and organotin reagents.[1] Especially, the palladium-catalyzed cross-coupling reaction of aryl- and alkenylboron reagents[2] has found wide applications in industrial processes as well as in laboratory syntheses. Recently, new rhodium-catalyzed addition reactions of arylboron compounds to unsaturated functionalities have been developed.[3] An arylrhodium species, generated from arylboron compounds via transmetalation, adds to α,β-unsaturated carbonyl compounds,[4] aldehydes,[5] imines,[6] alkynes,[7] and alkenes.[8]

On the other hand, carbon–carbon bond cleavage reactions by means of transition metals have also attracted much attention. They achieve an otherwise inaccessible organic transformation.[9] We have explored the catalytic carbon–carbon bond cleavage reactions of cyclobutanones, wherein a rhodium(I) complex inserts between the carbonyl carbon and the α-carbon.[10] In search of a rhodium complex with higher catalytic activity, we envisaged that an arylrhodium(I) species, which is more electron-rich than a rhodium(I) halide, could be more easily oxidized to a rhodium(III) species.[11] Hence, its insertion into the carbon–carbon single bond would be more facilitated. Thus, we investigated the rhodium-catalyzed reaction of cyclobutanones with arylboronic acids. We report here a full account of the rhodium-catalyzed addition/ring-opening reaction of cyclobutanones with organoboronic acids.[12] The related reaction with a benzocyclobutenone is also described.

Results and Discussion

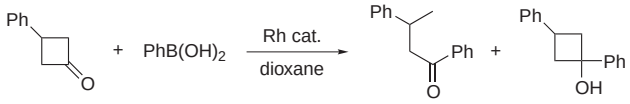
A mixture of 3-phenylcyclobutanone (**1a**) and phenylboronic acid (**2a**, 3.0 equiv to **1a**) in 1,4-dioxane was heated at 100 °C in the presence of a rhodium(I) complex (5 mol %) generated in situ from [Rh(acac)(C_2H_4)$_2$] (acac = acetylacetonato) and tri-*t*-butylphosphine (Rh:P = 1:2) (Table 1, Entry 1). The cyclobutanone **1a** was consumed within 30 min, and a mixture of the 1,2-addition product **4aa** and the ring-opened ketone **3aa** was formed, with the former predominating. As the reaction progressed, **4aa** decreased, and after heating for 8 h, **3aa** was formed as the exclusive product. This observation indicated that cyclobutanol **4aa** was initially produced, and then underwent isomerization to the ketone **3aa** under the reaction conditions (vide infra). The reaction required three equivalents of boronic acid and 5 mol % of rhodium catalyst to reach completion. Reducing the amount of **2a** decreased the yield (Entries 2 and 3). With lower catalyst loadings (1 or 3 mol %), the reaction was incomplete even after 45 h, probably due to deterioration of the catalyst (Entries 4 and 5). No reaction occurred with the use of [Rh(acac)(cod)] and [Rh(OH)(cod)]$_2$ having cycloocta-1,5-diene (cod) instead of ethylene ligands (Entries 6 and 7). An Rh:P ratio of 1:2 gave the best yield of **3aa** (Entries 8 and 9). Tricyclohexylphosphine showed moderate activity, while triphenylphosphine failed to promote the reaction (Entries 10 and 11). The reaction temperature was also important to obtain **3aa** in high yield. Lowering the reaction temperature led to the predominant formation of **4aa**, suggesting that conversion from **4aa** to **3aa** requires a higher temperature (Entries 12–14). The addition of water to the solvent (1,4-dioxane:water = 10:1) retarded the reaction (Entry 15).

The results obtained with sterically more demanding *o*-tolylboronic acid (**2b**) are given in Table 2. The reaction of cyclobutanone **1a** with **2b** was sluggish (Table 2), and **1a** remained even after 48 h (Entry 1). To our delight, the addition of an inorganic base as an additive (1 equiv to **1a**) facilitated the reaction. In particular, the use of Cs_2CO_3 led to the quantitative conversion of **1a** within 3 h.

Next, the reactivity of the isolated tertiary cyclobutanol was examined. When **4aa** and **4ab**[13] were heated under identical conditions, the ring-opening reaction took place to afford the

Published on the web August 4, 2005; DOI 10.1246/bcsj.78.1528

Table 1. Reaction of 3-Phenylcyclobutanone (**1a**) with Phenylboronic Acid (**2a**) in the Presence of Rhodium(I)–Phosphine Catalysts[a)]

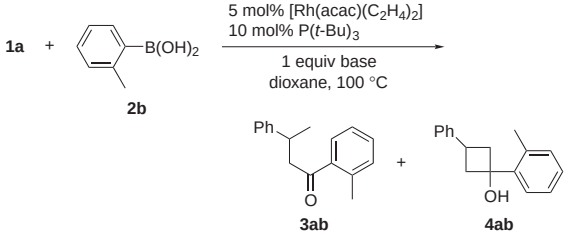


1a **2a** **3aa** **4aa**

Entry	**2a**/equiv	Rh complex/mol %	Phosphine ligand/mol %	Temp	Time/h	**3aa**/%	**4aa**/%
1	3.0	$[Rh(acac)(C_2H_4)]_2$/5	P(*t*-Bu)$_3$/10	100 °C	0.5	15	80
					2	52	44
					8	97	—
2	2.0	$[Rh(acac)(C_2H_4)]_2$/5	P(*t*-Bu)$_3$/10	100 °C	8	82	—
3	1.2	$[Rh(acac)(C_2H_4)]_2$/5	P(*t*-Bu)$_3$/10	100 °C	8	67	—
4	3.0	$[Rh(acac)(C_2H_4)]_2$/3	P(*t*-Bu)$_3$/6	100 °C	45	12	55
5	3.0	$[Rh(acac)(C_2H_4)]_2$/1	P(*t*-Bu)$_3$/2	100 °C	45	2	35
6	3.0	[Rh(acac)(cod)]/5	P(*t*-Bu)$_3$/10	100 °C	24	0	0
7	3.0	$[Rh(OH)(cod)]_2$/2.5	P(*t*-Bu)$_3$/10	100 °C	24	0	—
8	3.0	$[Rh(acac)(C_2H_4)]_2$/5	P(*t*-Bu)$_3$/5	100 °C	8	68	29
9	3.0	$[Rh(acac)(C_2H_4)]_2$/5	P(*t*-Bu)$_3$/15	100 °C	8	78	18
10	3.0	$[Rh(acac)(C_2H_4)]_2$/5	P(*c*-Hex)$_3$/10	100 °C	24	65	14
11	3.0	$[Rh(acac)(C_2H_4)]_2$/5	PPh_3/10	100 °C	24	5	—
12	3.0	$[Rh(acac)(C_2H_4)]_2$/5	P(*t*-Bu)$_3$/10	80 °C	8	38	53
13	3.0	$[Rh(acac)(C_2H_4)]_2$/5	P(*t*-Bu)$_3$/10	60 °C	8	11	89
14	3.0	$[Rh(acac)(C_2H_4)]_2$/5	P(*t*-Bu)$_3$/10	rt	8	3	55
15[b)]	3.0	$[Rh(acac)(C_2H_4)]_2$/5	P(*t*-Bu)$_3$/10	100 °C	8	12	63
					24	34	43

a) Unless otherwise noted, the reaction was carried out with 3-phenylcyclobutanone (**1a**, 0.50 mmol), phenylboronic acid (**2a**, 1.50 mmol) in 1,4-dioxane (1.0 mL) in the presence of rhodium catalysts, and the yields were determined by GC analysis. b) The reaction was carried out in 1,4-dioxane–H_2O (10:1).

Table 2. Effect of Base on the Rhodium-Catalyzed Reaction of **1a** with *o*-Tolylboronic Acid **2b**[a)]

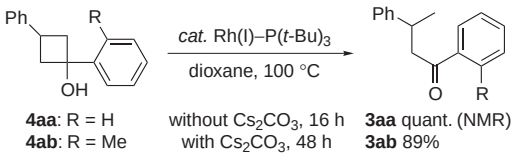


2b **3ab** **4ab**

Entry	Base	Time/h	**3ab**/%[b)]	**4ab**/%[b)]
1	none	48	51	15
2	$NaHCO_3$	24	54	12
3	KF	24	81	—
4	KOH	3	75	11
		24	94	—
5	Cs_2CO_3	3	90	10
		24	99	—

a) A mixture of **1a** (0.50 mmol), **2b** (1.50 mmol), $[Rh(acac)(C_2H_4)_2]$ (0.025 mmol), P(*t*-Bu)$_3$ (0.050 mmol), and base (0.50 mmol) was heated in 1,4-dioxane (1.0 mL) at 100 °C. b) Determined by GC.

corresponding butyrophenone derivatives, **3aa** and **3ab**, respectively, in high yield (Scheme 1). On the other hand, the ring-opening failed to occur in the absence of the rhodium catalyst, suggesting that the ring-opening process was also catalyzed by rhodium. These results are consistent with our proposed mechanism for the reaction of **1** with **2** (vide infra).



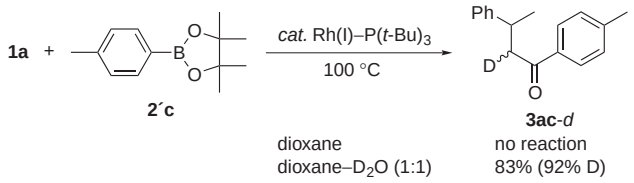
4aa: R = H
4ab: R = Me

without Cs_2CO_3, 16 h **3aa** quant. (NMR)
with Cs_2CO_3, 48 h **3ab** 89%

Scheme 1.

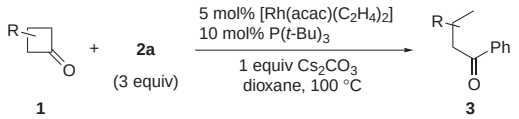
In contrast to boronic acid **2c**, the corresponding boronic ester **2′c** failed to react with **1a** in anhydrous 1,4-dioxane. The reaction of **2′c** worked well, however, in a mixed solvent of 1,4-dioxane–water (1:1). It is likely that the reaction requires protic hydrogens to regenerate the rhodium catalyst from the produced rhodium compound. In the reaction with boronic acid **2**, protons of the boronic acid moiety served as the proton source. These results led us to carry out a deuterium experiment using **2′c** in order to obtain mechanistic information. When the reaction of **2′c** was carried out in 1,4-dioxane–D_2O (1:1), deuterium was incorporated not at the expected γ-position of the produced ketone, but exclusively at the α-position (Scheme 2).[14]

The formation of the intermediary cyclobutanol **4** suggested that the insertion of rhodium into the carbonyl carbon and the α-carbon giving a five-membered cyclic acylrhodium inter-



Scheme 2.

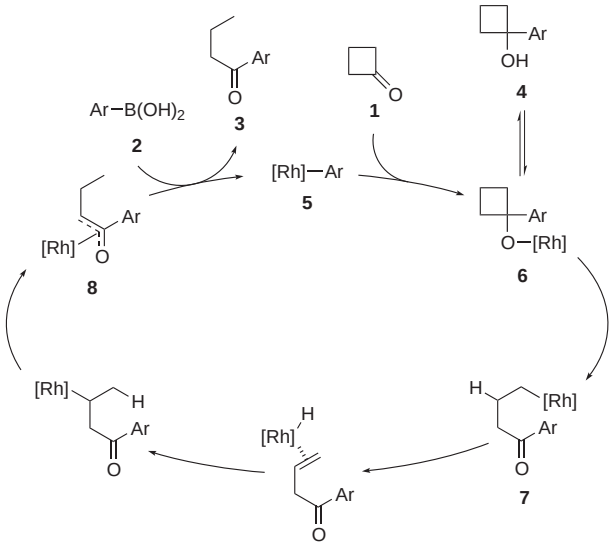
Table 3. Rhodium-Catalyzed Addition/Ring-Opening Reaction of Cyclobutanones **1** with Phenylboronic Acid (**2a**)[a)]



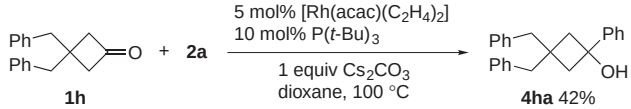
Entry	Cyclobutanone **1**	Product **3**	Yield/%[b)]
1	**1a**	**3aa**	95
2	**1b**	**3ba**	78
3	**1c**	**3ca**	79
4	**1d**	**3da**	75
5	**1e**	**3ea** + **3′ea** (77:23)[c),d)]	52
6	**1f**	**3fa** (*cis*:*trans* = 28:27)[c)]	76
7	**1g**		0

a) All reaction were carried out with cyclobutanone **1** (0.50 mmol), phenylboronic acid (**2a**, 1.50 mmol), [Rh(acac)-$(C_2H_4)_2$] (5 mol%), P(*t*-Bu)$_3$ (10 mol%), and Cs_2CO_3 (0.50 mmol) in 1,4-dioxane (1.0 mL) at 100 °C for 24–72 h. b) Isolated yield. c) Obtained as a mixture of isomers. The ratios were determined by ^{1}H NMR. d) Cyclobutanol was also isolated in 10% yield.

mediate is unlikely. Rather, we assume a mechanism that involves the 1,2-addition of arylrhodium to the carbonyl group[15] of cyclobutanone **1**, and a subsequent ring-opening of the resulting rhodium cyclobutanolate through β-carbon elimination. Scheme 3 summarizes our mechanistic hypothesis. The catalytic cycle involves (i) the addition of arylrhodium species **5** to **1**, (ii) ring-opening of rhodium cyclobutanolate **6** by β-carbon elimination to alkylrhodium intermediate **7**,[16] (iii) repetition of a β-hydride elimination/re-addition process[17] twice leading to η^3-oxaallylrhodium **8**, and (iv) protonolysis and transmetalation with boronic acid **2**, generating butyrophenone **3** and arylrhodium species **5**.



Scheme 3.



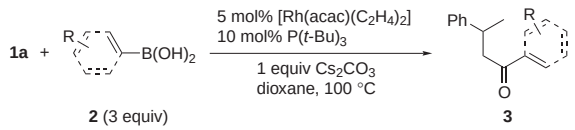
Scheme 4.

Other examples of the rhodium-catalyzed addition/ring-opening reaction of a series of cyclobutanones under the optimized reaction conditions using Cs_2CO_3 are listed in Table 3. The reaction of 3-aryl or 3-alkylcyclobutanones **1a–d** afforded the corresponding products **3aa–3da** in good yield (Entries 1–4). In the reaction of 2-phenylcyclobutanone (**1e**), β-carbon elimination took place either at the C(1)–C(4) or C(1)–C(2) bond to yield two products, **3ea** and **3′ea**, with the former predominating (Entry 5). Regioselective β-carbon elimination at the less-substituted carbon was observed with indene-derived cyclobutanone **1f** to give product **3fa** as a mixture of *cis*- and *trans*-isomers (Entry 6). This stereoisomerism is consistent with the proposed mechanism involving an η^3-oxaallylrhodium species. No reaction occurred with 2,2-disubstituted cyclobutanone **1g** due to steric reasons (Entry 7).

3,3-Disubstituted cyclobutanone **1h** gave cyclobutanol **4ha** in 42% yield upon a treatment with **2a** (Scheme 4).[18] β-Carbon elimination from **6** might be sterically hampered by disubstitution at the 3-position.

Analogous reactions were attempted with other less-strained cyclic ketones. No reaction occurred with cycloalkanones with five- to eight-membered rings under the present reaction conditions. The increased reactivity of cyclobutanones is ascribed to the strain of the four-membered ring;[19] the carbonyl sp^2 car-

Table 4. Rhodium-Catalyzed Addition/Ring-Opening Reaction of 3-Phenylcyclobutanone (**1a**) with Boronic Acids **2**[a)]



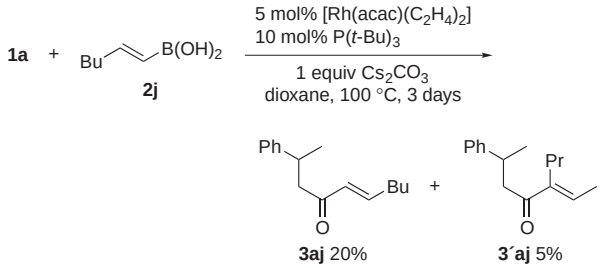
2 (3 equiv) **3**

Entry	Boronic acid **2**	Time/h	Product **3**	Yield/%[b)]
1	**2b**	24	**3ab**	72
2	**2c**	24	**3ac**	82
3	**2d**	24	**3ad**	77
4[c)]	**2′c**	24	**3ac**	73
5	**2e**	72	**3ae**	38
6	**2f**	24	**3af**	42
7	**2g**	120	**3ag**	39
8	**2h**	72	**3ah**	44
9	**2i**	72	**3ai**	47

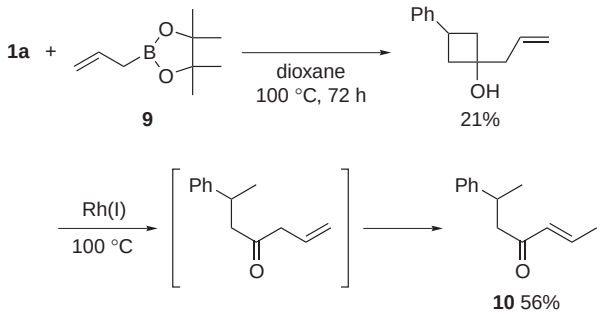
a) All reaction were carried out with 3-phenylcyclobutanone (**1a**, 0.50 mmol), boronic acid **2** (1.50 mmol), Rh(acac)-$(C_2H_4)_2$ (5 mol%), P(*t*-Bu)$_3$ (10 mol%), and Cs_2CO_3 (0.50 mmol) in 1,4-dioxane (1.0 mL) at 100 °C. b) Isolated yield by preparative TLC. c) The reaction was carried out in 1,4-dioxane–H_2O (1.0 mL:1.0 mL).

bon changes to an sp^3 carbon upon adding the arylrhodium, thereby diminishing the ring strain. The β-carbon elimination step would also be facilitated by release of the ring strain.

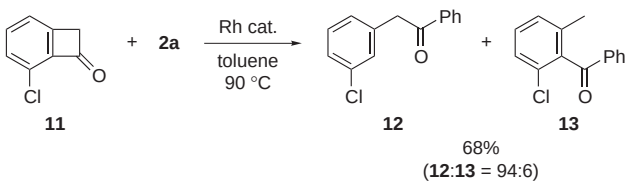
As summarized in Table 4, various organoboronic acids **2** can participate in the addition/ring-opening with cyclobutanone **1a**. Three isomeric tolylboronic acids **2b–d** gave the corresponding butyrophenones **3ab–3ad** in good yield (Entries 1–3). Pinacol ester **2′c** also underwent the reaction in the presence of water (Entry 4). Sterically bulkier mesitylboronic acid **2e** was less reactive, giving a 38% yield of **3ae** (Entry 5). Only moderate yields were obtained with both electron-donating and -withdrawing aromatic substituents (Entries 6 and 7). Some alkenylboronic acids, **2h** and **2i**, afforded the corresponding α,β-unsaturated ketones, **3ah** (44%) and **3ai** (47%), respectively (Entries 8 and 9).



Scheme 5.



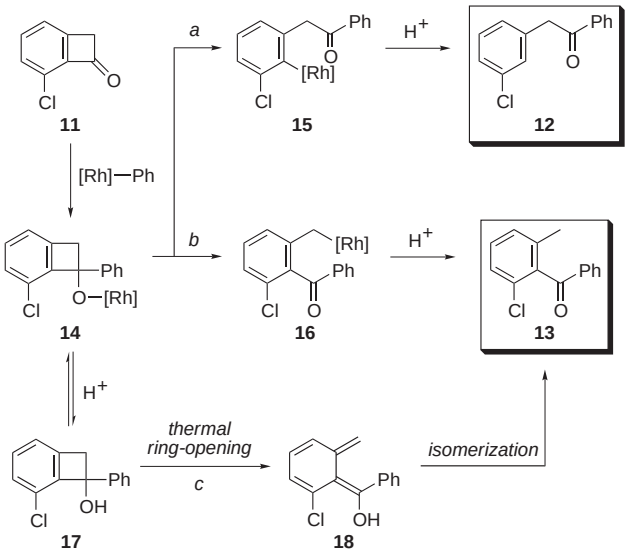
Scheme 6.



Scheme 7.

In the reaction of **1a** with (*E*)-hex-1-enylboronic acid (**2j**), a small amount of by-product **3′aj** was isolated along with ordinary product **3aj** (Scheme 5). It is likely that the by-product was formed via the isomerization of **2j** to allylboronic acid, the allylation of cyclobutanone **1a**, the rhodium-catalyzed ring-opening of the tertiary cyclobutanol, and isomerization of the resulting β,γ-unsaturated ketone to α,β-unsaturated ketone **3′aj** under the reaction conditions. In fact, when allylboronic ester **9** was reacted with **1a**, the α,β-unsaturated ketone **10** was produced through rhodium-catalyzed ring-opening/isomerization (Scheme 6).

When benzocyclobutenone **11** was subjected to identical reaction conditions, two ring-opened products, 2-phenylacetophenone **12** and 2-methylbenzophenone **13**, were obtained in a ratio of 94:6 (Scheme 7).



Scheme 8.

A mechanistic explanation for the formation of **12** and **13** from **11** is illustrated in Scheme 8. The addition of arylrhodium to **11** gives the rhodium alcoholate **14**. β-Carbon elimination with the aromatic *ipso* carbon produces phenylrhodium **15**. Protonolysis of **15** furnishes **12** (path *a*). For the minor product **13**, there are two possible reaction pathways. Like path *a*, β-carbon elimination with the benzylic carbon of **14** affords **16**, and then the protonolysis of **16** gives **13** (path *b*). On the other hand, **14** or protonated tertiary alcohol **17** might undergo a thermal ring-opening reaction in a concerted manner to give the *o*-quinodimethane derivative **18** (path *c*).[20] Prototropic isomerization would also lead to **13**. In fact, benzocyclobutenol **17**, independently prepared, underwent thermal ring-opening at 90 °C to give **13**, suggesting that the pathway is also conceivable.

Conclusion

We developed a rhodium(I)-catalyzed addition/ring-opening reaction of aryl- and alkenylboronic acids to cyclobutanones. The reaction gave ring-opened ketones through β-carbon elimination from a rhodium cyclobutanolate and successive β-hydride elimination/re-addition of the resulting alkylrhodium species, leading to an η^3-oxaallylrhodium. It was demonstrated that β-carbon elimination from transition metal cyclobutanolates occurs with rhodium(I) as well as with palladium(II).[16] The synthetic potential of the ring-opening protocol of transition metal cycloalkanolates will be further exploited.

This work was supported by a Grant-in-Aid for Young Scientists (B) (No. 15750085) from the Ministry of Education, Culture, Sports, Science and Technology, Japan. We thank H. Ushitora for obtaining the HRMS data.

Supporting Information

Experimental procedures and characterization data for new compounds. This material is available free of charge on the Web at http://www.csj.jp/journals/bcsj/.

References

1 a) H. C. Brown, "Organic Syntheses via Boranes," Wiley-Interscience, New York (1975). b) D. S. Matteson, "Stereodirected Synthesis with Organoboranes," Springer-Verlag, Berlin (1995).

2 a) N. Miyaura and A. Suzuki, *Chem. Rev.*, **95**, 2457 (1995). b) A. Suzuki, *J. Organomet. Chem.*, **576**, 147 (1999). c) A. Suzuki, "Metal-Catalyzed Cross-Coupling Reactions," ed by F. Diederich and P. J. Stang, VCH, Weinheim (1998), p. 49.

3 a) K. Fagnou and M. Lautens, *Chem. Rev.*, **103**, 169 (2003). b) T. Hayashi and K. Yamasaki, *Chem. Rev.*, **103**, 2829 (2003).

4 a) M. Sakai, H. Hayashi, and N. Miyaura, *Organometallics*, **16**, 4229 (1997). b) S. Sakuma and N. Miyaura, *J. Org. Chem.*, **66**, 8944 (2001). c) T. Hayashi, M. Takahashi, Y. Takaya, and M. Ogasawara, *J. Am. Chem. Soc.*, **124**, 5052 (2002). d) M. Kuriyama, K. Nagai, K.-i. Yamada, Y. Miwa, T. Taga, and K. Tomioka, *J. Am. Chem. Soc.*, **124**, 8932 (2002). e) R. Itooka, Y. Iguchi, and N. Miyaura, *J. Org. Chem.*, **68**, 6000 (2003). f) R. Shintani, K. Ueyama, I. Yamada, and T. Hayashi, *Org. Lett.*, **6**, 3425 (2004). g) J.-G. Boiteau, R. Imbos, A. J. Minnaard, and B. L. Feringa, *Org. Lett.*, **5**, 681 (2003).

5 a) M. Sakai, M. Ueda, and M. Miyaura, *Angew. Chem., Int. Ed.*, **37**, 3279 (1998). b) M. Ueda and N. Miyaura, *J. Org. Chem.*, **65**, 4450 (2000). c) M. Pucheault, S. Darses, and J.-P. Genet, *J. Am. Chem. Soc.*, **126**, 15356 (2004).

6 a) M. Ueda, A. Saito, and N. Miyaura, *Synlett*, **2000**, 1637. b) M. Kuriyama, T. Soeta, X. Hao, Q. Chen, and K. Tomioka, *J. Am. Chem. Soc.*, **126**, 8128 (2004). c) N. Tokunaga, Y. Otomaru, K. Okamoto, K. Ueyama, R. Shintani, and T. Hayashi, *J. Am. Chem. Soc.*, **126**, 13584 (2004).

7 a) T. Hayashi, K. Inoue, N. Taniguchi, and M. Ogasawara, *J. Am. Chem. Soc.*, **123**, 9918 (2001). b) M. Lautens and M. Yoshida, *Org. Lett.*, **4**, 123 (2002). c) M. Murakami and H. Igawa, *Helv. Chim. Acta*, **85**, 4182 (2002). d) M. Lautens and M. Yoshida, *J. Org. Chem.*, **68**, 762 (2003).

8 a) M. Lautens, A. Roy, K. Fukuoka, K. Fagnou, and B. Martin-Matute, *J. Am. Chem. Soc.*, **123**, 5358 (2001). b) M. Lautens, C. Dockendorff, K. Fagnou, and A. Malicki, *Org. Lett.*, **4**, 1311 (2002). c) M. Murakami and H. Igawa, *Chem. Commun.*, **2002**, 390.

9 a) R. H. Crabtree, *Chem. Rev.*, **85**, 245 (1985). b) M. Murakami and Y. Ito, "Activation of Unreactive Bond and Organic Synthesis," in "Topics in Organometallic Chemistry," ed by S. Murai, Springer, Berlin (1999), Vol. 3, p. 97. c) B. Rybtchinski and D. Milstein, *Angew. Chem., Int. Ed.*, **38**, 870 (1999). d) T. Mitsudo and T. Kondo, *Synlett*, **2001**, 309. e) C.-H. Jun, C. W. Moon, and D.-Y. Lee, *Chem.—Eur. J.*, **8**, 2422 (2002).

10 a) M. Murakami, H. Amii, and Y. Ito, *Nature*, **370**, 540 (1994). b) M. Murakami, H. Amii, K. Shigeto, and Y. Ito, *J. Am. Chem. Soc.*, **118**, 8285 (1996). c) M. Murakami, K. Takahashi, H. Amii, and Y. Ito, *J. Am. Chem. Soc.*, **119**, 9307 (1997). d) M. Murakami, T. Itahashi, H. Amii, K. Takahashi, and Y. Ito, *J. Am. Chem. Soc.*, **120**, 9949 (1998). e) M. Murakami, T. Tsuruta, and Y. Ito, *Angew. Chem., Int. Ed.*, **39**, 2484 (2000). f) M. Murakami, T. Itahashi, and Y. Ito, *J. Am. Chem. Soc.*, **124**, 13976 (2002). g) T. Matsuda, A. Fujimoto, M. Ishibashi, and M. Murakami, *Chem. Lett.*, **33**, 876 (2004).

11 L. S. Hegedus, S. M. Lo, and D. E. Bloss, *J. Am. Chem. Soc.*, **95**, 3040 (1973).

12 A part of this work appeared as a preliminary communication: T. Matsuda, M. Makino, and M. Murakami, *Org. Lett.*, **6**, 1257 (2004).

13 Tertiary cyclobutanols **4aa** and **4ab** were synthesized independently by the reaction of **1a** with the corresponding Grignard reagents and used as a diastereomeric mixture (**4aa**: *cis*:*trans* = 96:4; **4ab**: *cis*:*trans* = 74:26).

14 The diastereomer ratio of **3ab**-*d* was determined to be 64:36 by ^{1}H NMR; however, the relative stereochemistries were not determined.

15 Insertion of aldehyde into rhodium–aryl bond was observed by Hartwig. C. Krug and J. F. Hartwig, *J. Am. Chem. Soc.*, **124**, 1674 (2002).

16 For a review on β-carbon elimination from Pd(II) cyclobutanolate, see: T. Nishimura and S. Uemura, *Synlett*, **2004**, 201.

17 For transition metal–hydride elimination followed by re-addition with the opposite regiochemistry, see: a) K. Yoshida and T. Hayashi, *J. Am. Chem. Soc.*, **125**, 2872 (2003). b) S. V. Gagnier and R. C. Larock, *J. Am. Chem. Soc.*, **125**, 4804 (2003). c) M. Suginome, T. Matsuda, and Y. Ito, *J. Am. Chem. Soc.*, **122**, 11015 (2000).

18 Ring-opened ketone was also isolated in 2%.

19 For synthetic applications of cyclobutane derivatives, see: J. C. Namyslo and D. E. Kaufmann, *Chem. Rev.*, **103**, 1485 (2003).

20 a) C. J. Bungard and J. C. Morris, *J. Org. Chem.*, **67**, 2361 (2002). b) J. L. Segura and N. Martín, *Chem. Rev.*, **99**, 3199 (1999). c) T. Hamura, M. Miyamoto, K. Imura, T. Matsumoto, and K. Suzuki, *Org. Lett.*, **4**, 1675 (2002).