

●Supporting Information●

Palladium(II)-Catalyzed Cycloisomerization of Functionalized 1,5-Hexadienes

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GENERAL EXPERIMENTAL METHODS

Methods and Materials: Unless otherwise stated, commercially available reagents were used as purchased. Solvents were dried by passage through activated alumina columns of a solvent purification system: tetrahydrofuran (THF), dichloromethane (CH_2Cl_2), 1,2-dichloroethane [$(\text{CH}_2\text{Cl})_2$], diethylether (Et_2O), acetonitrile (MeCN), *N,N*-Dimethylformamide (DMF), and toluene (PhMe). Diisopropylamine [$(i\text{-Pr})_2\text{NH}$] and triethylamine (Et_3N) were distilled from CaH_2 and stored over activated 3 Å molecular sieves. Methanol was distilled from magnesium and stored over activated 3 Å molecular sieves. Isopropanol was distilled from sodium and stored over activated 3 Å molecular sieves. CDCl_3 was stored under argon over activated 4 Å molecular sieves.

Allyl vinyl ether **S11e** was prepared according to a published procedure.¹

The concentration of *n*-BuLi was determined employing diphenylacetic acid as indicator.²

All moisture-sensitive reactions were performed in flame-dried septum-sealed glassware under an atmosphere of argon. Reagents were transferred by means of syringe or cannula.

Analytical TLC was performed using pre-coated silica gel foils (4 cm). Visualization was achieved using 254 nm ultraviolet irradiation followed by staining with the Kāgi-Miescher reagent³ (*p*-anisaldehyde 2.53 vol%, acetic acid 0.96 vol%, ethanol 93.06 vol%, conc. H_2SO_4 3.45 vol%) or the KMnO_4 reagent (3 g KMnO_4 , 20 g K_2CO_3 , 5 mL NaOH (5%), 300 mL H_2O).

Flash chromatography⁴ was performed using silica gel (particle size 0.040–0.063 mm) and mixtures of cyclohexane and ethyl acetate, heptane and ethyl acetate or *n*-pentane and diethyl ether were used as eluents.

^1H NMR spectra were recorded at 300 MHz, 400 MHz, 500 MHz, or 600 MHz. Chemical shifts are reported in ppm relative to chloroform (δ 7.26 ppm).⁵ Signal splitting patterns are labeled by the following abbreviations: s = singlet, d = doublet, t = triplet, q = quartet, spt = septet, m = multiplet or overlap of non equivalent resonances. ^{13}C NMR spectra were recorded at 76 MHz, 101 MHz or 126 MHz. Chemical shifts are reported in ppm relative to CDCl_3 (77.16 ppm) or $\text{DMSO}-d_6$ (39.51 ppm).⁵ The assignment of CH_2 is based on APT (attached proton test) or DEPT (distortionless enhancement by polarization transfer) experiments. The terms “major” and “minor” are used to distinguish between NMR resonances of diastereomers. Where appropriate, the peak assignments were confirmed by 2D NMR experiments: ^1H , ^1H -COSY, ^1H , ^1H -NOESY, ^1H , ^{13}C -HSQC, and ^1H , ^{13}C -HMBC.

For NMR kinetic experiments, ^1H NMR measurements were performed with a 500 MHz NMR spectrometer UnityINOVA-500 (Varian) equipped with a 5 mm triple resonance probe H(C,X). All measurements used the same conditions (spectral width 5500 Hz, acquisition time 5.96 s, 64 kB data, 90° pulse width 10.3 μs). The kinetic measurements were setup as array experiments. In this case the preacquisition time was arrayed from 0 to 69 hours. Each spectrum was measured with a single scan. The processing was executed by using zero filling (256 kB).

¹ Körner, M.; Hiersemann, M. *Synlett* **2006**, 121–123.

² Juaristi, E.; Martinez-Richa, A.; Garcia-Rivera, A.; Cruz-Sanchez, J. S. *J. Org. Chem.* **1983**, 48, 2603–2606.

³ a) Miescher, K. *Helv. Chim. Acta* **1946**, 29, 743–752. b) Stahl, E., Kaltenbach. U. *J. Chromatog.* **1961**, 5, 351–355.

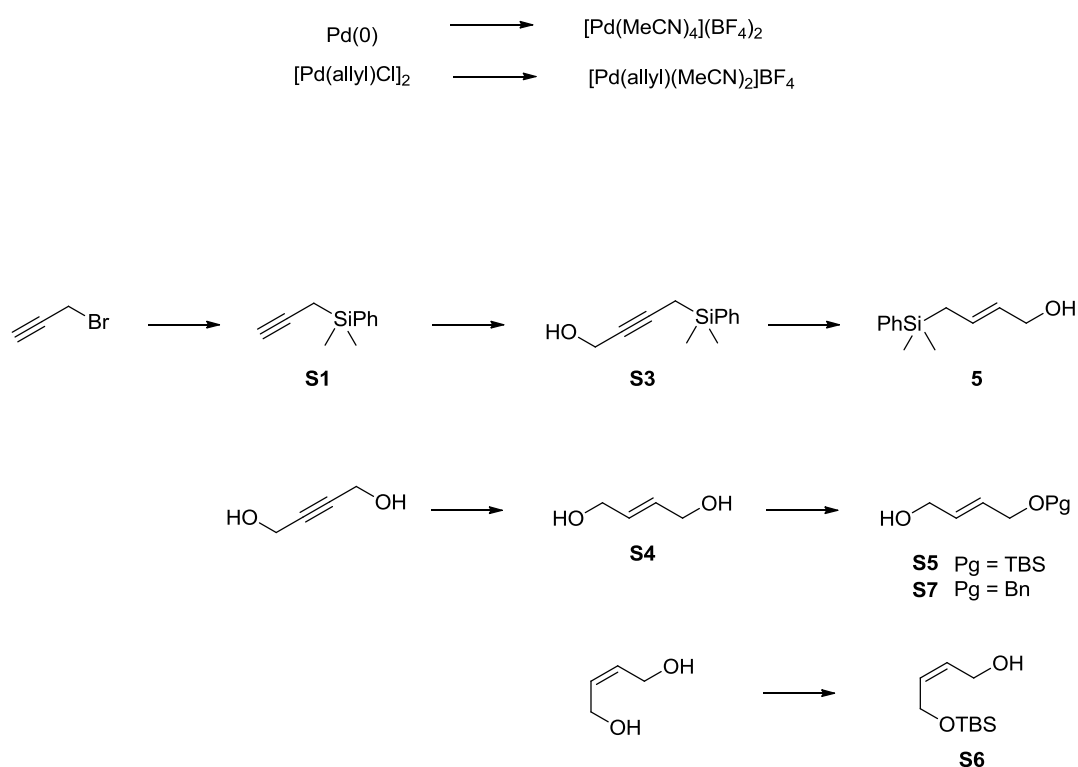
⁴ Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, 43, 2923–2925.

⁵ a) Fulmer, G. R.; Miller, A. J. M.; Sherden, N. H.; Gottlieb, H. E.; Nudelman, A.; Stoltz, B. M.; Bercaw, J. E.; Goldberg, K. I. *Organometallics* **2010**, 29, 2176–2179. b) Gottlieb, H. E.; Kotlyar, V.; Nudelman, A. *J. Org. Chem.* **1997**, 62, 7512–7515.

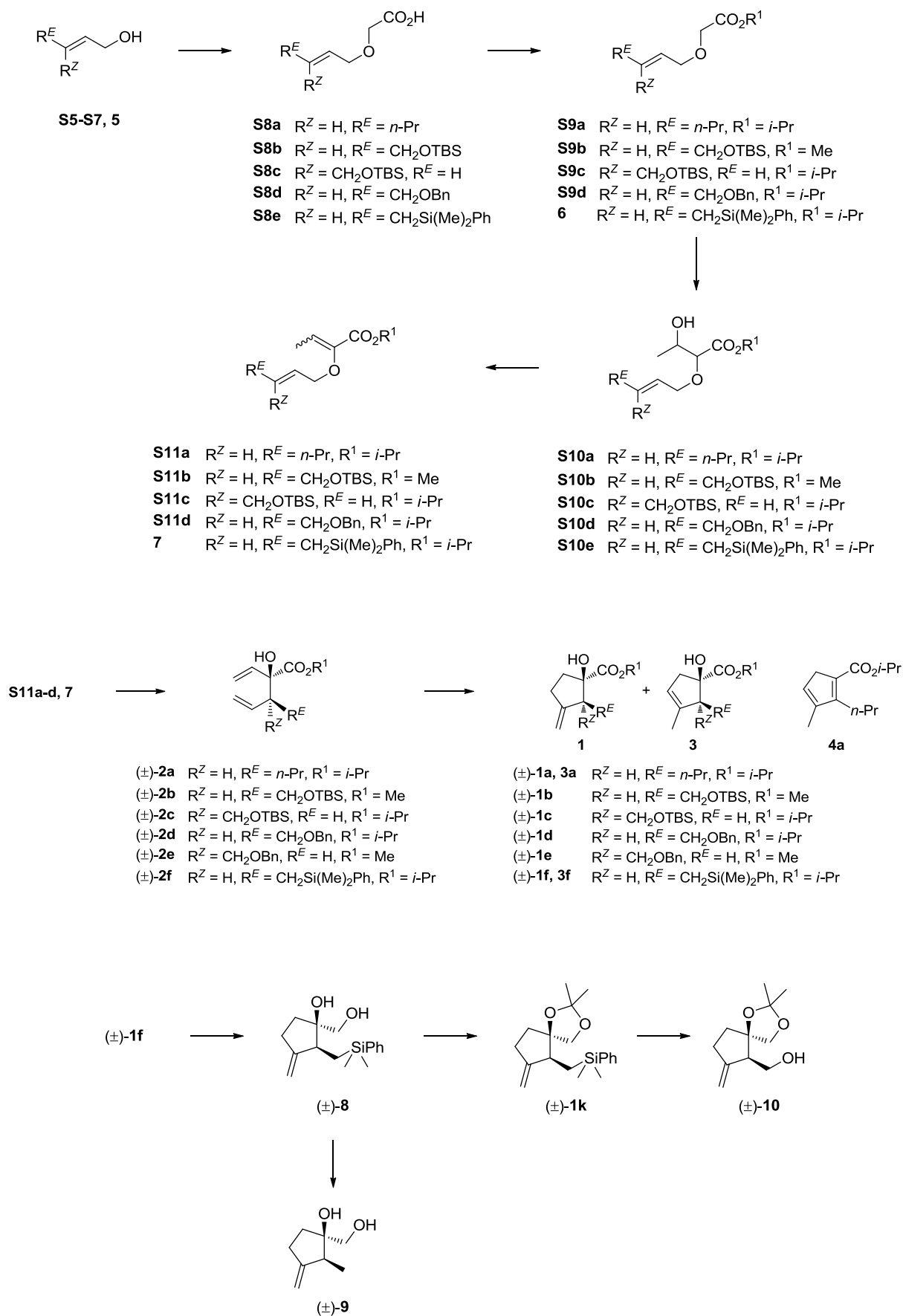
Infrared spectra were recorded as a thin film on a KBr disk (“film on KBr”). Absorption bands are reported in reciprocal wave length (cm^{-1}). The intensity of the absorption bands is labeled by the following abbreviations: s = strong, m = middle, w = weak, br = broad; the vibration modes are labeled as follows: ν = valence vibration, δ = deformation vibration. The assignment of functional groups is based on tabulated values.⁶

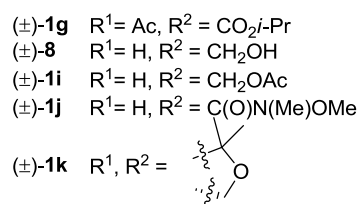
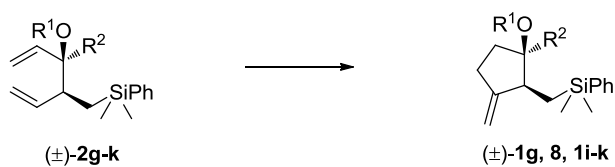
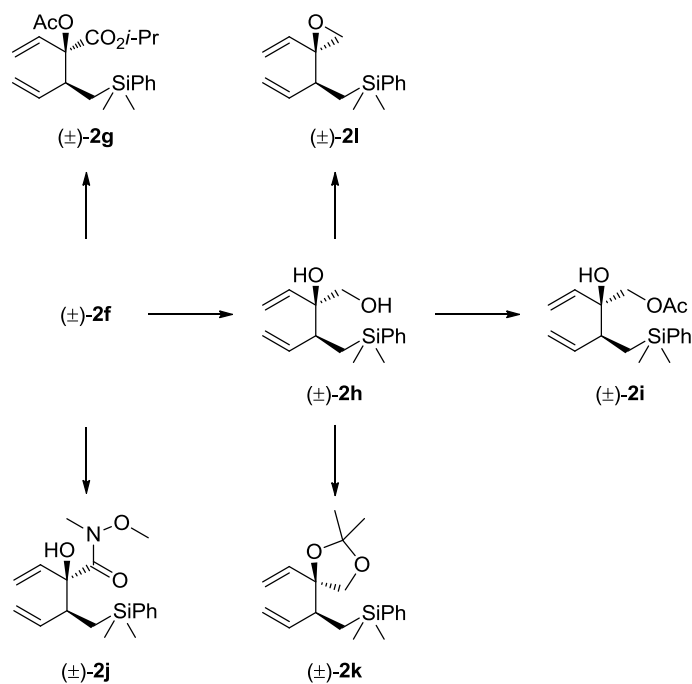
Molecular formula assignment was confirmed by combustion elemental analysis. High resolution mass spectra were recorded on a LTQ Orbitrap spectrometer by electrospray ionization (ESI).

CHART OF ALL SYNTHESIZED COMPOUNDS (SI1-10)

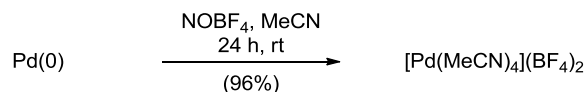


⁶ Hesse, M.; Meier, H.; Zeeh, B. *Spektroskopische Methoden in der organischen Chemie*, Georg Thieme Verlag **1995**, 6, 43–65.



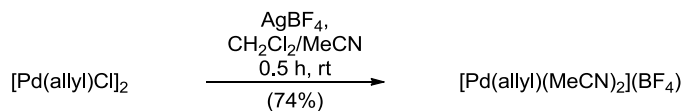


EXPERIMENTAL PROCEDURES AND ANALYTICAL DATA



[Pd(MeCN)₄](BF₄)₂⁷: Pd(0)-Sponge (0.16 g, 1.5 mmol, 1 eq) and NOBF₄ (0.35 g, 3 mmol, 2 eq) were successively added to MeCN (7.5 ml, 5ml/mmol Pd) (degassed by three cycles of “freeze-pump-thaw”) in a Schlenk-tube. The resulting mixture was stirred at room temperature under a slow flow of argon (24 h – 7 d, scale dependent) and exclusion of light. The yellow solution was filtered carefully into a Schlenk-tube containing anhydrous Et₂O (100 ml), where a yellow precipitate formed. The mixture was allowed to settle and the solvent was removed with a syringe. The yellow precipitate was washed with anhydrous Et₂O (20 ml) and subsequently dried under vacuum (5×10⁻² mbar) to afford [Pd(MeCN)₄](BF₄)₂ (0.64 g, 1.45 mmol, 96%) as a bright yellow powder. ¹H NMR (CD₃NO₂, 400 MHz, δ): 2.65 (s, 9H, 4×CH₃); IR (nujol) (cm⁻¹): 2355(w) (ν C≡N), 1060-1035(m) (BF₄⁻), 765(w) (BF₄⁻); Anal. Calcd. for C₈H₁₂B₂F₈N₄Pd: C, 21.6; H, 2.7; N, 12.6; Found: C, 21.4; H, 2.7; N, 13.0; C₈H₁₂B₂F₈N₄Pd, M = 444.24 g/mol.

The catalyst was stored in a Schlenk-tube under exclusion of light and used as long as it maintained a yellow to light-orange color. In our hands, commercial and self-synthesized batches of [Pd(MeCN)₄](BF₄)₂ exerted a discrete phenotype and reactivity: the latter one generally showed a higher activity in cycloisomerization reactions which was reflected in shorter reaction times. The commercial batches⁸ of [Pd(MeCN)₄](BF₄)₂ appeared as off-white powder which ultimately changed its color to brown upon storage in a Schlenk-tube under exclusion of light over several months.

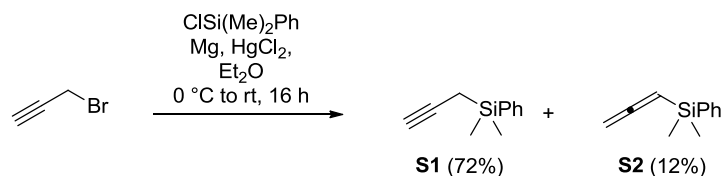


[Pd(allyl)(MeCN)₂](BF₄)⁹: [Pd(allyl)Cl]₂ (0.1 g, 0.27 mmol, 1 eq) and AgBF₄ (0.11 g, 0.56 mmol, 2.05 eq) were successively added to a solution of MeCN/CH₂Cl₂ (2.8 ml, 1/1, 5 ml/mmol Pd) in a Schlenk-tube. The resulting mixture was stirred for 0.5 h at room temperature, until a white precipitate formed. The precipitate was filtered off and the clear solution was added dropwise into a Schlenk-flask containing anhydrous Et₂O (50 ml). Upon addition, an off-white precipitate formed which was washed with Et₂O (10 ml) and ultimately dried under vacuum (5×10⁻² mbar) to afford [Pd(allyl)(MeCN)₂](BF₄) (0.13 g, 0.40 mmol, 74%) as an off-white powder. ¹H NMR (CDCl₃, 400 MHz, δ): 2.39 (s, 6 H), 3.18 (d, ³J = 12.5 Hz, 2H), 4.34 (d, ³J = 6.9 Hz, 2H), 5.63 (tt, ³J = 12.5, 6.9 Hz, 1H); IR (cm⁻¹): 2360(w) (ν C≡N), 2325(w), 1620(m) (ν C=C), 1385(s) (δ CH₃), 1055(s) (BF₄⁻), 795(w) (BF₄⁻); Anal. Calcd. for C₇H₁₁BF₄N₂Pd: C, 26.6; H, 3.5; N, 8.9; Found: C, 26.5; H, 3.8; N, 8.7; C₇H₁₁BF₄N₂Pd, M = 316.40 g/mol.

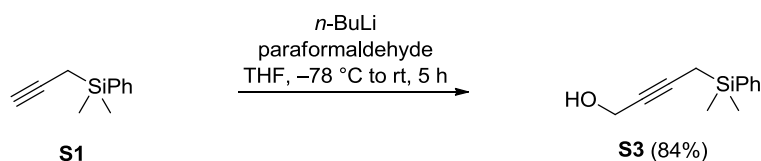
⁷ a) Schramm, R. F.; Wayland, B. B. *Chem. Commun.* **1968**, 898–899. b) Lai, T. W.; Sen, A. *Organometallics* **1984**, *3*, 866–870.

⁸ purchased from ACROS Organics: 1 g, 99%.

⁹ Sen, A.; Lai, T. W. *Organometallics* **1983**, *2*, 1059–1060.



Propynyl silane S1¹⁰: To an oven dried, three-necked-flask (equipped with a reflux condenser, a dropping funnel and a stopper, which is ultimately switched with a thermometer) under an atmosphere of argon was added Mg powder (5.1 g, 210 mmol, 2.1 eq) and HgCl₂ (0.9 g, 3.3 mmol, 0.03 eq). The flask was heated with a heatgun, sealed with a septum and allowed to cool down to room temperature under an atmosphere of argon before Et₂O (50 mL, 0.25 mL/mmol Mg) was added carefully. The flask was cooled to 0 °C and propargylbromide (21.6 mL, 200 mmol, 2 eq, 80% in toluene) in Et₂O (50 mL, 0.25 mL/mmol bromide) was added dropwise over a period of 1.5 h. After addition of the first few drops the solution became cloudy and started to boil. The rate of the addition was adjusted to maintain the internal temperature between 0 °C and 20 °C. The dark solution was stirred further for 45 min at 0 °C before chlorodimethyl(phenyl)silane (16.5 mL, 100 mmol, 1 eq) in Et₂O (50 mL, 0.5 mL/mmol silane) was added dropwise over a period of 2 h. The resulting reaction mixture was allowed to warm to room temperature overnight (16 h) and was then diluted by the careful addition of saturated aqueous NH₄Cl solution and *n*-pentane (150 mL). The aqueous layer was extracted with *n*-pentane (3×) and the combined organic phases were dried (MgSO₄) and concentrated under reduced pressure (≥ 5 mbar). Purification by repeated flash chromatography (*n*-pentane/Et₂O 500/1 → 100/1) afforded propynyl silane **S1** (12.6 g, 72 mmol, 72% combined) as a clear oil along with allene **S2**¹¹ (12%, determined by ¹H NMR spectroscopy of a mixed fraction of **S1** and **S2**, which was further purified by flash chromatography). *R_f* 0.54 (cyclohexane/ethyl acetate 20/1); ¹H NMR (CDCl₃, 400 MHz, δ): 0.41 (s, 6H), 1.72 (d, ⁴*J* = 3.0 Hz, 2H), 1.86 (t, ⁴*J* = 3.0 Hz, 1H), 7.35–7.42 (m, 3H), 7.54–7.59 (m, 2H); ¹³C NMR (CDCl₃, 101 MHz, δ): –3.4 (2×CH₃), 6.4 (CH₂), 67.6 (CH), 82.2 (C), 128.0 (2×CH_{ar}), 129.6 (CH_{ar}), 133.7 (2×CH_{ar}), 137.5 (C_{ar}); IR (cm^{–1}): 3310(m) (ν C–H, alkyne), 3070(w) (ν C–H, aromatic), 3050(m), 3025(w), 2960(m), 2895(w), 2120(m) (ν C≡C), 1620(m) (ν C=C), 1430(m), 1385(s), 1250(s), 1146(m), 1115(s); C₁₁H₁₄Si, *M* = 174.31 g/mol.

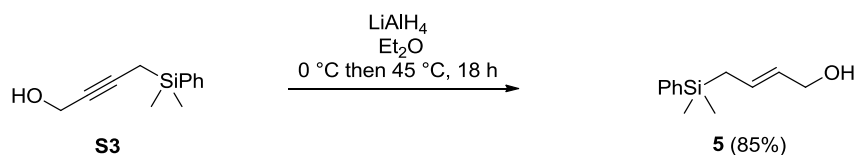


Propargylic alcohol S3^{10b}: *n*-BuLi (24.2 mL, 59.2 mmol, 2.45 M solution in hexanes) was added dropwise to a solution of propynyl silane **S1** (10.3 g, 59.2 mmol, 1 eq) in THF (300 mL, 5 mL /mmol **S1**) at –78 °C over a period of 20 min. The resulting pale yellow solution was stirred for 1 h at 0 °C before powdered paraformaldehyde (3.6 g, 118.4 mmol, 2 eq) was added in a single portion at 0 °C.

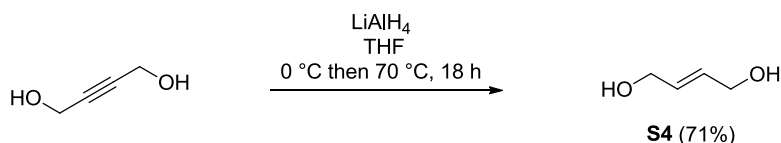
¹⁰ a) Kira, M.; Taki, T.; Sakurai, H. *J. Org. Chem.* **1989**, *54*, 5647–5648. b) Le Menez, P.; Fargeas, V.; Berque, I.; Poisson, J.; Ardisson, J.; Lallemand, J.-Y.; Pancrazi, A. *J. Org. Chem.* **1995**, *60*, 3592–3599.

¹¹ analytical data for **S2**^{10a}: *R_f* 0.68 (cyclohexane/ethyl acetate 20/1); ¹H NMR (CDCl₃, 400 MHz, δ): 0.39 (s, 6H), 4.39 (d, ⁴*J* = 7.1 Hz, 2H), 5.06 (t, ⁴*J* = 7.1 Hz), 7.35–7.40 (m, 2H), 7.52–7.60 (m, 2H); ¹³C NMR (CDCl₃, 101 MHz, δ): –2.3 (2×CH₃), 67.6, 79.5, 127.9 (2×CH_{ar}), 129.3 (CH_{ar}), 133.8 (2×CH_{ar}), 138.5 (C_{ar}), 213.6 (=C=); IR (cm^{–1}): 3070(m), 3050(w), 3020(w), 3010(w), 3000(w), 2960(s), 2890(w), 1930(s) (ν C=C=C, allene), 1620(w), 1430(s), 1415(w), 1385(w), 1250(s), 1215(s), 1115(s); C₁₁H₁₄Si, *M* = 174.31 g/mol.

The reaction mixture was allowed to warm to room temperature over a period of 4 h and was then diluted by the addition of saturated aqueous NH_4Cl solution. The aqueous layer was extracted with Et_2O (3 \times) and the combined organic phases were dried (MgSO_4) and concentrated under reduced pressure. Purification by flash chromatography (cyclohexane/ethyl acetate 50/1 \rightarrow 10/1) afforded propargylic alcohol **S3** (10.1 g, 49.6 mmol, 84%) as a clear oil. R_f 0.43 (cyclohexane/ethyl acetate 2/1); ^1H NMR (CDCl_3 , 400 MHz, δ): 0.40 (s, 6H), 1.38 (br t, $^3J = 6.0$ Hz, 1H), 1.75 (t, $^5J = 2.5$ Hz, 2H), 4.23 (dt, $^3J = 6.0$ Hz, $^5J = 2.5$ Hz, 2H), 7.34–7.43 (m, 3H), 7.52–7.59 (m, 2H); ^{13}C NMR (CDCl_3 , 101 MHz, δ): –3.3 (2 $\times\text{CH}_3$), 6.7 (CH_2), 51.8 (CH_2), 77.9 (C), 84.2 (C), 128.0 (2 $\times\text{CH}_{\text{ar}}$), 129.6 (CH_{ar}), 133.7 (2 $\times\text{CH}_{\text{ar}}$), 137.5 (C_{ar}); IR (cm^{-1}): 3335 (br, m) (ν O–H), 3070 (w) (ν C–H, aromatic), 3050(w), 2960(m), 2880(w), 2220(m) (ν C \equiv C), 1425(s), 1385(m), 1250(s), 1115(s), 1010(s); $\text{C}_{12}\text{H}_{16}\text{OSi}$, $M = 204.34$ g/mol.



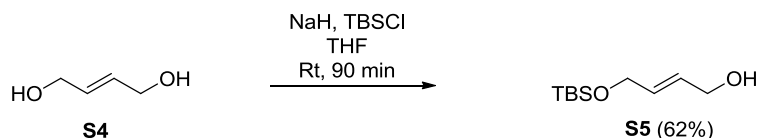
Allylic alcohol 5^{10b}: A solution of propargylic alcohol **S3** (10.1 g, 49.6 mmol, 1 eq) in Et_2O (50 mL, 1 mL/mmol **S3**) was added dropwise to a suspension of LiAlH_4 (2.8 g, 74.4 mmol, 1.5 eq) in Et_2O (200 mL, 4 mL/mmol **S3**) at 0 °C. After complete addition the resulting grey suspension was heated to 45 °C for a period of 18 h. The mixture was cooled to 0 °C and hydrolyzed by the careful addition of ethyl acetate (20 mL) and saturated aqueous Na/K tartrate solution (200 mL) until a light grey slurry has formed. The aqueous layer was extracted with ethyl acetate (3 \times) and the combined organic phases were dried (MgSO_4) and concentrated under reduced pressure. Purification by flash chromatography (cyclohexane/ethyl acetate 50/1 \rightarrow 5/1) afforded allylic alcohol **5** (8.7 g, 42.1 mmol, 85%) as a clear oil. R_f 0.43 (cyclohexane/ethyl acetate 2/1); ^1H NMR (CDCl_3 , 500 MHz, δ): 0.29 (s, 6H), 1.09 (br s, 1H), 1.74 (d, $^3J = 8.0$ Hz, 2H), 4.03 (d, $^3J = 6.2$ Hz, 2H), 5.46–5.55 (m, 1H), 5.63–5.71 (m, 1H), 7.32–7.40 (m, 3H), 7.47–7.53 (m, 2H); ^{13}C NMR (CDCl_3 , 101 MHz, δ): –3.3 (2 $\times\text{CH}_3$), 22.0 (CH_2), 64.2 (CH_2), 127.9 (2 $\times\text{CH}_{\text{ar}}$), 128.3 (CH), 129.2 (CH), 130.0 (CH_{ar}), 133.7 (2 $\times\text{CH}_{\text{ar}}$), 138.5 (C_{ar}); IR (cm^{-1}): 3350(br m) (ν O–H), 3070(w), 3050(w), 3020(w), 2955(m), 1660(w), 1425(s), 1405(m), 1250(s), 1155(m), 1115(s), 1080(m), 1000(s), 970(s), 835(s); $\text{C}_{12}\text{H}_{18}\text{OSi}$, $M = 206.36$ g/mol.



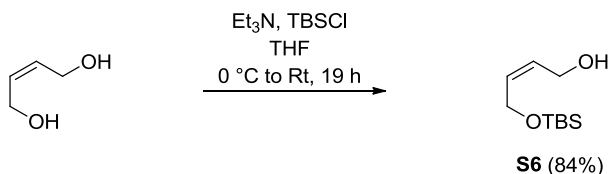
Diol S4¹²: A solution of but-2-yne-1,4-diol (10 g, 116 mmol, 1 eq) in THF (50 mL, 0.4 mL/mmol alcohol) was added dropwise to a suspension of LiAlH_4 (10.2 g, 255 mmol, 2.2 eq) in THF (150 mL, 1.3 mL/mmol alcohol) at 0 °C. After complete addition the resulting suspension was heated to 70 °C for a period of 18 h. The reaction mixture was cooled to 0 °C and celite[®] (2.5 g) and THF (50 mL) were added and the resulting mixture carefully hydrolyzed by the addition of saturated aqueous NH_4Cl solution (13 mL). The reaction mixture was filtered and washed with THF and the solids extracted by soxhlet extraction (THF, 70 °C, 2 d). The combined organic phases were dried (MgSO_4) and concentrated under reduced pressure. Kugelrohr distillation (3 mbar, 120 °C) afforded diol **S4** (7.3 g, 82

¹² Bauman, H.; Duthaler, R. O. *Helv. Chim. Acta* **1988**, *71*, 1025–1034.

mmol, 71%) as a clear oil. R_f 0.23 (ethyl acetate); ^1H NMR (CDCl_3 , 400 MHz, δ): 1.51 (br s, 2H), 4.17–4.20 (m, 4H), 4.85–4.95 (s, 2H); ^{13}C NMR ($\text{DMSO}-d_6$, 101 MHz, δ): 61.1 ($2\times\text{CH}_2$), 130.0 ($2\times\text{CH}$); IR (cm^{-1}): 3340(br s) (ν OH), 2875(s), 2870(s), 1385(m), 1085(s), 990(m) (δ CH=CH); $\text{C}_4\text{H}_8\text{O}_2$, $M = 88.15$ g/mol.



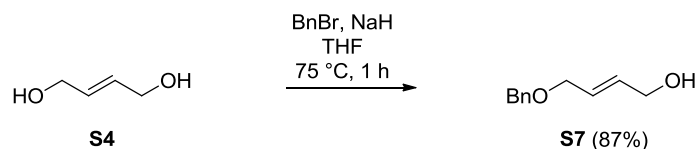
Silyl ether S5¹³: Allylic alcohol **S4** (2.3 g, 26.1 mmol, 1 eq) was added dropwise to a suspension of NaH (1 g, 26.1 mmol, 1 eq, 60% in mineral oil) [washed with *n*-hexane (3 \times)] in THF (52 mL, 2 mL/mmol **S4**) at room temperature and the resulting mixture was stirred for a period of 45 min. During this time a white precipitate formed. TBSCl (3.9 g, 26.1 mmol, 1 eq) was added and the reaction mixture was stirred further for 45 min at room temperature. Subsequently water was added and the aqueous layer was extracted with CH_2Cl_2 (3 \times). The combined organic phases were dried (MgSO_4) and concentrated under reduced pressure. Purification by flash chromatography (cyclohexane/ethyl acetate 10/1 \rightarrow 2/1) afforded silyl ether **S5** (3.3 g, 16.1 mmol, 62%) as a clear oil. R_f 0.40 (cyclohexane/ethyl acetate 5/1); ^1H NMR (CDCl_3 , 400 MHz, δ): 0.07 (s, 6H), 0.90 (s, 9H), 1.59 (br s, 1H), 4.11–4.16 (m, 2H), 4.16–4.20 (m, 2H), 5.74–5.82 (m, 1H), 5.83–5.91 (m, 1H); ^{13}C NMR (CDCl_3 , 101 MHz, δ): –5.1 ($2\times\text{CH}_3$), 18.6 (C), 26.1 ($3\times\text{CH}_3$), 63.2 (CH_2), 63.3 (CH_2), 129.1 (CH), 131.0 (CH); IR (cm^{-1}): 3350(br m) (ν OH), 2930(s), 2860(s), 1260(s), 1100(s), 840(s); $\text{C}_{10}\text{H}_{22}\text{O}_2\text{Si}$, $M = 202.37$ g/mol.



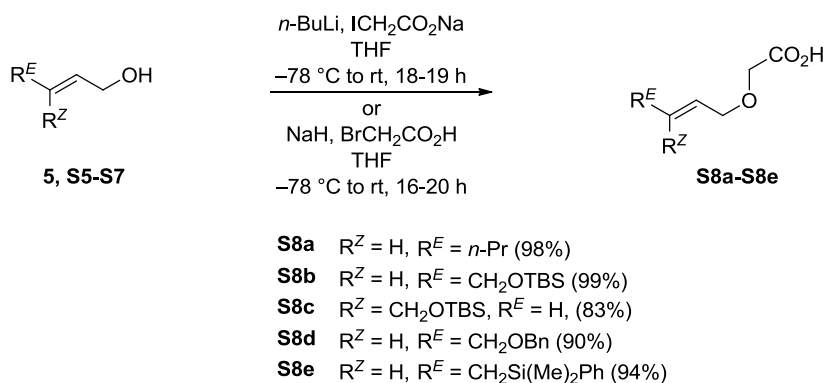
Silyl ether S6¹⁴: An ice-cooled solution of (*Z*)-but-2-ene-1,4-diol (10 mL, 121.7 mmol, 3 eq) in THF (10 mL, 0.09 mL/mmol alcohol) was treated successively with Et_3N (6.8 mL, 48.7 mmol, 1.2 eq) and a solution of TBSCl (6.1 g, 40.6 mmol, 1 eq) in THF (41 mL, 1 mL/mmol TBSCl) (dropwise over a period of 1 h). After complete addition the cooling bath was removed and the resulting suspension was allowed to warm to room temperature overnight (19 h). The reaction mixture was diluted with water (150 mL) and the aqueous layer extracted with CHCl_3 (3 \times). The combined organic phases were dried (MgSO_4) and concentrated under reduced pressure. Purification by flash chromatography (cyclohexane/ethyl acetate 50/1 \rightarrow 10/1) afforded silyl ether **S7** (6.9 g, 34.0 mmol, 84%) as a clear oil. R_f 0.54 (cyclohexane/ethyl acetate 2/1); ^1H NMR (CDCl_3 , 400 MHz, δ): 0.09 (s, 6H), 0.91 (s, 9H), 2.01 (t, $^3J = 5.7$ Hz, 1H), 4.20 (dd, $^3J = 5.5, 5.6$ Hz, 2H), 4.26 (d, $^3J = 4.8$ Hz, 2H), 5.63–5.76 (m, 2H); ^{13}C NMR (CDCl_3 , 101 MHz, δ): –5.1 ($2\times\text{CH}_3$), 18.5 (C), 26.0 ($3\times\text{CH}_3$), 59.0 (CH_2), 59.8 (CH_2), 130.2 (CH), 131.5 (CH); IR (cm^{-1}): 3350(br s) (ν OH), 2955(m), 2930(m), 2885(m), 2860(m), 1470(m), 1460(m), 1090(s), 1040(m) (ν C–O), 840(s), 780(s); $\text{C}_{10}\text{H}_{22}\text{O}_2\text{Si}$, $M = 202.37$ g/mol.

¹³ Ziegler, F. E.; Lim, H. *J. Org. Chem.* **1984**, *49*, 3278–3281.

¹⁴ Howe, G. P.; Wang, S.; Procter, G. *Tetrahedron Lett.* **1987**, *28*, 2629–2632.



Benzyl ether S7¹⁵: NaH (0.87 g, 22 mmol, 1.1 eq, 60% in mineral oil) was added to a solution of diol **S4** (3.5 g, 40 mmol, 2 eq) in THF (20 mL, 0.5 mL/mmol **S4**) at 0 °C in several portions. The resulting suspension was stirred for 1 h at 0 °C before benzyl bromide (3.4 g, 20 mmol, 1 eq) was added dropwise. The reaction mixture was stirred for 1 h at 75 °C and subsequently cooled down to room temperature. Saturated aqueous NH₄Cl solution was added and the aqueous layer was extracted with CH₂Cl₂. The combined organic phases were dried (MgSO₄) and concentrated under reduced pressure. Purification by flash chromatography (heptane/ethyl acetate) afforded benzyl ether **S7** (2.9 g, 17.3 mmol, 87%) as a clear oil. ¹H NMR (CDCl₃, 300 MHz, δ): 4.03 (d, ³J = 4.9 Hz, 2H), 4.15 (d, ³J = 4.2 Hz, 2H), 4.52 (s, 2H), 5.79–5.98 (m symm, 2H), 7.26–7.36 (m, 5H). C₁₁H₁₄O₂, M = 178.23 g/mol.



General procedure SI-A1: Etherification with sodium iodoacetate: A solution of the allylic alcohol (1 eq) in THF (1–3 mL/mmol alcohol) was treated dropwise with *n*-BuLi (1.05 eq) at –78 °C. The cooling bath was removed and the solution was stirred at room temperature for 30 min. Sodium iodoacetate (1.05 eq) was added in a single portion and the resulting brown slurry stirred at room temperature overnight (18–19 h). After that time the reaction mixture was carefully diluted by the addition of 1 M KOH solution. The organic layer was extracted with 1 M KOH solution (3×). The combined KOH phases were cooled to 0 °C and treated with conc. HCl solution until pH ≤ 2 was reached and an organic layer formed. The acid aqueous layer was subsequently extracted with CH₂Cl₂ (3×). The combined organic phases were dried (MgSO₄) and concentrated under reduced pressure. The crude acid **S8** was used without further purification.

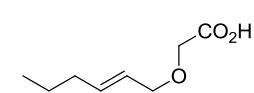
General procedure SI-A2: Etherification with bromoacetic acid¹⁶: NaH (3 eq, 60% in mineral oil) was added to a cooled (–78 °C) solution of bromoacetic acid (1–1.05 eq) in THF (1 mL/mmol alcohol) in multiple portions. The resulting suspension was stirred at –78 °C until the gas evolution had ceased (about 30 min). Subsequently, a solution of the allylic alcohol (1 eq) in THF (0.5–2 mL/mmol alcohol) was added dropwise and the resulting suspension was allowed to warm to room temperature overnight (16–20 h). After that time the reaction mixture was carefully diluted by the

¹⁵ Katsuki, T.; Lee, A. W. M.; Ma, P.; Martin, V. S.; Masamune, S.; Sharpless, K. B.; Tuddenham, D.; Walker, F. J. *J. Org. Chem.* **1982**, 47, 1373–1378.

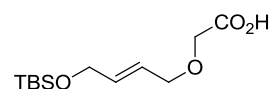
¹⁶ a) Nakai, T.; Mikami, K.; Taya, S.; Kimura, Y.; Mimura, T. *Tetrahedron Lett.* **1981**, 22, 69–72. b) Bedford, S. B.; Bell, K. E.; Bennett, F.; Hayes, C. J.; Knight, D. W.; Shaw, D. E. *J. Chem. Soc., Perkin Trans. 1* **1999**, 2143–2153.

addition of 1 M KOH solution until the precipitate completely disappeared. The organic layer was extracted with 1 M KOH solution (3×). The combined KOH phases were cooled to 0 °C and treated with conc. HCl solution until pH ≤ 2 was reached and an organic layer formed. The acid aqueous layer was subsequently extracted with CH₂Cl₂ (3×). The combined organic phases were dried (MgSO₄) and concentrated under reduced pressure. The crude acid **S8** was used without further purification.

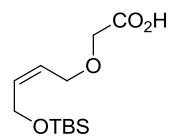
Acid S8a¹⁷: According to the general procedure **SI-A2**, the reaction of (*E*)-hex-2-en-1-ol (5.9 mL, 50 mmol, 1 eq) with NaH (6.0 g, 150 mmol, 3 eq, 60% in mineral oil) and bromoacetic acid (7.0 g, 50 mmol, 1 eq) in THF (100 mL) for 18 h afforded the crude acid **S8a** (7.7 g, 48.7 mmol, 98%) as a yellow oil. *R_f* 0.02 (cyclohexane/ethyl acetate 1/2); ¹H NMR (CDCl₃, 400 MHz, δ): 0.89 (t, ³*J* = 7.4 Hz, 3H), 1.41 (qt, ³*J* = 7.4, 7.4 Hz, 2H), 2.03 (dt, ³*J* = 7.3, 6.9 Hz, 2H), 4.05 (d, ³*J* = 6.5 Hz, 2H), 4.10 (s, 2H), 5.49–5.60 (m, 1H), 5.69–5.78 (m, 1H), 10.96 (br s, 1H); ¹³C NMR (CDCl₃, 101 MHz, δ): 13.8 (CH₃), 22.2 (CH₂), 34.4 (CH₂), 66.2 (CH₂), 72.4 (CH₂), 125.0 (CH), 136.9 (CH), 175.7 (C); C₈H₁₄O₃, M = 158.20 g/mol.



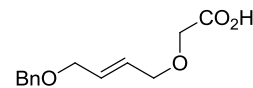
Acid S8b: According to the general procedure **SI-A1**, the reaction of allylic alcohol **S5** (3.2 g, 16.0 mmol, 1 eq) with *n*-BuLi (8.2 mL, 16.8 mmol, 1.05 eq, 2.10 M in hexanes) and sodium iodoacetate (3.5 g, 16.8 mmol, 1.05 eq) in THF (25 mL) for 19 h afforded the crude acid **S8b** (4.2 g, 15.9 mmol, 99%) as a brown oil. *R_f* 0.03 (cyclohexane/ethyl acetate 1/2). ¹H NMR (CDCl₃, 400 MHz, δ): 0.07 (s, 6H), 0.91 (s, 9H), 4.11 (s, 2H), 4.13 (d, ³*J* = 5.3 Hz, 2H), 4.17–4.22 (m, 2H), 5.75–5.90 (m, 2H), COOH unknowable; C₁₂H₂₄O₄Si, M = 260.40 g/mol.



Acid S8c: According to the general procedure **SI-A1**, the reaction of allylic alcohol **S6** (6.9 g, 34.0 mmol, 1 eq) with *n*-BuLi (14.8 mL, 34.0 mmol, 1 eq, 2.30 M in hexanes) and sodium iodoacetate (7.4 g, 35.7 mmol, 1.05 eq) in THF (34 mL) for 18.5 h afforded the crude acid **S8c** (7.3 g, 28.2 mmol, 83%) as a brown oil. *R_f* 0.03 (cyclohexane/ethyl acetate 1/2); ¹H NMR (CDCl₃, 400 MHz, δ): 0.07 (s, 6H), 0.91 (s, 9H), 4.12 (s, 2H), 4.21 (d, ³*J* = 6.3 Hz, 2H), 4.25 (d, ³*J* = 6.0 Hz, 2H), 5.56–5.65 (m, 1H), 5.73–5.81 (m, 1H), COOH unknowable; C₁₂H₂₄O₄Si, M = 260.40 g/mol.

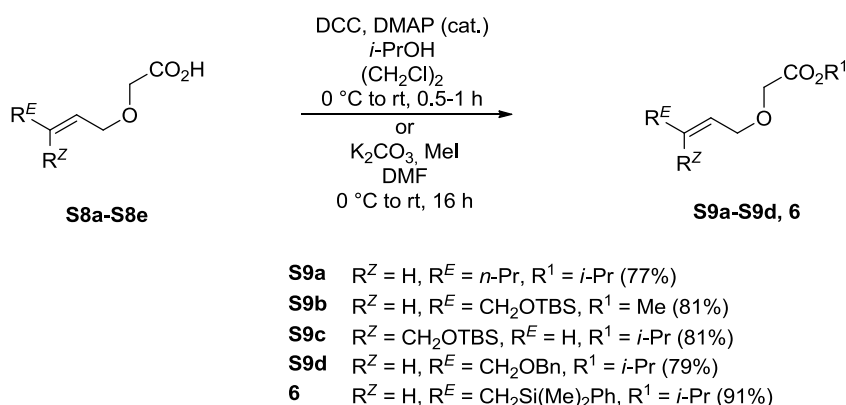
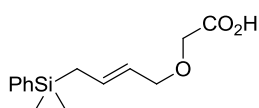


Acid S8d: According to the general procedure **SI-A1**, the reaction of allylic alcohol **S7** (3.3 g, 20 mmol, 1 eq) with *n*-BuLi (8 mL, 20 mmol, 1 eq, 2.5 in hexanes) and sodium iodoacetate (4.3 g, 21 mmol, 1.05 eq) in THF (20 mL) for 18 h afforded the crude acid **S8d** (4.2 g, 18 mmol, 90%) as a viscous oil. ¹H NMR (CDCl₃, 300 MHz, δ): 4.04 (d ³*J* = 3.9 Hz, 2H), 4.11 (s, 2H), 4.12 (d, ³*J* = 5.2 Hz, 2H), 4.52 (s, 2H), 5.79–5.85 (m, symm, 2H), 7.26–7.39 (m, 5H) COOH unknowable; C₁₃H₁₆O₄, M = 236.26 g/mol.



¹⁷ a) Enders, D.; Backhaus, D.; Runsink, J. *Tetrahedron* **1996**, 52, 1503–1528. b) Hiersemann, M.; Lauterbach, C.; Pollex, A. *Eur. J. Org. Chem.* **1999**, 2713–2724.

Acid S8e: According to the general procedure **SI-A1**, the reaction of allylic alcohol **5** (8.2 g, 39.9 mmol, 1 eq) with *n*-BuLi (17.1 mL, 41.9 mmol, 1.05 eq, 2.45 M in hexanes) and sodium iodoacetate (8.7 g, 41.9 mmol, 1.05 eq) in THF (120 mL) for 18 h afforded the crude acid **S8e** (9.9 g, 37.4 mmol, 94%) as a brown viscous oil. R_f 0.03 (cyclohexane/ethyl acetate 1/2); ^1H NMR (CDCl_3 , 400 MHz, δ): 0.29 (s, 6H), 1.77 (d, $^3J = 8.1$ Hz, 2H), 3.98 (s, 2H), 4.02 (d, $^3J = 6.8$ Hz, 2H), 5.32–5.42 (m, 1H), 5.66–5.76 (m, 1H), COOH unknowable; ^{13}C NMR (CDCl_3 , 101 MHz, δ): –3.2 ($2\times\text{CH}_3$), 22.3 (CH_2), 65.8 (CH_2), 72.5 (CH_2), 123.8 (CH), 128.0 ($2\times\text{CH}_{\text{ar}}$), 129.3 (CH_{ar}), 133.7 ($2\times\text{CH}_{\text{ar}}$), 133.8 (CH), 138.2 (C_{ar}), COOH unknowable; IR (cm^{-1}): 3440(br m) (ν OH), 3070(m), 3010(m), 2955(m), 1731(s) (ν C=O), 1660(m) (ν C=C), 1430(m), 1385(m), 1250(m), 1220(w), 1115(s) (ν C-O-C ether), 1070(w); $\text{C}_{14}\text{H}_{20}\text{O}_3\text{Si}$, $M = 264.39$ g/mol.



General procedure SI-B1: Steglich Esterification¹⁸: An ice-cooled solution of the crude acid **S8** (1 eq) in 1,2-dichloroethane [$(\text{CH}_2\text{Cl})_2$, 1–2 mL/mmol acid] was treated with DMAP (0.05 eq), a solution of DCC (1.0–1.1 eq) in $(\text{CH}_2\text{Cl})_2$ (1 mL/mmol acid), and *i*-PrOH (2–3 eq). The cooling bath was removed and the reaction mixture stirred at room temperature (0.5–18 h). The off-white precipitate was removed by filtration over a short silica-gel plug and the filter cake was washed thoroughly with CH_2Cl_2 . The filtrate was concentrated under reduced pressure. Purification by Kugelrohr distillation or by flash chromatography (cyclohexane/ethyl acetate 50/1 \rightarrow 10/1) afforded the ester **S9, 6** as a yellow to clear oil.

General procedure SI-B2: Esterification by alkylation of carboxylate salts¹⁹: An ice-cooled solution of the crude acid **S8** (1 eq) in DMF (1 mL/mmol acid) was treated with K_2CO_3 (4 eq) and MeI (3 eq). The resulting suspension was allowed to warm to room temperature overnight (16 h). The reaction mixture was poured into water (50 mL) and the organic layer was washed with water ($5\times$). The organic phase was dried (MgSO_4) and concentrated under reduced pressure. The crude product was purified by flash chromatography (cyclohexane/ethyl acetate 50/1 \rightarrow 5/1) to afford ester **S9** as a clear oil.

Ester S9a²⁰: According to the general procedure **SI-B1**, the reaction of acid **S8a** (7.7 g, 48.7 mmol) in $(\text{CH}_2\text{Cl})_2$ (98 mL) with DMAP (0.3 g, 2.4 mmol), DCC (10.6 g, 51.6 mmol, 1.05 eq) solved in $(\text{CH}_2\text{Cl})_2$ (49 mL), and *i*-PrOH (7.5 mL, 97.4 mmol) for 0.5 h afforded ester **S9a** (7.5 g, 37.4 mmol,

¹⁸ a) Neises, B.; Steglich, W. *Angew. Chem.* **1978**, *90*, 556–557. b) Hassner, A.; Alexanian, V. *Tetrahedron Lett.* **1978**, *19*, 4475–4478. c) Hassner, A.; Krepski, L. R.; Alexanian, V. *Tetrahedron* **1978**, *34*, 2069–2076.

¹⁹ Pfeffer, P. E.; Silbert, L. S. *J. Org. Chem.* **1976**, *41*, 1373–1379.

²⁰ a) Hiersemann, M. *Synlett* **1999**, 1823–1825. b) Hiersemann, M. *Synthesis* **2000**, 1279–1290.

77%) after Kugelrohr distillation (bp 84–90 °C, 1 mbar) as a clear oil. R_f 0.63 (cyclohexane/ethyl acetate 2/1); ^1H NMR (CDCl_3 , 400 MHz, δ): 0.90 (t, $^3J = 7.4$ Hz, 3H), 1.26 (d, $^3J = 6.3$ Hz, 6H), 1.40 (qt, $^3J = 7.4$, 7.4 Hz, 2H), 2.03 (dt, $^3J = 7.2$, 7.2 Hz, 2H), 4.01 (s, 2H), 4.03 (d, $^3J = 6.4$ Hz, 2H), 5.10 (spt, $^3J = 6.3$ Hz, 1H), 5.51–5.61 (m, 2H), 5.67–5.76 (m, 1H); ^{13}C NMR (CDCl_3 , 101 MHz, δ): 13.8 (CH_3), 22.0 ($2\times\text{CH}_3$), 22.3 (CH_2), 34.5 (CH_2), 67.2 (CH_2), 68.5 (CH), 72.3 (CH_2), 125.6 (CH), 136.2 (CH), 170.2 (C); IR (cm^{-1}): 2980(m), 2960(m), 2935(m), 2875(m), 1750(s) (ν C=O), 1730(m) (ν C=C), 1465(w), 1385(m), 1280(m) (ν C-O-C ester), 1205(s), 1135(s), 1110 (s) (ν C-O-C ether), 972(m); $\text{C}_{11}\text{H}_{20}\text{O}_3$, $M = 200.28$ g/mol.

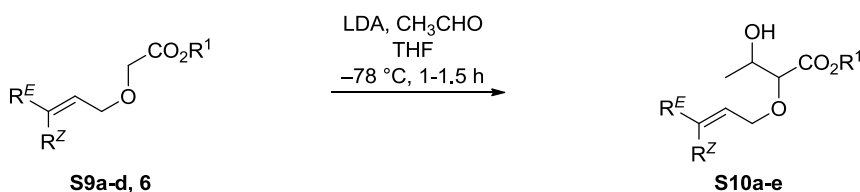
Ester S9b: According to the general procedure **SI-B2**, the reaction of acid **S8b** (4.2 g, 15.9 mmol) in DMF (16 mL) with K_2CO_3 (8.8 g, 64.0 mmol) and MeI (3.0 mL, 48.0 mmol) for 16 h afforded ester **S9b** (3.5 g, 12.9 mmol, 81%) as a light yellow oil. R_f 0.34 (cyclohexane/ethyl acetate 5/1); ^1H NMR (CDCl_3 , 400 MHz, δ): 0.04 (s, 6H), 0.88 (s, 9H), 3.73 (s, 3H), 4.03–4.10 (m, 2H+2H), 4.17 (s, 2H), 5.73–5.84 (m, 2H); ^{13}C NMR (CDCl_3 , 101 MHz, δ): -5.3 ($2\times\text{CH}_3$), 18.3 (C), 25.9 ($3\times\text{CH}_3$), 51.8 (CH_3), 62.8 (CH_2), 66.9 (CH_2), 71.4 (CH_2), 124.9 (CH), 133.8 (CH), 170.8 (C); IR (cm^{-1}): 2955(s), 2855(s), 1760(s) (ν C=O), 1255(m) (ν C-O-C ester), 1210(m), 1130(s) (ν C-O-C ether), 840(s); Anal. Calcd. for $\text{C}_{13}\text{H}_{26}\text{O}_4\text{Si}$: C, 56.9; H, 9.6; Found: C, 56.9; H, 9.5; $\text{C}_{13}\text{H}_{26}\text{O}_4\text{Si}$, $M = 274.43$ g/mol.

Ester S9c: According to the general procedure **SI-B1**, the reaction of acid **S8c** (7.3 g, 28.2 mmol) in $(\text{CH}_2\text{Cl})_2$ (25 mL) with DMAP (0.17 g, 1.4 mmol), DCC (6.4 g, 31.0 mmol, 1.1 eq) solved in $(\text{CH}_2\text{Cl})_2$ (25 mL), and *i*-PrOH (6.5 mL, 84.5 mmol, 3 eq) for 1 h afforded ester **S9c** (6.9 g, 22.8 mmol, 81%) after purification by flash chromatography as a clear oil. R_f 0.53 (cyclohexane/ethyl acetate 5/1); ^1H NMR (CDCl_3 , 400 MHz, δ): 0.07 (s, 6H), 0.89 (s, 9H), 1.26 (d, $^3J = 6.3$ Hz, 6H), 4.02 (s, 2H), 4.17 (d, $^3J = 6.5$ Hz, 2H), 4.24 (d, $^3J = 5.8$ Hz, 2H), 5.10 (spt, $^3J = 6.2$ Hz, 1H), 5.55–5.66 (m, 1H), 5.69–5.78 (m, 1H); ^{13}C NMR (CDCl_3 , 101 MHz, δ): -5.0 ($2\times\text{CH}_3$), 18.5 (C), 22.0 ($2\times\text{CH}_3$), 26.1 ($3\times\text{CH}_3$), 59.6 (CH_2), 67.1 (CH_2), 67.6 (CH_2), 68.6 (CH), 126.1 (CH), 133.8 (CH), 170.1 (C); IR (cm^{-1}): (2955)(s), 2930(s), 2860(s), 1750(s) (ν C=O), 1715(m) (ν C=C), 1470(w), 1385(s), 1375(m), 1360(m), 1260(m) (ν C-O-C ester), 1215(s), 1110(s) (ν C-O-C ether), 910(s); Anal. Calcd. for $\text{C}_{15}\text{H}_{30}\text{O}_4\text{Si}$: C, 59.6; H, 10.0; Found: C, 59.5; H, 9.8; $\text{C}_{15}\text{H}_{30}\text{O}_4\text{Si}$, $M = 302.48$ g/mol.

Ester S9d: According to the general procedure **SI-B1**, the reaction of acid **S8d** (4.2 g, 18 mmol) in $(\text{CH}_2\text{Cl})_2$ (36 mL) with DMAP (0.11 g, 0.9 mmol), DCC (4.1 g, 19.8 mmol, 1.1 eq), and *i*-PrOH (3.4 mL, 56 mmol, 2 eq) afforded ester **S9d** (3.9 g, 14 mmol, 79%) after purification by flash chromatography (heptane/ethyl acetate). ^1H NMR (CDCl_3 , 300 MHz, δ): 1.25 (d, $^3J = 6.2$ Hz, 6H), 4.02–4.06 (m, 4H), 4.09–4.13 (m, 2H), 4.51 (s, 2H), 5.09 (spt, $^3J = 6.3$ Hz, 1H), 5.83–5.90 (m symm, 2H), 7.26–7.35 (m, 5H). ^{13}C NMR (CDCl_3 , 76 MHz, δ): 21.9 ($2\times\text{CH}_3$), 67.6 (CH_2), 68.6 (CH), 70.1 (CH_2), 71.5 (CH_2), 72.4 (CH_2), 127.8 (CH), 127.9 ($2\times\text{CH}_{\text{ar}}$), 128.5 ($2\times\text{CH}_{\text{ar}}$), 128.6 (CH_{ar}), 130.7 (CH), 138.3 (C_{ar}), 170.0 (C); IR (cm^{-1}): 2980, 2860, 1750 (ν C=O); Anal. Calcd. for $\text{C}_{16}\text{H}_{22}\text{O}_4$: C, 69.04; H, 8.09; Found: C, 68.98; H, 8.09; $\text{C}_{16}\text{H}_{22}\text{O}_4$, $M = 278.35$ g/mol.

Ester 6: According to the general procedure **SI-B1**, the reaction of acid **S9e** (9.9 g, 37.4 mmol) in $(\text{CH}_2\text{Cl})_2$ (75 mL) with DMAP (0.23 g, 1.9 mmol), DCC (7.7 g, 37.4 mmol, 1.0 eq) solved in $(\text{CH}_2\text{Cl})_2$

(37 mL), and *i*-PrOH (5.7 mL, 74.8 mmol) for 1 h afforded ester **6** (10.5 g, 34.1 mmol, 91%) after purification by flash chromatography as a clear oil. R_f 0.4 (cyclohexane/ethyl acetate 10/1); ^1H NMR (CDCl_3 , 400 MHz, δ): 0.28 (s, 6H), 1.26 (d, $^3J = 6.3$ Hz, 6H), 1.75 (d, $^3J = 8.0$ Hz, 2H), 3.94 (s, 2H), 4.00 (d, $^3J = 6.7$ Hz, 2H), 5.09 (spt, $^3J = 6.3$ Hz, 1H), 5.41 (dt, $^3J = 15.1, 6.7$ Hz, 1H), 5.68 (dt, $^3J = 15.1, 8.0$ Hz, 1H), 7.32–7.39 (m, 3H), 7.46–7.52 (m, 2H); ^{13}C NMR (CDCl_3 , 101 MHz, δ): –3.2 ($2\times\text{CH}_3$), 22.0 ($2\times\text{CH}_3$), 22.2 (CH_2), 66.7 (CH_2), 68.5 (CH), 72.3 (CH_2), 124.7 (CH), 128.0 ($2\times\text{CH}_{\text{ar}}$), 129.2 (CH_{ar}), 132.6 (CH), 133.7 ($2\times\text{CH}_{\text{ar}}$), 138.4 (C_{ar}), 170.3 (C); IR (cm^{-1}): 3070(m), 3050(m), 2980(s), 2955(s), 1750(s) ($\nu \text{ C=O}$), 1730(s) ($\nu \text{ C=C}$), 1705(m), 1660(m), 1470(m), 1455(m), 1430(s), 1385(s), 1375(s), 1345(m), 1250(s) ($\nu \text{ C-O-C ester}$), 1205(s), 1110(s) ($\nu \text{ C-O-C ether}$), 1070(m), 970(m); Anal. Calcd. for $\text{C}_{17}\text{H}_{26}\text{O}_3\text{Si}$: C, 66.6; H, 8.6; Found: C, 66.7; H, 8.3; $\text{C}_{17}\text{H}_{26}\text{O}_3\text{Si}$, $M = 306.47$ g/mol.



- S10a** $R^Z = \text{H}$, $R^E = n\text{-Pr}$, $R^1 = i\text{-Pr}$ (87%, dr 3/1)
S10b $R^Z = \text{H}$, $R^E = \text{CH}_2\text{OTBS}$, $R^1 = \text{Me}$ (82%, dr 3/1)
S10c $R^Z = \text{CH}_2\text{OTBS}$, $R^E = \text{H}$, $R^1 = i\text{-Pr}$ (76%, dr 73/27)
S10d $R^Z = \text{H}$, $R^E = \text{CH}_2\text{OBn}$, $R^1 = i\text{-Pr}$ (89%, dr 77/23)
S10e $R^Z = \text{H}$, $R^E = \text{CH}_2\text{Si}(\text{Me})_2\text{Ph}$, $R^1 = i\text{-Pr}$ (91%, dr 72/28)

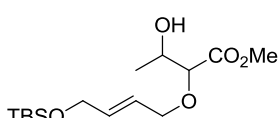
General procedure SI-C: Aldol addition: A solution of LDA [prepared *in situ* from (*i*-Pr) $_2\text{NH}$ (1.3 eq) and *n*-BuLi (1.2 eq)] in THF (2 mL/mmol ester **S9**, **6**) was treated dropwise with a cooled (-78°C) solution of the ester (1 eq) in THF (3 mL/mmol ester). After being stirred at -78°C for 15–30 min, freshly distilled (1 atm, 40°C), cooled acetaldehyde (2 eq) was added and the yellow solution was stirred further for 1–1.5 h at -78°C . Subsequently aqueous saturated NH_4Cl solution was added at -78°C and the reaction mixture was allowed to warm to room temperature. The aqueous layer was extracted with CH_2Cl_2 (3 \times). The combined organic phases were dried (MgSO_4) and concentrated under reduced pressure. Purification by flash chromatography (cyclohexane/ethyl acetate 50/1 \rightarrow 10/1 or 5/1) afforded the β -hydroxy ester **S10** as a mixture of diastereomers.²¹

Aldol adduct S10a²⁰: According to the general procedure **SI-C**, the reaction of ester **S9a** (7.5 g, 37.3 mmol) with (*i*-Pr) $_2\text{NH}$ (6.8 mL, 48.4 mmol), *n*-BuLi (18.6 mL, 44.7 mmol, 2.4 M in hexanes) and acetaldehyde (4.2 mL, 74.5 mmol) in THF (111 mL + 74 mL) for 1 h afforded the β -hydroxy ester **S10a** (7.9 g, 32.5 mmol, 87%) as a mixture of diastereomers (dr = 3/1). R_f 0.38 (cyclohexane/ethyl acetate 2/1); ^1H NMR (CDCl_3 , 400 MHz, mixture of diastereomers dr = 3/1, δ): 0.90 (t, $^3J = 7.3$ Hz, 3H), 1.20 (d, $^3J = 6.3$ Hz, 3H), 1.28 (d, $^3J = 6.3$ Hz, 6H), 1.40 (qt, $^3J = 7.4, 7.4$ Hz, 2H), 2.02 (dt, $^3J = 7.0, 7.0$ Hz, 2H), 2.34 (d, $^3J = 6.8$ Hz, 0.8H^{major}), 2.51 (d, $^3J = 5.3$ Hz, 0.2H^{minor}), 3.66 (d, $^3J = 5.8$ Hz, 0.2H^{minor}), 3.86 (d, $^3J = 4.5$ Hz, 0.8H^{major}), 3.88–3.99 (m, 1H), 4.01–4.10 (m, 1H), 4.11–4.20 (m, 1H), 5.11 (spt, $^3J = 6.3$ Hz, 1H), 5.49–5.60 (m, 1H), 5.64–5.75 (m, 1H); ^{13}C NMR (CDCl_3 , 101 MHz, mixture of diastereomers dr = 3/1, δ): 13.8 (CH_3), 18.4/18.9 (CH_3), 21.9/22.0 (CH_3), 22.0/22.0 (CH_3), 22.3/22.3 (CH_2), 34.5 (CH_2), 68.5/68.5 (CH_2), 68.8/68.8 (CH), 71.9/71.9 (CH), 81.2/82.3 (CH),

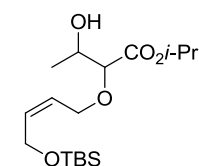
²¹ The relative configuration was not assigned.

125.4/125.6 (CH), 136.2/136.4 (CH), 170.5/170.8 (C); IR (cm⁻¹): 3465(br m) (ν OH), 2980(s), 2960(s), 2875(s), 1740(s) (ν C=O), 1670 (w) (ν C=C), 1465(m), 1460(m), 1375(s), 1330(w), 1270(s) (ν C-O-C ester), 1200(s), 1150(s), 1105(s) (ν C-O-C ether), 1050(m); C₁₃H₂₄O₄, M = 244.33 g/mol.

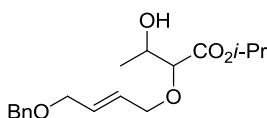
Aldol adduct S10b: According to the general procedure **SI-C**, the reaction of ester **S9b** (1.9 g, 7 mmol) with (*i*-Pr)₂NH (1.3 mL, 9.2 mmol), *n*-BuLi (3.5 mL, 8.5 mmol, 2.4 M in hexanes) and acetaldehyde (0.8 mL, 14.1 mmol) in THF (21 mL + 14 mL) for 1.5 h afforded the β-hydroxy ester **S10b** (1.9 g, 5.8 mmol, 82%) as a mixture of diastereomers (dr = 3/1). R_f 0.43 (cyclohexane/ethyl acetate 2/1); ¹H NMR (CDCl₃, 400 MHz, mixture of diastereomers dr = 3/1, δ): 0.06 (s, 6H), 0.87–0.92 (m, 9H), 1.17–1.25 (m, 3H), 2.34 (d, ³J = 6.7 Hz, 0.8H^{major}), 2.46 (d, ³J = 6.0 Hz, 0.2H^{minor}), 3.74 (s, 0.4H^{minor}), 3.76 (s, 2.6H^{major}), 3.88–4.13 (m, 2H+1H), 4.17 (s, 2H), 4.19–4.28 (m, 1H), 5.72–5.86 (m, 2 H); ¹³C NMR (CDCl₃, 101 MHz, mixture of diastereomers dr = 3/1, δ): -5.1 (2×CH₃), 18.4/18.5 (CH₃), 19.0 (C) 26.1 (3×CH₃), 52.1/52.2 (CH₃), 63.0/63.0 (CH₂), 68.5/68.6 (CH), 71.3/71.3 (CH₂), 81.7/82.2 (CH), 125.0/ 125.1 (CH), 134.0/134.2 (CH), 171.4/171.7 (C); IR (cm⁻¹): 3470(br s) (ν OH), 2955(s), 2930(s), 2860(s), 1750(s) (ν C=O), 1385(m), 1260(s) (ν C-O-C ester), 1110(s) (ν C-O-C ether), 840(s); Anal. Calcd. for C₁₅H₃₀O₅Si: C, 56.6; H, 9.5; Found: C, 56.4; H, 9.1; C₁₅H₃₀O₅Si, M = 318.48 g/mol.



Aldol adduct S10c: According to the general procedure **SI-C**, the reaction of ester **S9c** (5.4 g, 17.8 mmol) with (*i*-Pr)₂NH (3.2 mL, 23 mmol), *n*-BuLi (9.2 mL, 21.3 mmol, 2.3 M in hexanes) and acetaldehyde (3 mL, 53.2 mmol, 3 eq) in THF (54 mL + 36 mL) for 1.5 h afforded the β-hydroxy ester **S10c** (4.7 g, 13.5 mmol, 76%) as a mixture of diastereomers (dr = 73/27). R_f 0.29 (cyclohexane/ethyl acetate 5/1); ¹H NMR (CDCl₃, 400 MHz, mixture of diastereomers dr = 73/27, δ): 0.07 (s, 9H), 0.89 (s, 9H), 1.20 (d, ³J = 6.5 Hz, 2H^{major}), 1.22 (d, ³J = 6.6 Hz, 1H^{minor}), 1.28 (d, ³J = 6.2 Hz, 3H), eclipsed by 1.29 (d, ³J = 6.3 Hz, 3H) 2.37 (d, ³J = 7.2 Hz, 0.7H^{major}), 2.48 (d, ³J = 5.5 Hz, 0.3H^{minor}), 3.66 (d, ³J = 5.6 Hz, 0.3H^{minor}), 3.86 (d, ³J = 4.3 Hz, 0.7H^{major}), 3.94–4.01 (m, 0.3H^{minor}), 4.02–4.12 (m, 1H+0.7H^{major}), 4.23 (d, ³J = 5.3 Hz, 2H), 4.27 (d, ³J = 5.7 Hz, 0.7H), 4.30 (d, ³J = 5.9 Hz, 0.3H^{minor}), 5.12 (spt, ³J = 6.3 Hz, 1H), 5.55–5.65 (m, 1H), 5.69–5.77 (m, 1H); ¹³C NMR (CDCl₃, 101 MHz, mixture of diastereomers dr = 73/27, δ): -5.0 (2×CH₃), 18.3/18.9 (CH₃), 18.5 (C), 22.0/22.0 (2×CH₃), 26.0 (3×CH₃), 59.6/59.6 (CH₂), 66.5/66.6 (CH₂) 68.5/68.5 (CH), 68.9/69.0 (CH), 81.9/82.8 (CH), 126.0/126.2 (CH), 133.7/133.8 (CH), 170.3/170.6 (C); IR (cm⁻¹): 3470(br m) (ν OH), 2960(s), 2930(s), 2885(m), 2860(s), 1745(s) (ν C=O), 1470(m), 1385(s), 1260(s) (ν C-O-C ester), 1205(w), 1145(m), 1105(s) (ν C-O-C ether), 1005(w); Anal. Calcd. for C₁₇H₃₄O₅Si: C, 58.9; H, 9.9; Found: C, 59.2; H, 9.8; C₁₇H₃₄O₅Si, M = 346.53 g/mol.

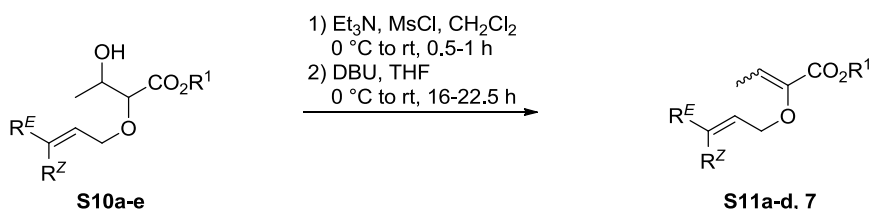
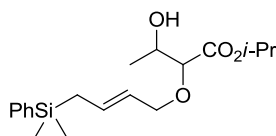


Aldol adduct S10d: According to the general procedure **SI-C**, the reaction of ester **S9d** (3.8 g, 14.6 mmol) with (*i*-Pr)₂NH (2.7 mL, 19 mmol), *n*-BuLi (7.0 mL, 17.5 mmol, 2.5 M in hexanes) and acetaldehyde (1.54 mL, 27 mmol) in THF (45 mL + 30 mL) for 1 h afforded the β-hydroxy ester **S10d** (4.0 g, 13 mmol, 89%) as a mixture of diastereomers (dr = 77/23). ¹H NMR (CDCl₃, 300 MHz, mixture of diastereomers dr = 77/23, δ): 1.21 (d, ³J = 6.5 Hz, 2H^{major}), 1.23 (d, ³J = 6.5 Hz, 1H^{minor}), 1.27 (d, ³J = 6.2 Hz, 3H), 1.28 (d, ³J = 6.2 Hz, 3H), 2.06–2.53 (br s, 1H), 3.69 (d, ³J = 5.5 Hz, 0.2H^{minor}), 3.87 (d, ³J = 4.5 Hz, 0.8H^{major}), 3.93–4.13 (m, 2H+2H), 4.17–4.30 (m, 1H), 4.52 (s, 2H), 5.11 (spt, ³J = 6.2 Hz, 1H), 5.79–5.92 (m symm, 2H), 7.25–7.37 (m, 5H); ¹³C NMR (CDCl₃, 76 MHz, mixture of diastereomers dr = 77/23, δ): 18.3/18.8 (CH₃), 21.8/21.8/21.9 (2×CH₃), 68.4/68.5, 68.8/68.9,



69.9/70.0, 72.4, 81.9/82.6 (CH), 127.7 (CH_{ar}), 127.8 (2×CH_{ar}), 128.3/128.5 (CH), 128.4 (2×CH_{ar}), 130.5/130.8 (CH), 138.2/138.2 (C_{ar}), 170.2/170.5 (C); IR (cm⁻¹): 3510(v OH), 2980–2860, 1740 (ν C=O); Anal. Calcd. for C₁₈H₂₆O₅: C, 67.06; H, 8.13; Found: C, 67.07; H, 8.14; C₁₈H₂₆O₅: M = 322.40 g/mol.

Aldol adduct 10e: According to the general procedure **SI-C**, the reaction of ester **6** (8.9 g, 28.9 mmol) with (*i*-Pr)₂NH (5.3 mL, 37.6 mmol), *n*-BuLi (14.2 mL, 34.7 mmol, 2.45 M in hexanes) and acetaldehyde (3.3 mL, 44.1 mmol) in THF (87 mL + 58 mL) for 1.5 h afforded the β-hydroxy ester **S10e** (9.2 g, 26.3 mmol, 91%) as a mixture of diastereomers (dr = 72/28). *R_f* 0.31 (cyclohexane/ethyl acetate 2/1); ¹H NMR (CDCl₃, 400 MHz, mixture of diastereomers dr = 72/28, δ): 0.28 (s, 6H), 1.18 (d, ³*J* = 6.5 Hz, 3H^{major}), 1.19 (d, ³*J* = 6.3 Hz, 3H^{minor}), 1.27 (d, ³*J* = 6.3 Hz, 6H), 1.75 (d, ³*J* = 8.1 Hz, 2H), 2.28 (d, ³*J* = 6.9 Hz, 0.7H^{major}), 2.47 (d, ³*J* = 5.3 Hz, 0.3H^{minor}), 3.64 (d, ³*J* = 5.7 Hz, 0.3H^{minor}), 3.83 (d, ³*J* = 4.3 Hz, 0.7H^{major}), 3.84–3.89 (m, 1H), 3.92–3.96 (m, 0.3H^{minor}), 3.98–4.07 (m, 0.7H^{major}), 4.10–4.19 (m, 1H), 5.11 (spt, ³*J* = 6.2 Hz, 1H), 5.34–5.44 (m, 1H), 5.60–5.73 (m, 1H), 7.31–7.40 (m, 3H), 7.46–7.54 (m, 2H); ¹³C NMR (CDCl₃, 101 MHz, mixture of diastereomers dr = 72/28, δ): -3.3 (CH₃), -3.2 (CH₃), 18.4/18.9 (CH₃), 21.9/22.0 (CH₃), 22.0 (CH₂), 22.2/22.3 (CH₃), 68.4/68.5 (CH), 68.8/68.8 (CH), 71.8 (CH₂), 80.7/81.6 (CH), 124.4/124.6 (CH), 128.0 (2×CH_{ar}), 129.4 (CH_{ar}), 132.7/132.9 (CH), 133.7 (2×CH_{ar}), 138.4/138.4 (C_{ar}), 170.5/170.8 (C); IR (cm⁻¹): 3470(br s) (ν OH), 3070(m), 3050(m), 2980(s), 1740(s) (ν C=O), 1655(m) (ν C=C), 1455(m), 1425(s), 1375(s), 1250(s) (ν C-O-C ester), 1200(m), 1145(s), 1105(s) (ν C-O-C ether), 1040(m), 970(s); Anal. Calcd. for C₁₉H₃₀O₄Si: C, 65.1; H, 8.6; Found: C, 65.2; H, 8.5; C₁₉H₃₀O₄Si, M = 350.53 g/mol.



- S11a** R^Z = H, R^E = *n*-Pr, R¹ = *i*-Pr (99%, *Z/E* 3/2)
S11b R^Z = H, R^E = CH₂OTBS, R¹ = Me (89%, *Z/E* 3/2)
S11c R^Z = CH₂OTBS, R^E = H, R¹ = *i*-Pr (92%, *Z/E* 3/2)
S11d R^Z = H, R^E = CH₂OBn, R¹ = *i*-Pr (76%, *Z/E* 65/35)
7 R^Z = H, R^E = CH₂Si(Me)₂Ph, R¹ = *i*-Pr (90%, *Z/E* 65/35)

General procedure SI-D: Mesylation-elimination sequence: An ice-cooled solution of aldol adduct **S10** (1 eq) in CH₂Cl₂ (2–3 mL/mmol **S10**) was successively treated with Et₃N (1.3 eq) and MsCl (1.2 eq). The cooling bath was removed and the reaction mixture was stirred at room temperature for a period of 0.5–1 h. The resulting suspension was diluted by the addition of saturated aqueous NaHCO₃ solution. The aqueous layer was extracted with CH₂Cl₂ (3×). The combined organic phases were dried (MgSO₄) and concentrated under reduced pressure to deliver the crude mesylate.

The crude mesylate was solved in THF (3 mL/mmol **S10**) and treated with DBU (3 eq) at 0 °C. The reaction mixture was allowed to warm to room temperature overnight (16–22.5 h) and was subsequently diluted by the addition of water. The aqueous layer was extracted with CH₂Cl₂ (3×) and the combined organic phases were dried (MgSO₄) and concentrated under reduced pressure. Purification by flash chromatography afforded allyl vinyl ether **S11**, **7** as a mixture of vinylic double bond isomers.

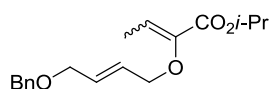
Allyl vinyl ether S11a²⁰: According to the general procedure **SI-D**, aldol adduct **S10a** (7.4 g, 30.3 mmol) was treated with Et₃N (5.5 mL, 39.3 mmol) and MsCl (2.81 mL, 36.3 mmol) in CH₂Cl₂ (91 mL) for 45 min to deliver the mesylate. The subsequent reaction with DBU (13.6 mL, 90.7 mmol) in THF (91 mL) for 22.5 h afforded the allyl vinyl ether **S11a** (6.75 g, 29.8 mmol, 99% over 2 steps) after purification by flash chromatography (cyclohexane/ethyl acetate 150/1) as a mixture of double bond isomers (*Z/E* = 60/40). *R*_f 0.59 (cyclohexane/ethyl acetate 5/1); ¹H NMR (CDCl₃, 500 MHz, mixture of double bond isomers *Z/E* = 60/40, δ): 0.89 (t, ³*J* = 7.4 Hz, 3H), 1.28 (d, ³*J* = 6.4 Hz, 4H^{major}), 1.31 (d, ³*J* = 6.2 Hz, 2H^{minor}), 1.41 (dq, ³*J* = 7.3 Hz, 1.2H^{major}), eclipsed by 1.40 (dq, ³*J* = 7.4 Hz, 0.8H^{minor}), 1.75 (d, ³*J* = 7.1 Hz, 1.8H^{major}), 1.93 (d, ³*J* = 7.4 Hz, 1.2H^{minor}), 1.99–2.06 (m, 2H), 4.19 (d, ³*J* = 5.7 Hz, 1.2H^{minor}), 4.27 (d, ³*J* = 6.4 Hz, 1.8H^{major}), 5.07 (sept, ³*J* = 6.2 Hz, 0.6H^{major}), eclipsed by 5.13 (spt, ³*J* = 6.4 Hz, 0.4H^{minor}), 5.40 (q, ³*J* = 7.4 Hz, 0.4H^{minor}), 5.56–5.67 (m, 1H), 5.67–5.76 (m, 1H), 6.31 (q, ³*J* = 7.1 Hz, 0.6H^{major}); ¹³C NMR (CDCl₃, 126 MHz, mixture of double bond isomers *Z/E* = 60/40, δ): 11.5/12.8 (CH₃), 13.8/13.8 (CH₃), 22.0 (2×CH₃), 22.3/22.3 (CH₂), 34.5/34.5 (CH₂), 68.3/68.5 (CH), 70.3/73.0 (CH₂), 113.0/124.0 (CH), 125.2/125.8 (CH), 135.4/136.1 (CH), 145.8/146.0 (C), 163.7/163.8 (C); IR (cm⁻¹): 2980(s), 2960(s), 2935(s), 2875(m), 1720(s) (ν C=O), 1650(m) (ν C=C), 1455(w), 1385(m), 1375(m), 1320(w), 1260(s) (ν C-O-C ester), 1180(m), 1145(m), 1110(s) (ν C-O-C ether), 1075(m), 1015(m); C₁₃H₂₂O₃, *m* = 226.31 g/mol.

Allyl vinyl ether S11b: According to the general procedure **SI-D**, aldol adduct **S10b** (1.6 g, 4.9 mmol) was treated with Et₃N (0.9 mL, 6.3 mmol) and MsCl (0.5 mL, 5.8 mmol) in CH₂Cl₂ (15 mL) for 45 min to deliver the mesylate. The subsequent reaction with DBU (2.2 mL, 14.6 mmol) in THF (15 mL) for 18 h afforded the allyl vinyl ether **S11b** (1.3 g, 4.3 mmol, 89% over 2 steps) after purification by flash chromatography (cyclohexane/ethyl acetate 100/1 → 20/1) as a mixture of double bond isomers (*Z/E* = 60/40). *R*_f 0.60 (cyclohexane/ethyl acetate 5/1); ¹H NMR (CDCl₃, 400 MHz, mixture of double bond isomers *Z/E* = 60/40, δ): 0.07 (s, 6H), 0.90 (s, 9H), 1.77 (d, ³*J* = 7.2 Hz, 1.8H^{major}), 1.97 (d, ³*J* = 7.4 Hz, 1.2H^{minor}), 3.76 (s, 1.8H^{major}), 3.80 (s, 1.2H^{minor}), 4.18 (d, ³*J* = 3.2 Hz, 2H), 4.27 (s, 0.8H^{minor}), 4.34 (d, ³*J* = 4.5 Hz, 1.2H^{major}), 5.42 (q, ³*J* = 7.4 Hz, 0.4H^{minor}), 5.79–5.91 (m, 2H), 6.36 (q, ³*J* = 7.1 Hz, 0.6H^{major}); ¹³C NMR (CDCl₃, 101 MHz, mixture of double bond isomers *Z/E* = 60/40, δ): -5.3 (2×CH₃), 11.6/12.7 (CH₃), 18.5/18.5 (C), 26.0 (3×CH₃), 51.9/51.9 (CH₃), 63.0/63.1 (CH₂), 69.2/72.3 (CH₂), 113.0/124.5 (CH), 124.9/125.2 (CH), 133.5/133.8 (CH), 145.0/145.4 (C), 164.3/164.5 (C); IR (cm⁻¹): 2955(s), 2930(m), 2860(s), 1730(s) (ν C=O), 1260(s) (ν C-O-C ester), 1135(m) (ν C-O-C ether), 840(s); Anal. Calcd. for C₁₅H₂₈O₄Si: C, 60.0; H, 9.4; Found: C, 60.0; H, 9.4; C₁₅H₂₈O₄Si, *M* = 300.47 g/mol.

Allyl vinyl ether S11c: According to the general procedure **SI-D**, aldol adduct **S10c** (4.6 g, 13.3 mmol) was treated with Et₃N (2.4 mL, 17.3 mmol) and MsCl (1.2 mL, 16 mmol) in CH₂Cl₂ (40 mL) for 45 min to deliver the mesylate. The subsequent reaction with DBU (6.0 mL, 39.9 mmol) in THF (40 mL) for 18 h afforded the allyl vinyl ether **S11c** (4.0 g, 12.2 mmol, 92% over 2 steps) after purification by flash chromatography (cyclohexane/ethyl acetate 100/1 → 20/1) as a mixture of double bond isomers (*Z/E* = 60/40). *R*_f 0.71 (cyclohexane/ethyl acetate 5/1); ¹H NMR (CDCl₃, 400 MHz, mixture of double bond isomers *Z/E* = 60/40, δ): 0.06 (s, 3.6H^{major}), 0.07 (s, 2.4H^{minor}), 0.89 (s, 5.4H^{major}), 0.90 (s, 3.6H^{minor}), 1.28 (d, ³*J* = 6.2 Hz, 3.6H^{major}), 1.32 (d, ³*J* = 6.3 Hz, 2.4H^{minor}), 1.76 (d, ³*J* = 7.1 Hz, 1.8H^{major}), 1.94 (d, ³*J* = 7.4 Hz, 1.2H^{minor}), 4.25 (d, ³*J* = 4.6 Hz, 2H), 4.34 (d, ³*J* = 5.6 Hz, 0.8H^{minor}), 4.41 (d, ³*J* = 5.8 Hz, 1.2H^{major}), 5.08 (spt, ³*J* = 6.2 Hz, 0.6H^{major}), eclipsed by 5.13 (spt, ³*J* = 6.2 Hz, 0.4H^{minor}), 5.38 (q, ³*J* = 7.4 Hz, 0.4H^{minor}), 5.61–5.74 (m, 2H), 6.33 (q, ³*J* = 7.1 Hz, 0.6H^{major}); ¹³C NMR (CDCl₃, 101

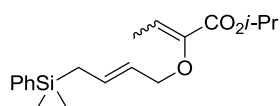
MHz, mixture of double bond isomers $Z/E = 60/40$, δ): $-5.1/-5.0$ ($2\times\text{CH}_3$), $11.5/12.8$ (CH_3), 18.5 (C), 22.0 ($2\times\text{CH}_3$), 26.0 ($3\times\text{CH}_3$), $59.6/59.9$ (CH_2), $65.4/67.7$ (CH_2), $68.5/68.6$ (CH), $112.5/124.3$ (CH), $125.8/126.0$ (CH), $132.8/133.5$ (CH), $145.6/146.0$ (C), $163.5/163.6$ (C); IR (cm^{-1}): $3030(\text{w})$, $2980(\text{s})$, $2960(\text{s})$, $2930(\text{s})$, $2855(\text{m})$, $2855(\text{s})$, $1720(\text{s})$ ($\nu \text{C=O}$), $1650(\text{m})$ ($\nu \text{C=C}$), $1470(\text{m})$, $1385(\text{s})$, $1315(\text{m})$, $1260(\text{s})$ ($\nu \text{C-O-C}$ ester), $1180(\text{m})$, $1140(\text{s})$, $1110(\text{s})$ ($\nu \text{C-O-C}$ ether), $1085(\text{s})$, $1025(\text{m})$, $1005(\text{m})$; Anal. Calcd. for $\text{C}_{17}\text{H}_{32}\text{O}_4\text{Si}$: C, 62.2; H, 9.8; Found: C, 62.3; H, 9.8; $\text{C}_{17}\text{H}_{32}\text{O}_4\text{Si}$, $M = 328.52$ g/mol.

Allyl vinyl ether S11d: According to the general procedure **SI-D**, aldol adduct **S10d** (2.6 g, 8 mmol) was treated with Et_3N (1.5 mL, 10.4 mmol) and MsCl (0.7 mL, 9.6 mmol) in CH_2Cl_2 (24 mL) for 30 min to deliver the mesylate. The subsequent reaction with DBU (2.2 mL, 14.6 mmol) in THF (24 mL) afforded the allyl vinyl ether **S11d** (1.8 g, 6 mmol, 76% over 2 steps) after purification by flash chromatography (heptane/ethyl acetate) as a mixture of double bond isomers ($Z/E = 65/35$). ^1H



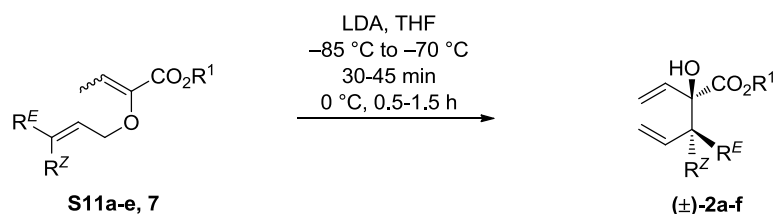
NMR (CDCl_3 , 300 MHz, mixture of double bond isomers $Z/E = 55/45$, δ): 1.28 (d, $^3J = 6.2$ Hz, $3.3\text{H}^{\text{major}}$), 1.32 (d, $^3J = 6.2$ Hz, $2.7\text{H}^{\text{minor}}$), 1.77 (d, $^3J = 7.1$ Hz, $1.6\text{H}^{\text{major}}$), 1.94 (d, $^3J = 7.1$ Hz, $1.4\text{H}^{\text{minor}}$), 4.01–4.08 (m, 2H), 4.25–4.29 (m, $0.9\text{H}^{\text{minor}}$), 4.35 (d, $^3J = 4.9$ Hz, $1.1\text{H}^{\text{major}}$), 5.08 (spt, $^3J = 6.2$ Hz, $0.6\text{H}^{\text{major}}$), eclipsed by 5.14 (spt, $^3J = 6.3$ Hz, $0.4\text{H}^{\text{minor}}$), 5.41 (q, $^3J = 7.5$ Hz, $0.4\text{H}^{\text{minor}}$), 5.83–5.99 (m, 2H), 6.33 (q, $^3J = 7.1$ Hz, $0.6\text{H}^{\text{major}}$), 7.25–7.38 (m, 5H); ^{13}C NMR (CDCl_3 , 76 MHz, mixture of double bond isomers $Z/E = 65/35$, δ): $11.6/14.1$ (CH_3), $21.6/22.0$ ($2\times\text{CH}_3$), 68.5 (CH), $70.0/70.3$ (CH_2), $72.1/72.2$ (CH_2), $72.3/72.7$ (CH_2), $118.7/124.1$ (CH), $127.7/127.8$ (CH), 127.9 ($2\times\text{CH}_{\text{ar}}$), $128.5/128.7$ (CH), 128.5 ($2\times\text{CH}_{\text{ar}}$), 130.7 (CH_{ar}), $138.0/138.3$ (C_{ar}), 146.0 (C), $161.0/163.5$ (C), resonances at $43.2/47.8$, 135.6 do not belong to **S11d**; IR (cm^{-1}): $2980-2860$, 1715 ; Anal. Calcd. for $\text{C}_{18}\text{H}_{24}\text{O}_4$: C, 71.03; H, 7.95; Found: C, 70.92; H, 8.10; $\text{C}_{18}\text{H}_{24}\text{O}_4$, $M = 328.52$ g/mol.

Allyl vinyl ether 7²²: According to the general procedure **SI-D**, aldol adduct **S10e** (3.5 g, 10 mmol) was treated with Et_3N (1.83 mL, 13 mmol) and MsCl (0.93 mL, 12 mmol) in CH_2Cl_2 (30 mL) for 1 h to deliver the mesylate. The subsequent reaction with DBU (4.48 mL, 30 mmol) in THF (30 mL) for 19 h afforded the allyl vinyl ether **7** (2.99 g, 9.0 mmol, 90% over 2 steps) after purification by flash chromatography (*n*-pentane/diethyl ether 50/1) as a mixture of double bond isomers ($Z/E = 65/35$). R_f



0.57 (cyclohexane/ethyl acetate 5/1); ^1H NMR (CDCl_3 , 400 MHz, mixture of double bond isomers $Z/E = 65/35$, δ): 0.28 (s, 4H^{major}), 0.28 (s, 2H^{minor}), 1.28 (d, $^3J = 6.3$ Hz, 4H^{major}), 1.31 (d, $^3J = 6.3$ Hz, 2H^{minor}), 1.70–1.78 (m, $2\text{H}^{\text{major}}+2\text{H}$), 1.92 (d, $^3J = 7.4$ Hz, 1H^{minor}), 4.17 (d, $^3J = 6.3$ Hz, $0.7\text{H}^{\text{minor}}$), 4.28 (d, $^3J = 6.8$ Hz, $1.3\text{H}^{\text{major}}$), 5.08 (spt, $^3J = 6.2$ Hz, $0.7\text{H}^{\text{major}}$), eclipsed by 5.13 (spt, $^3J = 6.3$ Hz, $0.3\text{H}^{\text{minor}}$), 5.36 (q, $^3J = 7.4$ Hz, $0.3\text{H}^{\text{minor}}$), 5.43–5.56 (m, 1H), 5.70 (dt, $J = 15.3$, 7.8 Hz, 1H), 6.30 (q, $^3J = 7.1$ Hz, $0.7\text{H}^{\text{major}}$), 7.31–7.40 (m, 3H), 7.45–7.53 (m, 2H); ^{13}C NMR (CDCl_3 , 101 MHz, mixture of double bond isomers $Z/E = 65/35$, δ): -3.3 ($2\times\text{CH}_3$), $11.5/12.8$ (CH_3), 22.0 ($2\times\text{CH}_3$), $22.2/22.2$ (CH_2), $68.3/68.5$ (CH), $70.3/73.0$ (CH_2), $112.8/124.8$ (CH), $124.0/124.1$ (CH), 127.9 ($2\times\text{CH}_{\text{ar}}$), 129.2 (CH_{ar}), $131.8/132.5$ (CH), $133.7/133.7$ ($2\times\text{CH}_{\text{ar}}$), 138.5 (C_{ar}), $145.6/145.8$ (C), $163.7/163.8$ (C); IR (cm^{-1}): $3070(\text{m})$, $3050(\text{m})$, $2980(\text{s})$, $2955(\text{s})$, $1715(\text{s})$ ($\nu \text{C=O}$), $1650(\text{m})$ ($\nu \text{C=C}$), $1455(\text{w})$, $1425(\text{m})$, $1385(\text{m})$, $1375(\text{m})$, $1320(\text{m})$, $1260(\text{s})$ ($\nu \text{C-O-C}$ ester), $1180(\text{m})$, $1135(\text{s})$, $1110(\text{s})$ ($\nu \text{C-O-C}$ ether), $1015(\text{m})$; Anal. Calcd. for $\text{C}_{19}\text{H}_{28}\text{O}_3\text{Si}$: C, 68.6; H, 8.5; Found: C, 68.8; H, 8.5; $\text{C}_{19}\text{H}_{28}\text{O}_3\text{Si}$, $M = 332.51$ g/mol.

²² Allyl vinyl ether (AVE) **7** slowly undergoes a Gosteli–Claisen rearrangement to the corresponding α -keto ester on exposure to 0°C , room temperature or elevated temperatures (e.g. reaction of **7** in CDCl_3 in a NMR tube for 19 d at ambient temperature afforded 88% α -keto ester as determined by ^1H NMR spectroscopy). Therefore, during reaction workup, concentration of the organic phases in vacuum should be conducted at temperature \leq room temperature. After purification, AVE **7** was used directly in the next step.



- (±)-**2a** $R^Z = \text{H}$, $R^E = n\text{-Pr}$, $R^1 = i\text{-Pr}$ (87%, *syn/anti* 88/12)
 (±)-**2b** $R^Z = \text{H}$, $R^E = \text{CH}_2\text{OTBS}$, $R^1 = \text{Me}$ (68%, *syn/anti* 92/8)
 (±)-**2c** $R^Z = \text{CH}_2\text{OTBS}$, $R^E = \text{H}$, $R^1 = i\text{-Pr}$ (81%, *syn/anti* 4/96)
 (±)-**2d** $R^Z = \text{H}$, $R^E = \text{CH}_2\text{OBn}$, $R^1 = i\text{-Pr}$ (57%, *syn/anti* 72/28)
 (±)-**2e** $R^Z = \text{CH}_2\text{OBn}$, $R^E = \text{H}$, $R^1 = \text{Me}$ (60%, *syn/anti* 16/84)
 (±)-**2f** $R^Z = \text{H}$, $R^E = \text{CH}_2\text{Si}(\text{Me})_2\text{Ph}$, $R^1 = i\text{-Pr}$ (89%, *syn/anti* 86/14)

General procedure SI-E: Dienolate [2,3]-Wittig rearrangement²³: A cooled (−85 °C) solution of LDA [prepared *in situ* from (*i*-Pr)₂NH (1.2–2 eq) and *n*-BuLi (1.1–1.8 eq)] in THF (2 mL/mmol **S11**, **7**) was treated dropwise with a cooled (−85 °C) solution of allyl vinyl ether **S11**, **7** (1 eq, mixture of double bond isomers) in THF (3 mL/mmol **S11**, **7**). The resulting light yellow solution was stirred for a period of 30–45 min (−85 °C → approx. −70 °C). The dry-ice bath was then replaced by a cooling-bath and the reaction mixture was stirred at 0 °C until TLC indicated complete conversion of the starting material (0.5–1.5 h). In most cases, successful reaction was accompanied by a color change from light yellow to orange/red. The solution was subsequently diluted by the addition of aqueous saturated NH₄Cl solution at 0 °C and warmed to room temperature. The aqueous layer was extracted with CH₂Cl₂ (3×). The combined organic phases were dried (MgSO₄) and concentrated under reduced pressure. Purification by flash chromatography (cyclohexane/ethyl acetate) afforded the 1,5-hexadiene (±)-**2** as a mixture of diastereomers. The reaction proved to be very sensitive to the quality of *n*-BuLi.²⁴ Therefore, it was freshly titrated² and used, while it appeared as a clear, colorless solution.

(±)-1,5-Hexadiene 2a²⁵: According to the general procedure **SI-E**, the reaction of allyl vinyl ether **S11a** (3.28 g, 14.5 mmol) with (*i*-Pr)₂NH (2.65 mL, 18.8 mmol, 1.3 eq) and *n*-BuLi (7.09 mL, 17.4 mmol, 1.1 eq, 2.45 M in hexanes) in THF (29 mL + 43 mL) at −85 °C → −70 °C (45 min) and 0 °C (1.5 h) provided 1,5-hexadiene (±)-**2a** (2.86 g, 12.7 mmol, 87%) after flash chromatography (cyclohexane/ethyl acetate 250/1) as a mixture of diastereomers (*syn/anti* = 88/12). *R_f* 0.60 (cyclohexane/ethyl acetate 5/1); 2D ¹H, ¹H-COSY, 2D ¹H, ¹³C-HSQC methods were used to confirm the NMR peak assignments: ¹H NMR (CDCl₃, 500 MHz, mixture of diastereomers *syn/anti* = 88/12, δ): 0.86 (t, ³*J* = 7.2 Hz, 3H, 9-CH₃), 1.07–1.20 (m, 2 H, 7-CH₂+8-CH₂), 1.25 (d, ³*J* = 6.8 Hz, 0.4H^{minor}, *i*-Pr-CH₃), eclipsed by 1.27 (d, *J* = 6.3 Hz, 2.6H^{major}, *i*-Pr-CH₃), 1.30 (d, *J* = 6.3 Hz, 3H, *i*-Pr-CH₃), 1.33–1.51 (m, 2 H, 7-CH₂+8-CH₂), 2.35 (ddd, *J* = 10.8, 10.0, 2.7 Hz, 0.1H^{minor}, 4-CH), 2.43 (ddd, *J* = 10.3, 2.4 Hz, 0.9H^{major}, 4-CH), 3.31 (s, 0.9H^{major}, OH), 3.33 (s, 0.1H^{minor}, OH), 5.01 (dd, ³*J* = 17.2, 1.9 Hz, 0.9H^{major}, 6-CH₂), eclipsed by 5.00–5.05 (m, 0.1H^{minor}, 6-CH₂), 5.05–5.13 (m, 2H, *i*-Pr-H+6-CH₂), 5.15 (dd, *J* = 10.6, 1.4 Hz, 0.9H^{major}, 1-CH₂), 5.24 (dd, *J* = 10.5, 1.5 Hz, 0.1H^{minor}, 1-CH₂), 5.41 (dd, *J* = 17.1, 1.4 Hz, 0.9H^{major}, 1-CH₂), 5.47–5.52 (m, 0.1H^{minor}, 1-CH₂), eclipsed by 5.54 (dt, ³*J* = 17.2, 9.9 Hz, 0.9H^{major}, 5-CH), 5.65 (dt, ³*J* = 17.2, 10.0

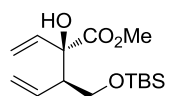
²³ a) Hiersemann, M. *Tetrahedron* **1999**, *55*, 2625–2638. b) Hiersemann, M.; Lauterbach, C.; Pollex, A. *Eur. J. Org. Chem.* **1999**, 2713–2724. c) Hiersemann, M.; Abraham, L.; Pollex, A. *Synlett* **2003**, 1088–1095.

²⁴ purchased from ACROS Organics; 800 mL, 2.5 M solution in hexanes.

²⁵ Hiersemann, M. *Synlett* **2000**, 415–417.

Hz, $0.1H^{\text{minor}}$, 5-CH), 5.87 (dd, $^3J = 17.1, 10.6$ Hz, $0.9H^{\text{major}}$, 2-CH), eclipsed by 5.88–5.93 (m, $0.1H^{\text{minor}}$, 2-CH); significant COSY cross peaks: 4-CH/5-CH; ^{13}C NMR (CDCl_3 , 126 MHz, mixture of diastereomers *syn/anti* = 88/12, δ): 14.0/14.1 (9-CH₃), 20.4/20.6 (8-CH₂), 21.8/21.9 (2×*i*-Pr-CH₃), 29.4/31.1 (7-CH₂), 51.1/51.1 (4-CH), 70.3 (*i*-Pr-CH), 79.8 (3-C), 115.2/116.1 (1-CH₂), 118.0/118.0 (6-CH₂), 136.8/137.4 (5-CH), 138.1/138.7 (2-CH), 174.7 (C=O); IR (cm^{-1}): 3515(br s) (ν OH), 3075(w), 2980(s), 2960(s), 2935(s), 2875(m), 1725(s) (ν C=O), 1640(m) (ν C=C), 1465(m), 1400(w), 1375(m), 1250(s) (ν C-O-C ester), 1230(m), 1160(s), 1105(s), 1000(m); Anal. Calcd. for $\text{C}_{13}\text{H}_{22}\text{O}_3$: C, 69.0; H, 9.8; Found: C, 69.4; H, 10.0; $\text{C}_{13}\text{H}_{22}\text{O}_3$, $M = 226.31$ g/mol. Separation of *syn-2a/anti-2a* was realized by preparative HPLC²⁶ [column: Nucleosil 50-7 (32×50 mm); eluent: *n*-heptane/ethyl acetate 99/1; flow: 20 ml/min; injection: 500 μL ; $c = 200$ mg/mL; $R_t(\text{anti-2a})$ 22.3 min, $R_t(\text{syn-2a})$ 24.9 min]; (\pm)-*anti-2a*: ^1H NMR (CDCl_3 , 400 MHz, δ): 0.86 (t, $^3J = 7.2$ Hz, 3H), 1.03–1.18 (m, 1H), 1.24 (d, $^3J = 6.2$ Hz, 3H), 1.26 (d, $^3J = 6.2$ Hz, 3H), eclipsed by 1.20–1.41 (m, 2H), 1.42–1.52 (m, 1H), 2.29–2.39 (m, 1H), 3.34 (s, 1H), 4.96–5.05 (m, 2H), 5.08 (dd, $J = 10.2, 2.1$ Hz, 1H), 5.24 (dd, $J = 10.3, 1.5$ Hz, 1H), 5.53 (dd, $J = 17.1, 1.5$ Hz, 1H), 5.65 (dt, $^3J = 17.2, 9.9$ Hz, 1H), 5.89 (dd, $^3J = 17.1, 10.5$ Hz, 1H); ^{13}C NMR (CDCl_3 , 101 MHz, δ): 14.1 (CH₃), 20.6 (CH₂), 21.9 (CH₃), 21.9 (CH₃), 29.4 (CH₂), 51.0 (CH), 70.3 (CH), 79.9 (C), 116.1 (CH₂), 118.0 (CH₂), 137.4 (CH), 138.0 (CH), 174.5 (C); (\pm)-*syn-2a*: ^1H NMR (CDCl_3 , 400 MHz, δ): 0.86 (t, $^3J = 7.0$ Hz, 3H), 1.05–1.21 (m, 2H), 1.27 (d, $^3J = 6.3$ Hz, 3H), 1.30 (d, $^3J = 6.3$ Hz, 3H), 1.32–1.51 (m, 2H), 2.38–2.48 (m, 1H), 3.32 (s, 1H), 5.01 (dd, $J = 17.2, 1.6$ Hz, 1H), 5.04–5.13 (m, 2H), 5.15 (dd, $J = 10.5, 1.5$ Hz, 1H), 5.41 (dd, $J = 17.1, 1.5$ Hz, 1H), 5.54 (dt, $^3J = 17.1, 10.0$ Hz, 1H), 5.87 (dd, $^3J = 17.1, 10.5$ Hz, 1H); ^{13}C NMR (CDCl_3 , 101 MHz, δ): 14.0 (CH₃), 20.4 (CH₂), 21.8 (2×CH₃), 31.0 (CH₂), 51.1 (CH), 70.3 (CH), 79.7 (C), 115.1 (CH₂), 118.0 (CH₂), 136.8 (CH), 138.6 (CH), 174.7 (C).

(\pm)-1,5-Hexadiene 2b: According to the general procedure **SI-E**, the reaction of allyl vinyl ether **S11b** (0.2 g, 0.7 mmol) with (*i*-Pr)₂NH (0.2 mL, 1.4 mmol, 2 eq) and *n*-BuLi (0.5 mL, 1.7 mmol, 1.8 eq, 2.4 M in hexanes) in THF (2 mL + 3 mL) at $-85^\circ\text{C} \rightarrow -70^\circ\text{C}$ (30 min) and room temperature instead of 0°C (30 min) provided 1,5-hexadiene (\pm)-**2b** (0.14 g, 0.5 mmol, 68%) after flash chromatography (cyclohexane/ethyl acetate 100/1) as a mixture of diastereomers (*syn/anti* =



92/8). R_f 0.63 (cyclohexane/ethyl acetate 5/1; ^1H NMR (CDCl_3 , 400 MHz, mixture of diastereomers *syn/anti* = 92/8, δ): 0.04 (s, 3H), 0.05 (s, 3H), 0.85–0.90 (m, 9H), 2.60–2.64 (m, $0.1H^{\text{minor}}$), 2.85 (td, $^3J = 7.9, 5.0$ Hz, $0.9H^{\text{major}}$), 3.65 (dd, $J = 10.1, 4.7$ Hz, 1H), 3.71–3.82 (m, 4H), 4.03 (s, $0.9H^{\text{major}}$), 4.21 (s, $0.1H^{\text{minor}}$), 5.02–5.33 (m, 3H), 5.46 (dd, $J = 17.0, 1.2$ Hz, $0.9H^{\text{major}}$), 5.58 (dd, $J = 17.0, 1.2$ Hz, $0.1H^{\text{minor}}$), 5.69 (dt, $^3J = 17.2, 9.7$ Hz, $0.9H^{\text{major}}$), 5.85 (dd, $^3J = 17.0, 10.5$ Hz, $0.9H^{\text{major}}$), 5.90–6.09 (m, $0.2H^{\text{minor}}$); ^{13}C NMR (CDCl_3 , 101 MHz, mixture of diastereomers *syn/anti* = 92/8, δ): -5.6 (CH₃), -5.4 (CH₃), 18.6 (C), 25.9/26.1 (3×CH₃), 51.8 (CH₃), 52.8 (CH), 64.4 (CH₂), 78.5 (C), 115.5/116.2 (CH₂), 118.7/118.9 (CH₂), 134.2 (CH), 138.0/138.2 (CH), 175.2 (C); IR (cm^{-1}): 3510(br m) (ν OH), 2950(s), 2860(m), 1740(s) (ν C=O), 1385(w), 1250(s) (ν C-O-C ester), 1170(s), 1110(m), 840(s); Anal. Calcd. for $\text{C}_{15}\text{H}_{28}\text{O}_4\text{Si}$: C, 60.0; H, 9.4; Found: C, 60.0; H, 9.3; $\text{C}_{15}\text{H}_{28}\text{O}_4\text{Si}$, $M = 300.47$ g/mol.

(\pm)-1,5-Hexadiene 2c: According to the general procedure **SI-E**, the reaction of allyl vinyl ether **S11c** (1.64 g, 5 mmol) with (*i*-Pr)₂NH (0.91 mL, 6.5 mmol, 1.3 eq) and *n*-BuLi (2.44 mL, 6.0 mmol, 1.2 eq, 2.45 M in hexanes) in THF (10 mL + 15 mL) at $-85^\circ\text{C} \rightarrow -70^\circ\text{C}$ (30 min) and 0°C (1 h) provided 1,5-hexadiene (\pm)-**2c** (1.33 g, 4.1 mmol, 81%) after flash chromatography (cyclohexane/ethyl

²⁶ System: Smartline Knauer HPLC, [pump K-1800, UV-detector 2600 (200 nm), autosampler 3900, Chromgate software V3.16]

acetate 500/1 \rightarrow 100/1) as a mixture of diastereomers (*syn/anti* = 4/96). R_f 0.57 (cyclohexane/ethyl acetate 5/1); 2D ^1H , ^1H -COSY, 2D ^1H , ^{13}C -HSQC methods were used to confirm the NMR peak assignments: ^1H NMR (CDCl_3 , 500 MHz, mixture of diastereomers *syn/anti* = 4/96, δ): 0.02 (s, 3H, TBS-CH₃), 0.03 (s, 3H, TBS-CH₃), 0.88 (s, 9H, TBS-*t*-Bu), 1.24 (d, 3J = 6.0 Hz, 3H, *i*-Pr-CH₃), 1.25 (d, 3J = 6.1 Hz, 2.8H^{major}, *i*-Pr-CH₃), 1.29 (d, 3J = 6.3 Hz, 0.2H^{minor}, *i*-Pr-CH₃), 2.63 (ddd, 3J = 10.0, 6.5, 4.1 Hz, 0.9H^{major}, 4-CH), 2.76–2.82 (m, 0.1H^{minor}, 4-CH), 3.69 (dd, J = 10.2, 5.5 Hz, 0.1H^{minor}, 4'-CH₂), 3.74 (dd, J = 10.1, 6.5 Hz, 0.9H^{major}, 4'-CH₂), 3.79 (dd, J = 10.2, 4.1 Hz, 1H, 4'-CH₂), 3.92 (s, 0.9H^{major}, OH), 3.97 (s, 0.1H^{minor}, OH), 5.03 (spt, 3J = 6.3 Hz, 1H, *i*-Pr-CH), 5.10–5.19 (m, 2H, 6-CH₂), 5.25 (dd, J = 10.5, 1.3 Hz, 1H, 1-CH₂), 5.45 (dd, J = 17.0, 1.3 Hz, 0.1H^{minor}, 1-CH₂), 5.56 (dd, J = 17.0, 1.4 Hz, 0.9H^{major}, 1-CH₂), 5.69–5.76 (m, 0.1H^{minor}, 5-CH), 5.82–5.85 (m, 0.1H^{minor}, 2-CH), eclipsed by 5.87 (ddd, J = 17.0, 10.3, 9.5 Hz, 0.9H^{major}, 5-CH), 6.00 (dd, 3J = 17.0, 10.5 Hz, 0.9H^{major}, 2-CH); significant COSY cross peaks: 4-CH/4'-CH₂, 4-CH/5-CH, 5-CH/6-CH₂; ^{13}C NMR (CDCl_3 , 126 MHz, mixture of diastereomers *syn/anti* = 4/96, δ): -5.3 (TBS-CH₃), -5.3 (TBS-CH₃), 18.4 (TBS-*t*-Bu-C), 21.9 (2 \times *i*-Pr-CH₃), 26.0 (TBS-*t*-Bu-CH₃), 52.5 (4-CH), 63.3 (4'-CH₂), 69.9 (*i*-Pr-CH), 79.7 (3-C), 115.9 (1-CH₂), 119.0 (6-CH₂), 135.2 (5-CH), 138.2 (2-CH), 173.1 (C=O); IR (cm⁻¹): 3505(br m) (ν OH), 3075(w), 2980(m), 2955(s), 2930(s), 2885(m), 2855(s), 1730(s) (ν C=O), 1640(w) (ν C=C), 1470(m), 1420(w), 1385(m), 1375(m), 1360(w), 1255(s) (ν C-O-C ester), 1175(s), 1145(s), 1105(s), 1005(m); Anal. Calcd. for C₁₇H₃₂O₄Si: C, 62.2; H, 9.8; Found: C, 62.4; H, 9.8; C₁₇H₃₂O₄Si, M = 328.52 g/mol.

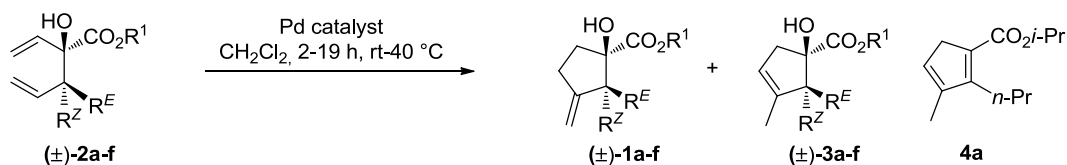
(\pm)-1,5-Hexadiene 2d: According to the general procedure **SI-E**, the reaction of allyl vinyl ether **S11d** (0.7 g, 2.3 mmol) with (*i*-Pr)₂NH (0.39 mL, 2.8 mmol, 1.2 eq) and *n*-BuLi (1.05 mL, 2.5 mmol, 1.1 eq, 2.4 M in hexanes) in THF (5 mL + 7 mL) at -85 °C to room temperature (overnight) instead of 0 °C provided 1,5-hexadiene (\pm)-**2d** (0.4 g, 1.3 mmol, 57%) after flash chromatography (heptane/ethyl acetate) as a mixture of separable diastereomers (*syn/anti* = 72/28). (\pm)-*syn*-**2d**: ^1H NMR (CDCl_3 , 300 MHz, δ): 1.12 (d, 3J = 6.5 Hz, 3H), 1.20 (d, 3J = 6.2 Hz, 3H), 2.98 (ddd, 3J = 8.4, 8.4, 5.5 Hz, 1H), 3.47 (dd, J = 9.4, 5.5 Hz, 1H), 3.60 (dd, J = 9.1, 8.1 Hz, 1H), 3.71 (s, 1H), 4.43 (s, 2H), 4.91 (spt, 3J = 6.3 Hz, 1H), 5.07–5.21 (m, 3H), 5.45 (dd, J = 17.0, 1.5 Hz, 1H), 5.67 (ddd, J = 17.0, 10.7, 9.1 Hz, 1H), 5.85 (dd, 3J = 17.0, 10.6 Hz, 1H), 7.22–7.38 (m, 5H); ^{13}C NMR (CDCl_3 , 76 MHz, δ): 21.5 (CH₃), 21.7 (CH₃), 50.4 (CH), 70.1 (CH), 70.3 (CH₂), 73.6 (CH₂), 77.6 (C), 115.3 (CH₂), 118.7 (CH₂), 127.8 (CH_{ar}), 128.1 (2 \times CH_{ar}), 128.4 (2 \times CH_{ar}), 134.3 (CH), 138.1 (C_{ar}), 138.5 (CH), 174.4 (C); IR (cm⁻¹): 3495, 2980–2860, 1725; Anal. Calcd. for C₁₈H₂₄O₄: C, 71.03; H, 7.95; Found: C, 70.66; H, 7.89; C₁₈H₂₄O₄, M = 304.38 g/mol.

(\pm)-1,5-Hexadiene 2e: According to the general procedure **SI-E**, the reaction of allyl vinyl ether **S11e**¹ (0.28 g, 1 mmol) with (*i*-Pr)₂NH (0.18 mL, 1.3 mmol, 1.3 eq) and *n*-BuLi (0.5 mL, 1.2 mmol, 1.2 eq, 2.4 M in hexanes) in THF (2 mL + 3 mL) at -85 °C \rightarrow -70 °C (30 min) and 0 °C (1 h) provided 1,5-hexadiene (\pm)-**2e** (0.16 g, 0.60 mmol, 60%) after flash chromatography (cyclohexane/ethyl acetate 200/1 \rightarrow 50/1) as a mixture of diastereomers (*syn/anti* = 16/84). R_f 0.34 (cyclohexane/ethyl acetate 5/1); 2D ^1H , ^1H -COSY, 2D ^1H , ^{13}C -HSQC methods were used to confirm the NMR peak assignments: ^1H NMR (CDCl_3 , 500 MHz, mixture of diastereomers *syn/anti* = 16/84, δ): 2.80 (ddd, 3J = 9.3, 6.4, 4.8 Hz, 0.8H^{major}, 4-CH), 3.01 (ddd, 3J = 8.8, 4.8 Hz, 0.2H^{minor}, 4-CH), 3.48 (dd, J = 9.5, 4.7 Hz, 0.3H^{minor}, 4'-CH₂), 3.57 (s, 0.5H^{minor}, OMe), 3.59–3.71 (m, 1.7H^{major}, 4'-CH₂), 3.70 (s, 1H, OH), 3.73 (s, 2.5H^{major}, OMe), 4.40–4.51 (m, 2H, OCH₂Ph), 5.08–5.21 (m, 2H, 6-CH₂), 5.24 (dd, J = 10.5, 1.3 Hz, 0.8H^{major}, 1-CH₂), 5.46 (dd, J = 17.0, 1.4 Hz, 0.2H^{minor}, 1-CH₂), 5.54 (dd, J = 17.0, 1.3 Hz, 0.8H^{major}, 1-CH₂), 5.66 (ddd, 3J = 17.3, 10.4, 9.0 Hz, 0.2H^{minor}, 5-CH), 5.81–5.88 (m, 0.2H^{minor}, 2-CH), eclipsed by 5.91 (ddd, 3J = 17.0, 10.4, 9.3 Hz,

0.8H^{major}, 5-CH), 6.00 (dd, ³J = 17.0, 10.5 Hz, 0.8H^{major}, 2-CH), 7.24–7.37 (m, 5H, Ar); significant COSY cross peaks: 4-CH/4'-CH₂, 4-CH/5-CH, 5-CH/6-CH₂; ¹³C NMR (CDCl₃, 126 MHz, mixture of diastereomers *syn/anti* = 16/84, δ): 50.6/51.3 (4-CH), 52.9/53.0 (OMe), 69.9/70.4 (4'-CH₂), 73.4/73.8 (OCH₂Ph), 77.6/80.0 (3-C), 115.5/116.1 (1-CH₂), 118.9/118.9 (6-CH₂), 127.8/127.9 (2×CH_{ar}), 128.2 (CH_{ar}), 128.4/128.5 (2×CH_{ar}), 133.9/135.5 (5-CH), 137.6/137.9 (2-CH), 138.2/138.3 (C_{ar}), 174.2/175.4 (C=O); IR (cm⁻¹): 3505(br s) (ν OH), 3065(w), 3030(m), 3010(w), 2980(w), 2955(m), 2925(m), 2905(m), 2865(m), 1730(s) (ν C=O), 1640(m), (ν C=C), 1495(m), 1455(s), 1435(s), 1420(m), 1360(m), 1250(s) (ν C-O-C ester), 1170(s), 1145(s), 1100(s), 995(s); Anal. Calcd. for C₁₆H₂₀O₄: C, 69.5; H, 7.3; Found: C, 69.5; H, 7.4; C₁₆H₂₀O₄, M = 276.33 g/mol.

(±)-1,5-Hexadiene 2f: According to the general procedure **SI-E**, the reaction of allyl vinyl ether **7** (2.99 g, 9 mmol) with (*i*-Pr)₂NH (1.52 mL, 10.8 mmol, 1.2 eq) and *n*-BuLi (4.04 mL, 9.9 mmol, 1.1 eq, 2.45 M in hexanes) in THF (18 mL + 27 mL) at -85 °C → -70 °C (30 min) and 0 °C (1 h) provided 1,5-hexadiene (±)-**2f** (2.65 g, 8.0 mmol, 89%) after flash chromatography (cyclohexane/ethyl acetate 250/1 → 100/1) as a mixture of diastereomers²⁷ (*syn/anti* = 86/14). The clear oil slowly crystallized upon storage in the freezer. *R*_f 0.60 (cyclohexane/ethyl acetate 5/1); 2D ¹H, ¹H-COSY, 2D ¹H, ¹³C-HSQC methods were used to firm the NMR peak assignments: ¹H NMR (CDCl₃, 500 MHz, mixture of diastereomers *syn/anti* = 86/14, δ): 0.24 (s, 0.4H^{minor}, SiCH₃), 0.25 (s, 2.6H^{major}, SiCH₃), 0.27 (s, 0.4H^{minor}, SiCH₃), 0.28 (s, 2.6H^{major}, SiCH₃), 0.59 (dd, *J* = 14.6 Hz, 2.2 Hz, 0.9H^{major}, 4'-CH₂), 0.87 (dd, *J* = 14.9, 12.1 Hz, 0.1H^{minor}, 4'-CH₂), 1.04 (dd, *J* = 14.9, 2.4 Hz, 0.1H^{minor}, 4'-CH₂), 1.12 (dd, *J* = 14.6, 12.5 Hz, 0.9H^{major}, 4'-CH₂), 1.21–1.23 (m, 0.6H^{minor}, *i*-Pr-CH₃), eclipsed by 1.24 (d, ³J = 6.2 Hz, 2.4H^{major}, *i*-Pr-CH₃), and 1.25 (d, ³J = 6.2 Hz, 3H, *i*-Pr-CH₃), 2.51 (ddd, ³J = 12.0, 9.8, 2.3 Hz, 0.1H^{minor}, 4-CH), 2.61 (ddd, ³J = 12.2, 10.0, 2.0 Hz, 0.9H^{major}, 4-CH), 3.30 (s, 0.1H^{minor}, OH), 3.35 (s, 0.9H^{major}, OH), 4.92 (dd, *J* = 17.2, 1.5 Hz, 0.9H^{major}, 6-CH₂), eclipsed by 4.90–5.10 (m, 2H, 6-CH₂, *i*-Pr-H), 5.14 (dd, *J* = 10.5, 1.5 Hz, 0.9H^{major}, 1-CH₂), 5.24 (dd, *J* = 10.5, 1.6 Hz, 0.1H^{minor}, 1-CH₂), 5.38 (dd, *J* = 17.1, 1.5 Hz, 0.9H^{major}, 1-CH₂), 5.48 (dt, ³J = 17.3, 10.1 Hz, 0.9H^{major}, 5-CH), eclipsed by 5.49–5.52 (m, 0.1H^{minor}, 1-CH₂), 5.62 (dt, ³J = 17.2, 10.0 Hz, 0.1H^{minor}, 5-CH), 5.79 (dd, *J* = 17.0, 10.5 Hz, 0.1H^{minor}, 2-CH), eclipsed by 5.83 (dd, *J* = 17.1, 10.6 Hz, 0.9H^{major}, 2-CH), 7.30–7.36 (m, 3H, CH_{ar}), 7.43–7.49 (m, 2H, CH_{ar}); significant COSY cross peaks: 4-CH/4'-CH₂, 4-CH/5-CH; ¹³C NMR (CDCl₃, 101 MHz, mixture of diastereomers *syn/anti* = 86/14, δ): -2.5/-2.3 (SiMe₂), -1.5/-1.4 (SiMe₂), 13.8/15.8 (4'-CH₂), 21.8/21.9 (2×*i*-Pr-CH₃), 47.6/47.8 (4-CH), 70.3 (*i*-Pr-CH), 80.9 (3-C), 115.3/116.6 (1-CH₂), 117.4/117.8 (6-CH₂), 127.7/127.9 (2×CH_{ar}), 128.9/128.9 (CH_{ar}), 133.7/133.8 (2×CH_{ar}), 138.0/138.8 (5-CH), 138.3 (2-CH), 139.4 (C_{ar}), 174.4/174.6 (C=O); IR (cm⁻¹): 3505(br m) (ν OH), 3070(w), 3050(w), 3020(w), 2980(m), 2955(m), 2920(w), 1725(s) (ν C=O), 1640(w) (ν C=C), 1620(w) (ν C=C), 1465(w), 1455(w), 1425(m), 1400(w), 1385(w), 1375(m), 1260(s) (ν C-O-C ester), 1190(s), 1140(m), 1105(s), 1085(m), 1000(m); Anal. Calcd. for C₁₉H₂₈O₃Si: C, 68.6; H, 8.5; Found: C, 68.6; H, 8.2; C₁₉H₂₈O₃Si, M = 332.51 g/mol.

²⁷ The relative configuration was confirmed by x-ray analysis from crystals of the major diastereomer of (±)-**2f**: Nelson, B.; Schürmann, M.; Preut, H.; Hiersemann, M. *Acta Crystallogr., Sect. E: Struct. Rep.* **2010**, *66*, o3102.



1a, 3a	$R^Z = \text{H}, R^E = n\text{-Pr}, R^1 = i\text{-Pr}$ (48%, 1a/3a 89/11) (+ 4a <5%)
1b	$R^Z = \text{H}, R^E = \text{CH}_2\text{OTBS}, R^1 = \text{Me}$ (15%)
1c	$R^Z = \text{CH}_2\text{OTBS}, R^E = \text{H}, R^1 = i\text{-Pr}$ (14%)
1d	$R^Z = \text{H}, R^E = \text{CH}_2\text{OBn}, R^1 = i\text{-Pr}$ (18%)
1e	$R^Z = \text{CH}_2\text{OBn}, R^E = \text{H}, R^1 = \text{Me}$ (14%)
1f, 3f	$R^Z = \text{H}, R^E = \text{CH}_2\text{Si}(\text{Me})_2\text{Ph}, R^1 = i\text{-Pr}$ (68%, 1f/3f 91/9)

General procedure SI-F: Pd(II)-catalyzed cycloisomerization: The Pd-catalyst (0.05–0.1 eq) was added to a solution of 1,5-hexadiene (±)-**2** (1 eq) in CH_2Cl_2 (10 mL/mmol **2**) and the resulting mixture was stirred at the given temperature (reaction at elevated temperatures were carried out in a glass pressure-tube,²⁸ sealed with a teflon screwcap) until TLC indicated complete conversion of the starting material (2–19 h). The reaction mixture was filtered through a short silica gel-plug (eluent CH_2Cl_2 or ethyl acetate) to remove the catalyst and was then concentrated under reduced pressure. Purification by flash chromatography (cyclohexane/ethyl acetate) afforded the corresponding methylene cyclopentane (±)-**1** along with methyl cyclopentene (±)-**3** as a mixture of diastereomers.

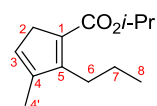
Cycloalkenes (±)-1a**, (±)-**3a** and **4a**:** According to the general procedure **SI-F**, 1,5-hexadiene (±)-**2a** (113 mg, 0.5 mmol) in CH_2Cl_2 (5 mL) was exposed to the cycloisomerization conditions with $[\text{Pd}(\text{MeCN})_4](\text{BF}_4)_2$ (11.1 mg, 0.025 mmol, 0.05 eq) at room temperature for 2 h. Purification by flash chromatography (cyclohexane/ethyl acetate 100/1) afforded methylene cyclopentane (±)-**1a** along with methyl cyclopentene (±)-**3a** (54 mg, 0.34 mmol, 48%, **1a/3a** = 89/11) as a mixture of diastereomers (*cis/trans* = 93/7). R_f 0.51 (cyclohexane/ethyl acetate 5/1); 2D $^1\text{H}, ^1\text{H}$ -COSY, 2D $^1\text{H}, ^{13}\text{C}$ -HSQC, 2D $^1\text{H}, ^{13}\text{C}$ -HMBC methods were used to confirm the NMR peak assignments:

^1H NMR (CDCl_3 , 500 MHz, mixture of regioisomers and diastereomers: **1a/3a** = 89/11, *cis-1a/trans-1a* = 93/7, δ): [$^{\text{“major”}}$ = *cis-1a*; $^{\text{“minor”}}$ = *trans-1a* + **3a**] 0.83–0.87 (m, $0.3\text{H}^{\text{minor}}$), 0.90 (t, $^3J = 7.3$ Hz, $2.7\text{H}^{\text{major}}$), 1.13–1.37 (m, 2H), eclipsed by 1.28 (d, $^3J = 6.2$ Hz, 3H), and 1.28 (d, $^3J = 6.2$ Hz, 3H), 1.39–1.54 (m, 2H), 1.69 (s, 0.3H), 1.82 (ddd, $J = 12.8, 8.4, 2.4$ Hz, $0.8\text{H}^{\text{major}}$), 1.86–1.98 (m, $0.2\text{H}^{\text{minor}}$), 2.09 (dt, $J = 12.6, 10.3$ Hz, $0.9\text{H}^{\text{major}}$), eclipsed by 2.12–2.18 (m, $0.1\text{H}^{\text{minor}}$), 2.27–2.42 (m, 0.2H), 2.47–2.66 (m, $1.8\text{H}^{\text{major}}$), 2.75–2.84 (m, $0.9\text{H}^{\text{major}}$), 2.92 (d, $J = 10.4$ Hz, $0.1\text{H}^{\text{minor}}$), 3.08 (s, $0.8\text{H}^{\text{major}}$), 3.23 (s, $0.1\text{H}^{\text{minor}}$), 3.33 (s, $0.1\text{H}^{\text{minor}}$), 4.82 (d, $J = 2.0$ Hz, $0.1\text{H}^{\text{minor}}$), 4.86 (d, $J = 2.4$ Hz, $0.9\text{H}^{\text{major}}$), 4.96 (d, $J = 2.2$ Hz, 1H), 5.04–5.08 (m, $0.1\text{H}^{\text{minor}}$), eclipsed by 5.10 (spt, $^3J = 6.2$ Hz, $0.9\text{H}^{\text{major}}$), 5.27–5.36 (m, $0.1\text{H}^{\text{minor}}$); (±)-*cis-1a*: R_f 0.51 (cyclohexane/ethyl acetate 5/1); ^1H NMR (CDCl_3 , 400 MHz, δ): 0.92 (t, $^3J = 7.3$ Hz, 3H, **8-CH₃**), 1.19–1.38 (m, 2H, **7-CH₂**), 1.30 (d, $^3J = 6.3$ Hz, 6H, *i*-Pr-CH₃), 1.53 (dt, $^3J = 7.3, 7.3$ Hz, 2H, **6-CH₂**), 1.84 (ddd, $J = 12.9, 8.2, 2.6$ Hz, 1H, **2-CH₂**), 2.11 (ddd, $J = 12.7, 10.3, 10.3$ Hz, 1H, **2-CH₂**), 2.52–2.68 (m, 2H, **3-CH₂**), 2.77–2.86 (m, 1H, **5-CH**), 3.12 (s, 1H, **OH**), 4.88 (d, $^3J = 2.3$ Hz, 1H, **4'-CH₂**), 4.98 (d, $^3J = 2.3$ Hz, 1H, **4'-CH₂**), 5.13 (spt, $^3J = 6.2$ Hz, 2H, *i*-Pr-H); ^{13}C NMR (CDCl_3 , 126 MHz, δ): 14.7 (**8-CH₃**), 21.1 (**7-CH₂**), 21.8 (*i*-Pr-CH₃), 21.9 (*i*-Pr-CH₃), 30.0 (**6-CH₂**), 30.4 (**3-CH₂**), 37.7 (**2-CH₂**), 51.8 (**5-CH**), 69.9 (*i*-Pr-CH), 81.9 (**1-C**), 105.8 (**4'-CH₂**), 153.5 (**4-C**), 176.7 (**C=O**); significant COSY cross peaks: 4'-CH₂/5-CH, 5-CH/6-CH₂, 3-CH₂/2-CH₂, significant HMBC cross peaks: 1-C/OH; IR (cm^{-1}): 3520(br m) (ν OH), 3075(w), 2980(s), 2960(s), 2935(s),

²⁸ SIGMA-Aldrich: Ace pressure tube, bushing type A, volume 15 mL (10.2 cm) or 35 mL (17.8 cm) with #7, Ace-Thred PTFE bushing and FETFE O-ring.

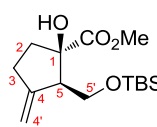
2875(m), 1720(s) (ν C=O), 1655(w) (ν C=C), 1465(m), 1375(m), 1295(m), 1270(s), 1235(s) (ν C-O-C ester), 1175(s), 1105(s), 1080(m), 1050(m); Anal. Calcd. for $C_{13}H_{22}O_3$: C, 69.0; H, 9.8; Found: C, 68.9; H, 9.7; $C_{13}H_{22}O_3$, $M = 226.31$ g/mol. (\pm)-**3a**: R_f 0.51 (cyclohexane/ethyl acetate 5/1); 1H NMR ($CDCl_3$, 500 MHz, mixture of diastereomers *cis/trans* = 91/9, δ): 0.90 (t, $^3J = 7.3$ Hz, 3H, **8-CH₃**), 1.10–1.23 (m, 1H, **7-CH₂**), 1.28 (d, $^3J = 6.3$ Hz, 3H, ***i*-Pr-CH₃**), eclipsed by 1.28 (d, $^3J = 6.3$ Hz, 3H, ***i*-Pr-CH₃**), and 1.30–1.39 (m, 1H, **7-CH₂**), 1.40–1.50 (m, 1H, **6-CH₂**), 1.52–1.61 (m, 1H, **6-CH₂**), 1.62–1.63 (m, 0.3H^{minor}, **4'-CH₃**), 1.69 (dd, $^4J = 2.6$, 1.1 Hz, 2.7H^{major}, **4'-CH₃**), 2.38 (d, $^3J = 16.3$ Hz, 0.9H^{major}, **2-CH₂**), 2.45–2.81 (m, 0.1H^{minor}, **2-CH₂**) 2.82 (ddd, $J = 16.2$, 4.5, 2.0 Hz, 1H, **2-CH₂**), 2.88–2.94 (m, 1H, **5-CH**), 3.23 (s, 0.9H^{major}, **OH**), 3.35 (s, 0.1H^{minor}, **OH**), 5.11 (spt, $^3J = 6.3$ Hz, 1H, ***i*-Pr-CH**), 5.32 (br s, 0.9H^{major}, **3-CH**), 5.67 (br s, 0.1H^{minor}, **3-CH**); ^{13}C NMR ($CDCl_3$, 126 MHz, mixture of diastereomers *cis/trans* > 95/5, δ): 14.6 (**8-CH₃**), 15.2 (**4'-CH₃**), 21.2 (**7-CH₂**), 21.8 (***i*-Pr-CH₃**), 28.9 (**6-CH₂**), 46.4 (**2-CH₂**), 55.6 (**5-CH**), 69.8 (***i*-Pr-CH**), 81.7 (**1-C**), 120.5 (**3-CH**), 140.9 (**4-C**), 177.6 (**C=O**); no significant COSY cross peaks; IR (cm^{-1}): 3520(br s) (ν OH), 3045(m), 2960(s), 2935(s), 1715(s) (ν C=O), 1660(m) (ν C=C), 1465(s), 1455(s), 1375(s), 1240(s) (ν C-O-C ester), 1200(s), 1180(s), 1105(s), 1050(s); Anal. Calcd. for $C_{13}H_{22}O_3$: C, 69.0; H, 9.8; Found: C, 96.0; H, 9.6; $C_{13}H_{22}O_3$, $M = 226.31$ g/mol.

At longer reaction times, small quantities of cyclopentadiene **4a** ($\leq 5\%$) could be isolated: **4a**: R_f 0.57 (cyclohexane/ethyl acetate 5/1); 2D 1H , 1H -COSY, 2D 1H , ^{13}C -HSQC, 2D 1H , ^{13}C -HMBC methods



were used to confirm the NMR peak assignments: 1H NMR ($CDCl_3$, 500 MHz, δ): 0.99 (t, $^3J = 7.4$ Hz, 3H, **8-CH₃**), 1.29 (d, $^3J = 6.3$ Hz, 6H, **2*x*-*i*-Pr-CH₃**), 1.47–1.56 (m, 2H, **7-CH₂**), 1.97 (d, $^3J = 1.6$ Hz, 3H, **4'-CH₃**), 2.72 (t, $^3J = 7.7$ Hz, 2H, **6-CH₂**), 3.18 (br s, 2H, **2-CH₂**), 5.11 (spt, $^3J = 6.2$ Hz, 1H, ***i*-Pr-H**), 6.21 (d, $J = 1.0$ Hz, 1H, **3-CH**), resonance at 0.85–0.87 (m) and 1.26 (br s) belong to H-grease⁵; ^{13}C NMR ($CDCl_3$, 126 MHz, δ): 13.8 (**4'-CH₃**), 14.5 (**8-CH₃**), 22.3 (***i*-Pr-CH₃**), 22.9 (**7-CH₂**), 29.4 (**6-CH₂**), 40.8 (**2-CH₂**), 66.7 (***i*-Pr-CH**), 130.5 (**1-C**), 132.8 (**3-CH**), 144.2 (**4-C**), 159.9 (**5-C**), 164.8 (**C=O**); resonance at 29.8 belongs to H-grease⁵; significant COSY cross peaks: **6-CH₂/7-CH₂**, **3-CH/2-CH₂**, **3-CH/4'-CH₃**; significant HMBC cross peaks: **3-CH/4'-CH₃**, **3-CH/1-C**, **3-CH/5-C**, **4'-CH₃/4-C**, **7-CH₂/5-C**; IR (cm^{-1}): 2960(w), 2925(m), 2855(w), 1700(s) (ν C=O), 1620(w) (ν C=C), 1555(w), 1455(w), 1385(s) (δ CH₃), 1310(m), 1245(m), 1225(s) (ν C-O-C ester), 1210(m), 1110(m), 1085(s); HRMS (ESI) Calcd. for $C_{13}H_{21}O_2$ ($[M+H]^+$): 209.15361, Found: 209.15359; $C_{13}H_{20}O_2$, $M = 208.30$ g/mol.

Methylene cyclopentane (\pm)-1b: According to the general procedure **SI-F**, 1,5-hexadiene (\pm)-**2b** (60 mg, 0.2 mmol) in CH_2Cl_2 (4 ml, 20 mL/mmol **2b**) was exposed to the cycloisomerization conditions with $[Pd(MeCN)_4](BF_4)_2$ (9 mg, 0.02 mmol, 0.1 eq) at 40 °C for 3 h. Purification by flash chromatography (cyclohexane/ethyl acetate 100/1) afforded methylene cyclopentane (\pm)-**1b** (9 mg, 0.03 mmol, 15%,) as a single diastereomer (*cis/trans* > 95/5). R_f 0.46 (cyclohexane/ethyl acetate 10/1); 2D



1H , 1H -COSY, 2D 1H , ^{13}C -HSQC methods were used to confirm the NMR peak assignments; the relative configuration was assigned by 2D 1H , 1H -NOESY experiments: 1H NMR ($CDCl_3$, 500 MHz, δ): 0.04 (s, 3H, **TBS-CH₃**), 0.04 (s, 3H, **TBS-CH₃**), 0.87 (s, 9H, **TBS-*t*-Bu-CH₃**), 1.88 (ddd, $J = 12.7$, 8.1, 1.3 Hz, 1H, **2-CH₂^{Re}**), 2.06 (ddd, $J = 12.0$, 9.4 Hz, 1H, **2-CH₂^{Si}**), 2.47–2.55 (m, 1H, **3-CH₂**), 2.58–2.68 (m, 1H, **3-CH₂**), 3.15 (ddd, $J = 8.2$, 5.4, 2.4 Hz, 1H, **5-CH**), 3.55 (br s, 1H, **OH**), 3.72–3.86 (m, 2H, **5'-CH₂**), eclipsed by 3.76 (s, 3H, **OMe**), 4.76 (d, $J = 2.2$ Hz, 1H, **4'-CH₂**), 4.98 (d, $J = 1.8$ Hz, 1H, **4'-CH₂**); ^{13}C NMR ($CDCl_3$, 126 MHz, δ): -5.5 (**TBS-CH₃**), -5.5 (**TBS-CH₃**), 18.4 (**TBS-*t*-Bu-C**), 26.0 (**3*x*-TBS-*t*-Bu-CH₃**), 31.2 (**3-CH₂**), 37.5 (**2-CH₂**), 52.7 (**OMe**), 54.1 (**5-CH**), 61.6 (**5'-CH₂**), 81.8 (**1-C**), 106.7 (**4'-CH₂**), 149.7 (**4-C**), 176.6 (**C=O**); significant COSY cross peaks: **3-CH₂/2-CH₂**, **5-CH/5'-CH₂**; significant NOESY cross peaks: **5-CH/2-CH₂^{Si}**, **OH/2-CH₂^{Re}**; IR (cm^{-1}): 3525(br m) (ν OH), 2955(s), 2930(s), 2860(m), 1735(s)

(ν C=O), 1240(s) (ν C-O-C ester), 1175(m), 1085(s), Anal. Calcd. for $C_{15}H_{28}O_4Si$: C, 60.0; H, 9.4; Found: C, 59.9; H, 9.5; $C_{15}H_{28}O_4Si$, M = 300.47 g/mol.

Methylene cyclopentane (\pm)-1c: According to the general procedure **SI-F**, 1,5-hexadiene (\pm)-**2c** (133 mg, 0.4 mmol) in CH_2Cl_2 (4 mL) was exposed to the cycloisomerization conditions with $[Pd(MeCN)_4](BF_4)_2$ (8.8 mg, 0.02 mmol, 0.05 eq) at room temperature for 16 h. Purification by flash chromatography (cyclohexane/ethyl acetate 200/1) afforded methylene cyclopentane (\pm)-**1c** (18 mg, 0.05 mmol, 14%,) as a single diastereomer (*cis/trans* < 5/95). R_f 0.54 (cyclohexane/ethyl acetate 5/1); 1H NMR ($CDCl_3$, 600 MHz, δ): 0.05 (s, 3H), 0.06 (s, 3H), 0.89 (s, 9H), 1.25 (d, $^3J = 6.1$ Hz, 3H), 1.26 (d, $^3J = 6.2$ Hz, 3H), 1.91 (ddd, $J = 13.2, 9.4$ Hz, 1H), 2.14 (ddd, $J = 13.3, 8.4, 4.9$ Hz, 1H), 2.48–2.60 (m, 3H), 2.85 (ddd, $J = 8.3, 5.9, 2.4$ Hz, 1H), 3.53 (br s, 1H), 3.65 (dd, $J = 10.1, 9.0$ Hz, 1H), 3.82 (dd, $J = 10.1, 6.2$ Hz, 1H), 4.77 (dd, $J = 2.3$ Hz, 1H), 4.87 (dd, $J = 2.1$ Hz, 1H), 5.05 (spt, $^3J = 6.3$ Hz, 1H); ^{13}C NMR ($CDCl_3$, 126 MHz, δ): -5.4 (CH_3), -5.4 (CH_3), 18.3 (C), 21.9 (CH_3), 22.0 (CH_3), 26.0 ($3\times CH_3$), 30.4 (CH_2), 35.6 (CH_2), 57.1 (CH), 63.4 (CH_2), 69.3 (CH), 83.2 (C), 106.4 (CH_2), 150.1 (C), 174.4 (C); IR (cm^{-1}): 3480(br m) (ν OH), 2955(s), 2930(s), 2855(m), 1725(s) (ν C=O), 1650(m) (ν C=C), 1470(m), 1385(s), 1255(s) (ν C-O-C ester), 1220(m), 1105(s); Anal. Calcd. for $C_{17}H_{32}O_4Si$: C, 62.2; H, 9.8; Found: C, 62.2; H, 9.6; $C_{17}H_{32}O_4Si$, M = 328.52 g/mol.

Methylene cyclopentane (\pm)-1d: According to the general procedure **SI-F**, 1,5-hexadiene (\pm)-**2d** in CH_2Cl_2 was exposed to the cycloisomerization conditions with $[Pd(MeCN)_4](BF_4)_2$ (0.05 eq) at room temperature for 4 h. Purification by flash chromatography afforded methylene cyclopentane (\pm)-**1d** (18%) as a single diastereomer (*cis/trans* > 95/5). 1H NMR ($CDCl_3$, 300 MHz, δ): 1.16 (d, $^3J = 6.2$ Hz, 3H), 1.22 (d, $^3J = 6.3$ Hz, 3H), 1.87 (ddd, $J = 12.8, 8.1, 1.7$ Hz, 1H), 2.09 (ddd, $J = 12.1, 9.4$ Hz, 1H), 2.49–2.57 (m, 1H), 2.58–2.68 (m, 1H), 3.20–3.28 (m, 1H), 3.42 (br s, 1H), 3.60–3.70 (m, 2H), 4.41–4.52 (m, 2H), 4.78 (dd, $J = 4.6, 2.3$ Hz, 1H), 4.97 (dd, $J = 4.6, 2.3$ Hz, 1H), 5.03 (spt, $^3J = 6.3$ Hz, 1H), 7.24–7.36 (m, 5 H); resonance at 0.85–0.87 (m) and 1.26 (br s) belong to H-grease⁵; ^{13}C NMR ($CDCl_3$, 76 MHz, δ): 21.6 (CH_3), 21.8 (CH_3), 30.9 (CH_2), 37.2 (CH_2), 52.3 (CH), 68.2 (CH_2), 69.7 (CH), 73.4 (CH_2), 81.4 (C), 106.7 (CH_2), 127.7 (CH_{ar}), 127.8 ($2\times CH_{ar}$), 128.4 ($2\times CH_{ar}$), 138.4 (C_{ar}), 149.7 (C), 175.7 (C); resonance at 29.8 belongs to H-grease⁵; IR (cm^{-1}): 3510, 3070–3030, 2980–2860, 1725; Anal. Calcd. for $C_{18}H_{24}O_4$: C, 71.03; H, 7.95; Found: C, 71.26; H, 8.27; $C_{18}H_{24}O_4$, M = 304.38 g/mol.

Methylene cyclopentane (\pm)-1e: According to the general procedure **SI-F**, 1,5-hexadiene (\pm)-**2e** (110 mg, 0.4 mmol) in CH_2Cl_2 (4 mL) was exposed to the cycloisomerization conditions with $[Pd(MeCN)_4](BF_4)_2$ (8.8 mg, 0.02 mmol, 0.05 eq) at room temperature for 16 h. Purification by flash chromatography (cyclohexane/ethyl acetate 100/1 \rightarrow 50/1) afforded methylene cyclopentane (\pm)-**1e** (18 mg, 0.05 mmol, 14%,) as a mixture of diastereomers (*cis/trans* = 6/94). R_f 0.26 (cyclohexane/ethyl acetate 5/1); 2D 1H , 1H -COSY, 2D 1H , ^{13}C -HSQC and 2D 1H , ^{13}C -HMBC methods were used to confirm the NMR peak assignments: 1H NMR ($CDCl_3$, 500 MHz, mixture of diastereomers *cis/trans* = 6/94, δ): 1.89–2.00 (m, 1H, 2- CH_2), 2.18–2.26 (m, 1H, 2- CH_2), 2.46–2.66 (m, 2H, 3- CH_2), 2.96–3.02 (m, 1H, 5-CH), 3.41–3.48 (m, 2H, OH+5'- CH_2), 3.61–3.67 (m, 4H, 5'- CH_2 +OMe), 4.40–4.49 (m, 2H, OCH_2Ph), 4.82 (d, $J = 2.3$ Hz, 0.9H^{major}, 4'- CH_2), 4.94 (d, $J = 1.9$ Hz, 0.9H^{major}, 4'- CH_2), 5.03–5.07 (m, 0.1H^{minor}, 4'- CH_2), 5.15–5.18 (m, 0.1H^{minor}, 4'- CH_2), 7.19–7.44 (m, 5H, Ar); ^{13}C NMR ($CDCl_3$, 126 MHz, mixture of diastereomers *cis/trans* = 6/94, δ): 30.4 (3- CH_2), 35.3 (2- CH_2), 52.4 (OMe), 56.0 (5-CH), 70.5 (5'- CH_2), 73.5 (OCH_2Ph), 83.3 (1-C), 107.2 (4'- CH_2), 127.8 ($2\times CH_{ar}$), 127.8 ($2\times CH_{ar}$), 128.5 (CH_{ar}), 138.0 (C_{ar}),

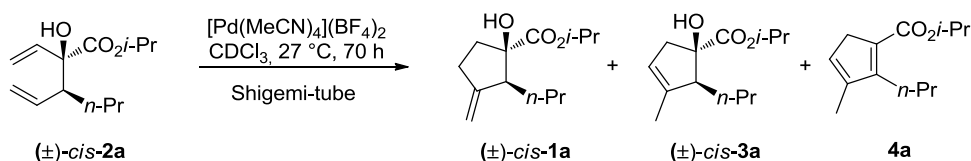
149.5 (4-C), 175.4 (C=O); significant COSY cross peaks: 4'-CH₂/3-CH₂, 5-CH/4'-CH₂, 5-CH/5'-CH₂; significant HMBC cross peaks: 3-CH₂/4'-CH₂, 3-CH₂/4-C, 2-CH₂/4-C; 3-CH₂/2-CH₂; IR (cm⁻¹): 3520(br w) (ν OH), 3030(w), 2955(m), 2865(m), 1730(s) (ν C=O), 1655(w) (ν C=C), 1495(w), 1455(m), 1385(m), 1265(m), 1220(m) (ν C-O-C ester), 1170(m), 1115(m); HRMS (ESI) Calcd. for C₁₆H₂₁O₄ ([M+H]⁺): 277.14344, Found: 277.14388; C₁₆H₂₀O₄, M = 276.33 g/mol.

Cycloalkenes (±)-1f and (±)-3f: According to the general procedure **SI-F**, 1,5-hexadiene (±)-**2f** (166 mg, 0.5 mmol) in CH₂Cl₂ (5 mL) was exposed to the cycloisomerization conditions with [Pd(MeCN)₄](BF₄)₂ (11 mg, 0.025 mmol, 0.05 eq) at 40 °C for 3.5 h. Purification by flash chromatography (cyclohexane/ethyl acetate 100/1 → 50/1) afforded methylene cyclopentane (±)-*cis*-**1f** (97 mg, 0.29 mmol, 58%, *cis/trans* = 95/5) along with cycloalkenes (±)-*trans*-**1f** and (±)-**3f** (16 mg, 0.05 mmol, 10%, (±)-*trans*-**1f**/(±)-**3f** = 39/61). (±)-*cis*-**1f**: R_f 0.43 (cyclohexane/ethyl acetate 5/1); 2D ¹H,¹H-COSY, 2D ¹H,¹³C-HSQC methods were used to confirm the NMR peak assignments; the relative configuration was assigned using 2D ¹H,¹H-NOESY experiments: ¹H NMR (CDCl₃, 500 MHz, mixture of diastereomers *cis/trans* = 95/5, δ): 0.28 (s, 3H, SiMe₂), 0.31 (s, 3H, SiMe₂), 0.82–0.84 (m, 0.2H^{minor}, 5'-CH₂), 0.87 (dd, *J* = 15.4, 3.3 Hz, 0.9H^{major}, 5'-CH₂), 0.96 (dd, *J* = 15.4, 8.8 Hz, 0.9H^{major}, 5'-CH₂), 1.15 (d, ³*J* = 6.2 Hz, 3H, *i*-Pr-CH₃), 1.23 (d, ³*J* = 6.2 Hz, 3H, *i*-Pr-CH₃), 1.86 (ddd, *J* = 13.0, 6.3, 6.2 Hz, 1H, 2-CH₂^{Re}), 2.19 (ddd, *J* = 13.4, 9.8 Hz, 1H, 2-CH₂^{Si}), 2.49–2.58 (m, 2H, 3-CH₂), 2.74–2.82 (m, 1H, 5-CH), 3.04 (s, 1H, OH), 4.66–4.68 (m, 0.1H^{minor}, 4'-CH₂), 4.71 (dd, *J* = 2.6 Hz, 0.9H^{major}, 4'-CH₂), 4.76–4.78 (m, 0.1H^{minor}, 4'-CH₂), 4.91 (dd, *J* = 2.6 Hz, 1H, 4'-CH₂), 4.96 (spt, ³*J* = 6.2 Hz, 1H, *i*-Pr-CH), 7.30–7.37 (m, 3H, Ar), 7.44–7.53 (m, 2H, Ar); ¹³C NMR (CDCl₃, 126 MHz, mixture of diastereomers *cis/trans* = 95/5, δ): -2.0 (SiMe₂), -1.9 (SiMe₂), 12.7 (5'-CH₂), 21.8 (*i*-Pr-CH₃), 21.9 (*i*-Pr-CH₃), 29.7 (3-CH₂), 35.6 (2-CH₂), 49.0 (5-CH), 70.0 (*i*-Pr-CH), 83.4 (1-C), 107.1 (4'-CH₂), 127.9 (2×CH_{ar}), 129.1 (CH_{ar}), 133.7 (2×CH_{ar}), 139.5 (C_{ar}), 153.9 (4-C), 175.6 (C=O); significant COSY cross peaks: 5-CH/4'-CH₂, 4'-CH₂/3-CH₂, 3-CH₂/2-CH₂, 5-CH/5'-CH₂; significant NOESY cross peaks: OH/2-H^{Re}, 5-H/2-H^{Si}; IR (cm⁻¹): 3515(br m) (ν OH), 3070(m), 3050(m), 2990(s), 2955(s), 1720(s) (ν C=O), 1660(m) (ν C=C), 1465(m), 1425(s), 1375(s), 1335(w), 1300(m), 1250(s) (ν C-O-C ester), 1215(m), 1185(s), 1145(m), 1075(s), 1050(m); Anal. Calcd. for C₁₉H₂₈O₃Si: C, 68.6; H, 8.5; Found: C, 68.6; H, 8.3; C₁₉H₂₈O₃Si, M = 332.51 g/mol. (±)-*trans*-**1f** and (±)-**3f**: R_f 0.51 (cyclohexane/ethyl acetate 5/1); ¹H NMR (CDCl₃, 400 MHz, mixture of regioisomers *trans*-**1f**/**3f** = 39/61, δ): 0.28–0.29 (m, 3.6H^{3f}), 0.32 (s, 2.4H^{1f}), 0.81–0.94 (m, 2H^{3f+1f}), 1.08–1.30 (m, 7H^{3f+1f}), 1.61 (br s, 1.75H^{3f}), 1.89 (ddd, *J* = 13.5, 11.1, 8.8 Hz, 0.4H^{1f}), 2.12 (ddd, *J* = 13.4, 9.5, 3.6 Hz, 0.4H^{1f}), 2.38–2.42 (m, 0.6H^{3f}), 2.47–2.51 (m, 0.4H^{1f}), 2.51–2.57 (m, 0.4H^{1f}), 2.61–2.65 (m, 0.4H^{1f}), 2.80 (dd, *J* = 16.6, 1.8 Hz, 0.6H^{3f}), 2.95–3.01 (m, 0.6H^{3f}), 3.16 (s, 0.6H^{3f}), 3.38 (s, 0.4H^{1f}), 4.66–4.71 (m, 0.4H^{1f}), 4.77–4.86 (m, 0.4H^{1f}), 4.96 (spt, ³*J* = 6.3 Hz, 0.6H^{3f}), eclipsed by 5.03 (spt, ³*J* = 6.3 Hz, 0.4H^{1f}), 5.26 (br s, 0.6H^{3f}), 7.30–7.37 (m, 3H^{3f+1f}), 7.45–7.56 (m, 2H^{3f+1f}); C₁₉H₂₈O₃Si, M^{3f,1f} = 332.51 g/mol.

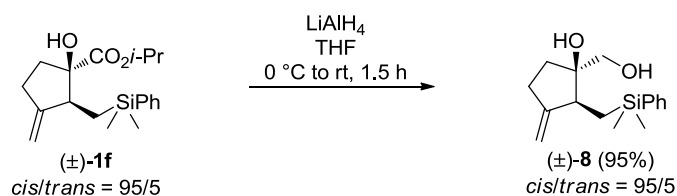
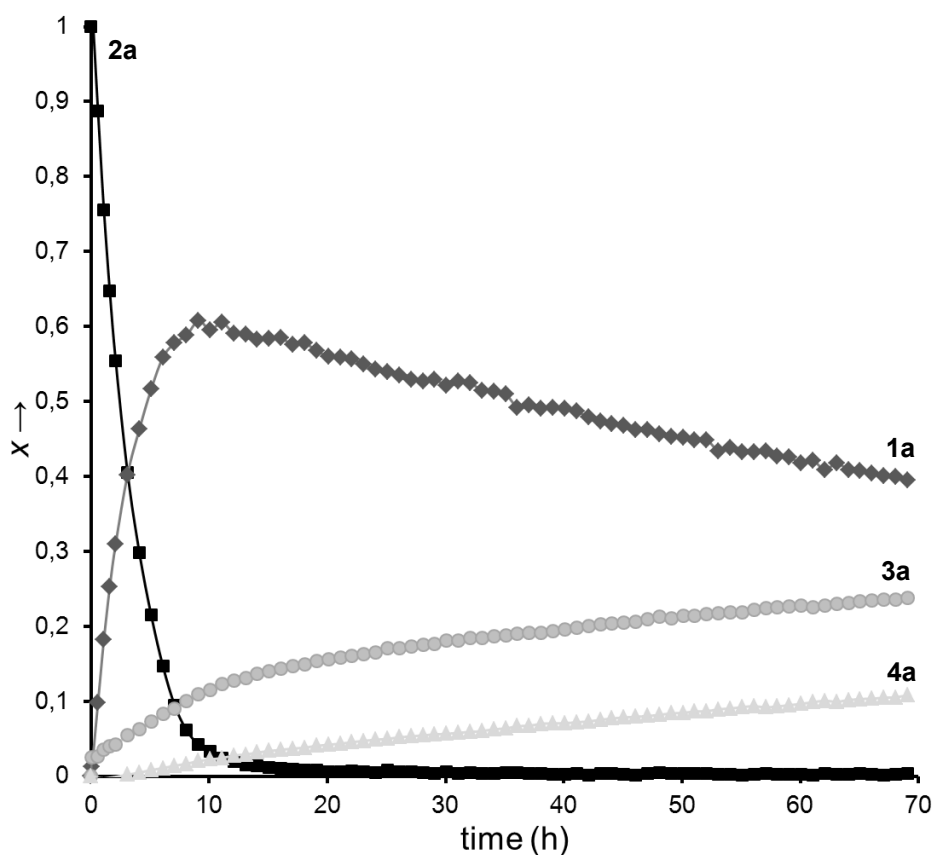
Table 1: product distribution for the cycloisomerization of (±)-**2f** under various conditions.

entry	scale (mmol)	catalyst batch	time (h)	yield ^a (%)	
				<i>cis</i> - 1f	<i>trans</i> - 1f + 3f
1	0.4	synth. (new)	4	56	8
2	1.5	comm. (new)	4	43 ^b	8 ^b
3	0.9	synth. (old)	3	39 ^b	13 ^b
4	0.5	comm. (new)	3	51	9
5	0.5	comm. (new)	3.5	58	10
6	0.5	comm. (new)	4	55	12

^a Isolated yield after column chromatography. ^b *cis*-**1f**/*trans*-**1f**/**3f** determined by ¹H NMR spectroscopy.



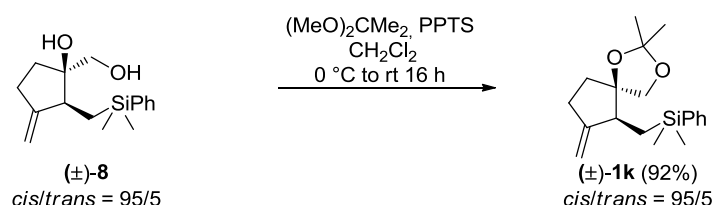
Pd(II)-catalyzed cycloisomerization: ^1H NMR kinetic experiment: A solution of hexadiene $(\pm)\text{-cis-2a}$ (4.5 mg, 0.02 mmol, 1 eq) in CDCl_3 (0.2 mL, 10 mL/mmol **2a**) was added to an oven-dried Shigemi-tube²⁹ under argon. The tube was sealed with a septum and a ^1H NMR spectrum was recorded (substrate spectrum). $[\text{Pd}(\text{MeCN})_4](\text{BF}_4)_2$ (0.05 mg, 0.001 mmol, 0.05 eq) was added and the evolution of the reaction was monitored by ^1H NMR spectroscopy in intervals of 0 h, 0.5 h, 1.5 h, 2 h, 3 h, ..., up to 69 h. The degree of conversion was determined in reference to the substrate spectrum.



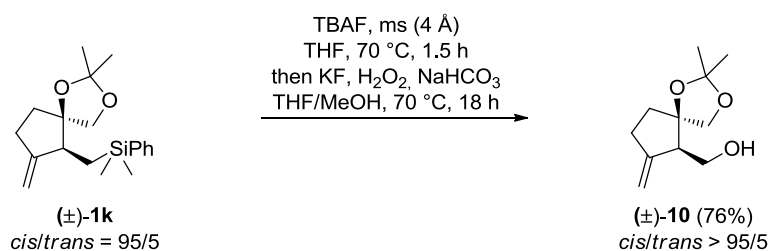
Diol $(\pm)\text{-8}$: Methylene cyclopentane **1f** (69 mg, 0.21 mmol, 1 eq) was added to a suspension of LiAlH_4 (24 mg, 0.62 mmol, 3 eq) in THF (1 mL, 5 mL/mmol **1f**) at 0°C . The cooling bath was removed and the reaction mixture was stirred at room temperature for a period of 1.5 h. The grey suspension was carefully diluted with ethyl acetate (5 mL) and saturated aqueous Na/K tartrate solution

²⁹ Rototec-Spintec GmbH: 5 mm OD Shigemi symmetrical microtube; solvent: CDCl_3 ; system: Varian.

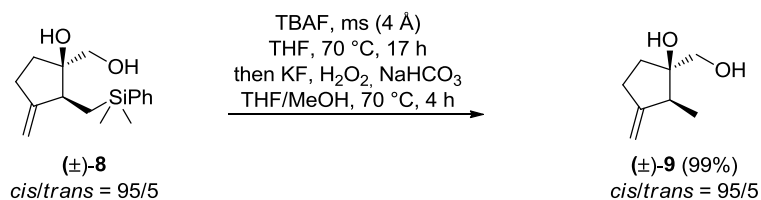
(10 mL) at 0 °C. The aqueous layer was extracted with ethyl acetate (3×) and the combined organic phases were dried (MgSO₄) and concentrated under reduced pressure. Purification by flash chromatography (cyclohexane/ethyl acetate 20/1 → 5/1) afforded diol (±)-**8** (55 mg, 0.2 mmol, 95%) as a mixture of diastereomers (*cis/trans* = 95/5). *R*_f 0.34 (cyclohexane/ethyl acetate 1/1); ¹H NMR (CDCl₃, 400 MHz, mixture of diastereomers *cis/trans* > 95/5, δ): 0.33 (s, 3H), 0.35 (s, 3H), 0.81 (dd, *J* = 15.2, 8.6 Hz, 1H), 1.07 (dd, *J* = 15.2, 3.2 Hz, 1H), 1.43 (br s, 1H), 1.66 (s, 1H), 1.77 (dd, *J* = 9.2, 7.4 Hz, 2H), 2.21–2.30 (m, 1H), 2.30–2.39 (m, 1H), 2.40–2.53 (m, 1H), 3.27 (dd, *J* = 11.1, 4.5 Hz, 1H), 3.40 (dd, *J* = 10.9, 2.3 Hz, 1H), 4.76 (dd, *J* = 4.4, 2.1 Hz, 1H), 4.89 (dd, *J* = 4.3, 2.0 Hz, 1H), 7.34–7.40 (m, 3H), 7.50–7.58 (m, 2H); ¹³C NMR (CDCl₃, 101 MHz, mixture of diastereomers *cis/trans* = 95/5, δ): –2.7 (CH₃), –2.0 (CH₃), 13.2 (CH₂), 28.5 (CH₂), 33.5 (CH₂), 45.8 (CH), 67.7 (CH₂), 82.2 (C), 107.4 (CH₂), 128.1 (2×CH_{ar}), 129.3 (CH_{ar}), 133.7 (2×CH_{ar}), 139.3 (C_{ar}), 155.2 (C); IR (cm^{–1}): 3410(br s) (ν OH), 3070(m), 3050(m), 2950(s), 1655(m) (ν C=C), 1425(s), 1385(m), 1250(s), 1115(s), 1070(m), 1030(m); Anal. Calcd. for C₁₆H₂₄O₂Si: C, 69.5; H, 8.8; Found: C, 69.5; H, 8.9; C₁₆H₂₄O₂Si, *M* = 276.45 g/mol.



Acetal (±)-1k: A solution of diol **8** (105 mg, 0.38 mmol, 1 eq) in CH₂Cl₂ (1 mL, 3 mL/mmol **8**) was subsequently treated with 2,2-dimethoxypropane (0.07 mL, 0.57 mmol, 1.5 eq) and pyridinium *p*-toluenesulfonate (PPTS) (14 mg, 0.06 mmol, 0.15 eq) at 0 °C. The cooling bath was removed and the resulting mixture was stirred overnight (16 h) at room temperature. The reaction mixture was diluted by the addition of saturated aqueous NaHCO₃ solution and the aqueous layer was extracted with CH₂Cl₂ (3×). The combined organic phases were dried (MgSO₄) and concentrated under reduced pressure. Purification by flash chromatography (cyclohexane/ethyl acetate 200/1) afforded acetal (±)-**1k** (111 mg, 0.35 mmol, 92%) as a mixture of diastereomers (*cis/trans* = 95/5). *R*_f 0.37 (cyclohexane/ethyl acetate 10/1); ¹H NMR (CDCl₃, 400 MHz, mixture of diastereomers *cis/trans* = 95/5, δ): 0.31 (s, 3H), 0.33 (s, 3H), 0.72 (dd, *J* = 14.8, 10.2 Hz, 0.1H^{minor}), 0.81 (dd, *J* = 15.3, 10.3 Hz, 0.9H^{major}), 1.10 (dd, *J* = 14.9, 1.9 Hz, 0.1H^{minor}), 1.24 (dd, *J* = 15.3, 2.4 Hz, 0.9H^{major}), 1.37 (s, 5.6H^{major}), eclipsed by 1.40 (s, 0.4H^{minor}), 1.72 (ddd, *J* = 13.2, 9.8, 6.2 Hz, 1H), 1.89–1.97 (m, 0.1H^{minor}), 2.08 (ddd, *J* = 13.2, 10.6, 5.7 Hz, 0.9H^{major}), 2.16–2.29 (m, 2H), 2.40–2.52 (m, 0.9H^{major}), 2.53–2.59 (m, 0.1H^{minor}), 3.61 (d, ²*J* = 8.5 Hz, 0.1H^{minor}), eclipsed by 3.64 (d, ²*J* = 8.4 Hz, 0.9H^{major}), 3.72 (d, ²*J* = 8.4 Hz, 0.9H^{major}), 3.84 (d, ²*J* = 8.6 Hz, 0.1H^{minor}), 4.69 (dd, *J* = 4.1, 2.2 Hz, 0.1H^{minor}), 4.73 (dd, *J* = 4.0, 2.7 Hz, 0.9H^{major}), 4.77 (d, *J* = 2.6 Hz, 0.1H^{minor}), eclipsed by 4.79 (dd, *J* = 4.0, 2.7 Hz, 0.9H^{major}), 7.32–7.38 (m, 3H), 7.49–7.56 (m, 2H); ¹³C NMR (CDCl₃, 101 MHz, mixture of diastereomers *cis/trans* = 95/5, δ): –2.3 (CH₃), –1.6 (CH₃), 13.4/14.0 (CH₂), 26.6 (CH₃), 26.9 (CH₃), 28.0 (CH₂), 34.2/35.5 (CH₂), 47.7/48.0 (CH), 69.7/73.2 (CH₂), 89.4 (C), 107.2/107.7 (CH₂), 109.5 (C), 127.9 (2×CH_{ar}), 129.0 (CH_{ar}), 133.8 (2×CH_{ar}), 139.6 (C_{ar}), 153.6 (C); IR (cm^{–1}): 3070(m), 3050(m), 2985(s), 2955(s), 2860(s), 1660(m) (ν C=C), 1455(m), 1425(s), 1380(s), 1370(s), 1250(s), 1210(s), 1155(s), 1115(s), 1060(s); Anal. Calcd. for C₁₉H₂₈O₂Si: C, 72.1; H, 8.9; Found: C, 72.2; H, 9.0; C₁₉H₂₈O₂Si, *M* = 316.51 g/mol.



Tamao–Fleming Oxidation^{30,31}: Alcohol (±)-10: To TBAF (1 mL, 1 mmol, 10 eq, 1 M in THF) in a pressure tube²⁸ were added pulverized, activated molecular sieves (4 Å) (200 mg, 0.2 g/mmol TBAF) and the resulting suspension was stirred at room temperature for 15 min. Subsequently, a solution of acetal (±)-1k (32 mg, 0.1 mmol, 1 eq) in THF (1 mL, 10 mL/mmol 1k) was added and the resulting mixture was stirred at 70 °C for a period of 1.5 h. The brown suspension was allowed to cool down to room temperature, where it was successively treated with KF (20 mg, 0.35 mmol, 3.5 eq), NaHCO₃ (19 mg, 0.23 mmol, 2.3 eq), MeOH (1 mL, 1 mL/mL THF) and H₂O₂ (0.3 mL, 3 mL/mmol 1k, 35% in H₂O). The resulting suspension was stirred at 70 °C overnight (18 h). The reaction mixture was filtered and the filter cake washed with ethyl acetate (3×3 mL) and water (10 mL). The aqueous layer was extracted with ethyl acetate (3×), the combined organic phases were dried (MgSO₄) and subsequently concentrated under reduced pressure. Purification by flash chromatography (cyclohexane/ethyl acetate 50/1 → 10/1) afforded alcohol (±)-10 (15 mg, 0.05 mmol, 76%) as a single diastereomer. *R_f* 0.2 (cyclohexane/ethyl acetate 5/1); 2D ¹H, ¹H-COSY, 2D ¹H, ¹³C-HSQC methods were used to confirm the NMR peak assignments: ¹H NMR (CDCl₃, 400 MHz, δ): 1.42 (s, 3H, O₂CMe₂), 1.46 (s, 3H, O₂CMe₂), 1.83 (ddd, *J* = 13.1, 8.1, 6.7 Hz, 1H, 2-CH₂), 1.99 (ddd, *J* = 12.9, 8.8, 7.3 Hz, 1H, 2-CH₂), 2.24–2.34 (m, 1H, 3-CH₂), 2.45–2.52 (m, 1H, 3-CH₂), 2.53–2.59 (m, 1H, 5-CH), 2.98 (dd, ³*J* = 8.4, 4.7 Hz, 1H, OH), 3.68 (ddd, *J* = 11.7, 8.3, 4.3 Hz, 1H, 5'-CH₂), 3.86 (ddd, *J* = 11.4, 8.3, 4.6 Hz, 1H, 5'-CH₂), 3.94 (s, 2H, 1'-CH₂), 4.92 (dd, *J* = 4.3, 2.2 Hz, 1H, 4'-CH₂), 5.00 (dd, *J* = 4.3, 2.1 Hz, 1H, 4'-CH₂); ¹³C NMR (CDCl₃, 101 MHz, δ): 26.4 (O₂CMe₂), 26.6 (O₂CMe₂), 29.9 (3-CH₂), 35.7 (2-CH₂), 52.8 (5-CH), 63.4 (5'-CH₂), 73.7 (1'-CH₂), 89.9 (1-C), 108.5 (4'-CH₂), 109.9 (O₂CMe₂), 149.0 (4-C); significant COSY cross peaks: 4'-CH₂/3-CH₂, 5'-CH₂/OH, 5'-CH₂/5-CH; IR (cm⁻¹): 3465(br s) (ν OH), 3075(w), 2985(s), 2960(s), 2930(s), 2870(s), 1710(m), 1655(m) (ν C=C), 1455(m), 1380(s), 1230(s), 1210(s), 1155(s), 1080(s), 1050(s), 1030(s); HRMS (ESI) Calcd. for C₁₁H₁₉O₃ ([M+H]⁺): 199.13287, Found: 199.13289; C₁₁H₁₈O₃, M = 198.26 g/mol.

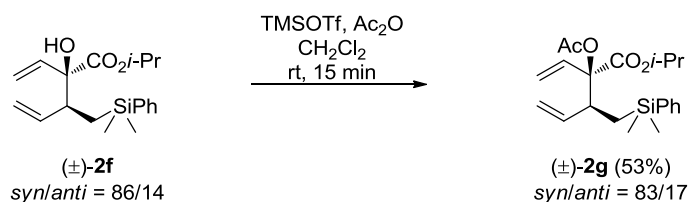
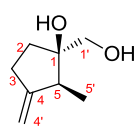


Attempted Tamao–Fleming Oxidation³¹: Protodesilylation product (±)-9: A solution of diol (±)-8 (28 mg, 0.1 mmol, 1 eq) in TBAF (1.55 mL, 1.55 mmol, 15.5 eq, 1 M in THF) was added to a

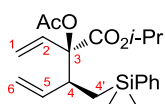
³⁰ a) Tamao, K.; Akita, M.; Kumada, M. *J. Organomet. Chem.* **1983**, 254, 13–22. b) Tamao, K.; Ishida, N.; Tanaka, T.; Kumada, M. *Organometallics* **1983**, 2, 1694–1696. c) Fleming, I.; Henning, R.; Plaut, H. *J. Chem. Soc., Chem. Commun.* **1984**, 29–31.

³¹ a) Knölker, H.-J.; Wanzl, G. *Synlett* **1995**, 378–382. b) Merten, J.; Hennig, A.; Schwab, P.; Fröhlich, R.; Tokalov, S. V.; Gutzeit, H. O.; Metz, P. *Eur. J. Org. Chem.* **2006**, 1144–1161.

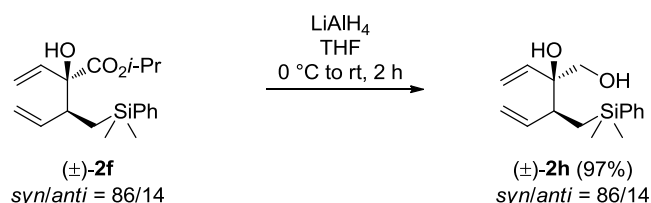
pressure tube²⁸ containing activated, pulverized molecular sieves (4 Å) (388 mg, 0.25 g/mmol TBAF). The resulting brown suspension was stirred at 70 °C for a period of 17 h. The reaction mixture was allowed to cool down to room temperature and was subsequently treated with KF (20 mg, 0.35 mmol, 3.5 eq), NaHCO₃ (19 mg, 0.23 mmol, 2.3 eq), MeOH (0.8 mL, 0.8 mL/mL THF) and H₂O₂ (0.36 mL, 3.6 mL/mmol **8**, 35% in H₂O). The resulting suspension was stirred at 70 °C further for 4 h. The reaction mixture was filtered and the filter cake washed with ethyl acetate and water. The aqueous layer was extracted with ethyl acetate (3×), the combined organic phases were dried (MgSO₄) and subsequently concentrated under reduced pressure. Purification by flash chromatography (cyclohexane/ethyl acetate 5/1) afforded protodesilylation product (±)-**9** (14 mg, 0.1 mmol, 99%) as mixture of diastereomers (*cis/trans* = 95/5). *R_f* 0.54 (ethyl acetate); 2D ¹H, ¹H-COSY, 2D ¹H, ¹³C-HSQC methods were used to confirm the NMR peak assignments: ¹H NMR (CDCl₃, 500 MHz, mixture of diastereomers *cis/trans* = 95/5, δ): 1.01–1.02 (m, 0.3H^{minor}, 5'-CH₃), 1.07 (d, ³*J* = 6.9 Hz, 2.7H^{major}, 5'-CH₃), 1.71–1.78 (m, 1H, 2-CH₂), 1.78–1.86 (m, 1H, 2-CH₂), 1.98 (br s, 2H, OH), 2.30–2.35 (m, 1H, 5-CH), 2.37–2.45 (m, 1H, 3-CH₂), 2.46–2.56 (m, 1H, 3-CH₂), 3.46 (d, ²*J* = 11.1 Hz, 0.1H^{minor}, 1'-CH₂), 3.55 (d, ²*J* = 10.7 Hz, 0.9H^{major}, 1'-CH₂), 3.61 (d, ²*J* = 11.1 Hz, 0.1H^{minor}, 1'-CH₂), 3.66 (d, ²*J* = 11.1 Hz, 0.9H^{major}, 1'-CH₂), 4.85 (d, *J* = 2.3 Hz, 1H, 4'-CH₂), 4.95 (d, *J* = 2.3 Hz, 1H, 4'-CH₂); ¹³C NMR (CDCl₃, 126 MHz, mixture of diastereomers *cis/trans* = 95/5, δ): 11.8 (5'-CH₃), 29.0 (3-CH₂), 34.8 (2-CH₂), 45.0 (5-CH), 68.5 (1'-CH₂), 81.9 (1-C), 106.2 (4'-CH₂), 155.1 (4-C); significant COSY cross peaks: 5'-CH₃/5-CH, significant HMBC cross peaks: 5'-CH₃/1-C, 5'-CH₃/4-C; IR (cm⁻¹): 3390(br s) (ν OH), 3075(w), 2965(s), 2935(s), 2875(m), 1655(m) (ν C=C), 1455(m), 1385(s) (δ CH₃), 1180(w), 1050(m), 1030(m), 1005(m); HRMS (ESI) Calcd. for C₈H₁₃O ([M-H₂O]⁺): 125.09609, Found: 125.09553; C₈H₁₄O₂, M = 142.20 g/mol.



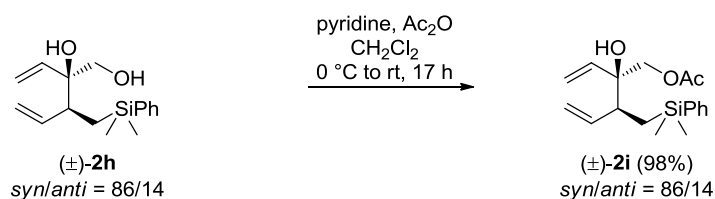
Acetate (±)-2g: A solution of hexadiene **2f** (115 mg, 0.35 mmol, 1 eq) in CH₂Cl₂ (0.7 mL, 2 mL/mmol **2f**) was successively treated with Ac₂O (0.14 mL, 1.4 mmol, 4 eq) and TMSOTf (one drop, transferred with a syringe needle) at room temperature. The resulting light pink solution was stirred for 15 min before silica gel (0.1 g) was added and the mixture was concentrated under reduced pressure. Purification by flash chromatography (*n*-pentane/diethyl ether 70/1 → 20/1) afforded acetate (±)-**2g** (70 mg, 0.19 mmol, 53%) as mixture of diastereomers (*syn/anti* = 83/17). *R_f* 0.49 (cyclohexane/ethyl acetate 5/1); 2D ¹H, ¹H-COSY, 2D ¹H, ¹³C-HSQC methods were used to confirm the NMR peak assignments: ¹H NMR (CDCl₃, 400 MHz, mixture of diastereomers *syn/anti* = 83/17, δ): 0.23–0.28 (m, 3H, SiMe₂), 0.30 (s, 3H, SiMe₂), 0.74 (dd, *J* = 14.7, 11.9 Hz, 1H, 4'-CH₂), 1.07–1.10 (m, 0.2H^{minor}, 4'-CH₂), 1.13 (dd, *J* = 14.7, 2.1 Hz, 0.8H^{major}, 4'-CH₂), 1.19 (d, ³*J* = 6.3 Hz, 2.5H^{major}, *i*-Pr-CH₃), eclipsed by 1.21–1.22 (m, 1H^{minor}), and 1.24 (d, ³*J* = 6.3 Hz, 2.5H^{major}, *i*-Pr-CH₃), 2.08 (s, 0.5H^{minor}, Ac-CH₃), 2.09 (s, 2.5H^{major}, Ac-CH₃), 2.57–2.67 (m, 0.2H^{minor}, 4-CH), 2.73 (ddd, *J* = 11.8, 10.0, 1.8 Hz, 0.8H^{major}, 4-CH), 4.91–5.08 (m, 4H, *i*-Pr-H, 1-CH₂, 6-CH₂), 5.18–5.24 (m, 0.2H^{minor}, 1-CH₂), eclipsed by 5.28 (d, *J* = 11.5 Hz, 0.8H^{major}, 1-CH₂), 5.37 (dt, *J* = 16.9, 10.0 Hz, 0.8H^{major}, 5-CH), 5.48 (dt, *J* = 17.1, 9.9 Hz, 0.2H^{minor}, 5-CH), 6.24 (dd, *J* = 17.6, 11.3 Hz, 0.8H^{major}, 1-CH), eclipsed by 6.29–6.38 (m, 0.2H^{minor}, 1-CH), 7.29–7.39 (m, 3H, Ar),



7.43–7.53 (m, 2H, Ar); ^{13}C NMR (CDCl_3 , 101 MHz, mixture of diastereomers *syn/anti* = 83/17, δ): –2.4 (SiMe_2), –1.6/–1.5 (SiMe_2), 14.6/15.2 ($4'\text{-CH}_2$), 21.0/21.1 (Ac-CH_3), 21.8/21.8 ($i\text{-Pr-CH}_3$), 21.9 ($i\text{-Pr-CH}_3$), 47.9/48.7 (4-CH), 69.1/69.3 ($i\text{-Pr-CH}$), 84.8/85.1 (3-C), 115.7/116.0 (1-CH_2), 118.2/118.5 (6-CH_2), 127.8 ($2\times\text{CH}_{\text{ar}}$), 129.0/129.0 (CH_{ar}), 132.2/133.3 (5-CH), 133.7/133.7 ($2\times\text{CH}_{\text{ar}}$), 137.3/137.5 (2-CH), 139.5 (C_{ar}), 169.1/169.2 (C=O), 169.4/169.6 (C=O); significant COSY cross peaks: $4\text{-CH}/5\text{-CH}$; IR (cm^{-1}): 3070(w), 3050(w), 2980(m), 2955(w), 2935(w), 1745(s) ($\nu\text{ C=O}$), 1640(w) ($\nu\text{ C=C}$), 1465(w), 1425(m), 1370(m), 1260(s) ($\nu\text{ C-O-C ester}$), 1230(s) ($\nu\text{ C-O-C ester}$), 1190(m), 1110(m), 1065(w), 1015(m); Anal. Calcd. for $\text{C}_{21}\text{H}_{30}\text{O}_4\text{Si}$: C, 67.3; H, 8.1; Found: C, 67.3; H, 8.0; $\text{C}_{21}\text{H}_{30}\text{O}_4\text{Si}$, $M = 374.55\text{ g/mol}$.

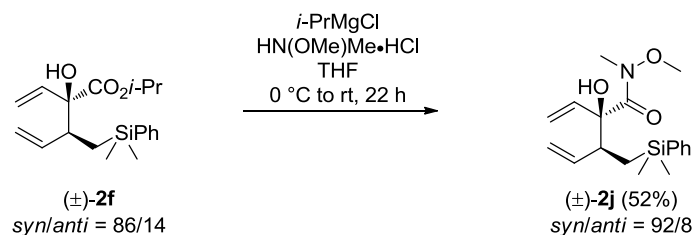


Diol (\pm)-2h: Hexadiene **2f** (500 mg, 1.5 mmol, 1 eq) was added to a suspension of LiAlH_4 (172 mg, 4.5 mmol, 3 eq) in THF (7.5 mL, 5 mL/mmol **2f**) at 0 °C. The cooling bath was removed and the reaction mixture was stirred at room temperature for a period of 2 h. The grey suspension was carefully hydrolyzed by the subsequent addition of ethyl acetate and saturated aqueous Na/K tartrate solution at 0 °C. The aqueous layer was extracted with ethyl acetate (5 \times) and the combined organic phases were dried (MgSO_4) and concentrated under reduced pressure. Purification by flash chromatography (cyclohexane/ethyl acetate 10/1) afforded diol (\pm)-**2h** (400 mg, 1.45 mmol, 97%) as a mixture of diastereomers (*syn/anti* = 86/14). R_f 0.34 (cyclohexane/ethyl acetate 2/1); ^1H NMR (CDCl_3 , 400 MHz, mixture of diastereomers *syn/anti* = 86/14, δ): 0.26 (s, 3H), 0.28 (s, $2.6\text{H}^{\text{major}}$), 0.29 (s, $0.4\text{H}^{\text{minor}}$), 0.69 (dd, $J = 14.6, 11.8\text{ Hz}$, $0.8\text{H}^{\text{major}}$), 0.82 (dd, $J = 14.4, 12.2\text{ Hz}$, $0.2\text{H}^{\text{minor}}$), 1.01 (dd, $J = 14.6, 2.0\text{ Hz}$, $0.2\text{H}^{\text{minor}}$), 1.15 (dd, $J = 14.8, 2.5\text{ Hz}$, $0.8\text{H}^{\text{major}}$), 1.64 (br s, $0.8\text{H}^{\text{major}}$), 1.74 (br s, $0.2\text{H}^{\text{minor}}$), 2.20 (br s, $0.2\text{H}^{\text{minor}}$), 2.23 (br s, $0.8\text{H}^{\text{major}}$), 2.32–2.37 (m, $0.2\text{H}^{\text{minor}}$), eclipsed by 2.41 (ddd, $^3J = 11.8, 10.0, 2.3\text{ Hz}$, $0.8\text{H}^{\text{major}}$), 3.40–3.63 (m, 2H), 4.98–5.07 (m, $1.8\text{H}^{\text{major}}$), 5.10 (dd, $J = 10.2, 1.6\text{ Hz}$, $0.2\text{H}^{\text{minor}}$), 5.25–5.39 (m, 2H), 5.51 (dt, $J = 17.5, 9.8\text{ Hz}$, 1H), 5.77 (dd, $J = 17.3, 11.0\text{ Hz}$, $0.8\text{H}^{\text{major}}$), eclipsed by 5.82–5.90 (m, Hz, $0.2\text{H}^{\text{minor}}$), 7.30–7.38 (m, 3H), 7.44–7.53 (m, 2H); ^{13}C NMR (CDCl_3 , 101 MHz, mixture of diastereomers *syn/anti* = 86/14, δ): –2.5/–2.4 (CH_3), –1.5 (CH_3), 14.7/15.8 (CH_2), 46.6/47.5 (CH), 66.8/67.6 (CH_2), 77.6 (C), 116.6/116.8 (CH_2), 117.6/118.4 (CH_2), 127.8 ($2\times\text{CH}_{\text{ar}}$), 128.9 (CH_{ar}), 133.8 ($2\times\text{CH}_{\text{ar}}$), 138.1 (CH), 138.8 (C_{ar}), 139.7 (CH); IR (cm^{-1}): 3440(m) ($\nu\text{ OH}$), 3070(w), 3010(w), 2955(m), 2890(m), 1640(w) ($\nu\text{ C=C}$), 1425(m), 1385(m) ($\delta\text{ CH}_3$), 1245(s), 1115(s), 1065(m); Anal. Calcd. for $\text{C}_{16}\text{H}_{24}\text{O}_2\text{Si}$: C, 69.5; H, 8.8; Found: C, 69.4; H, 8.7; $\text{C}_{16}\text{H}_{24}\text{O}_2\text{Si}$, $M = 276.45\text{ g/mol}$.



Acetate (\pm)-2i: An ice-cooled solution of diol **2h** (100 mg, 0.36 mmol, 1 eq) in CH_2Cl_2 (1 mL, 3 mL/mmol **2h**) was treated successively with pyridine (0.09 mL, 1.08 mmol, 3 eq) and Ac_2O (0.04 mL,

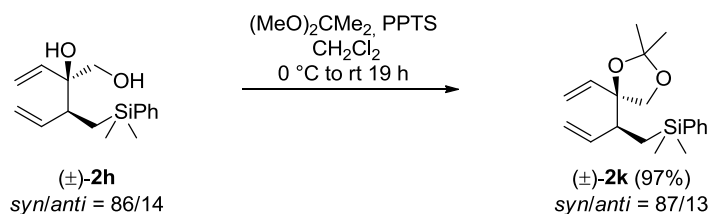
0.43 mmol, 1.2 eq) and the resulting mixture was allowed to warm to room temperature overnight (17 h). The reaction mixture was diluted with saturated aqueous NH_4Cl solution and the aqueous layer was extracted with CH_2Cl_2 (3 \times). The combined organic phases were dried (MgSO_4) and concentrated under reduced pressure. Purification by flash chromatography (cyclohexane/ethyl acetate 50/1 \rightarrow 10/1) afforded acetate (\pm)-**2i** (112 mg, 0.35 mmol, 98%) as a mixture of diastereomers (*syn/anti* = 86/14). R_f 0.66 (cyclohexane/ethyl acetate 2/1); ^1H NMR (CDCl_3 , 400 MHz, mixture of diastereomers *syn/anti* = 86/14, δ): 0.27 (s, 3H), 0.29 (s, 3H), 0.69 (dd, J = 14.6, 11.8 Hz, $0.8\text{H}^{\text{major}}$), 0.78–0.90 (m, $0.2\text{H}^{\text{minor}}$), 1.02 (dd, J = 14.3, 1.8 Hz, $0.2\text{H}^{\text{minor}}$), 1.20 (dd, J = 14.7, 2.4 Hz, $0.8\text{H}^{\text{major}}$), 2.02 (s, $0.4\text{H}^{\text{minor}}$), 2.04 (s, $2.6\text{H}^{\text{major}}$), 2.22 (s, 1H), 2.31–2.39 (m, $0.2\text{H}^{\text{minor}}$), 2.44 (ddd, 3J = 11.8, 10.0, 2.3 Hz, $0.8\text{H}^{\text{major}}$), 4.00 (d, 2J = 11.3 Hz, $0.8\text{H}^{\text{major}}$), 4.03–4.09 (m, $0.2\text{H}^{\text{minor}}$), 4.10–4.14 (m, $0.2\text{H}^{\text{minor}}$), 4.18 (d, 2J = 11.5 Hz, $0.8\text{H}^{\text{major}}$), 4.94–5.07 (m, $1.8\text{H}^{\text{major}}$), 5.11 (dd, J = 10.0, 1.5 Hz, $0.2\text{H}^{\text{minor}}$), 5.23–5.40 (m, 2H), 5.50 (dt, J = 17.1, 10.0 Hz, $0.8\text{H}^{\text{major}}$), eclipsed by 5.56–5.62 (m, $0.2\text{H}^{\text{minor}}$), 5.76 (dd, J = 17.3, 10.8 Hz, $0.8\text{H}^{\text{major}}$), eclipsed by 5.80–5.89 (m, $0.2\text{H}^{\text{minor}}$), 7.30–7.38 (m, 3H), 7.45–7.56 (m, 2H); ^{13}C NMR (CDCl_3 , 101 MHz, mixture of diastereomers *syn/anti* = 86/14, δ): –2.5/–2.4 (CH_3), –1.6/–1.6 (CH_3), 14.3/15.7 (CH_2), 21.0 (CH_3), 46.7/47.5 (CH), 68.2/69.2 (CH_2), 76.4/76.6 (C), 116.5/116.6 (CH_2), 117.9/118.6 (CH_2), 127.7/127.8 ($2\times\text{CH}_{\text{ar}}$), 128.9/129.0 (CH_{ar}), 133.7/133.7 ($2\times\text{CH}_{\text{ar}}$), 137.4/138.4 (CH), 139.0/139.4 (CH), 139.5 (C_{ar}), 171.1 (C=O); IR (cm^{-1}): 3480(m) (ν OH), 3070(w), 3050(w), 3000(w), 2955(m), 2920(w), 1745(s) (ν C=O), 1640(w) (ν C=C), 1425(s), 1380(s) (δ CH_3), 1245(s) (ν C-O-C ester), 1115(s), 1045(s), 995(m); Anal. Calcd. for $\text{C}_{18}\text{H}_{26}\text{O}_3\text{Si}$: C, 67.9; H, 8.2; Found: C, 68.0; H, 8.2; $\text{C}_{18}\text{H}_{26}\text{O}_3\text{Si}$, M = 318.48 g/mol.



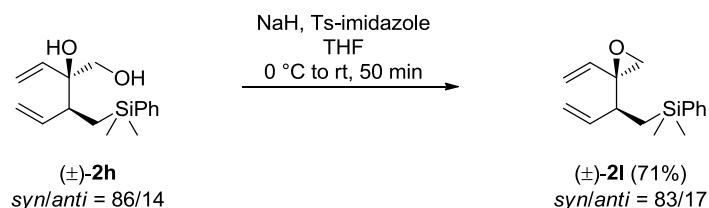
Weinreb amide formation³²: Amide (\pm)-2j**:** An ice-cooled solution of hexadiene **2f** (240 mg, 0.72 mmol, 1 eq) in THF (6 mL, 8 mL/mmol **2f**) was successively treated with dried (5×10^{-2} mbar, 70 $^\circ\text{C}$, 1 h) *N,O*-dimethylhydroxylamine hydrochloride (232 mg, 2.38 mmol, 3.3 eq) and *i*-PrMgCl (2.75 mL, 5.49 mmol, 7.6 eq, 2 M in THF). The cooling bath was removed and the resulting mixture was stirred at room temperature overnight (22 h). After 3 h, a further equivalent of *i*-PrMgCl (0.36 mL, 0.72 mmol, 1 eq, 2 M in THF) was added. The reaction mixture was cooled to 0 $^\circ\text{C}$, carefully hydrolyzed by the addition of saturated aqueous NH_4Cl solution and the aqueous layer was extracted with CH_2Cl_2 (3 \times). The combined organic phases were dried (MgSO_4) and concentrated under reduced pressure. Purification by flash chromatography (cyclohexane/ethyl acetate 50/1 \rightarrow 20/1) afforded Weinreb amide (\pm)-**2j** (124 mg, 0.37 mmol, 52%) as a mixture of diastereomers (*syn/anti* = 92/8) along with reisolated hexadiene (\pm)-**2f** (92 mg, 0.28 mmol, 38%). R_f 0.34 (cyclohexane/ethyl acetate 5/1); 2D ^1H , ^1H -COSY, 2D ^1H , ^{13}C -HSQC methods were used to confirm the NMR peak assignments: ^1H NMR (CDCl_3 , 500 MHz, mixture of diastereomers *syn/anti* = 92/8, δ): 0.25 (s, 3H, SiMe_2), 0.28 (s, 3H, SiMe_2), 0.52 (dd, J = 14.7, 2.2 Hz, $0.9\text{H}^{\text{major}}$, 4'- CH_2), 0.92–1.05 (m, $0.2\text{H}^{\text{minor}}$, 4'- CH_2), 1.10 (dd, J = 14.7, 12.2 Hz, $0.9\text{H}^{\text{major}}$, 4'- CH_2), 2.82 (ddd, 3J = 12.0, 9.9, 2.1 Hz, $0.9\text{H}^{\text{major}}$, 4-CH), eclipsed by 2.85–2.89 (m, $0.1\text{H}^{\text{minor}}$, 4-CH), 3.15 (s, $0.3\text{H}^{\text{minor}}$, *NMe*), 3.20 (s, $2.7\text{H}^{\text{major}}$, *NMe*), 3.49–3.55 (m, 3H,

³² Williams, J. M.; Jobson, R. B.; Yasuda, N.; Marchesini, G.; Dolling, U.-H.; Grabowski, E. J. J. *Tetrahedron Lett.* **1995**, 36, 5461–5464.

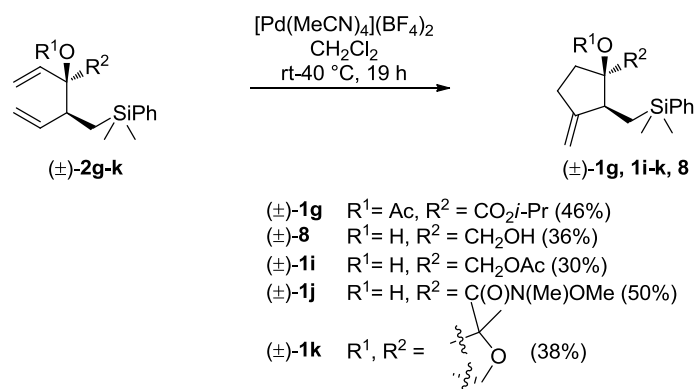
NMe), 4.44 (s, 0.1H^{minor}, OH), 4.52 (s, 0.9H^{major}, OH), 4.90 (dd, $J = 17.4, 1.8$ Hz, 0.1H^{minor}, 6-CH₂), 4.95 (dd, $J = 17.2, 1.7$ Hz, 0.9H^{major}, 6-CH₂), 5.04 (dd, $J = 10.1, 1.9$ Hz, 1H, 6-CH₂), 5.16 (dd, $J = 10.6, 1.6$ Hz, 0.9H^{major}, 1-CH₂), 5.27 (dd, $J = 10.5, 1.7$ Hz, 0.1H^{minor}, 1-CH₂), 5.42 (dd, $J = 17.2, 1.6$ Hz, 1H, 1-CH₂), 5.52–5.67 (m, 0.1H^{minor}, 5-CH), eclipsed by 5.59 (dt, $J = 17.3, 9.8$ Hz, 0.9H^{major}, 5-CH), 5.84 (dd, $J = 17.1, 10.5$ Hz, 0.1H^{minor}, 2-CH), 6.00 (dd, $J = 17.2, 10.6$ Hz, 0.9H^{major}, 2-CH), 7.29–7.36 (m, 3H, Ar), 7.43–7.52 (m, 2H, Ar); ¹³C NMR (CDCl₃, 126 MHz, mixture of diastereomers *syn/anti* = 92/8, δ): –2.3 (SiMe₂), –1.3 (SiMe₂), 15.6 (4'-CH₂), 33.9 (NMe), 46.5 (4-CH), 60.7 (NOMe), 80.6/81.5 (3-C), 116.0/116.4 (1-CH₂), 117.3/117.6 (6-CH₂), 127.7 (2×CH_{ar}), 128.9 (CH_{ar}), 133.8/133.9 (2×CH_{ar}), 138.7 (2-CH), 139.2 (5-CH), 139.7 (C_{ar}), 174.6 (C=O); significant COSY cross peaks: 4-CH/5-CH; IR (cm⁻¹): 3420(m) (ν OH), 3070(m), 2975(m), 2955(m), 2900(w), 1645(s) (ν C=O), 1425(m), 1350(s), 1250(m), 1175(m), 1115(s), 995(s); Anal. Calcd. for C₁₈H₂₇NO₃Si: C, 64.8; H, 8.2; N, 4.2; Found: C, 64.9; H, 8.2; N, 4.1; C₁₈H₂₇NO₃Si, M = 333.50 g/mol.



Acetal (±)-2k: A solution of diol **2h** (150 mg, 0.54 mmol, 1 eq) in CH₂Cl₂ (1.6 mL, 3 mL/mmol **2h**) was successively treated with 2,2-dimethoxypropane (0.1 mL, 0.81 mmol, 1.5 eq) and pyridinium *p*-toluenesulfonate (PPTS) (20 mg, 0.08 mmol, 0.15 eq) at 0 °C. The cooling bath was removed and the resulting mixture was stirred overnight (19 h) at room temperature. The reaction mixture was diluted by the addition of saturated aqueous NaHCO₃ solution and the aqueous layer was extracted with CH₂Cl₂ (3×). The combined organic phases were dried (MgSO₄) and concentrated under reduced pressure. Purification by flash chromatography (cyclohexane/ethyl acetate 200/1) afforded acetal (±)-**2k** (166 mg, 0.53 mmol, 97%) as a mixture of diastereomers (*syn/anti* = 87/13). *R_f* 0.57 (cyclohexane/ethyl acetate 5/1); ¹H NMR (CDCl₃, 400 MHz, mixture of diastereomers *syn/anti* = 87/13, δ): 0.26 (s, 2.7H^{major}), 0.27 (s, 0.3H^{minor}), 0.29 (s, 2.7H^{major}), 0.31 (s, 0.3H^{minor}), 0.68 (dd, $J = 14.7, 11.9$ Hz, 0.9H^{major}), 0.86 (dd, $J = 14.7, 11.9$ Hz, 0.1H^{minor}), 0.98 (dd, $J = 14.5, 2.1$ Hz, 0.1H^{minor}), 1.26 (dd, $J = 14.8, 2.2$ Hz, 0.9H^{major}), 1.36 (s, 2.7H^{major}), 1.39 (s, 2.7H^{major}), 1.40 (s, 0.3H^{minor}), 1.43 (s, 0.3H^{minor}), 2.26 (ddd, $^3J = 11.7, 9.5, 2.1$ Hz, 0.1H^{minor}), 2.38 (ddd, $^3J = 11.8, 10.1, 2.0$ Hz, 0.9H^{major}), 3.74 (d, $^2J = 8.7$ Hz, 0.9H^{major}), 3.83 (d, $^2J = 8.3$ Hz, 0.1H^{minor}), 3.92 (d, $^2J = 8.3$ Hz, 0.1H^{minor}), 3.99 (d, $^2J = 8.7$ Hz, 0.9H^{major}), 4.93–5.10 (m, 2H), 5.17–5.22 (m, 0.1H^{minor}), eclipsed by 5.22 (dd, $J = 10.8, 1.8$ Hz, 0.9H^{major}), 5.33 (dd, $J = 17.2, 1.7$ Hz, 0.1H^{minor}), eclipsed by 5.35 (dd, $J = 17.2, 1.8$ Hz, 0.9H^{major}), 5.48 (dt, $J = 17.1, 9.9$ Hz, 0.9H^{major}), 5.59 (dt, $J = 17.0, 9.8$ Hz, 0.1H^{minor}), 5.85 (dd, $J = 17.1, 10.8$ Hz, 0.9H^{major}), eclipsed by 5.90–5.94 (m, 0.1H^{minor}), 7.32–7.39 (m, 3H), 7.43–7.57 (m, 2H); ¹³C NMR (CDCl₃, 101 MHz, mixture of diastereomers *syn/anti* = 87/13, δ): –2.5/–2.3 (CH₃), –1.5/–1.5 (CH₃), 15.2/16.3 (CH₂), 26.4/26.5 (CH₃), 26.7/27.2 (CH₃), 48.3/49.2 (CH), 71.8/72.1 (CH₂), 86.3/86.6 (C), 110.0 (C), 114.8/115.5 (CH₂), 117.2/117.4 (CH₂), 127.7/127.8 (2×CH_{ar}), 128.8/128.9 (CH_{ar}), 133.7/133.8 (2×CH_{ar}), 137.9 (CH), 139.5/139.7 (C_{ar}), 139.9/140.3 (CH); IR (cm⁻¹): 3070(m), 3050(m), 2985(s), 2955(m), 2875(m), 1640(m) (ν C=C), 1455(w), 1430(m), 1405(m), 1380(s), 1370(s), 1260(s), 1230(m), 1210(s), 1115(s), 1055(s), 995(s); Anal. Calcd. for C₁₉H₂₈O₂Si: C, 72.1; H, 8.9; Found: C, 72.3; H, 9.1; C₁₉H₂₈O₂Si, M = 316.51 g/mol.



Epoxide formation³³: Oxirane (\pm)-2l: An ice-cooled solution of diol **2h** (114 mg, 0.41 mmol, 1 eq) in THF (8 mL, 20 mL/mmol **2h**) was treated with NaH (41 mg, 1 mmol, 2.5 eq, 60% in mineral oil) and the resulting suspension was stirred for 30 min at room temperature. The mixture was cooled to 0 °C, and 1-tosylimidazole (100 mg, 0.45 mmol, 1.1 eq) was added and the resulting mixture was stirred for 20 min at room temperature. The reaction mixture was carefully hydrolyzed by the addition of saturated aqueous NH_4Cl solution and the aqueous layer was extracted with CH_2Cl_2 (3 \times). The combined organic phases were dried (MgSO_4) and concentrated under reduced pressure. Purification by flash chromatography (cyclohexane/ethyl acetate 200/1 \rightarrow 100/1) afforded oxirane (\pm)-**2l** (75 mg, 0.29 mmol, 71%) as a mixture of diastereomers ($\text{syn/anti} = 83/17$). R_f 0.51 (cyclohexane/ethyl acetate 20/1); $^1\text{H NMR}$ (CDCl_3 , 500 MHz, mixture of diastereomers $\text{syn/anti} = 83/17$, δ): 0.27–0.29 (m, 3H), 0.29–0.31 (m, 3H), 0.79 (dd, $J = 14.8, 11.4$ Hz, $0.2\text{H}^{\text{minor}}$), 0.93 (dd, $J = 14.8, 10.4$ Hz, $0.8\text{H}^{\text{major}}$), 1.01–1.09 (m, $0.2\text{H}^{\text{minor}}$), 1.12 (dd, $J = 14.8, 4.3$ Hz, $0.8\text{H}^{\text{major}}$), 2.06–2.13 (m, $0.8\text{H}^{\text{major}}$), 2.23–2.31 (m, $0.2\text{H}^{\text{minor}}$), 2.55 (d, $^2J = 5.6$ Hz, $0.2\text{H}^{\text{minor}}$), 2.62 (d, $^2J = 5.6$ Hz, $0.8\text{H}^{\text{major}}$), 2.70 (d, $^2J = 5.6$ Hz, $0.2\text{H}^{\text{minor}}$), 2.77 (d, $^2J = 5.6$ Hz, $0.8\text{H}^{\text{major}}$), 4.95–5.08 (m, 2H), 5.15 (dd, $J = 10.7, 1.8$ Hz, $0.2\text{H}^{\text{minor}}$), eclipsed by 5.17 (dd, $J = 10.7, 1.6$ Hz, $0.8\text{H}^{\text{major}}$), 5.27 (dd, $J = 17.2, 1.6$ Hz, $0.2\text{H}^{\text{minor}}$), eclipsed by 5.30 (dd, $J = 17.1, 1.7$ Hz, $0.8\text{H}^{\text{major}}$), 5.55–5.65 (m, $0.2\text{H}^{\text{minor}}$), 5.71 (ddd, $J = 17.0, 10.4, 8.3$ Hz, $0.8\text{H}^{\text{major}}$), 6.00 (dd, $J = 17.1, 10.8$ Hz, 1H), 7.31–7.38 (m, 3H), 7.45–7.53 (m, 2H); $^{13}\text{C NMR}$ (CDCl_3 , 126 MHz, mixture of diastereomers $\text{syn/anti} = 83/17$, δ): –2.4/–2.2 (CH_3), –1.8/–1.6 (CH_3), 17.1/17.2 (CH_2), 44.2/45.8 (CH), 55.0/56.3 (CH_2), 62.4/62.9 (C), 116.4/116.5 (CH_2), 116.7/116.7 (CH_2), 127.8/127.9 ($2\times\text{CH}_{\text{ar}}$), 128.9/129.1 (CH_{ar}), 133.7/133.8 ($2\times\text{CH}_{\text{ar}}$), 134.0/135.0 (CH), 139.5 (C_{ar}), 139.7/139.7 (CH); IR (cm^{-1}): 3070(m), 3050(w), 2980(w), 2955(m), 2905(m), 1640(m) ($\nu\text{ C=C}$), 1620(m) ($\nu\text{ C=C}$), 1425(m), 1385(m), 1250(s), 1115(s), 990(w), 925(s); $\text{C}_{16}\text{H}_{22}\text{OSi}$, $M = 258.43$ g/mol



Methylene cyclopentane (\pm)-1g: According to the general procedure SI-F [Pd(II)-catalyzed cycloisomerization], 1,5-hexadiene (\pm)-**2g** (69 mg, 0.18 mmol) in CH_2Cl_2 (1.8 mL, 10 mL/mmol **2g**) was exposed to the cycloisomerization conditions with $[\text{Pd}(\text{MeCN})_4](\text{BF}_4)_2$ (4 mg, 0.009 mmol, 0.05 eq) at room temperature for 19 h. Purification by flash chromatography (cyclohexane/ethyl acetate 150/1 \rightarrow

³³ Hicks, D. R.; Fraser-Reid, B. *Synthesis* **1974**, 203.

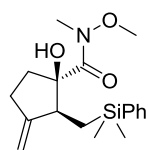
100/1) afforded methylene cyclopentane (±)-**1g** (32 mg, 0.09 mmol, 46%)³⁴ as a mixture of diastereomers (*cis/trans* = 86/14) along with recovered hexadiene (±)-**2g** (13 mg, 0.03 mmol, 19%). (±)-**1g**: *R_f* 0.46 (cyclohexane/ethyl acetate 10/1); 2D ¹H, ¹H-COSY, 2D ¹H, ¹³C-HSQC methods were used to confirm the NMR peak assignments: ¹H NMR (CDCl₃, 500 MHz, mixture of diastereomers *cis/trans* = 86/14, contaminated with (±)-**2g**, δ): 0.29 (s, 2.6H^{major}, SiMe₂), 0.31 (s, 2.6H^{major}, SiMe₂), 0.32–0.34 (m, 0.8H^{minor}, SiMe₂), 0.94 (dd, *J* = 15.6, 9.6 Hz, 1H, 5'-CH₂), 1.15 (d, ³*J* = 6.2 Hz, 3H, *i*-Pr-CH₃), 1.22 (d, ³*J* = 6.3 Hz, 3H, *i*-Pr-CH₃), 1.32 (dd, *J* = 15.7, 2.2 Hz, 1H, 5'-CH₂), 2.03 (s, 2.6H^{major}, Ac-CH₃), 2.04 (s, 0.4H^{minor}, Ac-CH₃), 2.25 (ddd, *J* = 13.5, 9.5, 3.8 Hz, 1H, 2-CH₂), 2.31–2.40 (m, 1H, 3-CH₂), 2.42–2.53 (m, 1H, 3-CH₂), 2.54–2.62 (m, 1H, 2-CH₂), 2.62–2.68 (m, 1H, 5-CH), 4.63–4.69 (m, 0.2H^{minor}, 4'-CH₂), 4.72 (d, *J* = 2.1 Hz, 0.8H^{major}, 4'-CH₂), 4.76–4.79 (m, 0.2H^{minor}, 4'-CH₂), 4.86 (d, *J* = 2.1 Hz, 0.8H^{major}, 4'-CH₂), 4.94 (spt, ³*J* = 6.3 Hz, 0.8H^{major}, *i*-Pr-CH), eclipsed by 5.02 (spt, ³*J* = 6.3 Hz, 0.2H^{minor}, *i*-Pr-CH), 7.31–7.39 (m, 3H, Ar), 7.49–7.54 (m, 2H, Ar); ¹H NMR (CDCl₃, 126 MHz, mixture of diastereomers *cis/trans* = 86/14, contaminated with (±)-**2g**, δ): -2.4/-2.2 (SiMe₂), -2.0 (SiMe₂), 12.7/12.8 (5'-CH₂), 21.3 (Ac-CH₃) 21.7/21.7 (*i*-Pr-CH₃), 21.9/21.9 (*i*-Pr-CH₃), 28.9 (3-CH₂), 31.6 (2-CH₂), 47.8/49.1 (5-CH), 68.9/69.1 (*i*-Pr-CH), 88.5 (1-C), 107.4 (4'-CH₂), 127.9 (2×CH_{ar}), 129.1/129.1 (CH_{ar}), 133.7/133.8 (2×CH_{ar}), 139.4 (C_{ar}), 153.2 (4-C), 170.4 (C=O), 170.6 (C=O); significant COSY cross peaks: 4'-CH₂/3-CH₂, 4'-CH₂/5-CH; IR (cm⁻¹): 3070(m), 2980(s), 2960(s), 2930(s)m, 1740(s) (ν C=O), 1455(m), 1430(s), 1375(s), 1255(s) (ν C-O-C ester), 1180(m), 1115(s), 1050(s); HRMS (ESI) Calcd. for C₂₁H₃₁O₄Si ([M+H]⁺): 375.19861, Found: 375.19822; C₂₁H₃₀O₄Si, M = 374.55 g/mol.

Methylene cyclopentane (±)-8: According to the general procedure SI-F [Pd(II)-catalyzed cycloisomerization], 1,5-hexadiene (±)-**2h** (50 mg, 0.18 mmol) in CH₂Cl₂ (1.8 ml, 10 mL/mmol **2h**) was exposed to the cycloisomerization conditions with [Pd(MeCN)₄](BF₄)₂ (4 mg, 0.009 mmol, 0.05 eq) at 40 °C for 19 h. Purification by flash chromatography (cyclohexane/ethyl acetate 150/1 → 100/1) afforded methylene cyclopentane (±)-**8** (32 mg, 0.09 mmol, 36%) as a mixture of diastereomers (*cis/trans* = 86/14) along with recovered hexadiene (±)-**2h** (11 mg, 0.04 mmol, 22%). Analytical data: see SI-27.

Methylene cyclopentane (±)-1i: According to the general procedure SI-F [Pd(II)-catalyzed cycloisomerization], 1,5-hexadiene (±)-**2i** (112 mg, 0.35 mmol) in CH₂Cl₂ (3.5 ml, 10 mL/mmol **2i**) was exposed to the cycloisomerization conditions with [Pd(MeCN)₄](BF₄)₂ (8 mg, 0.018 mmol, 0.05 eq) at room temperature for 19 h. Purification by flash chromatography (cyclohexane/ethyl acetate 100/1 → 50/1) afforded methylene cyclopentane (±)-**1i** (33 mg, 0.1 mmol, 30%) as a mixture of diastereomers (*cis/trans* = 94/6) along with recovered hexadiene (±)-**2i** (25 mg, 0.08 mmol, 22%). *R_f* 0.14 (cyclohexane/ethyl acetate 5/1); ¹H NMR (CDCl₃, 400 MHz, mixture of diastereomers *syn/anti* = 94/6, δ): 0.33 (s, 6H), 0.83 (dd, *J* = 15.2, 8.8 Hz, 1H), 1.00–1.06 (m, 0.1H^{minor}), 1.10 (dd, *J* = 15.2, 3.1 Hz, 0.9H^{major}), 1.71–1.84 (m, 3H), 2.02 (s, 2.8H^{major}), 2.08 (s, 0.2H^{minor}), 2.28–2.40 (m, 2H), 2.43–2.56 (m, 1H), 3.86 (d, ²*J* = 11.4 Hz, 1H), 3.97 (d, ²*J* = 11.4 Hz, 1H), 4.76 (d, *J* = 2.1 Hz, 1H), 4.81–4.84 (m, 0.1H^{minor}), 4.89 (d, *J* = 2.0 Hz, 0.9H^{major}), 7.31–7.42 (m, 3H), 7.45–7.58 (m, 2H); IR (cm⁻¹): 3465(br s) (ν OH), 3070(m), 3050(m), 2955(s), 1745(s) (ν C=O), 1660(m) (ν C=C), 1425(s), 1385(s), 1250(s) (ν C-O-C ester), 1115(s), 1045(s); HRMS (ESI) Calcd. for C₁₈H₂₇O₃Si ([M+H]⁺): 319.17240, Found: 319.17213; C₁₈H₂₆O₃Si, M = 318.48 g/mol.

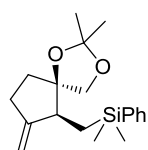
³⁴ slightly contaminated by hexadiene (±)-**2g**. Yield determined by ¹H NMR spectroscopy.

Methylene cyclopentane (±)-1j: According to the general procedure **SI-F [Pd(II)-catalyzed cycloisomerization]**, 1,5-hexadiene (±)-**2j** (77 mg, 0.23 mmol) in CH₂Cl₂ (2.3 ml, 10 mL/mmol **2j**) was exposed to the cycloisomerization conditions with [Pd(MeCN)₄](BF₄)₂ (5 mg, 0.01 mmol, 0.05 eq) at room temperature for 19 h. Purification by flash chromatography (cyclohexane/ethyl acetate 50/1 →



20/1) afforded methylene cyclopentane (±)-**1j** (38 mg, 0.1 mmol, 50%) as a mixture of diastereomers (*cis/trans* = 95/5). *R_f* 0.31 (cyclohexane/ethyl acetate 5/1); ¹H NMR (CDCl₃, 400 MHz, mixture of diastereomers *cis/trans* = 95/5, δ): 0.29 (s, 3H), 0.30 (s, 3H), 0.92 (d, *J* = 5.8 Hz, 2H), 1.87 (ddd, *J* = 13.2, 8.7, 4.6 Hz, 1H), 2.19–2.34 (m, 1H), 2.40–2.62 (m, 2H), 2.86–2.98 (m, 1H), 3.12 (s, 2.8H^{major}), 3.15 (s, 0.2H^{minor}), 3.45 (s, 0.2H^{minor}), 3.51 (s, 2.8H^{major}), 3.95 (s, 1H), 4.72 (d, *J* = 2.0 Hz, 0.9H^{major}), 4.92 (d, *J* = 1.8 Hz, 0.9H^{major}), 4.96–5.01 (m, 0.1H^{minor}), 5.04–5.11 (m, 0.1H^{minor}), 7.29–7.38 (m, 3H), 7.45–7.55 (m, 2H); ¹³C NMR (CDCl₃, 101 MHz, mixture of diastereomers *cis/trans* = 95/5, δ): –2.1 (CH₃), –1.8 (CH₃), 12.6 (CH₂), 30.2 (CH₂), 33.9 (CH₃), 34.9 (CH₂), 47.0 (CH), 60.8 (CH₃), 83.6 (C), 106.4 (CH₂), 127.8 (2×CH_{ar}), 128.9 (CH_{ar}), 133.8 (2×CH_{ar}), 139.7 (C_{ar}), 154.3 (C), 175.1 (C); IR (cm^{–1}): 3440(br s) (ν OH), 3070(m), 3050(m), 2955(s), 1635(s) (ν C=O), 1455(m), 1425(s), 1360(s), 1250(s), 1175(m), 1110(s), 1070(s); Anal. Calcd. for C₁₈H₂₇NO₃Si: C, 64.8; H, 8.2; N, 4.2; Found: C, 65.0; H, 8.4; N, 3.9; C₁₈H₂₇NO₃Si, *M* = 333.50 g/mol.

Methylene cyclopentane (±)-1k: According to the general procedure **SI-F [Pd(II)-catalyzed cycloisomerization]**, 1,5-hexadiene (±)-**2k** (70 mg, 0.22 mmol) in CH₂Cl₂ (2.2 mL, 10 mL/mmol **2k**) was exposed to the cycloisomerization conditions with [Pd(MeCN)₄](BF₄)₂ (5 mg, 0.01 mmol, 0.05 eq) at 40 °C for 19 h. Purification by flash chromatography (cyclohexane/ethyl acetate 200/1) afforded alkenes (±)-**1k** and (±)-**2k** (53 mg, 0.17 mmol, 76%) as inseparable mixture of regioisomers (**2k/1k** =



1/1). *R_f* 0.57 (cyclohexane/ethyl acetate 5/1); ¹H NMR (CDCl₃, 400 MHz, mixture of regioisomers **2k/1k** = 1/1, δ): 0.24 (s, 1.5H^{1k}), 0.27 (s, 1.5H^{1k}), 0.31 (s, 1.5H^{2k}), 0.33 (s, 1.5H^{2k}), 0.65 (dd, *J* = 14.7, 11.9 Hz, 0.5H^{1k}), 0.81 (dd, *J* = 15.4, 10.4 Hz, 0.5H^{2k}), 1.24 (dd, *J* = 14.9, 1.9 Hz, 1H), 1.32–1.42 (m, 6H), 1.72 (ddd, *J* = 13.2, 9.7, 6.2 Hz, 0.5H^{1k}), 2.08 (ddd, *J* = 13.1, 10.6, 5.6 Hz, 0.5H^{1k}), 2.15–2.31 (m, 1H^{1k+2k}), 2.30–2.64 (m, 1H^{1k}), 3.61–3.67 (m, 0.5H^{2k}), 3.72 (d, *J* = 7.8 Hz, 1H^{2k+1k}), 3.96 (d, *J* = 8.7 Hz, 0.5H^{2k}), 4.67–4.82 (m, 1H^{1k}), 4.91–5.08 (m, 1H^{2k}), 5.19 (d, *J* = 10.8 Hz, 0.5H^{2k}), 5.32 (dd, *J* = 17.2, 1.5 Hz, 0.5H^{2k}), 5.46 (dt, *J* = 17.2, 9.9 Hz, 0.5H^{2k}), 5.83 (dd, *J* = 17.2, 10.8 Hz, 0.5H^{2k}), 7.29–7.39 (m, 3H), 7.45–7.57 (m, 2H);

Analytical data for pure (±)-**1k**: see SI-28.