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# Stereoselective Synthesis of *syn*-Configured α-Allenols by Rhodium-Catalyzed Reaction of Alkynyl Oxiranes with Arylboronic Acids

Tomoya Miura,[†] Masahiko Shimada,[†] Paula de Mendoza,[§] Carl Deutsch,[‡] Norbert Krause,[‡] and Masahiro Murakami*,[†]

[†]*Department of Synthetic Chemistry and Biological Chemistry, Kyoto University, Katsura, Kyoto 615-8510, Japan, and* [‡]*Organic Chemistry II, Dortmund University of Technology, Otto-Hahn-Strasse 6, D-44227 Dortmund, Germany.* [§]*On leave from Institute of Chemical Research of Catalonia (ICIQ), Av. Països Catalans 16, 43007 Tarragona, Spain*

*murakami@sbchem.kyoto-u.ac.jp*

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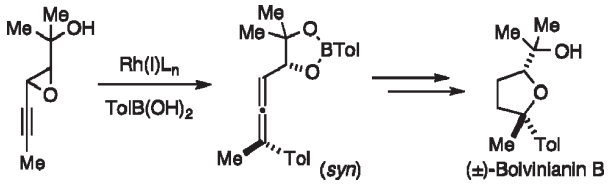


A rhodium-catalyzed reaction of alkynyl oxiranes with arylboronic acids affords *syn*-configured α-allenols with high diastereoselectivity. The reaction is initiated by addition of an arylrhodium(I) species onto the alkyne moiety of the alkynyl oxirane. The resulting alkenylrhodium(I) intermediate undergoes *β*-oxygen elimination to open the oxirane ring in a *syn*-selective fashion. Protonolysis of the rhodium(I) alkoxide with arylboronic acid releases the corresponding α-allenol along with the rhodium(I) boronate, which undergoes *β*-aryl elimination to regenerate the arylrhodium(I) species. The utility of this method is demonstrated by an application to a concise synthesis of (±)-Boivinianin B.

## Introduction

Allenes are an important class of building blocks in organic synthesis.[1] In particular, substituted α-allenols are useful precursors for the stereoselective construction of dihydrofurans and tetrahydrofurans possessing chiral centers at the 2- and/or 5-positions,[2] which are a structural motif often found in natural products of potent biological activities, such as the mycotoxins[3] and kalihinanes.[4] Therefore, methods to prepare substituted α-allenols in a stereocontrolled way are in high demand. The $S_N2'$-type reaction of alkynyl oxiranes with organometallic reagents presents one of the most reliable procedures. Organocopper and organocuprate reagents preferentially afford *anti*-configured[5] α-allenols,[6] with a few exceptions.[7] Palladium-catalyzed

(1) Reviews: (a) *Modern Allene Chemistry*; Krause, N., Hashmi, A. S. K., Eds.; Wiley-VCH: Weinheim, Germany, 2004; Vols. 1 and 2. (b) Ma, S. *Chem. Rev.* **2005**, *105*, 2829. (c) Ma, S. *Aldrichimica Acta* **2007**, *40*, 91.

(2) Reviews: (a) Bates, R. W.; Satcharoen, V. *Chem. Soc. Rev.* **2002**, *31*, 12. (b) Ma, S. *Acc. Chem. Res.* **2003**, *36*, 701. (c) Krause, N.; Belting, V.; Deutsch, C.; Erdsack, J.; Fan, H.-T.; Gockel, B.; Hoffmann-Röder, A.; Morita, N.; Volz, F. *Pure Appl. Chem.* **2008**, *80*, 1063. For recent examples, see: (d) Erdsack, J.; Krause, N. *Synthesis* **2007**, 3741. (e) Deng, Y.; Yu, Y.; Ma, S. *J. Org. Chem.* **2008**, *73*, 585. (f) Deng, Y.; Shi, Y.; Ma, S. *Org. Lett.* **2009**, *11*, 1205.

(3) Whang, K.; Venkataraman, H.; Kim, Y. G.; Cha, J. K. *J. Org. Chem.* **1991**, *56*, 7174 and references therein .

(4) White, R. D.; Keaney, G. F.; Slown, C. D.; Wood, J. L. *Org. Lett.* **2004**, *6*, 1123 and references therein .

(5) A hydroxyl group and an introduced substituent are oriented to a same face in *syn*-configured isomers and to opposite faces in *anti*-configured isomers.

(6) Reviews: (a) Krause, N.; Hoffmann-Röder, A. In *Modern Organocopper Chemistry*; Krause, N., Ed.; Wiley-VCH: Weinheim, 2002; pp 145−166. (b) Krause, N.; Hoffmann-Röder, A. *Tetrahedron* **2004**, *60*, 11671. For selected examples, see: (c) Oehlschlager, A. C.; Czyzewska, E. *Tetrahedron Lett.* **1983**, *24*, 5587. (d) Johnson, C. R.; Dhanoa, D. S. *J. Org. Chem.* **1987**, *52*, 1885. (e) Marshall, J. A.; Pinney, K. G. *J. Org. Chem.* **1993**, *58*, 7180. (f) Bertozzi, F.; Crotti, P.; Macchia, F.; Pineschi, M.; Arnold, A.; Feringa, B. L. *Tetrahedron Lett.* **1999**, *40*, 4893. (g) Deutsch, C.; Lipshutz, B. H.; Krause, N. *Angew. Chem., Int. Ed.* **2007**, *46*, 1650. (h) Deutsch, C.; Hoffmann-Röder, A.; Domke, A.; Krause, N. *Synlett* **2007**, 737.

(7) For a CuBr-catalyzed *syn*-selective reaction of **1a** with *alkyl* Grignard reagents in the presence of TMSCl, see: (a) Alexakis, A.; Marek, I.; Mangeney, P.; Normant, J. F. *Tetrahedron* **1991**, *47*, 1677. For a $Cu(OTf)_2$-catalyzed *syn*-selective reaction of **1k** with dialkylzinc reagents in the presence of TADDOL derived phosphorus amidites, see: (b) Bertozzi, F.; Crotti, P.; Macchia, F.; Pineschi, M.; Arnold, A.; Feringa, B. L. *Tetrahedron Lett.* **1999**, *40*, 4893.



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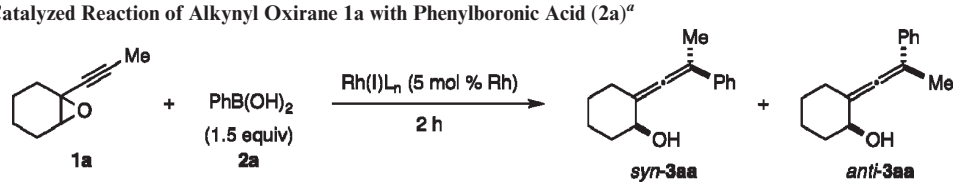
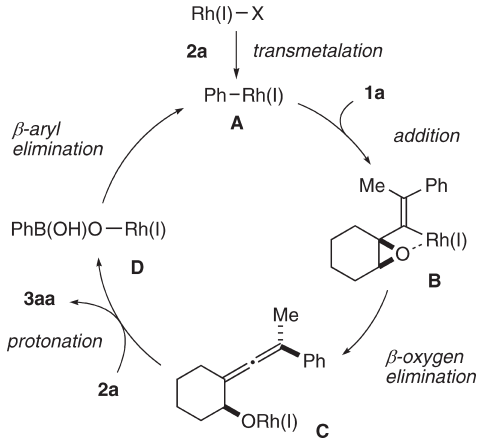
**TABLE 1. Rh(I)-Catalyzed Reaction of Alkynyl Oxirane 1a with Phenylboronic Acid (2a)[a]**




| entry | $Rh(I)L_n$ | ligand | base (equiv) | solvent | temp (°C) | yield (%) | *syn*/*anti*[b] |
|---|---|---|---|---|---|---|---|
| 1 | $[RhCl(cod)]_2$ | $P(OEt)_3$ | $NaHCO_3$ (1.5) | EtOH | 70 | 33 | 40/60 |
| 2 | $[RhCl(cod)]_2$ | $P(OEt)_3$ | $NaHCO_3$ (1.5) | THF | 70 | 18 | 90/10 |
| 3 | $[RhCl(cod)]_2$ | $P(OEt)_3$ | KOH (0.5) | THF | 70 | 58 | 98/2 |
| 4 | $[RhCl(cod)]_2$ | none | KOH (0.5) | THF | 70 | 59 | 98/2 |
| 5 | $[RhCl(cod)]_2$ | none | KOH (0.6) | THF | rt | 58 | 99/1 |
| 6 | $[RhCl(nbd)]_2$ | none | KOH (0.6) | THF | rt | 81 | 99/1 |

[a]Reaction conducted on a 0.35−0.40 mmol scale. [b]Determined by HPLC analysis.

**SCHEME 1. Proposed Reaction Pathway**

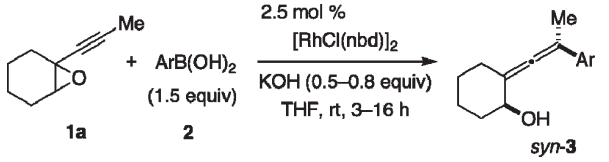



reactions with organostannanes,[8] organoborons,[9] and alkynylcoppers[10] also give the corresponding *anti*-configured products. On the other hand, *syn*-configured α-allenols are stereoselectively produced by the iron-catalyzed reaction of alkynyl oxiranes with *alkyl* Grignard reagents.[11] The reaction with *aryl* Grignard reagents, however, exhibits only moderate diastereoselectivity. During the course of our studies on the rhodium-catalyzed addition reaction of organoboron reagents to unsaturated organic compounds,[12] we became interested in employing alkynyl oxiranes as acceptors of arylrhodium(I) intermediates. In this paper, we describe the stereoselective synthesis of *syn*-configured α-allenols from alkynyl oxiranes and arylboronic acids under the catalysis of rhodium.[13]

## Results and Discussion

We have previously reported the rhodium-catalyzed substitution reaction of propargylic acetates with arylboronic acids, wherein an alkenylrhodium(I) intermediate undergoes *β*-oxygen elimination to afford trisubstituted allenes.[14] Similar reaction conditions were initially applied to the reaction of alkynyl oxirane **1a** with phenylboronic acid (**2a**). A mixture of **1a** (1.0 equiv) and **2a** (1.5 equiv) in EtOH was heated at 70 °C in the presence of $NaHCO_3$ (1.5 equiv) and the rhodium complex (5 mol %) generated in situ from $[RhCl(cod)]_2$ (cod = cycloocta-1,5-diene) and $P(OEt)_3$ (Rh/P = 1:2) (Table 1, entry 1). The reaction reached completion in 2 h, and an extractive workup followed by chromatographic isolation afforded α-allenol **3aa** in 33% yield with low diastereoselectivity (*syn*/*anti* = 40/60).[15] When THF was used in place of EtOH as the solvent, the diastereoselectivity was dramatically improved for *syn*-configured α-allenol (*syn*/*anti* = 90/10), albeit in a decreased yield (entry 2). Changing the base to KOH (0.5 equiv) gave better results in terms of both yield and diastereoselectivity (entry 3).[16] In the absence of $P(OEt)_3$, the reaction occurred even at room temperature (entry 5). Finally, we found that the reaction proceeded

**TABLE 2. Scope of Arylboronic Acids[a]**

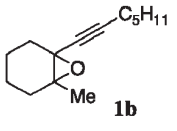
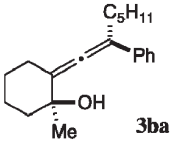
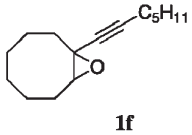
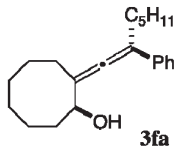
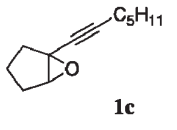
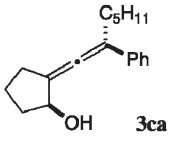
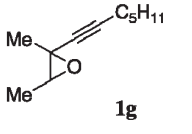
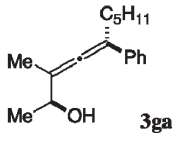
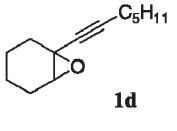
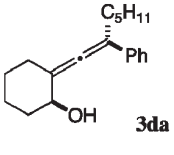
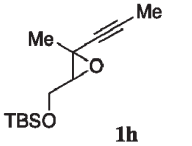
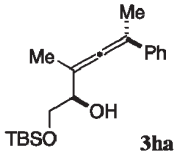
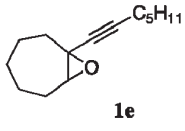
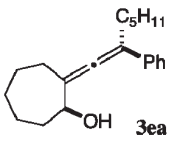
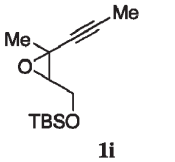
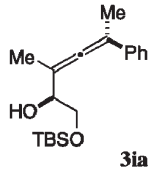



| entry | $ArB(OH)_2$ | product | yield (%) | *syn*/*anti*[b] |
|---|---|---|---|---|
| 1 | **2b** Ar = 4-F-$C_6H_4$ | **3ab** | 76 | 98/2 |
| 2 | **2c** Ar = 4-Br-$C_6H_4$ | **3ac** | 86 | 99/1 |
| 3 | **2d** Ar = 4-Me-$C_6H_4$ | **3ad** | 77 | 98/2 |
| 4 | **2e** Ar = 3-MeO-$C_6H_4$ | **3ae** | 80 | 99/1 |
| 5 | **2f** Ar = 3-Cl-$C_6H_4$ | **3af** | 74 | 99/1 |
| 6 | **2g** Ar = 3-CHO-$C_6H_4$ | **3ag** | 72 | 96/4 |
| 7 | **2h** Ar = 2-Me-$C_6H_4$ | **3ah** | 83 | 83/17 |
| 8 | **2i** Ar = 2-thiophene | **3ai** | 75 | 97/3 |

[a]Reaction conditions: **1a** (0.40 mmol), **2** (0.60 mmol), KOH (0.20−0.30 mmol), $[RhCl(ndb)]_2$ (0.01 mmol, 5 mol % Rh) in THF (4.0 mL) at rt for 3−16 h. [b]Determined by HPLC analysis.

(8) Kjellgren, J.; Sundén, H.; Szabó, K. *J. Am. Chem. Soc.* **2005**, *127*, 1787.
(9) Yoshida, M.; Ueda, H.; Ihara, M. *Tetrahedron Lett.* **2005**, *46*, 6705.
(10) Yoshida, M.; Hayashi, M.; Shishido, K. *Org. Lett.* **2007**, *9*, 1643.
(11) Fürstner, A.; Méndez, M. *Angew. Chem., Int. Ed.* **2003**, *42*, 5355.
(12) A review: Miura, T.; Murakami, M. *Chem. Commun.* **2007**, 217.
(13) A preliminary communication: Miura, T.; Shimada, M.; Ku, S.-Y.; Tamai, T.; Murakami, M. *Angew. Chem., Int. Ed.* **2007**, *46*, 7101.
(14) Murakami, M.; Igawa, H. *Helv. Chim. Acta* **2002**, *85*, 4182.
(15) The relative stereochemistry (*syn*/*anti*) was assigned by comparison with the NMR spectra reported in ref 7a for the *syn*- and *anti*-configured isomers of **3aa**.
(16) A hydroxide anion would replace a chloride ion on rhodium in the initial cycle. A hydroxide or alkoxide ion is nucleophilic enough to promote transmetalation with phenylboronic acid, and thus preferred over a chloride ion. Although 5 mol % of KOH would be enough, it was hardly possible to weigh hygroscopic KOH less than 0.5 equiv at a 0.4 mmol scale.

**TABLE 3. Scope of Alkynyl Oxiranes**[a]

| entry | substrate | *syn*-product | yield (%) | *syn*/*anti*[b] | entry | substrate | *syn*-product | yield (%) | *syn*/*anti*[b] |
|---|---|---|---|---|---|---|---|---|---|
| 1 |  **1b** |  **3ba** | 65 | 99/1 | 5 |  **1f** |  **3fa** | 83 | 99/1 |
| 2 |  **1c** |  **3ca** | 82 | 97/3 | 6 |  **1g** |  **3ga** | 85 | 99/1 |
| 3 |  **1d** |  **3da** | 74 | 97/3 | 7 |  **1h** |  **3ha** | 86 | 98/2 |
| 4 |  **1e** |  **3ea** | 83 | 99/1 | 8 |  **1i** |  **3ia** | 77 | 77/23 |

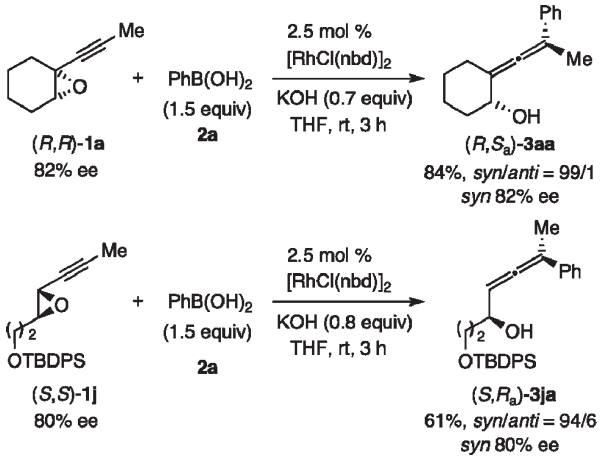
[a]The reaction conditions are the same as those in Table 2. [b]Determined by HPLC analysis.

more cleanly with a norbornadiene (nbd) complex than with the cod complex, producing **3aa** in the highest yield of 81% with excellent diastereoselectivity (*syn*/*anti* = 99/1, entry 6).[17]

The proposed mechanism is shown in Scheme 1. Initially, phenylrhodium(I) species **A** is generated by transmetalation between phenylboronic acid (**2a**) and a rhodium(I) complex. Subsequently, *cis* 1,2-addition of **A** across the carbon−carbon triple bond of **1a** takes place to generate alkenylrhodium(I) intermediate **B**. Noteworthy was that addition of the phenylrhodium(I) species to the alkynyl oxirane **1a** occurred at room temperature, compared to related examples that require heating to more than 70 °C.[14,18] The alkenylrhodium(I) intermediate **B** then undergoes $\beta$-oxygen elimination in a *syn* mode to open the oxirane ring.[19] We presume that the high stereoselectivity as well as the enhanced reactivity can be ascribed to precoordination of the oxygen atom of the oxirane ring to rhodium, as is the case in the iron-catalyzed reaction.[11] Protonolysis of rhodium(I) alkoxide **C** with **2a** releases α-allenol **3aa** along with rhodium(I) boronate **D**, which undergoes $\beta$-aryl elimination to regenerate phenylrhodium(I) species **A**.[20]

A variety of arylboronic acids **2** were subjected to reaction with alkynyl oxirane **1a** (Table 2). The catalytic process was effective with heteroarylboronic acid **2i** as well as with a

**SCHEME 2. Reaction of Enantiomerically Enriched Alkynyl Oxiranes**




functionally diverse array of arylboronic acids **2b**−**2g** to give *syn*-configured α-allenols **3ab**−**3ai** with diastereoselectivities higher than 96:4 (entries 1−6 and 8), except the case of the sterically hindered *o*-tolylboronic acid (**2h**, 83:17, entry 7).[21] The reaction conditions were mild enough to tolerate a formyl group, which would be incompatible with Grignard reagents. Alkyl- and alkenylboronic acids failed to take part in the reaction under the present reaction conditions.

The results of the rhodium-catalyzed reaction of various alkynyl oxiranes **1** with phenylboronic acid (**2a**) are summarized

(17) Other ligands such as $P(OCH_2CF_3)_3$, cyclohexan-1,4-diene, bicyclo-[2.2.2]octa-2,5-diene, 1,3-divinyltetramethyldisiloxane, and oct-4-yne gave inferior results to norbornadiene.

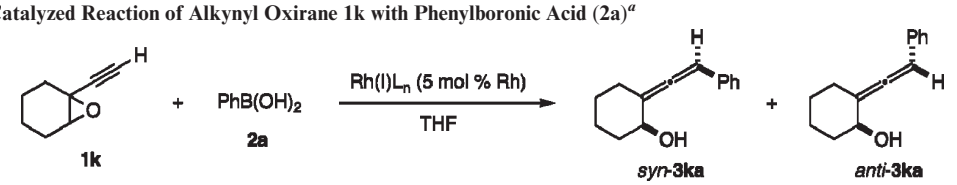
(18) (a) Hayashi, T.; Inoue, K.; Taniguchi, N.; Ogasawara, M. *J. Am. Chem. Soc.* **2001**, *123*, 9918. (b) Lautens, M.; Yoshida, M. *Org. Lett.* **2002**, *4*, 123. (c) Genin, E.; Michelet, V.; Genêt, J.-P. *Tetrahedron Lett.* **2004**, *45*, 4157.

(19) $\beta$-Oxygen elimination of the alkenylrhodium(I) intermediate can occur in an *anti* mode, leading to the formation of *anti*-configured α-allenols.[14]

(20) Zhao, P.; Incarvito, C. D.; Hartwig, J. F. *J. Am. Chem. Soc.* **2007**, *129*, 1876.

(21) $\beta$-Oxygen elimination takes place more facilely in both *syn* and *anti* modes to release steric congestion, lowering diastereoselectivity.

**TABLE 4. Rh(I)-Catalyzed Reaction of Alkynyl Oxirane 1k with Phenylboronic Acid (2a)[a]**



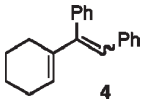

| entry | Rh(**I**)$L_n$ | base (equiv) | **2a** (equiv) | time (h) | temp (°C) | yield (%) | *syn*/*anti*[b] |
|---|---|---|---|---|---|---|---|
| 1 | $[RhCl(nbd)]_2$ | KOH (0.6) | 1.5 | 4.0 | rt | 19 | 83/17 |
| 2 | $[Rh(OH)(cod)]_2$ | none | 1.5 | 4.0 | rt | 27 | 85/15 |
| 3 | $[Rh(OH)(cod)]_2$ | none | 1.5 | 3.5 | 0 | 50 | 94/6 |
| 4 | $[Rh(OH)(cod)]_2$ | none | 1.1 | 1.5 | 0 | 71 | 97/3 |

[a]Reaction conducted on a 0.40 mmol scale. [b]Determined by HPLC analysis.

in Table 3. Substrate **1b** having a tetrasubstituted oxirane moiety was converted to tertiary alcohol **3ba** in 65% yield (*syn*/*anti* = 99/1, entry 1). The reactions of substrates **1c**−**1f** with cyclic structures of five- to eight-membered rings proceeded well to give the corresponding α-allenols **3ca**−**3fa** in good yields with high stereoselectivities (entries 2−5). Acyclic substrates **1g**−**1i** also participated in the reaction (entries 6−8). Higher diastereoselectivity was observed with *trans*-oxirane **1h** than with the corresponding *cis*-oxirane **1i**.

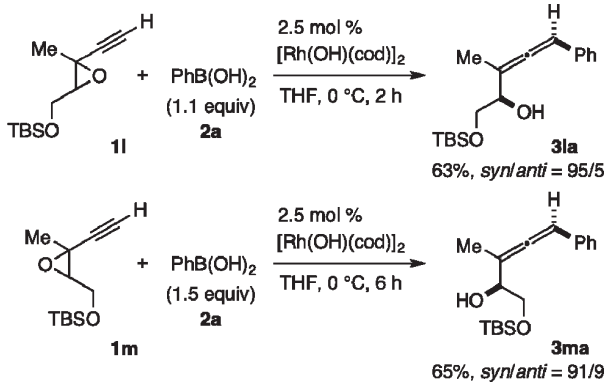
Enantiomerically enriched alkynyl oxiranes (*R*,*R*)-**1a**[22] and (*S*,*S*)-**1j**[23] were treated with **2a**, and the enantiomeric purities observed with the resulting *syn*-configured (*R*,*S*a)-**3aa** and (*S*,*R*a)-**3ja** were identical to those of the starting oxiranes, confirming that the reaction is stereospecific (Scheme 2).[24]

Next, the reaction of alkynyl oxiranes having an unsubstituted terminal alkyne was examined (Table 4). When substrate **1k** was subjected to the reaction with 1.5 equiv of **2a** in the presence of $[RhCl(nbd)]_2$ (5 mol %) and KOH (0.6 equiv), the desired product **3ka** was obtained in only 19% yield along with a small amount of the diphenyl-substituted 1,3-diene **4**, which arose from an overreaction of the resulting **3ka** with **2a** via $S_N2'$-type substitution (entry 1).[25] In contrast to the case of **1a**, the use of a rhodium catalyst possessing cycloocta-1,5-diene as the ligand gave a slightly better result (entry 2). Lowering the reaction temperature to 0 °C increased both the yield and the diastereoselectivity (entry 3). When the amount of **2a** was reduced to 1.1 equiv in order to suppress the overreaction, **3ka** was produced in the best yield of 71% with high diastereoselectivity (*syn*/*anti* = 97/3, entry 4).




Under the optimized reaction conditions, a pair of acyclic substrates **1l** and **1m** having a terminal alkyne moiety was converted to the corresponding α-allenols **3la** and **3ma** in 63% and 65% yield, respectively (Scheme 3). The *trans*-substrate **1l**

**SCHEME 3. Reaction of Alkynyl Oxiranes 1l and 1m**




gave a marginally higher diastereoselectivity than the *cis*-substrate **1m**. This deviation, observed to a greater extent with the reaction of the *cis* and *trans* isomers (**1h** and **1i**) having an internal alkyne moiety (Table 3, entries 7 and 8), is explained by assuming that coordination of the oxygen atom of the oxirane ring to rhodium would be required for the alkenylrhodium(I) intermediate to undergo β-oxygen elimination in a *syn*-selective way and that the sterically repulsive effect of the *cis* substituent would weaken coordination of the oxirane ring to the alkenylrhodium(I) intermediate.

Finally, the synthetic potential of the rhodium-catalyzed reaction of alkynyl oxiranes with arylboronic acids was demonstrated by applying it to the total synthesis of (±)-Boivinianin B (7,10-epoxy-1,3,5-bisabolatrien-11-ol) (Scheme 4).[26] 7,10-Epoxy-1,3,5-bisabolatrien-11-ol was isolated from the red alga *Laurencia tristicha* by Shi and co-workers in 2005. Later in 2006 Mulholland and co-workers also isolated it from the Meliaceae *Cipadessa boiviniana* and named it as Boivinianin B.[27,28] To deploy our reaction in the synthesis of a challenging molecule, we chose (±)-Boivinianin B as our

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(24) For the synthesis of optically active α-allenols, see: (a) Xu, D.; Li, Z.; Ma, S. *Chem.—Eur. J.* **2002**, *8*, 5012. (b) Inoue, M.; Nakada, M. *Angew. Chem., Int. Ed.* **2006**, *45*, 252. (c) Hernandez, E.; Burgos, C. H.; Alicea, E.; Soderquist, J. A. *Org. Lett.* **2006**, *8*, 4089. (d) Xia, G.; Yamamoto, H. *J. Am. Chem. Soc.* **2007**, *129*, 496 and references therein .
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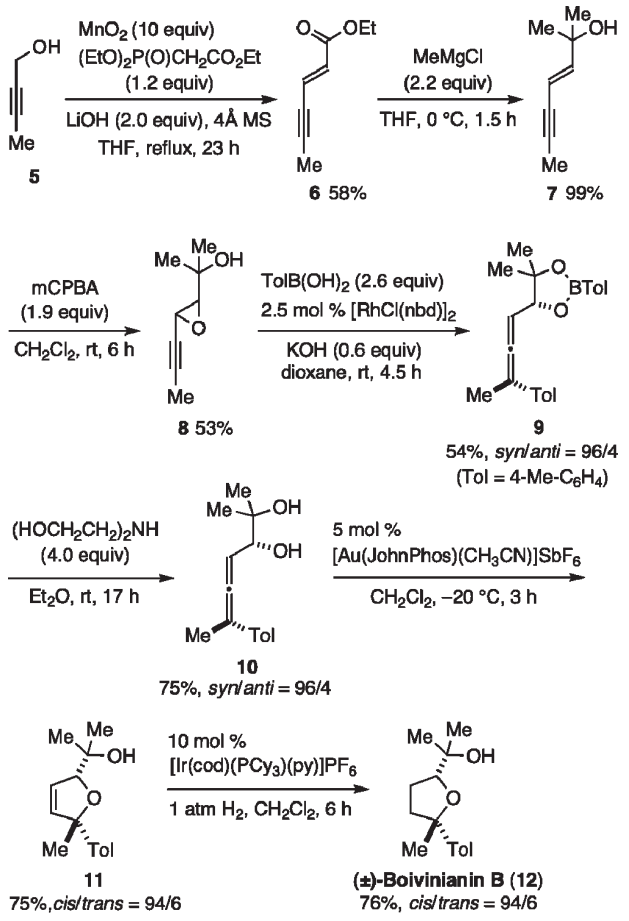
(28) A nonstereoselective synthesis of 7,10-epoxy-1,3,5-bisabolatrien-11-ol ((±)-Boivinianin B) was reported before it was isolated from natural sources: (a) Kirtany, J. K.; Paknikar, S. K. *Indian J. Chem.* **1974**, *12*, 1202. (b) Ho, T.; Liu, S. *Synth. Commun.* **1983**, *13*, 463.

**SCHEME 4. Synthesis of (±)-Boivinianin B**




target. Initially, the required alkynyl oxirane **8** was prepared from commercially available but-2-yn-1-ol (**5**) in three steps; the alcohol **5** was oxidized by $MnO_2$ and the resulting aldehyde was subjected directly to the Horner−Wadsworth−Emmons (HWE) olefination reaction to afford the unsaturated ester **6** (58% yield).[29] Treatment of **6** with 2.2 equiv of MeMgCl furnished tertiary allylic alcohol **7** (99% yield). Epoxidation with mCPBA gave alkynyl oxirane **8** in 53% yield with only *trans* geometory.[30] The rhodium-catalyzed reaction of **8** thus prepared with *p*-tolylboronic acid (2.6 equiv) was immediately followed by esterification with *p*-tolylboronic acid to afford cyclic boronate **9** in 54% yield with good diastereoselectivity of *syn*/*anti* = 96/4. Subsequent transesterification using diethanolamine furnished tolyl-substituted α-allenol **10** in 75% yield.[31] Next, gold-catalyzed cycloisomerization of **10** was carried out according to the procedure reported previously.[32] Cationic complex [Au(JohnPhos)($CH_3CN$)]$SbF_6$[33,34] was used as the catalyst, and the reaction was conducted at −20 °C in order to suppress epimerization, which otherwise would be expected to occur readily.[35] Almost complete stereospecificity was observed in the transformation to the resulting 2,5-dihydrofuran **11** (75% yield, *cis*/*trans* = 94/6). Hydrogenation of **11** was then carried out using palladium on charcoal as the catalyst, which resulted in some epimerization to afford the desired product with reduced diastereoselectivity (*cis*/*trans* = 83/17). It is likely that epimerization occurred via a π-allylpalladium intermediate. On the other hand, an iridium-catalyzed hydrogenation reaction of **11** furnished (±)-Boivinianin B (**12**) without any loss of stereochemical integrity (76% yield, *cis*/*trans* = 94/6), and the spectral data obtained were identical with those reported.[27b] Thus, the total synthesis of (±)-Boivinianin B (**12**) was completed in seven steps using only commercially available substances as the reagents as well as the starting material.

## Conclusions

We have developed a rhodium-catalyzed stereoselective synthesis of *syn*-configured aryl-substituted α-allenols from alkynyl oxiranes and arylboronic acids. Precoordination of the oxygen atom of the oxirane ring to rhodium is important for attaining high diastereoselectivity as well as enhanced reactivity. This method was successfully applied to the total synthesis of (±)-Boivinianin B in only seven steps.

## Experimental Section

**Representative Procedure for Rhodium-Catalyzed α-Allenol Synthesis with Arylboronic Acids (Table 1, Entry 6).** To an oven-dried, Ar-purged flask were added $[RhCl(nbd)]_2$ (4.6 mg, 0.01 mmol), **2a** (73.2 mg, 0.6 mmol), KOH (13.5 mg, 0.24 mmol), THF (2.0 mL), and a solution of **1a** (54.5 mg, 0.4 mmol) in THF (2.0 mL). The reaction mixture was stirred at room temperature for 2 h and quenched with water (10 mL). The aqueous layer was extracted with ethyl acetate (3 × 10 mL). The combined extracts were washed with brine and dried over $MgSO_4$. The solvent was removed under reduced pressure, and the residue was purified by preparative thin-layer chromatography (hexane/ethyl acetate = 5/1) to give **3aa** (69.4 mg, 81%). IR (neat): 3412, 2932, 1954, 1493, 1445, 1075 $cm^{-1}$. $^1H$ NMR: δ 1.38−1.57 (m, 3H), 1.73−1.99 (m, 3H), 2.01−2.28 (m, 2H), 2.14 (s, 3H), 2.44−2.56 (m, 1H), 4.00−4.17 (m, 1H), 7.18−7.25 (m, 1H), 7.29−7.38 (m, 2H), 7.41−7.48 (m, 2H). $^{13}C$ NMR: δ 17.5, 24.0, 27.2, 30.2, 36.8, 69.5, 104.9, 110.2, 125.5, 126.7, 128.3, 137.5, 194.5. HRMS ($CI^+$): calcd for $C_{15}H_{18}O$, $M^+$ 214.1358; found *m*/*z* 214.1355. [HPLC (Nacalai COSMOSIL 5SL-II, hexane/*i*-PrOH = 99.7/0.3, flow rate = 0.6 mL/min, λ = 220 nm): $t_1$ = 20.7 min (*syn*), $t_2$ = 22.0 min (*anti*).]

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**Supporting Information Available:** Experimental details and structural data for all new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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