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Rhodium-Catalyzed Asymmetric Coupling Reaction of Allylic Ethers with Arylboronic Acids

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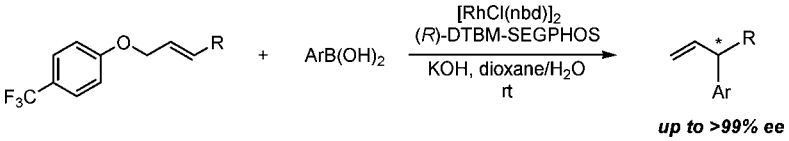
ABSTRACT



An asymmetric allylic substitution of simple allylic ethers with arylboronic acids in the presence of a rhodium(I)/(*R*)-DTBM-SEGPHOS catalyst has been developed. The reactions proceeded smoothly at room temperature to give the corresponding branch products with excellent regioselectivities and good to excellent enantioselectivities.

A coupling reaction of alkenes with organoboron reagents catalyzed by rhodium complexes has become a promising method for C−C bond formation.[1] In 1997, Miyaura et al. reported the rhodium-catalyzed 1,4-addition of organoboronic acids to α,β-unsaturated compounds,[2] and an asymmetric 1,4-addition, catalyzed by the rhodium(I)−BINAP system, was subsequently developed by Hayashi and Miyaura et al.[3] Hayashi et al. clarified that these reactions proceeded via the addition of the arylrhodium(I) species to the carbon−carbon double bond of α,β-unsaturated compounds.[4] Subsequently, the arylrhodium(I) species have been found to react with strained alkenes as well as electron-deficient alkenes. Murakami et al. and Lautens et al. independently reported the addition of arylboronic acids to oxanorbornenes,[5] norbornenes,[6] and allylic diol derivatives.[7] These reactions are thought to progress through the addition of arylrhodium(I) species to the carbon−carbon double bond, followed by β-elimination. The palladium- or rhodium-catalyzed allylic substitution of simple allylic acetates or alcohols with arylboronic acids has also been investigated.[8,9] These reactions selectively gave linear allylic arenes when the corresponding γ-substituted allylic alcohols or esters were used, probably proceeding via π-allyl complex intermediates (eq 1).

If the γ-substituted allylic alcohols or their derivatives undergo addition of arylrhodium species followed by β-oxy elimination, the reaction is expected to give branched allylic arenes with chiral centers. Such transformations

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(1) For reviews, see: (a) Hayashi, T. *Synlett* **2001**, 879. (b) Bolm, C.; Hildebrand, J. P.; Muñiz, K.; Hermanns, N. *Angew. Chem., Int. Ed.* **2001**, *40*, 3284. (c) Fagnou, K.; Lautens, M. *Chem. Rev.* **2003**, *103*, 169. (d) Hayashi, T.; Yamasaki, K. *Chem. Rev.* **2003**, *103*, 2829. (e) Miura, T.; Murakami, M. *Chem. Commun.* **2007**, 217. (f) Christoffers, J.; Koripelly, G.; Rosiak, A.; Rössle, M. *Synthesis* **2007**, 1279. (g) Youn, S. W. *Eur. J. Org. Chem.* **2009**, 2597.

(2) Sakai, M.; Hayashi, H.; Miyaura, N. *Organometallics* **1997**, *16*, 4229.

(3) Takaya, Y.; Ogasawara, M.; Hayashi, T.; Sakai, M.; Miyaura, N. *J. Am. Chem. Soc.* **1998**, *120*, 5579.

(4) Hayashi, T.; Takahashi, M.; Takaya, Y.; Ogasawara., M. *J. Am. Chem. Soc.* **2002**, *124*, 5052.

(5) (a) Murakami, M.; Igawa, H. *Chem. Commun.* **2002**, 390. (b) Lautens, M.; Dockendorff, C.; Fagnou, K.; Malicki, A. *Org. Lett.* **2002**, *4*, 1311.

(6) (a) Miura, T; Murakami, M. *Org. Lett.* **2005**, *7*, 3339. (b) Menard, F.; Lautens, M. *Angew. Chem., Int. Ed.* **2008**, *47*, 2085.

(7) (a) Menard, F.; Chapman, T. M.; Dockendorff, C.; Lautens, M. *Org. Lett.* **2006**, *8*, 4569. (b) Miura, T.; Takahashi, Y.; Murakami, M. *Chem. Commun.* **2007**, 595. (c) Yu, B.; Menard, F.; Isono, N.; Lautens, M. *Synthesis* **2009**, 853.

(8) (a) Uozumi, Y.; Danjo, H.; Hayashi, T. *J. Org. Chem.* **1999**, *64*, 3384. (b) Bouyssi, D.; Gerusz, V.; Balme, G. *Eur. J. Org. Chem.* **2002**, 2445. (c) Kayaki, Y.; Koda, T.; Ikariya, T. *Eur. J. Org. Chem.* **2004**, 4989.

(9) Kabalka, G. W.; Dong, G.; Venkataiah, B. *Org. Lett.* **2003**, *5*, 893.

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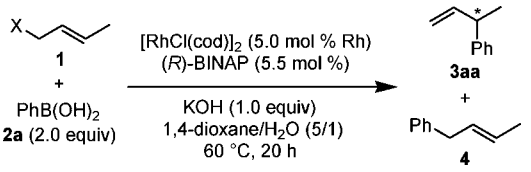
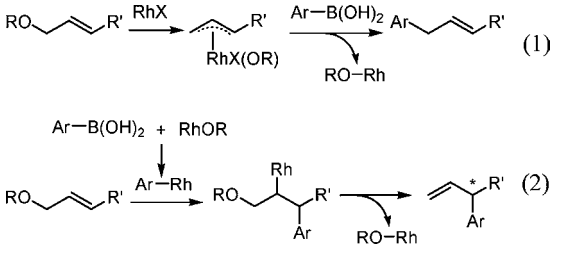
Table 1. Effects of Substrate Leaving Group[a]



			3aa		4
entry	X		yield (%)[b]	ee (%)[b]	yield (%)[b]
1	4-$CF_3C_6H_4O$	**1a**	22	77	<1
2	4-$NO_2C_6H_4O$	**1b**	25	64	7
3	PhO	**1c**	14	48	0
4	4-$MeOC_6H_4O$	**1d**	11	40	0
5	HO	**1e**	0	–	0
6	AcO	**1f**	14	71	3
7	Cl	**1g**	24	77	20
8[c]	4-$CF_3C_6H_4O$	**1a**	61	81	<1

[a] Reaction conditions: **1** (0.25 mmol), **2a** (0.5 mmol), $[RhCl(cod)]_2$ (5.0 mol % Rh), (*R*)-BINAP (5.5 mol %), KOH (0.25 mmol) in 1, 4-dioxane/H_2O (5/1, 0.6 mL). [b] Yield and enantiomeric excess were determined by GC analysis. [c] Reaction conditions: **1a** (0.25 mmol), **2a** (1.0 mmol), $[RhCl(nbd)]_2$ (5.0 mol % Rh), (*R*)-BINAP (7.5 mol %), KOH (2.0 mmol) in 1,4-dioxane/H_2O (5/1, 0.6 mL).

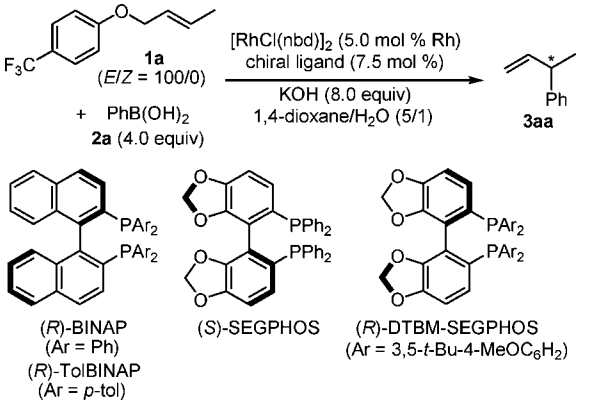
have the potential to be developed into asymmetric reactions (eq 2).



Here, we report that the regioselective and enantioselective allylic substitution of simple allylic ethers with arylboronic acids proceeded using chiral rhodium(I) complexes as catalysts. The reactions provide optically active simple alkenes, which are very useful sources of chiral compounds.

Initially, the effects of the allylic compound leaving group on the rhodium-catalyzed asymmetric coupling reaction of (*E*)-crotyl compounds **1a**–**g** with phenylboronic acid **2a** were investigated (Table 1). The substrate leaving group is an important factor in the reactivity, regioselectivity, and enantioselectivity of the reactions. When aryl (*E*)-crotyl ethers **1a**–**d** were used as substrates, the reactions proceeded regioselectively, giving the branched product **3aa** with moderate yields (Table 1, entries 1–4). Using alcohol **1e** did not result in a reaction (Table 1, entry 5). Acetate **1f** and chloride **1g** gave isomeric linear product **4** and branched product **3aa** (Table 1, entries 6 and 7). Using (*E*)-crotyl 4-trifluoromethylphenyl ether **1a** as the substrate, further investigations into the catalyst, the amounts of phenylboronic acid **2a**, and the amount of ligand and base used resulted in improvements in branched isomer **3aa** yield and enantiomeric excess, to 61% yield and 81% ee (Table 1, entry 8).

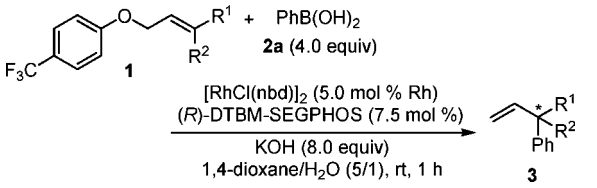
Table 2. Effects of Chiral Ligand in the Reaction of **1a** with **2a**[a]



entry	chiral ligand	temp (°C)	time (h)	yield[b] (%)	ee[b] (%)
1	(*R*)-BINAP	60	20	61	81
2	(*R*)-TolBINAP	60	20	71	85
3	(*S*)-SEGPHOS	60	20	63	82
4	(*R*)-DTBM-SEGPHOS	60	20	71	90
5	(*R*)-BINAP	rt	20	4	82
6	(*R*)-TolBINAP	rt	20	3	83
7	(*S*)-SEGPHOS	rt	20	5	78
8[c]	**(*R*)-DTBM-SEGPHOS**	**rt**	**1**	**75**	**92**

[a] Reaction conditions: **1a** (0.25 mmol), **2a** (1.0 mmol), $[RhCl(nbd)]_2$ (5.0 mol % Rh), chiral ligand (7.5 mol %), KOH (2.0 mmol) in 1,4-dioxane/H_2O (5/1, 0.6 mL). [b] Yield and enantiomeric excess were determined by GC analysis. [c] (*E*)-1-Phenylbut-2-ene **4** was also obtained in 1% yield.

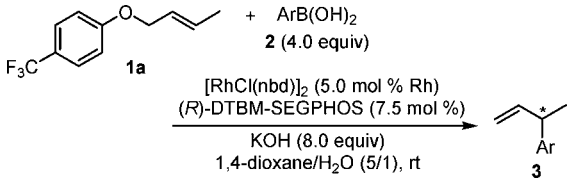
Table 3. Rh-Catalyzed Asymmetric Coupling Reaction of Allylic Ether **1** with **2a**[a]



	substrate **1**						
entry	R^1	R^2	(*E*/*Z*)		product **3**[b]	yield (%)	ee (%)[e]
1	Me	H	(100/0)	**1a**	**3aa**	75[c]	92 (*S*)
2	Et	H	(99/1)	**1h**	**3ba**	84[c]	85 (*S*)
3	*n*-Pr	H	(99/1)	**1i**	**3ca**	89[d]	85 (n.d.)[f]
4	H	Me	(3/97)	**1j**	**3aa**	82[c]	89 (*R*)
5	H	Et	(2/98)	**1k**	**3ba**	86[c]	87 (*R*)

[a] Reaction conditions: **1** (0.25 mmol), **2a** (1.0 mmol), $[RhCl(nbd)]_2$ (5.0 mol % Rh), (*R*)-DTBM-SEGPHOS (7.5 mol %), KOH (2.0 mmol) in 1,4-dioxane/H_2O (5/1, 0.6 mL) at rt for 1 h. [b] The yields of the linear products **4** were below 1%. [c] GC yield. [d] Isolated yield. [e] Enantiomeric excess values were determined by GC analysis. [f] The absolute configuration was not determined.

Table 4. Rh-Catalyzed Asymmetric Coupling Reaction of **1a** with Arylboronic Acids **2**[a]



	arylboronic acid **2**					
entry	Ar		time (h)	product **3**[b]	yield (%)	ee (%)[e]
1	Ph	**2a**	1	**3aa**	75[c]	92 (*S*)
2	4-MeC_6H_4	**2b**	1	**3ab**	87[c]	90 (*S*)
3	3-MeC_6H_4	**2c**	1	**3ac**	74[c]	92 (n.d.)[f]
4	2-MeC_6H_4	**2d**	4	**3ad**	45[c]	99 (n.d.)[f]
5	4-MeOC_6H_4	**2e**	1	**3ae**	85[d]	92 (*S*)
6	4-BrC_6H_4	**2f**	5	**3af**	71[d]	92 (*S*)
7	1-naphthyl	**2g**	6	**3ag**	36[d]	>99 (*S*)
8	2-naphthyl	**2h**	6	**3ah**	64[d]	96 (*S*)
9	6-MeO-2-naphthyl	**2i**	20	**3ai**	63[d]	91 (*S*)

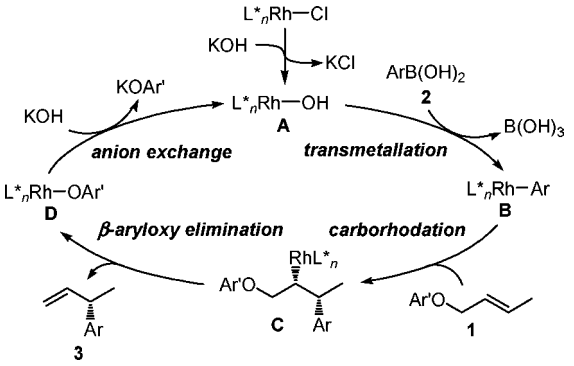
[a] Reaction conditions: **1a** (0.25 mmol), **2** (1.0 mmol), [RhCl(nbd)]$_2$ (5.0 mol % Rh), (*R*)-DTBM-SEGPHOS (7.5 mol %), KOH (2.0 mmol) in 1,4-dioxane/H_2O (5/1, 0.6 mL) at room temperature. [b] The yields of the linear products **4** were below 1%. [c] GC yield. [d] Isolated yield. [e] Enantiomeric excess values were determined by GC analysis. [f] The absolute configuration was not determined.

Next, the reaction of **1a** with phenylboronic acid **2a** was performed using various chiral ligands (Table 2). The reaction using (*R*)-TolBINAP or (*S*)-SEGPHOS, instead of (*R*)-BINAP, gave **3aa** with a better yield and ee (Table 2, entries 1−3), and (*R*)-DTBM-SEGPHOS gave a still higher yield and ee (Table 2, entry 4). The reaction proceeded smoothly even at room temperature using (*R*)-DTBM-SEGPHOS as the ligand, giving **3aa** at 75% yield and 92% ee after 1 h (Table 2, entry 8). However, the reactions were considerably slower using (*R*)-BINAP, (*R*)-TolBINAP, and (*S*)-SEGPHOS (Table 2, entries 5−7).

Under the optimized reaction conditions, using (*R*)-DTBM-SEGPHOS as the ligand, we examined the reactions of γ-substituted allylic ethers **1h**−**k** with phenylboronic acid **2a**. The results are summarized in Table 3. Regardless of the substrate steric hindrance and geometrical isomerism, in all cases, the reaction provided the branched products **3aa**−**3ca** with excellent regioselectivities and good yields and enantioselectivities (Table 3, entries 2−5). The reactions also proceeded stereospecifically: (*E*)-substrates **1a** and **1h** gave (*S*)-products (Table 3, entries 1 and 2), and (*Z*)-substrates **1j** and **1k** gave (*R*)-products (Table 3, entries 4 and 5).

Then, we investigated the scope of arylboronic acid in the reaction with **1a**. The results are summarized in Table 4. Using *p*- or *m*-tolylboronic acids **2b** and **2c** gave the corresponding products **3ab** and **3ac** with good yields and high enantioselectivities, as in the case of **2a** (Table 4, entries 1−3). The reaction with bulky *o*-tolylboronic acid **2d** gave **3ad** with excellent enantioselectivity (99% ee) but in a slightly lower yield. The other 4-substituted phenylboronic acids **2e**−**g**, which have either an electron-donating or -withdrawing group, gave branched products **3ae**−**3af** with moderate to good yields and high enantioselectivities (Table 4, entries 5−7). Replacing the phenyl group with a 1- or 2-naphthyl group gave the products **3ag** or **3ah** with excellent enantioselectivities, but longer reaction times were required (Table 4, entries 7 and 8). The coupling reaction of **1a** with 6-methoxy-2-naphthylboronic acid (**2i**) gave the allylic substituted product **3ai**, which is a precursor of the nonsteroidal anti-inflammatory drug naproxen, with a 63% yield and 91% ee (Table 4, entry 9).

Scheme 1. Possible Mechanism



The catalytic coupling reaction of allyl aryl ethers with arylboronic acids may involve the carborhodation of the carbon−carbon double bond, followed by β-alkoxy elimination (eq 2), as proposed by Murakami et al. and Lautens et al.[5−7] A possible reaction mechanism is shown in Scheme 1. A hydroxorhodium(I) species **A** is initially generated by anion exchange of a chlororhodium(I) complex with potassium hydroxide. Subsequent transmetalation between **A** and the arylboronic acid **2** gives an arylrhodium intermediate **B**. Enantioselective carborhodation gives intermediate **C**, and then β-aryloxy elimination gives the coupling product **3** and generates aryloxorhodium(I) species **D**. Anion exchange of **D** with potassium hydroxide regenerates the initial species **A**. The stereospecificity of the reaction (Table 3, entry 1 vs 4 and entry 2 vs 5) supports this addition−elimination mechanism. The bulky aryl groups on DTBM-SEGPHOS would promote the β-aryloxy elimination and enhance the enantioselectivity.

In summary, we have developed a regio- and enantioselective allylic substitution of simple allylic ethers with arylboronic acids using a rhodium(I)/(*R*)-DTBM-SEGPHOS catalyst system. The reactions proceeded in high yields with excellent regioselectivities, under very mild conditions, to give optically active simple alkenes. Further studies are in progress to expand the scope and investigate the mechanistic details of this reaction system.

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Supporting Information Available. Experimental procedures and characterization data for substrates and products. This material is available free of charge via the Internet at http://pubs.acs.org.

The authors declare no competing financial interest.