Oxonia-Cope Prins Cyclizations: a Facile Method for the Synthesis of Tetrahydropyranones Bearing Quaternary Centers

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General Experiment Details

All moisture- and air-sensitive reactions were carried out in flame- or oven-dried glassware using magnetic stirring under a positive pressure of argon gas. Standard syringe/septa techniques were employed. Reaction solvents were distilled or obtained from an alumina filtration system when necessary. Thin layer chromatography was performed on Whatman silica gel PE SIL G/UV plates. Concentration of organic solutions was performed using a Büchi rotary evaporator. Flash chromatography was performed on EM Science 230-400 mesh silica gel. Infrared spectra were recorded on a MIDAC Grams/Prospect FT-IR. NMR spectra were recorded on Bruker GN 500, Bruker Omega 500, and Bruker DRX 400 MHz FTNMR instruments. Proton NMR spectra were obtained using CDCl₃ as solvent and referenced to residual protiated solvent (δ 7.26 ppm) or C₆D₆ and referenced to δ 7.16 ppm. Carbon NMR spectra were recorded in ppm relative to the residual solvent signal: CDCl₃ (δ 77.0 ppm) or C₆D₆ (δ 128.4 ppm). Mass spectra were determined on an AE2-MS 30, a PG 7070E-HF, a CG Analytical 7070E, or a Fisons autospec spectrometer. Optical rotations were measured with a Jasco DIP-370 digital polarimeter. Tetrahydrofuran, ethyl ether and methylene chloride were dried by filtration through alumina according to the procedure by Grubbs.¹ Capillary GC analysis was performed on a Hewlett Packard Model 6890 instrument equipped with a FID detector. All reagents were purchased from Aldrich Chemical Co. or Acros and were used as received, unless otherwise stated. Elemental analyses were performed by M-H-

¹ Pangborn, A. B.; Giardello, M. A.; Grubbs, R. H.; Rosen, R. K.; Timmers, F. J. *Organometallics* **1996**, *15*, 1518–1520.

W Laboratories (Phoenix, AZ). Structures not numbered in the article were numbered consecutively starting with **101**.

Acetic acid 1-phenethylbut-3-enyl ester (101). Acetic anhydride (8.2 mL, 86.9 mmol, 2.0 equiv.), pyridine (5.3 mL, 65.3 mmol, 1.5 equiv.) and 4-(dimethylamino)pyridine (1.6 g, 13.1 mmol, 0.3 equiv.) were added to a stirred solution of 1-phenyl-hex-5-en-3-ol (7.7 g, 43.5 mmol, 1.0 equiv.) in 50 mL of CH₂Cl₂. After 5 h, the reaction mixture was diluted with 100 mL of diethyl ether, washed with 1 N aq. HCl (50 mL), satd. aq. NaHCO₃ (50 mL) and brine (50 mL). The organic layer was dried over anhydrous MgSO₄, and concentrated to provide 8.7 g (92%) of the known acetate² as a colorless oil: IR (neat) 3028, 2951, 1738, 1643, 1373, 1241, 1029 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.38–7.33 (m, 2 H), 7.28–7.23 (m, 3 H), 5.84 (dddd, *J* = 16.9, 10.1, 7.1, 7.1 Hz, 1 H), 5.20–5.13 (m, 2 H), 5.10–5.03 (m, 1 H), 2.80–2.64 (m, 2 H), 2.43 (dd, *J* = 7.3, 7.3 Hz, 2 H), 2.11 (s, 3 H), 2.00–1.93 (m, 2 H); ¹³C NMR (100 MHz, CDCl₃) δ 170.5, 141.3, 133.4, 128.3, 128.3, 128.2, 128.2, 125.8, 117.6, 72.7, 38.5, 35.1, 31.6, 21.0.

Tert-Butyldimethyl-[1-(1-phenethylbut-3-enyloxy)vinyl]oxy]silane (8). To a cooled (0 °C) solution of diisopropylamine (0.16 mL, 1.12 mmol, 1.15 equiv.) was added *n*-butyllithium (0.57 mL, 1.88 M in hexanes, 1.07 mmol, 1.1 equiv.). After 20 min. of stirring, the reaction mixture was cooled to –78 °C and the acetate **101** (212 mg, 0.97

² Falck, J. R.; Bhatt, R. K.; Ye, J. J. *Am. Chem. Soc.* **1995**, 117, 5973–5982.

mmol, 1.0 equiv.) was added dropwise *via* syringe. After 15 min. of stirring at $-78\text{ }^{\circ}\text{C}$, hexamethylphosphoramide (0.16 mL) was added followed by *tert*-butyldimethylsilyl chloride (154 mg, 1.02 mmol, 1.05 equiv.). After 30 min. of stirring at $-78\text{ }^{\circ}\text{C}$, the reaction mixture was slowly warmed to room temperature and the volatiles were removed on a rotary evaporator. Purification was deemed unnecessary and 312 mg (96%) of the title compound was isolated as a colorless oil: IR (neat) 3028, 2931, 1651, 1271, 1002, 829 cm^{-1} ; ^1H NMR (400 MHz, C_6D_6) δ 7.18–7.14 (m, 2 H), 7.11–7.03 (m, 3 H), 5.71 (m, 1 H), 5.01–4.97 (m, 2 H), 3.96–3.90 (m, 1 H), 3.60 (d, $J = 2.4\text{ Hz}$, 1 H), 2.70–2.53 (m, 2 H), 2.38–2.21 (m, 2 H), 1.92–1.71 (m, 2 H), 1.00 (s, 9 H), 0.24 (s, 3 H), 0.23 (s, 3 H); ^{13}C NMR (125 MHz, C_6D_6) δ 160.4, 142.4, 134.6, 129.1, 128.7, 128.2, 126.6, 117.9, 76.4, 63.2, 38.2, 35.8, 32.3, 26.2, 18.6, -3.8 , -3.9 .

3-(*tert*-Butyldimethylsilyloxy)but-3-enoic acid 1-phenethylbut-3-enyl ester (102).

A sample of 811 mg of **8** was converted to 707 mg (77%) of **102**, isolated as a colorless oil: IR (neat) 2931, 1740, 1473, 1254, 1030, 840, 699 cm^{-1} ; ^1H NMR (400 MHz, C_6D_6) δ 7.16–7.14 (m, 2 H), 7.09–7.04 (m, 3 H), 5.75–5.63 (m, 1 H), 5.08–4.95 (m, 3 H), 4.23 (s, 1 H), 4.20 (s, 1 H), 2.97 (s, 2 H), 2.66–2.45 (m, 2 H), 2.27–2.13 (m, 2 H), 1.87–1.61 (m, 2 H), 0.96 (s, 9 H), 0.17 (s, 3 H), 0.16 (s, 3 H); ^{13}C NMR (100 MHz, C_6D_6) δ 169.5, 153.6, 142.3, 134.3, 129.1, 129.1, 129.1, 129.1, 126.6, 118.1, 93.8, 73.4, 43.4, 39.3, 36.1, 32.5, 26.2, 18.6, -4.4 , -4.4 ; HRMS (EI) calcd for $[\text{C}_{22}\text{H}_{34}\text{O}_3\text{Si}+\text{H}]^+$ 375.2355, found 375.2342.

Acetic acid 3-(*tert*-butyldimethylsilanyloxy)-1-(1-phenethylbut-3-enyloxy)but-3-enyl ester (10). A sample of 492 mg of **102** was converted to 536 mg (98%) of **10**, isolated as 1:1.3 mixture of diastereomers: IR (neat) 2931, 1741, 1463, 1006, 926, 699 cm^{-1} ; ^1H NMR (500 MHz, C_6D_6) δ 7.20–7.03 (m, 6 H), 6.47–6.43 (m, 1 H), 5.92–5.76 (m, 1 H), 5.07–4.98 (m, 2 H), 4.16 (d, $J = 3.7$ Hz, 1 H), 4.14 (d, $J = 3.3$ Hz, 1 H), 3.81–3.73 (m, 1 H), 2.86–2.79 (m, 0.4 H), 2.75–2.67 (m, 0.6 H), 2.69–2.51 (m, 3 H), 2.35–2.20 (m, 2 H), 1.87–1.65 (m, 2 H), 1.73 (s, 3 H), 0.98 (s, 3 H), 0.96 (s, 5.4 H), 0.15 (s, 1.2 H), 0.14 (s, 1.2 H), 0.13 (s, 1.8 H), 0.10 (s, 1.8 H); ^{13}C NMR (125 MHz, C_6D_6) δ 170.5, 170.4, 154.9, 142.9, 135.5, 134.9, 129.1, 129.1, 129.1, 129.1, 129.0, 126.5, 126.4, 118.0, 117.3, 96.2, 95.0, 93.3, 93.0, 79.4, 77.7, 43.8, 43.6, 40.1, 39.4, 37.0, 32.5, 32.1, 26.2, 21.3, 21.2, 18.5, –4.2, –4.2, –4.6, –4.7; HRMS (EI) calcd for $[\text{C}_{24}\text{H}_{38}\text{O}_4\text{Si}+\text{Na}]^+$ 441.2437, found 441.2447.

2-Allyl-6-phenethyltetrahydropyran-4-one (17). A sample of 40 mg of **10** was converted to 23 mg (99%) of **17**, isolated as a colorless oil: IR (neat) 2928, 1720, 1455, 1060 cm^{-1} ; ^1H NMR (400 MHz, C_6D_6) δ 7.19–7.15 (m, 2 H), 7.11–7.02 (m, 3 H), 5.75 (dddd, $J = 17.0, 10.2, 7.0, 7.0$ Hz, 1 H), 5.06–4.94 (m, 2 H), 3.16–3.05 (m, 2 H), 2.70–2.48 (m, 2 H), 2.18–1.93 (m, 4 H), 1.86–1.74 (m, 2 H), 1.74–1.62 (m, 1 H), 1.46–1.34 (m, 1 H); ^{13}C NMR (125 MHz, C_6D_6) δ 205.1, 142.3, 134.6, 129.1, 129.1, 128.7, 128.2, 126.6, 117.9, 76.5, 76.1, 48.0, 47.6, 41.1, 38.6, 32.1. HRMS (EI) calcd for $[\text{C}_{16}\text{H}_{20}\text{O}_2+\text{Na}]^+$ 267.1361, found 267.1362. Anal. Calcd for $\text{C}_{16}\text{H}_{20}\text{O}_2$: C, 78.65; H, 8.25. Found: C, 78.44; H, 8.14.

General Procedure for the Synthesis of Silyl Enol Ethers (Method A): **3-(*tert*-Butyldimethylsilyloxy)-hex-3-enoic acid 1-phenethylbut-3-enyl ester (**103**).**

Butyryl chloride (0.2 mL, 2.0 mmol, 1.7 equiv.) was cooled to 0 °C in THF (2.0 mL). Silyl ketene acetal **8** (392 mg, 1.18 mmol, 1.0 equiv.) was added, followed by triethylamine (0.28 mL, 2.0 mmol, 1.7 equiv.). The reaction mixture was slowly warmed to room temperature and allowed to stir at this temperature for 16 h. The reaction mixture was then diluted with diethyl ether (20 mL) and washed with water (2 × 5 mL). The organic layer was dried over anhydrous MgSO₄ and concentrated to provide a yellow oil. Purification (SiO₂, 1:9 ether/hexanes, 1.5% Et₃N, R_f = 0.38) provided 407 mg (86%) of **103** (single *Z*-alkene isomer by NOE studies) as a colorless oil: IR (neat) 2959, 1738, 1362, 1254, 1152, 839 cm⁻¹; ¹H NMR (500 MHz, C₆D₆) δ 7.18–7.13 (m, 2 H), 7.10–7.03 (m, 3 H), 5.74–5.65 (m, 1 H), 5.06–4.95 (m, 3 H), 4.60 (t, *J* = 7.0 Hz, 1 H), 2.96 (s, 2 H), 2.66–2.59 (m, 1 H), 2.55–2.46 (m, 1 H), 2.25–2.08 (m, 4 H), 1.81–1.76 (m, 1 H), 1.72–1.64 (m, 1 H), 0.98 (s, 9 H), 0.94 (t, *J* = 7.5 Hz, 3 H), 0.15 (s, 3 H), 0.14 (s, 3 H); ¹³C NMR (125 MHz, C₆D₆) δ 169.9, 144.0, 142.3, 134.4, 129.1, 129.1, 128.7, 126.6, 118.1, 114.6, 73.4, 43.6, 39.3, 36.2, 32.4, 26.3, 19.6, 18.8, 14.8, –3.6, –3.6; HRMS (EI) calcd for [C₂₄H₃₈O₃Si+H]⁺ 403.2668, found 403.2650.

General Procedure for the DIBAL-H Reductive Acetylation of Esters:

Acetic acid 3-(*tert*-butyldimethylsilyloxy)-1-(1-phenethylbut-3-enyloxy)hex-3-enyl ester (11**).** Diisobutylaluminum hydride (0.45 mL, 447 μ L, 1.5 equiv.) was added to a cooled (-78 $^{\circ}$ C) solution of the ester **103** (120 mg, 298 μ mol, 1.0 equiv.) in CH_2Cl_2 (1.8 mL). After 1.5 h, the ester was consumed (monitored by LRMS) and pyridine (60 μ L, 745 μ mol, 2.5 equiv.) was added, followed by 4-(dimethylamino)pyridine (91 mg in 1 mL of CH_2Cl_2 , 745 μ mol, 2.5 equiv.) and acetic anhydride (141 μ L, 1.49 mmol, 5.0 equiv.). The reaction mixture was stirred for 16 h at -78 $^{\circ}$ C then slowly warmed to 0 $^{\circ}$ C over 3 h. The reached mixture was carefully quenched with Rochelle's salt (2 mL) and water (2 mL) then extracted with diethyl ether (3×10 mL). The organic extracts were washed with satd. aq. NaHCO_3 (5 mL) and brine (50 mL) then dried over anhydrous MgSO_4 , and concentrated to provide 130 mg (98%) of α -acetoxo ether **11** as a colorless oil as a 1:1 mixture of diastereomers: IR (neat) 2932, 1741, 1373, 1007, 838 cm^{-1} ; ^1H NMR (400 MHz, C_6D_6) δ 7.23–7.20 (m, 4 H), 7.16–7.13 (m, 6 H), 6.48 (t, $J = 5.4$ Hz, 1 H), 6.46 (t, $J = 5.0$ Hz, 1 H), 5.97–5.82 (m, 2 H), 5.10–5.00 (m, 4 H), 4.62 (t, $J = 7.1$ Hz, 2 H), 3.84–3.75 (m, 2 H), 2.91–2.74 (m, 2 H), 2.71–2.51 (m, 6 H), 2.42–2.22 (m, 4 H), 2.16–2.08 (m, 4 H), 1.93–1.78 (m, 4 H), 1.73 (s, 3 H), 1.72 (s, 3 H), 1.03 (s, 9 H), 1.02 (s, 9 H), 0.97 (t, $J = 7.4$ Hz, 3 H), 0.93 (t, $J = 7.5$ Hz, 3 H), 0.18 (s, 3 H), 0.18 (s, 3 H), 0.14 (s, 3 H), 0.13 (s, 3 H); ^{13}C NMR (125 MHz, C_6D_6) δ 170.5, 170.4, 145.2, 145.2, 143.0, 142.9, 135.5, 134.9, 129.1, 129.1, 129.0, 129.0, 129.0, 129.0, 126.5, 126.4, 126.4, 117.9, 117.3, 114.6, 114.3, 96.7, 95.3, 79.4, 77.8, 43.7, 43.5, 40.2, 39.2, 36.9, 32.5, 31.9, 31.9,

26.3, 26.3, 21.3, 21.2, 19.6, 19.6, 18.8, 18.8, 14.9, 14.9, -3.4, -3.6; HRMS (EI) calcd for $[\text{C}_{26}\text{H}_{42}\text{O}_4\text{Si}+\text{Na}]^+$ 469.2750, found 469.2755.

General Procedure for TMSOTf-Mediated Cyclizations:

6-Allyl-3-ethyl-2-phenethyltetrahydropyran-4-one (18). Trimethylsilyl

trifluoromethanesulfonate (36 μL , 201 μmol , 3.0 equiv.) was added to a cooled ($-78\text{ }^{\circ}\text{C}$) solution of α -acetoxy ether **11** (30 mg, 67 μmol , 1.0 equiv.) in CH_2Cl_2 (1.3 mL). After 30 min. of stirring at $-78\text{ }^{\circ}\text{C}$, no starting acetoxy ether remained and the reaction mixture was quenched with satd. aq. NaHCO_3 (2 mL). The aqueous was extracted with diethyl ether ($3 \times 10\text{ mL}$), washed with brine (10 mL), dried (MgSO_4) and concentrated. Purification (SiO_2 , 5 $\rightarrow$ 10% ether/hexanes, $R_f = 0.20$) provided 11 mg (61%) of **18eq** and 7 mg (38%) of **18ax**.

C-3 equatorial product **18eq** (confirmed by NOESY studies): IR (neat) 2927, 1715, 1456, 1111 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 7.31–7.29 (m, 2 H), 7.22–7.17 (m, 3 H), 5.89 (dddd, $J = 17.0, 10.1, 7.1, 7.1\text{ Hz}$, 1 H), 5.18–5.11 (m, 2 H), 3.64–3.56 (m, 1 H), 3.31 (ddd, $J = 9.8, 9.8, 2.4\text{ Hz}$, 1 H), 2.96–2.88 (m, 1 H), 2.77–2.68 (m, 1 H), 2.49–2.28 (m, 4 H), 2.20–2.14 (m, 1 H), 2.06–1.97 (m, 1 H), 1.91–1.81 (m, 1 H), 0.82 (t, $J = 7.4\text{ Hz}$, 3 H); ^{13}C NMR (125 MHz, CDCl_3) δ 208.4, 141.9, 133.8, 128.5, 128.4, 125.9, 117.7, 79.1, 76.6, 56.4, 47.9, 40.7, 35.8, 31.6, 17.1, 11.6. Anal. Calcd for $\text{C}_{18}\text{H}_{24}\text{O}_2$: C, 79.37; H, 8.88. Found: C, 79.50; H, 9.05.

C-3 axial product **18ax**: IR (neat) 2926, 1717, 1456, 1095 cm^{-1} ; ^1H NMR (500 MHz, C_6D_6) δ 7.18–7.15 (m, 2 H), 7.12–7.04 (m, 3 H), 5.77 (dddd, $J = 17.1, 10.2, 7.0, 7.0$ Hz, 1 H), 5.04–4.95 (m, 2 H), 3.24–3.16 (m, 2 H), 2.68 (ddd, $J = 13.7, 9.8, 5.2$ Hz, 1 H), 2.45 (dddd, $J = 9.3, 6.8, 6.8, 6.8$ Hz, 1 H), 2.19–2.13 (m, 1 H), 2.08–1.98 (m, 3 H), 1.90–1.82 (m, 1 H), 1.53–1.28 (m, 4 H), 0.75 (t, $J = 7.6$ Hz, 3 H); ^{13}C NMR (125 MHz, C_6D_6) δ 208.6, 142.4, 134.6, 129.1, 129.1, 128.7, 128.7, 126.6, 117.9, 79.1, 77.3, 57.3, 44.9, 41.2, 34.5, 33.0, 18.7, 12.0. Anal. Calcd for $\text{C}_{18}\text{H}_{24}\text{O}_2$: C, 79.37; H, 8.88. Found: C, 79.50; H, 8.96.

3-(tert-Butyldimethylsilyloxy)-hexa-3,5-dienoic acid 1-phenethylbut-3-enyl ester (104). A sample of 369 mg of **8** was converted to 425 mg (80%) of **104**, isolated as the *Z*-alkene (confirmed by NOE studies): IR (neat) 2931, 1737, 1751, 1421, 1002, 840, 699 cm^{-1} ; ^1H NMR (400 MHz, C_6D_6) δ 7.19–7.13 (m, 2 H), 7.10–7.04 (m, 3 H), 6.85 (ddd, $J = 17.2, 10.5, 10.5$ Hz, 1 H), 5.68 (dddd, $J = 17.9, 9.3, 7.1, 7.1$ Hz, 1 H), 5.43 (d, $J = 10.7$ Hz, 1 H), 5.09–4.90 (m, 5 H), 2.95 (s, 2 H), 2.65–2.45 (m, 2 H), 2.25–2.12 (m, 2 H), 1.85–1.61 (m, 2 H), 0.96 (s, 9 H), 0.14 (s, 3 H), 0.13 (s, 3 H); ^{13}C NMR (100 MHz, C_6D_6) δ 169.3, 146.6, 142.3, 134.2, 131.9, 129.1, 126.6, 118.2, 114.5, 114.0, 73.7, 43.7, 39.3, 36.1, 32.4, 26.2, 18.8, -3.6 ; HRMS (EI) calcd for $[\text{C}_{24}\text{H}_{36}\text{O}_3\text{Si}+\text{Na}]^+$ 423.2332, found 423.2333.

Acetic acid 3-(tert-butyldimethylsilyloxy)-1-(1-phenethylbut-3-enyloxy)hexa-3,5-dienyl ester (12). A sample of 231 mg of **104** was converted to 250 mg (92%) of **12**,

isolated as a 1:1 mixture of diastereomers: IR (neat) 2931, 1741, 1651, 1420, 1002, 839, 699 cm^{-1} ; ^1H NMR (500 MHz, C_6D_6) δ 7.23–7.04 (m, 5 H), 6.87–6.78 (m, 1 H), 6.45–6.39 (m, 1 H), 5.92–5.77 (m, 1 H), 5.47 (d, $J = 10.7$ Hz, 0.5 H), 5.46 (d, $J = 10.7$ Hz, 0.5 H), 5.10–4.99 (m, 3 H), 4.99–4.89 (m, 1 H), 3.79–3.70 (m, 1 H), 2.86–2.70 (m, 1 H), 2.66–2.53 (m, 3 H), 2.36–2.20 (m, 2 H), 1.87–1.69 (m, 2 H), 1.70 (s, 3 H), 1.00 (s, 4.5 H), 0.98 (s, 4.5 H), 0.16 (s, 3 H), 0.13 (s, 1.5 H), 0.12 (s, 1.5 H); ^{13}C NMR (125 MHz, C_6D_6) δ 170.5, 170.4, 148.2, 148.2, 143.0, 142.9, 135.4, 134.7, 132.1, 129.2, 129.1, 129.0, 129.0, 128.7, 126.5, 118.1, 117.3, 114.7, 114.5, 113.7, 113.6, 96.7, 95.2, 79.7, 77.9, 43.7, 43.5, 40.2, 39.2, 36.9, 36.8, 32.5, 31.9, 26.3, 21.3, 21.2, 18.8, –3.4, –3.5; HRMS (EI) calcd for $[\text{C}_{26}\text{H}_{40}\text{O}_4\text{Si}+\text{Na}]^+$ 467.2594, found 467.2604.

6-Allyl-3-ethylidene-2-phenethyltetrahydropyran-4-one (105). A sample of 70 mg of **12** was converted to 35 mg (84%) of **19**. Proton NMR analysis of the crude mixture allowed a 2:1 ratio of equatorial and axial products **19** to be assigned. However, upon attempted separation on triethylamine-deactivated silica gel produced **105**, isolated as a single *E*-ethylidene isomer (NOE): IR (neat) 2925, 1696, 1622, 1091 cm^{-1} ; ^1H NMR (500 MHz, C_6D_6) δ 7.18–7.14 (m, 2 H), 7.12–7.05 (m, 3 H), 6.64 (dq, $J = 7.3, 2.1$ Hz, 1 H), 5.77 (dddd, $J = 17.0, 10.3, 7.1, 7.1$ Hz, 1 H), 5.06–4.98 (m, 2 H), 4.49–4.45 (m, 1 H), 3.38–3.32 (m, 1 H), 2.81–2.69 (m, 2 H), 2.20–2.12 (m, 3 H), 2.00–1.93 (m, 1 H), 1.82–1.73 (m, 2 H), 1.16 (d, $J = 7.5$ Hz, 3 H); ^{13}C NMR (125 MHz, C_6D_6) δ 196.8, 142.6, 140.1, 134.7, 129.3, 129.0, 128.7, 128.3, 126.5, 117.7, 74.5, 72.5, 45.4, 40.5, 38.3, 31.8, 14.1; HRMS (EI) calcd for $[\text{C}_{18}\text{H}_{22}\text{O}_2+\text{Na}]^+$ 293.1518, found 293.1505.

General Procedure for the Synthesis of Silyl Enol Ethers (Method B):

3-(*tert*-Butyldimethylsilyloxy)-4-methylpent-3-enoic acid 1-phenethylbut-3-enyl ester (106). To a cooled (0 °C) suspension of zinc dust (118 mg, 1.80 mmol, 6.0 equiv.) in THF was added α -bromoisobutyryl bromide (0.11 mL, 0.90 mmol, 3.0 equiv.). After 30 min, the green solution was transferred *via* cannula to a 0 °C solution of silyl ketene acetal **8** (80 mg, 0.24 mmol, 1.0 equiv.) in THF. The reaction mixture was stirred at room temperature for 16 h. The reaction mixture was diluted with diethyl ether, washed with H₂O then satd. aq. NaCl and dried over anhydrous MgSO₄. After concentration and purification (10% diethyl ether/hexanes, R_f = 0.38), 70 mg (72%) of **106** was isolated as a colorless oil: IR (neat) 2930, 1737, 1455, 1256, 1197, 836 cm⁻¹; ¹H NMR (500 MHz, C₆D₆) δ 7.18–7.14 (m, 2 H), 7.10–7.04 (m, 3 H), 5.72–5.63 (m, 1 H), 5.05–4.95 (m, 3 H), 3.14 (d, J = 15.7 Hz, 1 H), 3.10 (d, J = 15.7 Hz, 1 H), 2.65–2.58 (m, 1 H), 2.54–2.46 (m, 1 H), 2.24–2.14 (m, 2 H), 1.84–1.75 (m, 1 H), 1.71–1.65 (m, 1 H), 1.73 (s, 3 H), 1.59 (s, 3 H), 2.24–2.14 (m, 2 H), 1.84–1.75 (m, 1 H), 1.71–1.65 (m, 1 H), 1.73 (s, 3 H), 1.59 (s, 3 H), 1.01 (s, 9 H), 0.18 (s, 3 H), 0.17 (s, 3 H); ¹³C NMR (125 MHz, C₆D₆) δ 170.1, 142.3, 138.7, 134.4, 129.1, 129.1, 128.7, 126.6, 118.0, 113.5, 73.3, 39.6, 39.4, 36.2, 32.4, 26.5, 19.6, 18.8, 18.6, –3.4, –3.4; HRMS (EI) calcd for [C₂₄H₃₈O₃Si+H]⁺ 403.2668, found 403.2666.

Acetic acid 3-(*tert*-butyldimethylsilanyloxy)-4-methyl-1-(1-phenethylbut-3-enyloxy)pent-3-enyl ester (13). A sample of 300 mg of **106** was converted to 306 mg (92%) of **13**, isolated as 1:1 mixture of diastereomers: IR (neat) 2930, 1741, 1682, 1124, 1007, 838, 700 cm^{-1} ; ^1H NMR (500 MHz, C_6D_6) δ 7.23–7.21 (m, 2 H), 7.16–7.04 (m, 3 H), 6.45–6.41 (m, 1 H), 5.92–5.79 (m, 1 H), 5.07–4.99 (m, 2 H), 3.79–3.73 (m, 1 H), 2.87–2.71 (m, 2 H), 2.65–2.53 (m, 2 H), 2.38–2.21 (m, 2 H), 1.87–1.74 (m, 2 H), 1.72 (s, 1.5 H), 1.72 (s, 1.5 H), 1.70 (s, 1.5 H), 1.68 (s, 1.5 H), 1.68 (s, 1.5 H), 1.67 (s, 1.5 H), 1.04 (s, 9 H), 0.18 (s, 1.5 H), 0.17 (s, 1.5 H), 0.13 (s, 1.5 H), 0.12 (s, 1.5 H); ^{13}C NMR (125 MHz, C_6D_6) δ 170.5, 170.3, 143.1, 143.0, 140.2, 140.1, 135.5, 134.8, 129.2, 129.1, 129.1, 129.0, 128.7, 128.2, 126.5, 126.4, 117.8, 117.3, 113.6, 113.4, 97.6, 96.2, 79.5, 77.9, 40.3, 39.2, 39.1, 38.9, 37.0, 36.9, 32.5, 31.6, 26.5, 26.4, 21.3, 21.3, 19.7, 19.6, 18.8, 18.8, 18.6, –3.2, –3.2, –3.4, –3.4; HRMS (EI) calcd for $[\text{C}_{26}\text{H}_{42}\text{O}_4\text{Si}+\text{Na}]^+$ 469.2750, found 469.2752.

6-Allyl-3,3-dimethyl-2-phenethyltetrahydropyran-4-one (20). A sample of 40 mg of **13** was converted to 22 mg (92%) of **20**, isolated as a colorless oil: IR (neat) 2932, 1712, 1455, 1127, 700 cm^{-1} ; ^1H NMR (500 MHz, C_6D_6) δ 7.19–7.15 (m, 2 H), 7.11–7.07 (m, 3 H), 5.84–5.74 (m, 1 H), 5.06–4.95 (m, 2 H), 3.22–3.14 (m, 1 H), 2.95 (d, J = 10.6 Hz, 1 H), 2.912–2.84 (m, 1 H), 2.60–2.52 (m, 1 H), 2.23–2.13 (m, 2 H), 2.07–1.95 (m, 2 H), 1.77–1.68 (m, 1 H), 1.51–1.43 (m, 1 H), 0.92 (s, 3 H), 0.90 (s, 3 H); ^{13}C NMR (125 MHz, C_6D_6) δ 209.9, 142.7, 134.6, 129.2, 129.1, 128.7, 128.2, 128.6, 117.9, 83.4, 77.1, 49.4,

44.4, 41.2, 33.4, 31.7, 19.5, 19.3; HRMS (EI) calcd for $[C_{18}H_{24}O_2+Na]^+$ 295.1674, found 295.1669. Anal. Calcd for $C_{18}H_{24}O_2$: C, 79.37; H, 8.88. Found: C, 79.50; H, 9.00.

1-Bromocyclohexanecarbonyl bromide (107). Known compound:³ IR (neat) 2941, 1770, 1081, 956, 627 cm^{-1} ; 1H NMR (400 MHz, C_6D_6) δ 1.90–1.70 (m, 4 H), 1.41–1.28 (m, 2 H), 1.22–1.10 (m, 2 H), 1.08–0.96 (m, 1 H), 0.92–0.79 (m, 1 H); ^{13}C NMR (100 MHz, C_6D_6) δ 170.7, 73.6, 39.0, 24.8, 23.9.

3-(*tert*-Butyldimethylsilyloxy)-3-cyclohexylidene-propionic acid 1-phenethylbut-3-enyl ester (108). A sample of 40 mg of **8** was converted to 36 mg (68%) of **108**, isolated as a colorless oil: IR (neat) 2929, 1737, 1450, 1032, 838 cm^{-1} ; 1H NMR (500 MHz, C_6D_6) δ 7.20–7.05 (m, 5 H), 5.76–5.65 (m, 1 H), 5.07–5.02 (m, 1 H), 5.01–4.96 (m, 2 H), 3.17 (d, J = 15.5 Hz, 1 H), 3.13 (d, J = 15.5 Hz, 1 H), 2.68–2.60 (m, 1 H), 2.56–2.48 (m, 1 H), 2.35–2.28 (m, 2 H), 2.24–2.16 (m, 2 H), 2.12–2.06 (m, 2 H), 1.87–1.78 (m, 1 H), 1.74–1.64 (m, 1 H), 1.57–1.41 (m, 6 H), 1.02 (s, 9 H), 0.19 (s, 3 H), 0.19 (s, 3 H); ^{13}C NMR (125 MHz, C_6D_6) δ 170.2, 142.4, 136.0, 134.4, 129.1, 128.7, 126.6, 121.8, 118.0, 73.3, 39.4, 39.2, 36.3, 32.4, 30.6, 28.5, 28.2, 27.9, 27.4, 26.7, 26.5, 18.9, –3.5, –3.5; HRMS (EI) calcd for $[C_{27}H_{42}O_3Si+H]^+$ 443.2982, found 443.2974.

³ Wagner, R. B.; Moore, J. A. *J. Am. Chem. Soc.* **1950**, 72, 974–977.

Acetic acid 3-(*tert*-butyldimethylsilanyloxy)-3-cyclohexylidene-1-(1-phenethylbut-3-enyloxy)propyl ester (14). A sample of 169 mg of **108** was converted to 172 mg (93%) of **14**, isolated as 1:1 mixture of diastereomers: IR (neat) 2928, 1739, 1448, 1250, 1007, 838 cm^{-1} ; ^1H NMR (500 MHz, C_6D_6) δ 7.24–7.14 (m, 5 H), 7.11–7.04 (m, 1 H), 6.47–6.42 (m, 1 H), 5.95–5.85 (m, 1 H), 5.10–5.00 (m, 2 H), 3.81–3.73 (m, 1 H), 2.90–2.75 (m, 2 H), 2.72–2.57 (m, 2 H), 2.43–2.12 (m, 6 H), 1.91–1.82 (m, 1 H), 1.75 (s, 1.5 H), 1.74 (s, 1.5 H), 1.62–1.42 (m, 6 H), 1.05 (s, 4.5 H), 1.04 (s, 4.5 H), 0.19 (s, 1.5 H), 0.18 (s, 1.5 H), 0.15 (s, 1.5 H), 0.15 (s, 1.5 H); ^{13}C NMR (125 MHz, C_6D_6) δ 170.2, 170.2, 143.0, 137.4, 135.6, 135.0, 129.2, 129.1, 129.0, 128.7, 126.5, 126.4, 121.8, 117.8, 117.3, 97.5, 96.1, 79.3, 77.8, 40.3, 39.3, 38.6, 38.5, 37.0, 36.9, 32.5, 31.8, 30.5, 28.8, 28.7, 28.3, 28.0, 27.9, 27.5, 27.5, 26.5, 26.5, 21.4, 21.3, 18.8, –3.2, –3.5; HRMS (EI) calcd for $[\text{C}_{29}\text{H}_{46}\text{O}_4\text{Si}+\text{Na}]^+$ 509.3063, found 509.3063.

3-Allyl-1-phenethyl-2-oxaspiro[5.5]undecan-5-one (21). A sample of 43 mg of **14** was converted to 26 mg (93%) of **21**, isolated as a colorless oil: IR (neat) 2930, 1706, 1455, 1239, 1120 cm^{-1} ; ^1H NMR (500 MHz, C_6D_6) δ 7.20–7.15 (m, 2 H), 7.12–7.07 (m, 3 H), 5.79 (dddd, $J = 17.1, 10.2, 7.0, 7.0$ Hz, 1 H), 5.05–4.97 (m, 2 H), 3.30–3.23 (m, 1 H), 2.94–2.86 (m, 2 H), 2.50 (ddd, $J = 13.5, 9.4, 7.2$ Hz, 1 H), 2.36 (dd, $J = 12.3, 12.3$ Hz, 1 H), 2.27–2.16 (m, 2 H), 2.07–1.99 (m, 3 H), 1.84–1.70 (m, 2 H), 1.64–1.50 (m, 3 H), 1.45–1.38 (m, 1 H), 1.25 (ddd, $J = 13.4, 13.4, 3.2$ Hz, 1 H), 1.02–0.88 (m, 2 H), 0.85 (ddd, $J = 12.8, 12.8, 4.7$ Hz, 1 H); ^{13}C NMR (125 MHz, C_6D_6) δ 211.3, 142.8, 134.7, 129.2, 129.1, 128.7, 126.6, 117.9, 85.2, 78.5, 55.1, 45.7, 41.2, 33.9, 31.9, 29.2, 28.6, 27.2,

23.5, 23.1; HRMS (EI) calcd for $[C_{21}H_{28}O_2+Na]^+$ 335.1987, found 335.1993. Anal. Calcd for $C_{21}H_{28}O_2$: C, 80.73; H 9.03. Found: C, 80.61; H, 9.07.

3-(*tert*-Butyldimethylsilyloxy)-4-phenylpent-3-enoic acid 1-phenethylbut-3-enyl ester (109). A sample of 100 mg of **8** was converted to 129 mg (92%) of **109**, isolated as a single *Z*-isomer (NOE): IR (neat) 2929, 1738, 1455, 1254, 829, 699 cm^{-1} ; 1H NMR (500 MHz, C_6D_6) δ 7.40–7.36 (m, 2 H), 7.20–7.11 (m, 6 H), 7.09–7.01 (m, 2 H), 5.74 (dddd, J = 17.7, 9.6, 7.0, 7.0 Hz, 1 H), 5.13–5.07 (m, 1 H), 5.04–4.99 (m, 2 H), 3.25 (d, J = 15.5 Hz, 1 H), 3.21 (d, J = 15.5 Hz, 1 H), 2.74–2.66 (m, 1 H), 2.61–2.53 (m, 1 H), 2.28–2.19 (m, 2 H), 1.92 (s, 3 H), 1.89–1.81 (m, 1 H), 1.74–1.66 (m, 1 H), 0.85 (s, 9 H), –0.11 (s, 3 H), –0.14 (s, 3 H); ^{13}C NMR (125 MHz, C_6D_6) δ 169.7, 412.6, 142.2, 140.7, 134.4, 134.4, 129.9, 129.1, 129.1, 128.6, 126.8, 126.7, 118.7, 118.2, 73.5, 40.6, 39.4, 36.2, 32.4, 26.3, 26.3, 20.0, 18.6, –3.9, –3.9; HRMS (EI) calcd for $[C_{29}H_{40}O_3Si+Na]^+$ 487.2644, found 487.2644.

Acetic acid 3-(*tert*-butyldimethylsilyloxy)-1-(1-phenethylbut-3-enyloxy)-4-phenylpent-3-enyl ester (15). A sample of 102 mg of **109** was converted to 110 mg (99%) of **15**, isolated as a 1:1 mixture of diastereomers: IR (neat) 2930, 1741, 1455, 1007, 837, 700 cm^{-1} ; 1H NMR (500 MHz, C_6D_6) δ 7.38–7.34 (m, 1 H), 7.33–7.29 (m, 1 H), 7.21–7.11 (m, 6 H), 7.10–6.99 (m, 2 H), 6.63–6.58 (m, 1 H), 5.98–5.86 (m, 1 H), 5.11–5.02 (m, 2 H), 3.86–3.77 (m, 1 H), 2.90–2.62 (m, 4 H), 2.41–2.27 (m, 2 H), 2.01–1.92 (m, 1

H), 1.98 (s, 3 H), 1.90–1.80 (m, 1 H), 1.76 (s, 1.5 H), 1.76 (s, 1.5 H), 0.88 (s, 4.5 H), 0.87 (s, 4.5 H), –0.14 (s, 1.5 H), –0.15 (s, 1.5 H), –0.17 (s, 1.5 H), –0.21 (s, 1.5 H); ^{13}C NMR (125 MHz, C_6D_6) δ 170.4, 170.3, 143.0, 142.9, 142.7, 142.0, 135.4, 134.8, 129.9, 129.1, 129.1, 129.0, 128.7, 128.7, 128.6, 128.5, 126.7, 126.7, 126.5, 126.5, 118.9, 118.8, 118.1, 117.4, 97.3, 96.1, 79.5, 77.9, 40.2, 40.0, 39.8, 39.3, 36.9, 36.8, 32.5, 32.2, 26.3, 21.3, 21.3, 20.0, 20.0, 18.6, –3.8, –3.8, –3.9, –3.9; HRMS (EI) calcd for $[\text{C}_{31}\text{H}_{44}\text{O}_4\text{Si}+\text{Na}]^+$ 531.2906, found 531.2908.

6-Allyl-3-methyl-2-phenethyl-3-phenyltetrahydropyran-4-one (22). A sample of 26 mg of **15** was converted to 15 mg (88%) of **22**, isolated as single diastereomer (confirmed by NOESY studies): IR (neat) 2927, 1713, 1445, 1098 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 7.31–7.13 (m, 6 H), 7.06–7.04 (m, 2 H), 7.00–6.97 (m, 2 H), 5.95 (dddd, J = 17.1, 10.2, 7.0, 7.0 Hz, 1 H), 5.23–5.16 (m, 2 H), 3.88–3.83 (m, 1 H), 3.82 (dd, J = 10.3, 1.5 Hz, 1 H), 2.86–2.80 (m, 1 H), 2.66 (dd, J = 15.5, 11.8 Hz, 1 H), 2.55–2.48 (m, 2 H), 2.44 (dd, J = 15.5, 3.0 Hz, 1 H), 2.42–2.37 (m, 1 H), 1.86–1.77 (m, 1 H), 1.57 (s, 3 H), 1.32–1.25 (m, 1 H); ^{13}C NMR (125 MHz, CDCl_3) δ 210.6, 141.5, 139.6, 133.6, 128.4, 128.2, 128.2, 127.9, 127.0, 125.8, 117.9, 82.9, 76.5, 58.1, 43.9, 40.5, 32.5, 30.5, 16.1; HRMS (EI) calcd for $[\text{C}_{23}\text{H}_{26}\text{O}_2+\text{Na}]^+$ 357.1830, found 357.1819.

3-(*tert*-Butyldiphenylsilyloxy)-2-methylpropionic acid (110). Known compound:⁴

¹H NMR (500 MHz, CDCl₃) δ 7.70–7.66 (m, 4 H), 7.46–7.38 (m, 6 H), 3.86 (dd, *J* = 9.9, 6.9 Hz, 1 H), 3.78 (dd, *J* = 9.9, 5.6 Hz, 1 H), 2.79–2.72 (m, 1 H), 1.21 (d, *J* = 7.1 Hz, 3 H), 1.09 (s, 1 H), 1.05 (s, 9 H); ¹³C NMR (125 MHz, CDCl₃) δ 190.9, 135.6, 135.6, 134.8, 133.2, 133.2, 129.7, 129.6, 127.7, 65.6, 42.2, 26.7, 26.5, 19.2, 13.2.

3-(*tert*-Butyldimethylsilyloxy)-5-(*tert*-butyldiphenylsilyloxy)-4-methylpent-3-

enoic acid 1-phenethylbut-3-enyl ester (111). A sample of 100 mg of **8** was converted to 167 mg (56%) of **111**, isolated as a 1:2 *E/Z* mixture (crude product, 1:1.5 *E/Z* mixture):

IR (neat) 2931, 1737, 1675, 1254, 1055, 834, 702 cm⁻¹; ¹H NMR (500 MHz, C₆D₆) δ 7.85–7.80 (m, 4 H), 7.26–7.03 (m, 11 H), 5.74–5.56 (m, 1 H), 5.07–4.89 (m, 3 H), 4.37 (s, 0.7 H), 3.14 (d, *J* = 16.3 Hz, 0.35 H), 3.06 (d, *J* = 16.3 Hz, 0.35 H), 3.04 (d, *J* = 15.9 Hz, 0.15 H), 3.00 (d, *J* = 15.9 Hz, 0.15 H), 2.62 (ddd, *J* = 13.4, 10.3, 5.3 Hz, 0.7 H), 2.58–2.48 (m, 1 H), 2.46–2.39 (m, 0.3 H), 2.26–2.15 (m, 1.4 H), 2.14–2.09 (m, 0.7 H), 1.95 (s, 1 H), 1.90 (s, 2 H), 1.87–1.79 (m, 0.7 H), 1.76–1.62 (m, 1.3 H), 1.20 (s, 6 H), 1.18 (s, 3 H), 1.01 (s, 3 H), 0.85 (s, 6 H), 0.20 (d, *J* = 1.7 Hz, 2 H), 0.06 (d, *J* = 2.7 Hz, 4 H); ¹³C NMR (125 MHz, C₆D₆) δ 169.8, 169.7, 142.3, 141.6, 139.8, 136.5, 136.4, 134.7, 134.7, 134.3, 134.2, 130.4, 130.2, 129.1, 129.1, 128.7, 128.6, 128.3, 126.6, 126.6, 118.1, 118.1, 117.7, 73.6, 73.5, 65.6, 63.0, 39.8, 39.4, 39.4, 39.3, 36.2, 36.1, 32.4, 32.3, 27.6, 27.5, 26.4, 26.3, 20.0, 19.9, 18.9, 18.7, 14.8, 14.8, -3.4, -3.7, -3.7; HRMS (EI) calcd for [C₄₀H₅₆O₄Si₂+Na]⁺ 679.3615, found 679.3585.

⁴ Heathcock, C. H.; Young, S. D.; Hagen, J. P.; Pilli, R.; Badertscher, U. *J. Org. Chem.* **1985**, *50*, 2095–2105.

Acetic acid 3-(*tert*-butyldimethylsilanyloxy)-5-(*tert*-butyldiphenylsilyloxy)-4-methyl-1-(1-phenethylbut-3-enyloxy)pent-3-enyl ester (16). A sample of 97 mg of **111** was converted to 95 mg (92%) of **16**, isolated as a diastereomeric mixture of alkene isomers: IR (neat) 2931, 1741, 1674, 1237, 1049, 838, 701 cm^{-1} ; ^1H NMR (500 MHz, C_6D_6) δ 7.87–7.76 (m, 4 H), 7.30–7.05 (m, 11 H), 6.50–6.45 (m, 0.8 H), 6.46–6.32 (m, 0.2 H), 5.94–5.74 (m, 1 H), 5.08–4.96 (m, 2 H), 4.57 (d, J = 8.1 Hz, 0.4 H), 4.54 (d, J = 8.1 Hz, 0.4 H), 4.50–4.37 (m, 1.2 H), 3.82–3.76 (m, 0.8 H), 3.72–3.68 (m, 0.2 H), 2.90–2.60 (m, 4 H), 2.38–2.16 (m, 2 H), 1.98 (s, 1 H), 1.94–1.80 (m, 2 H), 1.76 (s, 1.5 H), 1.75 (s, 1.5 H), 1.67 (s, 0.5 H), 1.66 (s, 0.5 H), 1.22 (s, 3 H), 1.21 (s, 2 H), 1.20 (s, 1 H), 1.19 (s, 3 H), 1.05 (s, 1 H), 1.03 (s, 1 H), 0.89 (s, 3.5 H), 0.88 (s, 3.5 H), 0.20 (s, 0.5 H), 0.20 (s, 0.5 H), 0.17 (s, 0.5 H), 0.16 (s, 0.5 H), 0.04 (s, 1 H), 0.02 (s, 1 H), 0.02 (s, 1 H), 0.01 (s, 1 H); ^{13}C NMR (125 MHz, C_6D_6) δ 170.5, 170.4, 170.2, 142.9, 142.8, 141.3, 141.3, 136.5, 135.4, 134.8, 130.3, 130.3, 130.2, 129.1, 129.1, 129.1, 129.1, 129.0, 129.0, 128.7, 128.6, 126.4, 118.0, 118.0, 117.9, 117.8, 117.4, 117.3, 96.9, 95.9, 95.7, 79.6, 79.3, 77.9, 65.5, 63.1, 63.0, 40.2, 39.3, 39.2, 39.1, 38.8, 36.9, 36.8, 36.7, 32.5, 32.4, 31.9, 27.6, 27.5, 26.4, 26.3, 21.3, 21.3, 21.2, 20.0, 18.9, 18.7, 15.0, 14.9, 14.9, –3.1, –3.3, –3.5, –3.6, –3.6; HRMS (EI) calcd for $[\text{C}_{42}\text{H}_{60}\text{O}_5\text{Si}_2+\text{Na}]^+$ 723.3877, found 723.3881.

6-Allyl-3-(*tert*-butyldiphenylsilyloxymethyl)-3-methyl-2-phenethyl-tetrahydropyran-4-one (23). A sample of 26 mg of **16** was converted to 15 mg (77%)

of **23**, isolated as a 1:1.2 mixture of diastereomers: IR (neat) 2930, 1717, 1428, 1112, 702 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 7.74–7.70 (m, 1 H), 7.62–7.55 (m, 2 H), 7.45–7.09 (m, 12 H), 5.99–5.89 (m, 0.7 H), 5.84–5.75 (m, 0.3 H), 5.20–5.07 (m, 2 H), 4.20 (d, J = 9.9 Hz, 0.3 H), 4.09 (d, J = 10.3 Hz, 0.7 H), 4.03 (d, J = 10.4 Hz, 0.7 H), 3.80–3.73 (m, 0.7 H), 3.65 (d, J = 9.9 Hz, 0.3 H), 3.55–3.49 (m, 0.3 H), 3.24 (d, J = 10.3 Hz, 0.7 H), 3.10–3.06 (m, 0.3 H), 3.02–2.94 (m, 0.7 H), 2.85–2.79 (m, 0.3 H), 2.72–2.64 (m, 0.7 H), 2.55–2.17 (m, 4.3 H), 1.04 (s, 0.9 H), 1.00 (s, 2.7 H), 0.96 (s, 6.3 H); ^{13}C NMR (125 MHz, CDCl_3) δ 210.0, 209.1, 142.1, 141.5, 135.8, 135.7, 135.7, 135.6, 133.6, 133.6, 133.3, 132.8, 129.8, 129.7, 129.7, 129.6, 128.5, 128.5, 128.4, 128.4, 127.7, 127.7, 127.6, 125.9, 125.9, 117.7, 82.8, 78.8, 77.3, 75.9, 66.1, 64.2, 55.9, 54.0, 45.2, 44.3, 40.7, 40.5, 33.0, 32.9, 31.4, 31.3, 29.7, 26.8, 19.3, 19.2, 15.4, 15.1; HRMS (EI) calcd for $[\text{C}_{34}\text{H}_{42}\text{O}_3\text{Si}+\text{Na}]^+$ 549.2801, found 549.2789. Anal. Calcd for $\text{C}_{34}\text{H}_{42}\text{O}_3\text{Si}$: C, 77.52; H 8.04. Found: C, 77.70; H, 7.99.

3-(tert-Butyldimethylsilyloxy)hex-3-enoic acid 1-[2-(tert-butyl-diphenyl-silyloxy)ethyl]-but-3-enyl ester (112). A sample of 100 mg of **8** was converted to 94 mg (82%) of **112**, isolated as a single *Z*-isomer (NOE): $[\alpha]_D^{22} +11.3$ (c 0.53, CHCl_3); IR (neat) 2931, 1738, 1428, 1112, 825 cm^{-1} ; ^1H NMR (400 MHz, C_6D_6) δ 7.81–7.74 (m, 4 H), 7.29–7.20 (m, 6 H), 5.75 (dddd, J = 16.0, 11.4, 7.0, 7.0 Hz, 1 H), 5.36–5.29 (m, 1 H), 5.02–4.96 (m, 2 H), 4.57 (t, J = 7.1 Hz, 1 H), 3.79–3.68 (m, 2 H), 2.94 (s, 2 H), 2.35–2.20 (m, 2 H), 2.16–2.07 (m, 2 H), 1.86–1.73 (m, 2 H), 1.18 (s, 9 H), 0.99 (s, 1 H), 0.94 (t, J = 7.6 Hz, 3 H), 0.14 (s, 3 H), 0.13 (s, 3 H); ^{13}C NMR (100 MHz, C_6D_6) δ 169.8, 143.9,

136.4, 136.4, 134.5, 134.4, 130.4, 128.6, 128.5, 118.1, 114.4, 71.3, 60.9, 43.5, 39.2, 37.0, 27.4, 26.3, 19.8, 19.6, 18.8, 14.8, -3.6, -3.6; HRMS (EI) calcd for $[C_{34}H_{52}O_4Si_2+Na]^+$ 603.3302, found 603.3301.

Acetic acid 3-(*tert*-butyldimethylsilanyloxy)-1-{1-[2-(*tert*-butyldiphenylsilyloxy)-ethyl]but-3-enyloxy-hex-3-enyl ester (113). A sample of 52 mg of **112** was converted to 55 mg (98%) of **113**, isolated as a 1:1 mixture of diastereomers: $[a]_D^{22} +8.3$ (c 0.855, $CHCl_3$); IR (neat) 2931, 1742, 1428, 1007, 825 cm^{-1} ; 1H NMR (400 MHz, C_6D_6) δ 7.82–7.75 (m, 4 H), 7.24–7.20 (m, 6 H), 6.48–6.43 (m, 1 H), 6.00–5.84 (m, 1 H), 5.09–4.98 (m, 2 H), 4.57 (t, $J = 7.1$ Hz, 0.5 H), 4.56 (t, $J = 7.1$ Hz, 0.5 H), 4.12–4.03 (m, 1 H), 3.96–3.78 (m, 2 H), 2.55–2.50 (m, 2 H), 2.41–2.27 (m, 2 H), 2.16–2.05 (m, 2 H), 1.98–1.75 (m, 2 H), 1.73 (s, 1.5 H), 1.73 (s, 1.5 H), 1.72 (s, 1.5 H), 1.20 (s, 4.5 H), 1.17 (s, 4.5 H), 1.01 (s, 9 H), 0.94 (t, $J = 7.5$ Hz, 1.5 H), 0.94 (t, $J = 7.5$ Hz, 1.5 H), 0.15 (s, 3 H), 0.12 (s, 1.5 H), 0.12 (s, 1.5 H); ^{13}C NMR (100 MHz, C_6D_6) δ 170.5, 170.3, 145.3, 145.2, 136.4, 136.4, 136.4, 136.3, 135.6, 134.9, 134.8, 134.6, 130.3, 130.3, 128.6, 117.9, 117.3, 114.3, 114.1, 96.3, 95.2, 77.0, 75.2, 61.4, 61.1, 43.4, 40.1, 39.1, 38.1, 37.7, 27.5, 27.5, 27.1, 26.4, 26.3, 21.3, 19.8, 19.5, 18.8, 18.8, 14.9, -3.4, -3.4, -3.4, -3.6; HRMS (EI) calcd for $[C_{36}H_{56}O_5Si_2+Na]^+$ 647.3564, found 647.3568.

6-Allyl-2-[2-(*tert*-butyldiphenylsilyloxy)ethyl]-3-ethyltetrahydropyran-4-one (25).

A sample of 36 mg of **113** was converted to 22 mg (85%) of **25**, isolated as a 2:1 mixture of C-3 epimers: IR (neat) 2961, 1715, 1428, 1112 cm^{-1} ; 1H NMR (500 MHz, C_6D_6) δ

7.79–7.74 (m, 4 H), 7.25–7.23 (m, 6 H), 5.72–5.61 (m, 1 H), 5.00–4.91 (m, 2 H), 4.00 (ddd, $J = 9.7, 9.7, 5.3$ Hz, 0.5 H), 3.88–3.70 (m, 1.5 H), 3.67 (ddd, $J = 8.9, 3.2, 3.2$ Hz, 0.5 H), 3.50 (ddd, $J = 10.0, 10.0, 2.0$ Hz, 0.5 H), 3.28–3.20 (m, 1 H), 2.20–1.88 (m, 5 H), 1.86–1.78 (m, 1 H), 1.62–1.42 (m, 2.5 H), 1.36–1.28 (m, 1.5 H), 1.17 (s, 4.5 H), 1.16 (s, 4.5 H), 0.96 (t, $J = 7.4$ Hz, 1.5 H), 0.73 (t, $J = 7.5$ Hz, 1.5 H); ^{13}C NMR (125 MHz, C_6D_6) δ 208.7, 206.6, 136.3, 134.4, 134.4, 130.4, 130.4, 128.9, 128.7, 128.6, 128.2, 117.9, 117.8, 77.2, 77.2, 76.6, 76.5, 61.3, 60.9, 57.3, 56.4, 48.1, 44.7, 41.1, 37.7, 35.8, 27.5, 19.8, 18.7, 18.0, 12.0; HRMS (EI) calcd for $[\text{C}_{28}\text{H}_{38}\text{O}_3\text{Si}+\text{Na}]^+$ 473.2488, found 472.2491.

Epimerization of the C-3 center: Treatment of **25** with 1:1 aq. NaOH (1.0 M)/THF at reflux enriched the C-3 equatorial product from 1:1 to 3.5:1 (99% mass recovery).

6-Allyl-2-[2-(*tert*-butyldiphenylsilyloxy)ethyl]-3-ethyltetrahydropyran-4-ol (26).

L-Selectride (27 μL , 27 μmol , 1.2 equiv.) was added to a -78 $^\circ\text{C}$ solution of pure C-3 equatorial **25** (8 mg, 12.8 μmol , 1.0 equiv) in 0.2 mL of THF. After 30 min, 1 drop of MeOH, 1 N NaOH and 30% H_2O_2 were sequentially added and the reaction mixture was allowed to stir with warming to room temperature over 1.5 h. After dilution with H_2O (2 mL), the aqueous was extracted with ethyl acetate (3×5 mL), then washed with H_2O and brine. The extracts were dried over anhydrous MgSO_4 and concentrated. Purification (20% EtOAc/hexanes, $R_f = 0.49$ in 30% EtOAc/hexanes) provided 7 mg (88%) of **26** as a single diastereomer: $[\alpha]_D^{22} -7.0$ (c 0.10, CHCl_3); IR (neat) 3412, 2930, 1428, 1112, 701 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 7.74–7.65 (m, 4 H), 7.44–7.35 (m, 6 H), 5.76 (dddd,

$J = 17.1, 10.0, 6.9, 6.9$ Hz, 1 H), 5.05–4.95 (m, 2 H), 4.15–4.12 (m, 1 H), 3.88–3.73 (m, 2 H), 3.71–3.61 (m, 2 H), 2.25–2.19 (m, 1 H), 2.12–2.05 (m, 1 H), 1.97–1.90 (m, 1 H), 1.79–1.75 (m, 1 H), 1.48–1.39 (m, 2 H), 1.29–1.16 (m, 4 H), 1.07 (s, 9 H), 0.93 (t, $J = 7.3$ Hz, 3 H); ^{13}C NMR (125 MHz, CDCl_3) δ 141.7, 135.6, 134.8, 129.7, 129.4, 127.7, 127.5, 120.9, 116.4, 72.5, 70.4, 66.5, 65.0, 60.5, 51.8, 45.8, 40.4, 39.2, 36.0, 26.9, 26.5, 19.3, 11.0; HRMS (EI) calcd for $[\text{C}_{28}\text{H}_{40}\text{O}_3\text{Si}+\text{Na}]^+$ 475.2644, found 475.2653.

Advanced Mosher analysis of the *R*- and *S*-MTPA esters:

$\delta S - \delta R$ values (ppm)