Supporting Information

Synthesis of Complex Allylic Esters via C—H Oxidation vs C—C Bond Formation

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General Information: All commercially obtained reagents were used as received: 2-phenyl-1,4-benzoquinone (ACROS); Pd(CH3CN)2(BF4)2 (Aldrich) was stored in a glove box under an argon atmosphere and weighed out in under argon prior to use, all other reagents were purchased from least expensive supplier and used directly unless otherwise stated. Solvents diethyl ether (Et2O) and methylene chloride (CH2Cl2) were purified prior to use by passage through a bed of activated alumina (Glass Contour, Laguna Beach, California). Anhydrous N,N-dimethylformamide (DMF) (Sure/Seal) was obtained from Sigma-Aldrich and used as received. All allylic oxidation reactions were run under air with no precautions taken to exclude moisture. All other reactions were run under a balloon of argon gas unless otherwise stated. Thin-layer chromatography (TLC) was conducted with E. Merck silica gel 60 F254 precoated plates (0.25 mm) and visualized with UV, potassium permanganate, and ceric ammonium molybdate staining. Flash column chromatography was performed as described by Still et al.1 using EM reagent silica gel 60 (230-400 mesh). 1H NMR spectra were recorded on a Varian Unity 400 (400 MHz), a Varian Unity 500 (500 MHz), or a Varian Unity Inova 500NB spectrometer and are reported in ppm using solvent as an internal standard (CDCl3 at 7.26 ppm). Data reported as: s = singlet, d = doublet, t = triplet, q = quartet, quint. = quintet, m = multiplet, br = broad, app = apparent; coupling constant(s) in Hz; integration, corresponding carbon atom. Proton-decoupled 13C-NMR spectra were recorded on a Varian Unity-500 (125 MHz) spectrometer and are reported in ppm using solvent as an internal standard (CDCl3 at 77.23 ppm). IR spectra were recorded as thin films on NaCl plates on a Perkin-Elmer Spectrum BX and are reported in frequency of absorption (cm⁻¹). All optical rotations were determined on a Perkin Elmer 341 Polarimeter using the sodium D line (589 nm). High-resolution mass spectra were obtained at the University of Illinois Mass Spectrometry Laboratory. Medium pressure liquid chromatography (MPLC) was used in cases with difficult silica chromatography separations and consists of a prep-HPLC pump, hand-packed 12g MPLC silica column and fraction collector.

Method Notes: These notes are intended to help with the preparation of compounds not described in this communication and should be used with discretion. The reaction is dependent on concentration with an optimal range of 1M or greater. Below this threshold of concentration the reaction is dramatically slower. Other solvents can be used. These consist mainly of other chlorinated hydrocarbons (chloroform, dichloroethane) but can be changed to ethereal solvents limited mainly by starting material, coupling acid solubility, and slightly diminished yields or selectivities. Stirring is crucial; appropriate stirring involves slow steady mixing at approximately 300 rpm (achieved after 1hr at 40°C when the reaction becomes black and viscous). Due to the high viscosity of the reaction mixture a bigger stir bar is more appropriate. The temperature is also important with an effective range of 40 to 45°C. Much lower temperatures result in dramatically slower reactivity and the inability to form a solution. Higher temperatures result in decreased yields due to by-product formation. The Pd(CH3CN)2(BF4)2 catalyst is moisture sensitive and decomposes to a wet dull yellow powder, easily distinguished from the bright yellow crystals of good catalyst.

General Procedure: To a 4 mL borosilicate vial was first added Pd(CH3CN)2(BF4)2 (44.4 mg, 0.1 mmol, 10 mol %) under argon atmosphere. The following reagents were then added in one portion under ambient atmosphere: phenyl benzoquinone (368 mg, 2.0 equiv.), CH2Cl2 (3.0 mmol, 3.0 equiv.), tBuOK (589 nm). High resolution mass spectra were obtained at the University of Illinois Mass Spectrometry Laboratory. Medium pressure liquid chromatography (MPLC) was used in cases with difficult silica chromatography separations and consists of a prep-HPLC pump, hand-packed 12g MPLC silica column and fraction collector.

Notes: (1) All yield are of column purified material with >20:1 L:B. E:Z ratios did not change after silica column purification unless otherwise noted. (2) All reference numbers in the tables and figures refer to the reference numbers from the text.
(E)-cinnamyl 3-(2,4-dimethoxyphenyl)acrylate (1) To a 4 mL borosilicate vial was added Pd(CH$_3$CN)$_2$(BF$_4$)$_2$ (44.4 mg, 0.1 mmol, 10 mol %) under argon atmosphere, followed by phenyl benzoquinone (368 mg, 2.0 mmol, 2 equiv.), (E)-3-(2,4-dimethoxyphenyl)acrylic acid (624 mg, 3.0 mmol, 3.0 equiv.), two 4Å molecular beads (50 mg) in one portion under ambient atmosphere. DMSO (100 µL, 1.1 mmol, 1.1 equiv.), CH$_2$Cl$_2$ (500 µL), and DIPEA (121.0 µL, 0.7 mmol, 0.7 equiv.) were added via glass syringe followed by a Teflon© stir bar. This solution was stirred at 41°C for 5 minutes before allyl benzene (118 mg, 1.0 mmol, 1.0 equiv.) was added neat using a microsyringe. The vial was then capped and stirred at 41°C for 72 hours. Upon completion (via NMR aliquate), the reaction was transferred to a separatory funnel using minimal methylene chloride (~2 mL). The solution was diluted with diethyl ether (50 mL) and washed with 5% K$_2$CO$_3$ (aq.) solution 2x. Note: If an inseparable emulsion forms filter the solution through a pressed pad of celite with 20-30 mL diethyl ether. The organic layer was dried with MgSO$_4$, filtered, and reduced in vacuo. Purification via flash silica gel chromatography (20% Et$_2$O/hexanes) gave (E)-cinnamyl 3-(2,4-dimethoxyphenyl)acrylate as a white solid. Note: Product streaks somewhat on silica gel with diethyl ether; however, to ensure good separation from PhBQ this mixture is necessary. The crude selectivities were determined to be L:B >20:1 and E:Z >20:1 by $^1$H NMR for entries 1-5 in table 1. Run 1 (224.0 mg, 0.69 mmol, 69%); run 2 (220.0 mg, 0.68 mmol, 68%); run 3 = (233.0 mg, 0.72 mmol, 72%) Average = 70% yield. 1.5 equivalents acid: Run 1 (185.0 mg, 0.57 mmol, 57%); run 2 (201.0 mg, 0.62 mmol, 62%); run 3 (204.0 mg, 0.63 mmol, 63%). Average = 61% yield. 24 hour reaction time: Run 1 (84.2 mg, 0.26 mmol, 52%); run 2 (85.9 mg, 0.27 mmol, 53%). Average = 53% yield. 5 mol % catalyst loading: Run 1 (103.7 mg, 0.32 mmol, 64%); run 2 (105.3 mg, 0.33 mmol, 65%). Average = 65% yield. 1.2 equiv. PhBQ: Run 1 (116.7 mg, 0.36 mmol, 72%) [not reported in Table 1]. R$_f$ = 0.2 (20% Et$_2$O/hexanes), $^1$H NMR (500 MHz, CDCl$_3$) δ 7.95 (d, $J = 16.0$ Hz, 1H), 7.45 (d, $J = 8.5$ Hz, 1H), 7.41 (d, $J = 7.0$ Hz, 2H), 7.33 (app. t, $J = 7.5$ Hz, 2H), 7.22 (s, 5H), 7.17 (app. t, $J = 7.5$ Hz, 2H), 7.05 (d, $J = 8.5$ Hz, 1H), 5.04 (s, 1H), 4.05 (s, 2H), 3.85 (s, 6H), 3.74 (s, 6H).
7.26 (t, J = 7.5, 1H), 6.70 (d, J = 16.0 Hz, 1H), 6.51 (dd, J = 9.0, 2.0 Hz, 1H), 6.48 (d, J = 16.0 Hz, 1H), 6.45 (d, J = 2.5 Hz, 1H), 6.37 (dt, J = 16.0, 6.0 Hz, 1H), 4.86 (dd, J = 6.0, 1.0 Hz, 2H), 3.87 (s, 3H), 3.84 (s, 3H). 13C NMR (100 MHz, CDCl3) δ 167.9, 162.9, 160.1, 140.7, 136.5, 134.1, 130.7, 128.8, 128.1, 126.8, 123.9, 116.7, 115.9, 105.4, 98.6, 65.0, 55.6 (2C). IR (neat, cm⁻¹) 3080, 3062, 3026, 2936, 2839, 1706, 1605, 1160. HRMS (ESI) m/z calculated for C20H20O4Na [M + Na]⁺: 347.1259; found: 347.1257. Spectral data has previously been reported for this compound.⁵

**(E)**-3-(benzo[d][1,3]dioxol-5-yl)allyl 2-bromo-3-(3,4,5-trimethoxyphenyl)propanoate (2) To a 4 mL borosilicate vial was added Pd(CH3CN)2(BF4)2 (11.1 mg, 0.025 mmol, 10 mol %) under argon atmosphere, followed by phenyl benzoquinone (92.0 mg, 0.5 mmol, 2 equiv.), 2-bromo-3-(3,4,5-trimethoxyphenyl)propionic acid³ (239.4 mg, 0.75 mmol, 3 equiv.), two 4Å molecular beads (30 mg) in one portion under ambient atmosphere. DMSO (25 µL, 0.29 mmol, 1.1 equiv.), CH3Cl (125 µL), and DIPEA (30 µL, 0.18 mmol, 0.7 equiv.) were added via glass syringe followed by a Teflon® stir bar. This solution was stirred at 41°C for 5 minutes before safrole (41 mg, 0.25 mmol, 1.0 equiv.) was added neat using a microsyringe. The vial was then capped and stirred at 41°C for 72 hours. Upon completion (via NMR aliquate), the reaction was transferred to a separatory funnel using minimal methylene chloride (~2 mL). The solution was diluted with 1:1 diethyl ether:hexanes (50 mL) and washed with 5% K2CO3 (aq.) solution 2x. Note: If an inseparable emulsion forms filter the solution through a pressed pad of celite with 20-30 mL diethyl ether. The organic layer was dried with MgSO4, filtered, and reduced in vacuo. Purification via flash silica gel chromatography (30% Et2O/hexanes) gave (E)-3-(benzo[d][1,3]dioxol-5-yl)allyl 2-bromo-3-(3,4,5-trimethoxyphenyl)propanoate as a pale yellow thick oil. The crude selectivities determined by 1H NMR in deutero-benzene are L:B >20:1 and E:Z 16:1. Run 1 (85.2 mg, 0.18 mmol, 71%); run 2 (80.1 mg, 0.17 mmol, 67%); run 3 = (80.4 mg, 0.17 mmol, 67%). **Average = 68% yield.** (16:1 E:Z after silica column purification). Rf = 0.15 (30% Et2O/hexanes). 1H NMR (400 MHz, CDCl3) δ 6.90 (d, J = 1.6 Hz, 1H), 6.80 (dd, J = 8.0, 1.6 Hz, 1H), 6.75 (d, J = 8.0 Hz, 1H), 6.56 (d, J = 16.0 Hz, 1H), 6.42 (s, 2H), 6.05 (dt, J = 16.0, 6.4 Hz, 1H), 5.96 (s, 2H), 4.80-4.71 (m, 2H), 4.41 (dd, J = 8.8, 6.8 Hz, 1H), 3.81 (s, 9H), 3.43 (dd, J = 14.0, 8.8 Hz, 1H), 3.18 (dd, J = 14.0, 6.8 Hz, 1H). 13C NMR (100 MHz, CDCl3) δ 169.2, 153.3, 148.1, 147.8, 134.8, 134.2, 130.3, 130.1, 121.6, 120.1, 108.3, 106.2, 105.8, 101.2, 66.6, 60.8, 56.1, 41.5, 41.4. IR (neat, cm⁻¹) 2998, 2940, 2839, 1738, 1591. HRMS (ESI) m/z calculated for C22H21BrO4 [M]+: 478.06271; found: 478.06254. Spectral data matches that previously reported.⁵

**(E)**-3-(4-hydroxy-3-methoxyphenyl)allyl palmitate (3) To a 4 mL borosilicate vial was added Pd(CH3CN)2(BF4)2 (44.4 mg, 0.1 mmol, 10 mol %) under argon atmosphere, followed by phenyl benzoquinone (368 mg, 2.0 mmol, 2 equiv.), palmatic acid (768 mg, 3.0 mmol, 3 equiv.), two 4Å molecular beads (50 mg) in one portion under ambient atmosphere. DMSO (100 µL, 1.1 mmol, 1.1 equiv.), CH3Cl (500 µL), and DIPEA (1210.0 µL, 0.7 mmol, 0.7 equiv.) were added via glass syringe followed by a Teflon® stir bar. This solution was stirred at 41°C for 5 minutes before 4-allyl-2-methoxyphenol (164 mg, 1.0 mmol, 1 equiv.) was added neat using a microsyringe. The vial was then capped and stirred at 41°C for 72 hours. Upon completion (via NMR aliquate), the reaction was transferred to a separatory funnel using minimal methylene chloride (~2 mL). The solution was diluted with 1:1 diethyl ether:hexanes (50 mL) and washed with NH4Cl (sat. aq.) solution 2x. Note: If an inseparable emulsion forms filter the solution through a pressed pad of celite with 20-30 mL diethyl ether. The organic layer was dried with MgSO4, filtered, and reduced in vacuo. Purification via flash silica gel chromatography (5% EtO/hexanes) gave (E)-3-(4-hydroxy-3-methoxyphenyl)allyl palmitate as a clear oil. The crude selectivities determined by 1H NMR are L:B >20:1 and E:Z >20:1. Run 1 (272.0 mg, 0.65 mmol, 65%); run 2 (263.0 mg, 0.63 mmol, 63%); run 3 = (268.0 mg, 0.64 mmol, 64%) **Average = 64% yield.** Rf = 0.2 (5% EtO/hexanes; elutes with and just after the brightly colored PhBQ). 1H NMR (400 MHz, CDCl3) δ 6.94-6.82 (m, 3H), 6.57 (d, J = 16.0 Hz, 1H), 6.14 (dt, J = 15.6, 6.8 Hz, 1H), 4.71 (dd, J = 6.8, 1.2 Hz, 2H), 3.91 (s, 3H), 2.34 (dt, J = 7.6, 2.8 Hz, 2H), 1.7-1.55 (m, 2H), 1.4-1.25 (s, 24H), 0.88 (t, J = 6.4 Hz, 3H). 13C NMR (100 MHz, CDCl3) δ 174.0, 146.8, 146.1, 134.6, 129.0, 121.1, 120.8, 114.6, 108.5, 65.3, 56.1, 34.6, 32.1, 29.9, 29.9, 29.8, 29.7, 29.6, 29.5, 29.4, 29.3, 25.2, 22.9, 14.4. IR (neat, cm⁻¹) 2921, 2850, 1732, 1708. HRMS (ESI) m/z calculated for C26H34O4 [M + H]+: 419.3161; found: 419.3155. Spectral data matches that previously reported.⁶

**(E)**-5-(tert-butyldimethysilyloxy)pent-2-enyl-2-(3,4-difluorophenyl)acetate (4) General Conditions: To a 4 mL borosilicate vial was added Pd(CH3CN)2(BF4)2 (22.2 mg, 0.05 mmol, 10 mol %) under argon atmosphere, followed by phenyl benzoquinone (184 mg, 1.0 mmol, 2 equiv.), 3,4-difluorophenylacetic acid (225 mg, 1.5 mmol, 3 equiv.), two 4Å molecular beads (30 mg) in one portion under ambient atmosphere. DMSO (50 µL, 0.57 mmol, 1.1 equiv.), CH3Cl (250 µL), and DIPEA (60 µL, 0.35 mmol, 0.7 equiv.) were added via glass syringe followed by a Teflon® stir bar. This solution was stirred at 41°C for 5 minutes before tert-butyldimethyl(pent-4-enyloxy)silane (100 mg, 0.5 mmol, 1 equiv.) was added neat using a microsyringe. The
vial was then capped and stirred at 41°C for 72 hours. Upon completion (via NMR aliquate), the reaction was transferred to a separatory funnel using minimal methylene chloride (~2 mL). The solution was diluted with 1:1 diethyl ether:hexanes (50 mL) and washed with 5% K₂CO₃ (aq.) solution 2×. Note: If an inseparable emulsion forms filter the solution through a pressed pad of celite with 20-30 mL diethyl ether. The organic layer was dried with MgSO₄, filtered, and reduced in vacuo. Purification via flash silica gel chromatography (5% EtO/hexanes) gave (E)-5-(tert-butylmethyisilyloxy)pent-2-enyl-2-(3,4-difluorophenyl)acetate as a clear oil. The crude selectivities determined by ¹H NMR are L:B=27:1, E:Z=17:1. Final yield = 60%.

Average = 60% yield. (11:1 E:Z and >20:1 L:B after silica column purification). Note: When 4 equiv. acid is used 133mg, 15% yield.

Previous Conditions: To a 4 mL borosilicate vial was added Pd(OAc)₂ (11.2 mg, 0.05 mmol, 10 mol %), phenyl benzoquinone (184 mg, 1.00 mmol, 2 equiv.), 3,4-difluorophenylacetic acid (259 mg, 1.5 mmol, 3 equiv.), and 4Å molecular sieves (50 mg). DMSO (190 μL), CH₂Cl₂ (60 μL), and DIPEA (43 μL, 0.25 mmol, 0.5 equiv.) were added via glass syringe followed by a Teflon® stir bar. tert-Butylbutyldimethylsilyl-enyl (100 mg, 0.5 mmol, 1 equiv.) was added neat using a microsyringe. The vial was then capped and stirred at 41°C for 72 hours. Upon completion (via NMR aliquate), the reaction was transferred to a separatory funnel using minimal methylene chloride (~2 mL). The solution was diluted with 1:1 diethyl ether:hexanes (50 mL) and washed with 5% K₂CO₃ (aq.) solution 2×. The organic layer was dried with MgSO₄, filtered, and reduced in vacuo. Purification via flash silica gel chromatography (5% EtO/hexanes) gave (E)-5-(tert-butylmethyisilyloxy)pent-2-enyl-2-(3,4-difluorophenyl)acetate as a clear oil. The crude selectivities determined by ¹H NMR are L:B=9:1 and E:Z=11:1. Run 1 (113.0 mg, 0.31 mmol, 62%); run 2 (113.0 mg, 0.30 mmol, 61%); run 3 = (106.0 mg, 0.29 mmol, 57%).

Average = 55% yield. (11:1 E:Z and >20:1 L:B after silica column purification). Note: 4Å molecular sieves was used.

Previous Conditions: To a 4 mL borosilicate vial was added Pd(OAc)₂ (11.2 mg, 0.05 mmol, 10 mol %), phenyl benzoquinone (184 mg, 1.00 mmol, 2 equiv.), 3,4-difluorophenylacetic acid (259 mg, 1.5 mmol, 3 equiv.), and 4Å molecular sieves (50 mg). DMSO (190 μL), CH₂Cl₂ (60 μL), and DIPEA (43 μL, 0.25 mmol, 0.5 equiv.) were added via glass syringe followed by a Teflon® stir bar. tert-Butylbutyldimethylsilyl-enyl (100 mg, 0.5 mmol, 1 equiv.) was added neat using a microsyringe. The vial was then capped and stirred at 41°C for 5 minutes before tert-butylbutyldimethyl(4-enyl)silyl (200 mg, 1 mmol, 1 equiv.) was added neat using a microsyringe. The vial was then capped and stirred at 41°C for 72 hours. Upon completion (via NMR aliquate), the reaction was transferred to a separatory funnel using minimal methylene chloride (~2 mL). The solution was diluted with 1:1 diethyl ether:hexanes (50 mL) and washed with 5% K₂CO₃ (aq.) solution 2×. Note: If an inseparable emulsion forms filter the solution through a pressed pad of celite with 20-30 mL diethyl ether. The organic layer was dried with MgSO₄, filtered, and reduced in vacuo. Purification via flash silica gel chromatography (15% EtO/hexanes) gave (E)-5-(4-enylmethyisilyloxy)pent-2-enyl-3-(3,4-difluorophenyl)propionate as a clear oil. The crude selectivities determined by ¹H NMR are L:B=9:1 and E:Z=11:1. Run 1 (197.0 mg, 0.51 mmol, 51%); run 2 (194.0 mg, 0.50 mmol, 50%); run 3 = (190.0 mg, 0.49 mmol, 49%).

Average = 50% yield. (11:1 E:Z and >20:1 L:B after silica column purification).
(S,E)-tert-butyl 6-(2-(((9H-fluoren-9-ylmethoxy)carbonylamino)-3-phenylpropanoamido)hex-4-enoate (6) To a 4 mL borosilicate vial was added Pd(CH$_2$CN)$_2$(BF$_4$)$_2$ (22.2 mg, 0.05 mmol, 10 mol %) under argon atmosphere, followed by phenyl benzoquinone (184.0 mg, 1.0 mmol, 2 equiv.), N-$\alpha$-Fmoc-L-phenylalanine (291.0 mg, 0.75 mmol, 1.5 equiv.), two 4Å molecular beads (50 mg) in one portion under ambient atmosphere. DMSO (50 µL, 0.55 mmol, 1.1 equiv.), CH$_2$Cl$_2$ (250 µL), and DIPEA (61.0 µL, 0.35 mmol, 0.7 equiv.) were added via glass syringe followed by a Teflon® stir bar. This solution was stirred at 41°C for 5 minutes before tert-butyl hex-5-enoate (85.0 mg, 0.55 mmol, 1.0 equiv.) was added neat using a microsyringe. The vial was then capped and stirred at 41°C for 72 hours. Upon completion (via NMR aliquate), the reaction was transferred to a separatory funnel using minimal methylene chloride (~2 mL). The solution was diluted with 1:1 diethyl ether:hexanes (50 mL) and washed with 5% K$_2$CO$_3$ (aq.) solution 2x. Note: If an inseparable emulsion forms filter the solution through a pressed pad of celite with 20-30 mL diethyl ether. The organic layer was dried with MgSO$_4$, filtered, and reduced in vacuo. Purification via flash silica gel chromatography (20% EtOAc/hexanes) gave (S,E)-tert-butyl 6-(2-(((9H-fluoren-9-ylmethoxy)carbonylamino)-3-phenylpropanoamido)hex-4-enoate as a clear thick oil. The crude selectivities are indistinguishable by $^1$H NMR. Column purified L:B selectivity was determined by $^1$H NMR to be ≥20:1. E:Z selectivity was determined to be 17:1 after methanalysis of the product followed by acetylation of the resulting alcohol. Run 1 (147.1 mg, 0.26 mmol, 53%); run 2 (149.9 mg, 0.27 mmol, 54%). 

Average = 54% yield. (≥20:1 L:B after silica column purification). $R_f$ = 0.1 (20% EtOAc/hexanes). $^1$H NMR (400 MHz, CDCl$_3$) δ 7.77 (d, J = 7.6 Hz, 2H), 7.57 (t, J = 6.0 Hz, 2H), 7.41 (t, J = 7.6 Hz, 2H), 7.34-7.24 (m, 5H), 7.10 (broad d, J = 6.4 Hz, 2H), 5.82-5.72 (m, 1H), 5.56 (dt, J = 15.2, 6.4 Hz, 1H), 5.27 (d, J = 8.0 Hz, 1H), 4.67 (app. q, J = 6.0 Hz, 1H), 4.56 (d, J = 6.8 Hz, 2H), 4.44 (dd, J = 10.8, 7.2 Hz, 1H), 4.33 (dd, J = 10.4, 6.8 Hz, 1H), 4.21 (t, J = 7.2 Hz, 1H), 3.20-3.06 (m, 2H), 2.40-2.26 (m, 4H), 1.44 (s, 9H). $^{13}$C NMR (100 MHz, CDCl$_3$) δ 172.4, 171.5, 155.7, 144.1, 140.0, 141.5, 135.9, 135.5, 129.7, 128.8, 128.0, 127.4, 127.3, 125.4, 125.3, 124.3, 124.2 (2C), 80.7, 67.1, 66.2, 55.0, 47.4, 38.4, 34.8, 28.3, 27.8. IR (neat, cm$^{-1}$) 3341, 2978, 1727. HRMS (ESI) m/z calculated for C$_{34}$H$_{38}$NO$_6$ [M + H]+: 556.2699; found: 556.2695. [α]$^D_{5}$ = +9.0° (c=1.1, CHCl$_3$). Spectral data has been previously reported.$^viii$

2-(9H-Fluoren-9-ylmethoxycarbonylamino)-succinic acid 1-tert-butyl ester 4-[5-(2-oxo-2-phenyl-ethoxycarbonyl)-pent-2-enyl]ester (7) To a 4 mL borosilicate vial was added Pd(CH$_2$CN)$_2$(BF$_4$)$_2$ (22.2 mg, 0.05 mmol, 10 mol %) under argon atmosphere, followed by a Teflon® stir bar, phenyl benzoquinone (184 mg, 1.0 mmol, 2 equiv.), Fmoc-L-aspartic acid 4-tert-butyl ester (617 mg, 1.5 mmol, 3 equiv.), two 4Å molecular beads (30 mg) in one portion under ambient atmosphere. DMSO (50 µL, 0.57 mmol, 1.1 equiv.), CH$_2$Cl$_2$ (250 µL), and DIPEA (60 µL, 0.35 mmol, 0.7 equiv.) were added via glass syringe. This solution was stirred at 41°C for 5 minutes before hex-5-enoic acid 2-oxo-2-phenyl-ethyl ester (116 mg, 0.55 mmol, 1 equiv.) was added neat using a microsyringe. The vial was then capped and stirred at 41°C for 72 hours. Upon completion (via NMR aliquate), the reaction was transferred to a separatory funnel using minimal methylene chloride (~2 mL). The solution was diluted with 1:1 diethyl ether:hexanes (50 mL) and washed with 5% K$_2$CO$_3$ (aq.) solution 2x. Note: If an inseparable emulsion forms filter the solution through a pressed pad of celite with 20-30 mL diethyl ether. The organic layer was dried with MgSO$_4$, filtered, and reduced in vacuo. Purification via flash silica gel chromatography (10-40% Et$_2$O/hexanes) gave 2-(9H-Fluoren-9-ylmethoxycarbonylamino)-succinic acid 1-tert-butyl ester 4-[5-(2-oxo-2-phenyl-ethoxycarbonyl)-pent-2-enyl]ester as a clear oil. The crude L:B selectivity was determined by $^1$H NMR to be ≥20:1. E:Z selectivity was determined to be 18:1 after methanalysis of the product followed by acetylation of the resulting alcohol. Run 1 (225.0 mg, 0.35 mmol, 70%); run 2 (231.0 mg, 0.36 mmol, 72%); run 3 (241.0 mg, 0.38 mmol, 75%); run 4 (221.1 mg, 0.35 mmol, 69%). Average = 72% yield. (≥20:1 L:B after silica column purification). $R_f$ = 0.2 (40% Et$_2$O/hexanes). $^1$H NMR (400 MHz, CDCl$_3$) δ 7.90 (app. d, J = 8.0 Hz, 2H), 7.76 (d, J = 7.6 Hz, 2H), 7.64-7.56 (m, 3H), 7.49 (t, J = 8.0 Hz, 2H), 7.40 (t, J = 7.2 Hz, 2H), 7.31 (t, J = 7.6 Hz, 2H), 5.90-5.76 (m, 2H), 5.66 (dt, J = 15.6, 6.4 Hz, 1H), 5.34 (s, 2H), 4.57 (d, J = 6.4 Hz, 2H), 4.65-4.50 (m, 1H), 4.34 (d, 2H), 4.23 (t, J = 6.8 Hz, 1H), 3.01 (dd, J = 16.8, 4.4 Hz, 1H), 2.85 (dd, J = 16.8, 4.4 Hz, 1H), 2.60 (app. t, J = 6.8 Hz, 2H), 2.47 (app. q, J = 6.8 Hz, 2H), 1.47 (s, 9H). $^{13}$C NMR (100 MHz, CDCl$_3$) δ 192.3, 172.4, 170.9, 169.8, 156.2, 144.1, 144.0, 141.5, 134.4, 134.2, 129.1, 128.0, 127.9, 127.3, 125.4, 125.1, 120.2 (2 peaks), 82.9, 67.4, 66.2, 65.6, 51.1, 47.3, 37.1, 33.3, 28.1, 27.6. IR (neat, cm$^{-1}$) 3358, 3067, 2928, 1737 (broad). HRMS (ESI) m/z calculated for C$_{36}$H$_{38}$NO$_6$ [M + H]+: 642.2703; found: 642.2695. [α]$^D_{5}$ = +12.3° (c=1.0, CHCl$_3$). Compound was found to be >99% ee through SCF (mobile phase CO$_2$, column chiralpak-AS, 12% MeOH, 2.5 mL/min, 125 barr) with retention times of 30.5 min for (+)-7 and 22.1 min for (+)-7. Spectral data matches previously reported data.$^ix}$
(5S,E)-1-tert-butyl 2-(6-(tert-butylidiphenylsilyloxy)hex-2-enyl) 5-(benzyloxy)methyl)pyrrolidine-1,2-dicarboxylate (8) To a 4 mL borosilicate vial was added Pd(CH₃CN)₄(BF₄)₂ (22.2 mg, 0.05 mmol, 10 mol %) under argon atmosphere, followed by phenyl benzoquinone (184 mg, 1.0 mmol, 2 equiv.), (5S)-5-(benzyloxy)methyl)-1-(tert-butoxycarbonyl)pyrrolidine-2-carboxylic acid (250 mg, 0.75 mmol, 1.5 equiv.), two 4Å molecular beads (30 mg) in one portion under ambient atmosphere. DMSO (50 µL, 0.57 mmol, 1.1 equiv.), CH₂Cl₂ (250 µL), and DIPEA (60 µL, 0.35 mmol, 0.7 equiv.) were added via glass syringe followed by a Teflon© stir bar. This solution was stirred at 41°C for 5 minutes before tert-butyl(hex-5-enyloxy)diphenylsilane (170 mg, 0.5 mmol, 1 equiv.) was added neat using a microsyringe. The vial was then capped and stirred at 41°C for 72 hours. Upon completion (via NMR aliquate), the reaction was transferred to a separatory funnel using minimal methylene chloride (~2 mL). The solution was diluted with 1:1 diethyl ether:hexanes (50 mL) and washed with 5% K₂CO₃ (aq.) solution 2x. Note: If an inseparable emulsion forms filter the solution through a pressed pad of celite with 20-30 mL diethyl ether. The organic layer was dried with MgSO₄, filtered, and reduced in vacuo. Purification via flash silica gel chromatography (10-40% Et₂O/hexanes) gave (5S,E)-1-tert-butyl 2-(6-(tert-butylidiphenylsilyloxy)hex-2-enyl) 5-(benzyloxy)methyl)pyrrolidine-1,2-dicarboxylate as a pail oil. The crude selectivities are >20:1 L:B (determined from crude ¹H NMR) and 15:1 E:Z (determined after hydrolysis to (E)-6-(tert-butylidiphenylsilyloxy)hex-2-en-1-ol). Run 1 (171.0 mg, 0.26 mmol, 51%); run 2 (184.5 mg, 0.28 mmol, 55%); run 3 = (168.0 mg, 0.25 mmol, 50%). Average = 52% yield. Rf= 0.2 (5% EtOAc/hexanes). Note: NMRs are a mixture of two diastereomers and two rotamers; ¹H NMR (500 MHz, CDCl₃) δ 7.65 (d, J = 7.5 Hz, 4H), 7.46-7.26 (m, 11H), 5.82-5.50 (m, 1H), 4.64-4.46 (m, 4H), 4.36-4.05 (m, 2H), 3.74-3.35 (m, 4H), 2.40-1.85 (m, 6H), 1.70-1.62 (m, 2H), 1.43 (s, 3H), 1.41 (s, 3H), 1.07 (s, 3H). ¹³C NMR (150 MHz, CDCl₃) δ 173.3, 172.8, 154.4, 154.0, 138.7, 138.5, 136.7, 136.2, 135.7, 134.1 (2 peaks), 129.8, 128.6, 128.5, 127.8, 127.7, 127.6, 124.0 (2 peaks), 80.3, 80.2, 73.4, 71.2, 70.9, 65.8, 63.3, 60.3, 59.9, 57.6, 57.4, 31.9 (2 peaks), 29.1, 28.8 (2 peaks), 28.6, 28.5, 28.0, 27.3, 27.0, 26.5, 19.4. IR ( neat, cm⁻¹) 2962, 2931, 2860, 1744, 1700. HRMS (ESI) m/z calculated for C₄₀H₄₄N₂O₆Si [M + H]⁺: 672.3720; found: 672.3737. [α]D²⁶ = -35.6° (c=1.0, CHCl₃). Spectral data matches previously reported data.¹
The organic layer was dried with MgSO\(_4\) (aq.) solution 2x. Note: If an inseparable emulsion forms filter the solution through a pressed pad of celite with minimal methylene chloride (~2 mL). The solution was diluted with 1:1 diethyl ether and stirred at 41°C for 10.9 min for 37. Average = 63% yield. R\(_f\) = 0.1 (5% EtOAc/hexanes). \(^1\)H NMR (500 MHz, CDCl\(_3\)) \(\delta\) 8.05 (d, \(J = 8.0\) Hz, 2H), 7.55 (t, \(J = 7.6\) Hz, 1H), 7.43 (t, \(J = 8.0\) Hz, 2H), 7.25 (d, \(J = 9.2\) Hz, 2H), 6.87 (d, \(J = 8.8\) Hz, 2H), 5.87 (dt, \(J = 15.2, 7.2\) Hz, 1H), 5.73 (dt, \(J = 15.2, 6.4\) Hz, 1H), 4.76 (d, \(J = 6.4\) Hz, 2H), 4.45 (s, 2H), 3.88 (app. quin., \(J = 5.6\) Hz, 1H), 3.80 (s, 3H), 3.40-3.30 (m, 2H), 2.45-2.35 (m, 1H), 2.30-2.20 (m, 1H), 0.87 (s, 9H), 0.04 (s, 6H). \(^13\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 166.6, 159.4, 133.0, 132.5, 130.7, 130.6, 129.8, 129.4, 128.5, 126.6, 114.0, 74.1, 73.2, 71.2, 65.7, 55.5, 38.0, 26.0, 18.4, -4.2, -4.5. IR (neat, cm\(^-1\)) 2959, 2926, 2857, 1720, 1700, 1594, 1581, 1533, 1462, 1377, 1270, 1249. HRMS (Cl\(_2\)) \(m/z\) calculated for C\(_{27}\)H\(_{37}\)O\(_2\)Si [M-H]: 469.24103; found: 469.24112. \(\alpha\)R \(_D\) = -10.9° (c=1.0, CHCl\(_3\)). (-)-8 was found to be >99% ee after TBS ether deprotection to form the free alcohol followed by SCF analysis (mobile phase CO\(_2\), column chiralpak-OD, 7% MeOH, 3.0 mL/min, 125 barr) with retention times of 15.0 min for (+)-8 (free alcohol) and 16.0 min for (-)-8 (free alcohol). Compound has previously been synthesized, however; no spectral data was provided.\(^{11}\)

\((E)-5-(tert-butyldimethylsiloxy)pent-2-enyl 2-(3,4-difluorophenyl)acetate (14)\) To a 4 mL borosilicate vial was added Pd(CH\(_3\)CN)\(_2\)(BF\(_4\))\(_2\) (44.4 mg, 0.1 mmol, 10 mol%) under argon atmosphere, followed by phenyl benzoquinone (368 mg, 2.0 mmol, 2 equiv.), benzoic acid (366 mg, 3 mmol, 3 equiv.), two 4Å molecular beads (50 mg) in one portion under ambient atmosphere. DMSO (100 \(\mu\)L, 1.1 mmol, 1.1 equiv.), CH\(_2\)Cl\(_2\) (500 \(\mu\)L), and DIPEA (121.0 \(\mu\)L, 0.7 mmol, 0.7 equiv.) were added via glass syringe followed by a Teflon\(_\copyright\) stir bar. This solution was stirred at 41°C for 5 minutes before (S)-(2-(4-methoxybenzoxoxy)hex-5-enyl)(tert-butyldimethylsiloxy)cyclohexylpent-2-enyl(3,4-difluorophenyl)acetate was added neat using a microsyringe. The vial was then capped and stirred at 41°C for 72 hours. Upon completion (via NMR aliquate), the reaction was transferred to a separatory funnel using minimal methylene chloride (~2 mL). The solution was diluted with 1:1 diethyl ether:hexanes (50 mL) and washed with 5% K\(_2\)CO\(_3\) (aq.) solution 2x. Note: If an inseparable emulsion forms filter the solution through a pressed pad of celite with 20-30 mL diethyl ether. The organic layer was dried with MgSO\(_4\), filtered, and reduced in vacuo. Purification via flash silica gel chromatography (5%
EtO/hexanes) gave (E)-5-(4-bromobenzoyloxy)methoxy)cyclohexylpent-2-enyl 2,4-dichlorobenzoate as a clear thick oil. MPLC was required to separate the branched ester (1% EtOAc:Hx). The crude selectivities determined by $^1$H NMR was L:B 8:1 and E:Z 15:1. Run 1 (111.0 mg, 0.20 mmol, 60%); run 2 (109.0 mg, 0.19 mmol, 59%); run 3 = (117.0 mg, 0.21 mmol, 63%) **Average = 61% yield.** (15:1 E:Z and >20:1 L:B after silica column purification). $R_f$ = 0.1 (10% Et$_3$O/pentane). $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 7.80-7.74 (m, 1H), 7.50-7.40 (m, 3H), 7.30-7.24 (m, 1H), 7.20 (d, $J$ = 6.4 Hz, 2H), 5.86 (dt, $J$ = 15.0, 7.0 Hz, 1H), 5.64 (dt, $J$ = 15.5, 6.5 Hz, 1H), 4.90-4.84 (m, 1H), 4.75 (d, $J$ = 6.5 Hz, 2H), 4.73-4.68 (m, 1H), 4.57 (s, 2H), 3.26-3.16 (m, 1H), 2.24-2.14 (m, 1H), 2.12-1.98 (m, 2H), 1.94-1.82 (m, 2H), 1.73 (br s, 1H), 1.63 (br d, $J$ = 10.0 Hz, 1H), 1.42-1.30 (m, 1H), 1.30-1.10 (m, 4H), 1.00-0.86 (m, 1H). $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 164.8, 138.5, 135.1, 133.1, 132.7, 131.7, 131.2, 129.6, 128.7, 127.2, 123.4, 121.7, 93.6, 80.7, 69.0, 66.7, 42.9, 32.4, 31.6, 30.4, 29.7, 25.4, 24.8. IR (neat, cm$^{-1}$) 3093, 3029, 2929, 2857, 1732, 1586. HRMS (Cl) m/z calculated for C$_{29}$H$_{30}$O$_2$BrCl$_2$[M + H]+: 555.07045; found: 555.07092. Compound has previously been synthesized; however, no spectral data was provided.\textsuperscript{xiii}

**Olefination Route**

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**Oxidation Route**

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(\(S,E\))-4-(6-oxo-1,3,5-dioxazepan-5-yl)but-2-enyl \(\rightarrow\) \((\text{Boc})\text{-Boc}\) 2-enyl 2,4-dichlorobenzoate (25) To a 2 mL borosilicate vial was added Pd(CH$_2$CN)$_2$(BF$_4$)$_2$ (11.1 mg, 0.025 mmol, 10 mol%) under argon atmosphere, followed by phenyl benzoquinone (97 mg, 0.5 mmol, 2 equiv.), Boc-L-phenalene (100 mg, 0.38 mmol, 1.5 equiv.), one 4Å molecular beads (20 mg) in one portion under ambient atmosphere. DMSO (25 µL, 0.29 mmol, 1.1 equiv.), CH$_2$Cl$_2$ (125 µL), and DIPEA (30 µL, 0.18 mmol, 0.7 equiv.) were added via glass syringe followed by a Teflon\textsuperscript{®} stir bar. This solution was stirred at 41°C for 5 minutes before homo-allylic lactam (77.0 mg, 0.25 mmol, 1 equiv.) was added neat using a microsyringe. The vial was then capped and stirred at 41°C for 72 hours. Upon completion (via NMR aluate), the reaction was transferred to a separatory funnel using minimal methyl chloride (~2 mL). The solution was diluted with 1:1 diethyl ether:hexanes (50 mL) and washed with 5% K$_2$CO$_3$ (aq.) solution x2. Note: If an inseparable emulsion forms filter the solution through a pressed pad of celite with 20-30 mL diethyl ether. The organic layer was dried with MgSO$_4$, filtered, and reduced *in vacuo*. Purification via flash silica gel chromatography (10-40% Et$_3$O/hexanes) gave (\(S,E\))-4-(6-oxo-1,3,5-dioxazepan-5-yl)but-2-enyl 2-(\((\text{Boc})\text{-Boc}\) 2-enyl)-2-phenylpropanoate (25) as a clear oil. The crude selectivities were determined to be >20:1 L:B (based on crude \(^1\)H NMR) and 17:1 E:Z (based on hydrolysis of the product and examination of the corresponding alcohol by \(^1\)H NMR). Run 1 (84.7 mg, 0.15 mmol, 59%); run 2 (86.1 mg, 0.15 mmol, 60%); run 3 = (28.5 mg, 0.05 mmol, 62%). **Average = 60% yield.** $R_f$ = 0.23 (50% EtOAc/hexanes). \(^1\)H NMR (500 MHz, CDCl$_3$) $\delta$ 7.32-7.20 (m, 3H), 7.13 (d, $J$ = 7.0 Hz, 2H), 5.82-5.54 (m, 2H), 5.02-4.92 (m, 1H), 4.64-4.52 (m, 3H), 4.20-3.92 (m, 4H), 3.58-3.50 (m, 2H), 3.48-3.36 (m, 4H), 3.36-3.24 (m, 2H), 3.14-3.00 (m, 2H), 1.80-1.24 (m, 25H). Note: Rotamer peaks are present in the \(^{13}\)C NMR. \(^{13}\)C NMR (100 MHz, CDCl$_3$) $\delta$ 171.9, 169.9, 169.5, 155.3, 136.2, 130.8, 130.6, 129.6, 129.5, 128.8, 127.3, 126.3, 125.5, 80.0, 71.9, 71.6, 70.9, 70.3, 70.2 (2 peaks), 70.2, 65.3, 64.9, 54.7, 47.8, 47.6, 46.7, 45.1, 38.6, 29.6, 28.8 (2 peaks), 28.6, 28.5, 28.2, 27.6, 27.5, 27.2, 26.8 (2 peaks), 26.0, 25.8, 25.2, 24.4, 24.3. IR (neat, cm$^{-1}$) 3443, 3324, 2932, 2859, 1742, 1715, 1645. HRMS (ESI) m/z calculated for C$_{29}$H$_{30}$N$_2$O$_2$ [M + H]: 575.3696; found: 575.3694. [\(\alpha\)]$_D^{20} = +4.1^\circ$ (c=0.7, CHCl$_3$). Spectral data matches previously reported data.\textsuperscript{xiii}
Table 2

2004 JACS Procedure: To a 4 mL borosilicate vial was first added Pd(OAc)$_2$ (11.2 mg, 0.05 mmol, 10 mol %) under argon atmosphere. The following reagents were then added in one portion under ambient atmosphere: benzoquinone (108 mg, 1.0 mmol, 2 equiv.) and 4Å molecular powder (108 mg). Finally, DMSO (1.5 mL, 1.65 g, 21 mmol, 42 equiv.), and starting material (0.5 mmol, 1.0 equiv.) were added sequentially via glass syringe followed by a Teflon© stir bar. The vial was then capped and stirred at 41°C for 72 hours. Upon completion as determined by NMR, the reaction was transferred to a separatory funnel using minimal methylene chloride (~2 mL) \[\text{Note 1}\]. The solution was diluted with diethyl ether (50 mL) and washed with 5% K$_2$CO$_3$ (aq.) solution twice \[\text{Note 2}\]. The organic layer was dried with MgSO$_4$, filtered, and reduced in vacuo. Purification was achieved via flash silica gel chromatography. Notes: (1) The excess quinone may be reduced by addition of solid Na$_2$SO$_3$ (2 g) to a reaction mixture diluted with 50 mL of EtOAc and 50 mL of a 5% K$_2$CO$_3$ (aq.) solution. The resulting biphasic mixture is then stirred rapidly for 30 minutes before continuing with the extraction. (2) If an inseparable emulsion forms, filter the solution through a pressed pad of celite with 20–30 mL diethyl ether.

2004 JACS Procedure with 3 equiv. acetic acid (0.33M): To a 4 mL borosilicate vial was first added Pd(OAc)$_2$ (11.2 mg, 0.05 mmol, 10 mol %) under argon atmosphere. The following reagents were then added in one portion under ambient atmosphere: benzoquinone (108 mg, 1.0 mmol, 2 equiv.) and 4Å molecular powder (108 mg). Finally, DMSO (1.5 mL, 1.65 g, 21 mmol, 42 equiv.), AcOH (86 µl, 90.2 mg, 1.5 mmol, 3 equiv.), and starting material (0.5 mmol, 1.0 equiv.) were added sequentially via glass syringe followed by a Teflon© stir bar. The vial was then capped and stirred at 41°C for 72 hours. Upon completion as determined by NMR, the reaction was transferred to a separatory funnel using minimal methylene chloride (~2 mL) \[\text{Note 1}\]. The solution was diluted with diethyl ether (50 mL) and washed with 5% K$_2$CO$_3$ (aq.) solution twice \[\text{Note 2}\]. The organic layer was dried with MgSO$_4$, filtered, and reduced in vacuo. Purification was achieved via flash silica gel chromatography. Notes: (1) The excess quinone may be reduced by addition of solid Na$_2$SO$_3$ (2 g) to a reaction mixture diluted with 50 mL of EtOAc and 50 mL of a 5% K$_2$CO$_3$ (aq.) solution. The resulting biphasic mixture is then stirred rapidly for 30 minutes before continuing with the extraction. (2) If an inseparable emulsion forms, filter the solution through a pressed pad of celite with 20–30 mL diethyl ether.
transferred to a separatory funnel using minimal methylene chloride (~2 mL) [Note 1]. The solution was diluted with diethyl ether (50 mL) and washed with 5% K$_2$CO$_3$ (aq.) solution twice [Note 2]. The organic layer was dried with MgSO$_4$, filtered, and reduced in vacuo. Purification was achieved via flash silica gel chromatography. Notes: (1) The excess quinone may be reduced by addition of solid Na$_2$SO$_3$ (2 g) to a reaction mixture diluted with 50 mL of EtOAc and 50 mL of a 5% K$_2$CO$_3$ (aq.) solution. The resulting biphasic mixture is then stirred rapidly for 30 minutes before continuing with the extraction. (2) If an inseparable emulsion forms, filter the solution through a pressed pad of celite with 20-30 mL diethyl ether.

**New General Procedure:** To a 4 mL borosilicate vial was first added Pd(CH$_3$CN)$_2$(BF$_4$)$_2$ (22.2 mg, 0.05 mmol, 10 mol %) under argon atmosphere. The following reagents were then added in one portion under ambient atmosphere: phenyl benzoquinone (184 mg, 1.0 mmol, 2 equiv.) and two 4Å molecular beads (50 mg). Finally, DMSO (50 µL, 0.7 mmol, 1.4 equiv.), CH$_2$Cl$_2$ (250 µL), and DIPEA (60.0 µL, 0.35 mmol, 0.7 equiv.), acetic acid (90 mg, 86 µL, 1.5 mmol, 3.0 equiv.) were added sequentially via glass syringe followed by a Teflon® stir bar. This solution was stirred at 41°C for 5 hours before starting material (0.5 mmol, 1.0 equiv.) was added neat using a microsyringe. The vial was then capped and stirred at 41°C for 72 hours. Upon completion as determined by NMR, the reaction was transferred to a separate funnel using minimal methylene chloride ( ~2 mL) [Note 1]. The solution was diluted with diethyl ether (50 mL) and washed with 5% K$_2$CO$_3$ (aq.) solution twice [Note 2]. The organic layer was dried with MgSO$_4$, filtered, and reduced in vacuo. Purification was achieved via flash silica gel chromatography. Notes: (1) The excess quinone may be reduced by addition of solid Na$_2$SO$_3$ (2 g) to a reaction mixture diluted with 50 mL of EtOAc and 50 mL of a 5% K$_2$CO$_3$ (aq.) solution. The resulting biphasic mixture is then stirred rapidly for 30 minutes before continuing with the extraction. (2) If an inseparable emulsion forms, filter the solution through a pressed pad of celite with 20-30 mL diethyl ether. **Note:** (1) All yield are of column purified material with >20:1 L:B. E:Z ratios did not change after silica column purification unless otherwise noted. (2) All reference numbers in the tables and figures refer to the reference numbers from the text.

(E)-5-(N-(tert-butoxycarbonyl)-4-methylphenylsulfonylamido)pent-2-en-1-yl acetate (31) from 1,1-dimethyl (4-methylphenyl)sulfonyl(4-pentenyl)carbamate.**x** Old: The crude selectivities were determined to be: L:B = 12:1 and E:Z = 8:1 by $^1$H NMR. Run 1 (102.0 mg, 0.25 mmol, 51%); run 2 (98.8 mg, 0.25 mmol, 50%); **Average = 51% yield.** (8:1 E:Z and >20:1 L:B after silica column purification). **New:** The crude selectivities were determined to be: L:B = >20:1 and E:Z = 9:1 by $^1$H NMR. Run 1 (150.4 mg, 0.37 mmol, 75%); run 2 (147.3 mg, 0.37 mmol, 74%); **Average = 75% yield.** (9:1 E:Z and >20:1 L:B after silica column purification). $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 7.76 (d, $J$ = 8.5 Hz, 2H), 7.28 (d, $J$ = 8.0 Hz, 2H), 5.76 (dt, $J$ = 15.5, 7.0 Hz, 1H), 5.66 (dt, $J$ = 15.5, 6.0 Hz, 1H), 4.50 (d, $J$ = 6.0 Hz, 2H), 3.86 (appt, $J$ = 7.5 Hz, 2H), 2.50 (q, $J$ = 7.5 Hz, 2H), 2.42 (s, 3H), 2.04 (s, 3H), 1.32 (s, 9H). $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 170.7, 150.8, 144.1, 137.4, 131.2, 129.2, 127.8, 126.8, 84.2, 64.7, 46.2, 33.0, 27.8, 21.5, 20.9. IR (neat, cm$^{-1}$) 2980, 2935, 1732. HRMS (ESI) m/z calculated for C$_{19}$H$_{27}$NO$_2$Na$^+$ [M + Na$^+$]: 420.1457; found: 420.1460.

(E)-3-(1,4-dioxaspiro[4.5]dec-6-yl)-2-propen-1-ol acetate (32) from 6-allyl-1,4-dioxaspiro[4.5]decane.$^x$ Old: The crude selectivities were determined to be: L:B >20:1 and E:Z >20:1 by $^1$H NMR. Run 1 (119 mg, 0.49 mmol, 49%); run 2 (120.5 mg, 0.50 mmol, 50%); **Average = 50% yield.** New: The crude selectivities were determined to be: L:B >20:1 and E:Z >20:1 by $^1$H NMR. Run 1 (75 mg, 0.31 mmol, 63%); run 2 (79.1 mg, 0.33 mmol, 65%); **Average = 64% yield.** $R_f$ = 0.1 (20% EtOAc/hexanes). $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 5.79 (dd, $J$ = 15.5, 7.5 Hz, 1H), 5.60 (dt, $J$ = 15.5, 6.0 Hz, 1H), 4.51 (d, $J$ = 6.0 Hz, 2H) 3.93-3.80 (m, 4H), 2.34-2.26 (m, 1H), 2.04 (s, 3H), 1.76-1.60 (m, 4H), 1.58-1.34 (m, 3H), 1.18-1.12 (m, 3H). $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 170.8, 135.1, 125.1, 109.9, 65.3, 65.1, 64.9, 48.2, 35.2, 30.0, 24.3, 23.8, 21.0. IR (neat, cm$^{-1}$) 2937, 2885, 2864, 1739. HRMS (ESI) m/z calculated for C$_{18}$H$_{20}$O$_2$Na$^+$ [M + Na$^+$]: 263.1259; found: 263.1258. Spectral data matches that previously reported.$^x$as

(E)-4-(2-(4-methoxyphenyl)-1,3-dioxolan-4-yl)but-2-en-1-yl acetate (33) from 2-(4-methoxyphenyl)-4-(pent-4-en-1-yl)-1,3-dioxolane.$^x$ Old: Run 1 (trace product); run 2 (trace product); **Average <5% yield.** New: The crude selectivities were determined to be: L:B = 12:1 and E:Z = 12:1 by $^1$H NMR. Run 1 (81.0 mg, 0.28 mmol, 55%); run 2 (73.0 mg, 0.25 mmol, 50%); **Average = 53% yield.** (12:1 E:Z and >20:1 L:B after silica column purification). $R_f$ = 0.5 (20% EtOAc/hexanes). $^1$H NMR (500 MHz, CDCl$_3$) $^1$H NMR (500 MHz, CDCl$_3$) Major Diastereomer: $\delta$ 7.42-7.36 (m, 2H), 6.94-6.86 (m, 2H), 5.86-5.77 (m, 1H), 5.75 (s, 1H), 5.75-5.67 (m, 1H) 4.53 (d, $J$ = 6.0 Hz, 2H), 4.34-4.20 (m, 1H), 4.07 (dd, $J$ = 8.0, 7.0 Hz, 1H), 3.81 (s, 3H), 3.76 (dd, $J$ = 7.5, 6.0 Hz, 1H), 2.56-2.32 (m, 2H), 2.06 (s, 3H). Minor Diastereomer: $\delta$ 5.88 (s, 1H), 4.53 (d, $J$ = 6.0 Hz, 2H), 4.32-4.25 (m, 2H), 3.81 (s, 3H), 3.65 (dd, $J$ = 8.0, 7.0 Hz,
1H. 13C NMR (100 MHz, CDCl3) Major Diastereomer: δ 170.7, 160.5, 130.4, 128.1, 127.8, 127.2, 113.8, 104.1, 75.9, 69.4, 64.8, 55.3, 36.6, 20.9. Minor Diastereomer: δ 160.3, 129.7, 103.3, 75.3, 70.1, 36.2. IR (neat, cm⁻¹) 3003, 2939, 2883, 2841, 1738. HRMS (ESI) m/z calculated for C16H20O3 [M + H]+: 293.1389; found: 293.1383.

(E)-5-((tert-butylidimethylsilyloxy)pent-2-en-1-yl)acetate (34) from tert-butylidimethyl(pent-4-en-1-yl)oxy)silane.¹⁻⁻⁻⁻ Old: The crude selectivities were determined to be L:B = 4:1 and E:Z = 8:1 by 1H NMR. Run 1 (23.0 mg, 0.09 mmol, 18%); run 2 (24.0 mg, 0.09 mmol, 19%); run 3 (16.8 mg, 0.07 mmol, 13%); Average = 17% yield. (8:1 E:Z and >20:1 L:B after silica column purification)

Old with 3 equiv. acetic acid (0.33M): The crude selectivities were determined to be L:B = 4:1 and E:Z = 5:1 by 1H NMR. Run 1 (11.0 mg, 0.043 mmol, 9%); run 2 (12.5 mg, 0.05 mmol, 10%); Average = 10% yield. Old with 3 equiv. acetic acid (0.17M): The crude selectivities were determined to be L:B = 3:1 and E:Z = 5:1 by 1H NMR. Run 1 (8.9 mg, 0.035 mmol, 7%); run 2 (9.0 mg, 0.035 mmol, 7%); Average = 7% yield. New: The selectivities were determined to be L:B = 8:1 (crude) and E:Z = 12:1 (after column) by 1H NMR. Run 1 (79.0 mg, 0.31 mmol, 61%); run 2 (70 mg, 0.27 mmol, 54%); Average = 58% yield. (12:1 E:Z and >20:1 L:B after silica column purification).

Rf = 0.1 (10% EtO/hexanes). 1H NMR (500 MHz, CDCl3) δ 7.57 (dt, J = 15.5, 7.0 Hz, 1H), 5.63 (dt, J = 15.5, 6.0 Hz, 1H), 4.51 (d, J = 6.5 Hz, 2H), 3.65 (t, J = 7.0 Hz, 2H), 2.27 (dq, J = 7.0 Hz, 2H), 2.05 (s, 3H), 0.88 (s, 9H), 0.04 (s, 6H). 13C NMR (125 MHz, CDCl3) δ 170.8, 132.8, 125.7, 65.1, 62.4, 35.8, 25.9, 21.0, 18.3, -5.3. IR (neat, cm⁻¹) 2953, 2931, 2897, 2858, 1743. HRMS (ESI) m/z calculated for C13H17O3Si [M + H]+: 259.1729; found: 259.1720.

(E)-5-(trityloxy)pent-2-en-1-yl acetate (35) from ((pent-4-en-1-yl)oxy)methanetriyl)tribenzene.¹⁻⁻⁻⁻ Old: The crude selectivities were determined to be L:B = 4:1 and E:Z = 8:1 by 1H NMR. Run 1 (63.0 mg, 0.16 mmol, 32%); run 2 (67.1 mg, 0.18 mmol, 35%); Average = 34% yield. (8:1 E:Z and >20:1 L:B after silica column purification).

New: The crude selectivities were determined to be L:B = 10:1 and E:Z = 11:1 by 1H NMR. Run 1 (133.0 mg, 0.34 mmol, 69%); run 2 (127.0 mg, 0.33 mmol, 66%); Average = 68% yield. (11:1 E:Z and >20:1 L:B after silica column purification).

Rf = 0.1 (10% EtO/hexanes). 1H NMR (500 MHz, CDCl3) δ 7.48-7.44 (m, 6H), 7.34-7.29 (m, 6H), 7.27-7.22 (m, 3H), 5.82 (dt, J = 15.5, 7.0 Hz, 1H), 5.65 (dt, J = 15.5, 6.0 Hz, 1H), 4.53 (dd, J = 7.0 Hz, 2H), 3.15 (t, J = 6.5 Hz, 2H), 2.40 (q, J = 6.0 Hz, 2H), 2.06 (s, 3H). 13C NMR (125 MHz, CDCl3) δ 170.7, 144.2, 132.9, 128.6, 127.7, 126.9, 125.7, 86.4, 65.0, 62.9, 33.0, 20.9. IR (neat, cm⁻¹) 3086, 3059, 3024, 2931, 2872, 1739. HRMS (ESI) m/z calculated for C26H26O3Si: 409.1780; found: 409.1784.

SELECTED STARTING MATERIAL (in order of product appearance in the manuscript)

tert-Butylidimethyl(pent-4-en-1-olysiloxy)silane (starting material for 4 and 5) To a 200mL round bottom flask was added 4-penten-1-ol (2.5 g, 58.0 mmol), THF (100 mL) and a Teflon© stir bar. The solution was cooled to 0°C and NaH (2.8 g, 4.0 equiv.) was added by portions. The reaction was allowed to stir for 30 minutes. After the solution turns a yellow color, t-Butyl(dimethyl)silyl chloride (TBSCI, 5.8 g, 1.5 equiv.) and tetrabutyl ammonium iodide (TBAI, 500 mg) were added. The reaction was monitored by TLC until completion (~2 hrs). The reaction was quenched with sat. aq. NH4Cl solution (10 mL) and the organics extracted with water. The organic layer was dried (MgSO4), filtered, and reduced in vacuo. Purification via flash silica gel chromatography (1% EtO/hexanes) gave 7.7 g of tert-butylidimethyl(pent-4-en-1-yl)oxy)silane as a clear oil (~90% yield). Previously prepared J. Chem. Soc. Perk. Trans. 2000, 1, 1915; Tetrahedron Lett. 1995, 36, 819. Rf = 0.3 (1% EtO/hexanes).

1H NMR (500 MHz, CDCl3) δ 5.86-5.78 (m, 1H), 5.02 (d, J = 17.0 Hz, 1H), 4.95 (d, J = 14.5 Hz, 1H), 3.62 (t, J = 7.0 Hz, 2H), 2.10 (app. q, J = 7.0 Hz, 2H), 1.62 (app. q, J = 6.5, 2H), 0.89 (s, 9H), 0.05 (s, 6H).

Hex-5-enoic acid 2-oxo-2-phenyl-ethyl ester (starting material for (+)-7) To a 100mL flame dried round bottom flask was added phenacylbromide (2.4 g, 12 mmol, 1.2 equiv.), potassium fluoride (1.75 g, 30 mmol, 2.5 equiv.), DMF (20 mL) and Teflon© stir bar. To this suspension was added 5-hexenoic acid (1.14 g, 10 mmol) in DMF (10 mL) and the reaction was stirred for 2 hours at room temperature. The reaction was diluted with diethyl ether (200 mL) and washed with a saturated sodium bicarbonate solution (2 x 50 mL). The organic layers were collected, dried (MgSO4), filtered, and concentrated in vacuo. Purification via flash silica gel chromatography (5% EtO/hexanes) gave 2 g of hex-5-enoic acid 2-oxo-2-phenyl-ethyl ester as a clear oil (~95% yield). Rf = 0.1 (2% EtO/hexanes).
Preparation of tert-butyl(hex-5-enynyl)diphenylsilane from 5-hexen-1-ol (13)  To a 200 mL round bottom flask was added 5-hexen-1-ol (5.0 g, 50.0 mmol), THF (100 mL) and a Teflon© stir bar. The solution was cooled to 0°C and sodium hydride (2.4 g, 100 mmol, 2 equiv.) was added portionwise. The solution was allowed to stir at room temperature for 0.5 hr. tert-Butyldiphenylchlorosilane (15.0 g, 55.0 mmol) and tetrabutylammoniumiodide (1.8 g, 50.0 mmol) were added and the reaction was monitored by TLC until all starting material was consumed. The reaction was quenched with 5.0 ml ammonium chloride solution (sat. aq.) and diluted with 200 ml of diethyl ether. The organics were extracted with from water, dried (MgSO₄), filtered, and reduced in vacuo. Purification via flash silica gel chromatography (1% Et₂O/hexanes) gave 15.0 g of tert-butyl(hex-5-enynyl)diphenylsilane as a clear oil (97% yield). R_f = 0.3 (1% Et₂O/hexanes). ¹H NMR (400 MHz, CDCl₃) δ 7.67 (d, J = 7.6 Hz, 4H), 7.46-7.34 (m, 6H), 5.80 (m, 1H), 5.02-4.92 (m, 2H), 3.67 (t, J = 6.4 Hz, 2H), 2.04 (app. q, J = 7.2 Hz, 2H), 1.63-1.42 (m, 4H), 1.05 (s, 9H). ¹³C NMR (100 MHz, CDCl₃) δ 139.2, 135.8, 134.3, 129.7, 127.8, 114.6, 64.0, 33.7, 32.2, 27.1, 25.3, 19.5. IR (neat, cm⁻¹) 3071, 3050, 2998, 2931, 2898, 2858. HRMS (ESI) m/z calculated for C₂³H₂₄O₂Si [M + H⁺]: 339.21443; found: 339.21422.

Preparation of 1-bromo-4-(((2-(pent-4-enyl)cyclohexyloxy)methoxy)methyl)benzene from 2-(pent-4-enyl)cyclohexanol (24)  To a 100 mL round bottom flask was added 2-(pent-4-enyl)cyclohexanol ¹⁵ (165.0 mg, 1.0 mmol, 1 equiv.), THF (20 mL) and a Teflon© stir bar. The solution was cooled to 0°C. Potassium bis(trimethylsilyl)amide (5.0 ml, 0.5 M in toluene, 2.5 mmol, 2.5 equiv.) was added dropwise and the solution was allowed to stir at room temperature for 1 hr. TBAI (38.0 mg, 0.1 mmol) and 1-bromo-4-(bromomethyl)benzene ¹⁶ (600 mg, 2.5 mmol) was added as a solution in 10 mL THF. The reaction was allowed to stir overnight. The reaction was quenched with 5 ml saturated aqueous NH₄Cl solution and diluted with diethyl ether. The organics were extracted with from water, dried (MgSO₄), filtered, and concentrated in vacuo. Purification via flash silica gel chromatography (1% Et₂O/hexanes) gave 329 mg of 1-bromo-4-(((2-(pent-4-enyl)cyclohexyloxy)methoxy)methyl)benzene as a clear oil (>90% yield). R_f = 0.2 (1% Et₂O/hexanes). ¹H NMR (400 MHz, CDCl₃) δ 7.47 (d, J = 8.0 Hz, 2H), 7.22 (d, J = 8.4 Hz, 2H), 5.86-5.74 (m, 1H), 5.02-4.94 (m, 1H), 4.95-4.90 (m, 1H), 4.87 (d, J = 6.8 Hz, 1H), 4.72 (d, J = 7.2 Hz, 1H), 4.58 (d, J = 4.5 Hz, 2H), 3.23-3.18 (m, 1H), 2.10-0.80 (m, 15H). ¹³C NMR (100 MHz, CDCl₃) δ 139.3, 137.3, 137.3, 131.7, 129.6, 121.7, 114.5, 93.5, 80.7, 68.9, 43.3, 34.5, 32.4, 32.0, 30.4, 26.2, 25.5, 24.9. HRMS (Cl⁺) m/z calculated for C₂₈H₂₃BrO₃ [M⁺]: 439.21991 observed: 439.21974; [α] D = −21.4° (c=1.0, CHCl₃).

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26.0, 25.9, 25.1, 24.5, 24.4. IR (neat, cm$^{-1}$) 2930, 2857, 1740, 1646. HRMS (ESI) m/z calculated for C$_{18}$H$_{34}$NO$_3$ [M + H]$^+$: 312.2539; found: 312.2542.

22 A similar procedure has been used on a similar molecule. Chou, S. S. P.; Liang, C. F.; Lee, T. M.; Liu, C. F. Tetrahedron, 2007, 63, 8267.