Supporting Information

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

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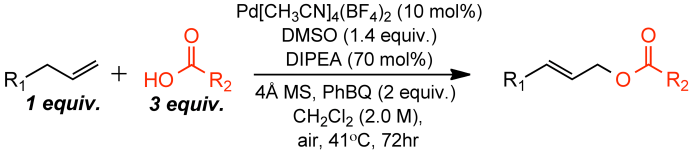
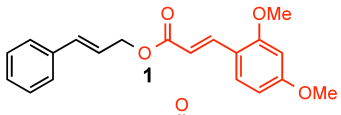
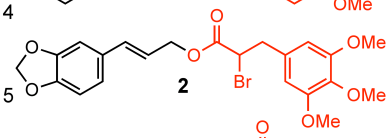
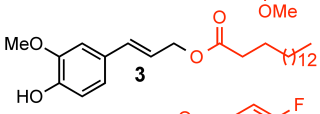
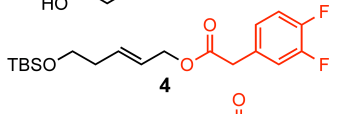
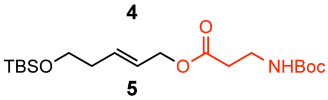
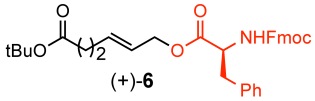
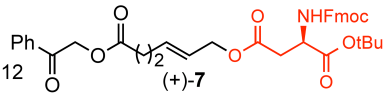
General Information: All commercially obtained reagents were used as received: 2-phenyl-1,4-benzoquinone (ACROS); $Pd(CH_3CN)_4(BF_4)_2$ (Aldrich) was stored in a glove box under a argon atmosphere and weighed out in under argon prior to use, all other reagents where purchased from least expensive supplier and used directly unless otherwise stated. Solvents diethyl ether (Et_2O) and methylene chloride (CH_2Cl_2) 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 pre-coated 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.[i] using EM reagent silica gel 60 (230-400 mesh). ^{1}H 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 ($CDCl_3$ at 7.26 ppm). Data reported as: s = singlet, d = doublet, t = triplet, q = quartet, quin. = quintet, m = multiplet, br = broad, app = apparent; coupling constant(s) in Hz; integration, corresponding carbon atom. Proton-decoupled ^{13}C-NMR spectra were recorded on a Varian Unity-500 (125 MHz) spectrometer and are reported in ppm using solvent as an internal standard ($CDCl_3$ 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^{o}C when the reaction becomes black and viscous). Due to the high viscosity of the reaction mixtures a bigger stir bar is more appropriate. The temperature is also important with an effective range of 40 to 45 ^{o}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 $Pd(CH_3CN)_4(BF_4)_2$ catalyst is moisture sensitive and decomposes to a wet dull yellow powder, easily distinguished from the bright yellow crystals of good catalyst.

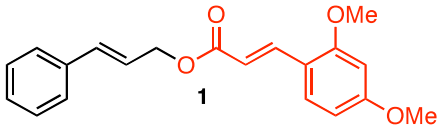
General Procedure: To a 4 mL borosilicate vial was first added $Pd(CH_3CN)_4(BF_4)_2$ (44.4 mg, 0.1 mmol, 10 mol %) under argon atmosphere. The following reagents were then added in one portion under ambient atmosphere: phenyl benzoquinone (368 mg, 2.0 mmol, 2 equiv.), carboxylic acid (3.0 mmol, 3.0 equiv.), two 4Å molecular beads (50 mg). Finally, DMSO (100 μL, 1.4 mmol, 1.4 equiv.), CH_2Cl_2 (500 μL), and DIPEA (121.0 μL, 0.7 mmol, 0.7 equiv.) were added sequentially via glass syringe followed by a Teflon© stir bar. This solution was stirred at 41^{o}C for 5 minutes before starting material (1.0 mmol, 1.0 equiv.) was added neat using a microsyringe. The vial was then capped and stirred at 41^{o}C for 72 hours. Upon completion as determined by NMR, the reaction was 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_2CO_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_2SO_3 (2 g) to a reaction mixture diluted with 50 mL of EtOAc and 50 mL of a 5% K_2CO_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.

Linear Allylic Oxidation (LAO)



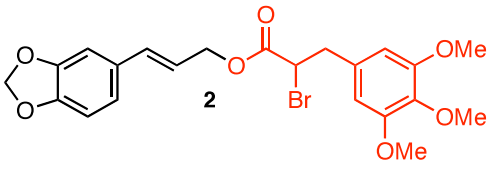
Entry		Isolated Yield[a]	*E:Z*[b]	L:B[b] (crude)	steps C-H	steps C-C
1	 **1**	70%	>20:1	>20:1	1	3
2		61%[c]	>20:1	>20:1		ref. 8
3		53%[d]	>20:1	>20:1		
4		65%[e]	>20:1	>20:1		
5	 **2**	68%	16:1	>20:1	2	5 ref. 9
6	 **3**	64%	>20:1	>20:1	1	3 ref. 10
7	 **4**	60%	11:1	6:1	2	4
8[f]		31%	10:1	9:1		ref. 11
9	 **5**	50%	11:1	9:1	2	4
10[f]		23%	7:1	11:1		ref. 12
11	 (+)-**6**	54%[c]	17:1[h]	>20:1[i]	2	2 ref. 14
12	 (+)-**7**	72%	18:1[h]	>20:1	2	4 ref. 15

[a] Isolated yields of >20:1 L:B. Unless otherwise noted, *E:Z* does not change after purification.[b] crude values by ^{1}H NMR. [c] 1.5 equiv. acid. [d] 24h reaction time. [e] 5 mol% $Pd[CH_3CN]_4(BF_4)_2$. [f] using previously published conditions, ref. 4b. [g] THP protected version of this compound was made. [h] determined after methanolysis and acetylation by ^{1}H NMR. [i] determined by ^{1}H NMR of purified material.

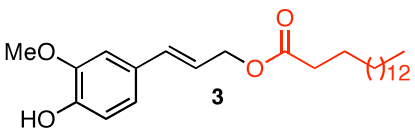


(*E*)-cinnamyl 3-(2,4-dimethoxyphenyl)acrylate (1) To a 4 mL borosilicate vial was added $Pd(CH_3CN)_4(BF_4)_2$ (44.4 mg, 0.1 mmol, 10 mol %) under argon atmosphere, followed by phenyl benzoquinone (368 mg, 2.0 mmol, 2 equiv.), (*E*)-3-(2,4-dimethoxyphenyl)acrylic acid (624 mg, 3.0 mmol, 3.0 equiv.), two 4Å molecular beads (50 mg) in one portion under ambient atmosphere. DMSO (100 µL, 1.1 mmol, 1.1 equiv.), CH_2Cl_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_2CO_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_2O/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_2O/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),

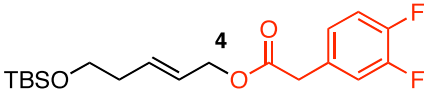
7.26 (t, J = 7.5, 1H), 6.70 (d, J = 16.0 Hz, 1H), 6.51 (dd, J = 9.0, 2.0 Hz, 1 H), 6.48 (d, J = 16.0 Hz, 1H), 6.45 (d, J = 2.5 Hz, 1H), 6.37 (dt, J = 16.0, 6.0 Hz, 1H), 4.86 (dd, J = 6.0, 1.0 Hz, 2H), 3.87 (s, 3H), 3.84 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.9, 162.9, 160.1, 140.7, 136.5, 134.1, 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, 3004, 2936, 2839, 1706, 1605, 1160. HRMS (ESI) m/z calculated for $C_{20}H_{20}O_4Na$ [M + Na]$^+$: 347.1259; found: 347.1257. Spectral data has previously been reported for this compound.[ii]



(*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 $Pd(CH_3CN)_4(BF_4)_2$ (11.1 mg, 0.025 mmol, 10 mol %) under argon atmosphere, followed by phenyl benzoquinone (92.0 mg, 0.5 mmol, 2.0 equiv.), 2-bromo-3-(3,4,5-trimethoxyphenyl)propionic acid[iii] (239.4 mg, 0.75 mmol, 3.0 equiv.), two 4Å molecular beads (30 mg) in one portion under ambient atmosphere. DMSO (25 μL, 0.29 mmol, 1.1 equiv.), CH_2Cl_2 (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% K_2CO_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 (30% Et_2O/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 ^{1}H 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). R_f= 0.15 (30% Et_2O/hexanes). ^{1}H NMR (400 MHz, $CDCl_3$) 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). ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.2, 153.3, 148.1, 147.8, 134.8, 132.3, 130.3, 121.6 , 120.1, 108.3, 106.2, 105.8, 101.2, 66.6, 60.8, 56.1, 45.1, 41.4. IR (neat, cm^{-1}) 2998, 2940, 2839, 1738, 1591. HRMS (EI) m/z calculated for $C_{22}H_{23}BrO_4$ [M]$^+$: 478.06271; found: 478.06254. Spectral data matches that previously reported.[5]



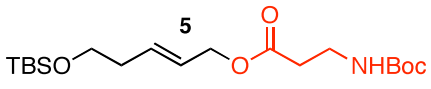
(*E*)-3-(4-hydroxy-3-methoxyphenyl)allyl palmitate (3) To a 4 mL borosilicate vial was added $Pd(CH_3CN)_4(BF_4)_2$ (44.4 mg, 0.1 mmol, 10 mol %) under argon atmosphere, followed by phenyl benzoquinone (368 mg, 2.0 mmol, 2 equiv.), palmitic acid (768 mg, 3.0 mmol, 3 equiv.), two 4Å molecular beads (50 mg) in one portion under ambient atmosphere. DMSO (100 μL, 1.1 mmol, 1.1 equiv.), CH_2Cl_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 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 NH_4Cl (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 $MgSO_4$, filtered, and reduced *in vacuo*. Purification via flash silica gel chromatography (5% Et_2O/hexanes) gave (*E*)-3-(4-hydroxy-3-methoxyphenyl)allyl palmitate as a clear oil. The crude selectivities determined by ^{1}H 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**. R_f= 0.2 (5% Et_2O/hexanes; elutes with and just after the brightly colored PhBQ). ^{1}H NMR (400 MHz, $CDCl_3$) 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), 1.4-1.2 (s, 24H), 0.88 (t, J = 6.4 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) 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 $C_{26}H_{43}O_4$ [M + H]$^+$: 419.3161; found: 419.3155. Spectral data matches that previously reported.[iv]



(*E*)-5-(tert-butyldimethylsilyloxy)pent-2-enyl 2-(3,4-difluorophenyl)acetate (4)
General Conditions: To a 4 mL borosilicate vial was added $Pd(CH_3CN)_4(BF_4)_2$ (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 (259 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_2Cl_2 (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

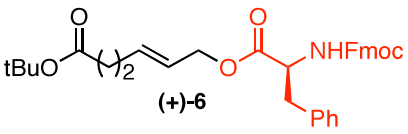
vial was then capped and stirred at 41°C for 72 hours. Upon completion (via NMR aliquate), the reaction was transferred to a separatory funnel using minimal methylene chloride (~2 mL). The solution was diluted with 1:1 diethyl ether:hexanes (50 mL) and washed with 5% K_2CO_3 (aq.) solution 2x. Note: 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% Et_2O/hexanes) gave (E)-5-(tert-butyldimethylsilyloxy)pent-2-enyl 2-(3,4-difluorophenyl)acetate as a clear oil. The crude selectivities determined by ^1H NMR are L:B 6:1 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 = 60% yield**. (11:1 E:Z and >20:1 L:B after silica column purification). Note: When 4 equiv. acid is used 133mg, 69% yield, L:B=27:1, E:Z=17:1.

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, 1.0 mmol, 2 equiv.), 3,4-difluorophenylacetic acid (259 mg, 1.5 mmol, 3 equiv.), and 4Å molecular sieves (50 mg). DMSO (190 µL), CH_2Cl_2 (60 µL), and DIPEA (43 µL, 0.25 mmol, 0.5 equiv.) were added via glass syringe followed by a Teflon© stir bar. *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% K_2CO_3 (aq.) solution 2x. The organic layer was dried with $MgSO_4$, filtered, and reduced *in vacuo*. Purification via flash silica gel chromatography (5% Et_2O/hexanes) gave (E)-5-(tert-butyldimethylsilyloxy)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 10:1. Run 1 (55.1 mg, 0.15 mmol, 30%); run 2 (57.0 mg, 0.15 mmol, 31%). **Average = 31% yield**. (10:1 E:Z and >20:1 L:B after silica column purification). R_f= 0.15 (5% Et_2O/hexanes). ^1H NMR (500 MHz, $CDCl_3$) δ 7.14-7.07 (m, 2H), 7.00-6.96 (m, 1H), 5.77 (dt, *J* = 15.5, 7.0 Hz, 1H), 5.61 (dtd, *J* = 16.5, 6.5, 1.0 Hz, 1H), 4.55 (d, *J* = 6.0 Hz, 2H), 3.64 (t, *J* = 6.5 Hz, 2H), 3.58 (s, 2H), 2.27 (app. q, *J* = 7.0, 2H), 0.89 (s, 9H), 0.04 (s, 6H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.8, 151.0 (dd, *J* = 65.9, 12.8 Hz), 149.1 (dd, *J* = 65, 12.9 Hz), 133.5, 130.9 (t, *J* = 5.0 Hz), 125.6 (app. s), 125.5, 118.5 (d, *J* = 17.4 Hz), 117.4 (d, *J* = 17.4 Hz), 65.9, 62.5, 40.5, 35.9, 29.8, 26.0, 18.5, -5.19. ^{19}F NMR (376 MHz, $CDCl_3$) δ -138.1 (quin., *J* = 9.4 Hz, 1F), -140.7 (m, 1F). IR (neat, cm^{-1}) 2953.6, 2929.6, 2903.9, 2858.5, 1740.0, 1520.3. HRMS (ESI) m/z calculated for $C_{19}H_{29}F_2O_3Si$ $[M + H]^+$: 371.1854; found: 371.1849. The TBS deprotected compound has been synthesized via standard TBAF deprotection and matches the spectral data previously reported.[v]



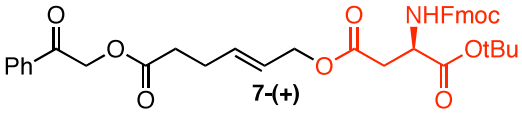
(*E*)-5-(*tert*-butyldimethylsilyloxy)pent-2-enyl 3-(*tert*-butoxycarbonyl)propanoate (5)
General Conditions: To a 4 mL borosilicate vial was added $Pd(CH_3CN)_4(BF_4)_2$ (44.4 mg, 0.1 mmol, 10 mol %) under argon atmosphere, followed by phenyl benzoquinone (368 mg, 2.0 mmol, 2 equiv.), Boc-β-Ala-OH (567.0 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.), CH_2Cl_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 *t*ert-butyldimethyl(pent-4-enyloxy)silane (200 mg, 1mmol, 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_2CO_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 (15% Et_2O/hexanes) gave (*E*)-5-(*tert*-butyldimethylsilyloxy))pent-2-enyl 3-(*tert*-butoxycarbonyl)propanoate) 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).

Previous Conditons: To a 4 mL borosilicate vial was added $Pd(OAc)_2$ (11.2 mg, 0.05 mmol, 10 mol %), phenyl benzoquinone (184 mg, 1.0 mmol, 2 equiv.), Boc-β-Ala-OH (283.5 mg, 1.5 mmol, 3 equiv.), 4Å molecular sieves (50 mg). DMSO (190 µL), CH_2Cl_2 (60 µL), and DIPEA (43 µL, 0.25 mmol, 0.5 equiv.) were added via glass syringe followed by a Teflon© stir bar. *t*ert-Butyldimethyl(pent-4-enyloxy)silane (100 mg, 0.5 mmol, 0.5 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_2CO_3 (aq.) solution 2x. The organic layer was dried with $MgSO_4$, filtered, and reduced *in vacuo*. Purification via flash silica gel chromatography (15% Et_2O/hexanes) gave (*E*)-5-(*tert*-butyldimethylsilyloxy))pent-2-enyl 3-(*tert*-butoxycarbonyl)propanoate) as a clear oil. The crude selectivities determined by ^1H NMR are L:B 11:1 and E:Z 7:1. Run 1 (45.0 mg, 0.12 mmol, 23%); run 2 (41.2 mg, 0.11 mmol, 21%); run 3 (46.4 mg, 0.12 mmol, 24%) **Average = 23% yield**. (7:1 E:Z and >20:1 L:B after silica column purification). R_f= 0.2 (20% Et_2O/hexanes). ^1H NMR (500 MHz, $CDCl_3$) δ 5.78 (dt, *J* = 15.0, 7.0 Hz, 1H), 5.62 (dt, *J* = 15.0, 6.5 Hz, 1H), 5.02 (br s, 1H), 4.54 (d, *J* = 6.0 Hz, 2H), 3.65 (t, *J* = 6.5 Hz, 2H), 3.39 (app q, *J* = 5.5 Hz, 2H), 2.52 (t, *J* = 6.0 Hz, 2H), 2.28 (app q, *J* = 6.5 Hz, 2H), 1.43 (s, 9H), 0.88 (s,9H), 0.04 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.6, 156.0, 133.3, 125.7, 65.6, 62.7, 36.3, 36.1, 34.8, 28.6, 26.1, 18.6, -5.1. IR (neat, cm^{-1}) 3371, 2955, 2930, 2858, 1719, 1506. HRMS (ESI) m/z calculated for $C_{19}H_{38}NO_5Si$ $[M + H]^+$: 388.2519; found: 388.2518. Spectral data is in agreement with that previously reported.[vi]



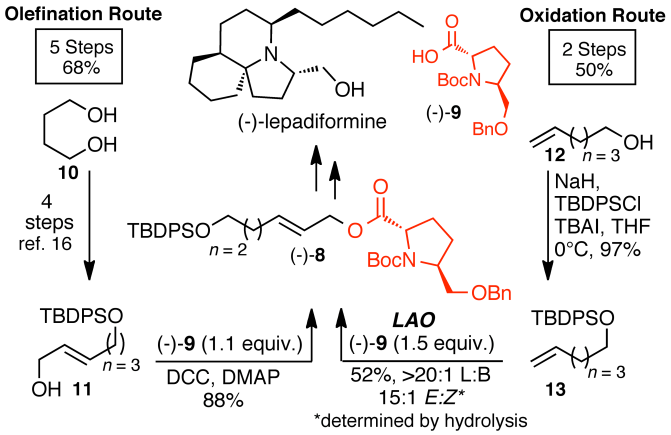
(+)-6

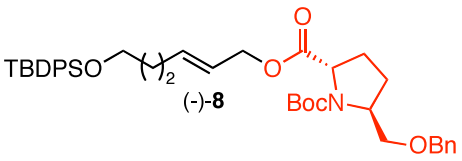
(*S*,*E*)-*tert*-butyl 6-(2-(((9*H*-fluoren-9-yl)methoxy)carbonylamino)-3-phenylpropanoyloxy)hex-4-enoate (6) To a 4 mL borosilicate vial was added $Pd(CH_3CN)_4(BF_4)_2$ (22.2 mg, 0.05 mmol, 10 mol %) under argon atmosphere, followed by phenyl benzoquinone (184.0 mg, 1.0 mmol, 2 equiv.), *N*-α-Fmoc-L-phenylalanine (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_2Cl_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[vii] (85.0 mg, 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 (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_2CO_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-(((9*H*-fluoren-9-yl)methoxy)carbonyl)-3-phenylpropanoyloxy)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 methanolysis 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, 144.0, 141.5, 135.9, 135.5, 129.7, 128.8, 128.0, 127.4, 127.3, 125.4, 125.3, 124.3, 120.2 (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. $[\alpha]^{25}_D$ = +9.0° (c=1.1, $CHCl_3$). Spectral data has been previously reported.[viii]



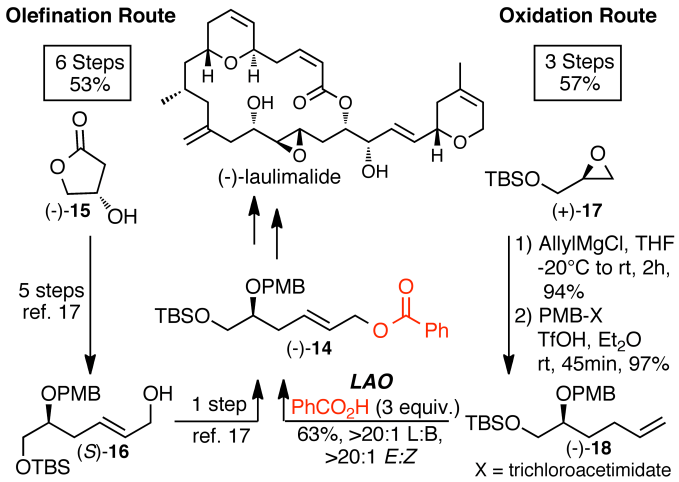
7-(+)

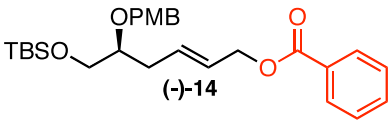
2-(9H-Fluoren-9-ylmethoxycarbonylamino)-succinic acid 1-tert-butyl ester 4-[5-(2-oxo-2-phenyl-ethoxycarbonyl)-pent-2-enyl]ester (7) To a 4 mL borosilicate vial was added $Pd(CH_3CN)_4(BF_4)_2$ (22.2 mg, 0.05 mmol, 10 mol %) under argon atmosphere, followed by a Teflon© stir bar, phenyl benzoquinone (184 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_2Cl_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, 0.5 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% K_2CO_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_2O/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 methanolysis 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_2O/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), 4.44-4.30 (m, 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 $C_{37}H_{40}NO_9$ $[M + H]^+$: 642.2703; found: 642.2695. $[\alpha]^{26}_D$ = +12.3° (c=1.0, $CHCl_3$). Compound was found to be >99% ee through SCF analysis (mobile phase CO_2, column chiralpak-AS, 12% MeOH, 2.5 mL/min, 125 barr) with retention times of 19.3 min for **(-)-7** and 22.1 min for **(+)-7**. Spectral data matches previously reported data.[ix]



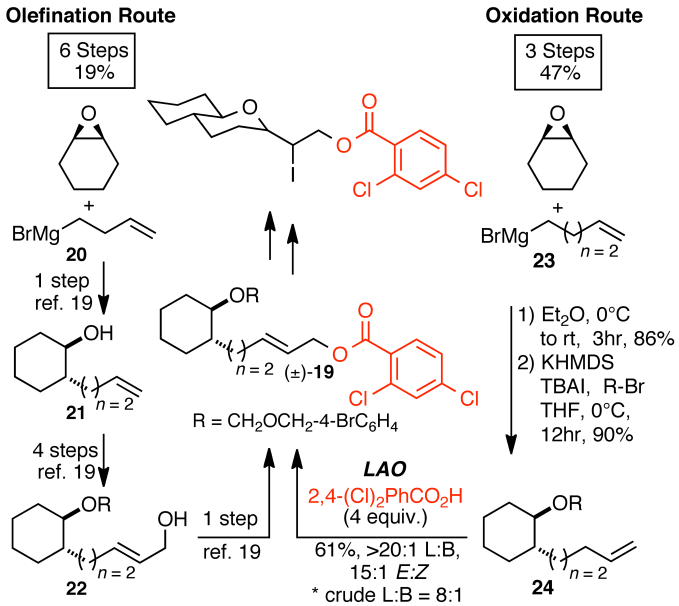


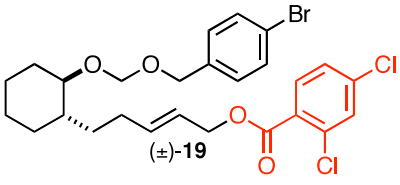
(5*S*,*E*)-1-*tert*-butyl 2-(6-(*tert*-butyldiphenylsilyloxy)hex-2-enyl) 5-(benzyloxymethyl)pyrrolidine-1,2-dicarboxylate (8) To a 4 mL borosilicate vial was added $Pd(CH_3CN)_4(BF_4)_2$ (22.2 mg, 0.05 mmol, 10 mol %) under argon atmosphere, followed by phenyl benzoquinone (184 mg, 1.0 mmol, 2 equiv.), (5*S*)-5-(benzyloxymethyl)-1-(*tert*-butoxycarbonyl)pyrrolidine-2-carboxylic acid (250 mg, 0.75mmol, 1.5 equiv.), two 4Å molecular beads (30 mg) in one portion under ambient atmosphere. DMSO (50 µL, 0.57 mmol, 1.1 equiv.), CH_2Cl_2 (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% K_2CO_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_2O/hexanes) gave (5*S*,*E*)-1-*tert*-butyl 2-(6-(*tert*-butyldiphenylsilyloxy)hex-2-enyl) 5-(benzyloxymethyl)pyrrolidine-1,2-dicarboxylate as a pail oil. The crude selectivities are >20:1 L:B (determined from crude ^{1}H NMR) and 15:1 *E:Z* (determined after hydrolysis to (*E*)-6-(*tert*-butyldiphenylsilyloxy)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**. R_f= 0.2 (5% EtOAc/hexanes). Note: NMRs are a mixture of two diastereomers and two rotamers: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.65 (d, *J* = 7.5 Hz, 4H), 7.46-7.26 (m, 11H), 5.82-5.70 (m, 1H), 5.62-5.50 (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, 6H), 1.07 (s, 9H). ^{13}C NMR (150 MHz, $CDCl_3$) 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 $C_{40}H_{54}NO_6Si$ $[M + H]^+$: 672.3720; found: 672.3737. $[\alpha]^{26}_D$ = -35.6° (c=1.0, $CHCl_3$). Spectral data matches previously reported data.[x]





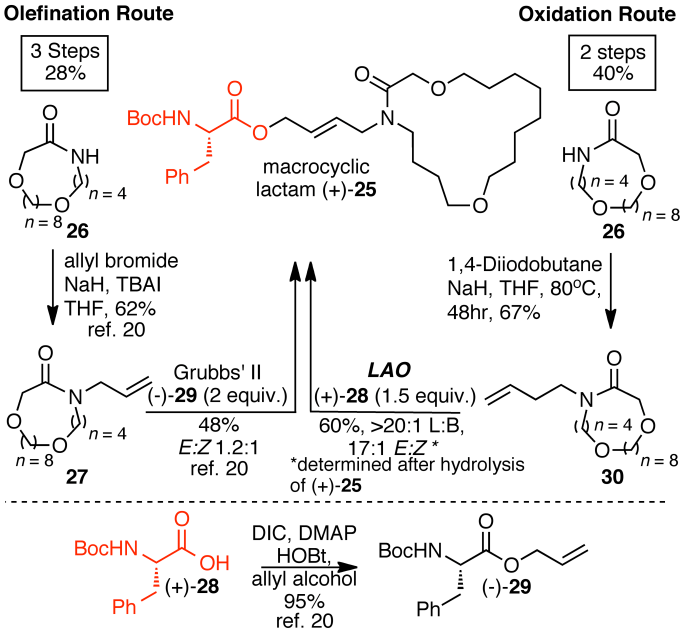
(*E*)-5-(*tert*-butyldimethylsilyloxy)pent-2-enyl 2-(3,4-difluorophenyl)acetate (14) To a 4 mL borosilicate vial was added $Pd(CH_3CN)_4(BF_4)_2$ (44.4 mg, 0.1 mmol, 10 mol %) under argon atmosphere, followed by phenyl benzoquinone (368 mg, 2.0 mmol, 2 equiv.), benzoic acid (366 mg, 3 mmol, 3 equiv.), two 4Å molecular beads (50 mg) in one portion under ambient atmosphere. DMSO (100 µL, 1.1 mmol, 1.1 equiv.), CH_2Cl_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 (*S*)-(2-(4-methoxybenzyloxy)hex-5-enyloxy)(*tert*-butyl)dimethylsilane (350 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% K_2CO_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% EtOAc/hexanes) gave (*E*)-5-(*tert*-butyldimethylsilyloxy)pent-2-enyl 2-(3,4-difluorophenyl)acetate as a clear thick oil. The crude selectivities determined by ^{1}H NMR are L:B >20:1 and E:Z >20:1. Run 1 (287.0 mg, 0.61 mmol, 61%); run 2 (291.0 mg, 0.62 mmol, 62%); run 3 = (306.0 mg, 0.65 mmol, 65%) **Average = 63% yield**. R_f = 0.1 (5% Et_2O/hexanes). ^{1}H NMR (500 MHz, $CDCl_3$) δ 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, 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, $CDCl_3$) δ 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, 1270, 1249. HRMS (CI^+) m/z calculated for $C_{27}H_{37}O_5Si$ $[M-H]^+$: 469.24103; found: 469.24112. $[\alpha]^{27}_D$ = -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.[xi]

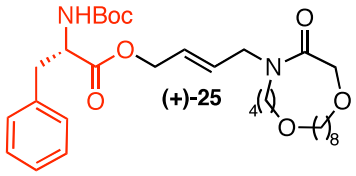




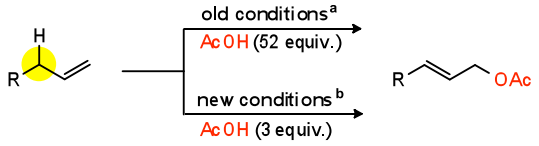
(*E*)-5-(2-((4-bromobenzyloxy)methoxy)cyclohexyl)pent-2-enyl 2,4-dichlorobenzoate (19) To a 2 mL borosilicate vial was added $Pd(CH_3CN)_4(BF_4)_2$ (15 mg, 0.03 mmol, 10 mol%) under argon atmosphere, followed by phenyl benzoquinone (122 mg, 0.66 mmol, 2 equiv.), 2, 4-dichlorobenzoic acid (254 mg, 1.3 mmol, 4 equiv.), one 4Å molecular beads (20 mg) in one portion under ambient atmosphere. DMSO (35 µL, 0.36 mmol, 1.1 equiv.), CH_2Cl_2 (170 µL), and DIPEA (40 µL, 0.23 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 1-bromo-4-(((2-(pent-4-enyl)cyclohexyloxy)methoxy)methyl)benzene (122 mg, 0.33 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_2CO_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%

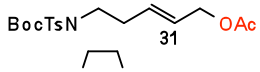
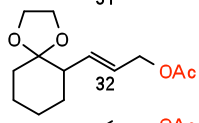
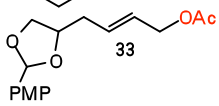
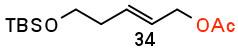
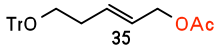
Et_2O/hexanes) gave (*E*)-5-(2-((4-bromobenzyloxy)methoxy)cyclohexyl)pent-2-enyl 2,4-dichlorobenzoate as a clear thick oil. MPLC was required to separate the branched ester (1% EtOAc:Hx). The crude selectivities determined by ^{1}H NMR are L:B 8:1 and *E:Z* 15:1. Run 1 (111.0 mg, 0.20 mmol, 60%); run 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_2O/pentane). ^{1}H NMR (500 MHz, $CDCl_3$) δ 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, $CDCl_3$) δ 164.8, 138.5, 137.7, 137.2, 135.1, 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 (CI) m/z calculated for $C_{26}H_{30}O_4BrCl_2$ $[M + H]^+$: 555.07045; found: 555.07092. Compound has previously been synthesized, however; no spectral data was provided.[xii]





(*S,E*)-4-(6-oxo-1,3,5-dioxazepan-5-yl)but-2-enyl 2-(*tert*-butoxycarbonylamino)-3-phenylpropanoate (25) To a 2 mL borosilicate vial was added $Pd(CH_3CN)_4(BF_4)_2$ (11.1 mg, 0.025 mmol, 10 mol%) under argon atmosphere, followed by phenyl benzoquinone (97 mg, 0.5 mmol, 2 equiv.), Boc-*L*-phenalanine (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_2Cl_2 (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 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 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_2CO_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_2O/hexanes) gave (*S,E*)-4-(6-oxo-1,3,5-dioxazepan-5-yl)but-2-enyl 2-(*tert*-butoxycarbonylamino)-3-phenylpropanoate 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, $CDCl_3$) δ 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, $CDCl_3$) δ 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 $C_{32}H_{51}N_2O_7$ $[M + H]^+$: 575.3696; found: 575.3694. $[\alpha]^{20}_D$ = +4.1° (c=0.7, $CHCl_3$). Spectral data matches previously reported data.[xiii]



Entry	Product	Conditions	Isolated Yield[c]	*E*:*Z*[d]	L:B (crude)[d]
1		old	51%	8:1	12:1
2		new	75%	9:1	>20:1
3		old	50%[e]	>20:1	>20:1
4		new	64%	>20:1	>20:1
5		old	<5%	---	---
6		new	53%	12:1	12:1
7		old	17%	8:1	4:1
8		new	58%	12:1	8:1
9		old[f, g]	7%	5:1	3:1
10		old	32%	8:1	4:1
11		new	69%	11:1	10:1

[a] $Pd(OAc)_2$ (10 mol%), DMSO: AcOH (1:1; 0.17M), 4Å MS, BQ (2 equiv.), air, 41°C, 72h. [b] $Pd[CH_3CN]_4(BF_4)_2$ (10 mol%), DMSO:CH_2Cl_2 (1:5; 2.0M), AcOH (3 equiv.), 4Å MS, PhBQ (2 equiv.), air, 41°C, 72h. [c] isolated yields of >20:1 L:B. Unless otherwise noted, *E*:*Z* does not change after purification. [d] crude values by 1H NMR [e] Previously reported, see ref. 4a. [f] $Pd(OAc)_2$ (10 mol%), DMSO (0.17M), AcOH (3 equiv.), 4Å MS, BQ (2 equiv.), air, 41°C, 72h. [g] When the reaction was run under the "old" conditions at 0.33M DMSO, 3 equiv. AcOH only trace reactivity was observed: 10% yield.

Table 2

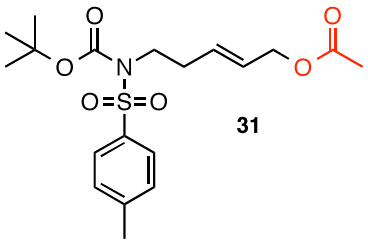
2004 JACS Procedure: To a 4 mL borosilicate vial was first added $Pd(OAc)_2$ (11.2 mg, 0.05 mmol, 10 mol %) under argon atmosphere. The following reagents were then added in one portion under ambient atmosphere: benzoquinone (108 mg, 1.0 mmol, 2 equiv.) and 4Å molecular powder (108 mg). Finally, DMSO (1.5 mL, 1.65 g, 21 mmol, 42 equiv.), AcOH (1.5 ml, 1.57g, 26 mmol, 52 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) [Note 1]. The solution was diluted with diethyl ether (50 mL) and washed with 5% K_2CO_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_2SO_3 (2 g) to a reaction mixture diluted with 50 mL of EtOAc and 50 mL of a 5% K_2CO_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, 90.2mg, 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) [Note 1]. The solution was diluted with diethyl ether (50 mL) and washed with 5% K_2CO_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_2SO_3 (2 g) to a reaction mixture diluted with 50 mL of EtOAc and 50 mL of a 5% K_2CO_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 (0.17M): 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 (2.91 mL, 3.21 g, 40.8 mmol, 82 equiv.), AcOH (86 µl, 90.2mg, 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

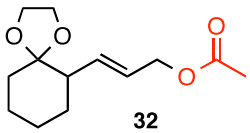
transferred to a separatory funnel using minimal methylene chloride (~2 mL) [Note 1]. The solution was diluted with diethyl ether (50 mL) and washed with 5% K_2CO_3 (aq.) solution twice [Note 2]. The organic layer was dried with $MgSO_4$, filtered, and reduced *in vacuo*. Purification was achieved via flash silica gel chromatography. Notes: (1) The excess quinone may be reduced by addition of solid Na_2SO_3 (2 g) to a reaction mixture diluted with 50 mL of EtOAc and 50 mL of a 5% K_2CO_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 $Pd(CH_3CN)_4(BF_4)_2$ (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_2Cl_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 minutes 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 separatory funnel using minimal methylene chloride (~2 mL) [Note 1]. The solution was diluted with diethyl ether (50 mL) and washed with 5% K_2CO_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_2SO_3 (2 g) to a reaction mixture diluted with 50 mL of EtOAc and 50 mL of a 5% K_2CO_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.



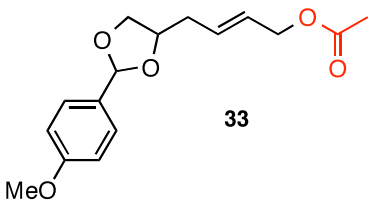
31

(E)-5-(N-(tert-butoxycarbonyl)-4-methylphenylsulfonamido)pent-2-en-1-yl acetate (31) from 1,1-dimethyl (4-methylphenyl)sulfonyl(4-pentenyl)carbamate.[xiv] 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). R_f= 0.15 (20% EtOAc/hexanes). ^{1}H NMR (500 MHz, $CDCl_3$) δ 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, $CDCl_3$) δ 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 $C_{19}H_{27}NO_6NaS$ $[M + Na]^+$: 420.1457; found: 420.1460.



32

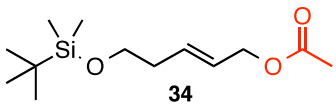
(E)-3-(1,4-dioxaspiro[4.5]dec-6-yl)-2-propen-1-ol acetate (32) from 6-allyl-1,4-dioxaspiro[4.5]decane.[xv] Old: The crude selectivities were determined to be L:B >20:1 and E:Z >20:1 by ^{1}H NMR. Run 1 (119 mg, 0.49 mmol, 49%); run 2 (120.5 mg, 0.50 mmol, 50%); **Average = 50% yield.**[xva] New: The 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, $CDCl_3$) δ 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) 3.96-3.80 (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, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 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 $C_{13}H_{20}O_4Na$ $[M + Na]^+$: 263.1259; found: 263.1258. Spectral data matches that previously reported.[16a]



33

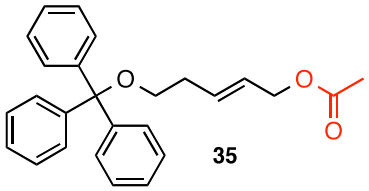
(E)-4-(2-(4-methoxyphenyl)-1,3-dioxolan-4-yl)but-2-en-1-yl acetate (33) from 2-(4-methoxyphenyl)-4-(pent-4-en-1-yl)-1,3-dioxolane.[xvi] Old: Run 1 (trace product); run 2 (trace product); **Average <5% yield.** New: The crude selectivities were determined to be L:B = 12:1 and E:Z = 12:1 by ^{1}H NMR. 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= 0.2 (5% EtOAc/hexanes). ^{1}H NMR (500 MHz, $CDCl_3$) ^{1}H NMR (500 MHz, $CDCl_3$) Major Diastereomer: δ 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: δ 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). ^{13}C NMR (100 MHz, $CDCl_3$) Major Diastereomer: δ170.7, 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 $C_{16}H_{21}O_5$ $[M + H]^+$: 293.1389; found: 293.1383.



34

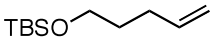
(E)-5-((tert-butyldimethylsilyl)oxy)pent-2-en-1-yl acetate (34) from tert-butyldimethyl(pent-4-en-1-yloxy)silane.[xvii] Old: The crude selectivities were determined to be L:B = 4:1 and E:Z = 8:1 by ^{1}H NMR. Run 1 (23.0 mg, 0.09 mmol, 18%); run 2 (24.0 mg, 0.09 mmol, 19%); run 3 (16.8 mg, 0.07 mmol, 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 ^{1}H 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 ^{1}H 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 ^{1}H 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). R_f= 0.1 (10% Et_2O/hexanes). ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.77 (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) . ^{13}C NMR (125 MHz, $CDCl_3$) 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 $C_{13}H_{27}O_3Si$ $[M + H]^+$: 259.1729; found: 259.1720.



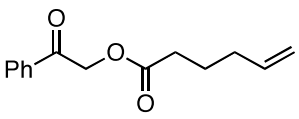
35

(E)-5-(trityloxy)pent-2-en-1-yl acetate (35) from ((pent-4-en-1-yloxy)methanetriyl)tribenzene.[xviii] Old: The crude selectivities were determined to be L:B = 4:1 and E:Z = 8:1 by ^{1}H 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 ^{1}H 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). R_f= 0.1 (10% Et_2O/hexanes). ^{1}H NMR (500 MHz, $CDCl_3$) 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). ^{13}C NMR (125 MHz, $CDCl_3$) δ170.7, 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 $C_{26}H_{26}O_3Na$ $[M + Na]^+$: 409.1780; found: 409.1784.

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

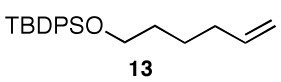


***tert*-Butyldimethyl(pent-4-enyloxy)silane** (starting material for **4** and **5**) To a 200mL round bottom flask was added 4-penten-1-ol (2.5 g, 58.0 mmol), THF (100 mL) and a Teflon© stir bar. The solution was cooled to 0°C and NaH (2.8 g, 4.0 equiv.) was added by portions. The reaction was allows to stir for 30 minutes. After the solution turns a yellow color, t-Butyl(dimethyl)silyl chloride (TBSCl, 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. NH_4Cl solution (10 mL) and the organics extracted with water. The organic layer was dried ($MgSO_4$), filtered, and reduced *in vacuo*. Purification via flash silica gel chromatography (1% Et_2O/hexanes) gave 7.7 g of *tert*-butyldimethyl(pent-4-enyloxy)silane as a clear oil (~90% yield). Previously prepared *J. Chem. Soc. Perk. Trans.* **2000**, *1,* 1915; *Tetrahedron Lett.* **1995**, *36*, 819. R_f= 0.3 (1% Et_2O/hexanes). ^{1}H NMR (500 MHz, $CDCl_3$) 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).



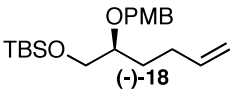
Hex-5-enoic acid 2-oxo-2-phenyl-ethyl ester (starting material for **(+)-7**) To a 100mL flame dried round bottom flask was added phenacylbromide (2.4 g, 12 mmol, 1.2 equiv.), potassium fluoride (1.75 g, 30 mmol, 2.5 equiv.), DMF (20 mL) and Teflon© stir bar. To this suspension was added 5-hexenoic acid (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 ($MgSO_4$), filtered, and concentrated *in vacuo*. Purification via flash silica gel chromatography (5% Et_2O/hexanes) gave 2 g of hex-5-enoic acid 2-oxo-2-phenyl-ethyl ester as a clear oil (~95% yield). R_f= 0.1 (2% Et_2O/hexanes). ^{1}H

NMR (500 MHz, $CDCl_3$) δ 7.91 (app. d, *J* = 7.5 Hz, 2H), 7.61 (t, *J* = 7.0 Hz, 1H), 7.48 (t, *J* = 8.0 Hz, 2H), 5.85-5.75 (m, 1H), 5.34 (s, 2H), 5.06 (d, *J* = 17.5 Hz, 1H), 5.00 (d, *J* = 10.0 Hz, 1H), 2.51 (t, *J* = 7.5 Hz, 2H), 2.16 (q, *J* = 7.5 Hz, 2H), 1.82 (quin., *J* = 8.0 Hz, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 192.5, 173.3, 137.9, 134.5, 134.1, 129.1, 128.0, 115.7, 66.1, 33.4, 33.2, 24.2. IR (neat, cm^{-1}) 3068, 2977, 2936, 2869, 1745, 1705. HRMS (ESI) m/z calculated for $C_{14}H_{17}O_3$ $[M + H]^+$: 233.1178; found: 233.1171.



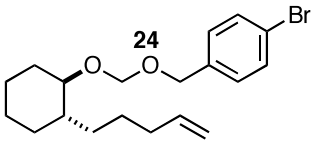
13

Prepartion of *tert*-butyl(hex-5-enyloxy)diphenylsilanefrom 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, 5.0 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 ($MgSO_4$), filtered, and reduced *in vacuo*. Purification via flash silica gel chromatography (1% Et_2O/hexanes) gave 15.0 g of *tert*-butyl(hex-5-enyloxy)diphenylsilane as a clear oil (97% yield). R_f = 0.3 (1% Et_2O/hexanes). ^1H NMR (400 MHz, $CDCl_3$) 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). ^{13}C NMR (100 MHz, $CDCl_3$) 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 $C_{22}H_{31}OSi$ $[M + H]^+$: 339.21443; found: 339.21422.

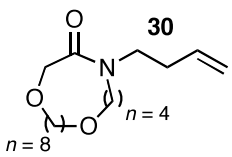


(-)-18

(*S*)-(2-(4-methoxybenzyloxy)hex-5-enyloxy)(*tert*-butyl)dimethylsilane ((-)-14) Previously made in 3 steps and 71% overall yield.[xix] Using the same method this material can be prepared in 2 steps from now commercially available tert-Butyldimethylsilyl (R)-(–)-glycidyl ether with 91% overall yield. R_f= 0.5 (5% Et_2O/hexanes). ^1H NMR (500 MHz, $CDCl_3$) δ 7.28-7.21 (m, 2H), 6.90-6.85 (m, 2H), 5.82 (m, 1H), 5.04-4.97 (m, 1H), 4.96-4.91 (m, 1H), 4.45 (s, 2H), 3.81 (s, 3H), 3.88-3.30 (m, 3H), 2.34-2.00 (m, 2H), 1.76-1.46 (m, 2H), 0.88 (s, 9H), 0.05 (s, 3H), 0.04 (s, 3H). HRMS (CI^+) m/z calculated for $C_{20}H_{33}O_3Si$ $[M-H]^+$: 349.21991 observed: 349.21974. $[\alpha]^{20}_D$ = -21.4° (c=1.0, $CHCl_3$). Spectral data matched previously reported data.



Prepartion of 1-bromo-4-(((2-(pent-4-enyl)cyclohexyloxy)methoxy)methyl)benzene from 2-(pent-4-enyl)cyclohexanol (24) To a 100 mLround bottom flask was added 2-(pent-4-enyl)cyclohexanol[xx] (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 a added dropwise and the solution was allows to stir at room temperature for 1 hr. TBAI (38.0 mg, 0.1 mmol) and 1-bromo-4-(bromomethyl)benzene[xxi] (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 NH_4Cl solution and diluted with diethyl ether. The organics were extracted with from water, dried ($MgSO_4$), filtered, and concentrated *in vacuo*. Purification via flash silica gel chromatography (1% Et_2O/hexanes) gave 329mg of 1-bromo-4-(((2-(pent-4-enyl)cyclohexyloxy)methoxy)methyl)benzene as a clear oil (>90% yield). R_f= 0.2 (1% Et_2O/hexanes). ^1H NMR (400 MHz, $CDCl_3$) 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). ^{13}C NMR (100 MHz, $CDCl_3$) δ 139.3, 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 (CI) m/z calculated for $C_{19}H_{28}O_2Br$ $[M + H]^+$: 367.12726; found: 367.12810.



4-(but-3-enyl)-1,9-dioxa-4-azacycloheptadecan-3-one (30)[xxii] To a flamed 200 mL round bottom flask was added 1,9-dioxa-4-azacycloheptadecan-3-one[13] (260.0 mg, 1.0 mmol), THF (2.5 mL) and a Teflon© stir bar. The solution was cooled to 0°C. NaH (120.0 mg, 5.0 mmol, 5.0 equiv.) was added in one portion and the solution was allows to stir for 0.5 hrs. 1,4-Diiodobutane (1.55 g, 5.0 mmol, 5.0 equiv.) was added in THF (2.5 mL) and the reaction was headed to 80°C in a sealed tube and stirred for 48 hours. [Note: TLC in 50% ethyl acetate:hexanes (CAM charred) should show complete consumption of starting materials. If two less polar spots are visible, dilute the reaction with 20 mL of benzene and add 15 equiv. DBU. Reseal the reaction vessel and heat to 80°C for 30 minutes. Extract with 1M H_3PO_4.] The reaction was quenched with 5.0 ml saturated NH_4Cl and diluted with 200 ml of ethyl acetate. The organics were extracted with from water (100 mL), dried over $MgSO_4$, filtered, and concentrated *in vacuo*. Purification via flash silica gel chromatography (50% EtOAc/hexanes) gave homo-allylic lactam as a clear oil. **Average Yield = 67%.** Run 1 (210.0 mg, 0.7 mmol, 70%), run 2 (204.0 mg, 0.68 mmol, 68%), run 3 (106.0 mg, 0.35 mmol, 64%). R_f= 0.5 (50% EtOAc/hexanes). Note: Rotamers are present in both NMR spectrum. ^1H NMR (500 MHz, $CDCl_3$) δ 5.85-5.68 (m, 1H), 5.12-4.98 (m, 2H), 4.12 (s, 1H), 4.06 (s, 1H), 3.58 (m, 10H), 2.34-2.24 (m, 2H), 1.80-1.20 (m, 16H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.8, 169.4, 135.8, 134.6, 117.9, 116.8, 71.8, 71.7, 71.5, 71.1, 70.3, 70.2, 70.2, 48.3, 46.1, 45.5, 44.7, 33.4, 32.2, 31.2, 30.6, 29.7, 28.9, 28.8, 28.6, 28.2, 27.7, 27.6, 27.2, 27.0, 26.9,

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.

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