J|A|C|S
COMMUNICATIONS

Published on Web 03/06/2007

Palladium-Catalyzed Asymmetric Silaborative C−C Cleavage of *meso*-Methylenecyclopropanes

Toshimichi Ohmura, Hiroki Taniguchi, Yoshiyuki Kondo, and Michinori Suginome*

Department of Synthetic Chemistry and Biological Chemistry, Graduate School of Engineering, Kyoto University, Katsura, Kyoto 615-8510, Japan

Received January 16, 2007; E-mail: suginome@sbchem.kyoto-u.ac.jp

Desymmetrization of cyclic compounds via asymmetric ring-opening reactions has been recognized as an important strategy for catalytic asymmetric synthesis. In these reactions, relatively reactive carbon−heteroatom bonds, such as C−O bonds in epoxides, acid anhydrides, and oxabicyclic alkenes, and C−N bonds in aziridines, are cleaved in the presence of chiral catalysts, including enzymes.[1] In view of the high synthetic utility of this method, it is highly desirable to expand the method to other cyclic systems by taking advantage of the rapid advances in catalyses involving the activation of unreactive bonds. A general scheme of desymmetrization of carbocycles via C−C bond cleavage is depicted in Scheme 1. Achiral carbocycles are converted into acyclic carbochains via selective cleavage of one of the two enantiotopic C−C σ-bonds. Despite the potential usefulness, this type of desymmetrization has only been realized in Rh-catalyzed hydrogenative C−C cleavage of cyclobutanones[2] and Pd-catalyzed arylative ring opening of cyclobutanols,[3] to the best of our knowledge.[4]

As a part of our silaboration study,[5] we have developed transition-metal-catalyzed silaborative C−C bond cleavage of methylenecyclopropanes (MCPs), which exhibits distinctive reaction pathways that depend critically on the catalysts used and the structure of the MCPs.[6,7] An example is shown by the reaction of 7-methylenebicyclo[4.1.0]heptane (**2**), whose proximal C−C bond cleavage is accompanied by regioselective introduction of a silyl and a boryl groups at the cleaved C−C bond. Herein, we describe a new asymmetric desymmetrization system utilizing silaborative C−C cleavage of *meso*-MCPs, which are easily prepared from *cis*-alkenes,[8] using a palladium catalyst bearing an optically active monodentate phosphorus ligand.

After brief screening of the catalysts, we decided to employ palladium−phosphine catalysts with a Pd/P ratio of 1/1 as these exhibit high catalyst activity in the silaboration of allenes.[5a] The original palladium catalyst bearing an isocyanide ligand[6] seemed unfavorable for the asymmetric induction because of the requirement for a relatively high reaction temperature (110 °C) and less flexibility in the design of chiral isocyanides.[9] We found that the palladium−phosphine catalyst showed high catalyst activity in the reaction of $Me_2PhSiB(pin)$ (**1a**) with **2**; the reaction proceeded even at 50 °C in the presence of $Pd(dba)_2$ (2.0 mol %) with PPh_3 (2.4 mol %), giving 2-(1-borylethenyl)-1-silylcyclohexane **3a** in 64% yield after 24 h. The catalyst activity was found to be highly dependent upon the Pd/P ratio. The reaction slowed down significantly in the absence of the phosphine ligand or in the presence of increased amounts of the ligand (Pd/P ratio of 1/2.4) (4 and 0% yield, respectively, under otherwise identical reaction conditions).[10]

With the modified reaction conditions, we examined asymmetric silaborative C−C cleavage of **2** with **1a** in the presence of palladium catalysts bearing various optically active monodentate phosphorus ligands (entries 1−6, Table 1). The reactions gave nonracemic **3a** at 50 °C in 41−91% yield after 72−120 h. Poor enantioselectivities were observed in the reactions using (+)-NMDPP, (*S*)-MONOPHOS, (*S*)-QUINAP, and (*S*)-MOP (entries 1, 2, 4, and 5), whereas (*R*,*R*)-**4** and (*R*)-**5a** gave **3a** with much better enantiomeric excesses (ee's) (61 and 71% ee, entries 3 and 6). To improve enantioselectivity, we carried out reactions using derivatives of **5** that have varied diarylphosphino groups on the 1,1′-binaphthyl skeleton.[11] We found that the highest enantioselectivity was attained with 2-bis(3,5-dimethylphenyl)phosphino-1,1′-binaphthyl [(*R*)-**5b**],[12] which afforded **3a** with 87% ee (entry 7).

Further improvement of enantioselectivity was achieved when $MePh_2SiB(pin)$ (**1b**) was used, resulting in 90% ee for the formation

Scheme 1. Asymmetric Ring Opening via C−C Bond Cleavage

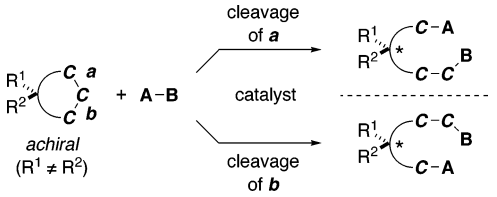
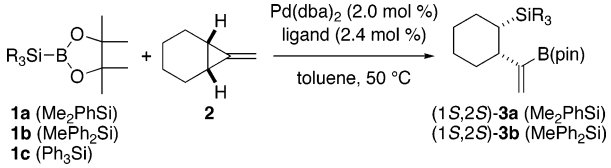
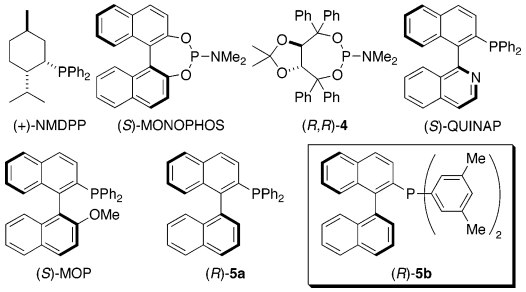


Table 1. Optimization of Reaction Conditions for Pd-Catalyzed Asymmetric Silaborative C−C Cleavage of **2** with **1**[a]



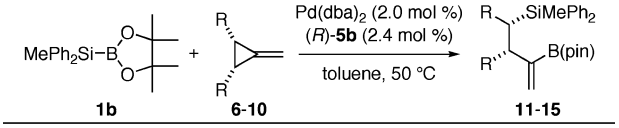
entry	Si–B	ligand	time (h)	yield (%)[b]	ee (%)[c]
1	**1a**	(+)-NMDPP	72	65	26[d]
2	**1a**	(*S*)-MONOPHOS	72	91	27
3	**1a**	(*R*,*R*)-**4**	72	71	61[d]
4	**1a**	(*S*)-QUINAP	120	41	1
5	**1a**	(*S*)-MOP	120	68	16
6	**1a**	(*R*)-**5a**	120	80	71
7	**1a**	(*R*)-**5b**	120	85	87
8	**1b**	(*R*)-**5b**	48	87	90
9	**1c**	(*R*)-**5b**	120	n.r.	

[a] **1** (0.40 mmol), **2** (0.60 mmol), $Pd(dba)_2$ (8.0 μmol), and ligand (9.6 μmol) were stirred in toluene (0.2 mL) at 50 °C unless otherwise noted. [b] Isolated yield. [c] Determined after conversion to the corresponding β-silyl ketones (see eq 1) that were analyzed by HPLC with a chiral stationary phase column. [d] (1*R*,2*R*)-**3a** was formed as major isomer.

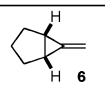
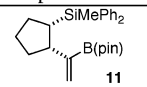
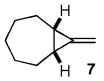
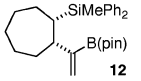
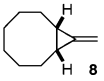
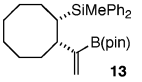
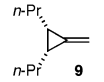
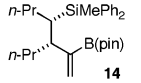
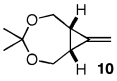
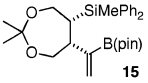


10.1021/ja0703170 CCC: $37.00

Table 2. Asymmetric Silaborative C−C Cleavage of MCPs[a]



1b 6-10 11-15

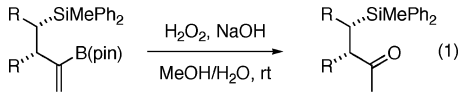
entry	MCP	product	time (h)	yield (%)[b]	ee (%)[c]
1[d]	 6	 11	80	72[e]	90
2	 7	 12	48	95	91
3	 8	 13	48	85	90
4[d]	 9	 14	40	72[e]	81
5[f]	 10	 15	99	50	89

[a] **1b** (0.40 mmol), MCP (0.60 mmol), $Pd(dba)_2$ (8.0 μmol), and (*R*)-**5b** (9.6 μmol) were stirred in toluene (0.2 ml) at 50 °C unless otherwise noted. [b] Isolated yield. [c] Determined after conversion to the corresponding β-silyl ketones (see eq 1) that were analyzed by HPLC with a chiral stationary phase column. [d] $Pd(dba)_2$ (3.0 mol %), (*R*)-**5b** (3.6 mol %), and MCP (2.0 equiv) were used. [e] Yield after conversion to the corresponding β-silyl ketones. [f] $Pd(dba)_2$ (4.0 mol %) and (*R*)-**5b** (4.8 mol %) were used.

of **3b** (entry 8). The more sterically demanding triphenylsilyl derivative **1c**, however, did not react at all under the same reaction conditions (entry 9). It is interesting to note that the optimized reaction conditions using silylborane **1b** and Pd/(*R*)-**5b** catalyst are identical to those for the enantioselective silaboration of allenes reported recently,[5d] indicating mechanistic similarity in the asymmetric induction step.

Various *meso*-MCPs were subjected to asymmetric silaborative C−C cleavage under the optimized conditions using silylborane **1b** and Pd/(*R*)-**5b** catalyst (Table 2). The reaction of bicyclic MCPs **6**−**8** that have fused five-, seven-, and eight-membered carbocycles gave **11**−**13** in high yield with high enantioselectivities (90−91% ee, entries 1−3). On the other hand, non-fused **9** afforded **14** with lower ee (81% ee, entry 4). We also carried out the reaction of cyclic acetal **10**, giving **15** with 89% ee, although the yield was modest (entry 5).

The enantioenriched silaboration products obtained are expected to be useful synthetic intermediates. An example is shown by the synthesis of β-silyl ketones (eq 1).[13]

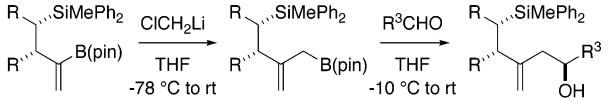


3b, **11**-**15** 72-90%

Oxidation of **3b** and **11**−**15** by treatment with H_2O_2 under basic conditions afforded the corresponding optically active β-silyl ketones in high yields with no epimerization.

Their synthetic utility was also demonstrated by a diastereoselective homologation−allylboration sequence (Table 3). Reaction of **3b** with $ClCH_2Li$ and treatment with EtCHO gave homoallylic alcohol **16a** in 78% yield with high diastereomeric ratio (94:6, entry 1). High diastereoselectivities were observed not only in the reaction of **3b** with *i*-PrCHO and PhCHO (entries 2 and 3) but also in the reactions of **11**, **12**, and **14** with PhCHO (entries 4−6). These reactions indicate that the stereochemistry of the β-substituent on allylic boronates efficiently controls the diastereoface selection in

Table 3. Diastereoselective Conversion of **3b**, **11**, **12**, and **14** via Homologation−Allylboration[a]



3b, **11**, **12**, **14** **16-19**

entry	substrate	R^3CHO	product	yield (%)[b]	dr[c]
1	**3b**	EtCHO	**16a**	78	94:6[d]
2	**3b**	*i*-PrCHO	**16b**	80	94:6
3	**3b**	PhCHO	**16c**	70	97:3
4	**11**	PhCHO	**17**	63	93:7
5	**12** (91% ee)	PhCHO	**18** (91% ee)	69	97:3
6	**14**	PhCHO	**19**	71	93:7

[a] In THF (0.23 mL), **3b**, **11**, **12**, or **14** (0.17 mmol) was reacted with $ClCH_2Li$ (0.26 mmol), and then the resulting mixture was treated with aldehydes (0.34 mmol). [b] Isolated yield. [c] Determined by HPLC analysis. [d] Determined by ^1H NMR.

the six-membered cyclic transition state.[14] As expected, enantioenriched **12** afforded **18** without a drop in ee (entry 5).

In conclusion, we developed Pd-catalyzed asymmetric silaborative C−C cleavage of *meso*-MCPs, affording synthetically useful 2-boryl-4-silyl-1-butene derivatives with high ee's.

Acknowledgment. This paper is dedicated to the memory of the late Professor Emeritus Yoshihiko Ito. This work is supported in part by Grant-in-Aid for Young Scientists (B) from MEXT (to T.O.).

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

References

(1) (a) Willis, M. C. *J. Chem. Soc., Perkin Trans. 1* **1999**, 1765. (b) Lautens, M.; Fagnou, K.; Hiebert, S. *Acc. Chem. Res.* **2003**, *36*, 48. (c) Chen, Y.; McDaid, P.; Deng, L. *Chem. Rev.* **2003**, *103*, 2965.
(2) Murakami, M.; Amii, H.; Ito, Y. *69th Annual Meeting of the Chemical Society of Japan*; Kyoto, Japan, March 1995; Abstr. No. 1H407.
(3) (a) Nishimura, T.; Matsumura, S.; Maeda, Y.; Uemura, S. *Chem. Commun.* **2002**, 50. (b) Matsumura, S.; Maeda, Y.; Nishimura, T.; Uemura, S. *J. Am. Chem. Soc.* **2003**, *125*, 8862.
(4) Related reactions involving catalytic enantioselective desymmetrization of carbocycles have been developed. Ring-opening metathesis of cyclic alkenes: (a) Schrock, R. R.; Hoveyda, A. H. *Angew. Chem., Int. Ed.* **2003**, *42*, 4592. Ring-expansion of cyclobutanones: (b) Matsuda, T.; Shigeno, M.; Makino, M.; Murakami, M. *Org. Lett.* **2006**, *8*, 3379. Baeyer−Villiger oxidation of cyclic ketones: (c) ten Brink, G.-J.; Arends, I. W. C. E.; Sheldon, R. A. *Chem. Rev.* **2004**, *104*, 4105. (d) García-Urdiales, E.; Alfonso, I.; Gotor, V. *Chem. Rev.* **2005**, *105*, 313.
(5) For recent examples, see: (a) Suginome, M.; Ohmura, T.; Miyake, Y.; Mitani, S.; Ito, Y.; Murakami, M. *J. Am. Chem. Soc.* **2003**, *125*, 11174. (b) Ohmura, T.; Suginome, M. *Org. Lett.* **2006**, *8*, 2503. (c) Ohmura, T.; Furukawa, H.; Suginome, M. *J. Am. Chem. Soc.* **2006**, *128*, 13366. (d) Ohmura, T.; Taniguchi, H.; Suginome, M. *J. Am. Chem. Soc.* **2006**, *128*, 13682. For recent reviews, see: (e) Suginome, M.; Ito, Y. *J. Organomet. Chem.* **2003**, *680*, 43. (f) Beletskaya, I.; Moberg, C. *Chem. Rev.* **2006**, *106*, 2320.
(6) Suginome, M.; Matsuda, T.; Ito, Y. *J. Am. Chem. Soc.* **2000**, *122*, 11015.
(7) For a review of catalytic addition to MCPs, see: Nakamura, I.; Yamamoto, Y. *Adv. Synth. Catal.* **2002**, *344*, 111.
(8) (a) Arora, S.; Binger, P. *Synthesis* **1974**, 801. (b) Kitatani, K.; Hiyama, T.; Nozaki, H. *Bull. Chem. Soc. Jpn.* **1977**, *50*, 3288.
(9) Suginome, M.; Nakamura, H.; Ito, Y. *Tetrahedron Lett.* **1997**, *38*, 555.
(10) For related studies of the metal/phosphine stoichiometry in Pt-catalyzed diboration, see: Thomas, R. L.; Souza, F. E. S.; Marder, T. B. *J. Chem. Soc., Dalton Trans.* **2001**, 1650 and references cited therein.
(11) Observed ee's (aryl groups of (*R*)-2-diarylphosphino-1,1′-binaphthyl are shown in parentheses): 79% ee (4-$MeOC_6H_4$), 44% ee (4-$CF_3C_6H_4$), 68% ee (4-MeC_6H_4), 79% ee (3-MeC_6H_4), and 7% ee (2-MeC_6H_4).
(12) (a) Uozumi, Y.; Suzuki, N.; Ogiwara, A.; Hayashi, T. *Tetrahedron* **1994**, *50*, 4293. (b) For a review of MOP ligand, see: Hayashi, T. *Acc. Chem. Res.* **2000**, *33*, 354.
(13) Walter, C.; Auer, G.; Oestreich, M. *Angew. Chem., Int. Ed.* **2006**, *45*, 5675 and references therein.
(14) (a) Kennedy, J. W. J.; Hall, D. G. *J. Org. Chem.* **2004**, *69*, 4412. For reviews on allylboration, see: (b) Yamamoto, Y.; Asao, N. *Chem. Rev.* **1993**, *93*, 2207. (c) Kennedy, J. W. J.; Hall, D. G. In *Boronic Acids*; Hall, D. G., Ed.; Wiley-VCH: Weinheim, Germany, 2005; p 241.

JA0703170