Ruthenium-Catalyzed Reductive Coupling Reaction of Propargylic Alcohols via Hydroboration of Allenylidene Intermediates

Gen Onodera,[†] Yoshiaki Nishibayashi,*[,‡] and Sakae Uemura[†]

Department of Energy and Hydrocarbon Chemistry, Kyoto University, Katsura, Nishikyo-ku, Kyoto 615-8510, Japan, and Institute of Engineering Innovation, The University of Tokyo, Yayoi, Bunkyo-ku, Tokyo 113-8656, Japan

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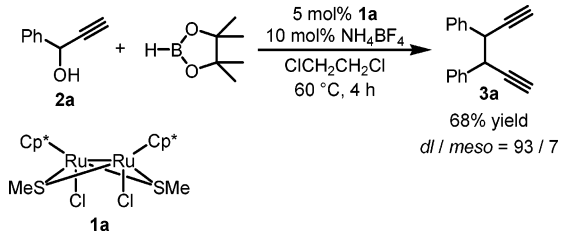
Summary: A novel ruthenium-catalyzed reductive coupling reaction of propargylic alcohols has been found to afford the corresponding 1,5-hexadiynes in good yields with high stereoselectivity. This catalytic reaction may proceed via hydroboration of the initially produced ruthenium−allenylidene intermediates with pinacolborane as a key step, disclosing a new reactivity of the allenylidene complexes.

We have recently disclosed that the ruthenium-catalyzed propargylic substitution reaction of propargylic alcohols with a variety of heteroatom- and carbon-centered nucleophiles afforded the corresponding functionalized propargylic compounds in high yields with complete regioselectivity.[1] It is noteworthy that the reactions are catalyzed by thiolate-bridged diruthenium complexes[2] such as $[Cp^*RuCl(\mu_2\text{-}SR)]_2$ ($Cp^* = \eta^5\text{-}C_5Me_5$; R = Me (**1a**), ^{n}Pr, ^{i}Pr (**1b**)) and $[Cp^*RuCl(\mu_2\text{-}SMe)_2RuCp^*(OH_2)]OTf$ (OTf = OSO_2CF_3; **1c**) but not by various mononuthenium complexes. On the basis of the data of some stoichiometric reactions as well as theoretical studies,[3] we assumed that the reaction proceeds via ruthenium−allenylidene complexes as key intermediates, where a synergistic effect of two ruthenium atoms in the diruthenium complexes is one of the essential factors in promoting the catalytic reaction.[1] More recently, we have also found several other kinds of catalytic reactions where the formations of the ruthenium−allenylidene intermediates as well as this synergistic effect are considered to be the key factors.[4]

As an extension of our study on these catalytic reactions, we have now envisaged a new type of catalytic reaction including hydroboration of allenylidene intermediates as a key step. Although hydroboration of carbon−carbon double and triple bonds is one of the most useful methods in organic synthesis,[5] its application to an allenylidene moiety has not yet been reported to our knowledge.[6] When we treated propargylic alcohols with pinacolborane in the presence of a catalytic amount of **1a**, the reductive homocoupling products of the propargylic alcohols were obtained unexpectedly. This reaction seems to proceed via hydroboration of the allenylidene intermediates, a preliminary result of which is presented here.

Treatment of 1-phenyl-2-propyn-1-ol (**2a**) with pinacolborane in the presence of **1a** (5 mol %) and NH_4BF_4 (10 mol %) in $ClCH_2CH_2Cl$ at 60 °C for 4 h afforded the propargylic group homocoupled product 3,4-diphenyl-1,5-hexadiyne (**3a**) in 68% isolated yield as a mixture of two diastereoisomers (*dl*/*meso* = 93/7) (Scheme 1). The reaction proceeded quite smoothly even

Scheme 1



at room temperature, though the yield of **3a** was slightly lower. One recrystallization of the diastereoisomers from CH_2Cl_2−*n*-hexane gave the major diastereoisomer in pure form. The stereochemistry of the major diastereoisomer of **3a** was unambiguously determined by X-ray analysis.[7] An ORTEP drawing of *dl*-**3a** is shown in Figure 1. When **1b** and **1c** were used as catalysts in place of **1a**, only lower yields of **3a** were obtained

* To whom correspondence should be addressed. E-mail: ynishiba@sogo.t.u-tokyo.ac.jp.

[†] Kyoto University.

[‡] The University of Tokyo.

(1) (a) Nishibayashi, Y.; Wakiji, I.; Hidai, M. *J. Am. Chem. Soc.* **2000**, *122*, 11019. (b) Nishibayashi, Y.; Wakiji, I.; Ishii, Y.; Uemura, S.; Hidai, M. *J. Am. Chem. Soc.* **2001**, *123*, 3393. (c) Nishibayashi, Y.; Yoshikawa, M.; Inada, Y.; Hidai, M.; Uemura, S. *J. Am. Chem. Soc.* **2002**, *124*, 11846. (d) Inada, Y.; Nishibayashi, Y.; Hidai, M.; Uemura, S. *J. Am. Chem. Soc.* **2002**, *124*, 15172. (e) Nishibayashi, Y.; Onodera, G.; Inada, Y.; Hidai, M.; Uemura, S. *Organometallics* **2003**, *22*, 873. (f) Nishibayashi, Y.; Inada, Y.; Yoshikawa, M.; Hidai, M.; Uemura, S. *Angew. Chem., Int. Ed.* **2003**, *42*, 1495. (g) Milton, M. D.; Onodera, G.; Nishibayashi, Y.; Uemura, S. *Org. Lett.* **2004**, *6*, 3993. (h) Nishibayashi, Y.; Milton, M. D.; Inada, Y.; Yoshikawa, M.; Wakiji, I.; Hidai, M.; Uemura, S. *Chem. Eur. J.* **2005**, *11*, 1433. (i) Onodera, G.; Matsumoto, H.; Milton, M. D.; Nishibayashi, Y.; Uemura, S. *Org. Lett.* **2005**, *7*, 4029.

(2) (a) The thiolate-bridged diruthenium complexes were found to provide a unique bimetallic reaction site for activation and transformation of various terminal alkynes; see: Nishibayashi, Y.; Yamanashi, M.; Wakiji, I.; Hidai, M. *Angew. Chem., Int. Ed.* **2000**, *39*, 2909 and references therein. (b) Nishibayashi, Y.; Imajima, H.; Onodera, G.; Hidai, M.; Uemura, S. *Organometallics* **2004**, *23*, 26. (c) Nishibayashi, Y.; Imajima, H.; Onodera, G.; Inada, Y.; Hidai, M.; Uemura, S. *Organometallics* **2004**, *23*, 5100. (d) The methanethiolate-bridged diruthenium complexes are commercially available from Wako Pure Chemical Industries (Japan) as met-DIRUX (*met*hanethiolate-bridged *diru*thenium complex) (**1a**) (130-14581) and met-DIRUX-OTf (**1c**) (132-14781).

(3) Ammal, S. C.; Yoshikai, N.; Inada, Y.; Nishibayashi, Y.; Nakamura, E. *J. Am. Chem. Soc.* **2005**, *127*, 9428.

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(5) For an example, see: Pelter, A.; Smith, K.; Brown, H. C. *Borane Reagents*; Academic Press: London, 1988.

(6) Miyaura and co-workers have recently reported the rhodium- or iridium-catalyzed trans hydroboration of terminal alkynes, where hydroboration of the vinylidene complexes is considered as a key intermediate: Ohmura, T.; Yamamoto, Y.; Miyaura, N. *J. Am. Chem. Soc.* **2000**, *122*, 4990.

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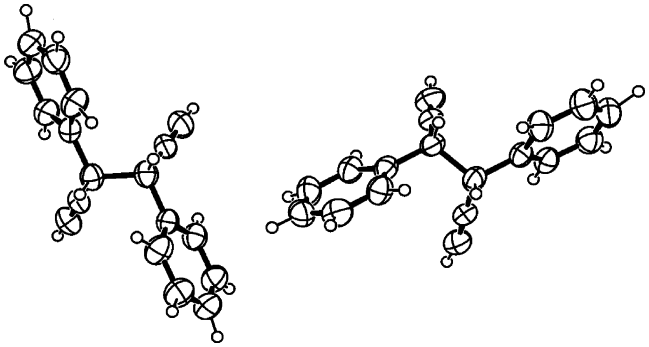
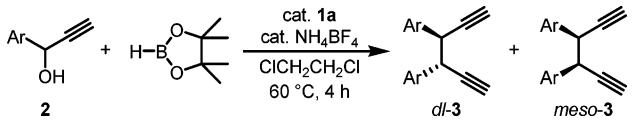


Figure 1. Crystal structure of *dl*-**3a**. Thermal ellipsoids are drawn at the 50% probability level.

Table 1. Reaction of Propargylic Alcohol 2 with Pinacolborane in the Presence of 1a and NH_4BF_4[a]



run	Ar	yield (%)[b]	(*dl*-**3**/*meso*-**3**)[c]
1	Ph (**2a**)	68	93/7
2	4-FC_6H_4 (**2b**)	66	96/4
3	4-ClC_6H_4 (**2c**)	60	92/8
4	3,5-$F_2C_6H_3$ (**2d**)	61	96/4
5	3,5-$Cl_2C_6H_3$ (**2e**)	60	91/9
6	4-$CF_3C_6H_4$ (**2f**)	23	97/3
7	4-$CH_3C_6H_4$ (**2g**)	30	78/22
8	4-$CH_3OC_6H_4$ (**2h**)	52	72/28
9	1-naphthyl (**2i**)	31	88/12
10	2-naphthyl (**2j**)	40	88/12

[a] All reactions of **2** (0.60 mmol) with pinacolborane (1.20 mmol) were carried out in the presence of **1a** (5 mol %) and NH_4BF_4 (10 mol %) in $ClCH_2CH_2Cl$ (5 mL). [b] Isolated yield. [c] Determined by ^1H NMR.

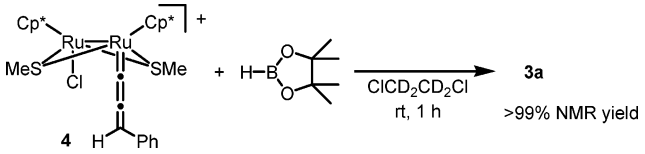
in both cases. Interestingly, reactions of **2a** with pinacolborane in the presence of mono- and polynuclear ruthenium complexes such as [(η^5-C_9H_7)RuCl(PPh_3)$_2$], [Cp*$RuCl_2$]$_2$, and [Cp*RuCl]$_4$ gave only a complex mixture of unidentified products in all cases. It is noteworthy that only thiolate-bridged diruthenium complexes **1** promoted the coupling reaction. In contrast to the reaction with pinacolborane, no formation of **3a** was observed in the reactions with catecholborane and 9-borabicyclo[3.3.1]-nonane (9-BBN). As a result, the combination of **1** and pinacolborane was revealed to be essential to promote this catalytic coupling reaction.

Next, reactions of other propargylic alcohols with pinacolborane were investigated. Typical results are shown in Table 1. The presence of electron-withdrawing groups such as fluoro and chloro groups in the benzene ring of propargylic alcohols did not give much effect on the yield of the coupling products (Table 1, runs 2−5). In sharp contrast, the yield of the coupling products was lower when a trifluoromethyl, methyl, or methoxy group was introduced to the benzene ring (Table 1, runs 6−8). In the case of reactions of propargylic alcohols bearing a naphthyl moiety, the corresponding coupling products were formed in moderate yields (Table 1, runs 9 and 10). Unfortunately, when 1,1-diphenyl-2-propyn-1-ol and 1-cyclohexyl-2-propyn-1-ol were used as substrates, the reaction did not proceed under the same reaction conditions.[8]

(7) The molecular structure of *dl*-**3a** has been unambiguously clarified by X-ray analysis. Crystal data for *dl*-**3a**: $C_{18}H_{14}$, M_r = 230.31, monoclinic, space group *Pa* (No. 7), a = 12.897(2) Å, b = 5.7782(7) Å, c = 17.568(3) Å, β = 90.649(4) °, V = 1309.1(3) Å^3, Z = 4, μ(Mo Kα) = 0.66 cm^{-1}, 9486 reflections measured, 7693 unique reflections, which were used in all calculations. Final R1 = 0.064 and wR2 = 0.078 (all data).

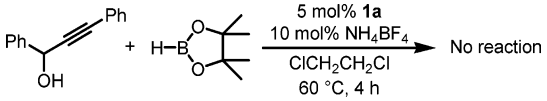
To elucidate the mechanism of this coupling reaction, the following stoichiometric and catalytic reactions were investigated. The reaction of the ruthenium−allenylidene complex[1,2] [Cp*RuCl(μ_2-SMe)$_2$RuCp*(C=C=CHPh)]BF_4 (**4**) with 1 equiv of pinacolborane at room temperature for 1 h in $ClCD_2CD_2Cl$ gave the coupling product **3a** quantitatively (Scheme 2). The

Scheme 2



catalytic reaction of 1,3-diphenyl-2-propyn-1-ol with pinacolborane under the same reaction conditions did not give any formation of the corresponding coupling products (Scheme 3).

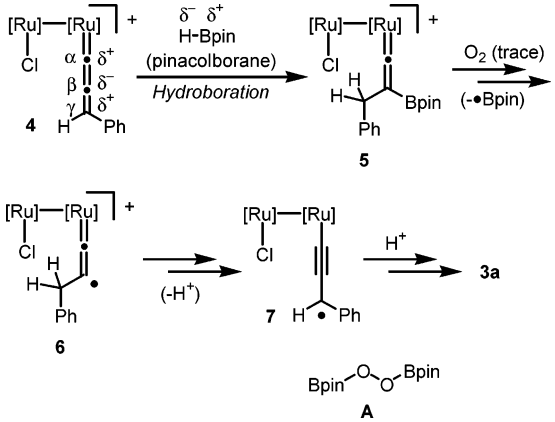
Scheme 3



These results indicate that this coupling reaction proceeds via an allenylidene complex such as **4**. On the other hand, the addition of a radical scavenger such as galvinoxyl or 1,1-diphenyl-2-picrylhydrazyl to the catalytic reaction system substantially lowered the yield of **3a** (31% and 25%, respectively). This result indicates that the present coupling of propargylic alcohols may involve some radical species in the main reaction course.

On the basis of these findings, a pathway of this catalytic reaction is proposed in Scheme 4. Hydroboration with pina-

Scheme 4



colborane occurs at the C_β−C_γ double bond of the initially produced ruthenium−allenylidene complex **4** to give the corresponding β-boravinylidene complex **5**. Then, the complex **5** is converted into the cationic radical complex **6** via radical fission assisted by adventitious molecular oxygen.[9] Elimination of a proton at C_γ and radical migration from C_β to C_γ in the

(8) (a) The reason the reaction of 1,1-diphenyl-2-propyn-1-ol with pinacolborane did not proceed is probably due to the steric hindrance between the diphenyl groups: Kaldis, J. H.; McGlinchey, M. J. *Tetrahedron Lett.* **2002**, *43*, 4049. (b) In the reaction using 1-cyclohexyl-2-propyn-1-ol under the same reaction conditions, the formation of a small amount of a vinylboron compound was observed, probably via hydroboration of the alkyne moiety of this alcohol.

complex **6** prefer to form the neutral radical complex **7**,[10] because the radical at C_γ of the complex is highly stabilized by the spin delocalization over the phenyl ring. Finally, an intermolecular reaction between two radical species results in the formation of the coupling product via vinylidene intermediates.[1h,3] The fact that only propargylic alcohols bearing an aryl moiety at the propargylic position are available for this catalytic coupling reaction may support our proposed reaction pathway. In addition, the formation of a boron compound such as **A** was observed in the reaction mixture by ^{11}B NMR and GCMS after the reaction of **2a** with pinacolborane.[11] This boron compound **A** may be formed as a terminated product from radical intermediates such as $>B-O-O^{\bullet}$. The addition of molecular oxygen to the catalytic reaction system, however, inhibited the formation of the coupling product, probably due to the decomposition of the reactive complexes. The presence of only a trace amount of molecular oxygen was effective in promoting this catalytic reaction.

Melikyan and co-workers have reported the stoichiometric coupling reaction of $Co_2(CO)_6$-complexed propargylic radicals, where several steps were necessary to obtain the coupling products.[12] Recently, Ding and co-workers have reported the coupling reaction of propargylic carbonates mediated by a stoichiometric amount of a titanium complex, where the corresponding 1-allenyl-5-alkynes were formed as side products in all cases.[13] In sharp contrast, the reaction described in this article is the first example of the catalytic and direct coupling reaction of propargylic alcohols to form 1,5-hexadiynes in good yields with high stereoselectivity.

In summary, a novel ruthenium-catalyzed reductive coupling reaction of propargylic alcohols has been found to afford the corresponding 1,5-hexadiynes in good yields with high stereoselectivity. This catalytic reaction may proceed via hydroboration of ruthenium−allenylidene intermediates with pinacolborane as a key step, disclosing a new reactivity of the allenylidene complexes.[14,15] Further investigation of the elucidation of the reaction mechanism in detail and of broadening the synthetic application of this coupling reaction is currently in progress.

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Supporting Information Available: Text giving experimental procedures and spectral data for all new compounds and a CIF file giving crystallographic data for **3a**. This material is available free of charge via the Internet at http://pubs.acs.org.

OM0509241

(9) Organoboranes have been known to work as good radical precursors. For an example, see: (a) Brown, H. C.; Negishi, E. *J. Am. Chem. Soc.* **1971**, *93*, 3777. For recent reviews, see: (b) Ollivier, C.; Renaud, P. *Chem. Rev*. **2001**, *101*, 3415. (c) Schaffner, A.-P.; Renaud, P. *Eur. J. Org. Chem.* **2004**, 2291.

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(11) Spectroscopic data of **A** are as follows: ^{11}B NMR (128 MHz, toluene-d_8) δ 22.1 ppm; GCMS (*m*/*z*) 286 (M^+).

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(15) For a recent example of stoichiometric reactions of ruthenium−allenylidene complexes, see: Nishibayashi, Y.; Imajima, H.; Onodera, G.; Uemura, S. *Organometallics* **2005**, *24*, 4106.