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Supporting Information

69451 Weinheim, Germany

The Deracemization of Quaternary Stereocenters by Palladium-Catalyzed Enantioconvergent Decarboxylative Allylation of Racemic β-Ketoesters

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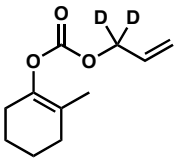
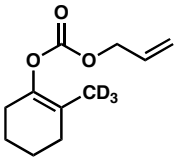
Materials and Methods. Unless otherwise stated, reactions were performed in flame-dried glassware under an argon or nitrogen atmosphere using dry, deoxygenated solvents. Solvents were dried by passage through an activated alumina column under argon. Brine solutions are saturated aqueous sodium chloride solutions. Tris(dibenzylideneacetone)dipalladium(0) ($Pd_2(dba)_3$) was purchased from Strem and stored in a glove box until immediately before use. (*S*)-*t*-BuPHOX and allyl cyanoformate were prepared by known methods.[1,2] Pimelic acid diallyl ester was prepared in a method analogous to the adipic acid esterification described by Tsuji.[3] Alkyl halides, diallyl carbonate, Select-fluor, and pimelic acid were purchased from Aldrich and used as received. 3-Methylcyclohex-2-en-1-one and cyclohex-2-en-1-one were purchased from Acros and used as received. Dimethyallyl carbonate was purchased from Alfa Aesar and used as received. Sodium hydride (NaH) was purchased as a 60% dispersion in mineral oil from Acros and used as such unless otherwise stated. Reaction temperatures were controlled by an IKAmag temperature modulator. Thin-layer chromatography (TLC) was performed using E. Merck silica gel 60 F254 precoated plates (0.25 mm) and visualized by UV fluorescence quenching, anisaldehyde, $KMnO_4$, or CAM staining. ICN Silica gel (particle size 0.032-0.063 mm) was used for flash chromatography. Analytical chiral HPLC was performed with an Agilent 1100 Series HPLC utilizing a Chiralcel OJ, AD, or OD-H column (4.6 mm x 25 cm) obtained from Daicel Chemical Industries, Ltd with visualization at 254 nm. Analytical chiral GC was performed with an Agilent 6850 GC utilizing a G-TA (30 m x 0.25 mm) column (1.0 mL/min carrier gas flow). Optical rotations were measured with a Jasco P-1010 polarimeter at 589 nm. ^1H and ^{13}C NMR spectra were recorded on a Varian Mercury 300 (at 300 MHz and 75 MHz respectively), and are reported relative to Me_4Si (δ 0.0). Data for ^1H NMR spectra are reported as follows: chemical shift (δ ppm) (multiplicity, coupling constant (Hz), integration). IR spectra were recorded on a Perkin Elmer Paragon 1000 spectrometer and are reported in frequency of absorption (cm^{-1}). High resolution mass spectra were obtained from the Caltech Mass Spectral Facility.

Deuterium Labeling Experiments.



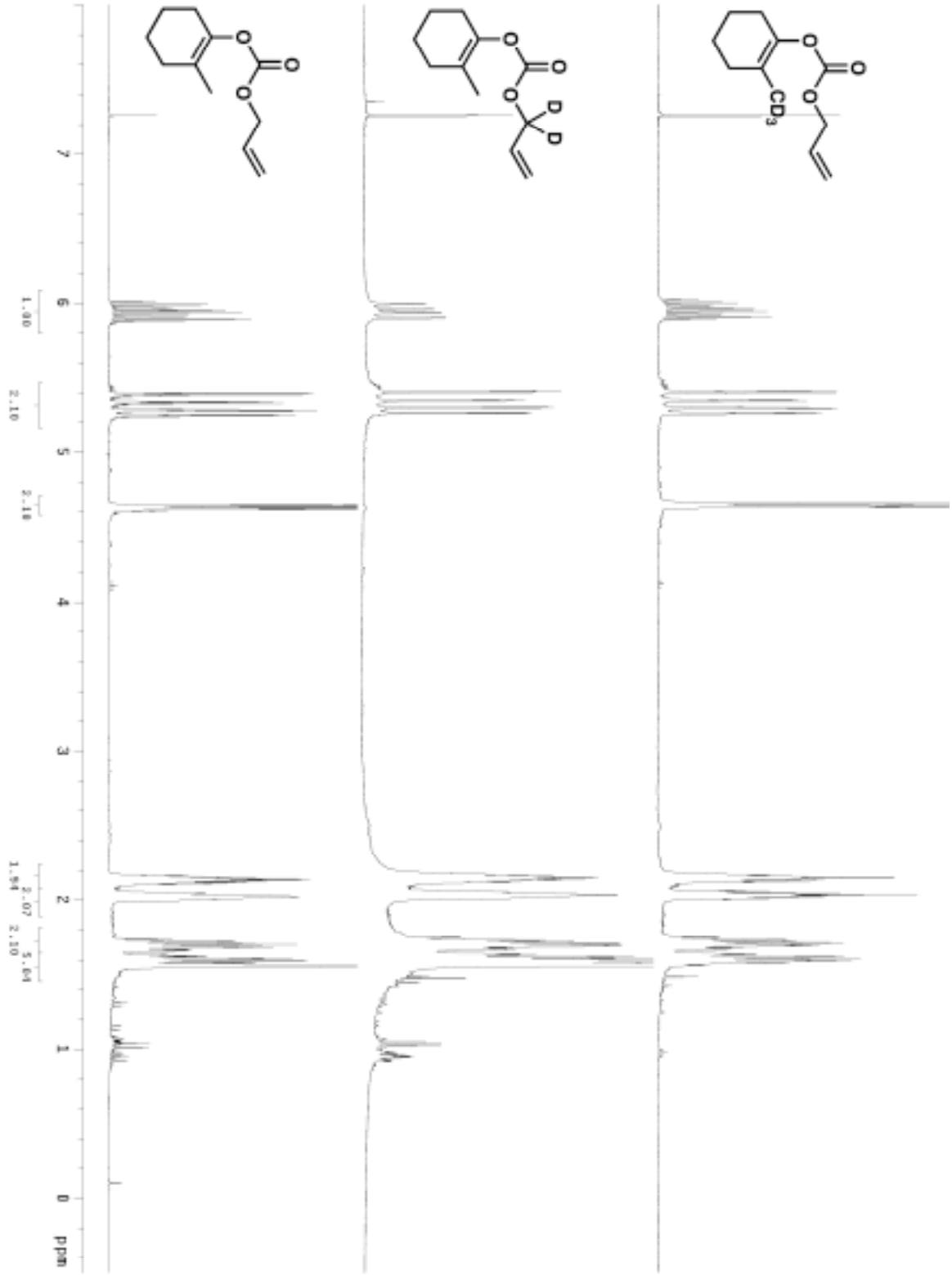
8

Compound **8** was prepared from dideuterioallyl chroroformate, which was synthesized from 1-dideuterioallyl alcohol[4] and 20% phosgene in toluene, and used without purification in our standard procedure.[5] Flash chromatography (SiO_2, 1→2.5% Et_2O in hexanes). 6.3% yield. R_f = 0.82 (25% Et_2O in hexanes); ^1H NMR (300 MHz, $CDCl_3$) δ 5.95 (dd, J = 17.0, 10.4 Hz, 1H), 5.38 (d, J = 17.1 Hz, 1H), 5.28 (d, J = 10.5 Hz, 1H), 2.21-2.09 (comp. m, 2H), 2.08-1.98 (comp. m, 2H), 1.77-1.66 (comp. m, 2H), 1.65-1.53 (comp. m, 2H), 1.57 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 153.1, 142.2, 131.4, 120.9, 119.0, 30.3, 26.6, 23.1, 22.3, 21.7, 15.8; IR (Neat Film NaCl) 2935, 2862, 1753, 1710, 1280, 1262, 1078 cm^{-1}; HRMS (EI) *m/z* calc'd for $C_{11}H_{14}D_2O_3$ $[M]^+$: 198.1225, found 198.1217.



9

Compound **9** was prepared from 2-trideuteriomethylcyclohexanone[6] by our standard procedure.[5] Flash chromatography (SiO_2, 2→2.5% Et_2O in hexanes). 22% yield. R_f = 0.82 (25% Et_2O in hexanes); ^1H NMR (300 MHz, $CDCl_3$) δ 5.96 (ddt, J = 17.1, 10.8, 6.0 Hz, 1H), 5.38 (d, J = 17.3 Hz, 1H), 5.28 (d, J = 10.5 Hz, 1H), 4.65 (d, J = 5.7 Hz, 2H), 2.21-2.09 (comp. m, 2H), 2.08-1.98 (comp. m, 2H), 1.77-1.66 (comp. m, 2H), 1.66-1.53 (comp. m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 153.1, 142.2, 131.5, 120.8, 118.8, 68.5, 30.0, 26.6, 23.1, 22.3; IR (Neat Film NaCl) 2936, 1755, 1705, 1367, 1276, 1247, 1216, 1034, 786 cm^{-1}; HRMS (EI) *m/z* calc'd for $C_{11}H_{13}D_3O_3$ $[M]^+$: 199.1288, found 199.1280.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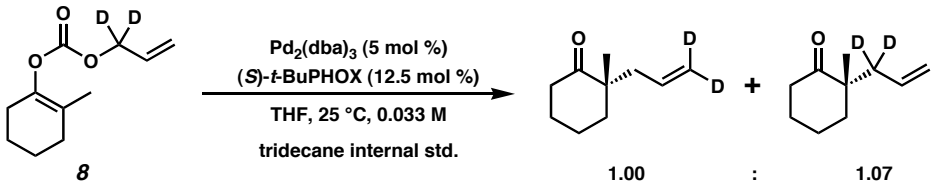
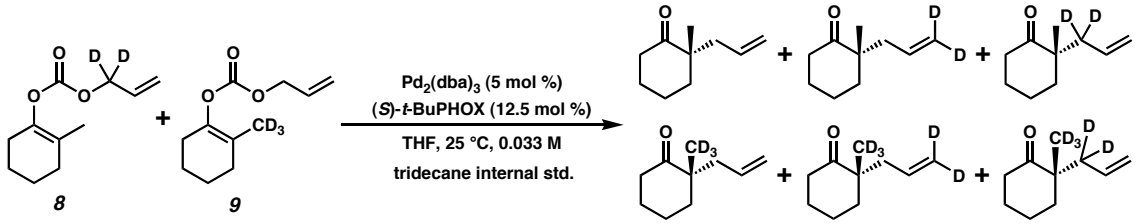
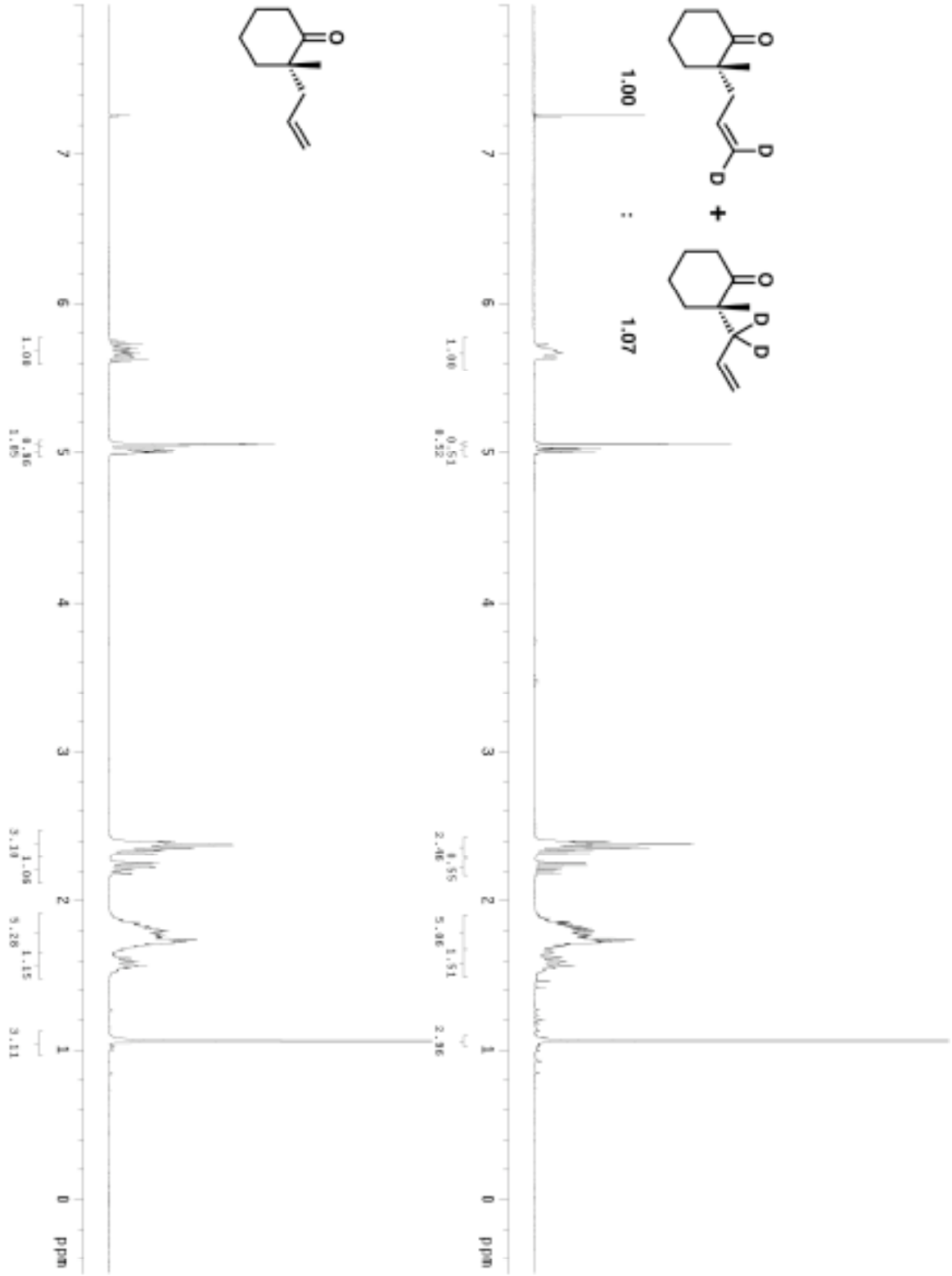
Asymmetric Tsuji Allylation of Deuterated Substrates



Enol carbonate **8** (39.7 mg, 0.2 mmol, 1.0 equiv) was reacted under our standard allylation conditions.[5] After 2 h, the reaction was complete by TLC. GC analysis showed an 88.1% yield and an 87% ee for the mixture of products. Flash chromatography (SiO_2, 1→2.5% Et_2O in pentane) afforded material for NMR analysis, which allowed the ratio of products to be quantified.



Enol carbonates **8** (19.9 mg, 0.1 mmol, 1.0 equiv) and **9** (19.8 mg, 0.1 mmol, 1.0 equiv) were simultaneously reacted under our standard conditions.[5] After 2 h, the reaction was complete by TLC. GC analysis showed an 88.4% yield and an 87% ee for the mixture of products. Flash chromatography (SiO_2, 1→2.5% Et_2O in pentane) afforded material for MS and NMR analysis, which allowed the ratio of products to be quantified.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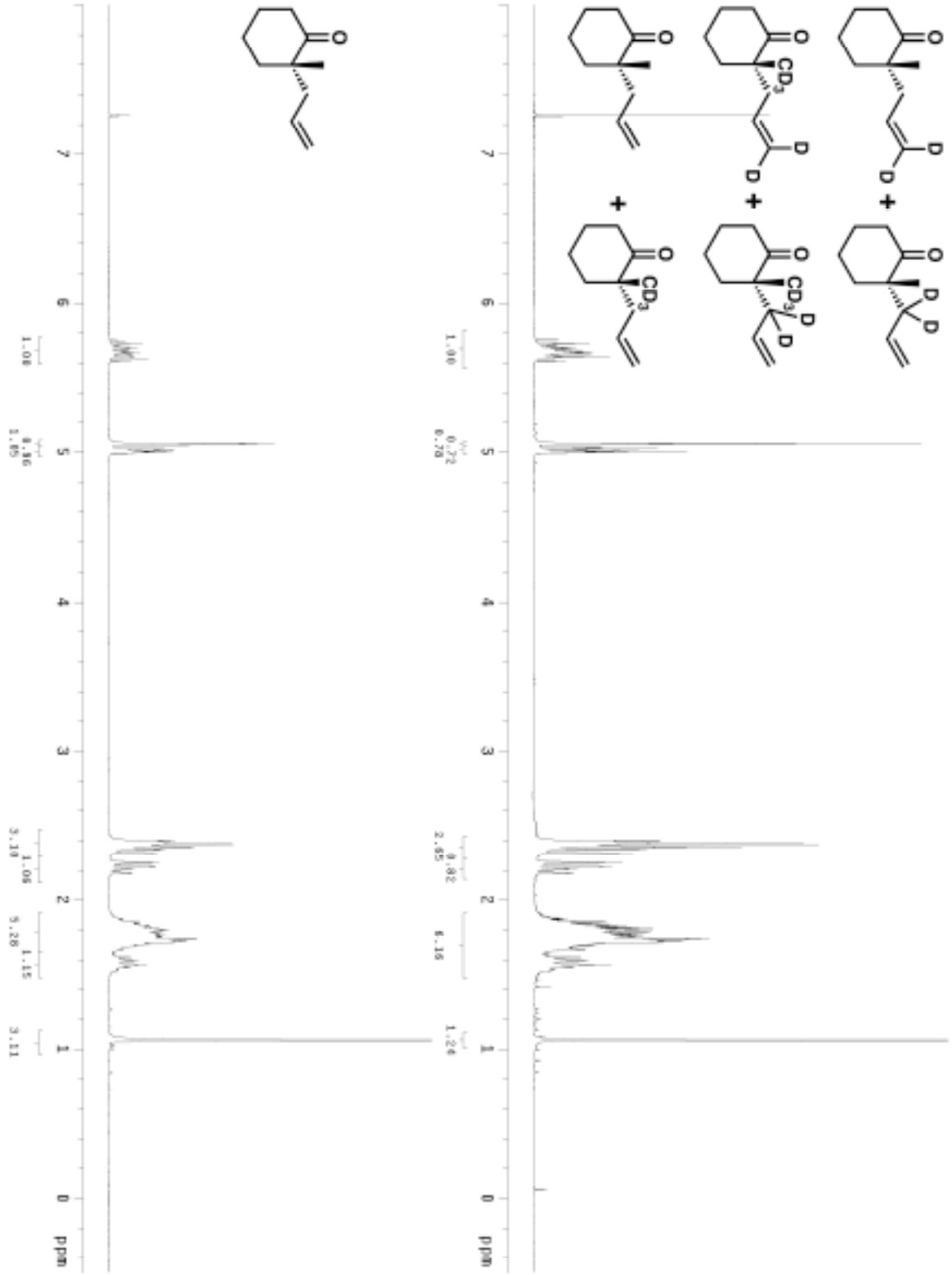
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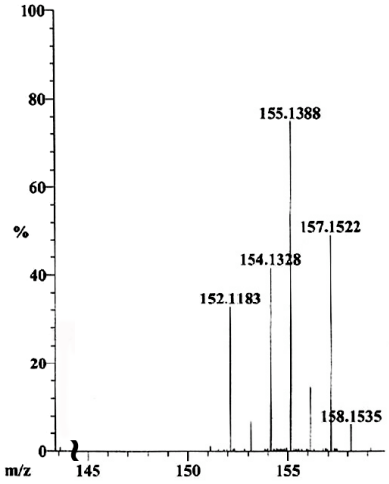
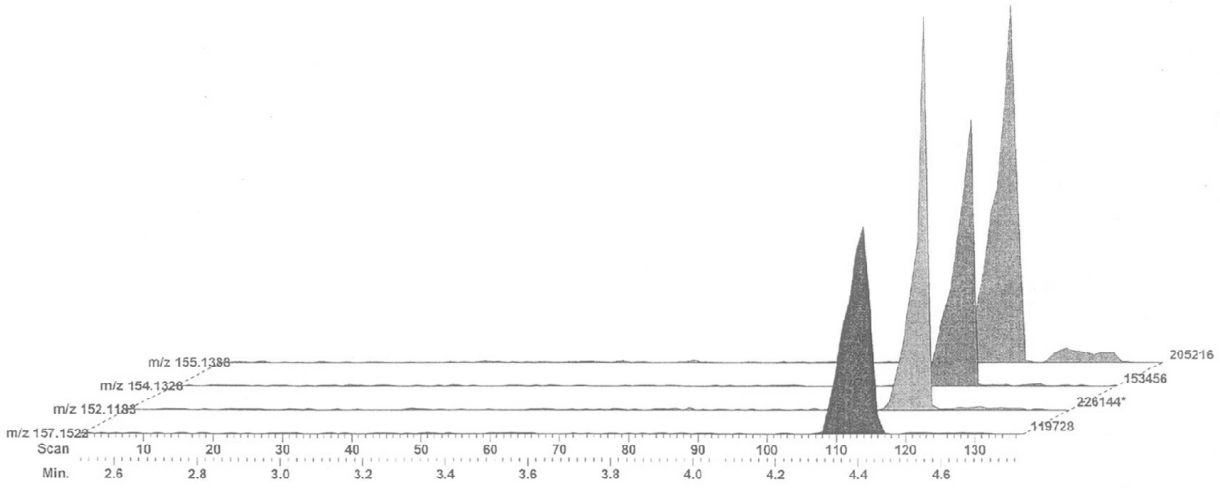
1.24

Mass Spectral Analysis of Crossover Experiments

A Representative MS Scan



Relative Abundance of Four Product Masses



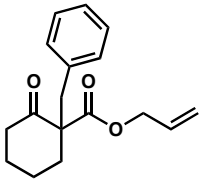
Mass	Scans	Integral	% Abundance
152.1183	110-118	459336	21.23 %
154.1328	110-118	478480	22.12 %
155.1388	108-118	720536	33.31 %
157.1522	107-118	504864	23.34 %
	Total	2163216	100 %

While the total ion counts are not rigorously quantitative, they clearly suggest that all four masses are present in nearly equal proportions. The slight excess of the 155 m/z ion is likely due to the natural abundance of ^{13}C present in the dideuterio material. Nearly identical distributions were obtained whether the reaction was run in THF, 1,4-dioxane, or benzene.

Representative Procedures for the Synthesis of β-Keto Allyl Esters.

Method 1 (Dieckmann Cyclization Method):[7]

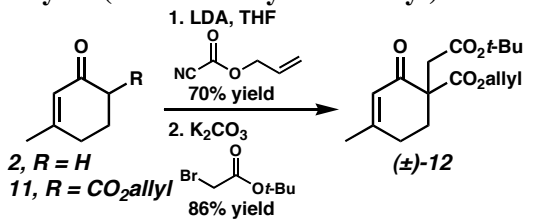
Allyl 1-benzyl-2-oxocyclohexanecarboxylate (Table 1, Entry 6):



To a suspension of NaH (166.4 mg, 4.16 mmol, 1.0 equiv) in toluene (2 mL) was added allyl alcohol (79.2 μL, 1.17 mmol, 0.28 equiv). Once gas evolution ceased, pimelic acid diallyl ester (1.00 g, 4.16 mmol, 1.0 equiv) was added slowly and the resulting mixture heated to 95 °C for 1 h. Additional toluene (~2 mL) was added during this time to maintain a fluid reaction mixture. The reaction mixture was cooled to rt and the solvent removed by rotary evaporation *in vacuo*. The resulting solid salt was placed under dry N_2 and dissolved in THF (9 mL) at rt. Benzyl bromide (643.2 μL, 5.4 mmol, 1.3 equiv) was then added dropwise. The resulting mixture was warmed to 50 °C for 2.5 h, cooled to rt, quenched with saturated aqueous NH_4Cl solution (5 mL) followed by H_2O (5 mL). The phases were separated and the aqueous phase was extracted with EtOAc (3 x 5 mL). The combined organic extracts were washed with brine (1 x 10 mL), then dried (Na_2SO_4), filtered, and concentrated in vacuo. The resulting oil was purified by flash chromatography (5 x 18 cm SiO_2, 10% Et_2O in pentane) to afford the quaternary compound as a colorless oil (781.4 mg, 70% yield). R_f = 0.30 (10% Et_2O in pentane); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.33-7.23 (comp. m, 3H), 7.20-7.13 (comp. m, 2H), 5.86 (dddd, J = 17.2, 10.3, 5.9, 5.9 Hz, 1H), 5.29 (m, 2H), 4.57 (m, 2H), 3.38 (d, 1H, J = 13.8 Hz), 2.94 (d, J = 13.8 Hz, 1H), 2.60-2.39 (comp. m, 3H), 2.14-1.97 (m, 1H), 1.83-1.60 (comp. m, 3H), 1.59-1.45 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 206.8, 170.5, 136.3, 131.2, 130.2, 127.9, 126.5, 119.0, 65.6, 62.1, 41.1, 40.3, 35.7, 27.4, 22.3; IR (Neat Film NaCl) 3029, 2942, 1713, 1452, 1179, 1085 cm^{-1}; HRMS (EI) *m/z* calc'd for $C_{17}H_{20}O_3$ $[M]^+$: 272.1412, found 272.1425.

Method 2 (Mander's Reagent Method):[8]

Allyl 1-(2-*tert*-butoxy-2-oxoethyl)-4-methyl-2-oxocyclohex-3-enecarboxylate ((±)-12):



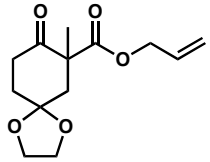
To a cooled (-78 °C) solution of LDA (18.70 mmol, 1.05 equiv) in THF (90 mL) was added 3-methylcyclohex-2-enone (**2**, 2.02 mL, 17.81 mmol, 1.0 equiv) in a dropwise fashion. The resulting solution was stirred at -78 °C for 30 min and then allyl cyanoformate (2.00 g, 18.17 mmol, 1.02 equiv) was added dropwise. The dry ice bath was removed and the reaction mixture slowly warmed to rt and stirred for 8 h. The reaction mixture was quenched with saturated aqueous NH_4Cl (15 mL) followed by H_2O (15 mL). The phases were separated and

the aqueous phase was extracted with EtOAc (3 x 15 mL). The combined organic extracts were washed with brine (1 x 30 mL), dried (Na_2SO_4), filtered and concentrated *in vacuo*. The resulting oil was purified by flash chromatography (5 x 24 cm SiO_2, 50% EtOAc in hexanes) to afford the β-keto ester **11** as a yellow oil (2.4152 g, 70% yield).

A portion of this β-keto ester (500.0 mg, 2.57 mmol, 1.0 equiv) was added to a suspension of anhydrous K_2CO_3 (711.8 mg, 5.15 mmol, 2.0 equiv) in acetone (2.5 mL). To the reaction mixture was added *t*-butyl bromoacetate (760.5 μL, 5.15 mmol, 2.0 equiv). The reaction mixture was then warmed to 50 °C and stirred for 48 h. The reaction mixture was then cooled, filtered, and the solids washed with acetone. The filtrate was concentrated and purified by flash chromatography (3 x 20 cm SiO_2, 10→30% EtOAc in hexanes) to afford the desired quaternary compound (±)-**12** as a colorless oil (684.7 mg, 86% yield; 60% overall yield for 2 steps). R_f = 0.28 (30% Et_2O in pentane). ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.93 (s, 1H), 5.87 (dddd, *J* = 17.3, 10.5, 5.4, 5.4 Hz, 1H), 5.23 (m, 2H), 4.61 (m, 2H), 2.83 (d, *J* = 16.4 Hz, 1H), 2.73 (d, *J* = 16.4 Hz, 1H), 2.58-2.36 (comp. m, 2H), 2.31-2.16 (comp. m, 2H), 1.94 (s, 3H), 1.42 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 194.2, 169.8, 161.9, 131.7, 125.6, 118.2, 81.1, 65.8, 54.2, 39.8, 30.5, 28.7, 28.0, 24.2; IR (Neat Film NaCl) 2979, 1733, 1677, 1368, 1153 cm^{-1}; HRMS (EI) *m/z* calc'd for $C_{17}H_{24}O_5$ $[M]^+$: 308.1624, found 308.1609.

Method 3 (Diallyl Carbonate Method):

Allyl 1-methyl-2-oxo-5-ethyleneketal-cyclohexanecarboxylate (Table 2, Entry 1):



Part 1 Acylation:

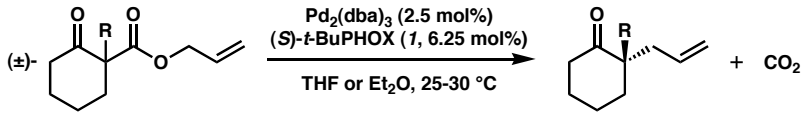
To a cooled (0 °C) suspension of NaH (9.22 g, 240.1 mmol, 2.5 equiv) in THF (125 mL) was added a solution of 1,4-cyclohexanedione *mono*-ethylene ketal (15.0 g, 96 mmol, 1.0 equiv) in THF (30 mL) dropwise over 15 min. The reaction mixture was warmed to rt and diallyl carbonate (20.65 mL, 144.0 mmol, 1.5 equiv) was added and the reaction mixture stirred for 16 h. The reaction was quenched with saturated aqueous NH_4Cl and 1 N HCl until a pH of 4 was reached. The phases were separated and the aqueous phase was extracted with EtOAc (7 x 150 mL). The combined organic extracts were dried (Na_2SO_4), filtered, concentrated, redissolved in DCM, dried ($MgSO_4$), filtered and concentrated.

Part 2 Alkylation:

The resulting oil was added to a suspension of anhydrous K_2CO_3 (26.5 g, 192.0 mmol, 2.0 equiv) in acetone (128 mL). To the reaction mixture was added iodomethane (12.0 mL, 192.0 mmol, 2.0 equiv) and the reaction mixture then heated to 50 °C for 14 h. The mixture was then cooled to r.t., filtered, and the solids washed with acetone. The filtrate was concentrated and the resulting oil purified by flash chromatography (SiO_2, 5→40% Et_2O in hexanes) to afford the desired quaternary compound as a colorless oil (18.0 g, 74% yield). R_f = 0.28 (30% Et_2O in pentane); ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.90 (dddd, *J* = 17.4, 10.5, 5.7, 5.7 Hz, 1H), 5.26 (m, 2H), 4.60 (m, 2H), 3.97 (comp. m, 4H), 3.02 (dt, *J* = 14.8, 10.2 Hz, 1H), 2.68 (dt, *J* = 14.0, 2.0 Hz, 1H), 2.49 (dt, *J* = 14.8, 4.4 Hz, 1H), 2.00 (comp. m, 2H), 1.72

(d, J = 14.1 Hz, 1H), 1.29 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 207.0, 172.9, 131.6, 118.5, 106.5, 65.9, 64.8, 64.3, 54.6, 43.6, 37.4, 35.2, 21.7; IR (Neat Film NaCl) 2939, 2891, 1733, 1717, 1304, 1141 cm^{-1}; HRMS (EI) m/z calc'd for $C_{13}H_{18}O_5$ $[M]^+$: 254.1154, found 254.1153.

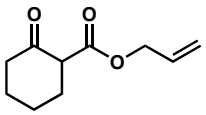
Table 1. Catalytic Enantioconvergent Decarboxylative Allylation of α-Substituted 2-Carboxyallyl Cyclohexanones.



entry	R	solvent	temp (°C)	time (h)	% yield[a]	% ee[b]
1	CH_3	THF	25	7.5	85	88
2	CH_3	Et_2O	25	4.75	89	88
3	prenyl	Et_2O	30	6	97	91
4	CH_2CH_2CN	Et_2O	25	6.5	97	88
5[c]	$CH_2CH_2CO_2Et$	Et_2O	25	6	96	90
6	$CH_2C_6H_5$	THF	25	0.5	99	85
7	$CH_2(4\text{-}CH_3OC_6H_4)$	THF	25	10	80	86
8	$CH_2(4\text{-}CF_3C_6H_4)$	THF	25	0.5	99	82
9[c]	$CH_2OTBDPS$	THF	25	5	86	81
10	F	Et_2O	30	3.5	80	91

[a] Isolated yield from reaction of 1.0 mmol substrate at 0.033 M in solvent, unless otherwise noted. [b] Determined by chiral GC or HPLC. [c] 4 mol% $Pd_2(dba)_3$, 10 mol% (*S*)-*t*-BuPHOX (**1**), 0.021 M.

Characterization data for substrate compounds:



SM1

SM1: Prepared by method 1. The reaction was quenched with 10% HCl. The product was isolated by bulb-to-bulb distillation once at 150-155 °C (bath temp, 2 torr), then at 136 °C (bath temp, 2 torr). 75% yield. R_f = 0.53 (10:1 Hexane:EtOAc); ^{1}H NMR (300 MHz, $CDCl_3$, mixture of enol tautomers) δ 12.14 (s, 0.7H), 5.99 (dddd, J = 5.7, 5.7, 10.8, 17.1 Hz, 0.7H), 5.96 (dddd, J = 5.7, 5.7, 10.2, 17.1 Hz, 0.3H), 5.38 (dddd, J = 1.5, 1.5, 1.5, 17.1 Hz, 0.3H), 5.37 (dddd, J = 1.5, 1.5, 1.5, 17.1 Hz, 0.7H), 5.24 (dddd, J = 1.5, 1.5, 1.5, 10.5 Hz, 1H), 4.72-4.55 (m, 2H), 3.41 (ddd, J = 1.5, 6.6, 9.6 Hz, 0.3H), 2.52 (dddd, J = 1.5, 5.4, 5.4, 14.1 Hz, 0.3H), 2.37 (m, 0.3H), 2.26 (m, 2.7H), 2.22-2.10 (m, 0.6H), 2.04-1.78 (m, 0.9H), 1.75-1.55 (m, 3.3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 205.9, 172.4, 172.2, 169.6, 132.3, 131.8, 118.4, 117.7, 97.5, 65.6, 64.6, 57.2, 41.5, 29.9, 29.1, 27.0, 23.3, 22.3, 22.3, 21.9; IR (Neat Film NaCl) 3086, 2941, 1746, 1716, 1659, 1617, 1299, 1259, 1217, 1176, 831 cm^{-1}; HRMS (EI) m/z calc'd for $C_{10}H_{14}O_3$ $[M]^+$: 182.0943, found 182.0941.

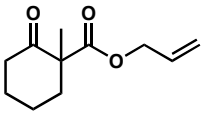


Table 1, Entry 1. Prepared by method 1. 62% yield. R_f = 0.38 (10:1 Hexane:EtOAc); ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.85 (dddd, *J* = 17.1, 10.2, 5.9, 5.9 Hz, 1H), 5.24 (m, 2H), 4.59 (d, *J* = 5.7 Hz, 2H), 2.58-2.34 (comp. m, 3H), 2.08-1.88 (m, 1H), 1.80-1.54 (comp. m, 3H), 1.52-1.37 (m, 1H), 1.27 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 207.9, 172.6, 131.4, 118.7, 65.6, 57.1, 40.5, 38.1, 27.4, 22.5, 21.1; IR (Neat Film NaCl) 3086, 2939, 2867, 1715, 1452, 1259, 1211, 1159, 1084, 976 cm^{-1}; HRMS (EI) *m/z* calc'd for $C_{15}H_{16}O_3$ $[M]^+$: 196.1099, found 196.1096.

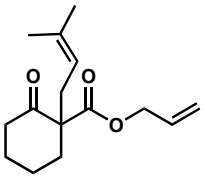


Table 1, Entry 3. Prepared by method 3 part B from **SM1** and prenyl bromide. Flash chromatography (SiO_2, 2→12% Et_2O in pentane). 20% yield. R_f = 0.24 (10% Et_2O in pentane); ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.87 (dddd, *J* = 17.1, 10.4, 5.8, 5.8 Hz, 1H), 5.31 (d, *J* = 17.1 Hz, 1H), 5.24 (d, *J* = 10.1 Hz, 1H), 5.06 (t, *J* = 7.7 Hz, 1H), 4.59 (d, *J* = 5.7 Hz, 2H), 2.65-2.27 (comp. m, 5H), 2.07-1.93 (m, 1H), 1.79-1.69 (m, 1H), 1.68 (s, 3H), 1.66-1.59 (m, 1H), 1.58 (s, 3H), 1.54-1.39 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 207.7, 171.4, 134.8, 131.6, 118.8, 118.5, 65.7, 61.3, 41.2, 35.5, 33.2, 27.5, 26.0, 22.5, 17.8; IR (Neat Film NaCl) 2938, 2863, 1714, 1451, 1438, 1210, 1178, 989 cm^{-1}; HRMS (EI) *m/z* calc'd for $C_{15}H_{22}O_3$ $[M]^+$: 250.1569, found 250.1574.

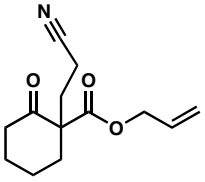


Table 1, Entry 4. Prepared by method 3 part B from **SM1** and acrylonitrile. Flash chromatography (SiO_2, 10% Et_2O in pentane). 55% yield. R_f = 0.27 (CH_2Cl_2); ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.91 (dddd, *J* = 17.6, 10.2, 6.0, 6.0 Hz, 1H), 5.41-5.25 (m, 2H), 4.68 (d, *J* = 6.0 Hz, 2H), 2.64-2.38 (comp. m, 4H), 2.37-2.13 (comp. m, 2H), 2.13-1.86 (comp. m, 2H), 1.85-1.40 (comp. m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 207.0, 170.6, 130.9, 120.0, 119.3, 66.4, 59.7, 40.9, 36.7, 30.8, 27.4, 22.4, 13.0; IR (Neat Film NaCl) 2945, 2868, 2248, 1713, 1450, 1192, 1136, 941 cm^{-1}; HRMS (EI) *m/z* calc'd for $C_{13}H_{17}NO_3$ $[M]^+$: 235.1208, found 235.1218.

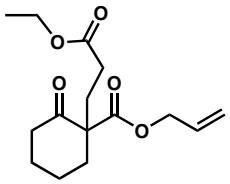


Table 1, Entry 5. Prepared by method 3 part B from **SM1** and ethyl acrylate. Flash chromatography (SiO_2, 10% Et_2O in pentane). 81% yield. R_f = 0.37 (30% Et_2O in pentane); ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.89 (dddd, *J* = 17.3, 10.3, 5.9, 5.9 Hz, 1H), 5.33 (dd, *J* = 17.3, 1.1 Hz, 1H), 5.26 (dd, *J* = 10.4, 1.3 Hz, 1H), 4.63 (app. t, *J* = 14.9 Hz, 2H), 4.11 (q, *J* = 7.2 Hz, 2H), 2.51-2.31 (comp. m, 4H), 2.31-2.11 (comp. m, 2H), 2.08-1.85 (comp. m, 2H), 1.84-1.57 (comp. m, 3H), 1.55-1.40 (m, 1H), 1.24 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 207.4, 173.0, 171.4, 131.3, 119.3, 65.9, 60.4, 60.1, 41.0, 36.2, 29.6, 29.5, 27.5, 22.5, 14.2; IR (Neat Film NaCl) 2943, 2868, 1734, 1715, 1456, 1181 cm^{-1}; HRMS (EI) *m/z* calc'd for $C_{15}H_{22}O_5$ [M]$^+$: 282.1467, found 282.1474.

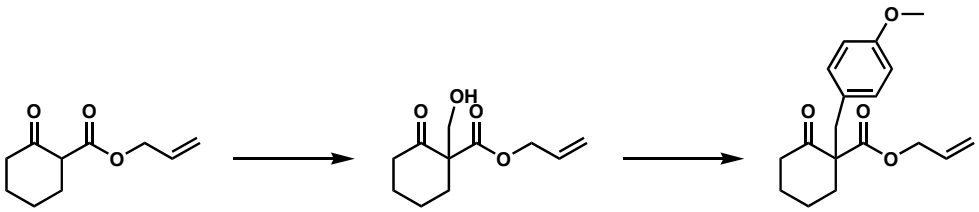


Table 1, Entry 7. To a cooled (0 °C) solution of **SM1** (4.00 g, 22.0 mmol, 1.0 equiv) in THF (40 ml) was added 35% aqueous formaldehyde (11.3 mL) and $KHCO_3$ (5.93 g, 65.9 mmol, 3.0 equiv). After 30 min at 0 °C the reaction mixture was allowed to warm to ambient temperature. After an additional 90 min, the reaction was quenched with water (100 mL) and DCM (100mL). After the layers were separated, the aqueous layer was extracted with DCM (4 x 50 mL), the combined organics dried (Na_2SO_4), and evaporated. The oil obtained was treated with THF (40 mL) and 3M HCl (4 drops) for 60 min, concentrated, and purified by flash chromatography (SiO_2, 10→45% EtOAc in hexanes) to give **SM2** (3.75g, 81% yield). To a cooled (0 °C) suspension of 60% NaH (251 mg, 6.28 mmol, 1.1 equiv) in DMF (20 mL) was added **SM2** (1.20g, 5.71 mmol, 1.0 equiv) in a dropwise manner over 2 min. Once gas evolution had ceased (10 min), Bu_4NI (527 mg, 1.43 mmol. 0.25 equiv) and PMB-Cl (930 μL, 6.85 mmol, 1.2 equiv) were added, and the reaction mixture slowly allowed to warm to ambient temperature. After 12 h, the reaction mixture was quenched with water (50 mL) and 2/1 DCM/hexanes (50 mL), the aqueous layer extracted with 2/1 DCM/hexanes (3 x 50 mL), dried (Na_2SO_4), evaporated, and purified by flash chromatography (SiO_2, 10→20% Et_2O in hexanes) to give the desired compound (485 mg, 28% yield). R_f = 0.30 (30% Et_2O in pentane); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.03 (d, *J* = 8.7 Hz, 2H), 6.77 (d, *J* = 8.7 Hz, 2H), 5.89-5.76 (m, 1H) 5.31-5.21 (m, 2H), 4.59-4.47 (m, 2H), 3.76 (s, 3H), 3.25 (d, *J* = 14.1 Hz, 1H), 2.84 (d, *J* = 14.1 Hz, 1H), 2.51-2.35 (m, 3H), 2.04-1.96 (m, 1H), 1.76-1.54 (m, 3H), 1.50-1.40 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 207.2, 170.8, 158.4, 131.4, 131.3, 128.4, 119.1, 113.4, 65.8, 62.3, 55.1, 41.3, 39.5, 35.8, 27.5, 22.5; IR (Neat Film NaCl) 2943, 1713, 1612, 1513, 1247, 1179 cm^{-1}; HRMS (EI) *m/z* calc'd for $C_{18}H_{22}O_4$ [M]$^+$: 302.1518, found 302.1514.

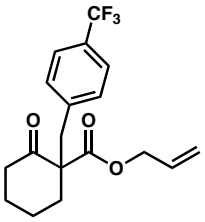


Table 1, Entry 8. Prepared by method 1 with 4-(trifluoroumethyl)benzyl bromide. Flash chromatography (SiO_2, 2→12% Et_2O in pentane). 56% yield. Mp 40-41 ºC; R_f = 0.63 (30% Et_2O in pentane); ^1H NMR (300 MHz, C_6D_6) δ 7.29 (d, J = 8.1 Hz, 2H), 7.02 (d, J = 8.1 Hz, 2H), 5.45 (dddd, J = 17.3, 10.4, 6.0, 6.0 Hz, 1H), 4.91 (m, 2H), 4.18 (m, 2H), 3.34 (d, J = 13.7 Hz, 1H), 2.78 (d, J = 13.7 Hz, 1H), 2.37-2.15 (comp. m, 3H), 1.57-1.38 (comp. m, 2H), 1.32-1.11 (comp. m, 2H), 1.09-0.94 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 206.7, 170.4, 140.8 (q, J_{CF} = 1.2 Hz), 131.0, 130.7, 129.0 (q, J_{CF} = 32.3 Hz), 124.9 (q, J_{CF} = 3.9 Hz), 124.2 (q, J_{CF} = 271.7 Hz), 119.4, 65.9, 62.2, 41.2, 40.2, 36.2, 27.5, 22.5; ^{19}F NMR (282 MHz, $CDCl_3$) δ -63.0; IR (Neat Film NaCl) 2945, 1715, 1326, 1164, 1123, 1068 cm^{-1}; HRMS (EI) m/z calc'd for $C_{18}H_{19}F_3O_3$ $[M]^+$: 340.1286, found 340.1277.

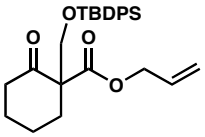


Table 1, Entry 9. To a solution of **SM2** (1.20 g, 5.71 mmol. 1.0 equiv), imidazole (583 mg, 8.57 mmol, 1.5 equiv), and DMAP (1.04 g, 8.57 mmol, 1.5 equiv) in DMF (20 mL) was added TBDPS-Cl (1.75 mL, 6.85 mmol, 1.2 equiv). After 24 h at ambient temperature, the reaction mixture was poured into water (75 mL) and 2/1 DCM/hexanes (150 mL), extracted with 2/1 DCM/hexanes (4 x 30 mL), dried (Na_2SO_4), and evaporated. Flash chromatography (SiO_2, 2.5→12% EtOAc in hexanes) gave the desired compound (1.85 g, 72% yield). Mp 59-60 °C; R_f = 0.24 (10% Et_2O in pentane); ^1H NMR (300 MHz, $CDCl_3$) δ 7.72-7.68 (m, 4H), 7.48-7.37 (m, 6H), 6.00-5.86 (m, 1H), 5.38-5.31 (m, 1H), 5.28-5.23 (m, 1H), 4.74-4.59 (m, 2H), 4.24 (d, J = 9.9 Hz, 1H), 3.82 (d, J = 9.9 Hz, 1H), 2.78 (dq, J = 13.4, 3.3 Hz, 1H), 2.53-2.38 (m, 2H), 2.10-1.99 (m, 1H), 1.88-1.54 (m, 4H) 1.07 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 206.4, 169.8, 135.6, 135.5, 133.1, 132.9, 131.5, 129.6, 127.6(2C), 118.8, 66.4, 65.8, 62.9, 41.2, 33.6, 27.3, 26.6, 22.1, 19.2; IR (Neat Film NaCl) 3072, 2933, 2858, 1715, 1428, 1200, 1112, 703 cm^{-1}; HRMS (EI) m/z calc'd for $C_{27}H_{33}O_4Si$ $[M-H]^+$: 449.2148, found 449.2165.

Allyl 2-Fluoro-2-Cyclohexanonecarboxylate:[9]

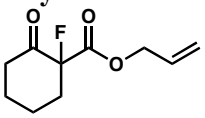
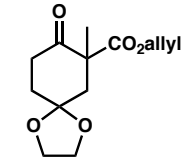
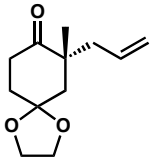
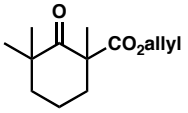
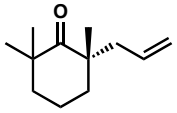
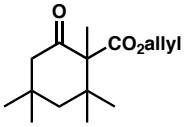
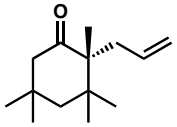
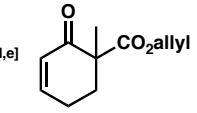
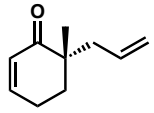
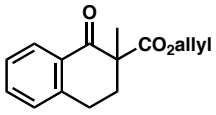
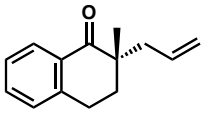
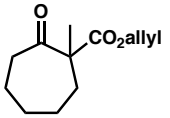
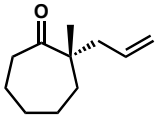
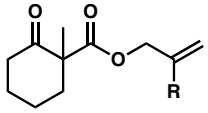
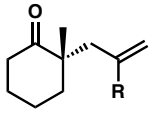
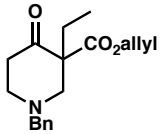
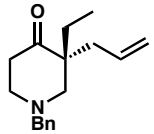


Table 1, Entry 10. To a solution of **SM1** (946.4 mg, 5.19 mmol, 1 equiv) in 50 mL CH_3CN, was added $TiCl_4$ (50 mL, 0.456 mmol, 0.09 equiv). Select-fluor (2.2224 g, 6.27 mmol, 1.2 equiv) was added after 10 min and the mixture stirred at rt for 2 h and 40 min, over which time the orange color disappeared. The mixture was partitioned between H_2O (200 mL) and Et_2O (50 mL). The aqueous layer was separated and washed with Et_2O (30 mL). The combined organic layers were dried ($MgSO_4$), concentrated to about 30 mL, passed through a pad of silica which was washed with Et_2O (5 x 10 mL), and evaporated *in vacuo*. The residue was the bulb-to-bulb distilled at 180-190 °C (bath temp, 2 torr) to afford the title compound

as a colorless oil (947.6 mg, 91% yield). R_f = 0.19 (10:1 Hexane:EtOAc); ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.93 (dddd, J = 5.7, 5.7, 10.5, 17.1 Hz, 1H), 5.37 (dddd, J = 1.5, 1.5, 1.5, 17.4 Hz, 1H), 5.29 (dddd, J = 1.5, 1.5, 1.5, 10.5 Hz, 1H), 4.73 (bd, J = 5.7 Hz, 2H), 2.80-2.67 (m, 1H), 2.66-2.38 (m, 2H), 2.24-2.10 (m, 1H), 1.98-1.80 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 201.5 (d, $J_{C\text{-}F}$ = 19.8 Hz), 166.4 (d, $J_{C\text{-}F}$ = 24.8 Hz), 130.8, 119.2, 96.2 (d, $J_{C\text{-}F}$ = 196.9 Hz), 66.5, 39.4, 35.8 (d, $J_{C\text{-}F}$ = 21.8 Hz), 26.4, 20.7 (d, $J_{C\text{-}F}$ = 6.0 Hz); IR (Neat Film NaCl) 3087, 2952, 1759, 1735, 1650, 1452, 1281, 1223, 1150, 1097, 990 cm^{-1}; HRMS (EI) m/z calc'd for $C_{10}H_{13}O_3F$ $[M]^+$: 200.0849, found 200.0858.

Table 2. *Enantioconvergent Decarboxylative Allylation of β-Ketoesters.*

entry	substrate	product	temp (°C)	time (h)	% yield[a]	% ee[b]
1			25	1.5	94	85
2[c]			25	24	94	86
3			30	9	89	90
4			25	5	90	85
5[d,e]			30	4	77	90
6[d]			25	10	97	92
7			25	9.5	83	87
8[d]			R = CH_3	35	6.5	87	92
9[d,e]			R = Cl	35	2.5	87	91
10			25	2.5	91	92

[a] Isolated yield from reaction of 1.0 mmol substrate, 2.5 mol% $Pd_2(dba)_3$, and 6.25 mol% (*S*)-*t*-BuPHOX (**1**) at 0.033 M in THF, unless otherwise noted. [b] Determined by chiral GC or HPLC. [c] 25 mmol substrate, 1.5 mol% $Pd_2(dba)_3$, and 3.75 mol% (*S*)-*t*-BuPHOX (**1**). [d] Performed in Et_2O. [c] 4 mol% $Pd_2(dba)_3$, and 10 mol% (*S*)-*t*-BuPHOX (**1**), at 0.021 M.

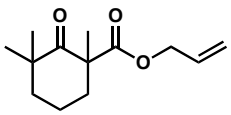


Table 2, Entry 3. To a cooled (-78 °C) solution of LDA (13.5 mmol, 1.12 equiv) in THF (30 mL) was added 2,2,6-trimethylcyclohexanone (1.6938 g, 12.08 mmol, 1.0 equiv) dropwise. The resulting solution was warmed to 0 °C for 1 hour, cooled to -78 °C and HMPA (2.2 mL, 12.6 mmol, 1.04 equiv) was added. After 5 min, allyl cyanoformate (1.5014g, 13.5 mmol, 1.12 equiv) was added dropwise. The reaction was warmed to rt and allowed to stir overnight. The reaction was then quenched with 50% saturated NH_4Cl (40 mL). The aqueous layer was separated and washed with EtOAc (3 x 20 mL). The combined organic extracts were washed with brine, dried (Na_2SO_4), filtered and concentrated *in vacuo*. The resulting oil was purified by flash chromatography (SiO_2, 3% Et_2O in hexanes) to afford the β-keto ester as a colorless oil (585.6 mg, 22%), along with the known enol carbonate (R_f = 0.53, 10:1 Hexane:EtOAc) as a colorless oil (1.3117 g, 48%). R_f = 0.50 (10:1 Hexane:EtOAc); ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.87 (dddd, *J* = 5.7, 5.7, 10.2, 16.8 Hz, 1H), 5.30 (dddd, *J* = 1.2, 1.2, 1.2, 17.1 Hz, 1H), 5.22 (dddd, *J* = 0.9, 0.9, 0.9, 10.2 Hz, 1H), 4.62 (dddd, *J* = 1.2, 1.2, 5.7, 13.2 Hz, 1H), 4.51 (dddd, *J* = 1.2, 1.2, 5.7, 13.2 Hz, 1H), 2.54 (dddd, *J* = 2.4, 3.9, 3.9, 13.8 Hz, 1H), 1.98 (ddddd, *J* = 3, 4.2, 12, 14.1, 15.6 Hz, 1H), 1.77-1.68 (m, 1H), 1.66-1.52 (m, 2H), 1.42 (ddd, *J* = 4.2, 12.3, 13.8, 1H), 1.32 (s, 3H), 1.09 (s, 3H), 1.06 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 211.4, 172.4, 131.5, 118.8, 65.7, 55.1, 46.1, 40.6, 36.8, 26.8, 25.5, 23.6, 18.5; IR (Neat Film NaCl) 3089, 2938, 1736, 1707, 1649, 1456, 1377, 1243, 1209, 1174, 1150, 972 cm^{-1}; HRMS (EI) *m/z* calc'd for $C_{13}H_{20}O_3$ $[M]^+$: 224.1413, found 224.1413.

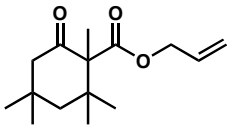


Table 2, Entry 4. Prepared by a modification of method 3. Part 1: Reaction of 3,3,5,5-tetramethylcyclohexanone in benzene (1 M) at 80 °C for 40 h using NaH (2 equiv) and diallylcarbonate (3 equiv) gave an ~1:1 mixture of mono and bisacylated material after flash chromatography (SiO_2, 1→8% Et_2O in hexanes). Part 2: Reaction in acetone (0.42 M) at 75 °C in a sealed flask for 24 h using Cs_2CO_3 (3 equiv) and MeI (4 equiv). Flash chromatography (SiO_2, 1→4% Et_2O in hexanes) gave the desired compound. 25% overall yield. R_f = 0.60 (25% Et_2O in pentane); ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.87 (dddd, *J* = 17.4, 10.5, 6.0, 6.0 Hz, 1H), 5.29 (d, *J* = 17.1 Hz, 1H), 5.22 (d, *J* = 10.5 Hz, 1H), 4.55 (d, *J* = 6.0 Hz, 2H), 2.78 (d, *J* = 13.5 Hz, 1H), 2.23-2.12 (comp. m, 2H), 1.33 (d, *J* = 14.4 Hz, 1H), 1.26 (s, 3H), 1.11 (s, 3H), 1.04 (s, 3H), 1.01 (s, 3H), 0.92 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 208.9, 171.5, 131.5, 118.8, 65.5, 62.6, 51.7, 49.4, 40.9, 34.8, 34.5, 29.6, 27.7, 26.9, 14.7; IR (Neat Film NaCl) 3087, 2959, 1715, 1456, 1371, 1216, 1101, 979 cm^{-1}; HRMS (EI) *m/z* calc'd for $C_{15}H_{24}O_3$ $[M]^+$: 252.1725, found 252.1719.

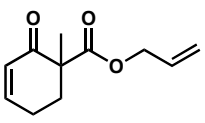


Table 2, Entry 5. Prepared by method 3 from cyclohex-2-en-1-one. Flash chromatography (SiO_2, CH_2Cl_2). 23% yield. R_f = 0.38 (30% Et_2O in pentane). ^{1}H NMR (300 MHz, $CDCl_3$)

δ 6.92 (m, 1H), 6.06 (dt, *J* = 10.1, 2.1 Hz, 1H), 5.86 (dddd, *J* = 17.3, 10.4, 5.6, 5.6 Hz, 1H), 5.24 (m, 2H), 4.61 (m, 2H), 2.57-2.41 (m, 2H), 2.41-2.27 (m, 1H), 1.97-1.82 (m, 1H), 1.41 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 196.8, 172.3, 149.4, 131.6, 128.9, 118.3, 65.7, 53.4, 33.3, 23.6, 20.3; IR (Neat Film NaCl) 2936, 1733, 1678, 1249, 1192, 1110 cm^{-1}; HRMS (EI) *m/z* calc'd for $C_{11}H_{14}O_3$ $[M]^+$: 194.0943, found 194.0941.

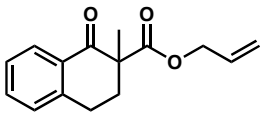


Table 2, Entry 6. Prepared by method 3 from 1-tetralone. Flash chromatography (SiO_2, 10% Et_2O in pentane). 60% yield. R_f = 0.61 (30% Et_2O in pentane); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.06 (d, *J* = 7.8 Hz, 1H), 7.47 (app. t, *J* = 7.5 Hz, 1H), 7.31 (app. t, *J* = 8.1 Hz, 1H), 7.22 (d, *J* = 7.8 Hz, 1H), 5.79 (dddd, *J* = 17.1, 10.7, 5.4, 5.4 Hz, 1H), 5.19-5.09 (m, 2H), 4.58 (m, 2H), 3.12-2.87 (m, 2H), 2.68-2.57 (m, 1H), 2.13-2.01 (m, 1H), 1.52 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 195.9, 172.5, 143.1, 133.4, 131.7, 131.5, 128.7, 128.0, 126.8, 118.0, 65.6, 53.9, 33.9, 26.0, 20.6; IR (Neat Film NaCl) 3071, 2982, 2938, 1736, 1690, 1602, 1456, 1377, 1308, 1228, 1189, 1112, 979, 743 cm^{-1}; HRMS (EI) *m/z* calc'd for $C_{15}H_{16}O_3$ $[M]^+$: 244.1099, found 244.1094.

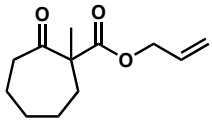


Table 2, Entry 7. Prepared by method 3 from cycloheptanone. Flash chromatography (SiO_2, 25→100% CH_2Cl_2 in pentane). 30% yield. R_f = 0.60 (30% Et_2O in pentane); ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.88 (dddd, *J* = 17.3, 10.4, 5.6, 5.6 Hz, 1H), 5.26 (m, 2H), 4.61 (m, 2H), 2.81-2.67 (m, 1H), 2.57-2.45 (m, 1H), 2.25-2.11 (m, 1H), 1.91-1.70 (comp. m, 3H), 1.69-1.49 (comp. m, 4H), 1.36 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 173.2, 131.6, 118.5, 65.6, 58.8, 42.0, 35.4, 30.1, 25.8, 24.7, 21.5; IR (Neat Film NaCl) 2936, 1740, 1710, 1229, 1151, 1105 cm^{-1}; HRMS (EI) *m/z* calc'd for $C_{12}H_{18}O_3$ $[M]^+$: 210.1256, found 210.1249.

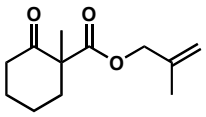


Table 2, Entry 8. Prepared by method 3 from cyclohexanone with dimethyallyl carbonate in part 1. Flash chromatography (SiO_2, 10% Et_2O in pentane). 46% yield. R_f = 0.24 (10% Et_2O in pentane); ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.94 (m, 2H), 4.54 (s, 2H), 2.58-2.42 (comp. m, 3H), 2.08-1.93 (m, 1H), 1.80-1.57 (comp. m, 6H), 1.55-1.40 (m, 1H), 1.32 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 208.1, 172.8, 139.4, 113.5, 68.4, 57.2, 40.6, 38.2, 27.5, 22.6, 21.3, 19.5; IR (Neat Film NaCl) 2940, 2867, 1715, 1452, 1260, 1211, 1160, 1086, 907 cm^{-1}; HRMS (EI) *m/z* calc'd for $C_{12}H_{18}O_3$ $[M]^+$: 210.1256, found 210.1256.

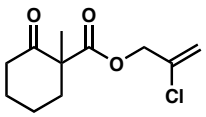


Table 2, Entry 9. Prepared by method 3 from cyclohexanone with 1.25 equiv of 2-chloroallyl carbonate (*vide infra*) in part 1. Flash chromatography (SiO_2, 10% Et_2O in

pentane). 62% yield. R_f = 0.20 (10% Et_2O in pentane); ^1H NMR (300 MHz, $CDCl_3$) δ 5.45 (m, 2H), 4.71 (m, 2H), 2.62-2.41 (comp. m, 3H), 2.10-1.93 (m, 1H), 1.81-1.62 (comp. m, 3H), 1.57-1.41 (m, 1H), 1.34 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 207.8, 172.3, 135.4, 115.8, 66.5, 57.2, 40.6, 38.2, 27.4, 22.5, 21.2; IR (Neat Film NaCl) 2942, 2868, 1716, 1640, 1453, 1248, 1221, 1153, 1084, 903 cm^{-1}; HRMS (EI) *m/z* calc'd for $C_{11}H_{15}O_3Cl$ $[M]^+$: 230.0710, found 230.0711.

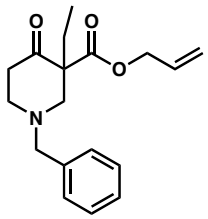


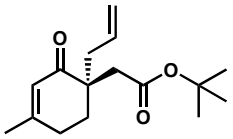
Table 2, Entry 10. Prepared by method 3 from 1-benzylpiperidin-4-one (part 1) and iodoethane (part 2). Flash chromatography (SiO_2, 2.5→20% EtOAc in hexanes). 55% yield. R_f = 0.50 (30% Et_2O in pentane); ^1H NMR (300 MHz, $CDCl_3$) δ 7.33-7.25 (m, 5H), 5.90 (dddd, *J* = 17.4, 10.7, 5.7, 5.7 Hz, 1H), 5.33 (dq, *J* = 17.1, 1.5 Hz, 1H), 5.24 (dq, *J* = 10.4, 1.5 Hz, 1H), 4.70 (ddt, *J* = 13.0, 6.0, 1.4 Hz, 1H), 4.62 (ddt, *J* = 13.0, 6.0, 1.4 Hz, 1H), 3.62 (d, *J* = 13.2 Hz, 1H), 3.56 (d, *J* = 13.2 Hz, 1H), 3.42 (dd, *J* = 11.4, 2.7 Hz, 1H), 3.04-2.80 (m, 2H), 2.45-2.35 (m, 2H), 2.25 (d, *J* = 11.7 Hz, 1H), 1.94-1.82 (m, 1H), 1.65-1.53 (m, 1H), 0.87 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 207.9, 171.3, 137.9, 131.7, 128.8, 128.2, 127.3, 118.7, 65.6, 61.8, 61.5, 61.0, 53.5, 40.6, 25.2, 9.1; IR (Neat Film NaCl) 2966, 2939, 1719, 1224, 1139, 699 cm^{-1}; HRMS (EI) *m/z* calc'd for $C_{18}H_{23}O_3$ $[M]^+$: 301.1678, found 301.1691.

General Procedure for Enantioconvergent Allylation.

(*S*)-2-allyl-2-methylcyclohexanone (Table 1, Entry 1):
A 100 mL rb flask was equipped with a magnetic stir bar and flame dried under vacuum. After cooling under dry nitrogen, $Pd_2(dba)_3$ (22.9 mg, 0.025 mmol, 0.025 equiv) and (*S*)-*t*-BuPHOX (24.2 mg, 0.0625 mmol, 0.0625 equiv) were added. The flask containing the solids was evacuated for 15 min and then refilled with dry nitrogen. Dry THF (30 mL) was then added and the resulting solution stirred at 25 ºC for 30 min. At this point, allyl 1-methyl-2-oxocyclohexanecarboxylate was added via syringe in one portion. When the reaction was complete by TLC, the reaction mixture was evaporated under reduced pressure and the residue purified by column chromatography (SiO_2, 1.5→2.5% Et_2O in pentane) to afford (*S*)-2-allyl-2-methylcyclohexanone (129.6 mg, 85% yield, 88% ee).

The absolute stereochemistry of this product matches that found in our previous work.[1b] The observed stereochemistry of all other known compounds produced in this work matched that of our previous work as well. The shown absolute stereochemistry for all new compounds is inferred by analogy.

Characterization data for new product compounds:



(–)-6

Reaction performed in Et_2O at 30 ºC . Flash chromatography (SiO_2, 3% Et_2O in pentane). 73% yield. R_f = 0.45 (30% Et_2O in pentane). ^1H NMR (300 MHz, $CDCl_3$) δ 5.84 (s, 1H), 5.70 (dddd, *J* = 16.8, 10.2, 7.3, 7.3 Hz, 1H), 5.12-5.11 (m, 2H), 2.71 (d, *J* = 15.6 Hz, 1H), 2.48-2.13 (comp. m, 6H), 1.93 (s, 3H), 1.91-1.81 (m, 1H), 1.40 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 201.0, 170.8, 160.3, 133.3, 125.4, 118.7, 80.5, 45.4, 40.5, 39.0, 29.8, 28.1, 27.8, 24.1; IR (Neat Film NaCl) 2978, 1728, 1670, 1367, 1213, 1152 cm^{-1}; HRMS (EI) *m/z* calc'd for $C_{16}H_{25}O_3$ $[M+H]^+$: 265.1804, found 265.1803; $[\alpha]_D^{25.4}$ –39.22° (*c* 1.05, CH_2Cl_2, 86% ee).

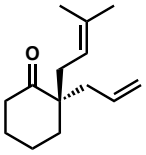


Table 1, Entry 3. Reaction performed in Et_2O at 30 ºC. Flash chromatography (SiO_2, 1.5→2.5% Et_2O in pentane). 97% yield. R_f = 0.38 (10% Et_2O in pentane); ^1H NMR (300 MHz, $CDCl_3$) δ 5.67 (dddd, *J* = 16.5, 10.6, 7.2, 7.2 Hz, 1H), 5.07-4.93 (comp. m, 3H), 2.44-2.24 (comp. m, 5H), 2.16 (dd, *J* = 14.6, 7.2 Hz, 1H), 1.89-1.64 (comp. m, 9H), 1.60 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 214.7, 134.2, 134.1, 119.0, 117.7, 52.1, 39.4, 39.3, 35.9, 33.3, 27.1, 26.0, 20.9, 18.0; IR (Neat Film NaCl) 3075, 2934, 2863, 1706, 1446, 1124, 914 cm^{-1}; HRMS (FAB) *m/z* calc'd for $C_{14}H_{23}O$ $[M+H]^+$: 207.1749, found 207.1744; $[\alpha]_D^{26.0}$ +1.95° (*c* 1.29, CH_2Cl_2, 91% ee).

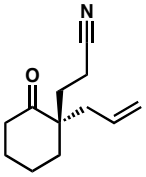


Table 1, Entry 4. Reaction performed in Et_2O. Flash chromatography (SiO_2, 25% Et_2O in pentane). 97% yield. R_f = 0.32 (CH_2Cl_2); ^1H NMR (300 MHz, $CDCl_3$) δ 5.60 (dddd, *J* = 16.7, 10.4, 7.4, 7.4 Hz, 1H), 5.17-5.07 (m, 2H), 2.53-2.16 (comp. m, 6H), 2.03-1.62 (comp. m, 8H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 213.2, 131.9, 120.0, 119.3, 50.8, 39.0, 38.9, 35.4, 30.6, 26.9, 20.5, 12.1; IR (Neat Film NaCl) 3081, 2939, 2863, 2246, 1702, 1453, 1126, 921 cm^{-1}; HRMS (EI) *m/z* calc'd for $C_{12}H_{17}NO$ $[M]^+$: 191.1310, found 191.1307; $[\alpha]_D^{25.6}$ -27.00° (*c* 1.56, CH_2Cl_2, 88% ee).

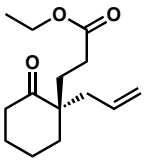


Table 1, Entry 5. Reaction performed in Et_2O. Flash chromatography (SiO_2, 5→14% Et_2O in pentane). 96% yield. R_f = 0.44 (30% Et_2O in pentane); ^1H NMR (300 MHz, $CDCl_3$)

δ 5.66 (dddd, *J* = 16.2, 10.9, 7.7, 7.2 Hz, 1H), 5.11-5.07 (m, 1H), 5.07-5.02 (m, 1H), 4.11 (app. q, *J* = 7.1 Hz, 2H), 2.48-2.18 (comp. m, 5H), 2.16-1.94 (comp. m, 2H), 1.90-1.65 (comp. m, 7H), 1.24 (app. t, *J* = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 214.2, 173.5, 133.3, 118.3, 60.4, 50.8, 39.1, 39.0, 36.2, 29.7, 28.8, 27.0, 20.7, 14.2; IR (Neat Film NaCl) 3076, 2937, 2866, 1735, 1704, 1454, 1377, 1309, 1181, 917 cm^{-1}; HRMS (EI) *m/z* calc'd for $C_{14}H_{22}O_3$ $[M]^+$: 238.1569, found 238.1574; $[\alpha]_D^{25.8}$ +9.60° (*c* 1.13, CH_2Cl_2, 90% ee).

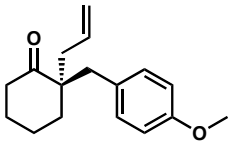


Table 1, Entry 7. Flash chromatography (SiO_2, 3% Et_2O in pentane). 80% yield. R_f = 0.54 (30% Et_2O in pentane); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.02 (d, *J* = 9.0 Hz, 2H), 6.79 (d, *J* = 8.4 Hz, 2H), 5.72 (dddd, *J* = 17.1, 9.8, 7.0, 7.0 Hz, 1H), 5.12-4.98 (m, 2H), 3.78 (s, 3H), 2.84 (s, 2H), 2.53-2.34 (m, 2H), 2.33-2.17 (m, 2H), 1.91-1.70 (comp. m, 4H), 1.70-1.61 (comp. m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 214.3, 158.1, 133.9, 131.5, 129.5, 118.1, 113.4, 55.2, 52.6, 40.1, 39.6, 39.3, 35.4, 26.8, 20.8; IR (Neat Film NaCl) 3076, 2935, 2863, 2361, 1702, 1611, 1513, 1456, 1249, 1179, 1036, 834 cm^{-1}; HRMS (EI) *m/z* calc'd for $C_{17}H_{22}O_2$ $[M]^+$: 258.1620, found 258.1627; $[\alpha]_D^{25.9}$ +3.60° (*c* 1.05, CH_2Cl_2, 86% ee).

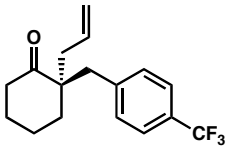


Table 1, Entry 8. Flash chromatography (SiO_2, 8→14% Et_2O in pentane). 99% yield. R_f = 0.85 (30% Et_2O in pentane); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.50 (d, *J* = 7.7 Hz, 2H), 7.24 (d, *J* = 8.0 Hz, 2H), 5.71 (dddd, *J* = 17.0, 10.1, 7.4, 6.9 Hz, 1H), 5.17-5.04 (m, 2H), 3.01 (d, *J* = 13.8 Hz, 1H), 2.88 (d, *J* = 13.8 Hz, 1H), 2.50-2.31 (comp. m, 3H), 2.29-2.17 (m, 1H), 1.97-1.82 (m, 1H), 1.82-1.69 (comp. m, 3H), 1.70-1.59 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 213.3, 142.0 (q, J_{CF} = 1.2 Hz), 133.0, 130.9, 128.4 (q, J_{CF} = 32.3 Hz), 124.7 (q, J_{CF} = 3.9 Hz), 124.2 (q, J_{CF} = 271.7 Hz), 118.5, 52.5, 40.4, 39.3, 39.3, 35.5, 26.6, 20.6; ^{19}F NMR (282 MHz, $CDCl_3$) δ -62.9; IR (Neat Film NaCl) 3076, 2940, 2867, 1705, 1618, 1418, 1326, 1164, 1123, 1068, 852 cm^{-1}; HRMS (EI) *m/z* calc'd for $C_{17}H_{19}F_3O$ $[M]^+$: 296.1388, found 296.1402; $[\alpha]_D^{26.6}$ –16.31° (*c* 1.17, CH_2Cl_2, 82% ee).

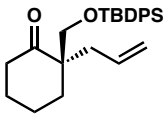


Table 1, Entry 9. Flash chromatography (SiO_2, 1→2.5% EtOAc in hexanes). 92% yield. R_f = 0.32 (5% EtOAc in hexanes); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.68-7.64 (m, 4H), 7.46-7.36 (m, 6H), 5.69-5.55 (m, 1H), 5.38-5.31 (m, 1H), 5.08-4.99 (m, 2H), 3.84 (d, *J* = 10.2 Hz, 1H), 3.66 (d, *J* = 10.2 Hz, 1H), 2.48 (d, *J* = 7.5 Hz, 2H), 2.40-2.20 (m, 2H), 1.90-1.60 (m, 6H), 1.06 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 213.4, 135.7, 133.8, 133.3(2C), 129.7, 129.6, 127.6(2C), 117.9, 66.4, 53.8, 39.7, 37.3, 34.0, 26.9(2C), 21.0, 19.3; IR (Neat Film NaCl) 3072, 2933, 2858, 1708, 1428, 1113, 703 cm^{-1}; HRMS (FAB) *m/z* calc'd for $C_{26}H_{35}O_2Si$ $[M+H]^+$: 407.2406, found 407.2398; $[\alpha]_D^{25}$ –3.96° (*c* 5.00, $CHCl_3$, 81% ee).

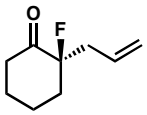


Table 1, Entry 10. Reaction performed in Et_2O at 30 ºC. Flash chromatography (SiO_2, 2% Et_2O/pentane). 80% yield. R_f = 0.36 (10:1 Hexane:EtOAc); ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.88-5.71 (m, 1H), 5.20-5.10 (m, 2H), 2.76-2.31 (m, 4H), 2.16-2.02 (m, 1H), 1.99-1.78 (m, 4H), 1.75-1.60 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 207.2 (d, $J_{C\text{-}F}$ = 20.0 Hz), 130.7 (d, $J_{C\text{-}F}$ = 3.8 Hz), 119.2, 97.7 (d, $J_{C\text{-}F}$ = 184.3 Hz), 39.4, 38.7 (d, $J_{C\text{-}F}$ = 22.7 Hz), 37.3 (d, $J_{C\text{-}F}$ = 22.2 Hz), 27.2, 21.4 (d, $J_{C\text{-}F}$ = 6.6 Hz); ^{19}F NMR (282 MHz, $CDCl_3$) δ -158.15; IR (Neat Film NaCl) 3080, 2946, 1729, 1642, 1453, 1433, 1126, 923 cm^{-1}; HRMS (EI) *m/z* calc'd for $C_9H_{13}OF$ $[M]^+$: 156.0950, found 156.0946; $[\alpha]_D^{24.4}$ -74.65° (*c* 1.05, CH_2Cl_2, 91% ee).

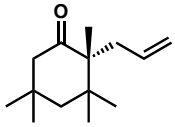


Table 2, Entry 4. Flash chromatography (SiO_2, 1→4% Et_2O in hexanes). 90% yield. R_f = 0.48 (10% Et_2O in hexanes); ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.63-5.46 (m, 1H), 5.10-4.94 (m, 2H), 2.61 (d, *J* = 13.5 Hz, 1H), 2.34 (d, *J* = 12.9 Hz, 1H), 2.11 (d, *J* = 12.9 Hz, 1H), 2.02 (d, *J* = 13.8 Hz, 1H), 1.83 (d, *J* = 14.6 Hz, 1H), 1.40 (d, *J* = 14.5 Hz, 1H), 1.02 (s, 3H), 0.99 (s, 3H), 0.95 (s, 3H), 0.92 (s, 3H), 0.90 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 215.5, 134.2, 117.9, 53.8, 51.0, 49.5, 40.5, 39.1, 35.7, 33.7, 29.8, 26.9, 26.3, 15.4; IR (Neat Film NaCl) 3077, 2957, 1708, 1639, 1460, 1392, 1370, 913 cm^{-1}; HRMS (EI) *m/z* calc'd for $C_{14}H_{24}O$ $[M]^+$: 208.1827, found 208.1837; $[\alpha]_D^{22.5}$ -4.14° (*c* 2.705, hexane, 85% ee).

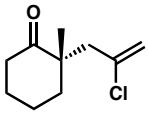


Table 2, Entry 9. Reaction performed in Et_2O at 35 ºC with 4 mol% $Pd_2(dba)_3$ (45.8 mg, 0.040 mmol), and 10 mol% (*S*)-*t*-BuPHOX (48.4 mg, 0.10 mmol). Flash chromatography (SiO_2, 1→2.5% Et_2O in pentane). 87% yield. R_f = 0.63 (30% Et_2O in pentane); ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.27 (app. d, *J* = 1.2 Hz, 1H), 5.15-5.09 (m, 1H), 2.80 (d, *J* = 14.4 Hz, 1H), 2.61 (d, *J* = 14.4 Hz, 1H), 2.56-2.37 (m, 2H), 1.94-1.61 (comp. m, 6H), 1.17 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 214.4, 138.7, 116.3, 48.4, 46.5, 39.2, 38.8, 27.4, 22.7, 21.1; IR (Neat Film NaCl) 2936, 2868, 1708, 1630, 1456, 1126, 887 cm^{-1}; HRMS (EI) *m/z* calc'd for $C_{10}H_{16}ClO$ $[M+H]^+$: 187.0890, found 187.0884; $[\alpha]_D^{26.6}$ –5.40° (*c* 3.21, CH_2Cl_2, 91% ee).

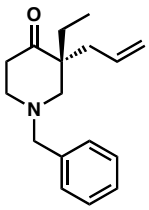


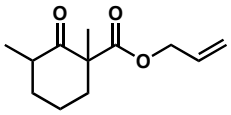
Table 2, Entry 10. Flash chromatography (SiO_2, 5 → 7% Et_2O in pentane). 91% yield. R_f = 0.29 (10% Et_2O in pentane); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.39-7.23 (comp. m, 5H), 5.62 (dddd, *J* = 12.3, 9.6, 7.2, 7.2 Hz, 1H), 5.03 (m, 1H), 4.99 (m, 1H), 3.56 (s, 2H), 2.83-2.69 (m,

1H), 2.65-2.33 (comp. m, 6H), 2.33-2.20 (m, 1H) 1.95 (dq, *J* = 15.3, 7.5 Hz, 1H), 1.51 (dq, *J* = 15.0, 7.5 Hz, 1H), 0.75 (dd, *J* = 7.5, 7.5 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 212.6, 138.6, 133.8, 128.7, 128.3, 127.2, 117.8, 62.2, 61.8, 53.4, 52.2, 39.3, 37.3, 26.7, 7.8; IR (Neat Film NaCl) 3065, 3028, 2965, 2801, 1709, 1454, 1352, 1200, 915, 699 cm^{-1}; HRMS (EI) *m/z* calc'd for $C_{17}H_{23}NO$ $[M]^+$: 257.1780, found 257.1772; $[\alpha]_D^{26.6}$ +31.21° (*c* 1.51, CH_2Cl_2, 92% ee).

Synthesis of substrate (±)-13.

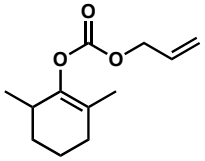
Allyl 2,6-Dimethyl-2-Cyclohexanonecarboxylate (SM3):

To a cooled (-78 °C) solution of LDA (8.0 mmol, 1.09 equiv) in THF (24 mL) was added 2,6-dimethylcyclohexanone (1 mL, 7.33 mmol, 1.0 equiv) dropwise. The resulting solution was warmed to 0 °C for 1 hour, cooled to -78 °C and HMPA (1.3 mL, 7.47 mmol, 1.02 equiv) was added. After 15 min, allyl cyanoformate (845.3 mg, 7.61 mmol, 1.04 equiv) was added dropwise. The reaction was warmed to RT for 30 min and then quenched with 50% saturated NH_4Cl. The aqueous layer was separated and washed with EtOAc (3 x 20 mL). The combined organic extracts were washed with brine, dried (Na_2SO_4), filtered and concentrated *in vacuo*. The resulting oil was purified by flash chromatography (3 x 20 cm, SiO_2, 4% Et_2O in hexanes, then 8% Et_2O in hexanes) to afford β-keto ester **SM3** as a colorless oil (629.1 mg, 41%), along with the corresponding enol carbonate as a colorless oil (187.1 mg, 12%).



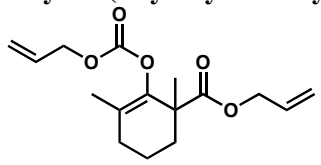
SM3

R_f = 0.43 (10:1 Hexane:EtOAc); ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.86 (dddd, *J* = 6.0, 6.0, 10.5, 17.4 Hz, 1H), 5.28 (dddd, *J* = 1.5, 1.5, 1.5, 17.1 Hz, 1H), 5.22 (dddd, *J* = 1.2, 1.2, 1.2, 10.5 Hz, 1H), 4.63 (dddd, *J* = 1.2, 1.2, 5.4, 13.2 Hz, 1H), 4.56 (dddd, *J* = 1.5, 1.5, 5.7, 13.2 Hz, 1H), 2.61-2.46 (m, 2H), 2.01 (dddd, *J* = 3.2, 3.2, 6.3, 16.2 Hz, 1H), 1.85-1.63 (m, 2H), 1.45-1.31 (m, 2H), 1.28 (s, 3H), 1.03 (d, *J* = 6.3 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 209.1, 172.9, 131.5, 118.7, 65.6, 57.1, 44.3, 38.9, 36.7, 22.8, 21.5, 14.7; IR (Neat Film NaCl) 3087, 2936, 1743, 1715, 1649, 1452, 1377, 1253, 1214, 1161, 976 cm^{-1}; HRMS (EI) *m/z* calc'd for $C_{12}H_{18}O_3$ $[M]^+$: 210.1256, found 210.1249.



R_f = 0.40 (10:1 Hexane:EtOAc); ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.96 (dddd, *J* = 5.7, 5.7, 10.8, 17.1 Hz, 1H), 5.38 (dddd, *J* = 1.2, 1.2, 1.2, 17.1 Hz, 1H), 5.28 (dddd, *J* = 1.2, 1.2, 1.2, 10.5 Hz, 1H), 4.70-4.60 (m. 2H), 2.54-2.40 (m, 1H), 2.04 (m, 2H), 1.92-1.80 (m, 1H), 1.73-1.51 (m, 2H), 1.55 (bs, 3H), 1.47-1.35 (m, 1H), 1.01 (d, *J* = 6.9 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 153.2, 146.0, 131.6, 121.1, 118.8, 68.5, 31.7, 31.2, 30.6, 20.0, 18.2, 16.0; IR (Neat Film NaCl) 3089, 2934, 1755, 1650, 1455, 1366, 1247, 1132, 1035 cm^{-1}; HRMS (EI) *m/z* calc'd for $C_{12}H_{18}O_3$ $[M]^+$: 210.1256, found 210.1249.

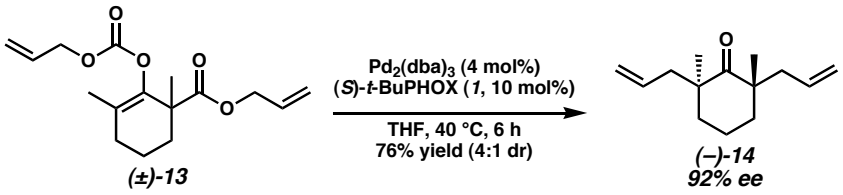
Allyl 2-(allyloxycarbonyloxy)-1,3-dimethylcycohex-2-enecarboxylate (13):



13

To a suspension of KH (155.9 mg, 3.89 mmol, 1.2 equiv, freed from a ~30% dispersion in mineral oil by washing with hexane) in 10 mL THF was added **SM3** (680.9 mg, 3.24 mmol, 1 equiv) dropwise. The mixture was stirred at RT for 2.5 h, at which time it was cooled to -78 °C. Allyl chloroformate (420 μL, 3.95 mmol, 1.2 equiv) was added and the mixture stirred 30 min at -78 °C, then 30 min at rt. The reaction was quenched with 50% saturated NH_4Cl (10 mL). Et_2O (5 mL) was added and the organic layer separated. The aqueous layer was washed with Et_2O (3 x 10 mL). The combined organic layers were dried (Na_2SO_4) and evaporated *in vacuo*. Silica gel chromatography (2 x 16 cm, 20:1 hexane:EtOAc) afforded the title compound **13** as a colorless oil (883 mg, 93% yield). R_f = 0.29 (10:1 Hexane:EtOAc); ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.94 (dddd, *J* = 5.7, 5.7, 10.2, 17.1 Hz, 1H), 5.90 (dddd, *J* = 5.7, 5.7, 10.5, 17.1 Hz, 1H), 5.37 (dddd, *J* = 1.2, 1.2, 1.2, 17.1 Hz, 1H), 5.31 (dddd, *J* = 1.2, 1.2, 1.2, 17.1 Hz, 1H), 5.27 (dddd, *J* = 1.2, 1.2, 1.2, 10.2 Hz, 1H), 5.20 (dddd, *J* = 1.5, 1.5, 1.5, 10.5 Hz, 1H), 4.66-4.58 (m. 3H), 4.55 (dddd, *J* = 1.2, 1.2, 5.4, 13.5 Hz, 1H), 2.25-2.10 (m, 3H), 1.80-1.52 (m, 3H), 1.58 (s, 3H), 1.35 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 174.6, 152.9, 142.0, 132.2, 131.5, 124.7, 118.9, 117.7, 68.7, 65.5, 46.7, 35.8, 30.6, 22.4, 19.2, 17.0; IR (Neat Film NaCl) 3087, 2942, 1760, 1732, 1649, 1452, 1366, 1235, 1168, 992 cm^{-1}; HRMS (EI) *m/z* calc'd for $C_{16}H_{22}O_5$ $[M]^+$: 294.1467, found 294.1464.

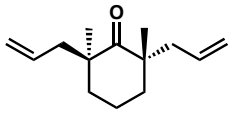
Scheme 5. Enantioselective allylation cascade generating two quaternary carbon stereocenters.



(2*S*,6*S*)-2,6-diallyl-2,6-dimethylcyclohexanone ((–)-14):

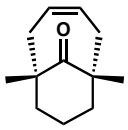
A 50 mL rb flask equipped with a magnetic stir bar was flame dried under vacuum. After cooling under nitrogen, $Pd_2(dba)_3$ (31.4 mg, 0.0343 mmol, 0.034 equiv) and *(S)-t*-Bu-PHOX (31.3 mg, 0.0808 mmol, 0.080 equiv) were added. After the flask was evacuated and filled with nitrogen three times, THF (32 mL) was added and the contents were stirred at 25 °C for 30 min, at which time allyl 2-(allyloxycarbonyloxy)-1,3-dimethylcycohex-2-enecarboxylate (**13**, 298 mg, 1.012 mmol, 1.0 equiv) was added by syringe in one portion. The reaction was stirred at 40 °C for 6 hours at which time TLC indicated complete reaction. The reaction mixture was allowed to cool and then concentrated to ~1 mL under reduced pressure and the residue chromatographed (100 mL pentane, then 1 → 2% Et_2O in pentane on 2 x 14 cm SiO_2) to afford the title compound **14** and a colorless, volatile oil (157.9 mg, 76% yield). GC analysis indicated the isolated compound was an 80:20 mixture (R_f = 0.51, 10:1 Hexane:EtOAc) of C_2-symmetric:meso diastereomers.

In order to obtain an analytical sample of the C_2-symmetric product, the following reaction was performed on the mixture of diastereomers: A solution of the diastereomeric ketones (50.4 mg, 0.244 mmol, 1.0 equiv) in 15 mL CH_2Cl_2 was degassed by bubbling Ar through the solution for 15 min. The second generation Grubbs catalyst (2 mg, 0.00236 mmol, 0.0097 equiv) was added and the mixture heated to 40 °C. After 90 min, GC analysis indicated none of the minor diastereomer was present. The reaction mixture was allowed to cool and then concentrated to ~1-2 mL under reduced pressure and the residue chromatographed (75 mL pentane, then 2→5% Et_2O in pentane on 1.5 x 24 cm SiO_2) to afford the C_2-symmetric diallyl cyclohexanone (–)-**14** (31 mg, 62%), the RCM product (8.3 mg) and 5.8 mg of a mixture of the two compounds.



(–)-14

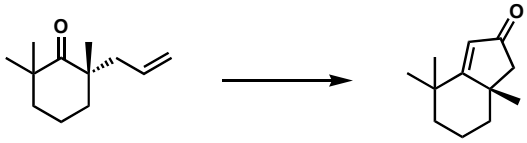
R_f = 0.17 (2% Et_2O in hexane); ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.65 (m, 2H), 5.10-4.95 (m, 4H), 2.33 (dd, J = 6.9, 13.8 Hz, 2H), 2.18 (dd, J = 7.8, 13.8 Hz, 2H), 1.87-1.68 (m, 4H), 1.59-1.48 (m, 2H), 1.06 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 218.6, 134.4, 118.0, 47.6, 43.9, 36.4, 25.0, 17.3; IR (Neat Film NaCl) 3076, 2930, 1694, 1639, 1461, 1374, 992, 914 cm^{-1}; HRMS (EI) m/z calc'd for $C_{14}H_{22}O$ $[M]^+$: 206.1671, found 206.1675; $[\alpha]_D^{23.6}$ -54.04° (*c* 0.95, hexane, 92% ee).



R_f = 0.13 (2% Et_2O in hexane); ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.83-5.72 (m, 2H), 2.53-2.35 (m, 3H), 2.03-1.85 (m, 4H), 1.75-1.62 (m. 2H), 1.48-1.37 (m, 1H), 1.09 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 217.9, 129.4, 48.5, 41.7, 39.0, 27.2, 20.0; IR (Neat Film NaCl) 2965, 1735, 1699, 1458, 1378, 1239 cm^{-1}; HRMS (EI) m/z calc'd for $C_{12}H_{18}O$ $[M]^+$: 178.1358, found 178.1360.

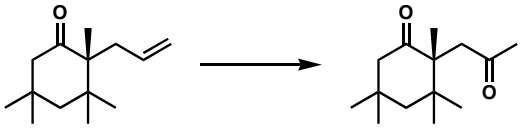
Procedures for Preparation of Derivatives.

Derivatization of (*S*)-2-allyl-2,6,6-trimethylcyclohexanone:



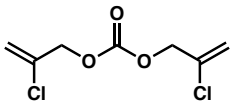
A reaction tube was charged with $PdCl_2$ (10.9 mg, 0.0615 mmol, 0.1 equiv) and $Cu(OAc)_2$ monohydrate (50.9 mg, 0.280 mmol, 0.5 equiv). Dimethylacetamide (DMA, 1.8 mL) and H_2O (0.4 mL) were added, followed by a solution of (*S*)-2-allyl-2,6,6-trimethylcyclohexanone (100 mg, 0.555 mmol, 1 equiv) in DMA (1 mL). The resulting suspension was subjected to three freeze (-78 °C), pump, thaw cycles; backfilling with O_2 each time. The reaction was then allowed to stir under a balloon of O_2 for 20 hours. The reaction mixture was directly applied to a column of silica (1.5 x 26 cm) and eluted with 20% Et_2O/pentane to afford (*S*)-2,2,6-trimethyl-6-(2-oxopropyl)cyclohexanone (80.1 mg, 74%) as

a colorless oil: R_f = 0.16 (10:1 Hexane:EtOAc); ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.27 (d, *J* = 18.3 Hz, 1H), 2.33 (d, *J* = 18 Hz, 1H), 2.06 (s, 3H), 2.01-1.75 (m, 3H), 1.70-1.55 (m, 2H), 1.54-1.44 (m, 1H), 1.17 (s, 3H), 1.12 (s, 3H), 1.11 (s, 3H). A screw cap vial was charged with (*S*)-2,2,6-trimethyl-6-(2-oxopropyl)cyclohexanone (68.6 mg, 0.349, 1 equiv), xylenes (1.4 mL) added, followed by freshly powdered KOH (5.6 mg, 0.1 mmol, 0.29 equiv). The vial was capped and the reaction heated to 110 °C for 10 h. The cooled reaction mixture was then applied to a column of silica (2 x 12 cm) and eluted first with pentane and then with 30% Et_2O/pentane to afford (*S*)-4,4,7a-trimethyl-5,6,7,7a-tetrahydro-1*H*-inden-2(4*H*)-one (61 mg, 98%) as a colorless oil. R_f = 0.11 (10:1 Hexane:EtOAc); ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.82 (s, 1H), 2.29 (s, 2H), 1.97-1.75 (m, *2*H), 1.71-1.53 (m, 2H), 1.47-1.33 (m, 2H), 1.35 (s, 3H), 1.25 (s, 3H), 1.19 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 207.9, 194.2, 126.2, 54.6, 44.1, 41.4, 40.5, 36.4, 31.1, 27.3, 26.1, 18.9; IR (Neat Film NaCl) 2927, 1713, 1697, 1601, 1460, 1260, 1166 cm^{-1}; HRMS (EI) *m/z* calc'd for $C_{12}H_{18}O$ $[M]^+$: 178.1358, found 179.1358; $[\alpha]_D^{23.9}$ -85.37° (*c* 1.07, CH_2Cl_2, 90% ee).



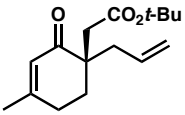
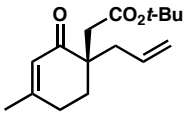
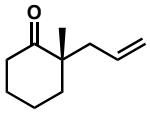
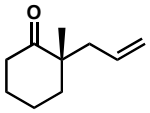
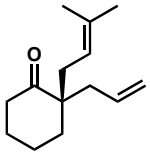
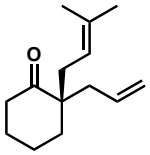
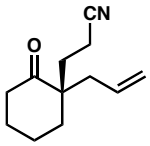
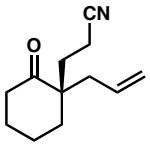
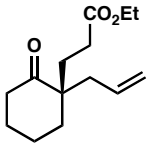
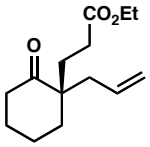
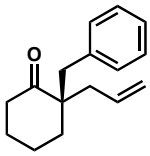
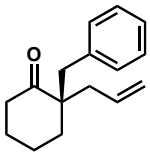
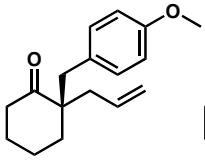
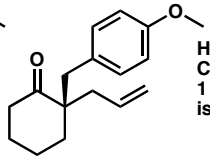
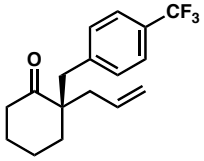
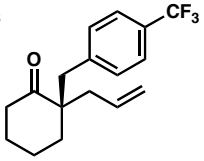
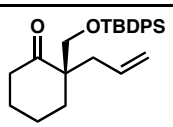
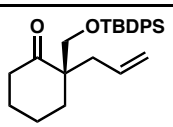
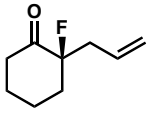
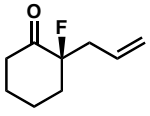
Oxidized via Wacker protocol.[5] Flash chromatography (SiO_2, 5→20% EtOAc in hexanes). 84% yield. R_f = 0.47 (35% EtOAc in hexanes); ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.05 (d, *J* = 16.8 Hz, 1H), 2.43 (d, *J* = 16.8 Hz, 1H), 2.32 (d, *J* = 12.3 Hz, 1H), 2.21 (d, *J* = 12.3 Hz, 1H), 2.17 (s, 3H), 1.59 (d, *J* = 15.0 Hz, 1H), 1.53 (d, *J* = 14.7 Hz, 1H), 1.16 (s, 3H), 1.02 (s, 3H), 1.00 (s, 3H), 0.93 (s, 3H), 0.90 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 213.4, 207.3, 52.5, 49.8, 49.3, 46.9, 41.2, 36.4, 32.1, 31.5, 31.0, 26.5, 25.8, 17.0; IR (Neat Film NaCl) 2956, 1710, 1696, 1411, 1367, 1174 cm^{-1}; HRMS (EI) *m/z* calc'd for $C_{14}H_{24}O_2$ $[M]^+$: 224.1776, found 224.1769; $[\alpha]_D^{24.3}$ -10.78° (*c* 1.04, absolute ethanol, 85% ee).

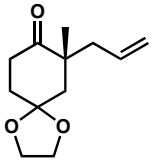
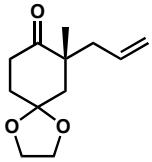
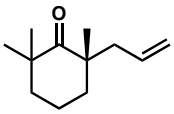
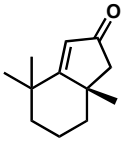
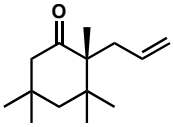
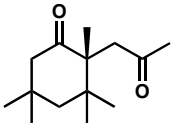
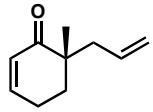
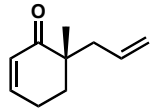
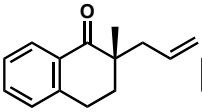
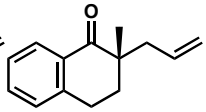
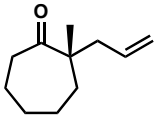
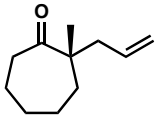
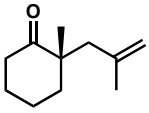
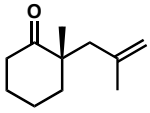
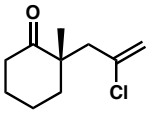
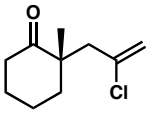
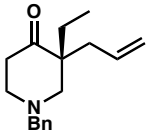
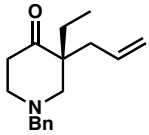
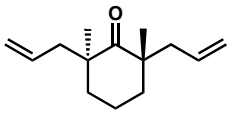
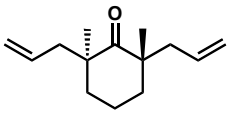
Characterization data for other new compounds:



Prepared by the method of Tsuji.[10] Purified by distillation (110 °C at 25 torr) to give 53% yield. R_f = 0.53 (10% Et_2O in pentane); ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.52 (m, 2H), 5.44 (m, 2H), 4.72 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 153.9, 134.9, 115.5, 69.3; IR (Neat Film NaCl) 3119, 2953, 2887, 1758, 1640, 1442, 1395, 1279, 974, 905 cm^{-1}; HRMS (EI) *m/z* calc'd for $C_7H_9O_3Cl_2$ $[M+H]^+$: 210.9929, found 210.9918.

Table 3. Methods for the determination of enantiomeric excess.

entry	product	compound assayed	assay conditions	retention time of major isomer (min)	retention time of minor isomer (min)	% ee
1			GC, G-TA 130 °C isotherm	59.355	61.189	86
2			GC, G-TA 100 °C isotherm	11.132	12.742	88
3			GC, G-TA 100 °C isotherm	55.506	52.560	91
4			GC, G-TA 150 °C isotherm	18.745	21.056	88
5			GC, G-TA 120 °C isotherm	90.978	94.220	90
6			HPLC Chiracel OJ 2 % EtOH in hexane isocratic, 1.0 mL/min	19.805	13.816	85
7			HPLC Chiracel AD 1 % EtOH in hexane isocratic, 1.0 mL/min	12.868	15.360	86
8			GC, G-TA 120 °C isotherm for 120 mins, then ramp 3 °C/min	127.738	126.429	82
9			HPLC Chiracel OD-H 100 % hexane isocratic, 1.0 mL/min	16.753	23.908	81
10			GC, G-TA 110 °C isotherm	6.274	8.015	91

entry	product	compound assayed	assay conditions	retention time of major isomer (min)	retention time of minor isomer (min)	% ee
11			GC, G-TA 120 °C isotherm	26.896	28.635	86
12			HPLC Chiracel AD 2 % IPA in hexane isocratic, 1.0 mL/min	14.070	12.272	90
13			GC, G-TA 120 °C isotherm	49.120	50.574	85
14			GC, G-TA 100 °C isotherm	15.314	18.040	90
15			HPLC Chiracel OD-H 0.1 % IPA in heptane isocratic, 0.7 mL/min	19.965	21.481	92
16			GC, G-TA 125 °C isotherm	15.599	17.076	87
17			GC, G-TA 100 °C isotherm	15.763	17.649	92
18			GC, G-TA 100 °C isotherm	44.907	50.063	91
19			HPLC Chiracel OJ 1 % EtOH in hexane isocratic, 1.0 mL/min	7.954	8.819	92
20			GC, G-TA 75 °C isotherm	118.507	127.365	92

References:

[1] a) M. Peer, J. C. de Jong, M. Kiefer, T. Langer, H. Rieck, H. Schell, P. Sennhenn, J. Sprinz, H. Steinhagen, B. Wiese, G. Helmchen, *Tetrahedron* **1996**, *52*, 7547-7583; b) D. C. Behenna, B. M. Stoltz, *J. Am. Chem. Soc.* **2004**, *126*, 15044-15045.

[2] D. M. X. Donnelly, J.-P. Finet, B. A. Rattigan, *J. Chem. Soc. Perkin Trans. 1* **1993**, 1729-1735.

[3] J. Tsuji, M. Nisar, I. Shimizu, I. Minami, *Synthesis* **1984**, *12*, 1009.

[4] S. Dua, M. S. Taylor, M. A. Buntine, J. H. Bowie, *J. Chem. Soc. Perkin Trans. 2* **1997**, 1991-1997.

[5] For procedure see supporting information for: D. C. Behenna, B. M. Stoltz, *J. Am. Chem. Soc.* **2004**, *126*, 15044-15045.

[6] H. O. House, W. L. Roelofs, B. M. Trost, *J. Org. Chem.* **1966**, *31*, 646-655.

[7] This procedure is a modification of the cyclization method reported by Tsuji.[3]

[8] This procedure is a modification of the acylation procedure reported in: L. N. Mander, S. P. Sethi, *Tetrahedron Lett.* **1983**, *24*, 5425-5428.

[9] Adapted from a procedure reported in: L. Hintermann, A. Togni, *Angew. Chem.* **2000**, *112*, 4530-4533; *Angew. Chem. Int. Ed.* **2000**, *39*, 4359-4362.

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