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Carbon–Carbon Bond-Forming Enantioselective Synthesis of Chiral Organosilicon Compounds by Rhodium/Chiral Diene-Catalyzed Asymmetric 1,4-Addition Reaction

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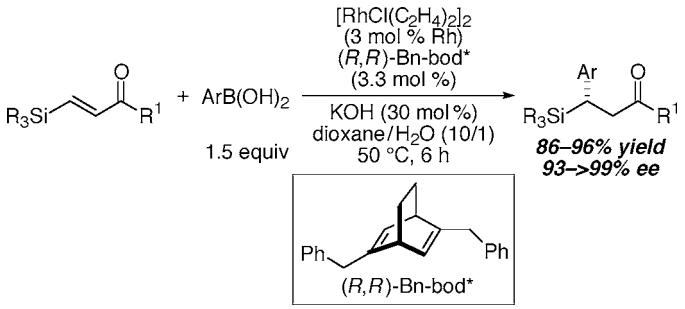
ABSTRACT



A new synthetic method for chiral organosilicon compounds through a rhodium-catalyzed asymmetric 1,4-addition of arylboronic acids to *β*-silyl α,*β*-unsaturated carbonyl compounds has been developed. By employing (*R*,*R*)-Bn-bod* as a ligand, a range of arylboronic acids can be coupled with these substrates in very high enantiomeric excess. The resulting *β*-silyl 1,4-adducts can be converted to *β*-hydroxy carbonyl compounds or allylsilanes while retaining their stereochemical information.

Organic molecules containing carbon−silicon bonds constitute an important class of compounds due to their wide utility in organic synthesis.[1] For example, carbon−silicon bonds can be readily oxidized to carbon−oxygen bonds by Tamao[2] or Fleming[3] oxidation, and allylsilanes are often used as effective allylating agents toward various carbonyl compounds to furnish homoallylic alcohol derivatives. These oxidation and allylation processes are known to proceed with high stereoselectivity when stereo-issues are involved.[1d,e] Therefore, construction of highly enantio-enriched chiral organosilicon compounds is an important objective, and achieving such an objective by asymmetric catalysis is highly desirable in view of efficiency.[4−7] In addition, if these compounds could be synthesized through transition-metal-catalyzed carbon−carbon bond forming reactions, the efficiency of the process would be further enhanced. Here we

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(2) (a) Tamao, K.; Ishida, N.; Tanaka, T.; Kumada, M. *Organometallics* **1983**, *2*, 1694. (b) Tamao, K.; Ishida, N. *J. Organomet. Chem.* **1984**, *269*, C37. (c) Tamao, K.; Nakajo, E.; Ito, Y. *J. Org. Chem.* **1987**, *52*, 4412. (d) Tamao, K. In *Organosilicon and Bioorganosilicon Chemistry*; Sakurai, H., Ed.; Ellis Horwood: Chichester, UK, 1985; p 231.

(3) (a) Fleming, I.; Henning, R.; Plaut, H. *J. Chem. Soc., Chem. Commun.* **1984**, 29. (b) Fleming, I.; Sanderson, P. E. J. *Tetrahedron Lett.* **1987**, *28*, 4229.

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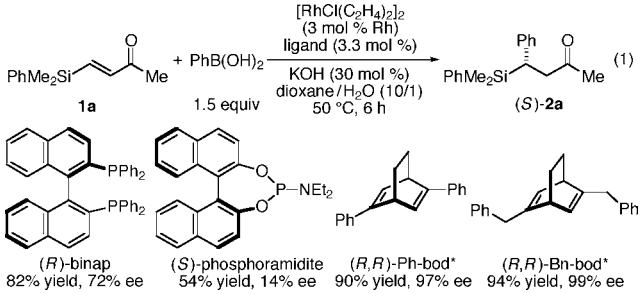
describe that a rhodium/chiral diene catalyst is highly effective for asymmetric 1,4-addition of arylboronic acids to β-silyl α,β-unsaturated carbonyl compounds, providing a new and useful method for the construction of chiral organosilicon compounds in high yield and enantioselectivity.

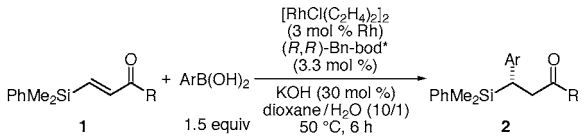
In an initial investigation, we examined the effect of ligand by employing β-phenyldimethylsilyl enone **1a** as a model substrate in the 1,4-addition of $PhB(OH)_2$ with 3 mol % of rhodium (eq 1). The use of (*R*)-binap[8] as a ligand produced

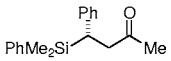
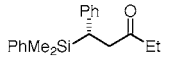
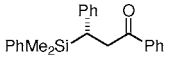
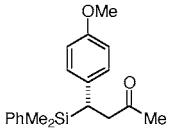
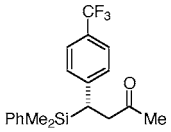
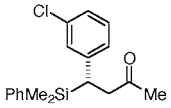
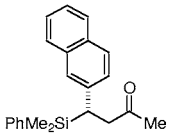
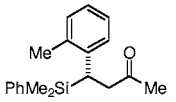


1,4-adduct **2a** in 82% yield with moderate ee of 72% (*S*).[9] Change of the ligand to (*S*)-phosphoramidite[10] (2.0 equiv to rhodium) resulted in lower yield and enantioselectivity (54% yield, 14% ee (*S*)). In contrast, the use of chiral diene ligands proved to be more effective for this 1,4-addition reaction, achieving higher yield and ee. Thus, the employment of (*R*,*R*)-Ph-bod*[11] as a ligand provided **2a** in 90% yield with 97% ee (*S*), and the change of substituents on the olefins from phenyl to benzyl ((*R*,*R*)-Bn-bod*)[11−13] further improved both yield and enantioselectivity (94% yield, 99% ee (*S*)).[14]

Under the optimized conditions with (*R*,*R*)-Bn-bod* as the ligand, the scope of the substrate and the nucleophile is illustrated in Table 1.[15] Thus, not only methyl enone, but also ethyl or phenyl enone can be phenylated effectively in excellent yield and ee (89−94% yield, 97−99% ee; entries 1−3). In addition, sterically and electronically diverse arrays of aryl groups can be installed under the same conditions,

Table 1. Rh/(*R*,*R*)-Bn-bod*-Catalyzed Asymmetric 1,4-Addition of Arylboronic Acids to β-Phenyldimethylsilyl Enones **1**



entry	product		yield (%)	ee (%)[a]
1		(**2a**)	94	99 (*S*)
2		(**2b**)	89	98 (*S*)
3		(**2c**)	94	97 (*S*)
4		(**2d**)	95	96 (*S*)
5		(**2e**)	94	95 (*S*)
6		(**2f**)	92	95 (*S*)
7		(**2g**)	96	93 (*S*)
8		(**2h**)	90	93 (*S*)[b]

[a] Ee was determined by chiral HPLC on a Chiralpak AD-H column with hexane/2-propanol. [b] Ee was determined by chiral HPLC on a Chiralcel OD-H column with hexane/2-propanol 90/10.

(4) For reviews of palladium-catalyzed asymmetric hydrosilylations, see: (a) Tang, J.; Hayashi, T. In *Catalytic Hetero-functionalization*; Togni, A., Grützmacher, H., Eds.; Wiley-VCH: Weinheim, Germany, 2001; p 73. (b) Tietze, L. F.; Ila, H.; Bell, H. P. *Chem. Rev.* **2004**, *104*, 3453 and the references therein. See also: (c) Suginome, M.; Ohmura, T.; Miyake, Y.; Mitani, S.; Ito, Y.; Murakami, M. *J. Am. Chem. Soc.* **2003**, *125*, 11174.

(5) For a review of asymmetric synthesis of allylsilanes by palladium-catalyzed cross-coupling reactions, see: Hayashi, T. In *Comprehensive Asymmetric Catalysis*; Jacobsen, E. N., Pfaltz, A., Yamamoto, H., Eds.; Springer: New York, 1999; Vol. 2, Chapter 25.

(6) For examples of a palladium-catalyzed asymmetric 1,4-addition of disilanes, see: (a) Hayashi, T.; Matsumoto, Y.; Ito, Y. *J. Am. Chem. Soc.* **1988**, *110*, 5579. (b) Matsumoto, Y.; Hayashi, T.; Ito, Y. *Tetrahedron* **1994**, *50*, 335.

(7) For examples of palladium-catalyzed asymmetric allylic silylations, see: (a) Matsumoto, Y.; Ohno, A.; Hayashi, T. *Organometallics* **1993**, *12*, 4051. (b) Hayashi, T.; Ohno, A.; Lu, S.; Matsumoto, Y.; Fukuyo, E.; Yanagi, K. *J. Am. Chem. Soc.* **1994**, *116*, 4221.

(8) Takaya, H.; Mashima, K.; Koyano, K.; Yagi, M.; Kumobayashi, H.; Taketomi, T.; Akutagawa, S.; Noyori, R. *J. Org. Chem.* **1986**, *51*, 629.

(9) (a) Takaya, Y.; Ogasawara, M.; Hayashi, T.; Sakai, M.; Miyaura, N. *J. Am. Chem. Soc.* **1998**, *120*, 5579. (b) For a review of rhodium-catalyzed asymmetric 1,4-additions, see: Hayashi, T.; Yamasaki, K. *Chem. Rev.* **2003**, *103*, 2829.

(10) (a) Boiteau, J.-G.; Minnaard, A. J.; Feringa, B. L. *J. Org. Chem.* **2003**, *68*, 9481. (b) Feringa, B. L. *Acc. Chem. Res.* **2000**, *33*, 346.

(11) (a) Tokunaga, N.; Otomaru, Y.; Okamoto, K.; Ueyama, K.; Shintani, R.; Hayashi, T. *J. Am. Chem. Soc.* **2004**, *126*, 13584. (b) Otomaru, Y.; Okamoto, K.; Shintani, R.; Hayashi, T. *J. Org. Chem.* **2005**, *70*, 2503. (c) Shintani, R.; Kimura, T.; Hayashi, T. *Chem. Commun.* **2005**, 3213. (d) Shintani, R.; Okamoto, K.; Hayashi, T. *Chem. Lett.* **2005**, 1294.

(12) (a) Shintani, R.; Okamoto, K.; Otomaru, Y.; Ueyama, K.; Hayashi, T. *J. Am. Chem. Soc.* **2005**, *127*, 54. (b) Shintani, R.; Tsurusaki, A.; Okamoto, K.; Hayashi, T. *Angew. Chem., Int. Ed.* **2005**, *44*, 3909.

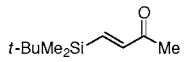
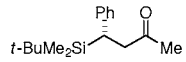
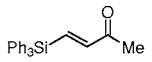
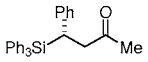
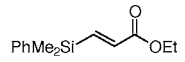
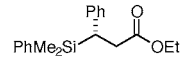
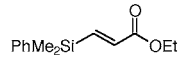
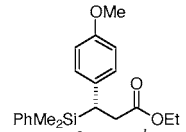
(13) For other chiral diene ligands in the literature, see: (a) Hayashi, T.; Ueyama, K.; Tokunaga, N.; Yoshida, K. *J. Am. Chem. Soc.* **2003**, *125*, 11508. (b) Shintani, R.; Ueyama, K.; Yamada, I.; Hayashi, T. *Org. Lett.* **2004**, *6*, 3425. (c) Otomaru, Y.; Tokunaga, N.; Shintani, R.; Hayashi, T. *Org. Lett.* **2005**, *7*, 307. (d) Otomaru, Y.; Kina, A.; Shintani, R.; Hayashi, T. *Tetrahedron*: *Asymmetry* **2005**, *16*, 1673. (e) Fischer, C.; Defieber, C.; Suzuki, T.; Carreira, E. M. *J. Am. Chem. Soc.* **2004**, *126*, 1628. (f) Defieber, C.; Paquin, J.-F.; Serna, S.; Carreira, E. M. *Org. Lett.* **2004**, *6*, 3873. (g) Paquin, J.-F.; Defieber, C.; Stephenson, C. R. J.; Carreira, E. M. *J. Am. Chem. Soc.* **2005**, *127*, 10850. (h) Paquin, J.-F.; Stephenson, C. R. J.; Defieber, C.; Carreira, E. M. *Org. Lett.* **2005**, *7*, 3821. (i) Läng, F.; Breher, F.; Stein, D.; Grützmacher, H. *Organometallics* **2005**, *24*, 2997. (j) Grundl, M. A.; Kennedy-Smith, J. J.; Trauner, D. *Organometallics* **2005**, *24*, 2831.

(14) The absolute configuration of compound **2a** was determined to be (*S*) by comparison of the optical rotation ($[\alpha]^{20}_D$ −9.3 (*c* 1.19, $CHCl_3$)) with the reported value in ref 6a ($[\alpha]^{20}_D$ +9.2 in $CHCl_3$ for (*R*)).

furnishing the corresponding 1,4-adducts uniformly in high yield and enantioselectivity (90−96% yield, 93−96% ee; entries 4−8).

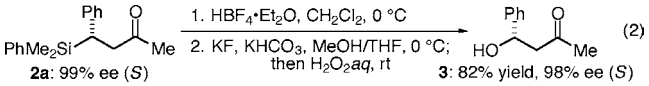
Furthermore, suitable substrates for this reaction are not limited to β-phenyldimethylsilyl enones. Thus, as shown in Table 2, other β-silyl enones (e.g., β-(*tert*-butyl)dimethylsilyl and β-triphenylsilyl enones) also undergo the present 1,4-addition reaction with high efficiency (91−95% yield, 97−>99% ee; entries 1 and 2). β-Silyl enoates can also be employed as substrates, providing the 1,4-adducts in high yield and ee as well (86−88% yield, 93−95% ee; entries 3 and 4).

Table 2. Rh/(*R*,*R*)-Bn-bod*-Catalyzed Asymmetric 1,4-Addition to Other β-Silyl α,β-Unsaturated Carbonyl Compounds[a]

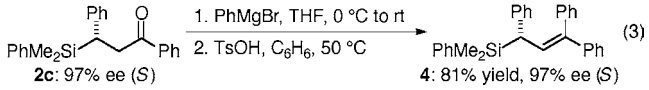
entry	substrate	product		yield (%)	ee (%)[b]
1			(**2i**)	95	>99 (*S*)[c]
2[d]			(**2j**)	91	97 (*S*)
3			(**2k**)	88	95 (*S*)
4			(**2l**)	86	93 (*S*)[e]

[a] See Table 1 for the reaction conditions. [b] Ee was determined by chiral HPLC on a Chiralpak AD-H column with hexane/2-propanol. [c] Ee was determined by chiral HPLC on a Chiralcel OJ-H column with hexane/2-propanol 200/1. [d] The reaction time was 12 h in the presence of 5 mol % of catalyst. [e] Ee was determined by chiral HPLC on a Chiralcel OD-H column with hexane/2-propanol 100/1.

Highly enantio-enriched chiral organosilicon compounds obtained through these rhodium-catalyzed 1,4-addition reactions are useful chiral building blocks for further derivatizations. For example, 1,4-adduct **2a** can be converted to the corresponding β-hydroxyketone (**3**) by oxidation of the carbon−silicon bond while retaining its stereochemical information.[1d,2,3] Thus, according to Tamao's procedure,[2] treatment of **2a** (99% ee) with tetrafluoroboric acid, followed by oxidation with hydrogen peroxide, provides β-hydroxyketone **3** with retention of configuration (82% yield, 98% ee; eq 2).[6,16] In addition, 1,4-adduct **2c** (97% ee) can be transformed into allylsilane **4** through a Grignard addition/dehydration sequence with no erosion of ee as well (81% yield, 97% ee; eq 3).



(2)



(3)

In summary, we have developed a new synthetic method for chiral organosilicon compounds through a rhodium-catalyzed asymmetric 1,4-addition of arylboronic acids to β-silyl α,β-unsaturated carbonyl compounds. By employing (*R*,*R*)-Bn-bod* as a ligand, we have efficiently coupled a range of arylboronic acids with these substrates in very high enantiomeric excess. The resulting β-silyl 1,4-adducts can be converted to β-hydroxy carbonyl compounds or allylsilanes while retaining their stereochemical information.

Acknowledgment. Support has been provided in part by a Grant-in-Aid for Scientific Research, the Ministry of Education, Culture, Sports, Science and Technology, Japan (21 COE on Kyoto University Alliance for Chemistry).

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

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(15) **General procedure:** KOH (0.10 mL, 60 μmol; 0.6 M in H_2O) was added to a solution of $[RhCl(C_2H_4)_2]_2$ (1.2 mg, 6.2 μmol Rh) and (*R*,*R*)-Bn-bod* (1.9 mg, 6.6 μmol) in 1,4-dioxane (0.50 mL), and the mixture was stirred for 5 min at room temperature. $ArB(OH)_2$ (0.30 mmol) and substrate **1** (0.20 mmol) were added to it with additional 1,4-dioxane (0.50 mL), and the resulting solution was stirred for 6 h at 50 °C. The reaction mixture was directly passed through a pad of silica gel with Et_2O and the solvent was removed under vacuum. The residue was purified by silica gel preparative TLC with Et_2O/hexane to afford the product.

(16) For recent examples of asymmetric synthesis of β-hydroxyketones by direct aldol reactions under organocatalysis, see: (a) Tang, Z.; Yang, Z.-H.; Chen, X.-H.; Cun, L.-F.; Mi, A.-Q.; Jiang, Y.-Z.; Gong, L.-Z. *J. Am. Chem. Soc.* **2005**, *127*, 9285. (b) Berkessel, A.; Koch, B.; Lex, J. *Adv. Synth. Catal.* **2004**, *346*, 1141.