Catalytic asymmetric reactions for organic synthesis: The combined C–H activation/siloxy-Cope rearrangement

Huw M. L. Davies, Rohan E. J. Beckwith.*

Department of Chemistry, University at Buffalo, State University of New York,

Buffalo, New York 14260-3000

Supporting Information

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EXPERIMENTAL

General: All reactions were carried out under an argon atmosphere and anhydrous conditions unless otherwise noted. Solvents used for C-H activation reactions were degassed prior to use. Degassing was conducted by bubbling Ar gas through the solution for 10 minutes. Tetrahydrofuran (THF), hexanes and 2,2-dimethylbutane were distilled from benzophenone sodium ketyl under argon in a standing still prior to use. Petrol refers to petroleum ether (b.p. 40-60 °C). All other solvents were of reagent grade. Reagents purchased from commercial sources were used without further purification unless otherwise stated. Analytical TLC was performed on 0.25 mm silica gel (60F-254) plates using UV light and phosphomolybdic acid (PMA) dip as visualizing agents. Purifications by flash column chromatography used silica 60 (230-400 mesh). ^{1}H NMR spectra were recorded on Nuclear Magnetic Resonance spectrometers at 300, 400, or 500 MHz and ^{13}C spectra were recorded at 75 or 125 MHz, calibrated by using residual undeuterated solvent as an internal standard. The following abbreviations apply- (app.) apparent, (b) broad, (s) singlet, (d) doublet, (t) triplet, (q) quartet, (m) multiplet, (dd) double doublet, etc. Chemical shifts are given in ppm. *J* values are recorded in Hz. Where necessary, proton and carbon assignments were assisted with ^{1}H COSY, DEPT or nOe sequences. The chemical shifts of multiplets corresponding to a single proton are quoted as a point, representing the center of the multiplet. Where the signals for two or more protons overlap, a range is quoted. Infrared spectra were obtained on a FT-IR spectrometer. Mass spectra were recorded on a GC-MS system using 70 eV electron impact (EI) ionization. Elemental analyses were determined by an external service provider. Diastereomeric ratios were determined by values derived from the 500 MHz ^{1}H NMR spectra of the crude reaction or by correlating these ^{1}H NMR values with GC-MS data. Optical rotations were determined by digital polarimeter. Enantiomeric excess was determined by either ^{1}H NMR using Eu tris[3-(heptafluoropropylhydroxymethylene)-(+)-camphorate] as a chiral shift reagent or high performance liquid chromatography (HPLC) using Diacel Chiralcel OD-H, Chiralpak AD-RH or (*R*,*R*) Whelk-O1 chiral analytical columns with 2-propanol in hexane as the eluent.

General Procedure for the Decomposition of Vinyldiazoacetates in the Presence of Allylic silyl ethers: Vinyldiazoacetate (1.00 mmol) in 2,2-dimethylbutane (10 mL) was added dropwise over 2 h via a

syringe pump to a rapidly stirred solution of allylic silyl ether (0.50 mmol) and Rh_2(*S*-DOSP)$_4$ (19 mg, 1.00 x 10^{-5} mol) in 2,2-dimethylbutane (1.0 mL) at 23 °C. On completion of the vinyldiazoacetate addition, the reaction mixture was allowed to stir for an additional 20 min prior to concentration in vacuo. Purification by flash chromatography on silica gel afforded the product(s).

Methyl (2*E*,4*R*,5*S*,6*Z*)-7-(*tert*-butyldimethylsiloxy)-5-methyl-4-phenylhepta-2,6-dienoate (16a) and methyl (2*S*,3*R*,*E*)-3-(*tert*-butyldimethylsiloxy)-*2*-((*E*)-styryl)hex-4-enoate (17a). As general procedure. The solvent was evaporated and the residue (**16a**:**17a**= 1.0:1.0 by ^{1}H NMR of the crude reaction mixture) was purified by flash chromatography [SiO_2; dichloromethane/petrol, 1:4], to provide **17a** (46 mg, 46% yield) and **16a** (43 mg, 43% yield). **17a**: colorless oil; R_f 0.62 (1:4 diethyl ether/hexane eluent); $[\alpha]_D^{25}$ -34.5 (*c* 0.94, $CHCl_3$); IR (film) 3024, 2953, 2929, 2885, 2856, 1736 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.40 (d, *J* = 7.6 Hz, 2H), 7.34 (app. t, *J* = 7.3 Hz, 2H), 7.26 (t, *J* = 7.2 Hz, 1H), 6.45 (d, *J* = 15.9 Hz, 1H), 6.32 (dd, *J* = 15.9, 9.5 Hz, 1H), 5.65 (dq, *J* = 15.3, 6.4 Hz, 1H), 5.50 (dd, *J* = 15.3, 7.6 Hz, 1H), 4.47 (app. t, *J* = 7.0 Hz, 1H), 3.70 (s, 3H), 3.25 (dd, *J* = 9.3, 6.5 Hz, 1H), 1.70 (d, *J* = 6.1 Hz, 3H), 0.88 (s, 9H), 0.03 (s, 3H), 0.02 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.7 (C), 137.1 (C), 133.7 (CH), 132.1 (CH), 128.6 (CH), 127.6 (CH), 127.5 (CH), 126.4 (CH), 124.9 (CH), 75.3 (CH), 57.8 (CH), 51.8 (CH_3), 25.8 (CH_3), 18.1 (C), 17.7 (CH_3), -4.1 (CH_3), -4.8 (CH_3); MS (ESI) *m*/*z* (relative intensity) 383 (M + Na, 70), 229 (100); HRMS (M + Na) calcd for $C_{21}H_{32}O_3NaSi$: 383.2013. Found 383.2013. HPLC analysis: ee 88% ((*R*,*R*)-Whelk-O1, 0.9% *i*-PrOH in hexane, 0.6 mL/min, λ= 254 nm, t_R= 9.6 min, major; t_R= 11.9 min, minor). Anal. Calcd for $C_{21}H_{32}O_3Si$: C, 69.95; H, 8.95. Found: C, 69.79; H, 9.08.

16a: colorless oil; R_f 0.54 (1:4 diethyl ether/hexane eluent); $[\alpha]_D^{25}$ -24.4 (*c* 1.33, $CHCl_3$); IR (film) 2955, 2929, 2860, 1725, 1653 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.34 (app. t, *J* = 7.3 Hz, 2H), 7.13-7.28 (m, 4H), 6.24 (d, *J* = 5.8 Hz, 1H), 5.75 (d, *J* = 15.9 Hz, 1H), 4.32 (dd, *J* = 8.9, 5.8 Hz, 1H), 3.70 (s, 3H), 3.14-3.25 (m, 2H), 0.98 (s, 9H), 0.85 (d, *J* = 6.1 Hz, 1H), 0.27 (s, 3H), 0.26 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 167.1 (C), 151.8 (CH), 141.8 (C), 138.7 (CH), 128.7 (CH), 128.4 (CH), 126.7 (CH), 120.9 (CH), 113.6 (CH), 55.4 (CH), 51.4 (CH_3), 33.5 (CH), 25.7 (CH_3), 19.5 (CH_3), 18.3 (C), -5.2 (CH_3), -5.3 (CH_3); MS (ESI) *m*/*z* (relative intensity) 383 (M + Na, 29), 361 (M + H, 84), 261 (100); HRMS (M + H) calcd for $C_{21}H_{33}O_3Si$: 361.2193. Found 361.2190. HPLC analysis: ee 89% (ChiralcelOD-H, 0.8% *i*-PrOH in hexane, 1.0 mL/min, λ= 254 nm, t_R= 4.5 min, major; t_R= 6.2 min, minor). Anal. Calcd for

$C_{21}H_{32}O_3Si$: C, 69.95; H, 8.95. Found: C, 69.71; H, 9.15.

Methyl (2*E*,4*R*,5*S*,6*E*)-5-((*Z*)-2-(*tert*-butyldimethylsiloxy)vinyl)-4-phenylocta-2,6-dienoate (16b) and methyl (2*S*,3*R*,4*E*,6*E*)-3-(*tert*-butyldimethylsiloxy)-2-((*E*)-styryl)octa-4,6-dienoate (17b). As general procedure. The solvent was evaporated and the residue (**16b**:**17b**= 2.5:1.0 by ^{1}H NMR analysis of the crude reaction mixture) was purified by flash chromatography [SiO_2; dichloromethane/petrol, 1:4], to provide **17b** (29 mg, 22% yield) and **16b** (63 mg, 47% yield). **17b:** colorless oil; R_f 0.56 (7:3 dichloromethane/pentane eluent); $[\alpha]_D^{25}$ -89.4 (*c* 0.83, $CHCl_3$); IR (film) 3027, 2952, 2928, 2886, 2856, 1737 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.38 (d, *J* = 7.5 Hz, 2H), 7.32 (app. t, *J* = 7.5 Hz, 2H), 7.24 (t, *J* = 7.1 Hz, 1H), 6.43 (d, *J* = 15.7 Hz, 1H), 6.30 (dd, *J* = 15.7, 9.3 Hz, 1H), 6.13 (dd, *J* = 15.0, 10.6 Hz, 1H), 6.02 (ddd, *J* = 14.7, 10.6, 1.5 Hz, 1H), 5.69 (dq, *J* = 14.7, 6.6 Hz, 1H), 5.54 (dd, *J* = 15.2, 7.9 Hz, 1H), 4.51 (app. t, *J* = 7.0 Hz, 1H), 3.68 (s, 3H), 3.25 (dd, *J* = 9.2, 6.2 Hz, 1H), 1.76 (d, *J* = 6.6 Hz, 3H), 0.86 (s, 9H), 0.02 (s, 3H), 0.01 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 172.5 (C), 137.1 (C), 133.9 (CH), 131.8 (CH), 131.0 (CH), 130.9 (CH), 130.2 (CH), 128.6 (CH), 127.5 (CH), 126.5 (CH), 124.7 (CH), 75.1 (CH), 57.9 (CH), 51.8 (CH_3), 25.8 (CH_3), 18.2 (CH_3), 18.2 (C), -4.1 (CH_3), -4.8 (CH_3); MS (ESI) *m*/*z* (relative intensity) 409 (M + Na, 100); HRMS (ESI) (M + Na) calcd for $C_{23}H_{34}O_3NaSi$: 409.2169. Found 409.2174. HPLC analysis: ee 91% (ChiralcelOD-H, 1.0% *i*-PrOH in hexane, 1.0 mL/min, λ= 254 nm, t_R= 4.1 min, major; t_R= 5.5 min, minor).

16b: yellow oil; R_f 0.51 (7:3 dichloromethane/pentane eluent); $[\alpha]_D^{25}$ -28.4 (*c* 1.33, $CHCl_3$); IR (film) 3034, 2953, 2929, 2891, 2856, 1735, 1663 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.30 (app. t, *J* = 7.0 Hz, 2H), 7.12-7.24 (m, 4H), 6.27 (d, *J* = 5.9 Hz, 1H), 5.74 (dd, *J* = 15.4, 0.7 Hz, 1H), 5.34 (dq, *J* = 15.2, 6.2 Hz, 1H), 5.21 (ddd, *J* = 15.0, 7.1, 1.5 Hz, 1H), 4.36 (dd, *J* =9.5, 5.9 Hz, 1H), 3.71 (m, 1H), 3.70 (s, 3H), 3.35 (app. t, *J* = 8.6 Hz, 1H), 1.54 (d, *J* = 6.2 Hz, 3H), 0.95 (s, 9H), 0.15 (s, 3H), 0.14 (s, 3H)**;** MS (ESI) *m*/*z* (relative intensity) 409 (M + Na, 100); HRMS (ESI) (M + Na) calcd for $C_{23}H_{34}O_3NaSi$: 409.2169. Found 409.2176. HPLC analysis: ee 92% (ChiralcelOD-H, 0.8% *i*-PrOH in hexane, 1.0 mL/min, λ= 254 nm, t_R= 5.1 min, major; t_R= 6.9 min, minor).

Methyl (2*E*,4*R*,5*S*,6*Z*)-7-(*tert*-butyldimethylsiloxy)-4,5-diphenylhepta-2,6-dienoate (16c) and methyl (2*S*,3*R*,*E*)-3-(*tert*-butyldimethylsiloxy)-5-phenyl-2-((*E*)-styryl)pent-4-enoate (17c). As general procedure. The solvent was evaporated and the residue (**16c**:**17c**= 1.4:1.0 by ^{1}H NMR analysis

of the crude reaction mixture) was purified by flash chromatography [SiO_2; dichloromethane/petrol, 2:3], to provide **17c** (93 mg, 41% yield) and **16c** (105 mg, 53% yield). **17c:** yellow oil; R_f 0.23 (3:7 dichloromethane/pentane eluent); $[\alpha]_D^{25}$ -87.2 (*c* 0.72, $CHCl_3$); IR (film) 3028, 2952, 2891, 2856, 1736, 1600 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.32-7.12 (m, 10H), 6.47 (d, *J* = 15.9 Hz, 1H), 6.39 (d, *J* = 15.9 Hz, 1H), 6.27 (dd, *J* = 15.9, 9.5 Hz, 1H), 6.12 (dd, *J* = 15.9, 7.6 Hz, 1H), 4.59 (app. t, *J* = 6.7 Hz, 1H), 3.59 (s, 3H), 3.26 (dd, *J* = 9.5, 6.4 Hz, 1H), 0.80 (s, 9H), -0.03 (s, 3H), -0.06 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.5 (C), 137.0 (C), 136.7 (C), 134.1 (CH), 131.2 (CH), 130.5 (CH), 128.6 (CH), 128.5 (CH), 127.8 (CH), 127.6 (CH), 126.7 (CH), 126.5 (CH), 124.5 (CH), 75.3 (CH), 57.8 (CH), 51.9 (CH_3), 25.8 (CH_3), 18.2 (C), -4.1 (CH_3), -4.8 (CH_3); MS (EI) *m/z* (relative intensity) 445 (M + Na, 100); HRMS (EI) (M) calcd for $C_{26}H_{34}O_3Si$: 422.2272. Found 422.2261 HPLC analysis: ee 91% (ChiralcelOD-H, 0.8% *i*-PrOH in hexane, 1.0 mL/min, λ= 254 nm, t_R= 5.3 min, major; t_R= 6.8 min, minor); Anal. Calcd for $C_{26}H_{34}O_3Si$: C, 73.89; H, 8.11. Found: C, 73.81; H, 8.12.

16c: yellow oil; R_f 0.19 (3:7 dichloromethane/pentane eluent); $[\alpha]_D^{25}$ -66.8 (*c* 1.82, $CHCl_3$); IR (film) 3030, 2951, 2893, 2858, 1724, 1651 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.26 (dd, *J* = 15.9, 8.5 Hz, 1H), 7.19-7.01 (m, 10H), 6.29 (d, *J* = 5.8 Hz, 1H), 5.80 (d, *J* = 15.9, 0.7 Hz, 1H), 4.75 (dd, *J* = 9.8, 5.8 Hz, 1H), 4.33 (app. t, *J* = 9.8 Hz, 1H), 3.74-3.66 (m, 4H), 0.95 (s, 9H), 0.15 (s, 3H), 0.10 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 167.0 (C), 150.9 (CH), 143.2 (C), 141.0 (C), 139.3 (CH), 128.4 (CH), 128.3 (CH), 128.1 (CH), 128.0 (CH), 126.5 (CH), 125.9 (CH), 121.4 (CH), 111.4 (CH), 55.0 (CH), 51.4 (CH_3), 45.4 (CH), 25.6 (CH_3), 18.2 (C), -5.3 (CH_3), -5.4 (CH_3); MS (EI) *m/z* (relative intensity) 445 (M + Na, 100%); HRMS (EI) (M) calcd for $C_{26}H_{34}O_3Si$: 422.2272. Found 422.2270. HPLC analysis: ee 91% (ChiralcelOD-H, 0.8% *i*-PrOH in hexane, 1.0 mL/min, λ= 254 nm, t_R= 5.3 min, major; t_R= 6.8 min, minor); Anal. Calcd for $C_{26}H_{34}O_3Si$: C, 73.89; H, 8.11. Found: C, 73.85; H, 8.10.

Methyl (4*S*,5*R*,*E*)-5-methyl-7-oxo-4-phenylhept-2-enoate (16d) and methyl (2*S*,3*R*,*E*)-2((*E*)-styryl)-3-(trimethylsiloxy)hex-4-enoate (17d). As general procedure. The solvent was evaporated and the residue (**16d**:**17d**= 1.3:1.0 by ^1H NMR analysis of the crude reaction mixture) was purified by flash chromatography [SiO_2; diethyl ether/petrol, 1:20 with 1% triethylamine], to provide **17d** (51 mg, 39% yield) as a yellow oil; R_f 0.52 (7:3 dichloromethane/pentane eluent); $[\alpha]_D^{25}$ -53.7 (*c* 1.42, $CHCl_3$); IR (film) 3027, 2954, 1736 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.39 (d, *J* = 7.0 Hz, 2H), 7.32 (app. t, *J* = 7.2

Hz, 2H), 7.24 (t, *J* = 7.2 Hz, 1H), 6.46 (d, *J* = 16.1 Hz, 1H), 6.27 (dd, *J* = 15.9, 9.4 Hz, 1H), 5.65 (dq, *J* = 15.3, 6.1 Hz, 1H), 5.49 (ddd, *J* = 15.3, 7.3, 1.4 Hz, 1H), 4.44 (app. t, *J* = 7.0 Hz, 1H), 3.69 (s, 3H), 3.23 (dd, *J* = 9.4, 7.0 Hz, 1H), 1.69 (dd, *J* = 6.5, 1.4 Hz, 3H), 0.08 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.6 (C), 137.0 (C), 133.8 (CH), 131.8 (CH), 128.6 (CH), 127.5 (CH), 127.5 (CH), 126.4 (CH), 124.9 (CH), 74.9 (CH), 57.6 (CH), 51.8 (CH_3), 17.7 (CH_3), 0.3 (CH_3); MS (EI) *m*/*z* (relative intensity) 303 (M - Me, 4), 143 (100); HRMS (EI) calcd for $C_{14}H_{20}O_2Si$: 248.1227. Found 248.1227. HPLC analysis: ee 90% (ChiralcelOD-H, 0.8% *i*-PrOH in hexane, 1.0 mL/min, λ= 254 nm, t_R= 5.1 min, major; t_R= 6.8 min, minor).

Further elution [diethyl ether/petrol, 2:3], afforded **16d** (53 mg, 43% yield) as a colorless oil; R_f 0.40 (1:1 diethyl ether/pentane eluent); $[\alpha]_D^{25}$ +10.7 (*c* 0.30, $CHCl_3$); IR (film) 2955, 1723, 1654 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.76 (br s, 1H), 7.34 (app. t, *J* = 7.6 Hz, 2H), 7.26 (t, *J* = 7.3 Hz, 1H), 7.19 (d, *J* = 7.3 Hz, 2H), 7.09 (dd, *J* = 15.6, 9.8 Hz, 1H), 5.88 (d, *J* = 15.6 Hz, 1H), 3.72 (s, 3H), 3.25 (app. t, *J* = 9.2 Hz, 1H), 2.62 (dd, *J* = 16.8, 4.0 Hz, 1H), 2.56 (m, 1H), 2.29 (ddd, *J* = 16.8, 8.5, 2.1 Hz, 1H), 0.86 (d, *J* = 6.4 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 201.6 (CH), 166.7 (C), 149.8 (CH), 140.5 (C), 128.9 (CH), 128.1 (CH), 127.2 (CH), 122.3 (CH), 54.7 (CH), 51.6 (CH_3), 48.8 (CH_2), 32.6 (CH), 18.2 (CH_3); LRMS (ESI) *m*/*z* 269 (M + Na, 100%); HRMS (M + Na) calcd for $C_{15}H_{18}O_3Na$: 269.1148. Found 269.1146. HPLC analysis: ee 91% (Chiralpak AD-RH, 2.5% *i*-PrOH in hexane, 0.97 mL/min, λ= 254 nm, t_R= 17.2 min, major; t_R= 18.0 min, minor); Anal. Calcd for $C_{15}H_{18}O_3$: C, 73.15; H, 7.37. Found: C, 73.19; H, 7.20.

Methyl (2*E*,4R,5*S*,6*E*)-5-(2-oxoethyl)-4-phenylocta-2,6-dienoate (16e) and methyl (2*S*,3*R*,4*E*,6*E*)-2((*E*)-styryl)-3-(trimethylsiloxy)octa-4,6-dienoate (17e). As general procedure. The solvent was evaporated and the residue (**16e**:**17e**= 4.2:1.0 by ^{1}H NMR analysis of the crude reaction mixture) was purified by flash chromatography [SiO_2; diethyl ether/petrol, 1:20 with 1% triethylamine], to provide **17e** (25 mg, 17% yield) as a colorless oil; R_f 0.58 (7:3 dichloromethane/pentane eluent); $[\alpha]_D^{25}$ -63.6 (*c* 0.55, $CHCl_3$); IR (film) 3035, 2954, 1735 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.39 (d, *J* = 7.0 Hz, 2H), 7.32 (app. t, *J* = 7.3 Hz, 2H), 7.24 (t, *J* = 7.3 Hz, 1H), 6.45 (d, *J* = 15.9 Hz, 1H), 6.27 (dd, *J* = 15.9, 9.2 Hz, 1H), 6.13 (dd, *J* = 15.3, 10.7 Hz, 1H), 6.02 (m, 1H), 5.69 (dq, *J* = 15.0, 6.7 Hz, 1H), 5.54 (dd, *J* = 15.0, 7.0 Hz, 1H), 4.49 (app. t, *J* = 7.0 Hz, 1H), 3.68 (s, 3H), 3.24 (d, *J* = 9.5, 7.0 Hz, 1H), 1.75 (d, *J* = 6.7 Hz, 3H), 0.07 (s, 9H),; ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.5 (C), 137.0 (C), 133.9 (CH), 131.6

(CH), 130.8 (CH), 130.7 (CH), 130.3 (CH), 128.6 (CH), 127.6 (CH), 126.5 (CH), 124.7 (CH), 74.7 (CH), 57.7 (CH), 51.9 (CH_3), 18.2 (CH_3), 0.3 (CH_3); MS (EI) *m*/*z* (relative intensity): 329 (M – CH_3, 3), 169 (100); HRMS (EI) calcd for $C_{20}H_{28}O_3Si$: 344.1802. Found 344.1799. HPLC analysis: ee 91% (Chiralcel OD-H, 0.8% *i*-PrOH in hexane, 1.0 mL/min, λ= 254 nm, t_R= 5.2 min, minor; t_R= 7.0 min, major).

Further elution [diethyl ether/petrol, 2:3], afforded **16e** (79 mg, 68%) as a yellow oil; R_f 0.10 (7:3 dichloromethane/pentane eluent); $[\alpha]_D^{25}$ +7.2 (*c* 0.97, $CHCl_3$); IR (film) 3027, 2950, 2853, 1723, 1662 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 9.68 (app. t, *J* = 1.2 Hz, 1H), 7.32 (app. t, *J* = 7.3 Hz, 2H), 7.24 (app. t, *J* = 6.9 Hz, 1H), 7.17-7.09 (m incorporating d, *J* = 7.3 Hz, 3H), 5.87 (d, *J* = 15.6 Hz, 1H), 5.38 (ddd, *J* = 15.3, 12.8, 6.4 Hz, 1H), 5.16 (dd, *J* = 15.3, 8.5 Hz, 1H), 3.73 (s, 3H), 3.44 (app. t, *J* = 8.5 Hz, 1H), 3.08 (m, 1H), 2.54 (dd, *J* = 16.5, 4.3 Hz, 1H), 2.39 (ddd, *J* = 16.8, 9.5, 2.4 Hz, 1H), 1.55 (d, *J* = 6.4 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 201.7 (CH), 166.7 (C), 149.4 (CH), 139.8 (C), 130.1 (CH), 128.6 (CH), 128.5 (CH), 128.4 (CH), 127.1 (CH), 122.3 (CH), 53.2 (CH), 51.6 (CH_3), 46.5 (CH_2), 41.9 (CH), 17.9 (CH_3); MS (EI) *m*/*z* (relative intensity) 272 (M^+, 39), 115 (100); HRMS (EI) calcd for $C_{17}H_{20}O_3$: 272.1407. Found 272.1419; HPLC analysis: ee 93% Chiralcel OD-H, 5.0% *i*-PrOH in hexane, 0.97 mL/min, λ= 254 nm, t_R= 16.7 min, minor; t_R= 17.6 min, major); Anal. Calcd for $C_{17}H_{20}O_3$: C, 74.97; H, 7.40. Found: C, 74.86; H, 7.27.

Methyl (4*R*,5*R*,*E*)-7-oxo-4,5-diphenylhept-2-enoate (16f) and methyl (2*S*,3*R*,*E*)-3-hydroxy-5-phenyl-2-((*E*)-styryl)pent-4-enoate (17f). As general procedure. The solvent was evaporated and the residue (**16f**:**17f**= 1.4:1.0 by ^1H NMR analysis of the crude reaction mixture) was purified by flash chromatography [SiO_2; diethyl ether/petrol, 2:3], to provide **16f** (80 mg, 53% yield) and **17f** (71 mg, 45% yield). **16f**: colorless oil; R_f 0.28 (2:3 diethyl ether/pentane eluent); IR (film) 1724 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 9.61 (br s, 1H), 7.21-7.07 (m, 7H), 7.02-6.98 (m, 4H), 5.93 (d, *J* = 15.3 Hz, 1H), 3.74 (s, 3H), 3.71-3.62 (m, 2H), 2.91 (ddd, *J* = 17.0, 4.9, 0.9 Hz, 1H), 2.85 (ddd, *J* = 17.0, 8.9, 2.1 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 200.8 (C), 166.6 (C), 149.2 (CH), 140.6 (C), 139.8 (C), 128.6 (CH), 128.4 (CH), 128.3 (CH), 128.2 (CH), 127.0 (CH), 126.9 (CH), 122.5 (CH), 55.2 (CH), 51.7 (CH_3), 50.0 (CH_2), 44.8 (CH); MS (EI) (relative intensity) *m*/*z* 308 (M, 7), 176 (93), 105 (100); HRMS (EI) calcd for $C_{20}H_{20}O_3$: 308.1407. Found 308.1395. HPLC analysis: ee 91% (Chiralpak AD-RH, 2.5% *i*-PrOH in hexane, 0.97 mL/min, λ= 254 nm, t_R= 18.2 min, major; t_R= 20.3 min, minor.

17f: colorless oil; R_f 0.26 (2:3 diethyl ether/pentane eluent); $[\alpha]_D^{25}$ -88.2 (*c* 1.25, $CHCl_3$); IR (film) 3457, 3027, 2952, 1730 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.44-7.23 (m, 10H), 6.69 (d, *J* = 15.9 Hz, 1H), 6.61 (d, *J* = 15.9 Hz, 1H), 6.37 (dd, *J* = 15.9, 9.2 Hz, 1H), 6.24 (dd, *J* = 15.9, 7.0 Hz, 1H), 4.68 (m, 1H), 3.74 (s, 3H), 3.44 (dd, *J* = 9.2, 5.5 Hz, 1H), 2.80 (d, *J* = 3.4 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 173.1 (C), 136.5 (C), 136.4 (C), 135.5 (CH), 132.5 (CH), 128.7 (CH), 128.6 (CH), 128.2 (CH), 128.1 (CH), 128.0 (CH), 126.7 (CH), 126.6 (CH), 122.7 (CH), 73.5 (CH), 56.0 (CH), 52.3 (CH_3), 25.8 (CH_3); LRMS (ES) *m/z* 331 (M + Na, 54%), 291 (100), 231 (64); HRMS (M + Na) calcd for $C_{20}H_{20}O_3Na$: 331.1305. Found 331.1312. HPLC analysis: ee 91% ((*R*,*R*)-Whelk-O1, 5.0% *i*-PrOH in hexane, 1.0 mL/min, λ= 254 nm, t_R= 24.5 min, major; t_R= 27.8 min, minor).

Methyl (2*E*,4*S*,5*R*,6*Z*)-4-(4-bromophenyl)-7-(*tert*-butyldimethylsilyloxy)-5-phenylhepta-2,6-dienoate (24) and methyl (2*R*,3*S*,*E*)-2-((*E*)-4-bromostyryl)-3-(*tert*-butyldimethylsilyloxy)-5-phenylpent-4-enoate (25). Methyl (*E*)-4-(4-bromophenyl)but-3-enoate **23** (562 mg, 2.00 mmol) in 2,2-dimethylbutane (20 mL) was added dropwise over 3 h via syringe pump to a rapidly stirred solution of TBS-protected cinnamyl alcohol (**15c**) (414 mg, 1.67 mmol) and Rh_2(*R*-DOSP)$_4$ (37 mg, 2.0 x 10^{-5} mol) in 2,2-dimethylbutane (1.0 mL) at 23 °C. On completion of the diazoacetate addition the reaction mixture was allowed to stir for an additional 20 min. The solvent was evaporated and the residue (**24**:**25**= 1.1:1.0 by ^1H NMR analysis of the crude reaction mixture) was purified by flash chromatography [SiO_2; dichloromethane/petrol, 2:3], to provide **24** (288 mg, 45% yield) and **25** (236 mg, 36% yield). **25**: pale yellow oil; R_f 0.51 (7:3 dichloromethane/pentane eluent); $[\alpha]_D^{22}$ +96.0 (*c* 0.55, $CHCl_3$); IR (film) 2952, 2900, 2880, 2856, 1736 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.47 (d, *J* = 8.5 Hz, 2H), 7.41 (d, *J* = 7.3 Hz, 2H), 7.36 (t, *J* = 7.3 Hz, 2H), 7.29 (d, *J* = 8.3 Hz, 3H), 6.62 (d, *J* = 15.9 Hz, 1H), 6.59-6.39 (m, 2H), 6.26 (dd, *J* = 15.9, 7.6 Hz, 1H), 4.74 (app. t, *J* = 6.7 Hz, 1H), 3.72 (s, 3H), 3.40 (dd, *J* = 8.2, 6.4 Hz, 1H), 0.94 (s, 9H), 0.11 (s, 3H), 0.09 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.1 (C), 136.6 (C), 135.8 (C), 132.9 (CH), 131.6 (CH), 131.3 (CH), 130.2 (CH), 128.6 (CH), 127.9 (CH), 127.8 (CH), 126.6 (CH), 125.3 (CH), 121.3 (C), 75.2 (CH), 57.7 (CH), 51.8 (CH_3), 25.7 (CH_3), 18.1 (C), -4.1 (CH_3), -4.8 (CH_3); MS (ESI) *m/z* (relative intensity): 501 (M, 100); HRMS (ESI) (M + Na) calcd for $C_{26}H_{33}O_3NaSi$: 523.1275. Found 523.1282. HPLC analysis: ee 89% (Chiralcel OD-H, 0.2% *i*-PrOH in hexane, 0.97 mL/min, λ= 254 nm, t_R= 16.6 min, minor; t_R= 18.1 min, major); Anal. Calcd for $C_{26}H_{33}BrO_3Si$: C, 62.27; H, 6.63; Br,

15.93. Found: C, 62.46; H, 6.63; Br 15.99.

24: colorless oil; R_f 0.43 (7:3 dichloromethane/pentane eluent); $[\alpha]_D^{22}$ +8.3 (*c* 1.16, $CHCl_3$); IR (film) 3029, 2952, 2930, 2857, 1725, 1652 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.29 (d, *J* = 8.2 Hz, 2H), 7.22 (dd, *J* = 15.6, 8.2 Hz, 1H), 7.12 (t, *J* = 7.3 Hz, 2H), 7.08 (t, *J* = 7.3 Hz, 1H), 7.04 (d, *J* = 7.0 Hz, 2H), 6.92 (d, *J* = 8.5 Hz, 2H), 6.30 (d, *J* = 5.8 Hz, 1H), 5.76 (d, *J* = 15.9 Hz, 1H), 4.73 (dd, *J* = 9.8, 5.8 Hz, 1H), 4.28 (app. t, *J* = 9.8 Hz, 1H), 3.72 (s, 3H), 3.69 (app. t, *J* = 9.5 Hz, 1H), 0.95 (d, 9H), 0.15 (s, 3H), 0.10 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.9 (C), 150.0 (CH), 142.9 (C), 140.2 (C), 139.6 (CH), 131.5 (CH), 130.2 (CH), 128.3 (CH), 128.0 (CH), 126.2 (CH), 121.9 (CH), 120.4 (C), 111.0 (CH), 54.3 (CH), 51.5 (CH_3), 45.4 (CH), 25.7 (CH_3), 18.2 (C), -5.3 (CH_3), -5.4 (CH_3); MS (ESI) *m/z* (relative intensity): 523 (M + Na, 72), 357 (100); HRMS (ESI) (M + Na) calcd for $C_{26}H_{33}O_3NaSi$: 523.1275. Found 523.1277. HPLC analysis: ee 90% (Chiralcel OD-H, 0.8% *i*-PrOH in hexane, 0.97 mL/min, λ= 254 nm, t_R= 6.7 min, minor; t_R= 7.2 min, major); Anal. Calcd for $C_{26}H_{33}BrO_3Si$: C, 62.27; H, 6.63; Br, 15.93. Found: C, 62.28; H, 6.62; Br 16.05.

Methyl (2*E*,7*Z*)-4-(4-bromophenyl)-7-(2-(2,4-dinitrophenyl)hydrazono)-5-phenylhept-2-enoate (26). Concentrated HCl (5 drops) was added to a solution of 2,4-dinitrophenylhydrazine (158 mg, 0.80 mmol) and silyl enol ether **24** (100 mg, 0.20 mmol) in ethanol (5 mL) at 23 ˚C. The resultant solution was stirred for 14 h prior to addition of sat. $NaHCO_3$(aq) (10mL) and diethyl ether (3 x 20 mL). The organic layers were combined and washed with brine (20 mL), dried ($MgSO_4$). The solvent was evaporated and the residue was purified by flash chromatography [SiO_2; diethyl ether/pentane, 3:2], to provide **26** (99 mg, 87% yield) as an orange solid (recrystallized from ethyl acetate/pentane); R_f 0.26 (3:2 diethyl ether/pentane eluent); $[\alpha]_D^{22}$ +54.7 (*c* 0.68, $CHCl_3$); IR (film) 3296, 1720, 1619, 1592, 1519, 14338, 1333, cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 10.8 (s, 1H), 9.07 (d, *J* = 2.4 Hz, 1H), 8.28 (dd, *J* = 9.5, 2.4 Hz, 1H), 7.79 (d, *J* = 9.5 Hz, 1H), 7.26-7.32 (m, 2H), 7.17-7.25 (m, 3H), 7.14 (app. t, *J* = 7.3 Hz, 1H), 7.00 (d, *J* = 7.3 Hz, 2H), 6.87 (d, *J* = 8.24 Hz, 2H), 5.97 (d, *J* = 15.6 Hz, 1H), 3.76 (s, 3H), 3.67 (app. t, *J* = 9.8 Hz, 1H), 3.34 (td, *J* = 9.8, 4.3 Hz, 1H), 2.96 (dt, *J* = 15.3, 5.0 Hz, 1H), 2.79 (ddd, *J* = 15.0, 11.3, 5.0 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.5, 149.8, 148.5, 144.9, 139.8, 139.0, 138.0, 131.7, 130.0, 129.8, 128.9, 128.7, 128.3, 127.3, 123.5, 122.9, 120.9, 116.5, 54.9, 51.8, 48.6, 36.9; MS (EI) *m/z* (relative intensity): 566 (M - H, 21), 313 (100); HRMS (EI) (M) calcd for $C_{26}H_{23}O_6N_4Br$: 566.0795. Found 566.0786. Anal.

Calcd for $C_{26}H_{23}O_6BrN_4$: C, 55.04; H, 4.09; Br 14.08; N, 9.87. Found: C, 54.95; H, 4.10; Br, 14.11; N, 9.76.

Methyl (4*R*,5*R*,*E*)-7-oxo-5-phenyl-4-((*E*)-styryl)hept-2-enoate (28a) and methyl (2*S*,3*E*,5*E*)-6-phenyl-2-((*R*,*E*)-3-phenyl-1-(trimethylsilyloxy)allyl)hexa-3,5-dienoate (29a). As general procedure. The solvent was evaporated and the residue (**28a**:**29a**= 1.6:1.0 by ^{1}H NMR analysis of the crude reaction mixture) was purified by flash chromatography [SiO_2; diethyl ether/petrol, 1:20 with 1% triethylamine], to provide **29a** (68 mg, 34% yield) as a yellow oil; R_f 0.55 (7:3 dichloromethane/pentane eluent); $[\alpha]_D^{25}$ –73.1 (*c* 0.78, $CHCl_3$); IR (film) 3026, 2953, 1734, 1598 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.43-7.35 (m, 4H), 7.32 (app. t, *J* = 7.6 Hz, 4H), 7.28-7.21 (m, 2H), 6.82 (dd, *J* = 15.6, 10.4 Hz, 1H), 6.54 (dd, *J* = 15.9, 11.0 Hz, 2H), 6.30 (dd, *J* = 15.3, 10.4 Hz, 1H), 6.20 (dd, *J* = 15.9, 7.3 Hz, 1H), 5.93 (dd, *J* = 15.3, 9.5 Hz, 1H), 4.63 (app. t, *J* = 6.7 Hz, 1H), 3.69 (s, 3H), 3.28 (dd, *J* = 9.2, 6.4 Hz, 1H), 0.12 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.4 (C), 137.3 (C), 136.7 (CH), 134.6 (CH), 132.4 (CH), 1301.1 (CH), 130.2 (CH), 128.7 (CH), 128.6 (CH), 128.5 (CH), 128.4 (CH), 127.8 (CH), 127.6 (CH), 126.7 (CH), 126.4 (CH), 75.0 (CH), 57.3 (CH), 52.0 (CH_3), 0.4 (CH_3); MS (ESI) *m*/*z* (relative intensity) 429 (M + Na, 100); HRMS (ESI) (M + Na) calcd for $C_{25}H_{30}O_3NaSi$: 429.1856. Found 429.1866. HPLC analysis: ee 83% Chiracel OD-H, 0.8% *i*-PrOH in hexane, 1.0 mL/min, λ= 254 nm, t_R= 6.6 min, major; t_R= 10.4 min, minor). Further elution [diethyl ether/petrol, 2:3], afforded **28a** (66 mg, 39%) as a yellow oil; R_f 0.14 (7:3 dichloromethane/pentane eluent); ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.67 (br s, 1H), 7.43-7.17 (m, 10H), 6.96 (dd, *J* = 15.7, 8.5 Hz, 1H), 6.08 (d, *J* = 15.3, 1H), 5.94 (dd, *J* = 15.3, 8.5 Hz, 1H), 5.87 (d, *J* = 15.3 Hz, 1H), 3.73 (s, 3H), 3.71-3.62 (m, 2H), 2.90 (ddd, *J* = 17.0, 4.9, 0.9 Hz, 1H), 2.86 (ddd, *J* = 17.0, 8.9, 2.1 Hz, 1H); MS (ESI) *m*/*z* (relative intensity): 357 (M + Na, 100), 335 (M + H, 82); HRMS (EI) calcd for $C_{22}H_{20}O_3$: 332.1407. Found 332.1411. HPLC analysis: ee 83% ((*R*,*R*)-Whelk-O1, 9.0% *i*-PrOH in hexane, 0.6 mL/min, λ= 254 nm, t_R= 7.3 min, major; t_R= 8.7 min, minor; Anal. Calcd for $C_{22}H_{22}O_3$: C, 79.02; H, 6.63; . Found: C, 78.22; H, 6.37.

Methyl (4*R*,5*R*,*E*)-4-methyl-7-oxo-5-phenylhept-2-enoate (28b) and methyl (2*S*,3*R*,*E*)-5-phenyl-2-((*E*)-prop-1-enyl)-3-(trimethylsilyloxy)pent-4-enoate (29b). As general procedure except diazoacetate addition was conducted over 4h. The solvent was evaporated and the residue (**28b**:**29b**= 1.0:1.5 by crude ^{1}H NMR) was purified by flash chromatography [SiO_2; diethyl ether/pentane,

1:20 with 1% triethylamine], to provide **29b** (65 mg, 41% yield) as a colorless oil; R_f 0.51 (7:3 dichloromethane/pentane eluent); $[\alpha]_D^{25}$ -33.3 (*c* 0.72, $CHCl_3$); IR (film) 2954, 1736 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.36 (d, *J* = 7.6 Hz, 2H), 7.32 (app.t, *J* = 7.6 Hz, 2H), 7.25 (app. t, *J* = 7.0 Hz, 1H), 6.51 (d, *J* = 15.9 Hz, 1H), 6.17 (dd, *J* = 15.9, 7.0 Hz, 1H), 5.62-5.52 (m, 2H), 4.54 (app. t, *J* = 6.9 Hz, 1H), 3.66 (s, 3H), 3.14 (app. t, *J* = 7.0 Hz, 1H), 1.73 (d, *J* = 4.6 Hz, 3H), 0.11 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.9 (C), 136.9 (C), 130.8 (CH), 130.5 (CH), 130.2 (CH), 128.6 (CH), 127.7 (CH), 126.6 (CH), 125.7 (CH), 74.8 (CH), 57.1 (CH), 51.8 (CH_3), 18.1 (CH_3), 0.4 (CH_3); MS (ESI) *m/z* (relative intensity): 687 (100), 364 (M + 2Na, 35); HRMS (ESI) (M + Na) calcd for $C_{18}H_{26}O_3NaSi$: 341.1543. Found 341.1555. HPLC analysis: ee 76% (Chiralcel OD-H, 0.8% *i*-PrOH in hexane, 1.0 mL/min, λ= 254 nm, t_R= 10.2 min, major; t_R= 11.0 min, minor). Further elution chromatography [SiO_2; diethyl ether/pentane, 3:7 with 1% triethylamine], to provide **28b** (31 mg, 25% yield) as a colorless oil; R_f 0.40 (1:1 diethyl ether/pentane eluent); $[\alpha]_D^{25}$ +65.2 (*c* 0.27, $CHCl_3$); IR (film) 2922, 1721, 1654 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 9.56 (t, *J* = 1.8 Hz, 1H), 7.32 (t, *J* = 7.3 Hz, 2H), 7.23 (t, *J* = 7.3 Hz, 1H), 7.18 (d, *J* = 7.3 Hz, 2H), 6.85 (dd, *J* = 15.6, 9.2 Hz, 1H), 5.87 (dd, *J* = 15.6, 0.6 Hz, 1H), 3.76 (s, 3H), 3.12 (m, 1H), 2.78-2.73 (m, 2H), 2.56 (m, 1H), 0.89 (d, *J* = 6.7 Hz, 3H),; ^{13}C NMR (125 MHz, $CDCl_3$) δ 201, 166.8, 152.1, 141.3, 128.8, 128.2, 127.1, 121.6, 51.7, 48.2, 45.0, 42.7, 18.1; MS (EI) *m/z* (relative intensity) 202 (11), 115 (100); HRMS (EI) calcd for $C_{15}H_{18}O_3$: 246.1250. Found 246.1260; HPLC analysis: ee 78% ((*R,R*-whelk, 7.0% *i*-PrOH in hexane, 1.0 mL/min, λ= 254 nm, t_R= 9.9 min, major; t_R= 10.8 min, minor); Anal. Calcd for $C_{15}H_{18}O_3$: C, 73.15; H, 7.37. Found: C, 72.83; H, 7.24.

Methyl (4*R*,5*R*,*E*)-4-ethyl-7-oxo-5-phenylhept-2-enoate (28c) and methyl (*S*,*E*)-2-((*R*,*E*)-3-phenyl-1-(trimethylsilyloxy)allyl)hex-3-enoate (29c). As general procedure except diazoacetate addition was conducted over 4h. The solvent was evaporated and the residue (**28c**:**29c**= 1.0:2.7 by crude ^1H NMR) was purified by flash chromatography [SiO_2; diethyl ether/petrol, 1:40 with 1% triethylamine], to provide **29c** (69 mg, 42% yield). **29c**: colorless oil; R_f 0.48 (3:2 dichloromethane/pentane eluent); $[\alpha]_D^{25}$ -33.5 (*c* 0.99, $CHCl_3$); IR (film) 3027, 2961, 1736 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.36 (d, *J* = 7.3 Hz, 2H), 7.32 (app. t, *J* = 7.3 Hz, 2H), 7.24 (t, *J* = 7.0 Hz, 1H), 6.51 (d, *J* = 15.9 Hz, 1H), 6.17 (dd, *J* = 15.9, 7.0 Hz, 1H), 5.61 (dt, *J* = 15.6, 6.1 Hz, 1H), 5.53 (dd, *J* = 15.6, 8.9 Hz, 1H), 4.53 (app. t, *J* = 7.0 Hz, 1H), 3.65 (s, 3H), 3.13 (dd, *J* = 8.9, 7.3 Hz, 1H), 2.08 (app. quintet, *J* = 7.3 Hz, 2H), 1.00 (t, *J* = 7.3 Hz,

3H), 0.11 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 1723.0 (C), 137.1 (CH), 136.9 (C), 130.8 (CH), 130.5 (CH), 128.6 (CH), 127.7 (CH), 6.6 (CH), 123.6 (CH), 74.8 (CH), 57.2 (CH), 51.8 (CH_3), 25.7 (CH_2), 13.6 (CH_3), 0.4 (CH_3); MS (ESI) *m*/*z* (relative intensity): 365 (100), 355 (M + Na, 47); HRMS (ESI) (M + Na) calcd for $C_{19}H_{28}O_3NaSi$: 355.1700. Found 355.1698. HPLC analysis: ee 80% (Chiralpak AD-RH, 100% hexane, 1.0 mL/min, λ= 254 nm, t_R= 7.0 min, major; t_R= 7.6 min, minor); Anal. Calcd for $C_{19}H_{28}O_3Si$: C, 68.63; H, 8.49. Found: C, 68.68; H, 8.68.

Further elution [diethylether/petrol, 3:7] afforded **28c** (20 mg, 15% yield). **28c**: colorless oil; R_f 0.30 (1:1 diethyl ether/pentane eluent); IR (film) 2930, 1720, 1659 cm^{-1}**;** ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.55 (s, 1H), 7.30 (t, *J* = 7.3 Hz, 2H), 7.23 (t, *J* = 7.3 Hz, 1H), 7.18 (d, *J* = 7.6 Hz, 2H), 6.73 (dd, *J* = 15.6, 10.1 Hz, 1H), 5.88 (d, *J* = 15.6 Hz, 1H), 3.77 (s, 3H), 3.17 (td, *J* = 9.5, 5.5 Hz, 1H), 2.78-2.68 (m, 2H), 2.30 (ddd, *J* = 12.8, 9.8, 3.1 Hz, 1H), 1.33 (m, 1H), 1.15 (m, 1H), 0.74 (t, *J* = 7.6 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 201.3, 166.6, 150.8, 141.7, 128.8, 128.2, 127.1, 123.4, 50.5, 48.6, 43.9, 25.0, 11.8; MS (ES) *m*/*z* (relative intensity): 260 (M, 5), 205 (35), 105 (100); HRMS (EI) (M) calcd for $C_{16}H_{20}O_3$: 260.1407. Found 260.1404. HPLC analysis: ee 81% ((*R*,*R*)-Whelk-O1, 9.0% *i*-PrOH in hexane, 0.6 mL/min, λ= 254 nm, t_R= 13.4 min, major; t_R= 14.3 min, minor); Anal. Calcd for $C_{16}H_{20}O_3$: C, 73.82; H, 7.74. Found: C, 73.85; H, 8.10.

Methyl (2*E*,4*R*,5*S*,6*Z*)-7-(*tert*-butyldimethylsiloxy)-4,5-dimethylhepta-2,6-dienoate (30) and methyl (2*S*,3*R*,*E*)-3-(*tert*-butyldimethylsiloxy)-2-((*E*)-prop-1-enyl)hex-4-enoate (31). Methyl (*E*)-2-diazo-pent-3-enoate **27b** (521 mg, 3.72 mmol) in 2,2-dimethylbutane (37 mL) was added dropwise over 3.5 h via cannula addition to a rapidly stirred solution of TBS-protected crotyl alcohol (**15a**) (340 mg, 1.84 mmol) and Rh_2(*S*-DOSP)$_4$ (69 mg, 3.72 x 10^{-5} mol) in 2,2-dimethylbutane (3.0 mL) at 23 °C. On completion of the diazoacetate addition the reaction mixture was allowed to stir for an additional 1 h. The solvent was evaporated and the residue (**30**:**31**= 1.2:1.0 by crude ^{1}H NMR) was purified by flash chromatography [SiO_2; dichloromethane-petrol, 1:4], to provide **31** (125 mg, 23% yield) and **30** (137 mg, 25% yield). **31**: colorless oil; $[\alpha]_D^{25}$ -29.9 (*c* 0.29, $CHCl_3$); IR (film) 2953, 2929, 2886, 2856, 1740 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.58 (dq, *J* = 15.4, 6.2 Hz, 1H), 5.49-5.54 (m, 2H), 5.42 (ddq, *J* = 15.4, 7.7, 1.5 Hz, 1H), 4.30 (app. t, *J* = 7.0 Hz, 1H), 3.65 (s, 3H), 3.02 (m, 1H), 1.72 (d, *J* = 4.8 Hz, 3H), 1.67 (dd, *J* = 6.6, 1.1 Hz, 3H), 0.86 (s, 9H), 0.02 (s, 3H), 0.00 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ

173.1 (C), 132.3 (CH), 129.6 (CH), 127.2 (CH), 126.2 (CH), 75.1 (CH), 57.5 (CH), 51.6 (CH_3), 25.8 (CH_3), 18.2 (C), 18.1 (CH_3), 17.6 (CH_3), - 4.1 (CH_3), - 4.8 (CH_3); LRMS (ESI) *m/z* 618 (M + 2Na, 70%), 321 (M + Na, 100), 299 (M + H, 30); HRMS (M + Na) calcd for $C_{16}H_{30}O_3NaSi$: 321.1856. Found 321.1865.ee 81% (by ^1H NMR using Eu tris[3-(heptafluoropropylhydroxymethylene)-(+)-camphorate]). Anal. Calcd for $C_{16}H_{30}O_3Si$: C, 64.38; H, 10.13. Found: C, 64.43; H, 10.20.

30: colorless oil; $[\alpha]_D^{25}$ -20.2 (*c* 0.97, $CHCl_3$); IR (film) 2957, 2929, 2856, 1727, 1654 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 6.94 (dd, *J* = 15.8, 8.1 Hz, 1H), 6.18 (d, *J* = 5.9 Hz, 1H), 5.78 (dd, *J* = 16.2, 0.3 Hz, 1H), 4.24 (dd, *J* = 9.5, 5.9 Hz, 1H), 3.74 (s, 3H), 2.80 (m, 1H), 2.30 (m, 1H), 1.04 (d, *J* = 7.0 Hz, 3H), 0.95 (d, *J* = 7.0 Hz, 3H), 0.94 (s, 9H), 0.14 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.1, 153.6, 138.6, 120.1, 113.1, 51.4, 42.2, 33.3, 29.8, 25.7, 18.5, 16.8, -5.3; LRMS (ESI) *m/z* 321 (M + Na, 100%); HRMS (M + Na) calcd for $C_{16}H_{30}O_3NaSi$: 321.1856. Found 321.1859. HPLC analysis: ee 82% (*R*,*R*)-Whelk-O1, 0.1% *i*-PrOH in hexane, 1.0 mL/min, λ= 254 nm, t_R= 9.9 min, major; t_R= 10.6 min, minor). Anal. Calcd for $C_{16}H_{30}O_3Si$: C, 64.38; H, 10.13. Found: C, 64.32; H, 10.16.

Methyl (4*S*,5*R*,*E*)-4,5-dimethyl-7-oxohept-2-enoate (32). Methyl (*E*)-2-diazo-pent-3-enoate **27b** (222 mg, 1.59 mmol) in 2,2-dimethylbutane (17 mL) was added dropwise over 2 h via addition funnel to a rapidly stirred solution of TMS-protected crotyl alcohol (**15f**) (2.08 g, 14.44 mmol) and Rh_2(*S*-DOSP)$_4$ (30 mg, 1.59 x 10^{-5} mol) in 2,2-dimethylbutane (1.0 mL) at 23 °C. On completion of the diazoacetate addition the reaction mixture was allowed to stir for an additional 1 h prior to concentration *in vacuo* to remove solvent and excess silyl ether **15f**. The crude reaction mixture was dissolved in α,α,α-trifluorotoluene (5 ml, degassed) and placed in a sealable vial containing 1-ethyl-3-methyl-1*H*-imidazolium (50 mg, 0.19 mmol). The vessel was sealed and irradiated with microwaves at 30 W, 240 °C for 30 min. The ionic liquid was removed by passing the crude reaction mixture through a plug of silica eluting with diethyl ether. The solvent was evaporated and the residue was purified by flash chromatography [SiO_2; diethyl ether/petrol, 3:7], to provide **32** (155 mg, 53% yield) as a colorless oil; R_f 0.14 (2:8 diethyl ether/pentane eluent); $[\alpha]_D^{22}$ +3.7 (*c* 0.93, $CHCl_3$); IR (film) 2966, 1723, 1657 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 9.74 (s, 1H), 6.86 (dd, *J* = 15.9, 8.2 Hz, 1H), 5.81 (d, *J* = 15.9 Hz, 1H), 3.73 (s, 3H), 2.48 (dd, *J* = 16.2, 3.7 Hz, 1H), 2.29 (dd, *J* = 13.4, 6.7 Hz, 1H), 2.26-2.12 (m, 2H), 1.04 (d, *J* = 6.7 Hz, 3H), 0.94 (d, *J* = 6.7 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 201.9 (CH), 167.0 (C), 152.3 (CH), 121.1 (CH),

51.6 (CH_3), 48.4 (CH_2), 41.2 (CH), 32.3 (CH), 17.0 (CH_3), 15.7 (CH_3); MS (ESI) *m/z* (relative intensity): 207 (M + Na, 21), 185 (M, 100); HRMS (ESI) (M + Na) calcd for $C_{10}H_{16}O_3Na$: 207.0992. Found 207.0991. HPLC analysis: ee 81% ((*R*,*R*)-Whelk-O1, 5.0% *i*-PrOH in hexane, 1.0 mL/min, λ= 254 nm, t_R= 17.4 min, major; t_R= 21.3 min, minor).

Methyl (4*R*,5*R*,*E*)-4,5-dimethyl-7-oxohept-2-enoate (34). Methyl (*E*)-2-diazo-pent-3-enoate **27b** (140 mg, 1.00 mmol) in 2,2-dimethylbutane (10 mL) was added dropwise over 3 h via syringe pump to a rapidly stirred solution of Rh_2(*R*-DOSP)$_4$ (19 mg, 1.00 x 10^{-5} mol) in TMS-protected *cis*-2-buten-1-ol (**33**) (1.44 g, 10.0 mmol) at 23 °C. The solvent and excess silyl ether was removed *in vacuo* and the resultant orange oil was dissolved in α,α,α-trifluorotoluene (5 mL, degassed), combined with 1-ethyl-3-methyl-1*H*-imidazolium (50 mg, 0.95 mmol) and exposed to microwave assisted heating at 30W, 240˚C for 30 min. The solvent was evaporated and the residue was purified by flash chromatography [SiO_2; diethyl ether-petrol, 1:3], to afford **34** (64 mg, 35% yield) as a colorless oil; R_f 0.57 (10:1 dichloromethane/diethyl ether eluent); $[\alpha]_D^{25}$ –41.8 (*c* 0.44, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.76 (br s, 1H), 6.88 (dd, *J* = 15.9, 7.9 Hz, 1H), 5.81 (d, *J* = 15.9 Hz, 1H), 3.75 (s, 3H), 2.45 (dd, *J* = 15.6, 3.8 Hz, 1H), 2.35 (m, 1H), 2.29-2.15 (m, 2H), 1.07 (d, *J* = 6.7 Hz, 3H), 0.95 (d, *J* = 6.7 Hz, 3H). HPLC analysis: ee 76% (*R*,*R*)-Whelk-O1, 5.0% *i*-PrOH in hexane, 0.97 mL/min, λ= 254 nm, t_R= 9.4 min, minor; t_R= 10.1 min, major). Data were in accordance with the previously reported literature.[5c]

Methyl (4*R*,5*R*,*E*)-5-methyl-7-oxo-4-phenylhept-2-enoate (35), methyl (2*R*,3*S*,*Z*)-2-((*E*)-styryl)-3-(trimethylsilyloxy)hex-4-enoate (36) and methyl (1*S*,2*S*,3*R*,*E*)-2-(hydroxymethyl)-3-methyl-1-styrylcyclopropanecarboxylate (37). As general procedure except using Rh_2(*R*-DOSP)$_4$ catalyst in place of Rh_2(*S*-DOSP)$_4$. The solvent was evaporated and the residue (**35**:**36**:**37**= 1.6:1.0:2.3 by crude ^{1}H NMR) was purified by flash chromatography [SiO_2; diethylether/pentane, 1:40 with 1% triethylamine], to provide **36** (33 mg, 21% yield) as a colorless oil; R_f 0.44 (7:3 dichloromethane/pentane eluent); $[\alpha]_D^{22}$ +34.2 (*c* 0.86, $CHCl_3$); IR (film) 2954, 1738 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.39 (d, *J* = 7.3 Hz, 2H), 7.32 (t, *J* = 7.3 Hz, 2H), 7.24 (t, *J* = 7.3 Hz, 1H), 6.46 (d, *J* = 15.9 Hz, 1H), 6.29 (dd, *J* = 16.2, 9.5 Hz, 1H), 5.54 (dq, *J* = 11.0, 7.0 Hz, 1H), 5.42 (ddd, *J* = 11.0, 9.2, 1.5 Hz, 1H), 4.83 (m, 1H), 3.68, (s, 3H), 3.25 (m, 1H), 1.69 (dd, *J* = 7.0, 1.5 Hz, 3H), 0.07 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.4 (C), 137.1 (C), 133.9 (CH), 131.7 (CH), 128.6 (CH), 127.6 (CH), 126.4 (CH), 125.6 (CH), 124.8

(CH), 69.0 (CH), 57.3 (CH), 51.8 (CH_3), 13.4 (CH_3), 0.2 (CH_3); MS (ESI) *m/z* (relative intensity): 341 (M + Na, 100); HRMS (ESI) (M + Na) calcd for $C_{18}H_{26}O_3NaSi$: 341.1543. Found 341.1536. HPLC analysis: ee 92% (ChiralcelOD-H, 100% hexane, 0.97 mL/min, λ= 254 nm, t_R= 16.0 min, major; t_R= 19.0 min, minor).

Further elution (diethyl ether/pentane, 3:7 with 1% triethylamine), to provide **35** (31 mg, 25% yield) as a colorless oil; R_f 0.40 (7:3 dichloromethane/pentane eluent); $[\alpha]_D^{22}$ –25.0 (*c* 0.72, $CHCl_3$); IR (film) 2954, 1723, 1659 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 9.59 (d, *J* = 0.9 Hz, 1H), 7.33 (t, *J* = 7.3 Hz, 2H), 7.25 (t, *J* = 7.3 Hz, 1H), 7.18 (d, *J* = 7.0 Hz, 2H), 7.11 (d, *J* = 15.6, 9.8 Hz, 1H), 5.87 (d, *J* = 15.6 Hz, 1H), 3.72 (s, 3H), 3.23 (t, *J* = 9.5 Hz, 1H), 2.54 (m, 1H), 2.34 (dd, *J* = 17.1, 4.0 Hz, 1H), 2.16 (ddd, *J* = 17.1, 8.9, 2.4 Hz, 1H), 1.04 (d, *J* = 6.7 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 201.5 (C), 166.8 (C), 149.6 (CH), 140.9 (C), 129.1 (CH), 128.0 (CH), 127.3 (CH), 122.2 (CH), 54.8 (C), 51.6 (CH_3), 48.9 (CH_2), 32.8 (CH), 18.5 (CH_3); MS (ESI) *m/z* (relative intensity): 269 (M + Na, 100); HRMS (ESI) (M + Na) calcd for $C_{15}H_{18}O_3Na$: 269.1148. Found 269.1141. HPLC analysis: ee 92% ((*R*,*R*)-Whelk-O1, 5.0% *i*-PrOH in hexane, 0.97 mL/min, λ= 254 nm, t_R= 10.1 min, major; t_R= 11.2 min, minor); Anal. Calcd for $C_{15}H_{18}O_3$: C, 73.15; H, 7.37. Found: C, 73.31; H, 7.31.

Further elution (diethyl ether/pentane, 7:3) provided **37** (49 mg, 40% yield) as a colorless oil; R_f 0.11 (1:1 diethyl ether/pentane eluent); $[\alpha]_D^{22}$ –3.9 (*c* 0.82, $CHCl_3$); IR (film) 3211, 2953, 1722, 1699 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.42 (d, *J* = 7.6 Hz, 2H), 7.34 (t, *J* = 7.6 Hz, 2H), 7.26 (t, *J* = 7.3 Hz, 1H), 6.68 (d, *J* = 16.2 Hz, 1H), 6.14 (d, *J* = 16.2 Hz, 1H), 3.74 (dd, *J* = 7.0, 2.1 Hz, 2H), 3.68 (s, 3H), 2.07 (dt, *J* = 9.5, 7.63 Hz, 1H), 1.89 (dq, *J* = 9.5, 6.7 Hz, 1H), 1.49 (br.s 1H), 1.16 (d, *J* = 6.4 Hz, 3H),; ^{13}C NMR (125 MHz, $CDCl_3$) δ 174.8, 137.6, 137.1, 128.6, 127.8, 126.3, 120.5, 59.1, 52.4, 32.7, 31.8, 25.6, 9.3; MS (ESI) *m/z* (relative intensity): 269 (M + Na, 100); HRMS (ESI) (M + Na) calcd for $C_{15}H_{18}O_3Na$: 269.1148. Found 269.1145. HPLC analysis: ee 88% (Chiralpak AD-RH, 5.0% *i*-PrOH in hexane, 0.97 mL/min, λ= 254 nm, t_R= 9.6 min, minor; t_R= 11.1 min, major).

Methyl 2-(1-benzyl-4-methyl-3-phenylpiperidin-2-yl)acetate (39). Prepared according to the method of Schnieder.[5g] Benzylamine (0.03 mL, 0.24 mmol) was added to a rapidly stirred solution of aldehyde (59 mg, 0.24 mmol) and anhydrous $MgSO_4$ in toluene (4 mL) at -15 °C and the resultant solution was stirred for 1.5 h. The reaction mixture was then filtered and the filtrate concentrated in vacuo.

The residue was dissolved in methanol (4 mL) and stirred under an atmosphere of hydrogen (1 atm) for 14 h at 23 °C. The solvent was evaporated and the residue (a 2:1 mixture of inseparable diastereomers) was purified by flash chromatography [SiO_2; diethyl ether/petrol, 1:4], to provide **39** (24 mg, 30% yield) as a colorless oil; R_f 0.20 (1:4 diethyl ether/pentane eluent). Only the major diastereoisomer could be fully characterized: IR (film) 3027, 2952, 2921, 2360, 2338, 1736 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.37-7.13 (m, 10H), 3.92 (d, *J* = 13.7 Hz, 1H), 3.68 (d, *J* = 13.7 Hz, 1H), 3.51 (m, 1H), 3.41 (s, 3H), 2.92 (dd, *J* = 11.9, 4.6 Hz, 1H), 2.76 (td, *J* = 13.4, 2.7 Hz, 1H), 2.68 (dd, *J* = 14.9, 8.5 Hz, 1H), 2.61 (bd, *J* = 13.1 Hz, 1H), 2.22 (dd, *J* = 14.9, 5.5 Hz, 1H), 2.14 (m, 1H), 1.58 (m, 1H), 1.48 (dd, *J* = 13.1, 4.6 Hz, 1H), 0.86 (d, *J* = 6.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 173.3 (C), 141.2 (C), 129.0 (CH), 128.7 (CH), 128.6 (CH), 128.3 (CH), 128.2 (CH), 127.0 (CH), 126.2 (CH), 62.1 (CH), 58.4 (CH_2), 51.3 (CH_3), 50.5 (CH), 44.3 (CH_2), 31.5 (CH_2), 30.4 (CH_2), 27.8 (CH), 20.6 (CH_3); MS (ESI) *m/z* (relative intensity) 264 (M - H, 100), 91 (82); HRMS (ESI) (M - H) calcd for $C_{19}H_{22}N$: 264.1747. Found 264.1742; Anal. Calcd for $C_{22}H_{27}NO_2$: C, 78.30; H, 8.06; N 4.15. Found: C, 78.01; H, 8.21; N 4.03.

Methyl 2-(3-methyl-5-oxo-2-phenylcyclopentyl)acetate (40). KHMDS (0.32 mL, 0.16 mmol, 0.5M in toluene) was added to 3-benzyl-5-(2-hydroxyethyl)-4-methylthiazolium chloride A (43 mg, 0.16 mmol) in DMF (20 mL) and stirred at 23 °C for 15 min. Aldehyde x in DMF (10 mL) was then added and the resultant solution was stirred for 24 h. The reaction was quenched by the addition of sat. NH_4Cl(aq) (10 mL) and extracted with diethyl ether (3 x 15 mL). The organics were combined and washed with HCl (aq) (10 mL, 1M), H_2O (5 x 10 mL), brine (10 mL) and dried (Na_2SO_4). The solvent was evaporated and the residue (71% de by crude ^1H NMR) was purified by flash chromatography [SiO_2; diethylether-pentane, 3:7], to provide **40** (117 mg, 59%) as a colorless oil; R_f 0.46 (1:1 diethyl ether/pentane eluent); IR (film) 2955, 1734, 1497, 1437 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.35 (t, *J* = 7.3 Hz, 2H), 7.28 (d, *J* = 7.6 Hz, 1H), 7.23 (d, *J* = 7.3 Hz, 2H), 3.52 (s, 3H), 2.76-2.67 (m, contains dd, *J* = 10.1, 7.3 Hz, 3H), 5.42 (dd, *J* = 10.1, 4.9 Hz, 1H), 2.33 (m, 1H), 2.08 (dd, *J* = 18.6, 11.6 Hz, 1H), 1.04 (d, *J* = 6.4 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 216.3 (C), 172.2 (C), 140.2 (C), 128.8 (CH), 127.8 (CH), 127.2 (CH), 55.8 (CH), 54.2 (CH), 51.6 (CH_3), 45.9 (CH_2), 37.3 (CH), 31.9 (CH_2), 17.9 (CH_3); MS (EI) *m/z* (relative intensity): 246 (M^+, 2), 173 (100); HRMS (EI) calcd for $C_{15}H_{18}O_3$: 246.1250. Found 246.1260; Anal. Calcd for $C_{15}H_{18}O_3$: C, 73.15; H, 7.37. Found: C, 73.23; H, 7.31.

Figure 2 : ORTEP Drawing of **26**