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Rhodium-Catalyzed Asymmetric 1,4-Addition of 2-Alkenyl-1,3,2-benzodioxaboroles to α,β-Unsaturated Ketones

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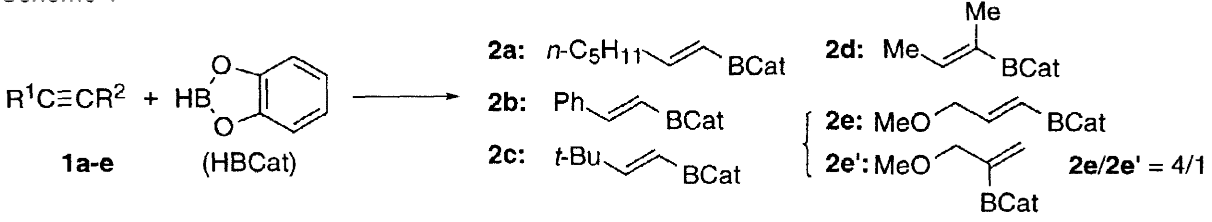
Abstract: Reaction of 2-alkenyl-1,3,2-benzodioxaboroles, which are readily accessible by hydroboration of alkynes with catecholborane, with α,β-unsaturated ketones in the presence of rhodium/(*S*)-binap catalyst and triethylamine in dioxane/H_2O (10/1) proceeded with high enantioselectivity at 100 °C to give high yields of optically active β-alkenyl ketones of over 90% ee. One pot synthesis of the 1,4-addition product is also successful in the rhodium-catalyzed asymmetric reaction by use of alkenylboranes generated *in situ* from alkyne and catecholborane.

In 1997 Miyaura has reported that a rhodium complex catalyzes 1,4-addition of aryl- and alkenylboronic acids to enones in an aqueous solution.[1] Very recently the rhodium-catalyzed reaction has been extended to catalytic asymmetric synthesis by use of a rhodium complex coordinated with (*S*)-binap.[2] In a typical transformation, the reaction of 2-cyclohexenone with phenylboronic acid in the presence of 3 mol % of the rhodium catalyst generated from $Rh(acac)(C_2H_4)_2$ and (*S*)-binap in dioxane/H_2O (10/1) at 100 °C for 5 h gave (*S*)-3-phenylcyclohexanone of 97% ee. Unfortunately, the preparation, isolation, and purification of the organoboronic acids are not always easy, and it would be more practically useful if boronic acid esters were used for the catalytic asymmetric 1,4-addition. Here we report that 2-alkenyl-1,3,2-benzodioxaboroles **2** that are readily accessible by hydroboration of alkynes **1** with catecholborane can be also used successfully for the rhodium-catalyzed asymmetric 1,4-addition to enones **3**.

Hydroboration of 1-heptyne (**1a**), phenylethyne (**1b**), 3,3-dimethyl-1-butyne (**1c**), 2-butyne (**1d**), 3-methoxy-1-propyne (**1e**), with catecholborane was carried out without solvent at 0~70 °C according to the standard procedures.[3] Distillation under reduced pressure gave high yields of the corresponding 2-alkenyl-1,3,2-benzodioxaboroles **2** (Scheme 1). The reaction of **1e** gave a mixture of regioisomers consisting of 3-methoxy-1-boryl-1-propene (**2e**) and 3-methoxy-2-boryl-1-propene (**2e'**) in a ratio of 4 to 1.

For the reaction of (*E*)-1-heptenylborane **2a** with 2-cyclohexenone (**3m**) catalyzed by the Rh-(*S*)-binap complex, several reaction conditions were examined (Scheme 2, Table 1). The chemical yield of 3-((*E*)-1-heptenyl)cyclohexanone (**4am**) was very low (29%, entry 1) under the conditions used for the reaction of aryl-

Scheme 1



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Scheme 2

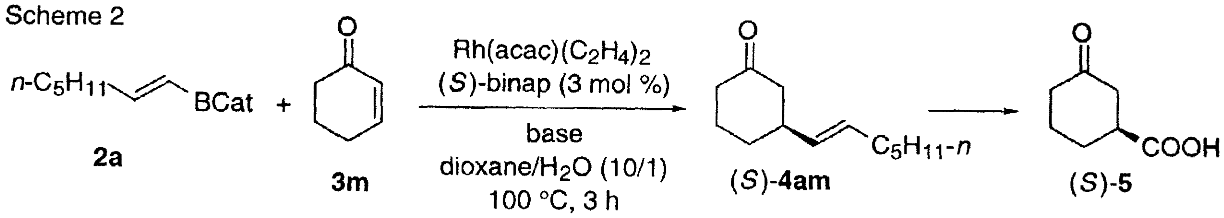


Table 1. Effects of Base on Asymmetric 1,4-Addition of 2-[(*E*)-1-Heptenyl]-1,3,2-benzodioxaborole (**2a**) to 2-cyclohexenone (**3m**)[a]

entry	base (equiv to **3m**)	yield (%)[b]	% ee[c] (config)
1	none	29	94 (*S*)
2	Et_3N (5.0)	78	95 (*S*)
3[d]	Et_3N (10.0)	92	96 (*S*)
4	*i*-Pr_2NEt (5.0)	29	94 (*S*)
5	NaOH (5.0)	26	94 (*S*)

[a] The reaction was carried out in dioxane/H_2O (10/1) for 3 h with 2.5 equiv of **2a** in the presence of 3 mol % of the catalyst generated from Rh(acac)$(C_2H_4)_2$ and (*S*)-binap. [b] Isolated yield by silica gel chromatography. [c] Determined by HPLC analysis with a chiral stationary phase column (Daicel Chiralpak AS, hexane/2-propanol = 90/10). [d] The reaction with 5.0 equiv of **2a**.

and alkenylboronic acids,[2] that is, in dioxane/H_2O (10/1) at 100 °C, though the enantioselectivity is high (94% ee). Considering that the alkenylcatecholborane undergoes hydrolysis under the reaction conditions generating alkenylboronic acid and catechol[4] which makes the reaction media acidic, several bases were added to the reaction mixture. The chemical yield was greatly improved by the addition of 5 equiv (to **3m**) of triethylamine, which gave 78% yield of **4am** in the reaction of **3m** with 2.5 equiv of **2a** (entry 2). Use of 5 equiv of **2a** in the presence of triethylamine increased the yield to 92% (entry 3). Other bases such as diisopropylethylamine or sodium hydroxide were less effective than triethylamine (entries 4 and 5). The enantioselectivity was kept high (94%~96% ee) with any bases. The absolute configuration of **4am** was determined to be (–)-(*S*) by correlation with known (+)-(*S*)-3-carboxycyclohexanone[5] (**5**) obtained by oxidative cleavage of the carbon-carbon double bond.[6]

Several other 2-alkenyl-1,3,2-benzodioxaboroles were also successfully used for the catalytic asymmetric 1,4-addition (Scheme 3, Table 2). Alkenyl groups, (*E*)-2-phenylethenyl (**2b**), (*E*)-3,3-dimethyl-1-butenyl (**2c**), and 2-buten-2-yl (**2d**), were introduced with high enantioselectivity into 2-cyclohexenone (**3m**) giving the corresponding 3-substituted cyclohexanones in over 91% ee in high yields (entries 2-4).[7] Interestingly, the reaction of **3m** with the mixture of linear isomer **2e** and branch isomer **2e'** (4 to 1 ratio), prepared by the hydroboration of propargyl ether **1e**, gave a single 1,4-addition product **4em** which results from 1-alkenylborane **2e** (entry 5).[7] High enantioselectivity was also achieved in the reaction of 2-cyclopentenone (**3n**) with alkenylboranes **2a** and **2d** (entries 6 and 7).[7]

One pot synthesis of optically active β-alkenyl ketones is also possible from alkynes and catecholborane without isolation of the hydroboration products (Scheme 4). For a typical example, catecholborane (245 mg, 2.00 mmol) was added to 1-heptyne (**1a**, 216 mg, 2.20 mmol) at 0 °C. The mixture was stirred at room

Scheme 3

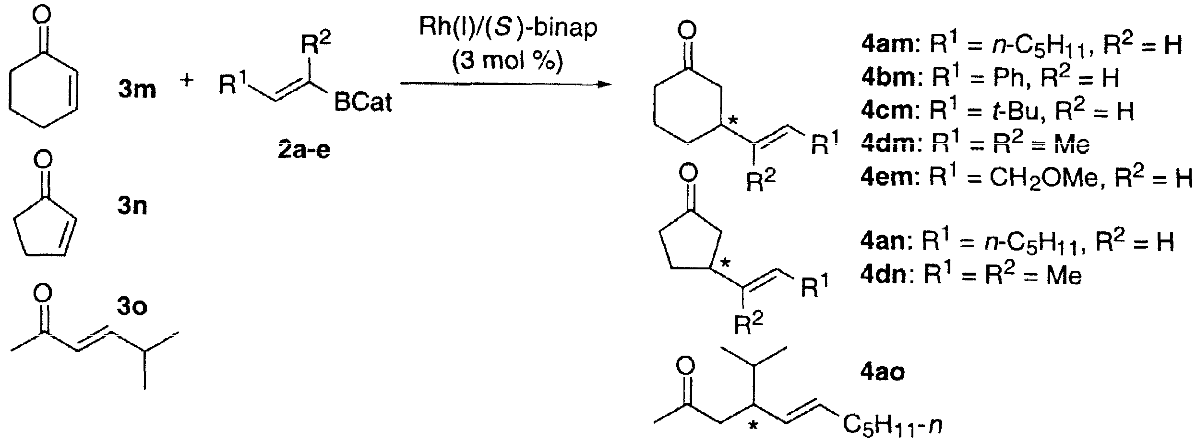


Table 2. Asymmetric 1,4-Addition of Bronic Esters **2** to Enones **3** Catalyzed by (*S*)-binap-Rhodium(I)[a]

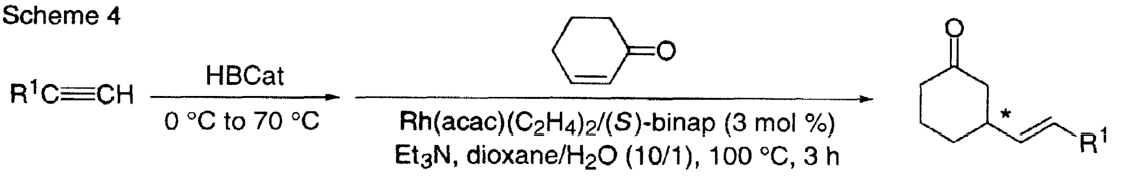
entry	enone **3**	boronic ester **2**	yield[b] (%) of **4**	% ee[c] of **4**	$[\alpha]_D^{20}$ (*c* in $CHCl_3$)
1	**3m**	**2a**	92 (**4am**)	96 (*S*)[d]	−16 (0.91)
2	**3m**	**2b**	76 (**4bm**)	92 (*S*)[d]	+7.6 (0.86)
3	**3m**	**2c**	77 (**4cm**)	91	−20 (1.31)
4	**3m**	**2d**	82 (**4dm**)	99	−14 (0.65)
5	**3m**	**2e** (+**2e'**)	89 (**4em**)	94	−8.5 (1.04)
6	**3n**	**2a**	83 (**4an**)	98	−78 (0.94)
7	**3n**	**2d**	81 (**4dn**)	95	−106 (0.61)
8	**3o**	**2a**	68 (**4ao**)	81	−5.9 (1.00)

[a] The reaction was carried out in dioxane/H_2O (10/1) for 3 h with 5 equiv of boronic ester **2** and 10 equiv of Et_3N, in the presence of 3 mol % of the catalyst generated from $Rh(acac)(C_2H_4)_2$ and (*S*)-binap. [b] Isolated yield by silica gel chromatography. [c] Determined by HPLC analysis with a chiral stationary phase column, Daicel Chiralpak AS (hexane/2-propanol = 90/10 for **4am**, **4bm**, **4dm**, and **4em**. hexane/2-propanol = 98/2 for **4cm**, **4an**, **4en**, and **4ao**). [d] Determined by correlation with (+)-(*S*)-3-carboxy-cyclohexanone (**5**) (see text).

temperature for 30 min and at 70 °C for 3 h. Unreacted materials were removed under reduced pressure. To the residue, were added a solution of 2-cyclohexenone (**3m**, 39 mg, 0.40 mmol), $Rh(acac)(C_2H_4)_2$ (3.1 mg, 12 μmol), and (*S*)-binap (7.5 mg, 12 μmol) in dioxane (1.0 mL), triethylamine (409 mg, 4.00 mmol), and H_2O (0.1 mL). The whole mixture was heated at 100 °C for 3 h. Addition of 20% aqueous sodium hydroxide followed by ether extraction and silica gel chromatography (hexane/ethyl acetate = 5/1) gave 66 mg (85% yield) of (*S*)-3-((*E*)-1-heptenyl)cyclohexanone (**4am**), whose enantiomeric purity was determined to be 95% ee by HPLC analysis with a chiral stationary phase column.

The present reaction of 2-alkenyl-1,3,2-benzodioxaboroles extends the scope of the rhodium-catalyzed asymmetric 1,4-addition forming optically active β-alkenyl ketones which generally proceeds on various types of α,β-unsaturated ketones with high enantioselectivity.

Scheme 4



R^1 = n-C_5H_{11} (**4am**): 85% yield, 95% ee (*S*)
R^1 = *t*-Bu (**4cm**): 75% yield, 92% ee

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References and notes

1. Sakai, M.; Hayashi, H.; Miyaura, N. *Organometallics* **1997**, *16*, 4229.
2. Takaya, Y.; Ogasawara, M.; Hayashi, T.; Sakai, M.; Miyaura, N. *J. Am. Chem. Soc.* **1998**, *120*, 5579.
3. (a) Brown, H. C.; Gupta, S. K. *J. Am. Chem. Soc.* **1975**, *97*, 5249. (b) Lane, C. F.; Kabalka, G. W. *Tetrahedron* **1976**, *32*, 981.
4. It was confirmed that alkenylcatecholborane **2a** undergoes hydrolysis giving the corresponding alkenylboronic acid on heating its aqueous solution (dioxane/H_2O = 10/1) at 100 °C.
5. Numata, A.; Suzuki, T.; Ohno, K.; Uyeo, S. *Yakugaku Zasshi* **1968**, *88*, 1298.
6. A sample of (–)-**4am** ($[\alpha]_D^{20}$ –16 (*c* 0.91, chloroform)) was oxidized with ruthenium trichloride and sodium metaperiodate according to the procedures reported by Sharpless (Carlsen, P. H. J.; Katsuki, T.; Martin, V. S.; Sharpless, K. B. *J. Org. Chem.* **1981**, *46*, 3936) to give a mixture of carboxycyclohexanone (**5**) and hexanoic acid. The mixture was esterified with diazomethane, and the methyl esters were separated by preparative TLC. Methyl ester of **5** was hydrolyzed (30% KOH/methanol) to give pure (*S*)-(+)-**5** ($[\alpha]_D^{20}$ +8.1 (*c* 1.16, methanol)) (ref. 5).
7. **4bm**: ^{1}H NMR ($CDCl_3$) δ 1.58-1.66 (m, 1H), 1.70-1.79 (m, 1H), 2.00-2.04 (m, 1H), 2.07-2.12 (m, 1H), 2.28-2.34 (m, 2H), 2.38-2.42 (m, 1H), 2.51-2.55 (m, 1H), 2.65-2.70 (m, 1H), 6.15 (dd, J = 16.2 and 6.9 Hz, 1H), 6.39 (d, J = 16.2 Hz, 1H), 7.22 (t, J = 7.4 Hz, 1H), 7.30 (t, J = 7.4 Hz, 2H), 7.34-7.36 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 24.99, 31.39, 41.27, 41.93, 47.34, 126.14, 127.35, 128.56, 129.12, 132.92, 137.12, 210.87. Anal. calcd. for $C_{14}H_{16}O$: C, 83.96; H, 8.05. Found: C, 83.74; H, 8.23. **4dm**: ^{1}H NMR ($CDCl_3$) δ 1.58 (d, J = 6.9 Hz, 3H), 1.61 (s, 3H), 1.63-1.69 (m, 2H), 1.84-1.86 (m, 1H), 2.03-2.08 (m, 1H), 2.23-2.37 (m, 5H), 5.26 (q, J = 6.9 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 13.26, 13.69, 25.21, 30.08, 41.28, 46.87, 47.54, 118.43, 137.66, 212.00. Anal. calcd. for $C_{10}H_{16}O$: C, 78.90; H, 10.59. Found: C, 78.88; H, 10.64. **4em**: ^{1}H NMR ($CDCl_3$) δ 1.49-1.56 (m, 1H), 1.67-1.74 (m, 1H), 1.93-1.96 (m, 1H), 2.04-2.09 (m, 1H), 2.19-2.30 (m, 2H), 2.36-2.54 (m, 3H), 3.33 (s, 3H), 3.88 (d, J = 5.9 Hz, 2H), 5.57 (dt, J = 15.7 and 5.9 Hz, 1H), 5.68 (dd, J = 15.7 and 6.4 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 24.92, 31.11, 41.17, 41.20, 47.16, 57.91, 72.84, 125.64, 136.39, 210.89. Anal. calcd. for $C_{10}H_{16}O_2$: C, 71.39; H, 9.59. Found: C, 71.66; H, 9.66. **4dn**: ^{1}H NMR ($CDCl_3$) δ 1.61 (d, J = 6.9 Hz, 3H), 1.64 (s, 3H), 1.74-1.81 (m, 1H), 2.08-2.21 (m, 3H), 2.30-2.36 (m, 2H), 2.72-2.79 (m, 1H), 5.30 (q, J = 6.9 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 13.30, 14.08, 28.02, 38.51, 43.51, 45.15, 118.35, 136.15, 219.28. Anal calcd. for $C_9H_{14}O$: C, 78.21; H, 10.21. Found: C, 78.50; H, 10.21. **4ao**: ^{1}H NMR ($CDCl_3$) δ 0.83 (d, J = 6.9 Hz, 3H), 0.87 (d, J = 6.9 Hz, 3H), 0.88 (t, J = 6.4 Hz, 3H), 1.22-1.36 (m, 6H), 1.55-1.61 (m, 1H), 1.97 (q, J = 6.9 Hz, 2H), 2.10 (s, 3H), 2.31-2.46 (m, 3H), 5.19 (dd, J = 15.2 and 8.4 Hz, 1H), 5.38 (dt, J = 15.2 and 6.9 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 14.06, 18.86, 20.45, 22.49, 29.21, 30.54, 31.33, 31.91, 32.55, 45.07, 47.14, 130.21, 132.42, 209.03. Anal calcd. for $C_{14}H_{26}O$: C, 79.94; H, 12.46. Found: C, 79.82; H, 12.20. For **4am**, **4cm**, and **4an**, see ref. 2.