Tetrahedron 71 (2015) 6442–6448

Contents lists available at ScienceDirect

Tetrahedron

journal homepage: www.elsevier.com/locate/tet

Alkene migration to the end-terminal carbon bearing a phenyl group over a chiral siloxy carbon center in Heck reaction

Akiko Ida, Naoyuki Hoshiya, Jun'ichi Uenishi *

Kyoto Phaemaceutical University, Yamashina, Kyoto 607-8412, Japan

ARTICLE INFO

Article history:
Received 16 January 2015
Received in revised form 4 March 2015
Accepted 5 March 2015
Available online 11 March 2015

On the celebration of Tetrahedron Prize 2014, this paper is dedicated to Professor Jiro Tsuji for his great contribution on Pd-chemistry

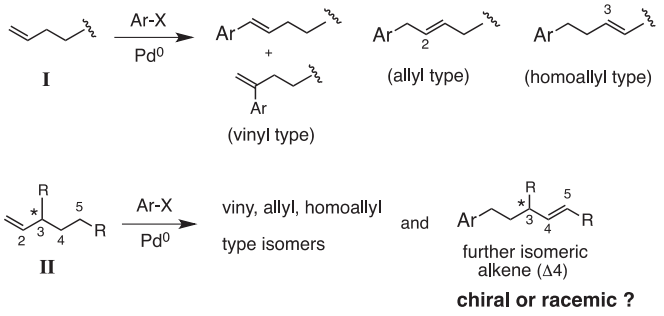
Keywords:
Alkene migration
Chiral center
Heck reaction
Pd-catalyst
Stereochemistry

ABSTRACT

The Heck reaction of aryl bromide with a terminal alkene substrate having a chiral center at the allylic position and a phenyl substituent at another terminal carbon is reported. An alkene migration to the phenyl-substituted end carbon is observed, along with the typical Heck reaction. This zipper-type migration occurs through multiple internal carbon bonds, and the stereochemistry of the internal chiral center is completely retained during this process.

1. Introduction

The Heck reaction is an important coupling reaction for the formation of carbon–carbon bonds.[1] The reaction involves the addition of ArPdX to an alkene, followed by β-hydride elimination to give an aryl substitution alkene.[2] Typically, electronically biased alkenes with no hydrogen atom at their allylic position are used.[3] Otherwise, the reaction becomes sluggish and gives complex regioisomeric mixtures.[4] The Heck arylation of a terminal alkene, such as **I**, affords two regioisomeric vinyl-type alkenes[5] also allyl- and homoallyl-type alkenes (Scheme 1). However, the stereochemistry of the internal chiral center in the substrate, such as in **II**, in the Heck reaction has not been investigated, most likely because minimal 4-alkenyl bond migration occurs.[6] The formation of the isomeric alkene decreases in the order of vinyl, allyl(Δ2), homoallyl(Δ3) and further isomeric(Δ4) types of alkenes. However, we are interested in the stereochemistry of the isomeric alkene(Δ4) product in the Heck reaction in which a chiral center exists at the allylic position of the terminal alkene, such as in the case of **II**.



Scheme 1. Heck reaction of terminal alkene with ArX.

For this purpose, the installation of an alkene-stabilizing substituent (R), e.g., a phenyl or ester group, may be required at the C-5 position of the substrate to increase its formation. Either racemization or retention of the chiral carbon center will provide details of the alkene migration process in the Heck reaction. In this study, we have found the following results: (i) the migration of an alkene through three to five bonds to give the terminal styrenyl product in 30–40% yield when a phenyl group is installed at the terminal

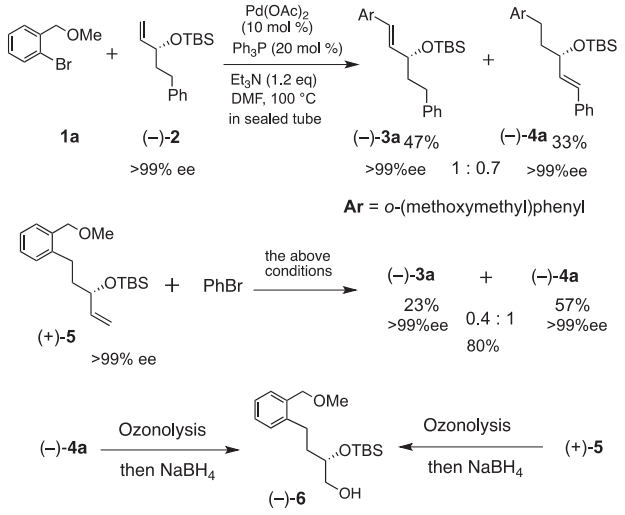
* Corresponding author. Tel.: +81 75 595 4665; fax: +81 75 595 4763; e-mail address: juenishi@mb.kyoto-phu.ac.jp (J. Uenishi).

http://dx.doi.org/10.1016/j.tet.2015.03.018
0040-4020/

carbon and (ii) the retention of the stereochemistry without racemization of the siloxy or methoxy chiral carbon center during the migration process.

2. Results and discussion

We first examined the Heck reaction of chiral alkene (−)-**2** having an (*R*)-TBSoxy group at the C-3 carbon with aryl bromide **1a**. The reaction was conducted in DMF at 100 °C with $Pd(OAc)_2$ and Ph_3P as the catalyst in the presence of Et_3N to give (−)-**3a** in 47% yield, along with its alkene regioisomer (−)-**4a** in 33% yield. No enol silyl ether product was detected in the reaction mixture. Surprisingly, product **4a** was optically pure, with greater than 99% ee, as determined by chiral HPLC.[7] The reaction of the reverse combination of terminal alkene (+)-**5** and bromobenzene gave the same products (−)-**3a** and (−)-**4a** in a ratio of 0.4:1 under the same reaction conditions. In both cases, the alkenyl bond migrated to the end-terminal position by chain walking of σ-Pd complex, which resembles a zipper reaction in the alkyne migration process (Scheme 2).[8]



Scheme 2. Heck reaction of aryl bromide and alkene.

We examined this Pd-catalyzed migration process for other terminal alkenes (−)-**2** and (+)-**7**–**11** with aryl bromides **1a**–**d** (Fig. 1); the results are shown in Table 1.

The reaction of (−)-**2** with *o*-(hydroxymethyl)bromobenzene **1b** gave (−)-**3b** and (−)-**4b** in 70% yield with a ratio of 1:0.5 (entry 2). Similarly, the reaction of (−)-**2** with *o*- and *p*-bromotoluenes **1c** and **1d** afforded a mixture of **3c** and **4c** in 82% yield with a 1:0.6 ratio and **3d** and **4d** in 81% yield with a 1:0.7 ratio (entries 3 and 4, respectively). Methyl ether (+)-**7** afforded compounds (−)-**3e** and (+)-**4e** in 51% and 30% yields with 99% ee, respectively (entry 5). A small amount of exomethylene isomer **3e′** was also isolated in this

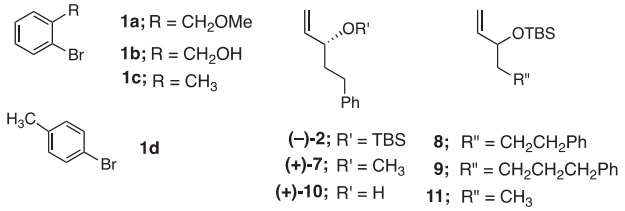
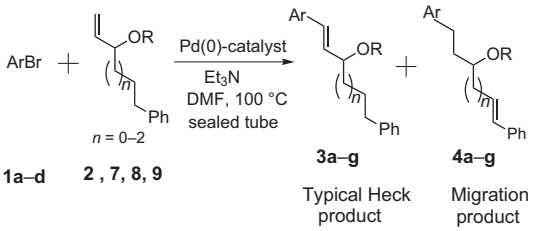


Fig. 1. Structures of ArBr and terminal alkenes.

Table 1
Heck reactions of ArBr and terminal alkenes

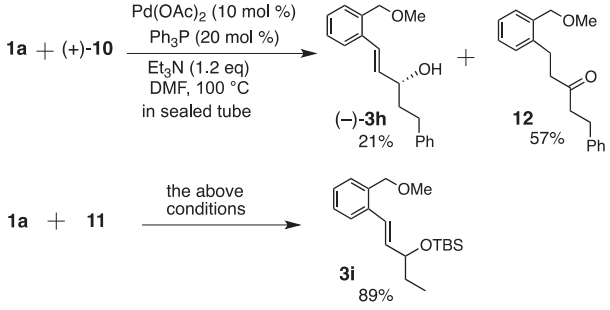


Entry	Compound	Alkene	Time (h)	Product **3**+**4**	Yield[a] (%)	Ratio[b] (**3**:**4**)
1	**1a**	(−)-**2**	24	**3a**+**4a**[c]	80	1:0.7
2	**1b**	(−)-**2**	20	**3b**+**4b**[c]	70	1:0.5
3	**1c**	(−)-**2**	27	**3c**+**4c**[d]	82	1:0.6
4	**1d**	(−)-**2**	19	**3d**+**4d**[d]	81	1:0.7
5	**1b**	(+)-**7**	24	**3e**+**4e**[e]	81	1:0.6
6	**1b**	**8**	24	**3f**+**4f**[c]	66	1:0.4
7	**1a**	**9**	14	**3g**+**4g**[c]	88	1:0.5

[a] Combined yield.
[b] Ratio was determined by ^1H NMR.
[c] Compounds are separable by HPLC.
[d] Compounds are inseparable by HPLC.
[e] Exomethylene isomer was produced in less than 5% yield.

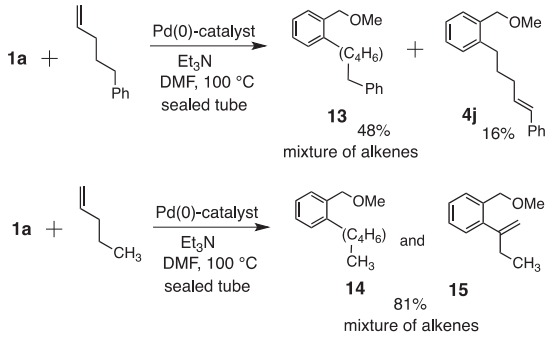
case. These results indicated that starting terminal α,β-unsaturated alkene (*n*=0) gave δ,ε-unsaturated product in Heck arylation reaction. The reaction of **8**, which is a one-carbon-extended substrate (*n*=1) between the siloxy carbon center and the terminal phenyl group, with **1b** gave compounds **3f** in 47% yield and **4f** in 19% yield with a ratio of 1:0.4 (entry 6). The alkene migration proceeded again to the terminal end to form ε,ζ-unsaturated product **4f**. The reaction of the two-carbon-extended alkene **9** (*n*=2) with **1b** also gave the typical Heck product **3g** with ζ,η-unsaturated product **4g** in 88% yield with a ratio of 1:0.5 (entry 7). All of the isomers **4a**–**g** were obtained as side products in which the alkenyl bond isomerized to the conjugated position with the terminal phenyl group. Surprisingly, in the case of **9**, σ-Pd complex moved over four carbon bonds by chain walking to reach 1,5-transposition and furnished styrenyl product.[9] It is noteworthy that the internal chiral center completely retain the stereochemistry during the process in all the cases. While, the internal alkenes produced in the migration process were poorly detected in the products.

When terminal alkene (+)-**10** bearing a hydroxy group instead of a silyloxy or methoxy group was used with **1a**, the typical Heck product (−)-**3h** formed as an optically pure form in 21% yield and no zipper product was produced. Instead, the migration process terminated at the enol intermediate to afford ketone **12** in 57% yield.[6,9] The reaction of a simple 3-silyloxypentene **11** with **1a** exclusively gave the typical Heck product **3i** in 89% yield (Scheme 3).



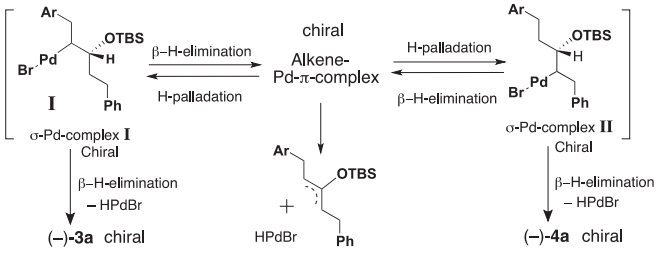
Scheme 3. Heck Reaction of **1a** with (+)-**10** and **11**.

We realized that the terminal phenyl group is essential for the formation of the zipper product[10] but questioned the necessity of the internal siloxy group. The reaction of 5-phenylpentene with **1a** gave a mixture of regioisomeric alkenes **13** and zipper product **4j** in 48% and 16% yields, respectively. However, the reaction of 1-hexene with **1a** gave a mixture of alkene isomers **14** and exomethylene product **15** in 81% total yield. These results indicated that no zipper reaction occurred in the absence of the terminal phenyl group (Scheme 4).



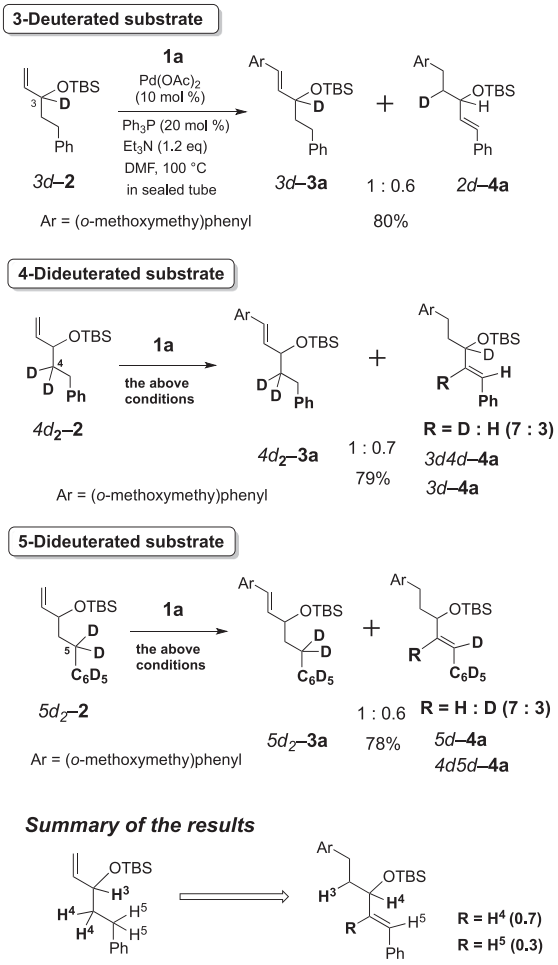
Scheme 4. Heck reaction of **1a** with 5-phenyl-1-pentene and *n*-hexene.

In the formation of **(−)-4a**, the migration process of the alkene involves β-hydride elimination of HPdBr from the σ-Pd complex and the subsequent hydropalladation to the intermediary alkene. Because zipper product **4a** is chiral, its precursors, including σ-Pd complex **I**, **II**, and other intermediates, must be chiral (Scheme 5). If HPdBr dissociates from the intermediate alkene completely, then re-addition of HPdBr to the alkene would form a racemic σ-Pd adduct. Therefore, the intermediate alkenes must exist as a chiral alkene π-Pd complex.



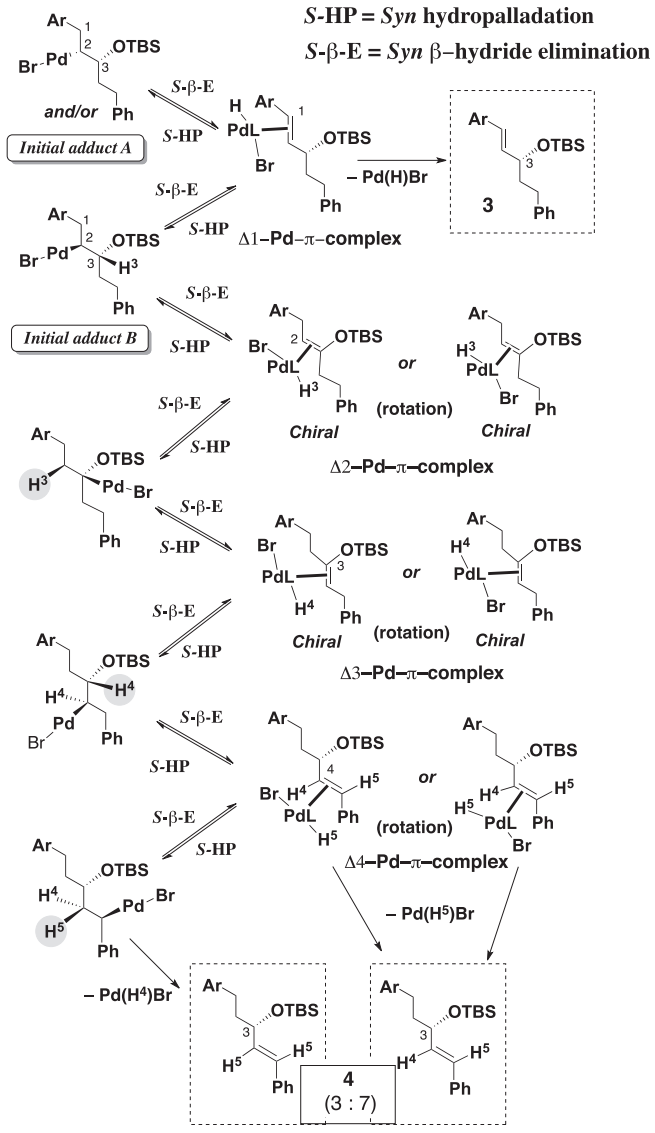
Scheme 5. Heck reaction intermediate.

During the migration, rearrangement of the protons occurs in the formation of compound **4a**. The identification of the protons of **4a** originating from those of **2** would provide useful information about the reaction mechanism.[11] Experiments using deuterated materials would reveal the process. Three deuterated analogs, *3d*-**2**, $4d_2$-**2**, and $5d_2$-**2**, incorporated with deuterium at more than 99% of the C-3, C-4, and C5 positions were prepared and subjected to the reaction (Scheme 6). Mono-deuterated compound *3d*-**2** gave *3d*-**3a** and *2d*-**4a** in a reaction where the deuterium at C-3 moved to the next carbon at C-2 completely. The reaction of $4d_2$-**2** gave $4d_2$-**3a** and two deuterated compounds, *3d4d*-**4a** and *3d*-**4a**, in a ratio of 7:3. One of the two C-4 deuterium atoms transferred to the C-3 position completely, and 70% of the other deuterium atom remained at the C-4 position. In the case of $5d_2$-**2**, in addition to $5d_2$-**3a**, 5-deuterio and 4,5-dideuterio compounds *5d*-**4a** and *4d5d*-**4a** were obtained in a ratio of 7:3, where 30% of one deuterium atom at C-5 moved to the C-4 position and the other deuterium remained at C-5. The rearrangement is summarized at the bottom of Scheme 6.



Scheme 6. Heck reaction of **1a** with deuterated **2**.

The reaction mechanism can be considered on the basis of these results. The plausible mechanism is shown in Scheme 7. First, the addition of ArPdBr derived from ArBr and the Pd^0-catalyst to alkene **2** generates two diastereoisomeric adducts A and B. The *syn*-β-hydride elimination (*S*-β-E) of A and part of B will provide **3** via the alkene(Δ1) π-Pd complex. On the other hand, the *S*-β-E of the initial adduct B with H^3 will give a chiral alkene(Δ2) π-Pd complex, and rotational hydropalladation (migratory insertion) to the alkene affords a chiral C-3 substituted σ-Pd complex. In this step, H^3 moves to the C-2 position. When the two steps repeat, a chiral C-4 substituted σ-Pd complex can form. The *S*-β-E with H^5 then leads to the alkene(Δ4) π-Pd complex. De-coordination of the complex provides **4a** consisting of C-4 (H^4) and C-5 (H^5) in a ratio of 70%. In another pathway, the benzyl σ-Pd complex is formed by rotational hydropalladation. Finally, the formation of product **4** consisting of the C-4 (H^5) and C-5 (H^5) protons in a ratio of 30% results in an *anti*-β-hydride elimination pathway.[12]



Scheme 7. Plausible reaction mechanism of Zipper process in the Heck reaction.

In summary, we observed that alkene migration takes place over multiple carbon–carbon bonds in terminal alkene substrates having a phenyl substituent at another terminal carbon in the Heck reaction. This migration proceeds without racemization at the internal chiral siloxy or methoxy carbon center. These results provided clear proof that a 1,3-transposition of the σ-Pd complex via the alkene π-Pd complex occurs by intramolecular migratory insertion without dissociation of the alkene and HPdBr. More detail of the study and synthetic applications are under progress.

3. Experimental

3.1. General

All reactions were run under an atmosphere of nitrogen. Solvents and reagents were dried prior to use. Et_2O and THF were distilled from sodium benzophenone ketyl. CH_2Cl_2 was distilled from P_2O_5 and toluene was distilled from CaH_2. ^1H NMR spectra were recorded on JEOLJNM-ALM-270 (270 MHz) and Agilent Unity Inova XL-400 (400 MHz). Proton chemical shifts were internally referenced to the residual proton resonance in $CDCl_3$ (δ 7.26) and CD_2Cl_2 (δ 5.32). ^{13}C NMR spectra were recorded on Agilent Unity Inova XL-400 (100 MHz). Carbon chemical shifts were internally referenced to the deuterated solvent signals in $CDCl_3$ (δ 77.00). Mass spectra (MS) were recorded on JEOL JMC-GC MATE. Electron impact (EI) spectra were performed at 70 eV for low and high resolution mass spectra. IR spectra were taken on a JASCO FT/IR-410 using a thin film on NaCl plate. Optical rotations were recorded on a JASCO P-2200. Chiral HPLC analyses were performed on a JASCO PU-2080 using UV-2075 detector. Analytical thin layer chromatography (TLC) was performed on Merck silica gel $60F_{254}$ plates. Flash column chromatography was performed with Merck silica gel 60 (40–63 μm pore size).

3.2. Typical Heck reaction of aryl bromide and terminal alkene

A mixture of alkene (0.1 mmol), aryl bromide (0.2 mmol), Ph_3P (20 mol %), Pd(OAc) (10 mol %) and Et_3N (0.12 mmol) were dissolved in anhydrous DMF (0.2 M) in a sealed tube. The mixture was heated at 100 °C under an argon atmosphere for the corresponding time described in Table. After cooling to room temperature, ether (70 mL) was added to the reaction mixture. The mixture was washed with water three times (5 mL×3), and then with brine (5 mL). The organic layer was dried over $MgSO_4$, filtered, and concentrated. The crude material was purified by flash chromatography on silica gel to give the corresponding products. Some of products were further purified by HPLC.

*3.2.1. (R,E)-3-tert-Butyldimethylsilyloxy-1-[(2-methoxymethyl)-phenyl]-5-phenylpent-1-ene (−)-**3a**.* Colorless oil; *Rf*=0.24 (2.5% EtOAc in hexane), 0.53 (40% CH_2Cl_2 in hexane); $[\alpha]_D^{22}$ −2.3 (*c* 0.78, $CHCl_3$); ^1H NMR (270 MHz, $CDCl_3$) δ 7.47 (1H, dd, *J*=7.2, 1.9 Hz), 7.36–7.15 (8H, m), 6.81 (1H, d, *J*=15.7 Hz), 6.12 (1H, dd, *J*=15.7, 6.3 Hz), 4.50 (2H, s), 4.37 (1H, m), 3.39 (3H, s), 2.75–2.67 (2H, m), 1.96–1.87 (2H, m), 0.94 (9H, s), 0.10 (3H, s), 0.07 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 142.4, 136.5, 135.3, 134.9, 129.1, 128.4, 128.3, 128.1, 127.2, 126.4, 126.1, 125.7, 73.1, 72.8, 58.1, 40.1, 31.5, 25.9, 18.3, −4.2, −4.8; LRMS (EI): *m*/*z* (rel. int. %) 396 (M^+, 0.1), 364 (31), 339 (19), 117 (base); HRMS (EI): Calcd for $C_{25}H_{36}O_2Si$ *m*/*z* 396.2484, found 396.2475; >99% ee, [HPLC conditions; column Daicel OD-H, eluent 0.5% 2-propanol in hexane, flow rate 1.0 mL/min, wavelength 254 nm, $t_r(S)$=5.1 min, $t_r(R)$=6.8 min].

*3.2.2. S,E)-3-tert-Butyldimethylsilyloxy-5-[(2-methoxymethyl)-phenyl]-1-phenylpent-1-ene (−)-**4a**.* Colorless oil; *Rf*=0.24 (2.5% EtOAc in hexane), 0.48 (40% CH_2Cl_2 in hexane); $[\alpha]_D^{22}$ −18.6 (*c* 0.11, $CHCl_3$); ^1H NMR (270 MHz, $CDCl_3$) δ 7.40–7.14 (9H, m), 6.54 (1H, d, *J*=15.9 Hz), 6.23 (1H, dd, *J*=15.9, 6.3 Hz), 4.46 (2H, s), 4.38 (1H, m), 3.38 (3H, s), 2.86–2.62 (2H, m), 1.90–1.81 (2H, m), 0.95 (9H, s), 0.11 (3H, s), 0.08 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 141.0, 137.1, 135.7, 133.0, 129.3, 129.2, 129.0, 128.5, 127.9, 127.4, 126.4, 125.9, 73.4, 72.6, 58.2, 39.8, 28.1, 25.9, 18.3, −4.2, −4.7; LRMS (EI): *m*/*z* (rel. int. %) 396 (M^+, 0.1), 364 (6), 339 (15), 232 (base); HRMS (EI): Calcd for $C_{25}H_{36}O_2Si$ *m*/*z* 396.2484, found 396.2476; >99% ee, [HPLC conditions: column Kromasil 5-AmyCoat, eluent 1% 2-propanol in hexane, flow rate 0.5 mL/min, wavelength 254 nm, $t_r(S)$=8.0 min, $t_r(R)$=10.5 min].

*3.2.3. (R,E)-3-tert-Butyldimethylsilyloxy-1-[(2-hydroxymethyl)-phenyl]-5-phenylpent-1-ene (−)-**3b**.* Colorless oil; *Rf*=0.40 (20% EtOAc in hexane); $[\alpha]_D^{20}$ −6.8 (*c* 0.50, EtOH); IR ($CHCl_3$, cm^{-1}): 3426; ^1H NMR (400 MHz, $CDCl_3$) δ 7.47 (1H, d, *J*=7.2 Hz), 7.38 (1H, d, *J*=7.2 Hz), 7.31–7.26 (4H, m), 7.21–7.16 (3H, m), 6.85 (1H, d, *J*=14.6 Hz), 6.15 (1H, dd, *J*=14.6, 6.2 Hz), 4.75 (2H, d, *J*=5.6 Hz), 4.37 (1H, q, *J*=6.2 Hz), 2.87–2.64 (2H, m), 1.99–1.86 (2H, m), 0.95 (9H, s), 0.10 (3H, s), 0.08 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 142.5, 137.7,

136.2, 135.9, 128.5, 128.5, 128.3, 128.3, 127.7, 126.4, 126.1, 125.9, 73.2, 63.5, 40.2, 31.7, 26.1, 18.4, −4.1, −4.6; LRMS (FAB) *m/z* 405 $(M+Na)^+$; HRMS (FAB) Calcd for $C_{24}H_{34}O_2SiNa$ $(M+Na)^+$ 405.2226, found 405.2229; >99% ee, [HPLC conditions: column Daicel OD-H, eluent 1% 2-propanol in hexane, flow rate 1.0 mL/min, wavelength 254 nm, $t_r(S)$=16 min, $t_r(R)$=24 min].

*3.2.4. (S,E)-3-tert-Butyldimethylsilyloxy-5-[(2-hydroxymethyl)-phenyl]-1-phenylpent-1-ene (−)-**4b**.* Colorless oil; *Rf*=0.40 (20% EtOAc in hexane); $[\alpha]_D^{20}$ −22.6 (*c* 0.40, EtOH); IR ($CHCl_3$, cm^{-1}): 3349; ^1H NMR (400 MHz, $CDCl_3$) δ 7.38–7.36 (3H, m), 7.34–7.30 (2H, t, *J*=10.0 Hz), 7.25–7.18(4H, m), 6.54 (1H, d, *J*=16.2 Hz), 6.21 (1H, dd, *J*=16.2, 6.4 Hz), 4.73 (2H, d, *J*=5.0 Hz), 4.39 (1H, q, *J*=6.4 Hz), 2.84 (1H, m), 2.72 (1H, m), 1.91–1.86 (2H, m), 1.68 (1H, t, *J*=5.9 Hz), 0.95 (9H, s), 0.11 (3H, s), 0.08 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 140.5, 138.3, 137.0, 132.8, 129.5, 129.3, 128.6, 128.3, 128.0, 127.4, 126.4, 126.2, 73.4, 63.1, 39.9, 27.9, 25.9, 18.3, −4.2, −4.7; LRMS (FAB) *m/z* 405 $(M+Na)^+$; HRMS (FAB) Calcd for $C_{24}H_{34}O_2SiNa$ $(M+Na)^+$ 405.2226, found 405.2229; >99% ee, [HPLC conditions: column Daicel AD-H, eluent 1% 2-propanol in hexane, flow rate 1.0 mL/min, wavelength 254 nm, $t_r(R)$=23 min, $t_r(S)$=27 min].

*3.2.5. (R,E)-3-tert-Butyldimethylsilyloxy-1-(2-methylphenyl)-5-phenylpent-1-ene (**3c**) and (S,E)-3-tert-butyldimethylsilyloxy-5-(2-methylphenyl)-1-phenylpent-1-ene (**4c**).* A mixture of **3c** and **4c**. Colorless oil; *Rf*=0.33 (2.5% EtOAc in hexane); ^1H NMR (400 MHz, $CDCl_3$) δ 7.45–7.11 (9H, m, **3c**+**4c**), 6.78 (0.62H, dd, *J*=15.7, 1.0 Hz, **3c**), 6.57 (0.38H, d, *J*=15.9 Hz, **4c**), 6.26 (0.38H, dd, *J*=15.9, 6.4 Hz, **4c**), 6.12 (0.62H, dd, *J*=15.7, 6.3 Hz, **3c**), 4.41–4.36 (1H, m, **3c**+**4c**), 2.81–2.65 (2H, m, **3c**+**4c**), 2.37 (1.86H, s, **3c**), 2.33 (1.14H, s, **4c**), 1.98–1.84 (2H, m, **3c**+**4c**), 0.98 (3.42H, s, **4c**), 0.97 (5.58H, s, **3c**), 0.14 (1.14H, s, **4c**), 0.13 (1.86H, s, **3c**), 0.10 (3H, s, **3c**+**4c**); ^{13}C NMR (100 MHz, $CDCl_3$) δ 142.4 (**3c**), 140.6 (**4c**), 137.1 (**4c**), 136.3 (**3c**), 135.9 (**4c**), 135.4 (**3c**), 134.4 (**3c**), 133.0 (**4c**), 130.2, 130.1, 129.3, 128.7, 128.5, 128.4, 128.3, 127.4, 127.3, 127.2, 126.4, 126.1 (**4c**), 125.9 (**4c**), 125.8, 125.7, 125.7, 73.4 (**4c**), 73.1 (**3c**), 40.1 (**3c**), 38.9 (**4c**), 31.5 (**3c**), 29.0 (**4c**), 25.9 (**3c**), 25.9 (**4c**), 19.9 (**3c**), 19.2 (**4c**), 18.3 (**3c**), 18.3 (**4c**), −4.2 (**3c**), −4.2 (**4c**), −4.7 (**3c**), −4.7 (**4c**).

*3.2.6. (R,E)-3-tert-Butyldimethylsilyloxy-1-(4-methylphenyl)-5-phenylpent-1-ene (**3d**) and (S,E)-3-tert-butyldimethylsilyloxy-5-(4-methylphenyl)-1-phenylpent-1-ene (**4d**).* A mixture of **3d** and **4d**. Colorless oil; *Rf*=0.33 (2.5% EtOAc in hexane); ^1H NMR (400 MHz, $CDCl_3$) δ 7.39–7.09 (9H, m, **3d**+**4d**), 6.53 (0.38H, dd, *J*=15.9, 2.6 Hz, **4d**), 6.47 (0.62H, d, *J*=15.8 Hz, **3d**), 6.20 (0.38H, ddd, *J*=15.9, 6.5, 2.5 Hz, **4d**), 6.15 (0.62H, dd, *J*=15.8, 6.7 Hz, **3d**), 4.36–4.29 (1H, m, **3d**+**4d**), 2.75–2.63 (2H, m, **3d**+**4d**), 2.34 (1.86H, s, **3d**), 2.32 (1.14H, s, **4d**), 1.96–1.83 (2H, m, **3d**+**4d**), 0.94 (3.42H, s, **4d**), 0.93 (5.58H, s, **3d**), 0.09 (1.86H, s, **3d**), 0.09 (1.14H, s, **4d**), 0.06 (1.14H, s, **4d**), 0.05 (1.86H, s, **3d**); ^{13}C NMR (100 MHz, $CDCl_3$) δ 142.4 (**3d**), 142.4 (**4d**), 139.3 (**4d**), 137.2 (**3d**), 137.1 (**4d**), 135.1 (**4d**), 134.3 (**3d**), 133.1 (**4d**), 133.1 (**3d**), 132.1 (**3d**), 129.3, 129.2, 129.0, 128.5, 128.4, 128.3, 128.3, 128.2, 127.4, 127.3, 126.4, 126.3, 125.7, 125.7, 73.2 (**3d**), 73.1 (**4d**), 40.2 (**4d**), 40.1 (**3d**), 31.6 (**3d**), 31.1 (**4d**), 25.9 (**3d**), 25.9 (**4d**), 21.2 (**3d**), 21.0 (**4d**), 18.3 (**3d**), 18.3 (**4d**), −4.1 (**4d**), −4.2 (**3d**), −4.7 (**3d**), −4.7 (**4d**).

*3.2.7. (R,E)-3-Methoxy[1-(2-methoxymethyl)phenyl]-5-phenyl-pent-1-ene (−)-**3e**.* Colorless oil; *Rf*=0.35 (10% EtOAc in hexane); $[\alpha]_D^{23}$ −9.5 (*c* 1.00, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.52 (1H, dd, *J*=7.5, 1.5 Hz), 7.37–7.18 (8H, m), 6.84 (1H, d, *J*=15.7 Hz), 5.98 (1H, dd, *J*=15.7, 7.9 Hz), 4.54 (1H, d, *J*=11.7 Hz), 4.51 (1H, d, *J*=11.7 Hz), 3.73 (1H, q, *J*=7.9 Hz), 3.40 (3H, s), 3.36 (3H, s), 2.78–2.73 (2H, m), 2.05 (1H, m), 1.90 (1H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 142.0, 136.1, 134.9, 132.3, 129.7, 129.3, 128.5, 128.3, 128.2, 127.5, 126.2, 125.8, 81.6, 72.8, 58.1, 56.2, 37.2, 31.6; LRMS (EI): *m/z* (rel. int. %) 296 (M^+, 2), 264 (24), 191 (34), 159 (base); HRMS (EI): Calcd for $C_{20}H_{24}O_2$ *m/z* 296.1776, found 296.1779; >99% ee, [HPLC conditions: column Daicel OD-H, eluent 1% 2-propanol in hexane, flow rate 0.5 mL/min, wavelength 254 nm, $t_r(S)$=21 min, $t_r(R)$=39 min].

*3.2.8. (S,E)-3-Mehoxy[5-(2-methoxymethyl)phenyl]-1-phenyl-pent-1-ene (+)-**4e**.* Colorless oil; *Rf*=0.35 (10% EtOAc in hexane); $[\alpha]_D^{24}$ +2.3 (*c* 0.40, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.42–7.40 (2H, m), 7.37–7.31 (3H, m), 7.28–7.17 (4H, m), 6.56 (1H, d, *J*=15.9 Hz), 6.10 (1H, dd, *J*=15.9, 7.9 Hz), 4.48 (2H, s), 3.74 (1H, q, *J*=7.9 Hz), 3.38 (3H, s), 3.35 (3H, s), 2.85–2.70 (2H, m), 1.99 (1H, m), 1.86 (1H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 140.6, 136.6, 135.7, 132.5, 130.0, 129.4, 129.1, 128.6, 128.0, 127.7, 126.5, 125.9, 81.8, 72.6, 58.2, 56.2, 37.0, 28.0; LRMS (EI): *m/z* (rel. int. %) 296 (M^+, 0.9), 264 (28), 159 (20), 147 (base); HRMS (EI): Calcd for $C_{20}H_{24}O_2$ *m/z* 296.1776, found 296.1773; >99% ee, [HPLC conditions: column Daicel AD-H column, eluent 1% 2-propanol in hexane, flow rate 0.5 mL/min, wavelength 254 nm, $t_r(R)$=24 min, $t_r(S)$=34 min].

*3.2.9. (R)-3-Methoxy[2-(2-methoxymethyl)phenyl]-1-phenyl-pent-1-ene (−)-**3e′**.* Colorless oil; *Rf*=0.45 (10% EtOAc in hexane); $[\alpha]_D^{23}$ −5.8 (*c* 0.65, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.45 (1H, dd, *J*=6.9, 1.6 Hz), 7.31–7.21 (5H, m), 7.17–7.08 (3H, m), 5.46 (1H, dd, *J*=2.0, 1.3 Hz), 5.14 (1H, dd, *J*=2.0, 0.4 Hz), 4.45 (1H, d, *J*=11.4 Hz), 4.39 (1H, d, *J*=11.4 Hz), 3.82 (1H, m), 3.48 (3H, s), 3.35 (3H, s), 2.80 (1H, ddd, *J*=13.7, 10.2, 5.0 Hz), 2.59 (1H, ddd, *J*=13.7, 10.0, 6.5 Hz), 1.79 (1H, m), 1.68 (1H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 146.6, 142.0, 139.9, 135.6, 129.1, 128.9, 128.4, 128.3, 127.3, 127.3, 125.7, 115.7, 84.1 72.3, 58.1, 57.0, 36.0, 31.9; LRMS (EI): *m/z* (rel. int. %) 296 (M^+, 13), 264 (10), 232 (9), 173 (base); HRMS (EI): Calcd for $C_{20}H_{24}O_2$ *m/z* 296.1776, found 296.1769.

*3.2.10. (E)-3-tert-Butyldimethylsilyloxy-1-[(2-hydroxymethyl)-phenyl]-6-phenylhex-1-ene (**3f**).* Colorless oil; *Rf*=0.26 (10% EtOAc in hexane); IR (neat, cm^{-1}) 3337; ^1H NMR (400 MHz, $CDCl_3$) δ 7.44 (1H, dd, *J*=7.5, 1.9 Hz), 7.34 (1H, dd, *J*=6.9, 2.0 Hz), 7.28–7.23 (4H, m), 7.17–7.14 (3H, m), 6.79 (1H, dd, *J*=15.6, 0.9 Hz), 6.08 (1H, dd, *J*=15.6, 6.3 Hz), 4.71 (2H, d, *J*=3.9 Hz), 4.31 (1H, dtd, *J*=6.3, 5.9, 0.9 Hz), 2.62 (2H, dd, *J*=7.8, 7.1 Hz), 1.80–1.53 (4H, m), 0.91 (9H, s), 0.07 (3H, s), 0.05 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 142.4, 137.5, 136.1, 136.0, 128.4, 128.3, 128.2, 128.1, 127.5, 126.2, 125.7, 125.6, 73.3, 63.4, 37.9, 35.9, 26.9, 25.9, 18.2, −4.3, −4.7; LRMS (FAB) *m/z* 419 $(M+Na)^+$; HRMS (FAB) Calcd for $C_{25}H_{36}O_2SiNa$ *m/z* 419.2382, found 419.2378.

*3.2.11. (E)-4-tert-Butyldimethylsilyloxy-6-[(2-hydroxymethyl)-phenyl]-1-phenylhex-1-ene (**4f**).* Colorless oil; *Rf*=0.26 (10% EtOAc in hexane); IR (neat, cm^{-1}) 3389; ^1H NMR (400 MHz, $CDCl_3$) δ 7.37–7.17 (9H, m), 6.41 (1H, dd, *J*=15.8, 1.2 Hz), 6.23 (1H, dt, *J*=15.8, 7.2 Hz), 4.71 (2H, d, *J*=1.2 Hz), 3.90 (1H, m), 2.84 (1H, ddd, *J*=13.7, 11.3, 5.5 Hz), 2.67 (1H, ddd, *J*=13.7, 11.5, 5.4 Hz), 2.44 (2H, ddd, *J*=7.2, 5.9, 1.2 Hz), 1.90–1.70 (2H, m), 0.94 (9H, s), 0.10 (3H, s), 0.10 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 140.7, 138.2, 137.6, 132.2, 129.3, 128.5, 128.3, 128.0, 127.0, 126.8, 126.2, 126.0, 72.1, 63.1, 41.0, 38.6, 28.1, 25.9, 18.1, −4.3, −4.5; LRMS (FAB) *m/z* 419 $(M+Na)^+$; HRMS (FAB) Calcd for $C_{25}H_{36}O_2SiNa$ $(M+Na)^+$ *m/z* 419.2382, found 419.2388.

*3.2.12. (E)-3-tert-Butyldimethylsilyloxy-1-[(2-hydroxymethyl)-phenyl]-7-phenylhept-1-ene (**3g**).* Colorless oil; *Rf*=0.47 (20% EtOAc in hexane); IR (neat, cm^{-1}) 3390; ^1H NMR (400 MHz, $CDCl_3$) δ 7.46 (1H, dd, *J*=7.1, 1.8 Hz), 7.37 (1H, dd, *J*=7.2, 2.0 Hz), 7.31–7.24 (4H, m), 7.19–7.15 (3H, m), 6.80 (1H, d, *J*=15.7 Hz), 6.10 (1H, dd, *J*=15.7, 6.3 Hz), 4.74 (2H, s), 4.29 (1H, dt, *J*=6.3, 5.7 Hz), 2.62 (2H, dd, *J*=8.0, 7.3 Hz), 1.69–1.39 (6H, m), 0.92 (9H, s), 0.08 (3H, s), 0.07 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 142.6, 137.5, 136.3, 136.1, 128.4, 128.2,

128.1, 128.1, 127.4, 126.3, 125.6, 125.5, 73.5, 63.4, 38.2, 35.9, 31.5, 25.9, 25.0, 18.3, −4.3, −4.8; LRMS (FAB) *m/z* 433 $(M+Na)^+$; HRMS (FAB) Calcd for $C_{26}H_{38}O_2SiNa$ $(M+Na)^+$ *m/z* 433.2539, found 433.2543.

*3.2.13. (E)-5-tert-Butyldimethylsilyloxy-7-[(2-hydroxymethyl)-phenyl]-1-phenylhept-1-ene (**4g**).* Colorless oil; *Rf*=0.47 (20% EtOAc in hexane); IR (neat, cm^{-1}) 3399; ^1H NMR (400 MHz, $CDCl_3$) δ 7.39–7.18 (9H, m), 6.40 (1H, d, *J*=15.8 Hz), 6.22 (1H, dt, *J*=15.8, 6.9 Hz), 4.73 (2H, s), 3.84 (1H, tt, *J*=5.7, 5.5 Hz), 2.80 (1H, ddd, *J*=13.7, 10.9, 6.0 Hz), 2.67 (1H, ddd, *J*=13.7, 10.8, 5.9 Hz), 2.28 (1H, dt, *J*=6.9, 6.8 Hz), 2.26 (1H, dt, *J*=6.9, 6.7 Hz), 1.86–1.67 (4H, m), 1.27 (1H, s), 0.94 (9H, s), 0.11 (3H, s), 0.10 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) 140.8, 138.2, 137.7, 130.6, 129.9, 129.3, 128.5, 128.3, 128.0, 126.9, 126.2, 125.9, 71.7, 63.1, 38.6, 36.6, 28.9, 28.0, 25.9, 18.1, −4.3, −4.4; LRMS (FAB) *m/z* 433 $(M+Na)^+$; HRMS (FAB) Calcd for $C_{26}H_{38}O_2SiNa$ $(M+Na)^+$ *m/z* 433.2539, found 433.2545.

*3.2.14. (R,E)-[1-(2-Methoxymethyl)phenyl]-5-phenylpent-1-en-3-ol (**3h**).* Colorless oil; *Rf*=0.15 (20% EtOAc in hexane); $[\alpha]_D^{25}$ −20.2 (*c* 0.30, $CHCl_3$); IR (neat, cm^{-1}): 3397; ^1H NMR (400 MHz, $CDCl_3$) δ 7.38 (1H, dd, *J*=7.3, 1.6 Hz), 7.23–7.07 (8H, m), 6.76 (1H, d, *J*=15.7 Hz), 6.07 (1H, dd, *J*=15.7, 6.8 Hz), 4.40 (2H, s), 4.23 (1H, m), 3.28 (3H, s), 2.73–2.61 (2H, m), 1.94–1.79 (3H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 141.8, 136.1, 134.9, 134.5, 129.3, 128.5, 128.4, 128.2, 127.5, 127.4, 126.1, 125.9, 72.8, 72.4, 58.0, 38.7, 31.7; LRMS (EI): *m/z* (rel. int. %) 282 (M^+, 2), 250 (35), 159 (10), 145 (base); HRMS (EI): Calcd for $C_{19}H_{22}O_2$ *m/z* 282.1620, found 282.1614; >99% ee, [HPLC conditions: column Daicel OJ-H, 3% eluent 2-propanol in hexane, flow rate 1.0 mL/min, wavelength 254 nm, $t_r(R)$=47 min, $t_r(S)$=50 min].

*3.2.15. [1-(2-Methoxymethyl)phenyl]-5-phenylpentan-3-one (**12**).* Colorless oil; *Rf*=0.27 (10% EtOAc in hexane); IR (neat, cm^{-1}): 1713; ^1H NMR (400 MHz, $CDCl_3$) δ 7.32–7.13 (9H, m), 4.44 (2H, s), 3.38 (3H, s), 2.94–2.89 (4H, m), 2.74–2.69 (4H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 209.3, 141.0, 140.0, 135.7, 129.5, 129.3, 128.5, 128.3, 128.3, 126.2, 126.1, 72.9, 58.2, 44.4, 44.3, 29.8, 26.3; LRMS (EI): *m/z* (rel. int. %) 282 (M^+, 1), 250 (49), 145 (39), 134 (base); HRMS (EI): Calcd for $C_{19}H_{22}O_2$ *m/z* 282.1620, found 282.1627.

*3.2.16. (E)-3-tert-Butyldimethylsilyloxy-1-[(2-methoxymethyl)-phenyl]pent-1-ene (**3i**).* Colorless oil; *Rf*=0.39 (5% EtOAc in hexane); ^1H NMR (400 MHz, $CDCl_3$) δ 7.48 (1H, dd, *J*=7.5, 1.6 Hz), 7.34 (1H, dd, *J*=7.3, 1.4 Hz), 7.30–7.21 (2H, m), 6.79 (1H, dd, *J*=15.7, 1.3 Hz), 6.09 (1H, dd, *J*=15.7, 6.2 Hz), 4.52 (1H, d, *J*=12.9 Hz), 4.49 (1H, d, *J*=12.9 Hz), 4.24 (1H, qd, *J*=6.2, 1.3 Hz), 3.40 (3H, s), 1.66–1.58 (2H, m), 0.94 (9H, s), 0.94 (3H, t, *J*=7.4 Hz), 0.11 (3H, s), 0.09 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 136.7, 135.6, 134.9, 129.0, 128.3, 128.0, 127.1, 126.1, 126.0, 74.8, 72.8, 58.1, 31.2, 25.9, 18.3, 9.6, −4.3, −4.8; LRMS (EI): *m/z* (rel. int. %) 320 (M^+, 0.5), 291 (23), 263 (20), 147 (base); HRMS (EI): Calcd for $C_{19}H_{32}O_2Si$ *m/z* 320.2172, found 320.2176.

*3.2.17. A mixture of alkenes; (E)-[1-(2-methoxymethyl)phenyl]-5-phenylpent-1-ene (**13j**), [1-(2-methoxymethyl)phenyl]-5-phenylpent-2-ene, and 3-ene (**13**Δ2+Δ3) (ratio **13j**:**13** Δ2+Δ3=1:0.5).* Colorless oil; *Rf*=0.36 (5% EtOAc in hexane); ^1H NMR (400 MHz, $CDCl_3$) δ 7.51 (0.67H, dd, *J*=7.7, 1.3 Hz, **3j**), 7.38–7.18 (8H, m, **13j**+**13**Δ**2**+Δ**3**), 7.16 (0.33H, dd, *J*=7.5, 1.9 Hz, **13**Δ**2**+Δ**3**), 6.70 (0.67H, d, *J*=15.7 Hz, **13j**), 6.19 (0.67H, dt, *J*=15.7, 6.9 Hz, **3j**), 5.65–5.47 (0.66H, m, **13**Δ**2**+Δ**3**), 4.54 (1.34H, s, **13j**), 4.49 (0.66H, s, **13**Δ**2**+Δ**3**), 3.44 (2.01H, s, **13j**), 3.42 (0.99H, s, **13**Δ**2**+Δ**3**), 3.42 (0.66H, d, *J*=9.7 Hz, **13**Δ**2**+Δ**3**), 2.83–2.70 (2H, m, **13j**+**13**Δ**2**+Δ**3**), 2.41–2.30 (2H, m, **13j**+**13**Δ**2**+Δ**3**), 1.90–1.83 (1.34H, m, **13j**); ^{13}C NMR (100 MHz, $CDCl_3$) δ 142.3 (**13j**), 141.9 (**13**Δ**2**+Δ**3**), 139.1 (**13**Δ**2**+Δ**3**), 137.2 (**13j**), 135.8 (**13**Δ**2**+Δ**3**), 134.4 (**13j**), 132.8 (**13j**), 130.9 (**13**Δ**2**+Δ**3**), 129.5 (**13**Δ**2**+Δ**3**), 129.1 (**13**Δ**2**+Δ**3**), 129.1 (**13j**), 128.8 (**13**Δ**2**+Δ**3**), 128.5 (**13j**), 128.5 (**13**Δ**2**+Δ**3**), 128.3 (**13j**), 128.2 (**13**Δ**2**+Δ**3**), 128.0 (**13j**), 128.0 (**13**Δ**2**+Δ**3**), 127.2 (**13j**), 126.8 (**13j**), 126.1 (**13**Δ**2**+Δ**3**), 125.9 (**13**Δ**2**+Δ**3**), 125.9 (**13j**), 125.7 (**13j**), 72.8 (**13j**), 72.6 (**3′j**), 58.2 (**13**Δ**2**+Δ**3**), 58.1 (**13j**), 35.9 (**13**Δ**2**+Δ**3**), 35.4 (**13**Δ**2**+Δ**3**), 35.3 (**13j**), 34.3 (**13**Δ**2**+Δ**3**), 32.8 (**13j**), 31.0 (**13j**).

*3.2.18. (E)-[5-(2-Methoxymethyl)phenyl]-1-phenylpent-1-ene (**4j**).* Colorless oil; *Rf*=0.36 (5% EtOAc in hexane); ^1H NMR (400 MHz, $CDCl_3$) δ 7.37–7.18 (9H, m), 6.43 (1H, dd, *J*=15.7, 1.4 Hz), 6.26 (1H, dt, *J*=15.7, 6.8 Hz), 4.48 (2H, s), 3.39 (3H, s), 2.74–2.70 (2H, m), 2.30 (2H, dtd, *J*=7.5, 6.8, 1.4 Hz), 1.83–1.76 (2H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 141.0, 137.8, 135.6, 130.5, 130.2, 129.3, 129.1, 128.5, 127.9, 126.9, 125.9, 125.9, 72.7, 58.2, 32.9, 31.8, 30.7; LRMS (EI): *m/z* (rel. int. %) 266 (M^+, 9), 234 (27), 143 (37), 130 (base); HRMS (EI): Calcd for $C_{19}H_{22}O$ *m/z* 266.1671, found 266.1668.

3.3. Structure determination of the Heck product (−)-4a

*3.3.1. Conversion of (−)-**4a** to (−)-**6**.* Compound (−)-**4a** (28 mg, 0.071 mmol) was dissolved in CH_2Cl_2 (0.7 mL, 0.1 M) and the solution was cooled to −78 °C. O_3 was bubbled through the solution until the starting material was consumed, which was monitored on TLC. Excess of O_3 was then removed by bubbling nitrogen through the solution until the blue color had dissipated. MeOH (0.7 mL) and sodium borohydride (26.7 mg, 0.705 mmol, 10 equiv) was then added slowly and the mixture was stirred at room temperature. After stirring for 0.5 h, water was added to the reaction mixture. The mixture was extracted with CH_2Cl_2 three times. The combined organic layer was dried over $MgSO_4$, filtered and concentrated. The crude product was chromatographed on silica gel to give (−)-**6** (14 mg) in 61% yield. *(S)-2-tert-Butyldimethylsilyloxy-4-[(2-methoxymethyl)phenyl]butan-1-ol (−)-**6**.* Colorless oil; *Rf*=0.30 (20% EtOAc in hexane); $[\alpha]_D^{25}$ −8.1 (*c* 0.30, EtOH); IR (neat, cm^{-1}) 3444; ^1H NMR (400 MHz, $CDCl_3$) δ 7.31 (1H, dd, *J*=7.1, 2.0 Hz), 7.25 (1H, m), 7.20–7.16 (2H, m), 4.50 (1H, d, *J*=11.4 Hz), 4.45 (1H, d, *J*=11.4 Hz), 3.85 (1H, m), 3.63 (1H, ddd, *J*=11.2, 6.4, 4.2 Hz), 3.55 (1H, ddd, *J*=11.2, 6.4, 5.1 Hz), 3.39 (3H, s), 2.73 (1H, ddd, *J*=13.7, 10.0, 7.1 Hz), 2.62 (1H, ddd, *J*=13.7, 10.1, 6.8 Hz), 1.99 (1H, t, *J*=6.4 Hz), 1.83–1.77 (2H, m), 0.93 (9H, s), 0.11 (3H, s), 0.10 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 140.9, 135.4, 129.4, 129.2, 128.2, 126.0, 72.8, 72.6, 66.1, 58.1, 35.4, 28.2, 25.8, 18.1, −4.5, −4.6; LRMS (EI): *m/z* (rel. int. %) 324 (M^+, 0.2), 307 (1), 293 (6), 235 (base); HRMS (EI): Calcd for $C_{18}H_{32}O_3Si$ *m/z* 324.2121, found 324.2128.

*3.3.2. Conversion of (+)-**5** to (−)-**6**.* The same reaction described above for (+)-**5** gave compound (−)-**6** in 70% yield.

Acknowledgements

The authors acknowledge financial support by the Minister of Education Science and Culture Japan.

Supplementary data

Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.tet.2015.03.018.

References and notes

1. (a) Heck, R. F. In *Comprehensive Organic Synthesis*; Trost, B. M., Ed.; Pergamon Press: New York, NY, 1991; Vol. 4, pp 833–863; (b) Heck, R. F. *Org. React.* **1982**, *27*, 345–390; (c) de Meijere, A.; Meyer, F. E. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 2379–2411; (d) Larhed, M.; Hallberg, A. In *Handbook of Organopalladium Chemistry for Organic Synthesis*; Negishi, E.-i., de Meijere, A., Eds.; Wiley: New

York, NY, 2002; pp 1133–1178; (e) Bräse, S.; de Meijere, A. In *Cross-coupling of Organyl Halides with Alkenes: the Heck Reaction in Metal-catalyzed Cross-coupling Reactions*; de Meijere, A., Diederich, F., Eds.; Wiley-VCH: New York, NY, 2004; pp 217–315; (f) Special issue for Heck Reaction *Synlett* **2006**, 2855–3184; (g) *Mizoroki-Heck Reaction*; Oestreich, M., Ed.; John-Wiley & Sons: Chichester, UK, 2009; (h) *Science of Synthesis, Cross Coupling and Heck-type Reactions*; Larhed, M., Ed.; Thieme: Stuttgart, Germany, 2013; Vol. 3.

2. Review for mechanism Beletskaya, I. P.; Cheprakov, A. V. *Chem. Rev.* **2000**, *100*, 3009–3066.
3. For example; acryl ester for electron deficient alkene or vinyl ether for electron rich alkene.
4. (a) Berthiol, F.; Doucet, H.; Santelli, M. *Tetrahedron Lett.* **2003**, *44*, 1221–1225; (b) Jeffery, T. *Tetrahedron Lett.* **2000**, *41*, 8445–8449.
5. Effort to control regiosiomer of styrenyl alkene. (a) Qin, L.; Ren, X.; Lu, Y.; Li, Y.; Zhou, J. *Angew. Chem., Int. Ed.* **2012**, *51*, 5915–5919; (b) Werner, E. W.; Sigman, M. S. *J. Am. Chem. Soc.* **2011**, *133*, 9692–9695; (c) Delcamp, J. H.; Brucks, A. P.; White, M. C. *J. Am. Chem. Soc.* **2008**, *130*, 11270–11271; (d) Zhu, S.-F.; Song, X.-G.; Li, Y.; Cai, Y.; Zhou, Q.-L. *J. Am. Chem. Soc.* **2010**, *132*, 16374–16376.
6. New type of stereo and regiocontrolled Heck reaction of alkenol substrates was reported. (a) Werner, E. W.; Mei, T.-S.; Burckle, A. J.; Sigman, M. S. *Science* **2012**, *338*, 1455–1458 The mechanistic study and computational investigations; (b) Xu, L.; Hilton, M. J.; Zhang, X.; Norrby, P.-O.; Wu, Y.-D.; Sigman, M. S.; Wiest, O. *J. Am. Chem. Soc.* **2014**, *136*, 1960–1967; (c) Dang, Y.; Qu, S.; Wang, Z.-X.; Wang, X. *J. Am. Chem. Soc.* **2014**, *136*, 986–998.
7. See their HPLC charts in Supplementary data.
8. Migration process is similar to the hydrozirconation in which chain walking of alkyl zirconium intermediate ends up to the terminal alkyl Cp_2zirconium halide. (a) Hart, D. W.; Schwarz, J. *J. Am. Chem. Soc.* **1974**, *96*, 8115–8116; (b) Gibson, T.; Tulich, L. *J. Org. Chem.* **1981**, *46*, 1921–1923; (c) Chirik, P. J.; Day, M. W.; Labinger, J. A.; Bercaw, J. E. *J. Am. Chem. Soc.* **1999**, *121*, 10308–10317; (d) Bushby, R. J. *Quat. Rev.* **1970**, *24*, 585–600.
9. Examples alkene migration of alkenol substrates in Heck reactions (1,2-alkene to n,n+1-alkene). 1,2 to 2,3-migration: (a) Jeffery, T. *Tetrahedron Lett.* **1991**, *32*, 2121–2124 1,2 to 3,4- and 4,5-migration;; (b) Berthiol, F.; Doucet, H.; Santelli, M. *Synthesis* **2005**, 3589–3602; (c) Crawley, M. L.; Phipps, K. M.; Goljer, I.; Mehlmann, J. F.; Lundquist, J. T.; Ullrich, J. W.; Yang, C.; Mahaney, P. E. *Org. Lett.* **2009**, *11*, 1183–1185 1,2 to 4,5-migration;; (d) Larock, R. C.; Leung, W.-Y.; Stolz-Dunn, S. *Tetrahedron Lett.* **1989**, *30*, 6629–6632 1,2 to 7,8-migration;; (e) Mei, T.-S.; Werner, E. W.; Burckle, A. J.; Sigman, M. S. *J. Am. Chem. Soc.* **2013**, *135*, 6830–6833.
10. The use of ester group instead of phenyl group did not provide any zipper product.
11. Related experiments for the chain walking process in Heck reaction of alkenol using deuterium substrates have appeared recently Hilton, M. J.; Xu, L.-P.; Norrby, P.-O.; Wu, Y.-D.; Wiest, O.; Sigman, M. S. *J. Org. Chem.* **2014**, *79*, 11841–11850.
12. Many possibilities may exist. We are not able to account this result fully. However, *anti*-β-hydride elimination was observed at particular benzylic position in some cases. See: Wu, X.; Zhou, J. *Chem. Commun.* **2013**, 4794–4796.