ORGANIC LETTERS

2007
Vol. 9, No. 22
4643−4645

Catalytic Asymmetric Synthesis of Allylsilanes through Rhodium/Chiral Diene-Catalyzed 1,4-Addition of Alkenyl[2-(hydroxymethyl)phenyl]dimethylsilanes

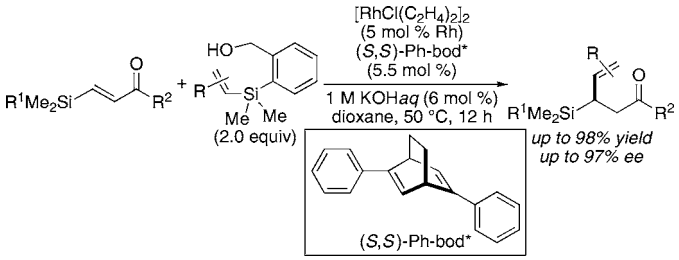
Ryo Shintani,*,† Yoshitaka Ichikawa,† Tamio Hayashi,*,† Jinshui Chen,‡ Yoshiaki Nakao,‡ and Tamejiro Hiyama*,‡

Department of Chemistry, Graduate School of Science, Kyoto University, Sakyo, Kyoto 606-8502, Japan, and Department of Material Chemistry, Graduate School of Engineering, Kyoto University, Nishikyo, Kyoto 606-8510, Japan

shintani@kuchem.kyoto-u.ac.jp; thayashi@kuchem.kyoto-u.ac.jp; thiyama@npc05.kuic.kyoto-u.ac.jp

Received August 29, 2007

ABSTRACT



A new synthetic method of chiral allylsilanes has been developed through a rhodium-catalyzed asymmetric 1,4-addition of alkenyl[2-(hydroxymethyl)phenyl]dimethylsilanes to β-silyl α,β-unsaturated ketones. By employing (*S*,*S*)-Ph-bod* as a ligand, a range of alkenyl nucleophiles have been installed to these substrates in high yield and enantiomeric excess. The resulting allylsilanes can be used for stereoselective intramolecular allylation reactions to control two contiguous tertiary and quaternary stereocenters.

Organic molecules containing carbon−silicon bonds are an important class of compounds due to their wide utility in organic synthesis.[1] In particular, allylsilanes are known to act as effective allylating agents toward various carbonyl compounds to give homoallyl alcohol derivatives, and these allylation processes proceed with high stereoselectivity when stereo issues are involved.[2] Therefore, the development of a catalytic asymmetric method of constructing highly enantioenriched chiral allylsilanes is of high value in view of the efficiency,[3] and it would be more desirable if these com-

† Graduate School of Science.
‡ Graduate School of Engineering.

(1) (a) Colvin, E. W. In *Chemistry of Organic Silicon Compounds*; Rappoport, Z., Apeloig, Y., Eds.; Wiley: Chichester, 1998; Part 2, p 1667. (b) Hiyama, T.; Shirakawa, E. In *Handbook of Organopalladium Chemistry for Organic Synthesis*; Negishi, E.-i., Ed.; John Wiley & Sons: Hoboken, 2002; Vol. 1, p 285. (c) Denmark, S. E.; Sweis, R. F. In *Metal-Catalyzed Cross-Coupling Reactions*, 2nd ed.; De Meijere, A., Diederich, F., Eds.; Wiley-VCH: Weinheim, 2004; Vol. 1, p 163. (d) Jones, G. R.; Landais, Y. *Tetrahedron* **1996**, *52*, 7599. (e) Chan, T. H.; Wang, D. *Chem. Rev.* **1992**, *92*, 995.

(2) For reviews, see: (a) Masse, C. E.; Panek, J. S. *Chem. Rev.* **1995**, *95*, 1293. (b) Fleming, I.; Barbero, A.; Walter, D. *Chem. Rev.* **1997**, *97*, 2063. (c) Chabaud, L.; James, P.; Landais, Y. *Eur. J. Org. Chem.* **2004**, 3173. See also: (d) Suginome, M.; Ito, Y. *J. Organomet. Chem.* **2003**, *685*, 218.

(3) (a) Hayashi, T.; Konishi, M.; Ito, H.; Kumada, M. *J. Am. Chem. Soc.* **1982**, *104*, 4962. (b) Hayashi, T.; Konishi, M.; Okamoto, Y.; Kabeta, K.; Kumada, M. *J. Org. Chem.* **1986**, *51*, 3772. (c) Hayashi, T.; Kabeta, K.; Yamamoto, T.; Tamao, K.; Kumada, M. *Tetrahedron Lett.* **1983**, *24*, 5661. (d) Hayashi, T.; Han, J. W.; Takeda, A.; Tang, J.; Nohmi, K.; Mukaide, K.; Tsuji, H.; Uozumi, Y. *Adv. Synth. Catal.* **2001**, *343*, 279. (e) Matsumoto, Y.; Ohno, A.; Hayashi, T. *Organometallics* **1993**, *12*, 4051. (f) Hayashi, T.; Ohno, A.; Lu, S.; Matsumoto, Y.; Fukuyo, E.; Yanagi, K. *J. Am. Chem. Soc.* **1994**, *116*, 4221. (g) Hayashi, T.; Iwamura, H.; Uozumi, Y. *Tetrahedron Lett.* **1994**, *35*, 4813. (h) Ohmura, T.; Taniguchi, H.; Suginome, M. *J. Am. Chem. Soc.* **2006**, *128*, 13682. (i) Kacprzynski, M. A.; May, T. L.; Kazane, S. A.; Hoveyda, A. H. *Angew. Chem., Int. Ed.* **2007**, *46*, 4638. See also: (j) Kacprzynski, M. A.; Kazane, S. A.; May, T. L.; Hoveyda, A. H. *Org. Lett.* **2007**, *9*, 3187.

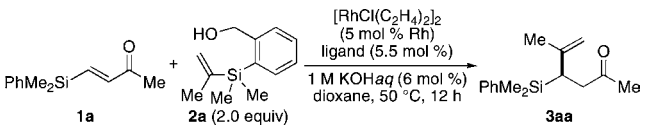
10.1021/ol702125q CCC: $37.00
Published on Web 10/03/2007

pounds could be synthesized through the formation of new carbon−carbon bonds.[3a,b,i,j] Herein we describe that a rhodium/chiral diene catalyst is highly effective for asymmetric 1,4-addition of alkenyl[2-(hydroxymethyl)phenyl]dimethylsilanes[4,5] to β-silyl α,β-unsaturated ketones, providing a new and useful method for the construction of chiral allylsilanes in high yield and ee.

In 2005, we reported a rhodium-catalyzed asymmetric 1,4-addition of arylboronic acids to β-silyl α,β-unsaturated carbonyl compounds for the synthesis of chiral organosilanes and demonstrated that high yield and enantioselectivity could be achieved by the use of a chiral diene ligand such as (*R*,*R*)-Bn-bod*.[6] On the basis of this study, we envisioned that the use of alkenyl nucleophiles would lead to the formation of enantio-enriched chiral allylsilanes. To implement this strategy, because some alkenylboronic acids are known to be unstable, we decided to focus on the employment of alkenyl[2-(hydroxymethyl)phenyl]dimethylsilanes as the nucleophile. Although these reagents are known to function as nucleophiles in the rhodium-catalyzed 1,4-addition reactions, their usage has been limited to the addition to simple α,β-unsaturated ketones so far.[5]

In an initial investigation, we examined the effect of ligand by using β-dimethylphenylsilyl enone **1a** as a model substrate in the 1,4-addition of 2-propenylsilyl reagent **2a** with 5 mol % rhodium at 50 °C (Table 1). As was the case with the addition of arylboronic acids,[6] the use of chiral diene ligands such as (*S*,*S*)-Bn-bod*[7,8] and (*S*,*S*)-Ph-bod*[7] gave the desired 1,4-adduct (**3aa**) in high yield and ee (96% yield, 93% ee; Table 1, entries 1 and 2). In comparison, typical phosphorus-based chiral ligands, such as (*R*)-binap,[9] (*R*)-phosphoramidite,[10] and (*R*)-MeO-mop,[11] turned out to be much less effective, giving **3aa** in lower yield and enantioselectivity (Table 1, entries 3−5).

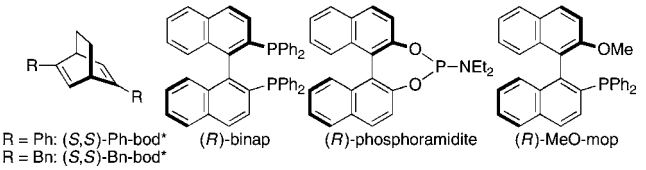
Table 1. Rhodium-Catalyzed Asymmetric 1,4-Addition of (2-Propenyl)[2-(hydroxymethyl)phenyl]dimethylsilane (**2a**) to (*E*)-4-Dimethylphenylsilyl-3-buten-2-one (**1a**)



1a **2a** (2.0 equiv) **3aa**

entry	ligand	yield (%)	ee (%)[a]
1	(*S*,*S*)-Bn-bod*	96	93
2	(*S*,*S*)-Ph-bod*	96	93
3	(*R*)-binap	10	22
4	(*R*)-phosphoramidite	54	16
5	(*R*)-MeO-mop	<2	–

[a] ee was determined by chiral HPLC on a Chiralpak AS column with hexane/2-propanol = 98/2.

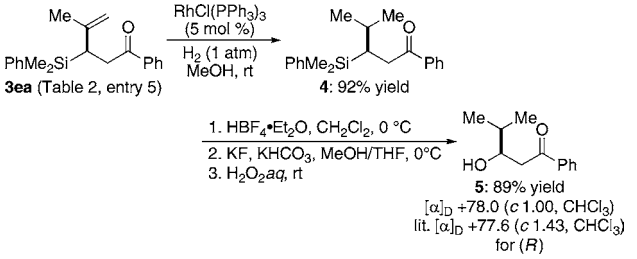


R = Ph: (*S*,*S*)-Ph-bod* R = Bn: (*S*,*S*)-Bn-bod* (*R*)-binap (*R*)-phosphoramidite (*R*)-MeO-mop

Under the conditions using (*S*,*S*)-Ph-bod* as a ligand, the scope of the substrate and the nucleophile is illustrated in Table 2. Thus, not only dimethylphenylsilyl group but also other silyl groups such as the *tert*-butyldimethylsilyl group can be employed at the β-position of the substrate (Table 2, entry 2). With respect to the substituent adjacent to the carbonyl group, primary alkyl, secondary alkyl, and aryl groups are all tolerated to give the corresponding allylsilanes in high yield and enantioselectivity (88−95% yield, 92−97% ee; Table 2, entries 3−5). In addition to 2-propenyl group, various other alkenyl groups are also successfully installed with high efficiency (90−98% yield, 91−94% ee; Table 2, entries 6−10). Unfortunately, somewhat lower enantioselectivity is observed by the use of a linear alkenyl nucleophile under the present reaction conditions (Table 2, entry 11).

The absolute configuration of 1,4-adduct **3ea** (Table 2, entry 5) was determined as shown in Scheme 1. Thus,

Scheme 1. Derivatization of Compound **3ea**



3ea (Table 2, entry 5) **4**: 92% yield **5**: 89% yield

$[\alpha]_D$ +78.0 (*c* 1.00, $CHCl_3$)
lit. $[\alpha]_D$ +77.6 (*c* 1.43, $CHCl_3$) for (*R*)

(4) (a) Nakao, Y.; Imanaka, H.; Sahoo, A. K.; Yada, A.; Hiyama, T. *J. Am. Chem. Soc.* **2005**, *127*, 6952. (b) Nakao, Y.; Sahoo, A. K.; Yada, A.; Chen, J.; Hiyama, T. *Sci. Technol. Adv. Mater.* **2006**, *7*, 536. (c) Nakao, Y.; Imanaka, H.; Chen, J.; Yada, A.; Hiyama, T. *J. Organomet. Chem.* **2007**, *692*, 585. (d) Nakao, Y.; Ebata, S.; Chen, J.; Imanaka, H.; Hiyama, T. *Chem. Lett.* **2007**, 606. (e) Nakao, Y.; Imanaka, H.; Chen, J.; Yada, A.; Hiyama, T. *J. Organomet. Chem.* **2007**, *692*, 585. See also: (f) Hudrlik, P. F.; Abdallah, Y. M.; Hudrlik, A. M. *Tetrahedron Lett.* **1992**, *33*, 6747. (g) Hudrlik, P. F.; Arango, J. O.; Hijji, Y. M.; Okoro, C. O.; Hudrlik, A. M. *Can. J. Chem.* **2000**, *78*, 1421.

(5) Nakao, Y.; Chen, J.; Imanaka, H.; Hiyama, T.; Ichikawa, Y.; Duan, W.-L.; Shintani, R.; Hayashi, T. *J. Am. Chem. Soc.* **2007**, *129*, 9137.

(6) Shintani, R.; Okamoto, K.; Hayashi, T. *Org. Lett.* **2005**, *7*, 4757.

(7) (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. (e) Shintani, R.; Okamoto, K.; Hayashi, T. *Org. Lett.* **2005**, *7*, 4757. (f) Nishimura, T.; Yasuhara, Y.; Hayashi, T. *Org. Lett.* **2006**, *8*, 979. (g) Shintani, R.; Duan, W.-L.; Hayashi, T. *J. Am. Chem. Soc.* **2006**, *128*, 5628. (h) Tokunaga, N.; Hayashi, T. *Adv. Synth. Catal.* **2007**, *349*, 513. (i) Duan, W.-L.; Imazaki, Y.; Shintani, R.; Hayashi, T. *Tetrahedron* **2007**, *63*, 8529.

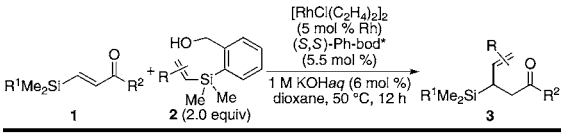
(8) (a) Shintani, R.; Okamoto, K.; Otomaru, Y.; Ueyama, K.; Hayashi, T. *J. Am. Chem. Soc.* **2005**, *127*, 54. (b) Shintani, R.; Tsurusaki, A.; Okamoto, K.; Hayashi, T. *Angew. Chem., Int. Ed.* **2005**, *44*, 3909. (c) Hayashi, T.; Tokunaga, N.; Okamoto, K.; Shintani, R. *Chem. Lett.* **2005**, 1480. (d) Chen, F.-X.; Kina, A.; Hayashi, T. *Org. Lett.* **2006**, *8*, 341. (e) Nishimura, T.; Katoh, T.; Hayashi, T. *Angew. Chem., Int. Ed.* **2007**, *46*, 4937.

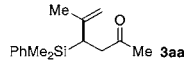
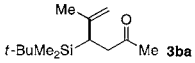
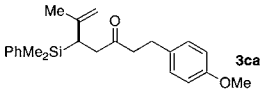
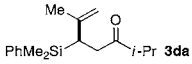
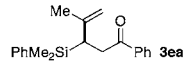
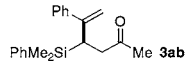
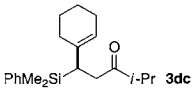
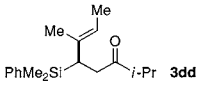
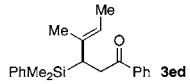
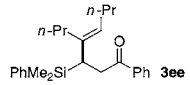
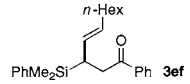
(9) Takaya, H.; Mashima, K.; Koyano, K.; Yagi, M.; Kumobayashi, H.; Taketomi, T.; Akutagawa, S.; Noyori, R. *J. Org. Chem.* **1986**, *51*, 629.

(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) Uozumi, Y.; Tanahashi, A.; Lee, S.-Y.; Hayashi, T. *J. Org. Chem.* **1993**, *58*, 1945. (b) Hayashi, T. *Acc. Chem. Res.* **2000**, *33*, 354.

Table 2. Rh/(*S*,*S*)-Ph-bod*-Catalyzed Asymmetric 1,4-Addition of Alkenyl[2-(hydroxymethyl)phenyl]dimethylsilanes **2** to *β*-Silyl α,*β*-Unsaturated Ketones **1**

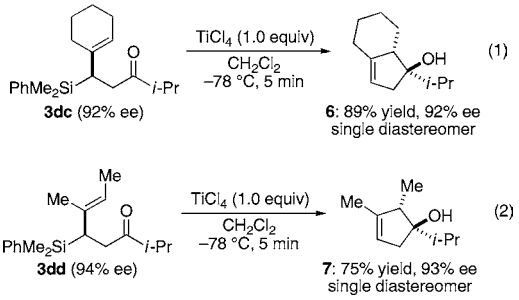


entry	product	yield (%)	ee (%)[a]
1	 **3aa**	96	93
2[b]	 **3ba**	95	97
3	 **3ca**	91	92
4	 **3da**	95	97
5[c]	 **3ea**	88	93
6[b]	 **3ab**	96	93
7	 **3dc**	90	92
8	 **3dd**	98	94
9[b]	 **3ed**	92	91
10	 **3ee**	92	93
11	 **3ef**	91	56

[a] ee was determined by chiral HPLC with hexan/2-propanol. [b] (*S*,*S*)-Bn-bod* was used as a ligand. [c] The reaction was conducted at 60 °C.

hydrogenation of the olefin by Wilkinson's catalyst, followed by Tamao oxidation,[12,13] gave 3-hydroxy-4-methyl-1-phenylpentan-1-one (**5**), retaining its stereochemical information. By comparing the optical rotation with the literature value,[14] the absolute configuration of compound **5** was assigned as (*R*), which determined the configuration of **3ea** to be (*R*).

Highly enantio-enriched chiral allylsilanes obtained through these rhodium-catalyzed 1,4-addition reactions are useful chiral building blocks for further derivatizations. For example, treatment of 1,4-adduct **3dc** with $TiCl_4$ at −78 °C rapidly gave intramolecular allylation product **6** in 89% yield as a single diastereomer with retaining the enantiomeric excess (eq 1).[15] Similarly, compound **3dd** was converted to compound **7** with complete stereoselectivity in 75% yield (eq 2).



In summary, we have developed a new synthetic method of chiral allylsilanes through a rhodium-catalyzed asymmetric 1,4-addition of alkenyl[2-(hydroxymethyl)phenyl]dimethylsilanes to *β*-silyl α,*β*-unsaturated ketones. By employing (*S*,*S*)-Ph-bod* as a ligand, we have efficiently installed a range of alkenyl nucleophiles to these substrates in high yield and enantiomeric excess. The resulting allylsilanes can be used in the context of stereoselective intramolecular allylation reactions to control two contiguous tertiary and quaternary stereocenters.

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.

OL702125Q

(12) (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, 1985; p 231.

(13) (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.

(14) Trost, B. M.; Ito, H. *J. Am. Chem. Soc.* **2000**, *122*, 12003.

(15) (a) Masse, C. E.; Dakin, L. A.; Knight, B. S.; Panek, J. S. *J. Org. Chem.* **1997**, *62*, 9335. (b) Mikami, K.; Maeda, T.; Kishi, N.; Nakai, T. *Tetrahedron Lett.* **1984**, *25*, 5151.