Available online at www.sciencedirect.com
ScienceDirect
Tetrahedron Letters 48 (2007) 3925–3928
Tetrahedron Letters

Palladium-catalyzed intra-molecular olefin insertion reaction of α-alkenyl-α-acyloxytrialkylsilane. Synthesis of optically active carbocycle

Kazuhiko Sakaguchi,* Takuya Okada, Takeshi Yamada and Yasufumi Ohfune*

Graduate School of Science, Department of Material Science, Osaka City University, Sugimoto, Sumiyoshi, Osaka 558-8585, Japan

Received 7 February 2007; revised 2 March 2007; accepted 6 March 2007
Available online 12 March 2007

Abstract—Pd-catalyzed intra-molecular olefin insertion/carbonylation reaction of optically active α-alkenyl-α-acyloxysilanes is described. The reactions proceeded in a stereoselective manner to give five- and six-membered optically active carbocycles having (*E*)-vinylsilane in their side chains. Under CO condition, optically active carbocycles containing one-carbon homologated side chain were produced by Pd-catalyzed tandem olefin insertion–carbonylation reaction.

Optically active α-alkenyl-α-acyloxysilane has received significant attention because of its chirality transferring property from the α- to γ-position through a cationic rearrangement[1] or an electrocyclic rearrangement of its acyloxy-derived enolate.[2] In the previous report, we demonstrated that a novel π-allyl palladium species, an equivalent of a putative α,γ-silylallyl cation (Fig. 1), could be generated from optically active α-alkenyl-α-acyloxysilane using a Pd catalyst.[3] This reactive species was trapped by an external or internal nucleophile to give an acyclic or cyclic γ-substituted vinylsilane, exclusively, where the α-silyl group played a crucial role for the regio- and stereo-selective C–C bond forming reactions owing to its steric and stereo-electronic features.[4]

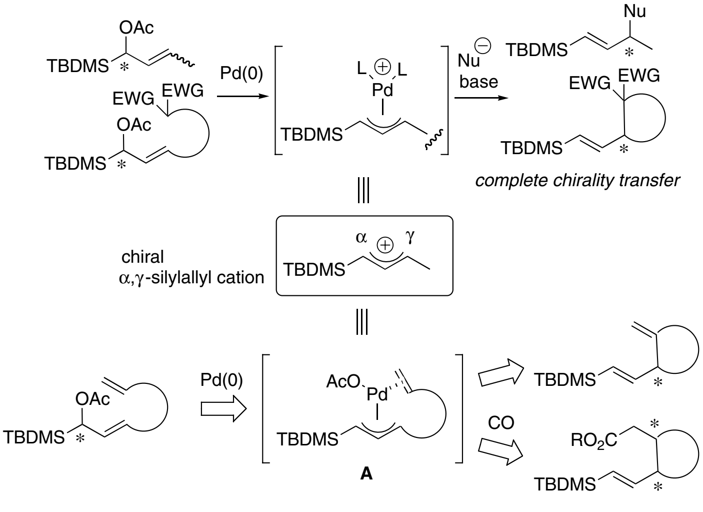


Figure 1.

Keywords: Pd-catalyzed cyclization; Olefin insertion; α-Acyloxysilane; π-Allyl palladium; Chirality transfer; Vinylsilane.

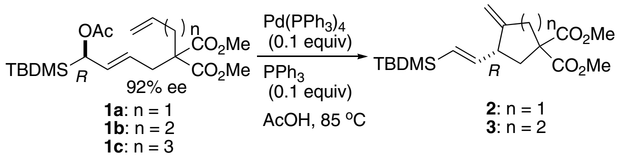
* Corresponding authors. Tel.: +81 6 6605 2571; fax: +81 6 6605 2522 (K.S.); e-mail: sakaguch@sci.osaka-cu.ac.jp

0040-4039/$ - see front matter © 2007 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tetlet.2007.03.029

The next stage of our synthetic work was to extend these results to a Pd-catalyzed olefin insertion reaction, which was initially developed by Oppolzer et al. and was proven to be a powerful method for the synthesis of five- and six-membered ring systems.[5] We envisaged that the olefin insertion reaction of optically active α-alkenyl-α-acetoxysilane would proceed via the π-allyl palladium intermediate **A** to produce carbocycle having a vinylsilane, where the original chirality at the acetoxy carbon would be transferred to the newly formed chiral center. Furthermore, in the presence of carbon monoxide, palladium would catalyze both olefin insertion and CO insertion to give a one-carbon homologated cyclic product.[6] These results are described in this Letter.

According to Oppolzer's protocol,[7] we examined Pd-catalyzed cyclization of α-alkenyl-α-acetoxysilanes **1a**–**c** (Table 1), prepared in optically active form (Supplementary data). Treatment of (*R*)-**1a** ($n = 1$, 92% ee) with $Pd(PPh_3)_4$ (0.1 equiv) and PPh_3 (0.1 equiv) in AcOH (degassed) at 85 °C for 1 h underwent olefin insertion reaction to afford cyclized product **2**[8] having (*E*)-vinylsilane in 89% yield (entry 1). Optical purity of **2** was determined to be 92% ee, and its absolute configuration was *R* (Supplementary data). Pd-catalyzed cyclization of (*R*)-**1b** ($n = 2$, 92% ee) required prolonged reaction period (20 h) under the same reaction conditions to afford six-membered cyclized product **3** (60%)[9–11] together with recovery of **1b** (20%) (entry 2). The ee of the starting **1b** was also completely retained in **3** (92% ee).[12] Using EtOH or THF as the solvent, conjugate diene **4** was produced together with recovery of **1b** (entry 3,4).[13] The reaction of **1c** ($n = 3$) under the standard conditions resulted in a complete recovery of the starting **1c**, probably due to a latent ring strain in construction of a medium-sized ring (entry 5). Under elevated temperature (110 °C), conjugate diene **5** (17%) was produced with recovery of **1c** (50%) (entry 6).

Table 1. Pd-catalyzed olefin insertion of α-alkenyl-α-acetoxysilanes **1a**–**c**



	Substrate	Time (h)	Product	Yield (%)	Recovery of **1** (%)
1	**1a**	1	**2**	89 (92% ee)	—
2	**1b**	20	**3**	60[a] (92% ee)[b]	20
3[c]		22	**3**	30[a]	20[d]
4[e]		22	**3**	—	63[f]
5	**1c**	22	—	—	quant
6[g]		6	—	—	50[h]

[a] See Ref. 10.

[b] See Ref. 12.

[c] EtOH was used as the solvent.

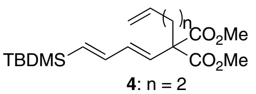
[d] Diene **4** (39%) was by-produced.

[e] THF was used as the solvent.

[f] Diene **4** (37%) was produced.

[g] 110 °C.

[h] Diene **5** (17%) was produced.



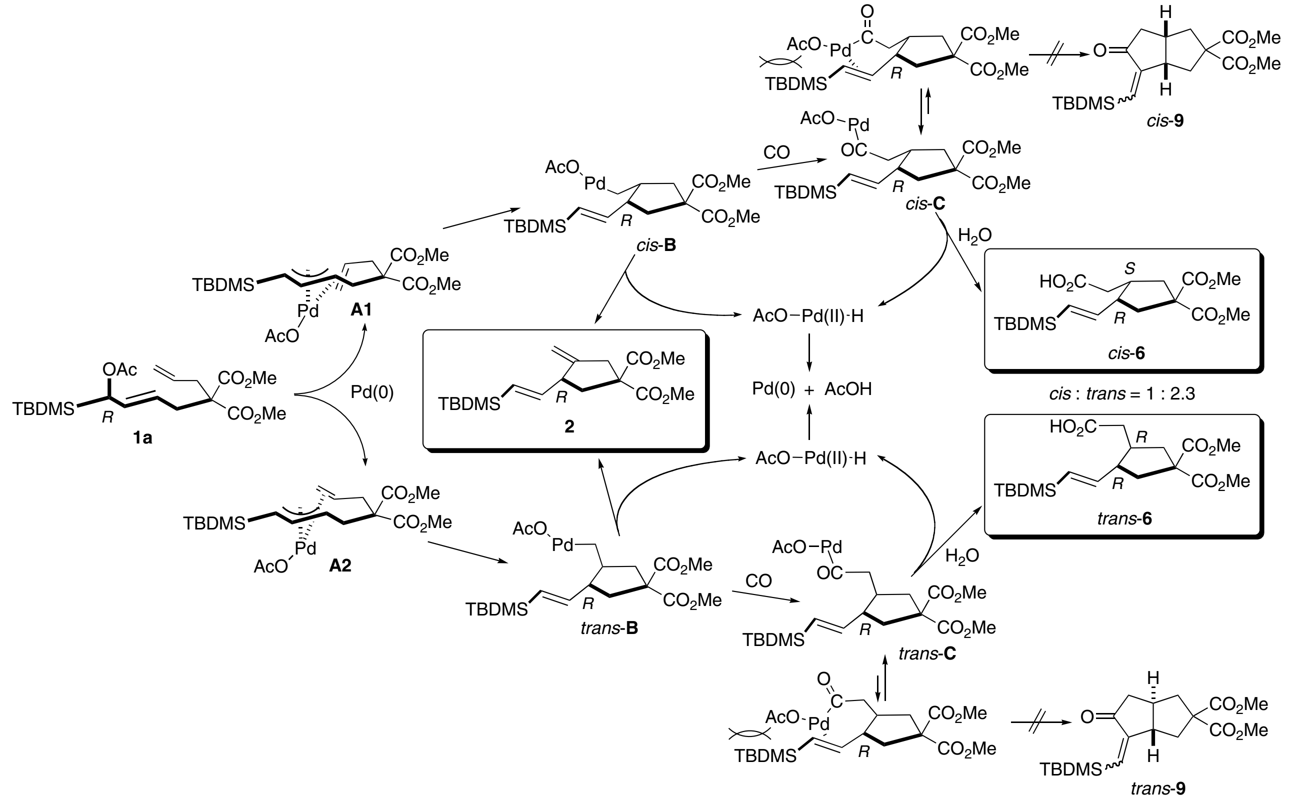
4: n = 2
5: n = 3

The present Pd-catalyzed cyclization reaction is characterized by the following points: (1) the reaction of the (*R*)-acyloxysilanes gave the (*R*)-enantiomer of the product without any loss of optical purity, (2) carbon–carbon bond formation occurred exclusively at the γ-position to silicone, and (3) the product had an (*E*)-vinylsilane moiety. Thus, oxidative addition of Pd(0) into (*R*)-**1a** would occur from the backside of the acetoxy group followed by coordination to the internal olefin to give optically active π-allyl palladium intermediates **A1** and/or **A2** (Scheme 1). The olefin insertion took place at the γ-position to afford σ-palladium complexes *cis*-**B** and/or *trans*-**B**. Subsequent β-hydride elimination of Pd(II) in **B** afforded (*R*)-**2**.[14]

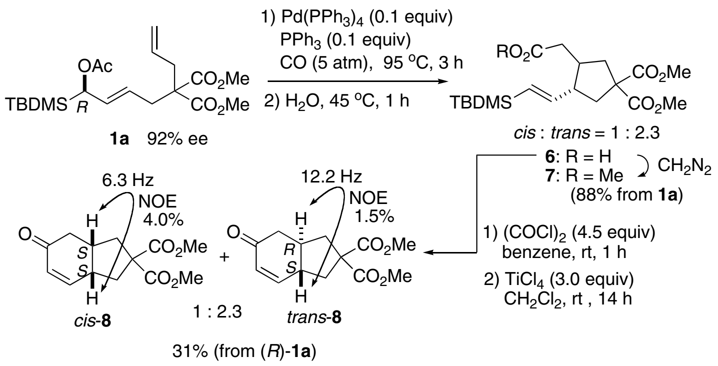
Next, we examined Pd-catalyzed tandem olefin insertion/carbonylation reaction of α-alkenyl-α-acyloxysilane **1a** (Scheme 2). Reaction of (*R*)-**1a** with $Pd(PPh_3)_4$ (0.1 equiv), PPh_3 (0.1 equiv) and CO (5 atm) at 95 °C for 3 h followed by treatment of the reaction mixture with H_2O gave carboxylic acid **6**, which, upon esterification with CH_2N_2, gave triester **7** (cis:trans = 1:2.3, 88% from **1a**). The relative configuration of **7** was confirmed by the conversion of **6** to a bicyclo[4.3.0]-ring system (vide infra). The reaction under 1 atm of CO gave a mixture of **7** (70%, cis:trans = 1:2.3) and the non-carbonylated (*R*)-**2** (22% yield, 92% ee) indicating that CO insertion took place over β-hydride elimination from *cis*-**B** and/or *trans*-**B** at higher pressure of CO. Now, it was clearly understood that cyclization to **2** occurred from both intermediates *cis*-**B** and *trans*-**B** via **A1** and **A2**, respectively, since tandem insertion/carbonylation reaction gave a mixture of *cis*-**6** and *trans*-**6** (1:2.3), as shown in Scheme 1. We expected that successive olefin insertion would occur from intermediate **C** to give optically active bicyclic compounds **9**.[15] However, such compounds were not obtained in this case, probably due to the steric hindrance of the TBDMS group, which would prevent the olefin coordination.[16]

Construction of a bicyclo[4.3.0]-ring system was achieved by a vinylsilane-terminated cationic cyclization of **6** (Scheme 2).[17,18] Treatment of the crude reaction mixture of **6** with $(COCl)_2$ (4.5 equiv) in benzene (rt, 1 h) followed by treatment with $TiCl_4$ (3 equiv) in CH_2Cl_2 (rt, 14 h) gave a separable mixture of unsaturated ketones **8**[19] in 31% yield (4 steps from (*R*)-**1a**, cis:trans = 1:2.3). Relative stereochemistry of *cis*-**8** and *trans*-**8** was determined by the *J* values (6.3 Hz: cis, 12.2 Hz: trans)[20] and the NOE experiments (4.0%: cis, 1.5%: trans) of their protons attached to the ring-junction.

In summary, we have succeeded in construction of optically active five- and six-membered carbocyclic systems having a vinylsilane in their side chains by chirality-transferring Pd-catalyzed intra-molecular olefin insertion of α-alkenyl-α-hydroxysilane, where the starting



Scheme 1.



Scheme 2.

ee was completely transferred to the product. The reaction in the presence of carbon monoxide underwent Pd-catalyzed olefin insertion–carbonylation reaction to produce cis and trans five-membered carbocycles having a carbonylated side chain. Further studies using the present chirality-transferring carbon–carbon bond forming reaction are in progress.

Acknowledgment

This study was financially supported by a Grant-in-Aid for Scientific Research from the Ministry of Education, Culture, Sports, Science and Technology, Japan.

Supplementary data

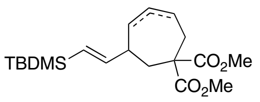
Supplementary data (preparation of cyclization precursor **1a**–**c**; determination of the optical purity and absolute configuration of **2**; determination of the optical purity of **3**) associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2007.03.029.

References and notes

1. Sakaguchi, K.; Higashino, M.; Ohfune, Y. *Tetrahedron* **2003**, *59*, 6647–6658.
2. (a) Sakaguchi, K.; Suzuki, H.; Ohfune, Y. *Chirality* **2001**, *13*, 357–365; (b) Morimoto, Y.; Takanishi, M.; Kinoshita, T.; Sakaguchi, K.; Shibata, K. *Chem Commun.* **2002**, 42–43; (c) Sakaguchi, K.; Yamamoto, M.; Kawamoto, T.; Yamada, T.; Shinada, T.; Shimamoto, K.; Ohfune, Y. *Tetrahedron Lett.* **2004**, *45*, 5869–5872.
3. Sakaguchi, K.; Yamada, T.; Ohfune, Y. *Tetrahedron Lett.* **2005**, *46*, 5009–5012.
4. (a) Apeloig, Y.; Stanger, A. *J. Am. Chem. Soc.* **1985**, *107*, 2806–2807; (b) Soderquist, J. A.; Hassner, A. *Tetrahedron*

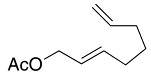
Lett. **1988**, *29*, 1899–1902; (c) Apeloig, Y.; Biton, R.; Bu-Freih, A. *J. Am. Chem. Soc.* **1993**, *115*, 2252–2253.

5. For reviews, see: (a) Oppolzer, W. *Angew. Chem., Int. Ed. Engl.* **1989**, *28*, 38–52; (b) Oppolzer, W. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Paquette, L. A., Eds.; Pergamon: Oxford, 1991; Vol. 5, pp 29–61, Chapter 1.2; (c) Tsuji, J. *Palladium Reagents and Catalysts*; John Wiley & Sons Ltd: Chichester, 2004; p 483.
6. (a) Yamamoto, K.; Terakado, M.; Murai, K.; Miyazawa, M.; Tsuji, J.; Takahashi, K.; Mikami, K. *Chem. Lett.* **1989**, 955–958; (b) Terakado, M.; Murai, K.; Miyazawa, M.; Yamamoto, K. *Tetrahedron* **1994**, *50*, 5705–5718.
7. Oppolzer, W.; Gaudin, J.-M. *Helv. Chim. Acta* **1987**, *70*, 1477–1481.
8. Compound (*R*)-**2**: $[\alpha]_D^{21}$ +13.9 (*c* 1.05, $CHCl_3$, 92% ee); ^1H NMR (300 MHz, $CDCl_3$) δ 5.82 (dd, J = 18.4, 7.1 Hz, 1H), 5.68 (d, J = 18.4 Hz, 1H), 4.98 (d, J = 2.0 Hz, 1H), 4.79 (d, J = 2.0 Hz, 1H), 3.74 (s, 3H), 3.72 (s, 3H), 3.17 (m, 1H), 3.07 (m, 1H), 2.94 (m, 1H), 2.58 (dd, J = 13.0, 7.7 Hz, 1H), 2.03 (dd, J = 13.0, 11.0 Hz, 1H), 0.86 (s, 9H), 0.01 (s, 6H).
9. Compound **3**: ^1H NMR (300 MHz, $CDCl_3$) δ 6.00 (dd, J = 18.7, 7.0 Hz, 1H), 5.70 (dd, J = 18.7, 0.9 Hz, 1H), 4.75 (d, J = 1.5, 1H), 4.61 (d, J = 1.5 Hz, 1H), 3.78 (s, 3H), 3.70 (s, 3H), 2.84 (m, 1H), 2.47–2.32 (4H), 1.83–1.66 (2H), 0.87 (s, 9H), 0.02 (s, 6H).
10. Calculated yield of the reaction mixture by ^1H NMR. The mixture was composed of **3** and its structural isomers **10** (**3**:**10** = 81:19). The mixture was inseparable by silica-gel chromatographic methods. The structures of **10** were tentatively assigned to internal double bond isomers since ^1H NMR showed signals corresponding to a *trans*-vinylsilane (5.6–6.0 ppm, J = 18.4–18.7 Hz) and an internal olefin.

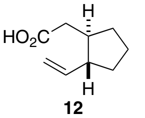


10

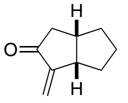
11. The yield of a Pd-catalyzed six-membered ring formation was also moderate (63%), see Ref. 7.
12. Calculated by ^1H NMR using the mixture of the corresponding MTPA esters (Supplementary data). Although the absolute configuration of **3** was not confirmed, it was suggested to be *R* by consideration of the result of **2**.
13. Screening of other Pd-catalysts, ligand and their concentration ($Pd(dba)_2$, $Pd_2(dba)_3$–$CHCl_3$, and DPPE) did not improve the yield of **3**.
14. Oppolzer, W.; Gaudin, J.-M.; Birkinshaw, T. N. *Tetrahedron Lett.* **1988**, *29*, 4705–4708.
15. It was reported that the Pd-catalyzed reaction of allyl acetate **11** ($Pd_2(dba)_3$–$CHCl_3$ (0.025 equiv), PPh_3 (0.15 equiv), CO (2 atm), AcOH, 80 °C, 20 h) gave not only five-membered *trans*-**12** (50%) but also additional olefin-insertion product *cis*-bicyclo[3.3.0]octane **13** (21%) and its *trans*-isomer (9%).[6b] Similar results, see: Yoo, S.-E.; Lee, S.-H.; Yi, K.-Y.; Jeong, N. *Tetrahedron Lett.* **1990**, *31*, 6877–6880.



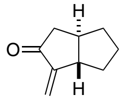
11



12



cis-**13**



trans-**13**

16. A similar tandem cyclization was completely prevented when the substrate possessed a vinylic acetoxy group. Holzapfel, C. W.; Marais, L. *Tetrahedron Lett.* **1998**, *39*, 2179–2182.
17. For reviews, see: Blumenkopf, T. A.; Overman, L. E. *Chem. Rev.* **1986**, *86*, 857–873.
18. Burke, S. D.; Murtiashaw, C. W.; Dike, M. S.; Smith Strickland, S. M.; Saunders, J. O. *J. Org. Chem.* **1981**, *46*, 2400–2402.
19. Compound *cis*-**8**: $[\alpha]_D^{25}$ −101.1 (*c* 1.30, $CHCl_3$); ^1H NMR (600 MHz, $CDCl_3$) δ 6.71 (dd, J = 10.2, 3.3 Hz, 1H), 5.60 (dd, J = 10.2, 1.9 Hz, 1H), 3.74 (s, 3H), 3.70 (s, 3H), 2.95 (m, 1H), 2.74 (m, 1H), 2.61 (dd, J = 14.0, 8.4 Hz, 1H), 2.57 (dd, J = 16.7, 5.3 Hz, 1H), 2.54 (dd, J = 14.0, 7.6 Hz, 1H), 2.46 (dd, J = 16.7, 5.7 Hz, 1H), 2.42 (dd, J = 14.0, 5.5 Hz, 1H), 2.04 (dd, J = 14.0, 9.2 Hz, 1H). *trans*-**8**: $[\alpha]_D^{25}$ −97.0 (*c* 1.25, $CHCl_3$); ^1H NMR (600 MHz, $CDCl_3$) δ 7.04 (dd, J = 9.9, 0.5 Hz, 1H), 6.00 (dd, J = 9.9, 2.6 Hz, 1H), 3.75 (s, 3H), 3.74 (s, 3H), 2.79 (dd, J = 12.8, 6.9 Hz, 1H), 2.74 (dd, J = 16.5, 3.6 Hz, 1H), 2.66 (dd, J = 12.8, 6.0 Hz, 1H), 2.41 (m, 1H), 2.20 (dd, J = 16.5, 13.7 Hz, 1H), 2.04 (m, 1H), 1.90 (dd J = 12.8, 6.6 Hz, 1H), 1.88 (dd, J = 12.8, 6.2 Hz, 1H).
20. The J values of the ring-junction protons of both *cis*-**8** and *trans*-**8** were obtained by the homonuclear decoupling method.