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Palladium-catalyzed allylic alkylation of optically active α-alkenyl-α-acyloxytrialkylsilane

Kazuhiko Sakaguchi,* Takeshi Yamada and Yasufumi Ohfune*

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

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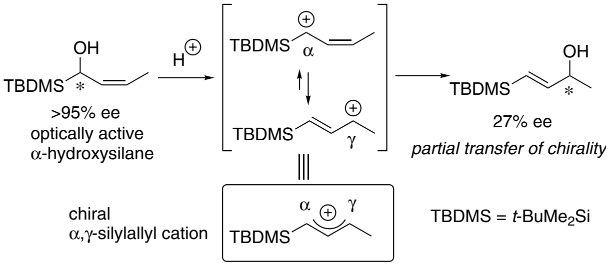
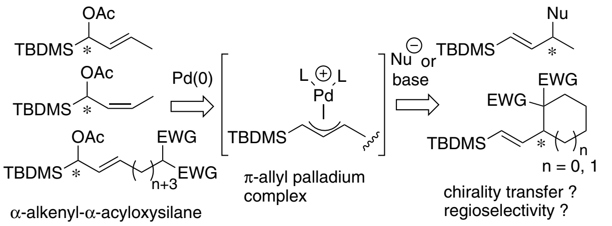
Abstract—Pd-catalyzed inter- and intramolecular allylic alkylations of optically active α-alkenyl-α-acyloxysilanes are described. The reactions proceeded in a regio- and stereoselective manner to give the corresponding (*E*)-vinylsilanes in which the ee of the starting material was completely transferred to the product.

During the course of our recent studies regarding the syntheses and reactions of optically active α-hydroxysilane,[1] we found that an acidic treatment of α-alkenyl-α-hydroxysilane (>95% ee) proceeded through a putative α-silyl cation[2] to give a rearranged γ-hydroxyvinylsilane with partial racemization (27% ee) (Eq. 1).[3] These results prompted us to examine a chirality-transferring carbon–carbon bond formation via the chiral cationic complex, which can be generated from α-alkenyl-α-acyloxysilane as a π-allyl palladium complex (Eq. 2). It is of interest to examine the regioselectivity upon alkylation and the extent of the chirality transfer. In this letter, we describe highly enantio- and regioselective inter- and intramolecular Pd-catalyzed allylic alkylations of α-alkenyl-α-acyloxysilanes with carbon nucleophiles.[4]

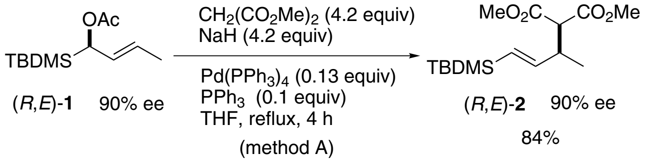


(1)



(2)

Initially attempted was an intermolecular Pd(0)-catalyzed allylic alkylation of optically active α-acyloxysilane **1**.[5] Reaction of (*R*,*E*)-**1** (90% ee)[3] with dimethyl malonate (4.2 equiv) under our standard reaction condition {NaH (4.2 equiv), Pd(PPh$_3$)$_4$ (0.13 equiv), and PPh$_3$ (0.1 equiv) under reflux in THF for 4 h} (method A) promoted intermolecular alkylation to give (*E*)-vinylsilane **2** in 84% yield (Scheme 1). The ee of the product was 90%, and its absolute configuration was *R* (Supplementary data).[6] Thus, we found that not only the optical purity of the starting material was completely transferred to the product but also the reaction occurred exclusively at γ to Si and the products had (*E*)-olefin. These results suggested that the allylic alkylation of



Scheme 1.

Keywords: Pd-catalyzed allylic alkylation; α-Acyloxysilane; α-Silyl cation; Chirality transfer.

* Corresponding authors. Tel.: +81 6660 52571; fax: +81 6660 52522; e-mail: sakaguch@sci.osaka-cu.ac.jp

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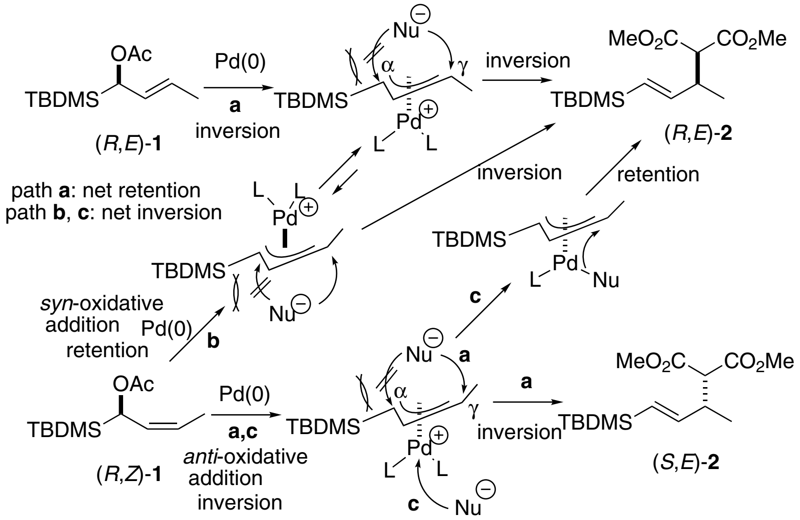


Scheme 2.

α-acyloxysilane **1** with $Pd(PPh_3)_4$ proceeded through an inversion–inversion (net retention) mechanism via a π-allyl palladium intermediate in the same manner as that of a conventional Pd(0)-catalyzed allylic alkylation (path a, Scheme 2).[7] The γ-regioselectivity would be explained by both (1) steric effect, that is, a sterically bulky TBDMS group compared to a methyl group (α:γ = < 1:>99), and (2) electric character, that is, the more electrophilic property of γ-carbon than that of α-carbon.[8]

We next examined the reaction of the (*Z*)-isomer of the α-acyloxysilane **1** (>95% ee)[3] under the same reaction conditions. However, the reaction was quite slow (23 h) and gave (*S*,*E*)-vinylsilane (38%, >95% ee) along with recovery of the starting **1** (52%, >95% ee) (Table 1, entry 1). To improve the yield of the reaction, $Pd_2(dba)_3$–$CHCl_3$ was employed as a catalyst (method B). The reaction under the standard conditions gave an increased yield of (*E*)-**2** (entry 2). However, the product possessed an *R* configuration that of a net inversion product, without loss of its optical purity.[6] We screened the reaction by changing the substrate, amount of the phosphine ligand, and the solvent as summarized in the following: (1) (*R*,*E*)-**1** gave a net retention product (*R*,*E*)-**2** (entry 3), (2) with increased amount of PPh_3, the product ee was decreased (entries 4 and 5) and the product configuration was inversed to *S* by the addition of 0.33 equiv of PPh_3 (entry 6), while without PPh_3 gave rise to (*S*,*E*)-**2** (entry 7),[9] (3) the use of CH_3CN as the solvent gave a net retention product (*S*,*E*)-**2** in 87% yield with 92% ee (entry 8) in contrast to the use of THF in entry 2.[10] To the fact that the reaction of (*R*,*Z*)-**1** using method B (0.04 equiv of PPh_3 in THF) gave a net inversion product (*R*,*E*)-**2**, it would be produced via internal *syn*-oxidative addition of Pd(0)[11] (retention) and subsequent attack of the nucleophile from the backside of the Pd atom (inversion) (path b) as shown in Scheme 2. The reaction with an increased amount of PPh_3 would proceed through paths a and b in a competitive manner. An alternative mechanism that involves a transmetalation followed by an internal delivery of the nucleophile

Table 1. Pd-catalyzed allylic alkylation of α-acyloxyallylsilane **1**

$$(R)\text{-}\mathbf{1} \xrightarrow[\text{NaH (4.2 equiv), THF, reflux}]{\text{Pd(0) (cat.), PPh}_3\text{, CH}_2(\text{CO}_2\text{Me})_2\text{ (4.2 equiv)}} (E)\text{-}\mathbf{2}$$

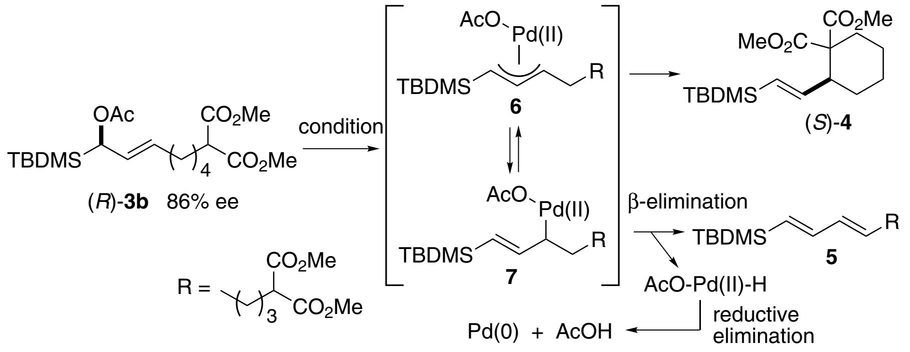
Entry	(*R*)-**1**[a]	Method[b]	PPh_3 (equiv)	Time (h)	(*E*)-**2**	Yield (%)	ee (%)	Recovery of **1** (%)[d]
1	*Z*	A	0.1	23	*S*	38	>95	52
2	*Z*	B	0.04	23	*R*	67	>95	27
3	*E*	B	0.04	4	*R*	86	73	0
4	*Z*	B	0.08	23	*R*	40	65	51
5	*Z*	B	0.16	23	*R*	62	38	31
6	*Z*	B	0.33	23	*S*	41	24	40
7	*Z*	B	None	23	*S*	6	19	78
8[c]	Z	B	0.04	23	*S*	87	92	6

[a] (*R*,*E*)-**1** (90% ee), (*R*,*Z*)-**1** (>95% ee).

[b] Method A: $Pd(PPh_3)_4$ (0.13 equiv), $CH_2(CO_2Me)_2$ (4.2 equiv), NaH (4.2 equiv), THF, reflux. Method B: $Pd_2(dba)_3$–$CHCl_3$ (0.04 equiv), $CH_2(CO_2Me)_2$ (4.2 equiv), NaH (4.2 equiv), THF, reflux.

[c] CH_3CN, 90 °C.

[d] In each case, the recovered **1** retained the optical purity of the starting **1**.



Condition: $Pd(PPh_3)_4$ (0.1 equiv), PPh_3 (0.1 equiv), NaH, reflux, 14 h

entry	NaH (equiv)	solvent	(*S*)-**4** (% ee) (%)	**5** (%)
1	1.0	THF	33 (87)	27
2	2.0	THF	37 (c)	0
3[a]	2.0	THF	55 (c)	0
4[a]	2.0	DMF[b]	84 (87)	0

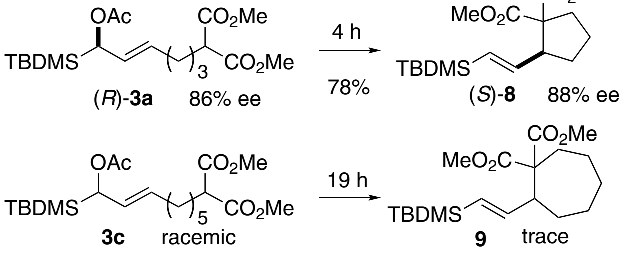
a) $Pd_2(dba)_3$-$CHCl_3$ (0.05 equiv), $PMePh_2$ (0.3 equiv). b) 100 °C, 3 h. (c) Not detected.

Scheme 3.

from the π-allyl-Pd complex generated by *anti*-oxidative addition (path c) is less likely under the reaction conditions because the transmetalation does not generally proceed in the case of soft nucleophile such as malonate anion.[4] The use of a polar solvent would accelerate path a to give (*S*,*E*)-**2**.[11] Thus, it was found that each enantiomer could be prepared in good yields by the use of $Pd_2(dba)_3$–$CHCl_3$ in THF or CH_3CN.

Next, we turned our attention to an intramolecular Pd(0)-catalyzed allylic alkylation of α-acyloxyallylsilane toward the construction of optically active carbocycles.[12] Three cyclization precursors **3a–c** ($n = 3$, 4, and 5) were synthesized in optically active forms except for $n = 5$ (Supplementary data). As a preliminary experiment, (*R*)-**3b** $n = 4$ was treated with NaH, $Pd(PPh_3)_4$, and PPh_3 in THF (Scheme 3). The reaction gave the esired six-membered carbocycle **4** having (*E*)-vinylsilane,[13] while the yield was low (33%) and diene **5** (27%) was a by-product (entry 1). The optical purity of the starting material was completely transferred to **4** (87% ee), and its absolute configuration was *S* (a net retention product, Supplementary data). Next, we attempted to optimize the reaction conditions relative to (1) amount of NaH, (2) other Pd catalysts, (3) effect of phosphine ligand, and (4) solvent. It was considered that in situ generated AcOH would accelerate β-elimination of the Pd(II) species in the η^1-allyl palladium(II) intermediate **7** to give diene **5**. The use of excess NaH would eliminate such reaction pathway. Indeed, the use of 2 equiv of NaH did not give the diene at all, but the yield of **4** was not satisfactory (entry 2).[14] To increase the yield of the cyclized product, we screened several phosphine ligands and Pd catalysts. The use of $Pd_2(dba)_3$–$CHCl_3$ (0.05 equiv) and $PMePh_2$ (0.3 equiv) was a suitable combination to give **4** in 55% yield (entry 3).[15] Finally, the reaction was optimized by the use of DMF (100 °C) as the solvent. The reaction was completed within 3 h to give (*S*)-**4** in 84% yield (87% ee) (entry 4).[16] This would be due to high solubility of the reactant in DMF since the use of benzene (18%) or acetonitrile (13%) resulted in low yields, respectively.[17] Reaction of (*R*)-**3a** ($n = 3$, 86% ee) under the optimized conditions afforded five-membered product (*S*)-**8** (88% ee) in 78% yield (Scheme 4).[13] On the other hand, reaction of **3c** ($n = 5$) gave only a trace amount of cyclized product **9**,[18] probably due to a latent ring strain in a medium-size ring. These results suggested that the present Pd(0)-catalyzed reaction would undergo an intramolecular allylic alkylation of α-alkenyl-α-acyloxysilane via a conventional net retention pathway through a π-allyl palladium intermediate.

In summary, Pd(0)-catalyzed allylic alkylations of optically active α-alkenyl-α-acyloxysilanes were examined. The reaction proceeded in a stereo- and regioselective manner to give the corresponding acyclic and cyclic



Scheme 4. Reagents and conditions: $Pd_2(dba)_3$–$CHCl_3$ (0.05 equiv), $PMePh_2$ (0.3 equiv), NaH (2 equiv), DMF, 100 °C.

(*E*)-vinylsilanes. The products completely retained the optical purity of the starting materials. Thus, a novel chiral α- or γ-silyl cation species was trapped as a π-allyl palladium intermediate. Further studies using the present chirality-transferring carbon–carbon bond forming reaction are in progress.

Acknowledgements

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Supplementary data

Supplementary data associated with this article can be found, in the online version at doi:10.1016/j.tetlet.2005.05.076.

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6. (*R*)-**2**: $[\alpha]_D^{20}$ −19.3 (*c* 1.14, CHCl$_3$, 90% ee, from (*R*,*E*)-**1**); $[\alpha]_D^{20}$ −25.9 (*c* 1.05, CHCl$_3$, >95% ee, from (*R*,*Z*)-**1**); ^{1}H NMR (300 MHz, CDCl$_3$) δ 5.93 (dd, $J = 18.6$, 7.4 Hz, 1H), 5.70 (dd, $J = 18.6$, 0.8 Hz, 1H), 3.72 (s, 3H), 3.67 (s, 3H), 3.33 (d, $J = 9.2$ Hz, 1H), 2.97 (dqd, $J = 9.2$, 6.8, 6.8 Hz, 1H), 1.08 (d, $J = 6.8$, 3H), 0.83 (s, 9H), 0.01 (s, 3H), −0.02 (s, 3H).
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8. According to the MP2/6-31G*//3-21G calculations, carbocation α to the SiH$_3$ group is 18.3 kcal/mol less stable than the corresponding carbocation α to a methyl group.[2a]
9. As a control experiment, the reaction of (*R*,*Z*)-**1** (>95% ee) using method B without carbon nucleophile resulted in a formation of 1-TBDMS-1,3-butadiene with a recovery of (*R*,*Z*)-**1** (>95% ee). This also suggests the present reaction proceeds through a π-allyl palladium(II) intermediate in Scheme 3.
10. The (*R*,*Z*)-α-acyloxysilane **1** (>95% ee) was converted to (*S*,*E*)-vinylsilane **2** (>95% ee) via Pd(II)-catalyzed allylic rearrangement in two steps (67%) by Panek's protocol: Panek, J. S.; Sparks, M. A. *J. Org. Chem.* **1990**, *55*, 5564–5566.
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13. (*S*)-**4**: $[\alpha]_D^{24}$ −32.7 (*c* 0.64, CHCl$_3$, 87% ee); ^{1}H NMR (400 MHz, CDCl$_3$) δ 6.25 (dd, $J = 18.6$, 8.5 Hz, 1H), 5.63 (d, $J = 18.6$ Hz, 1H), 3.67 (s, 3H), 3.66 (s, 3H), 2.78 (dt, $J = 12.0$, 4.0 Hz, 1H), 2.15 (m, 1H), 1.97 (m, 1H), 1.80 (m, 1H), 2.78–1.53 (2H), 1.50–1.34 (3H), 0.84 (s, 9H), −0.01 (s, 3H), −0.03 (s, 3H). (*S*)-**8**: $[\alpha]_D^{18}$ −59.1 (*c* 1.51, CHCl$_3$, 88% ee); ^{1}H NMR (400 MHz, CDCl$_3$) δ 5.96 (dd, $J = 18.6$, 7.3 Hz, 1H), 5.71 (dd, $J = 18.6$, 1.2 Hz, 1H), 3.72 (s, 3H), 3.62 (s, 3H), 3.29 (dt, $J = 7.2$, 7.2 Hz, 1H), 2.47 (dt, $J = 13.7$, 8.3 Hz, 1H), 2.08 (ddd, $J = 13.8$, 9.0, 4.8 Hz, 1H), 1.99–1.81 (2H), 1.75–1.50 (2H), 0.84 (s, 9H), −0.02 (s, 6H).
14. The reaction using a carbonate instead of acetate without a base under the same conditions did not proceed at all, while heating under reflux for 7 h gave diene **5** (34%). The use of 2 equiv of NaH gave a mixture of **4** (24%) and **5** (10%) when heated under reflux for 7 h.
15. The use of DPPE, DPPB, or DPPF gave **4** in 44%, 46%, and 38%, respectively. On the other hand, P(*n*-Bu)$_3$, P(Cy)$_3$, PMe$_2$Ph, P(*o*-tol)$_3$, AsPh$_3$, or DPPP by-produced the diene **5**.
16. The reaction of **3b** using Pd(PPh$_3$)$_4$ and PPh$_3$ without a base (THF, reflux, 14 h) gave the diene **5** in 92% yield; however, the reaction using Pd$_2$(dba)$_3$–CHCl$_3$ (0.05 equiv) and PMePh$_2$ (0.05 equiv) (DMF, 100 °C, 19 h) gave **5** (32%) with recovery of **3b** (56%).
17. Using DMF as the solvent, the reaction of **3b** with Pd(PPh$_3$)$_4$ (0.1 equiv) and PPh$_3$ (0.1 equiv) instead of Pd$_2$(dba)$_3$–CHCl$_3$ and PMePh$_2$ gave **4** (72%) as the sole product.
18. Trace amounts of diene were detected from the crude product by ^{1}H NMR.