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Rh-Catalyzed Reductive Coupling Reaction of Aldehydes with Conjugated Dienes Promoted by Triethylborane

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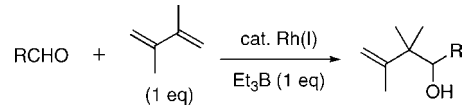
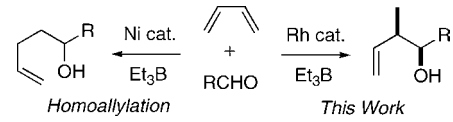
ABSTRACT



Rh(I) catalyzes the reductive coupling reaction of a wide variety of aldehydes with conjugated dienes in the presence of a stoichiometric amount of triethylborane to provide homoallyl alcohols in a single operation.

Reductive coupling reactions are among the most efficient strategies for C−C bond formation in modern organic and organometallic chemistry.[1] Conjugated dienes are significant building blocks for the manufacturing of polymers and are utilized as constituents of physiologically active molecules, such as terpenoids. In 1998, we first developed the Ni-catalyzed homoallylation of aldehydes with a wide variety of conjugated dienes via reductive coupling processes promoted by triethylborane as a reducing agent to provide bishomoallyl alcohols (Scheme 1).[2] In this case, isoprene reacts with aldehydes at the C1 position to afford 1,3-*anti*-3-methyl-4-penten-1-ol in excellent yield with high regio- and stereoselectivities in an anti-Markovnikov addition manner.

Scheme 1. Transition-Catalyzed Reductive Coupling Reaction of Aldehyde and Diene



Recently, it has been found that Rh catalysts allow hydrogen to serve as a reducing agent for C−C bond formation with partitioning of homolytic and heterolytic hydrogen active species.[3] Rh-catalyzed reductive condensations of conjugated dienes with aldehydes under hydrogen atmosphere were developed by M. J. Krische et al.[4] However, in this case, the scope of the transformation was limited to the reaction of 1,3-cyclohexadiene with activated aldehydes such as aralkyl glyoxals.

Herein, we would like to report that Rh(I) catalyst in combination with Et_3B nicely promotes the reductive cou-

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(1) (a) Metal Catalyzed Reductive C-C Bond Formation. *Topics in Current Chemistry*; Krische, M. J., Ed.; Springer-Verlag: Berlin, Heidelberg, 2007; Vol. 279. (b) *Modern Organonickel Chemistry*; Tamaru, Y., Ed.; Wiley-VCH: Weinheim, 2005.

(2) (a) Kimura, M.; Ezoe, A.; Mori, M.; Iwata, K.; Tamaru, Y. *J. Am. Chem. Soc.* **2006**, *128*, 8559–8568. (b) Tamaru, Y.; Kimura, M. *Org. Synth.* **2006**, *83*, 88–96. (c) Kimura, M.; Ezoe, A.; Tanaka, S.; Tamaru, Y. *Angew. Chem., Int. Ed.* **2001**, *40*, 3600–3602. (d) Shibata, K.; Kimura, M.; Shimizu, M.; Tamaru, Y. *Org. Lett.* **2001**, *3*, 2181–2183. (e) Kimura, M.; Fujimatsu, H.; Ezoe, A.; Shibata, K.; Shimizu, S; Matsumoto, S.; Tamaru, Y. *Angew. Chem., Int. Ed.* **1999**, *38*, 397–400. (f) Kimura, M.; Ezoe, A.; Shibata, K.; Tamaru, Y. *J. Am. Chem. Soc.* **1998**, *120*, 4033–4034.

(3) *Modern Rhodium-Catalyzed Organic Reactions*; Evans, P. A., Ed.; Wiley-VCH: Weinheim, 2005.

(4) (a) Jang, H.- Y.; Krische, M. J. *Acc. Chem. Res.* **2004**, *37*, 653–661. (b) Jang, H.- Y.; Huddleston, R. R.; Krische, M. J. *Angew. Chem., Int. Ed.* **2003**, *42*, 4074–4077.

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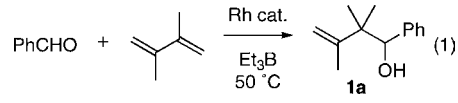
pling reaction of cyclic and acyclic conjugated dienes with a wide variety of aldehydes to provide homoallyl alcohols according to Markovnikov's fashion (Scheme 1). It is noteworthy that the regioselectivity of the reductive coupling reaction of conjugated dienes and aldehydes by the Rh/Et_3B system is apparently in contrast to that of the Ni/Et_3B system; the former is allylation and the latter is homoallylation. Although many methods for the synthesis of homoallyl alcohols promoted by transition metal catalysts have been well developed so far,[5] the direct allylation of carbonyls with 1,3-dienes in a single operation without isolation of the allylmetal species is extremely rare.

The reaction was conducted by exposing benzaldehyde and a conjugated diene to a mixture of Rh catalyst and Et_3B at 50 °C under nitrogen atmosphere (eq 1). Table 1 shows a summary of a various Rh(I) catalysts used to promote the reductive coupling reaction of benzaldehyde with 2,3-dimethyl-1,3-butadiene. The reaction outcome changes dramatically depending on the class of Rh(I) complexes. Chloro, acetylacetonate, and triflate groups are inappropriate counterions, and no reaction takes place at all (entries 1−5, Table 1).

Table 1. Rh-Catalyzed Reductive Coupling Reaction of PhCHO and 2,3-Dimethyl-1,3-diene[a]

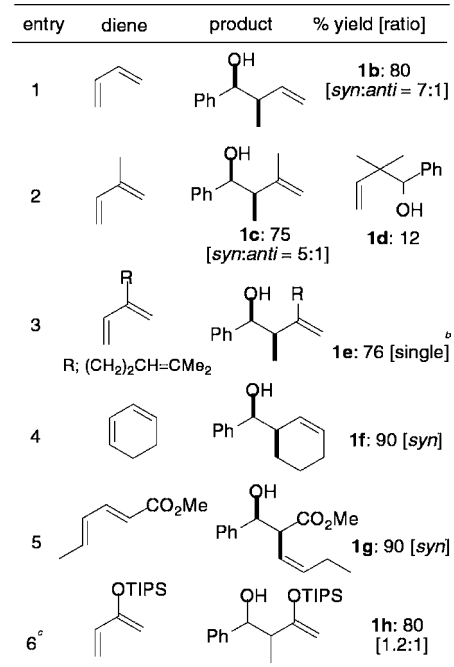


entry	Rh catalyst	mmol catalyst	yield of **1a** (%)
1	$RhCl(PPh_3)_3$	0.1	0
2	$Rh(CO)_2(acac)$	0.1	0
3	$[Rh(cod)_2][BF_4]$	0.1	0
4	$Rh(OTf)(cod)_2$	0.1	0
5	$[RhCl(cod)]_2$	0.05	0[b]
6	$[Rh(OH)(cod)]_2$	0.05	99[c]
7	$[Rh(OH)(cod)]_2$	0.005	78
8	$[RhH(cod)]_4$	0.025	94

[a] The reaction was undertaken in the presence of PhCHO (1 mmol), 2,3-dimethyl-1,3-butadiene (4 mmol), Rh catalyst, and Et_3B (3 mmol) in THF (5 mL) at 50 °C for 24 h under nitrogen atmosphere. [b] Addition of a catalytic amount of 4 M KOH solution (25 mL, 0.1 mmol) promoted the reaction to give **1a** in 80% yield. [c] Stoichiometric amount of each reagent, PhCHO (1 mmol), 2,3-dimethyl-1,3-butadiene (1 mmol), and Et_3B (1 mmol) were used to give **1a** in 89% yield.

In contrast, the addition of a catalytic amount of KOH aqueous solution to an $[RhCl(cod)]_2$ catalytic system induced the reductive coupling reaction with aldehyde and diene to afford homoallyl alcohol **1a** in 80%.[6] $[Rh(OH)(cod)]_2$ catalyst promoted the reaction effectively to provide **1a** in quantitative yield (entry 6, Table 1). Under similar catalytic system, the lower use of RhOH catalyst (0.01 equiv) was tolerated in the reaction with reasonable yield (entry 7). Furthermore, $[RhH(cod)]_4$, which was prepared from $[RhCl(cod)]_2$ and EtLi according to the literature,[7] participated in the desired reaction giving rise to **1a** in excellent yield (entry 8, Table 1). It was proved that RhH catalyst works as an active species as well as RhOH catalyst. These results might imply that the hydroxy group of RhOH plays a crucial role to form RhEt by transmetalation with Et_3B followed by β-hydride elimination to give an important RhH active species at the initial stage of the catalytic system.

Table 2. Rh(OH)-Catalyzed Reductive Coupling of PhCHO with Various Conjugated Dienes[a]



[a] The reaction was undertaken in the presence of PhCHO (1 mmol), diene (1 mmol), $[Rh(OH)(cod)]_2$ (0.05 mmol), and Et_3B (1 mmol) in THF (5 mL) for 24 h at 50 °C under nitrogen atmosphere. [b] Stereochemistry of **1e** is not determined. [c] At 67 °C for 24 h.

Although RhH was considered to be active species to promote the reaction, $[Rh(OH)(cod)]_2$ complex was actually used as an appropriate catalyst owing to the stability and easy storage. Once a suitable Rh catalyst was identified, the reductive coupling reaction was extended to a wide variety of conjugated dienes (Table 2). 1,3-Butadiene underwent the reductive allylation to provide **1b** in high yield with a 7:1

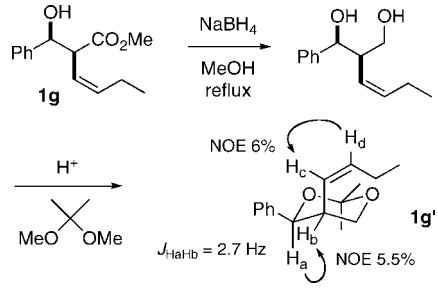
(5) (a) Tsuji, J.; Hara, M.; Ohno, K. *Tetrahedron* **1974**, *30*, 2143–2145. (b) Ojima, I. *J. Organomet. Chem.* **1977**, *134*, C1–C5. (c) Ojima, I.; Kumagai, M. *J. Organomet. Chem.* **1978**, *157*, 2143–2146. (d) Cornish, A. J.; Lappert, M. F.; MacQuitty, J. J.; Maskell, R. K. *J. Organomet. Chem.* **1979**, *177*, 153–161. (e) Satoh, M.; Nomoto, Y.; Miyaura, N.; Suzuki, A. *Tetrahedron Lett.* **1989**, *30*, 3789–3792. (f) Kobayashi, S.; Nishio, K. *J. Org. Chem.* **1994**, *59*, 6620–6628. (g) Hayashi, N.; Honda, H.; Yasuda, M.; Shibata, I.; Baba, A. *Org. Lett.* **2006**, *8*, 4553–4556. (h) Ru-catalyzed coupling reaction of diene with alcohols: Shibahara, F.; Bower, J. F.; Krische, M. J. *J. Am. Chem. Soc.* **2008**, *130*, 6338–6339.

(6) The allylation using $[RhCl(cod)]_2$ catalyst and 0.1 equiv of KOH proceeded smoothly. The formation of RhOH active species might be required at the initial stage of the reaction: see footnote [b] in Table 1.

(7) RhH is generated from RhEt species through β-hydride elimination, which is derived from $[RhCl(cod)]_2$ and EtLi; see:Kulzick, M.; Price, R. T.; Muetterties, E. L. *Organometallics* **1982**, *1*, 1256–1258.

ratio of *syn* and *anti* stereoisomers (entry 1, Table 2). Isoprene reacted with benzaldehyde at the C-3 and C-2 positions to give a regioisomeric mixture of **1c** and **1d** in a 6:1 ratio (entry 2, Table 2). Myrcene reacted with aldehyde at the less-substituted alkene to provide **1e** as a single isomer (entry 3, Table 2). 1,3-Cyclohexadiene serves as a pertinent allylating agent to exert *syn*-homoallyl alcohol exclusively (run 4, Table 2). Rh-catalyzed allylation with cyclic diene is more selective than that of the Ni-catalyzed allylation, which has shown marginal success of *syn* stereoselectivity (*syn*:*anti* = 4:1).[2a] An electron-deficient diene, methyl sorbate, reacted with benzaldehyde at the α-carbon position with excellent stereoselecivity to provide **1g** as a single isomer (entry 5, Table 2). The stereochemistry of **1g** was unequivocally determined as the *syn*-(*Z*) form on the basis of specral data of the converted acetonide **1g′**, which was derived from **1g** by the reduction with $NaBH_4$ followed by acetonization (Scheme 2). 2-Siloxy-1,3-butadiene underwent reductive coupling at the C-3 position with high regioselectivity to afford homoallyl alcohol **1h** possessing a silyl enol ether framework (entry 6, Table 2). However, in this case, exclusive *syn* stereoselectivity was not observed, and a mixture of *syn*- and *anti*-**1h** was obtained in good yield.

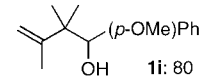
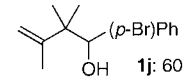
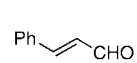
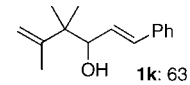
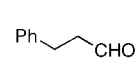
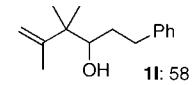
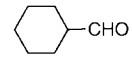
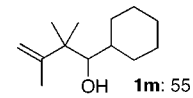
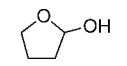
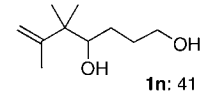
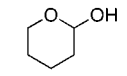
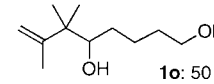
Scheme 2. Structure Determination of Homoallyl Alcohol **1g**



The results using a wide variety of aldehydes with 2,3-dimethyl-1,3-butadiene are shown in Table 3. Irrespective of the substituents and electronic nature of the aromatic ring, both *p*-anisaldehyde and *p*-bromobenzaldehyde provided homoallyl alcohols in good to excellent yields (entries 1 and 2, Table 3). α,β-Unsaturated aldehyde and alkylaldehyde also took part in the reaction in a similar way (entries 3−5, Table 3). Encouraged by the compatibility of the Ni/Et_3B-promoted homoallylation of lactols,[2c] we examined the applicability of the present reaction system to the allylation of five- and six-membered lactols to give the corresponding homoallyl alcohols in reasonable yields (entries 6 and 7, Table 3). These results also might greatly contribute to the reaction of carbohydrate and related chemistry from now on.

At this momonet, it is premature to give the rationale behind these regio- and stereoselectivities; however, a plausible reaction mechanism for Rh-catalyzed allylation of aldehydes with conjugated diene promoted by Et_3B is illustrated in Scheme 3. RhOH reacts with Et_3B to form RhEt species, which readily undergoes β-hydride elimination to

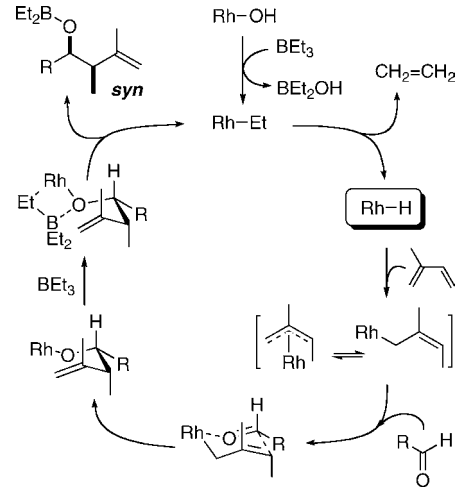
Table 3. Rh-Catalyzed Reductive Coupling Reaction of Carbonyls with 2,3-Dimethyl-1,3-butadiene[a]

entry	aldehyde	time (h)	product	% yield
1	(*p*-OMe)PhCHO	34		**1i**: 80
2	(*p*-Br)PhCHO	22		**1j**: 60
3		24		**1k**: 63
4		72		**1l**: 58
5		72		**1m**: 55
6		72		**1n**: 41
7		72		**1o**: 50

[a] The reaction was undertaken in the presence of carbonyl (1 mmol), 2,3-dimethyl-1,3-butadiene (4 mmol), Et_3B (3 mmol), and $[Rh(OH)(cod)]_2$ (0.05 mmol) in THF (5 mL) at 50 °C for 72 h under nitrogen atmosphere.

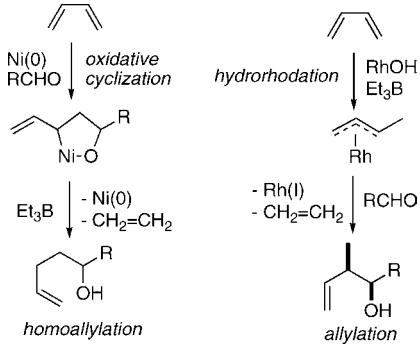
generate a fine active RhH species along with evolution of ethylene.[7] RhH active species readily adds to conjugated diene to form π-allylrhodium intermediate, which subsequently serves as an allylic carbanion equivalent toward the aldehyde to provide homoallyl alcohol through the six-membered ring transition state. The stereochemical outcome

Scheme 3. Rh-Catalyzed Allylation of Aldehyde with 1,3-Diene Promoted by Et_3B



seems to derive from the stability of the π-allylrhodium. Finally, ethyl group transfer from Et_3B to the alkoxyrhodium intermediate results in the formation of RhH active species via β-hydride elimination of RhEt, hence accomplishing the Rh(I) catalytic cycle.

Scheme 4. Reductive Coupling Reaction of Aldehyde with Diene Promoted by Ni/Et_3B versus Rh/Et_3B



A comparison between Ni/Et_3B-promoted homoallylation and Rh/Et_3B-promoted allylation of aldehyde with diene would be worth considering (Scheme 4). Under the Ni/Et_3B system, oxidative cyclization of a Ni(0) species across the conjugated diene and aldehyde successfully proceeds to form an oxanickelacycle intermediate, which undergoes σ-bond metathesis with Et_3B giving rise to bis-homoallyl alcohols.[2] In this case, the regio- and stereoselectivities stem from the structure of the oxanickelacycle intermediates. On the other hand, RhOH catalyst readily reacts with Et_3B to generate RhH active species. Assuming that the hydrorhodation of RhH toward the conjugated diene is extremely faster than the oxidative cyclization of a Rh(I) species across a diene and aldehyde, the nucleophilic allylation of aldehyde with π-allylrhodium would predominate over the homoallylation. Thus, the reaction feature of the reductive coupling reaction of aldehyde with diene promoted by Rh/Et_3B might be in marked contrast to that of Ni/Et_3B.

In conclusion, we have developed the Rh(I)-catalyzed reductive coupling reaction of aldehydes with a wide variety of conjugated dienes in the presence of Et_3B to provide homoallyl alcohols in a single operation. Asymmetric allylation of aldimines and polyhydroxy aldehydes such as carbohydrates with 1,3-dienes are currently underway in our laboratories, and these results will be reported in due course.

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Supporting Information Available: Experimental procedures and NMR spectra for all homoallyl alcohols. This material is available free of charge via the Internet at http://pubs.acs.org.

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