Supporting Information for:

Asymmetric, Organocatalytic, Three-Step Syntehsis of α-Hydroxy-(*E*)-β,γ-Unsaturated Esters

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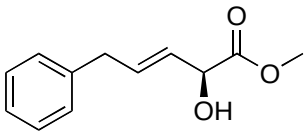
Experimental Procedures.

All air and moisture sensitive reactions were carried out in flame-dried or oven dried (120 ^{o}C) glassware under an inert atmosphere of argon. All reactive liquids were transferred by syringe of cannula and were added into the flask through a rubber septum. All other solvents and reagents were used as received unless otherwise stated. Melting points were obtained on Mel-temp metal block apparatus and are not corrected. ^{1}H and ^{13}C NMR were obtained on a Bruker 400 MHz spectrometer. All NMR spectra were obtained in a solution of $CDCl_3$ or acetone-d_6. Chemical shifts (δ) are reported in parts per million (ppm). Multiplicities of signals in the ^{1}H spectra are reported as follows, s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet), dd (doublet of doublets), etc. Infrared spectra were obtained on a Perkin Elmer 1600 FR-IR spectrometer as liquid films or as a thin layer with NaCl cells. Intensities were repoted as s (strong 67-100 %), m (medium 34-66%), and w (0-33 %) with the following notations, br (broadened), sh (shoulder), etc. Optical rotations were recorded on JASCO, P-1100 model polarimeter (Japan Spectroscopic Co., Ltd.) with sodium D line at the temperatures as indicated in the experimental for the specific compounds. Analytical Thin Layer Chromatography (TLC) was performed on Merck silica gel plates (Merck Kieselgel, 60, 0.25-mm thickness) with F_{254} indicator. Compounds were visualized under UV lamp and/or by developing with (p)-anisaldehyde, iodine, vanillin, $KMnO_4$ or phosphomolibdic acid followed by heating with a heat gun. High Pressure Liquid Chromatography (HPLC) was performed on a Rainin HPLX system equipped with two 25 mL pump heads and a Rainin Dynamaz UV-C duel beam variable wavelength detector set at 254 nm. FAB mass spectra were obtained using a VG70S double focusing magnetic sector mass spectrometer (VF Analytical, Manchester, UK, now Micromass/Waters) equipped with a Xe gas FAB gun (8 kV @ 1.2 mA), an off-axis electron multiplier and an MSS data system (MasCom,

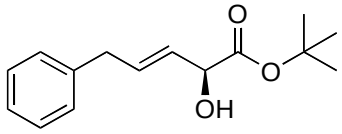
Bremen, Germany) at Johns Hopkins University. ESI spectra were obtained on a Bruker Apex-120Q FTMS instrument, and Apex-Qe with a high performance 12 Tesla magnet at Old Dominion University.



Compound 12. A flame-dried 5 mL round bottom flask was charged with freshly distilled 3-phenylpropanal **1a** (75 μL, 0.57 mmol) in 3 mL of anhydrous toluene and catalyst (2S)-**2** (68 mg, 0.11 mmol) and stirred at rt under Ar for 30 min. The reaction mixture was cooled to -20 °C and N-(phenylseleno)- phthalimide (188 mg, 0.62 mmol) was added. The reaction stirred for 2 h, then was cooled to -40 °C and diluted with 2 mL anhydrous THF. To this was added a solution of methyl(triphenylphosphoranylidene)acetate (265 mg, 0.62 mmol) in 2 mL anhydrous THF dropwise via syringe over 10 minutes. After stirring for 1 h, the mixture was warmed slowly to 0 °C over 4 h, then stirred an additional 10 h. The reaction was quenched with NH_4Cl (4 mL) and extracted with Et_2O (3 x 5 mL), dried over $MgSO_4$ and filtered. The filtrated was concentrated *in vacuo*, and the crude product was purified by flash column chromatography (0-10 % ethyl acetate in hexanes) to afford **5** (193 mg, 0.56 mmol, 99 % over 2 steps) as a colorless oil, which was used directly in the next step.

A 5 mL round bottom flask equipped with a stirbar under argon was charged with phenyl selenenyl olefin **5** (79 mg, 0.23 mmol) in 3 mL THF and 1 mL pyridine and cooled to -20 °C. To this was added H_2O_2 (0.1 mL, 30 % wt solution in H_2O) and the reaction stirred at -20 °C for 2 h. The reaction was was added to a saturated aqueous solution of ammonium chloride (5 mL), and extracted with diethyl ether (3 x 5 mL). The organics were washed with brine, dried over

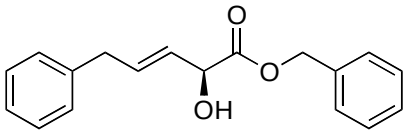
$MgSO_4$ and filtered. The filtrate was concentrated *in vacuo* and the crude product was purified via column chromatography (0-15 % ethyl acetate in hexanes) to afford α-hydroxy-β,γ-unsaturated ester **12** (41 mg, 0.19 mmol, 87 %) as a clear oil. Enantiomeric purity of **12** was determined to be 95 % based on analytical HPLC analysis using (S,S)-Whelk-O1 column with 1 % 2-propanol in hexanes. $[\alpha]_D^{22}$ = +47.4 (c = 1.98, $CHCl_3$); IR (thin film) 3467, 3027, 2953, 2896, 1740, 1495, 1453, 1436, 1211, 1127, 973, 748, 699 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.32-7.17 (m, 5 H), 6.10-6.03 (m, 1H), 5.59 (dd, 1H, *J* = 6.4, 15.6 Hz) 4.66 (d, 1H, *J* = 5.6 Hz), 3.80 (s, 3H), 3.41 (d, 2H, *J* = 6.8 Hz), 3.01 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.9, 139.4, 132.9, 128.5, 128.4, 127.4, 126.2, 71.2, 52.8, 38.4; HRMS (FAB) calc 207.1021 for $C_{12}H_{15}O_2$ $[(MH)^+]$, found 207.1018.



Compound 13. A flame-dried 5 mL round bottom flask was charged with freshly distilled 3-phenylpropanal **1a** (75 μL, 0.57 mmol) in 3 mL of anhydrous toluene and catalyst (2S)-**2** (67 mg, 0.11 mmol) and stirred at rt under Ar for 30 min. The reaction mixture was cooled to -20 °C and N-(phenylseleno)-phthalimide (205 mg, 0.68 mmol) was added. The reaction stirred for 2 h, then was cooled to -40 °C and diluted with 2 mL anhydrous THF. To this was added a solution of (tert-butoxycarbonylmethylene)triphenylphosphorane(256 mg, 0.67 mmol) in 2 mL anhydrous THF dropwise via syringe over 10 minutes. After stirring for 1 h, the mixture was warmed slowly to 0 °C over 4 h, and stirred an additional 10 h. The reaction was quenched with NH_4Cl (4 mL) and extracted with Et_2O (3 x 5 mL), dried over $MgSO_4$ and filtered. The filtrated was concentrated *in vacuo*, and the crude product was purified by flash column chromatography (0-

10 % ethyl acetate in hexanes) to afford **6** (160 mg, 0.41 mmol, 73 % over 2 steps) as a colorless oil, which was used directly in the next step.

A 5 mL round bottom flask equipped with a stirbar under argon was charged with phenyl selenenyl olefin **6** (160 mg, 0.41 mmol) in 3 mL THF and 1 mL pyridine and cooled to -20 °C. To this was added H_2O_2 (0.1 mL, 30 % wt solution in H_2O) and the reaction stirred at -20 °C for 2 h. The reaction was was added to a saturated aqueous solution of ammonium chloride (5 mL), and extracted with diethyl ether (3 x 5 mL). The organics were washed with brine, dried over $MgSO_4$ and filtered. The filtrate was concentrated *in vacuo* and the crude product was purified via column chromatography (0-15 % ethyl acetate in hexanes) to afford α-hydroxy-β,γ-unsaturated ester **13** (64 mg, 0.26 mmol, 63 %) as a clear oil. Enantiomeric purity of **13** was determined to be 95 % based on analytical HPLC analysis using (S,S)-Whelk-O1 column with 0.5 % 2-propanol in hexanes. $[\alpha]_D^{22}$ = +45.8 (c = 1.49, $CHCl_3$); IR (thin film) 3502 (w, br), 3027(w, sh), 2979 (w), 2932 (w), 1727(s), 1454 (w), 1393 (w), 1369 (m), 1277 (w, sh), 1256 (m), 1158 (s), 969 (w), 698 (m) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.31-7.26 (m, 2 H), 7.22-7.17 (m, 3H), 6.05-6.01 (m, 1H), 5.59-5.54 (dd, 1H, *J* = 6, 15 Hz) 4.51(d, 1H, *J* = 5 Hz), 3.41 (d, 2H, *J* = 7 Hz), 3.04 (s, 1H), 1.48 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.8, 139.7, 132.2, 128.5, 128.4, 128.3, 126.1, 81.8, 71.3, 38.4, 27.9; HRMS (FAB) calc 249.1491for $C_{15}H_{21}O_3$ $[(MH)^+]$, found 249.1485.

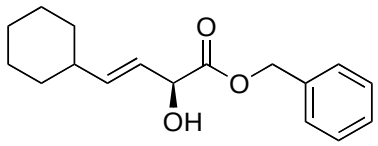


Compound 14. A flame-dried 5 mL round bottom flask was charged with freshly distilled 3-phenylpropanal **1a** (75 μL, 0.51 mmol) in 3 mL of anhydrous toluene and catalyst (2S)-**2** (67 mg,

0.11 mmol) and stirred at rt under Ar for 30 min. The reaction mixture was cooled to -20 °C and N-(phenylseleno)-phthalimide (205 mg, 0.68 mmol) was added. The reaction stirred for 2 h, then was cooled to -40 °C and diluted with 2 mL anhydrous THF. To this was added a solution of (benzyloxycarbonylmethylene)triphenylphosphorane (302 mg, 0.74 mmol) in 2 mL anhydrous THF dropwise via syringe over 10 minutes. After stirring for 1 h, the mixture was warmed slowly to 0 °C over 4 h, and stirred an additional 10 h. The reaction was quenched with NH_4Cl (4 mL) and extracted with Et_2O (3 x 5 mL), dried over $MgSO_4$ and filtered. The filtrated was concentrated *in vacuo*, and the crude product was purified by flash column chromatography (0-10 % ethyl acetate in hexanes) to afford **7** (192 mg, 0.46 mmol, 81 % over 2 steps) as a colorless oil, which was used directly in the next step.

A 5 mL round bottom flask equipped with a stirbar under argon was charged with phenyl selenenyl olefin **7** (57 mg, 0.14 mmol) in 3 mL THF and 1 mL pyridine and cooled to -20 °C. To this was added H_2O_2 (0.1 mL, 30 % wt solution in H_2O) and the reaction stirred at -20 °C for 2 h. The reaction was was added to a saturated aqueous solution of ammonium chloride (5 mL), and extracted with diethyl ether (3 x 5 mL). The organics were washed with brine, dried over $MgSO_4$ and filtered. The filtrate was concentrated *in vacuo* and the crude product was purified via column chromatography (0-15 % ethyl acetate in hexanes) to afford α-hydroxy-β,γ-unsaturated ester **14** (27 mg, 0.095 mmol, 70 %) as a clear oil. Enantiomeric purity of **14** was determined to be 95 % based on analytical HPLC analysis using (S,S)-Whelk-O1 column with 3 % 2-propanol in hexanes. $[\alpha]_D^{23}$ = +10.9 (c = 1.24, $CHCl_3$); IR (thin film) 3488 (w, br), 3062 (w), 3028 (w), 2897 (w), 1735(s), 1496 (w), 1453 (w), 1261 (w), 1194 (m), 1125 (m), 1047 (w), 971 (m), 748 (m), 607 (s) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.47-7.13 (m, 10H), 6.10-6.03 (m, 1H), 5.63-5.56 (dd, 1H, *J* = 6, 15 Hz) 5.27-5.19 (q, 2H, *J* = 12 Hz), 4.70 (d, 2H, *J* = 6 Hz), 3.40

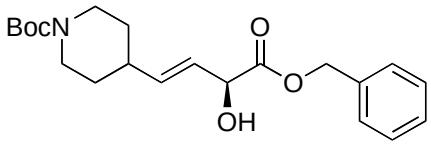
(d, 2H, J = 7 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.4, 139.4, 135.1, 133.2, 128.6, 128.57, 128.51, 128.4, 128.2, 127.4, 126.2, 71.2, 67.5, 38.4; HRMS (EI) calc 305.1148 $C_{18}H_{18}O_3Na$ [$(MNa)^+$], found 305.1148.



Compound 15. A flame-dried 5 mL round bottom flask was charged with freshly distilled 2-cyclohexylethanal **1b** (50 mg, 0.39 mmol) in 3 mL of anhydrous toluene and catalyst (2S)-**2** (46 mg, 0.078 mmol) and stirred at rt under Ar for 30 min. The reaction mixture was cooled to -20 °C and N-(phenylseleno)-phthalimide (141 mg, 0.47 mmol) was added. The reaction stirred for 2 h, then was cooled to -40 °C and diluted with 2 mL anhydrous THF. To this was added a solution of (benzyloxycarbonylmethylene)triphenylphosphorane (207 mg, 0.51 mmol) in 2 mL anhydrous THF dropwise via syringe over 10 minutes. After stirring for 1 h, the mixture was warmed slowly to 0 °C over 4 h, and stirred an additional 10 h. The reaction was quenched with NH_4Cl (4 mL) and extracted with Et_2O (3 x 5 mL), dried over $MgSO_4$ and filtered. The filtrated was concentrated *in vacuo*, and the crude product was purified by flash column chromatography (0-10 % ethyl acetate in hexanes) to afford **8** (127 mg, 0.31 mmol, 79 % over 2 steps) as a colorless oil, which was used directly in the next step.

A 5 mL round bottom flask equipped with a stirbar under argon was charged with phenyl selenenyl olefin **8** (63 mg, 0.15 mmol) in 3 mL THF and 1 mL pyridine and cooled to -20 °C. To this was added H_2O_2 (0.1 mL, 30 % wt solution in H_2O) and the reaction stirred at -20 °C for 2 h. The reaction was was added to a saturated aqueous solution of ammonium chloride (5 mL), and extracted with diethyl ether (3 x 5 mL). The organics were washed with brine, dried over

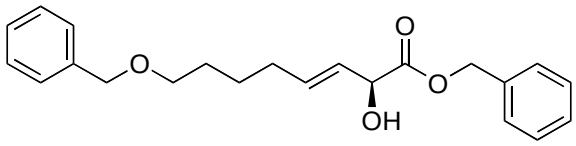
$MgSO_4$ and filtered. The filtrate was concentrated *in vacuo* and the crude product was purified via column chromatography (0-15 % ethyl acetate in hexanes) to afford α-hydroxy-β,γ-unsaturated ester **15** (28 mg, 0.10 mmol, 67 %) as a clear oil. Enantiomeric purity of **15** was determined to be 95 % based on analytical HPLC analysis using (S,S)-Whelk-O1 column with 4 % 2-propanol in hexanes. $[\alpha]_D^{23}$ = +8.4 (c = 1.5, $CHCl_3$); IR (thin film) 3462 (w, br), 2924 (m), 2850 (m), 1737 (s), 1448 (w), 1262 (w), 1191 (w), 1145 (w), 967 (m), 1047 (w), 749 (m), 696 (m) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.39-7.29 (m, 5H), 5.87-5.81 (dd, 1H, *J* = 7, 16 Hz), 5.50-5.44 (dd, 1H, *J* = 6, 15 Hz) 5.26-5.17 (q, 2H, *J* = 12 Hz), 4.64 (s, 1H), 2.90 (d, 2H, *J* = 5 Hz), 2.02-1.86 (m, 1H), 1.73-1.62 (m, 5H), 1.31-0.91 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.7, 140.4, 135.2, 128.6, 128.4, 128.1, 123.6, 76.7, 71.5, 67.3, 40.2, 32.5, 32.4, 26.1, 25.9 ; HRMS (EI) calc 297.1461 $C_{17}H_{22}O_3Na$ [$(MNa)^+$], found 297.1459.



Compound 16. A flame-dried 5 mL round bottom flask was charged with freshly distilled N-Boc-4-piperidineethanal **1c** (54 mg, 0.24 mmol) in 3 mL of anhydrous toluene and catalyst (2S)-**2** (29 mg, 0.048 mmol) and stirred at rt under Ar for 30 min. The reaction mixture was cooled to -20 °C and N-(phenylseleno)-phthalimide (108 mg, 0.36 mmol) was added. The reaction stirred for 2 h, then was cooled to -40 °C and diluted with 2 mL anhydrous THF. To this was added a solution of (benzyloxycarbonylmethylene)triphenylphosphorane (294 mg, 0.72 mmol) in 2 mL anhydrous THF dropwise via syringe over 10 minutes. After stirring for 1 h, the mixture was warmed slowly to 0 °C over 4 h, and stirred an additional 10 h. The reaction was quenched with NH_4Cl (4 mL) and extracted with Et_2O (3 x 5 mL), dried over $MgSO_4$ and filtered. The filtrated

was concentrated *in vacuo*, and the crude product was purified by flash column chromatography (0-10 % ethyl acetate in hexanes) to afford **9** (102 mg, 0.20 mmol, 83 % over 2 steps) as a colorless oil, which was used directly in the next step.

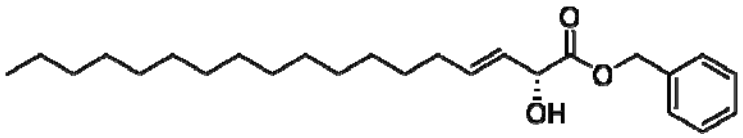
A 5 mL round bottom flask equipped with a stirbar under argon was charged with phenyl selenenyl olefin **9** (60 mg, 0.12 mmol) in 3 mL THF and 1 mL pyridine and cooled to -20 °C. To this was added H_2O_2 (0.1 mL, 30 % wt solution in H_2O) and the reaction stirred at -20 °C for 2 h. The reaction was was added to a saturated aqueous solution of ammonium chloride (5 mL), and extracted with diethyl ether (3 x 5 mL). The organics were washed with brine, dried over $MgSO_4$ and filtered. The filtrate was concentrated *in vacuo* and the crude product was purified via column chromatography (0-15 % ethyl acetate in hexanes) to afford α-hydroxy-β,γ-unsaturated ester **16** (29 mg, 0.078 mmol, 67 %) as a clear oil. Enantiomeric purity of **16** was determined to be 94 % based on analytical HPLC analysis using (S,S)-Whelk-O1 column with 10 % 2-propanol in hexanes. $[\alpha]_D^{23}$ = -1.22 (c = 1.1, $CHCl_3$); IR (thin film) 3425 (w, br), 2973 (s), 2931 (s), 2851 (w), 1743 (m), 1687 (s), 1393 (m), 1337 (w), 1274 (w), 1214 (w), 1168 (s), 969 (w), 866 (w), 697 (w) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.39-7.31 (m, 5H), 5.86-5.80 (dd, 1H, *J* = 6, 15 Hz), 5.54-5.49 (dd, 1H, *J* = 5.6, 15 Hz) 5.25-5.18 (q, 2H, *J* = 12 Hz), 4.65 (t, 1H, *J* = 5.6 Hz), 4.05 (s, 2H), 2.98 (d, 1H, *J* = 6 Hz), 2.71 (d, 2H, *J* = 12), 2.13 (s, 1H), 1.64-1.61 (m, 3H), 1.45 (s, 9H), 1.29-1.23 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.4,154.8, 137.8, 135.1, 128.6, 128.5, 128.2, 124.8, 79.4, 71.2, 67.5, 38.4, 31.3, 28.4; HRMS (EI) calc 375.20457 $C_{21}H_{29}NO_5$ [$(M)^+$], found 375.2055.



Compound 17. A flame-dried 5 mL round bottom flask was charged with freshly distilled 6-benzyloxyhexanal **1d** (53 mg, 0.26 mmol) in 3 mL of anhydrous toluene and catalyst (2S)-**2** (31 mg, 0.052 mmol) and stirred at rt under Ar for 30 min. The reaction mixture was cooled to -20 °C and N-(phenylseleno)-phthalimide (116 mg, 0.39 mmol) was added. The reaction stirred for 2 h, then was cooled to -40 °C and diluted with 2 mL anhydrous THF. To this was added a solution of (benzyloxycarbonylmethylene)triphenylphosphorane (316 mg, 0.77 mmol) in 2 mL anhydrous THF dropwise via syringe over 10 minutes. After stirring for 1 h, the mixture was warmed slowly to 0 °C over 4 h, and stirred an additional 10 h. The reaction was quenched with NH_4Cl (4 mL) and extracted with Et_2O (3 x 5 mL), dried over $MgSO_4$ and filtered. The filtrated was concentrated *in vacuo*, and the crude product was purified by flash column chromatography (0-10 % ethyl acetate in hexanes) to afford **10** (62 mg, 0.13 mmol, 49 % over 2 steps) as a colorless oil, which was used directly in the next step.

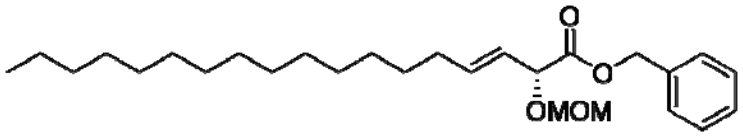
A 5 mL round bottom flask equipped with a stirbar under argon was charged with phenyl selenenyl olefin **10** (62 mg, 0.13 mmol) in 3 mL THF and 1 mL pyridine and cooled to -20 °C. To this was added H_2O_2 (0.1 mL, 30 % wt solution in H_2O) and the reaction stirred at -20 °C for 2 h. The reaction was was added to a saturated aqueous solution of ammonium chloride (5 mL), and extracted with diethyl ether (3 x 5 mL). The organics were washed with brine, dried over $MgSO_4$ and filtered. The filtrate was concentrated *in vacuo* and the crude product was purified via column chromatography (0-15 % ethyl acetate in hexanes) to afford α-hydroxy-β,γ-unsaturated ester **17** (40 mg, 0.11 mmol, 90 %) as a clear oil. Enantiomeric purity of **17** was

determined to be 97 % based on analytical HPLC analysis using (S,S)-Whelk-O1 column with 5 % 2-propanol in hexanes. $[\alpha]_D^{23}$ = +6.45 (c = 1.65, $CHCl_3$); IR (thin film) 3422 (w, br), 3031 (s), 2939 (s), 2861 (w), 1738 (s), 1496 (w), 1454 (m), 1261 (w, sh), 1198 (m), 1101 (m), 969 (m), 735 (m), 696 (s) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.40-7.27 (m, 10H), 5.92-5.85 (m, 1H), 5.60-5.51 (td, 1H, *J* = 2, 12.4, 19 Hz) 5.22 (s, 2H), 4.65 (d, 1H, *J* = 5.6 Hz), 4.5 (s, 2H), 3.46 (t, 2H, *J* = 6 Hz), 2.98 (s, 1H), 2.11-2.03 (q, 2H, *J* = 7 Hz), 1.65-1.43 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.5, 138.5, 135.1, 143.5, 128.6, 128.5, 128.3, 128.1, 127.6, 127.5, 126.2, 72.8, 71.4, 70.0, 67.4, 31.8, 29.1, 25.4; HRMS (EI) calc 377.1723 $C_{22}H_{26}O_4Na$ [$(M+Na)^+$], found 377.1719.

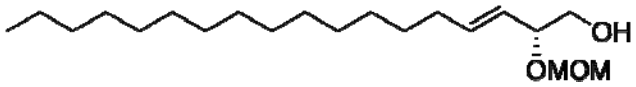


Compound 18. A flame-dried 5 mL round bottom flask was charged with freshly distilled hexdecanal **1e** (119 mg, 0.49 mmol) in 3 mL of anhydrous toluene and catalyst (2*R*)-**2** (60 mg, 0.09 mmol) and stirred at rt under Ar for 30 min. The reaction mixture was cooled to -20 °C and N-(phenylseleno)-phthalimide (224 mg, 0.74 mmol) was added. The reaction stirred for 2 h, then was cooled to -40 °C and diluted with 2 mL anhydrous THF. To this was added a solution of (benzyloxycarbonylmethylene)triphenylphosphorane (500 mg, 1.2 mmol) in 2 mL anhydrous THF dropwise via syringe over 10 minutes. After stirring for 1 h, the mixture was warmed slowly to 0 °C over 4 h, and stirred an additional 10 h. The reaction was quenched with NH_4Cl (4 mL) and extracted with Et_2O (3 x 5 mL), dried over $MgSO_4$ and filtered. The filtrated was concentrated *in vacuo*, and the crude product was purified by flash column chromatography (0-10 % ethyl acetate in hexanes) to afford **11** (201 mg, 0.38 mmol, 77 % over 2 steps) as a colorless oil, which was used directly in the next step.

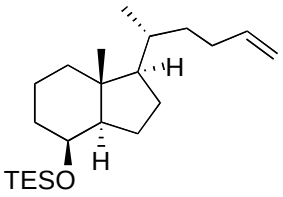
A 5 mL round bottom flask equipped with a stirbar under argon was charged with phenyl selenenyl olefin **11** (92 mg, 0.17 mmol) in 3 mL THF and 1 mL pyridine and cooled to -20 °C. To this was added H_2O_2 (0.2 mL, 30 % wt solution in H_2O) and the reaction stirred at -20 °C for 2 h. The reaction was was added to a saturated aqueous solution of ammonium chloride (5 mL), and extracted with diethyl ether (3 x 5 mL). The organics were washed with brine, dried over $MgSO_4$ and filtered. The filtrate was concentrated *in vacuo* and the crude product was purified via column chromatography (0-15 % ethyl acetate in hexanes) to afford α-hydroxy-β,γ-unsaturated ester **18** (56 mg, 0.14 mmol, 83 %) as a clear oil. Enantiomeric purity of **18** was determined to be 95 % based on analytical HPLC analysis using (S,S)-Whelk-O1 column with 3 % 2-propanol in hexanes. $[\alpha]_D^{23}$ = -9.4 (c = 0.23, $CHCl_3$); IR (thin film) 3487 (w, br), 2923 (s), 2852 (m), 1736 (s), 1456 (w), 1277 (w), 1210 (w), 1191 (w), 1138 (w), 1109 (w), 1029 (w), 967 (w), 733 (w), 683 (w) cm^{-1}; ^1H NMR (400 MHz, acetone) δ 7.42-7.37 (m, 5H), 5.92-5.88 (m, 1H), 5.65-5.59 (td, 1H, *J* = 2, 12.4, 19 Hz) 5.22 (m, 2H), 4.69 (t, 1H, *J* = 5.2 Hz), 4.41 (d, 1H, *J* = 5.6 Hz), 2.11-2.05 (m, 2H), 1.43-1.33 (m with s at 1.32, 26H), 9.22 (t, 3H, *J* = 6.4 Hz); ^{13}C NMR (100 MHz, D-6 acetone) δ173., 136.9, 133.9, 129.0, 128.7, 128.6, 128.1, 72.2, 66.7, 32.6, 32.4, 30.2, 30.1, 29.8, 29.6, 29.5, 23.1, 14.2; HRMS (EI) calc 411.2869 $C_{25}H_{40}O_3Na$ $[(M+Na)^+]$, found 411.2865.



Compound 21. A flame dried 5 mL round bottom flask equipped with a stirbar under argon was charged with α-hydroxy-β,γ-unsaturated ester **18** (56 mg, 0.14 mmol) in 2 mL anhydrous CH_2Cl_2 and cooled to -5 °C. To this was added methoxymethylbromide (57 μL, 0.71 mmol) and diisopropylethylamine (246 μL, 1.4 mmol) reaction warmed to rt over 30 minutes. After stirring for 48 h, the reaction was added to water (5 mL), and extracted with methylene chloride (3 x 5 mL). The organics were washed with brine, dried over $MgSO_4$ and filtered. The filtrate was concentrated *in vacuo* and the crude product was purified via column chromatography (0-15 % diethyl ether in hexanes) to afford MOM-protected α-hydroxy-β,γ-unsaturated ester **21** (34 mg, 0.079 mmol, 55 %) as a clear oil. Enantiomeric purity of **20** was determined to be 97 % based on analytical HPLC analysis using (S,S)-Whelk-O1 column with 0.5 % 2-propanol in hexanes. $[\alpha]_D^{23}$ = -33.5 (c = 0.2, $CHCl_3$); IR (thin film) 2924 (w), 2851 (w), 1751(s), 1540 (w), 1506 (w), 1471 (w), 1436 (w), 1318 (w), 1212 (w), 1107 (w), 1035 (w), 968 (w), 871 (w), 799 (w), 734 (w), 720 (w), 695 (w) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.37-7.31 (m, 5H), 5.91-5.84 (m, 1H), 5.53-5.48 (dd, 1H, *J* = 7.2, 15.2 Hz) 5.19 (s, 2H), 4.73 (d, 1H, *J* = 6.8 Hz), 4.67 (d, 1H, *J* = 6.8 Hz), 4.63 (d, 1H, *J* = 7.2 Hz), 3.35 (s, 3H), 2.08-2.03 (m, 2H), 1.43-1.26 (m with s at 1.26, 25 H), 0.88 (t, 3H, 6.8 Hz); ^{13}C NMR (100 MHz, D-6 acetone) 170.9, 137.3, 135.6, 128.5, 128.2, 128.1, 123.9, 94.7, 75.8, 66.6, 55.8, 32.2, 31.9, 29.64, 29.63, 29.6, 29.4, 29.3, 29.1, 28.7, 22.7, 14.1; HRMS (EI) calc 455.3132 $C_{27}H_{44}O_4Na$ $[(M+Na)^+]$, found 455.3127.

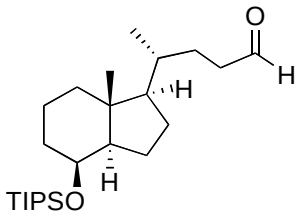


Compound (-)-19. A flame dried 5 mL round bottom flask equipped with a stirbar under argon was charged with ester **21** (28 mg, 0.064 mmol) in 2 mL anhydrous diethyl ether and cooled to -5 °C. To this was added lithium aluminum hydride (5 mg, 0.12 mmol). After stirring for 1 h, the reaction was added to water (5 mL), and extracted with diethyl ether (3 x 5 mL). The organics were washed with brine, dried over $MgSO_4$ and filtered. The filtrate was concentrated *in vacuo* and the crude product was purified via column chromatography (25 % diethyl ether in hexanes) to afford (-)-**19** (17 mg, 0.052 mmol, 80 %) as a white solid. $[\alpha]_D^{23}$ = -77 (c = 0.85, $CHCl_3$); IR (thin film) 3237(w, br), 2952 (w), 2917 (s), 2851 (m), 1467 (w), 1359 (w), 1228 (w), 1156 (w), 1035 (m), 966 (m), 816 (m) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 5.78-5.74 (m, 1H), 5.33-5.28 (m, 1H), 4.75 (d, 1H, *J* = 6.8 Hz), 4.6 (d, 1H, *J* = 6.8 Hz), 4.09-4.07 (m, 1H), 3.57 (s, 2H), 3.39 (s, 3H), 2.3 (s, 1H), 2.06-2.01 (m, 2H), 1.40-1.26 (m with s at 1.26, 25 H), 0.87 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 136.6, 125.8, 94.2, 78.8, 65.7, 55.5, 32.4, 31.9, 29.67, 29.65, 29.64, 29.58, 29.4, 29.3, 29.1, 28.9, 22.7, 14.1; HRMS (EI) calc 351.2869 $C_{20}H_{40}O_3Na$ $[(M+Na)^+]$, found 351.2868.



Compound 23. A flame dried 5 mL round bottom flask equipped with a stirbar under argon was charged with iodide **22** (260 mg, 0.60 mmol) in 4 mL anhydrous tetrahydrofuran and cooled to -5 °C. To this was added allylmagnesium bromide (0.65 mL, 0.65 mmol, 1.0 M solution). The reaction was allowed to slowly warm to rt over 30 minutes. After stirring for 96 h, the reaction

was added to a saturated solution of NH_4Cl (10 mL), and extracted with diethyl ether (3 x 5 mL). The organics were washed with brine, dried over $MgSO_4$ and filtered. The filtrate was concentrated *in vacuo* and the crude product was purified via column chromatography (100 % hexanes) to afford **23** (196 mg, 0.56 mmol, 94 %) as a clear oil. $[\alpha]_D^{23}$ = +49.9 (c = 0.62, $CHCl_3$); IR (thin film) 2949 (s), 2909 (m), 2875 (s), 1520 (w), 1456 (w), 1413 (w), 1372 (w), 1306 (w), 1235 (w), 1083 (m), 1070 (m), 972 (m), 921 (m), 722 (m) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 5.86-5.76 (m, 1H), 5.01 (d, 1H, *J* = 17 Hz), 4.91 (d, 1H, *J* = 10 Hz), 4.05 (s, 1H), 2.21-2.18 (m, 1H), 1.99-1.07 (m, 16H), 0.98-0.91 (m, 15H), 0.59-0.54 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 139.7, 113.8, 69.4, 56.8, 53.2, 42.2, 40.9, 35.1, 34.9, 34.7, 30.6, 27.3, 23.1, 18.5, 17.7, 13.5, 6.9, 5.3, 4.9; HRMS (FAB) calc 349.2927 $C_{22}H_{41}OSi$ [$(M-H)^+$], found 349.2927.

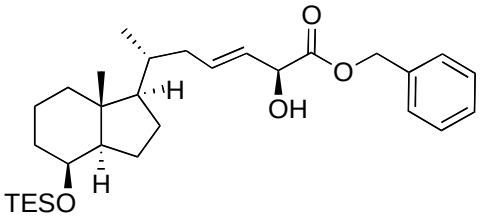


Compound 24. A flame dried 5 mL round bottom flask equipped with a stirbar under argon was charged with olefin **23** (78 mg, 0.22 mmol) in 2 mL acetonitrile. To this was added hydrogen fluoride (0.1 mL, 49 % aq). After stirring for 1 h, the reaction was added to a saturated solution of sodium bicarbonate (5 mL), and let stir for 30 minutes until gas ceased to evolve. The aqueous layer was extracted with ethl acetate (3 x 5 mL). The organics were washed with brine, dried over $MgSO_4$ and filtered. The filtrate was concentrated *in vacuo* and the crude product was taken directly onto the next step. A flame dried 5 mL round bottom flask equipped with a stirbar under argon was charged with the crude alcohol intermediate (52 mg, 0.22 mmol) in 3 mL anhydrous methylene chloride, and cooled to -78 °C. To this was added 2,6-Lutidine (105 μL,

0.91 mmol) and triisopropyl trifluoromethanesulfonate (84 μL, 0.31 mmol). The reaction was slowly warmed to rt over the next 6 h, and stirred an addition 6 h upon which it was added to water (5 mL) and extracted with diethyl ether (3 x 5 mL). The organics were washed with brine, dried over $MgSO_4$ and concentrated *in vacuo* and purified via column chromatography (100 % hexanes) to afford intermediate TIPS protected product (90 mg, 0.21 mmol, 94 % 2 step yeild) as a colorless oil. $[\alpha]_D^{23}$ = +45.6 (c = 0.98, $CHCl_3$); IR (thin film) 2942 (s), 2866 (s), 1463 (w), 1372 (w), 1237 (m), 1164 (m), 1067 (m), 1023 (m), 906 (m), 882 (m), 845 (w), 801 (w), 765 (w), 673 (m) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 5.84-5.77 (m, 1H), 5.0 (d, 1H, J = 17 Hz), 4.91 (d, 1H, *J* = 10 Hz), 4.21 (s, 1H), 2.18-2.14 (m, 1H), 1.99-1.23 (m, 15H), 1.15-1.02 (m with s at 1.07, 28H), 0.95 (s, 3H), 0.91 (d, 2H, J = 6 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 139.7, 113.8, 70.4, 56.7, 53.5, 42.1, 40.9, 35.1, 34.9, 34.6, 30.6, 27.3, 23.3, 18.5, 18.3, 18.2, 18.1, 17.9, 17.8, 13.8, 13.4, 12.9, 12.7, 6.6; HRMS (EI) calc 393.3547 $C_{25}H_{48}OSi$ $[(M+Na)^+]$, found 393.3547. This TIPS protected intermediate was taken on to the next step.

A flame dried 5 mL round bottom flask equipped with a stirbar under argon was charged with TIPS protected intermediate (27 mg, 0.062 mmol) in 3 mL of a 9:4 Dioxane/H_2O mixture. To this was added osmium tetraoxide (77 μL, 0.006 mmol, 2.5 % wt solution in 2-propanol) and the reaction stirred for 30 minutes, at which time sodium metaperiodate (33 mg, 0.16 mmol) was added. After stirring for 24 h, the reaction was diluted with brine, and extracted with ethylacetate (3 x 5 mL), dried over $MgSO_4$ and concentrated *in vacuo* and purified via flash silica column chromatography (0-5 % diethyl ether in hexanes) to afford aldehyde **24** (17 mg, 0.038 mmol, 62 %) as a colorless oil. $[\alpha]_D^{23}$ = +54.3 (c = 1.1, $CHCl_3$); IR (thin film) 2942 (s), 2866 (s), 2711 (w), 1728 (m), 1463 (w), 1373 (w), 1238 (m), 1164 (m), 1068 (w), 1026 (m), 948 (w), 922 (w), 882 (w), 845 (w), 801 (w), 673 (m) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 9.76 (s,

1H), 4.19 (s, 1H), 2.44-2.41 (m, 1H), 2.36-2.34 (m, 1H), 1.95 (d, 1H, *J* = 12 Hz), 1.84-1.67 (m, 6H), 1.44-1.22 (m, 9H), 1.14-1.01 (m with s at 1.05, 24H), 0.94 (s, 3H), 0.90 (d, 3H, 6Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 203.3, 69.9, 56.4, 53.4, 42.1, 40.9, 40.8, 34.9, 34.5, 27.8, 27.3, 23.3. 18.4, 18.3, 18.2, 17.8, 13.9, 12.6; HRMS (EI) calc 895.7365 $(C_{27}H_{52}O_2Si)_2Na$ [$(M_2+Na)^+$], found 895.7377.



Compound 26. A flame-dried 5 mL round bottom flask was charged with aldehyde **24** (32 mg, 0.074 mmol) in 1.5 mL of anhydrous toluene and catalyst (2S)-**2** (9 mg, 0.015 mmol) and stirred at rt under Ar for 30 min. The reaction mixture was cooled to -20 °C and N-(phenylseleno)-phthalimide (24.4 mg, 0.081 mmol) was added. The reaction stirred for 2 h, then was cooled to -40 °C and diluted with 1.5 mL anhydrous THF. To this was added a solution of (benzyloxycarbonylmethylene)triphenylphosphorane (90 mg, 0.22 mmol) in 1 mL anhydrous THF dropwise via syringe over 10 minutes. After stirring for 1 h, the mixture was warmed slowly to 0 °C over 4 h, and stirred an additional 10 h. The reaction was quenched with NH_4Cl (4 mL) and extracted with Et_2O (3 x 5 mL), dried over $MgSO_4$ and filtered. The filtrated was concentrated *in vacuo*, and the crude product was purified by flash column chromatography (0-3 % ethyl acetate in hexanes) to afford **25** (37.4 mg, 0.052 mmol, 70 % over 2 steps) as a colorless oil, which was used directly in the next step.

A 5 mL round bottom flask equipped with a stirbar under argon was charged with phenyl selenenyl olefin **25** (37 mg, 0.052 mmol) in 2 mL THF and 0.66 mL pyridine and cooled to -25

°C. To this was added H_2O_2 (0.15 mL, 30 % wt solution in H_2O) and the reaction stirred at -20 °C for 2 h. The reaction was was added to a saturated aqueous solution of ammonium chloride (5 mL), and extracted with diethyl ether (3 x 5 mL). The organics were washed with brine, dried over $MgSO_4$ and filtered. The filtrate was concentrated *in vacuo* and the crude product was purified via column chromatography (0-10 % ethyl acetate in hexanes) to afford α-hydroxy-β,γ-unsaturated ester **26** (19 mg, 0.032 mmol, 62 %) as a clear oil. $[\alpha]_D^{23}$ = +32.0 (c = 0.94, $CHCl_3$); IR (thin film) 3474 (w, br), 2942 (s), 2890 (sh, m), 2866 (s), 1738 (s), 1457 (m), 1373 (w), 1263 (w), 1164 (m), 1084 (m), 1023 (m), 971 (m), 882 (w), 845 (w), 801 (w), 673 (m) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.39-7.33 (m, 5H), 5.88-5.80 (m, 1H), 5.52-5.47 (dd, 1H, *J* = 6, 23 Hz) 5.25-5.19 (m, 2H), 4.65 (t, 1H, *J* = 6 Hz), 4.19 (s, 1H), 2.16-2.12 (m, 1H), 1.94-1.18 (m, 16H), 1.14-1.02 (m with s at 1.07, 24H), 0.93 (s, 3H), 0.85 (d, *J* = 6 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.7, 135.2, 133.4, 128.6, 128.5, 128.2, 127.3, 71.5, 69.9, 67.4, 56.2, 53.4, 42.1, 40.7, 38.7, 35.4, 34.5, 27.3, 23.3, 18.7, 18.3, 18.2, 17.8, 13.9, 12.6; HRMS (EI) calc 565.3684 $C_{22}H_{26}O_4Na$ $[(M+Na)^+]$, found 565.3684.