Supporting Information for

Enantioselective Pd-Catalyzed Decarboxylative Allylic Alkylation of Thiopyranones. Access to Acyclic, Stereogenic α-Quaternary Ketones.

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Materials and Methods

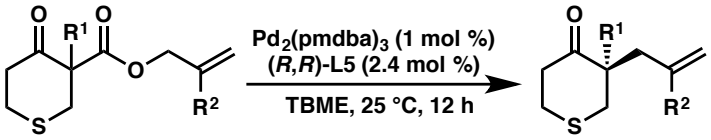
Unless otherwise stated, reactions were performed in flame-dried glassware under an argon or nitrogen atmosphere using dry, deoxygenated solvents. Solvents were dried by passage through an activated alumina column under argon.[1] Reaction progress was monitored by thin-layer chromatography (TLC) or Agilent 1290 UHPLC-MS. TLC was performed using E. Merck silica gel 60 F254 precoated glass plates (0.25 mm) and visualized by UV fluorescence quenching, *p*-anisaldehyde, or $KMnO_4$ staining. Silicycle Silia*Flash*® P60 Academic Silica gel (particle size 40–63 nm) was used for flash chromatography. ^{1}H NMR spectra were recorded on Varian Inova 500 MHz and Bruker 400 MHz spectrometers and are reported relative to residual $CHCl_3$ (δ 7.26 ppm). ^{13}C NMR spectra were recorded on a Varian Inova 500 MHz spectrometer (125 MHz) and Bruker 400 MHz spectrometers (100 MHz) and are reported relative to $CHCl_3$ (δ 77.16 ppm). Data for ^{1}H NMR are reported as follows: chemical shift (δ ppm) (multiplicity, coupling constant (Hz), integration). Multiplicities are reported as follows: s = singlet, d = doublet, t = triplet, q = quartet, p = pentet, sept = septuplet, m = multiplet, br s = broad singlet, br d = broad doublet. Data for ^{13}C NMR are reported in terms of chemical shifts (δ ppm). IR spectra were obtained by use of a Perkin Elmer Spectrum BXII spectrometer or Nicolet 6700 FTIR spectrometer using thin films deposited on NaCl plates and reported in frequency of absorption (cm^{-1}). Optical rotations were measured with a Jasco P-2000 polarimeter operating on the sodium D-line (589 nm), using a 100 mm path-length cell. Analytical SFC was performed with a Mettler SFC supercritical CO_2 analytical chromatography system utilizing Chiralpak (AD-H, AS-H or IC) or Chiralcel (OD-H, OJ-H, or OB-H) columns (4.6 mm x 25 cm) obtained from Daicel Chemical Industries, Ltd. High resolution mass spectra (HRMS) were obtained from Agilent 6200 Series TOF with an Agilent G1978A Multimode source in electrospray ionization (ESI+), atmospheric pressure chemical ionization (APCI+), or mixed ionization mode (MM: ESI-APCI+), or obtained from Caltech mass spectrometry laboratory.

Reagents were purchased from Sigma-Aldrich, Acros Organics, Strem, or Alfa Aesar and used as received unless otherwise stated. Ligands **(*S*)-L1**,[2] **(*S*)-L2**,[3] **(*R*,*R*)-L4**,[4] and **(*R*,*R*)-L5**[5] and substrate **1a**[6] were prepared by known methods.

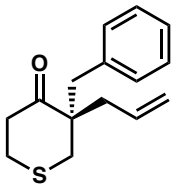
List of Abbreviations:

ee – enantiomeric excess, SFC – supercritical fluid chromatography, TLC – thin-layer chromatography, TBME – *tert*-butyl methyl ether, IPA – isopropanol

General Procedure for Pd-Catalyzed Allylic Alkylation Reactions



In a nitrogen-filled glovebox, $Pd_2(pmdba)_3$ (1.0 mol %, 2.2 mg) and **(*R,R*)-*L5*** (2.4 mol %, 3.9 mg) were added to a 1 dram vial followed by 1.0 mL of TBME. The resulting mixture was stirred at 25 °C for 30 minutes at which time a solution of β-ketoester substrate (0.2 mmol) in 1.0 mL TBME was added. The vial was then sealed with a Teflon-lined cap and electrical tape, removed from the glovebox, and stirred at 25 °C for 12 h. The crude reaction mixture was filtered through Celite®, and the Celite® rinsed with Et_2O. The crude product was purified by silica gel flash chromatography to provide the desired alkylation product.

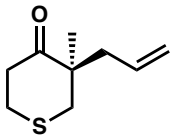


(*S*)-3-allyl-3-benzyltetrahydro-4*H*-thiopyran-4-one (2a)

Purified by column chromatography (10% Et_2O in hexanes) to provide a colorless oil (45.2 mg, 92% yield); 94% ee, $[\alpha]_D^{25}$ +11.0 (*c* 1.05, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 7.32–7.19 (m, 3H), 7.17–7.10 (m, 2H), 5.72 (dddd, *J* = 16.9, 10.3, 7.9, 6.7 Hz, 1H), 5.17–5.07 (m, 2H), 3.14 (d, *J* = 13.8 Hz, 1H), 3.02 (d, *J* = 13.8 Hz, 1H), 2.95–2.85 (m, 2H), 2.83–2.69 (m, 4H), 2.56 (ddt, *J* = 14.4, 7.8, 1.2 Hz, 1H), 2.47 (ddt, *J* = 14.4, 6.7, 1.4 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 211.1, 136.7, 133.2, 130.8, 128.3, 126.8, 119.2, 54.0, 41.6, 40.2, 38.8, 38.0, 29.7; IR (Neat Film, NaCl) 3062, 3028, 2976, 2946, 2913, 1703, 1638, 1604, 1582, 1495, 1453, 1434, 1419, 1312, 1274, 1223, 1129, 1086, 1031, 988, 965, 918, 806, 750, 726, 703 cm^{-1}; HRMS (FAB+) *m/z* calc'd for $C_{15}H_{19}OS$ $[M+H]^+$: 247.1157, found 247.1168; SFC Conditions: 15% IPA, 2.5 mL/min, Chiralcel OJ-H column, λ = 210 nm, t_R (min): minor = 2.87, major = 3.48.

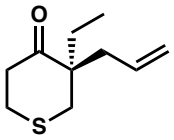
Procedure for Preparatory Scale Preparation of 2a

In a nitrogen-filled glovebox, $Pd_2(pmdba)_3$ (1.0 mol %, 33.0 mg) and **(*R,R*)-*L5*** (2.4 mol %, 58.5 mg) were dissolved in 15.0 mL of TBME, and the resulting mixture was stirred at 25 °C. After 30 minutes, a solution of β-ketoester substrate **1a** (3.0 mmol, 871.1 mg) in 15.0 mL TBME was added, and the reaction flask sealed and removed from the glovebox. After stirring at 25 °C for 12 h, the crude reaction mixture was filtered through Celite®, and the Celite® rinsed with Et_2O. The crude product was purified by silica gel flash chromatography (10% Et_2O in hexanes) to provide **2a** as a colorless oil (649.0 mg, 88% yield): 91% ee.



(*R*)-3-allyl-3-methyltetrahydro-4*H*-thiopyran-4-one (2b)

Purified by column chromatography (10% Et_2O in hexanes) to provide a colorless oil (25.1 mg, 74% yield); 93% ee, $[\alpha]_D^{25}$ +33.6 (*c* 1.25, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.66 (ddt, *J* = 17.0, 10.2, 7.4 Hz, 1H), 5.14–5.06 (m, 2H), 2.96–2.83 (m, 2H), 2.81–2.61 (m, 5H), 2.45–2.37 (m, 1H), 1.19 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 211.9, 132.9, 119.0, 50.0, 41.3, 41.2, 40.9, 30.6, 22.0; IR (Neat Film, NaCl) 3075, 2976, 2929, 2907, 1703, 1638, 1452, 1432, 1420, 1376, 1324, 1270, 1221, 1133, 1090, 996, 976, 919, 811 cm^{-1}; HRMS (FAB+) *m/z* calc'd for $C_9H_{14}OS$ $[M+H]^{\bullet}$: 170.0765, found 170.0790; SFC Conditions: 2% IPA, 2.5 mL/min, Chiralpak AD-H column, λ = 210 nm, t_R (min): minor = 5.09, major = 6.37.

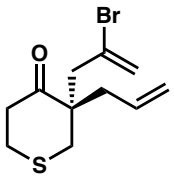


(*R*)-3-allyl-3-ethyltetrahydro-4*H*-thiopyran-4-one (2c)

Purified by column chromatography (5% Et_2O in hexanes) to provide a colorless oil (26.0 mg, 70% yield); 82% ee,* $[\alpha]_D^{25}$ +18.3 (*c* 0.85, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.71–5.56 (m, 1H), 5.08 (dddd, *J* = 13.3, 3.7, 2.2, 1.0 Hz, 2H), 2.94–2.82 (m, 2H), 2.81 (dd, *J* = 14.1, 1.0 Hz, 1H), 2.78–2.67 (m, 2H), 2.69–2.59 (m, 1H), 2.54 (ddt, *J* = 14.3, 7.8, 1.1 Hz, 1H), 2.42–2.33 (m, 1H), 2.10 (dq, *J* = 14.9, 7.5 Hz, 1H), 1.66–1.54 (m, 1H), 0.80 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR (101

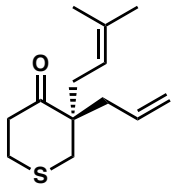
*e.e. determined following cross-metathesis with methyl acrylate

MHz, $CDCl_3$) δ 211.6, 133.3, 118.8, 53.1, 41.3, 39.4, 37.9, 30.4, 26.9, 7.9; IR (Neat Film, NaCl) 3385, 3075, 2966, 2942, 1702, 1639, 1460, 1433, 1420, 1384, 1339, 1313, 1279, 1244, 1104, 1082, 996, 918, 812, 782, 723, 673 cm^{-1}; HRMS (FAB+) *m/z* calc'd for $C_{10}H_{16}OS$ $[M+H]^{\bullet}$: 184.0922, found 184.0941; SFC Conditions*: 20% IPA, 2.5 mL/min, Chiralpak IC column, λ = 210 nm, t_R (min): minor = 7.87, major = 8.61.



(*S*)-3-allyl-3-(2-bromoallyl)tetrahydro-4*H*-thiopyran-4-one (2d)

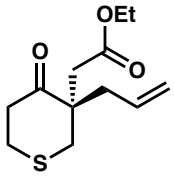
Purified by column chromatography (5% Et_2O in hexanes) to provide a colorless oil (45.2 mg, 82% yield); 50% ee, $[\alpha]_D^{25}$ +6.2 (*c* 2.26, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 5.71–5.59 (m, 2H), 5.58 (d, *J* = 1.7 Hz, 1H), 5.16–5.07 (m, 2H), 3.17 (dd, *J* = 15.3, 0.9 Hz, 1H), 2.96 (d, *J* = 1.0 Hz, 1H), 2.94–2.84 (m, 5H), 2.81–2.68 (m, 2H), 2.57 (ddt, *J* = 14.4, 7.0, 1.3 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 210.2, 132.5, 128.3, 122.0, 119.7, 53.1, 45.1, 41.7, 39.3, 38.5, 30.4; IR (Neat Film, NaCl) 3387, 3075, 3004, 2976, 2947, 2911, 2836, 1703, 1637, 1623, 1431, 1420, 1332, 1311, 1275, 1221, 1136, 1105, 993, 966, 920, 897, 809, 739, 673, 618 cm^{-1}; HRMS (FAB+) *m/z* calc'd for $C_{11}H_{16}BrOS$ $[M+H]^+$: 275.0105, found 275.0110; SFC Conditions: 1% IPA, 2.5 mL/min, Chiralcel OJ-H column, λ = 210 nm, t_R (min): minor = 5.16, major = 5.68.



(*S*)-3-allyl-3-(3-methylbut-2-en-1-yl)tetrahydro-4*H*-thiopyran-4-one (2e)

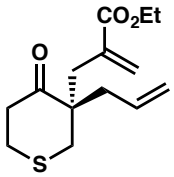
Purified by column chromatography (10% Et_2O in hexanes) to provide a colorless oil (33.9 mg, 76% yield); 78% ee, $[\alpha]_D^{25}$ –6.0 (*c* 1.65, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 5.73–5.59 (m, 1H), 5.11–5.03 (m, 2H), 4.97 (tdq, *J* = 7.5, 2.9, 1.5 Hz, 1H), 2.87 (t, *J* = 6.3 Hz, 2H), 2.82–2.74 (m, 2H), 2.76–2.63 (m, 2H), 2.67–2.53 (m, 2H), 2.41 (ddt, *J* = 14.1, 7.0, 1.3 Hz, 1H), 2.36–2.27 (m, 1H), 1.70 (t, *J* = 1.4 Hz, 3H), 1.62 (d, *J* = 1.3 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 211.4, 135.3, 133.3, 118.8, 118.3, 53.6, 41.4, 39.1, 38.8, 32.8, 30.3, 26.2, 18.3; IR (Neat Film, NaCl)

3387, 3075, 2975, 2912, 2857, 1703, 1638, 1435, 1420, 1377, 1326, 1311, 1274, 1221, 1130, 1116, 989, 917, 848, 810, 783, 729, 676, 616 cm^{-1}; HRMS (FAB+) *m/z* calc'd for $C_{13}H_{21}OS$ $[M+H]^+$: 225.1313, found 225.1335; SFC Conditions: 2% IPA, 2.5 mL/min, Chiralcel OB-H column, λ = 210 nm, t_R (min): major = 2.77, minor = 3.21.



Ethyl (*S*)-2-(3-allyl-4-oxotetrahydro-2*H*-thiopyran-3-yl)acetate (2f)

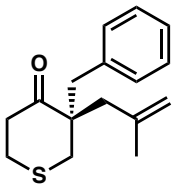
Purified by column chromatography (20% Et_2O in hexanes) to provide a colorless oil (44.2 mg, 91% yield); 69% ee, $[\alpha]_D^{25}$ +43.5 (*c* 2.21, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 5.68–5.56 (m, 1H), 5.15–5.07 (m, 2H), 4.08 (qd, *J* = 7.1, 1.6 Hz, 2H), 3.22 (d, *J* = 13.8 Hz, 1H), 3.00 (ddd, *J* = 13.3, 10.0, 3.8 Hz, 1H), 2.89–2.58 (m, 7H), 2.52 (dd, *J* = 14.0, 7.9 Hz, 1H), 1.22 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 209.8, 171.6, 132.1, 119.9, 60.7, 51.6, 41.2, 39.5, 39.2, 38.4, 30.0, 14.2; IR (Neat Film, NaCl) 3077, 2980, 2916, 1732, 1706, 1639, 1438, 1418, 1372, 1345, 1317, 1279, 1247, 1222, 1182, 1135, 1114, 1096, 995, 920 cm^{-1}; HRMS (FAB+) *m/z* calc'd for $C_{12}H_{19}O_3S$ $[M+H]^+$: 243.1055, found 243.1053; SFC Conditions: 2% IPA, 2.5 mL/min, Chiralpak AD-H column, λ = 210 nm, t_R (min): major = 5.66, minor = 7.67.



Ethyl (*S*)-2-((3-allyl-4-oxotetrahydro-2*H*-thiopyran-3-yl)methyl)acrylate (2g)

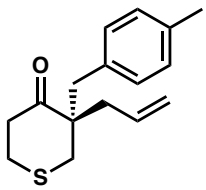
Purified by column chromatography (15% Et_2O in hexanes) to provide a colorless oil (46.8 mg, 87% yield); 66% ee, $[\alpha]_D^{25}$ +7.8 (*c* 2.34, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 6.26 (d, *J* = 1.4 Hz, 1H), 5.72–5.59 (m, 1H), 5.59 (q, *J* = 1.1 Hz, 1H), 5.13–5.04 (m, 2H), 4.16 (qt, *J* = 7.2, 1.5 Hz, 2H), 3.10 (dd, *J* = 14.2, 1.1 Hz, 1H), 2.93–2.81 (m, 4H), 2.77 (dd, *J* = 19.6, 1.3 Hz, 1H), 2.73–2.65 (m, 1H), 2.62 (d, *J* = 14.1 Hz, 1H), 2.55–2.41 (m, 2H), 1.28 (td, *J* = 7.2, 1.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 210.4, 167.5, 136.9, 133.0, 129.2, 119.2, 61.1, 53.3, 41.5, 38.9, 38.8, 36.1, 29.7, 14.3; IR (Neat Film, NaCl) 3076, 2979, 2938, 2910, 1712, 1638, 1626, 1436,

1417, 1369, 1333, 1308, 1276, 1209, 1174, 1159, 1096, 1027, 992, 960, 920, 858.9, 819, 684, 665 cm^{-1}; HRMS (FAB+) *m/z* calc'd for $C_{14}H_{21}O_3S$ $[M+H]^+$: 269.1211, found 269.1204; SFC Conditions: 10% IPA, 3.5 mL/min, Chiralpak AD-H column, λ = 210 nm, t_R (min): major = 3.04, minor = 3.95.



(*S*)-3-benzyl-3-(2-methylallyl)tetrahydro-4*H*-thiopyran-4-one (2h)

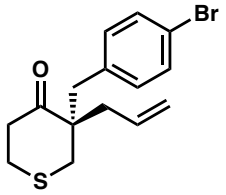
Purified by column chromatography (10% Et_2O in hexanes) to provide a colorless oil (15.3 mg, 29% yield); 80% ee, $[\alpha]_D^{25}$ –1.0 (*c* 0.77, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 7.31 – 7.24 (m, 2H), 7.26–7.19 (m, 1H), 7.17–7.11 (m, 2H), 4.89 (m, 1H), 4.70–4.66 (m, 1H), 3.23 (d, *J* = 13.7 Hz, 1H), 2.95 (d, *J* = 13.7 Hz, 1H), 2.92–2.78 (m, 3H), 2.77–2.67 (m, 3H), 2.64 (dd, *J* = 15.2, 1.1 Hz, 1H), 2.52 (dd, *J* = 15.2, 1.2 Hz, 1H), 1.70 (t, *J* = 1.0 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 212.1, 141.7, 136.9, 131.0, 128.3, 126.7, 114.9, 53.8, 42.1, 41.5, 40.8, 38.2, 29.7, 25.1; IR (Neat Film, NaCl) 3063, 3027, 2915, 1702, 1640, 1494, 1452, 1376, 1311, 1274, 1216, 1124, 1079, 1031, 988, 897, 808, 748, 704 cm^{-1}; HRMS (FAB+) *m/z* calc'd for $C_{16}H_{21}OS$ $[M+H]^+$: 261.1313, found 261.1323; SFC Conditions: 5% IPA, 2.5 mL/min, Chiralcel OB-H column, λ = 210 nm, t_R (min): major = 4.18, minor = 5.16.



(*S*)-3-allyl-3-(4-methylbenzyl)tetrahydro-4*H*-thiopyran-4-one (2i)

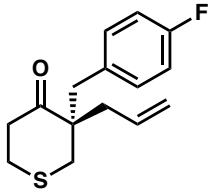
Purified by column chromatography (10% Et_2O in hexanes) to provide a colorless oil (44.8 mg, 86% yield); 90% ee, $[\alpha]_D^{25}$ +3.9 (*c* 2.20, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 7.08 (d, *J* = 7.8 Hz, 2H), 7.02 (d, *J* = 8.0 Hz, 2H), 5.72 (dddd, *J* = 16.9, 10.2, 7.8, 6.6 Hz, 1H), 5.16–5.06 (m, 2H), 3.09 (d, *J* = 13.9 Hz, 1H), 2.99 (d, *J* = 13.8 Hz, 1H), 2.89 (m, 2H), 2.83–2.68 (m, 4H), 2.58–2.49 (m, 1H), 2.46 (ddt, *J* = 14.4, 6.7, 1.4 Hz, 1H), 2.32 (s, 3H); ^{13}C NMR (101 MHz,

$CDCl_3$) δ 211.2, 136.3, 133.5, 133.3, 130.6, 129.0, 119.0, 54.0, 41.6, 39.8, 38.7, 38.0, 29.7, 21.1; IR (Neat Film, NaCl) 3075, 3049, 3020, 3005, 2946, 2918, 1703, 1638, 1514, 1434, 1419, 1313, 1274, 1222, 1128, 1115, 989, 919, 830, 797 cm^{-1}; HRMS (FAB+) *m/z* calc'd for $C_{16}H_{21}OS$ $[M+H]^+$: 261.1313, found 261.1331; SFC Conditions: 10% IPA, 2.5 mL/min, Chiralcel OJ-H column, λ = 210 nm, t_R (min): minor = 3.34, major = 4.14.



(*S*)-3-allyl-3-(4-bromobenzyl)tetrahydro-4*H*-thiopyran-4-one (2j)

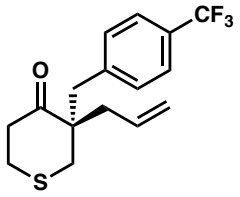
Purified by column chromatography (10% Et_2O in hexanes) to provide a colorless oil (58.8 mg, 91% yield); 91% ee, $[\alpha]_D^{25}$ +4.6 (*c* 2.94, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 7.42–7.35 (m, 2H), 7.05–6.98 (m, 2H), 5.68 (dddd, *J* = 16.9, 10.2, 7.7, 6.7 Hz, 1H), 5.17–5.06 (m, 2H), 3.11 (d, *J* = 13.8 Hz, 1H), 2.95–2.84 (m, 3H), 2.78–2.69 (m, 4H), 2.55 (ddt, *J* = 14.4, 7.7, 1.2 Hz, 1H), 2.43 (ddt, *J* = 14.3, 6.7, 1.3 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 210.7, 135.8, 132.8, 132.5, 131.4, 120.8, 119.4, 53.8, 41.5, 39.6, 38.9, 37.9, 29.7; IR (Neat Film, NaCl) 3075, 2946, 2914, 1703, 1638, 1487, 1434, 1404, 1313, 1274, 1073, 1012, 989, 921, 837, 788 cm^{-1}; HRMS (FAB+) *m/z* calc'd for $C_{15}H_{18}BrOS$ $[M+H]^+$: 325.0262, found 325.0265; SFC Conditions: 7% IPA, 2.5 mL/min, Chiralpak AD-H column, λ = 210 nm, t_R (min): minor = 11.06, major = 11.92.



(*S*)-3-allyl-3-(4-fluorobenzyl)tetrahydro-4*H*-thiopyran-4-one (2k)

Purified by column chromatography (10% Et_2O in hexanes) to provide a colorless oil (43.9 mg, 83% yield); 91% ee, $[\alpha]_D^{25}$ +9.3 (*c* 2.20, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 7.14–7.06 (m, 2H), 7.00–6.91 (m, 2H), 5.69 (dddd, *J* = 17.0, 10.3, 7.7, 6.7 Hz, 1H), 5.17–5.06 (m, 2H), 3.13 (d, *J* = 14.0 Hz, 1H), 2.95 (d, *J* = 14.0 Hz, 1H), 2.88 (dd, *J* = 7.6, 5.0 Hz, 2H), 2.79–2.70 (m, 4H), 2.58–2.49 (m, 1H), 2.44 (ddt, *J* = 14.4, 6.7, 1.4 Hz, 1H); ^{19}F (282 MHz, $CDCl_3$) δ –116.25 (tt, *J* = 8.8, 5.4 Hz); ^{13}C NMR (101 MHz, $CDCl_3$) δ 210.9, 161.9 (d, *J* = 245.1 Hz), 133.0, 132.3 (d, *J*

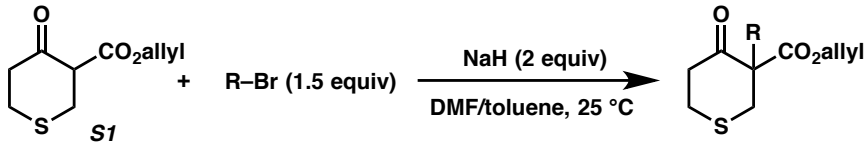
= 3.3 Hz), 132.2 (d, *J* = 7.9 Hz), 119.3, 115.2 (d, *J* = 21.0 Hz), 53.9, 41.5, 39.4, 38.8, 37.9, 29.7; IR (Neat Film, NaCl) 3075, 2947, 2915, 1703, 1638, 1604, 1509, 1435, 1417, 1335, 1314, 1275, 1223, 1160, 1130, 1098, 1016, 988, 965, 921, 843, 813, 772 cm^{-1}; HRMS (FAB+) *m/z* calc'd for $C_{15}H_{18}FOS$ $[M+H]^+$: 265.1062, found 265.1055; SFC Conditions: 10% IPA, 2.5 mL/min, Chiralcel OB-H column, λ = 210 nm, t_R (min): major = 2.70, minor = 3.75.



(*S*)-3-allyl-3-(4-(trifluoromethyl)benzyl)tetrahydro-4*H*-thiopyran-4-one (2l)

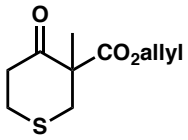
Purified by column chromatography (10% Et_2O in hexanes) to provide a colorless oil (50.5 mg, 80% yield); 93% ee, $[\alpha]_D^{25}$ +12.5 (*c* 2.53, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 7.52 (d, *J* = 8.0 Hz, 2H), 7.26 (d, *J* = 8.0 Hz, 2H), 5.69 (dddd, *J* = 17.0, 10.2, 7.7, 6.8 Hz, 1H), 5.19–5.09 (m, 2H), 3.22 (d, *J* = 13.7 Hz, 1H), 3.03 (d, *J* = 13.8 Hz, 1H), 2.89 (t, *J* = 6.2 Hz, 2H), 2.84–2.67 (m, 4H), 2.60 (ddt, *J* = 14.4, 7.7, 1.2 Hz, 1H), 2.44 (ddt, *J* = 14.4, 6.7, 1.3 Hz, 1H); ^{19}F NMR (282 MHz, $CDCl_3$) δ –62.48 (s); ^{13}C NMR (101 MHz, $CDCl_3$) δ 210.5, 141.1 (d, *J* = 1.4 Hz), 132.6, 131.1, 129.1 (q, *J* = 32.5 Hz), 125.2 (q, *J* = 3.7 Hz), 122.9 (q, *J* = 272.7), 119.6, 53.9, 41.5, 40.0, 38.9, 38.1, 29.7; IR (Neat Film, NaCl) 3076, 2917, 1703, 1638, 1618, 1436, 1417, 1326, 1275, 1165, 1123, 1068, 1019, 922, 856 cm^{-1}; HRMS (FAB+) *m/z* calc'd for $C_{16}H_{18}F_3OS$ $[M+H]^+$: 315.1030, found 315.1042; SFC Conditions: 2% IPA, 2.5 mL/min, Chiralcel OD-H column, λ = 210 nm, t_R (min): major = 10.24, minor = 11.19.

General Procedure for Preparation of Thiopyranone β-Ketoesters Substrates



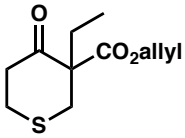
To an oven dried 20 mL vial was added NaH (3 mmol) and the vial evacuated and backfilled with argon three times. To the vial was added anhydrous DMF (1.0 mL), toluene (1.0 mL), and alkyl bromide (3 mmol) and the resulting suspension stirred for 5 minutes. A solution of **S1** (2 mmol) in anhydrous toluene (1.0 mL) was then added dropwise over 10 min. Following the

addition, the reaction was continued until all **S1** was consumed as seen by TLC. If necessary, additional toluene (1.0 to 2.0 mL) was added to ensure proper stirring of the reaction mixture. After diluting with Et_2O, the reaction was quenched with 1.0 M HCl, and the layers separated. The aqueous layer was extracted with Et_2O, and the combined organic layers were washed with water then brine, and dried over Na_2SO_4. The resulting crude residue was then purified by silica gel flash chromatography to provide the desired product.



Allyl 3-methyl-4-oxotetrahydro-2*H*-thiopyran-3-carboxylate (1b)

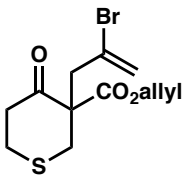
Purified by column chromatography (15% Et_2O in hexanes) to provide a colorless oil (224.3 mg, 52% yield); ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.91 (ddt, *J* = 17.2, 10.4, 5.8 Hz, 1H), 5.34 (dq, *J* = 17.2, 1.5 Hz, 1H), 5.26 (dq, *J* = 10.4, 1.3 Hz, 1H), 4.74–4.62 (m, 2H), 3.33 (dd, *J* = 13.9, 2.9 Hz, 1H), 3.01–2.82 (m, 3H), 2.84–2.76 (m, 1H), 2.71 (d, *J* = 13.9 Hz, 1H), 1.41 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 205.5, 171.8, 131.5, 119.1, 66.3, 59.2, 42.9, 40.0, 30.8, 21.0; IR (Neat Film, NaCl) 3086, 2985, 2937, 1731, 1714, 1649, 1454, 1417, 1374, 1358, 1315, 1294, 1277, 1233, 1192, 1160, 1125, 1100, 1064, 974, 938, 855, 817, 770, 738, 713, 682 cm^{-1}; HRMS (FAB+) *m/z* calc'd for $C_{10}H_{15}O_3S$ $[M+H]^+$: 215.0742, found 215.0741.



Allyl 3-ethyl-4-oxotetrahydro-2*H*-thiopyran-3-carboxylate (1c)

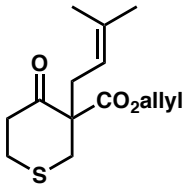
Purified by column chromatography (7% Et_2O in hexanes) to provide a colorless oil (157.4 mg, 35% yield); ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.92 (ddt, *J* = 17.3, 10.5, 5.8 Hz, 1H), 5.35 (dq, *J* = 17.1, 1.5 Hz, 1H), 5.27 (dq, *J* = 10.3, 1.2 Hz, 1H), 4.75–4.62 (m, 2H), 3.30 (dd, *J* = 13.9, 2.9 Hz, 1H), 3.01–2.89 (m, 2H), 2.89–2.82 (m, 1H), 2.81–2.70 (m, 2H), 2.08–1.97 (m, 1H), 1.74 (dq, *J* = 14.6, 7.5 Hz, 1H), 0.90 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 205.5, 170.8, 131.6, 119.2, 66.1, 63.4, 43.4, 38.4, 31.0, 27.6, 9.3; IR (Neat Film, NaCl) 3085, 2967, 2940, 2883, 1727, 1712, 1460, 1425, 1381, 1360, 1308, 1270, 1248, 1227, 1196, 1149, 1128, 986, 971, 936,

814, 796, 779, 732, 682 cm^{-1}; HRMS (FAB+) *m/z* calc'd for $C_{11}H_{17}O_3S$ $[M+H]^+$: 229.0898, found 229.0894.



Allyl 3-(2-bromoallyl)-4-oxotetrahydro-2*H*-thiopyran-3-carboxylate (1d)

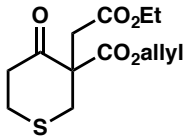
Purified by column chromatography (10% Et_2O in hexanes) to provide a colorless oil (330.1 mg, 52% yield); ^1H NMR (500 MHz, $CDCl_3$) δ 5.99–5.86 (m, 1H), 5.68 (dt, *J* = 1.7, 0.8 Hz, 1H), 5.60 (d, *J* = 1.7 Hz, 1H), 5.37 (dq, *J* = 17.2, 1.5 Hz, 1H), 5.27 (dq, *J* = 10.4, 1.3 Hz, 1H), 4.75–4.63 (m, 2H), 3.53 (dd, *J* = 14.0, 2.7 Hz, 1H), 3.23 (dd, *J* = 15.0, 0.7 Hz, 1H), 3.02 (dd, *J* = 15.0, 0.7 Hz, 1H), 3.01–2.72 (m, 5H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 203.7, 169.2, 131.4, 126.3, 122.8, 119.4, 66.7, 62.5, 44.7, 43.3, 37.7, 30.6; IR (Neat Film, NaCl) 3085, 2952, 2923, 1714, 1649, 1624, 1425, 1360, 1313, 1298, 1279, 1263, 1196, 1143, 1115, 1054, 985, 969, 936, 901, 854, 839, 814, 736, 683 cm^{-1}; HRMS (FAB+) *m/z* calc'd for $C_{12}H_{14}O_3S^{81}Br$ $[(M+H)–H_2]^+$: 318.9827, found 318.9828.



Allyl 3-(3-methylbut-2-en-1-yl)-4-oxotetrahydro-2*H*-thiopyran-3-carboxylate (1e)

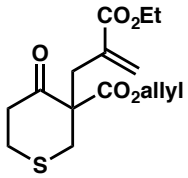
Purified by column chromatography (15% Et_2O in hexanes) to provide a colorless oil (369.8 mg, 69% yield); ^1H NMR (500 MHz, $CDCl_3$) δ 5.90 (ddt, *J* = 17.1, 10.4, 5.8 Hz, 1H), 5.34 (dq, *J* = 17.2, 1.5 Hz, 1H), 5.25 (dq, *J* = 10.4, 1.2 Hz, 1H), 5.06 (dddt, *J* = 8.4, 7.0, 2.9, 1.5 Hz, 1H), 4.69–4.61 (m, 2H), 3.30 (dd, *J* = 13.9, 2.8 Hz, 1H), 2.98–2.86 (m, 2H), 2.90–2.81 (m, 1H), 2.84–2.72 (m, 2H), 2.65–2.49 (m, 2H), 1.68 (m, *J* = 1.3 Hz, 3H), 1.70–1.59 (m, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 205.3, 170.5, 135.8, 131.6, 119.1, 118.0, 66.2, 63.3, 43.4, 37.9, 33.0, 30.8, 26.1,

18.1; IR (Neat Film, NaCl) 2912, 1712, 1426, 1377, 1315, 1263, 1223, 1185, 1114, 933 cm^{-1}; HRMS (FAB+) *m/z* calc'd for $C_{14}H_{21}O_3S$ $[M+H]^+$: 269.1211, found 269.1204.



Allyl 3-(2-ethoxy-2-oxoethyl)-4-oxotetrahydro-2*H*-thiopyran-3-carboxylate (1f)

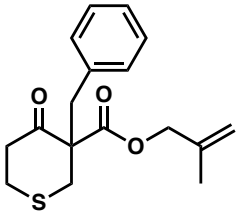
Purified by column chromatography (30% Et_2O in hexanes) to provide a colorless oil (472.0 mg, 83% yield); ^1H NMR (500 MHz, $CDCl_3$) δ 5.92 (ddt, *J* = 17.2, 10.4, 5.8 Hz, 1H), 5.35 (dq, *J* = 17.2, 1.5 Hz, 1H), 5.26 (dq, *J* = 10.4, 1.3 Hz, 1H), 4.69 (qdt, *J* = 13.1, 5.8, 1.4 Hz, 2H), 4.12 (q, *J* = 7.1 Hz, 2H), 3.30 (dd, *J* = 13.9, 2.6 Hz, 1H), 3.18 (dd, *J* = 13.9, 0.6 Hz, 1H), 3.08 (ddd, *J* = 14.0, 11.0, 5.5 Hz, 1H), 2.96 (m, 2H), 2.94–2.85 (m, 1H), 2.82 (ddd, *J* = 14.0, 4.6, 3.5 Hz, 1H), 2.75 (d, *J* = 16.3 Hz, 1H), 1.25 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 204.2, 170.2, 170.2, 131.5, 119.1, 66.7, 61.0, 60.9, 42.5, 38.9, 38.1, 30.3, 14.2; IR (Neat Film, NaCl) 3085, 2982, 2936, 1736, 1718, 1711, 1420, 1373, 1346, 1281, 1182, 1132, 1097, 1047, 1028, 987, 970, 934, 870, 850, 821 cm^{-1}; HRMS (FAB+) *m/z* calc'd for $C_{13}H_{19}O_5S$ $[M+H]^+$: 287.0953, found 287.0951.



Allyl 3-(2-(ethoxycarbonyl)allyl)-4-oxotetrahydro-2*H*-thiopyran-3-carboxylate (1g)

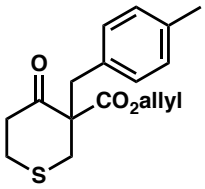
Purified by column chromatography (20% Et_2O in hexanes) to provide a white, waxy solid (431.1 mg, 69% yield); ^1H NMR (500 MHz, $CDCl_3$) δ 6.28 (d, *J* = 1.3 Hz, 1H), 5.91 (ddt, *J* = 17.1, 10.4, 5.8 Hz, 1H), 5.58 (q, *J* = 1.1 Hz, 1H), 5.34 (dq, *J* = 17.2, 1.5 Hz, 1H), 5.26 (dq, *J* = 10.4, 1.2 Hz, 1H), 4.62 (dq, *J* = 5.8, 1.3 Hz, 2H), 4.26–4.10 (m, 2H), 3.31 (dd, *J* = 13.9, 3.1 Hz, 1H), 3.18 (dd, *J* = 14.2, 0.9 Hz, 1H), 3.01–2.85 (m, 2H), 2.89–2.76 (m, 2H), 2.75–2.63 (m, 2H), 1.29 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 204.4, 169.7, 167.0, 135.8, 131.5, 129.3, 119.2, 66.4, 62.5, 61.2, 43.6, 38.1, 35.2, 30.6, 14.3; IR (Neat Film, NaCl) 2982, 2938, 2908, 1714, 1649, 1628, 1434, 1416, 1370, 1337, 1311, 1294, 1278, 1262, 1194, 1175, 1156, 1117,

1096, 1058, 1025, 947, 860, 812, 683 cm^{-1}; HRMS (FAB+) *m/z* calc'd for $C_{15}H_{21}O_5S$ $[M+H]^+$: 313.1110, found 313.1115.



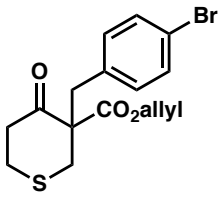
2-Methylallyl 3-benzyl-4-oxotetrahydro-2*H*-thiopyran-3-carboxylate (1h)

Purified by column chromatography (15% Et_2O in hexanes) to provide a colorless oil (301.2 mg, 49.5% yield); ^1H NMR (500 MHz, $CDCl_3$) δ 7.34–7.11 (m, 5H), 4.93 (dt, *J* = 12.0, 1.5 Hz, 2H), 4.47 (s, 2H), 3.35 (d, *J* = 13.7 Hz, 1H), 3.31–3.24 (m, 1H), 3.11 (d, *J* = 13.7 Hz, 1H), 2.99–2.82 (m, 4H), 2.85–2.73 (m, 1H), 1.68 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 204.8, 170.0, 139.1, 135.7, 130.6, 128.3, 127.1, 114.2, 69.0, 64.3, 43.6, 39.9, 38.1, 30.7, 19.7; IR (Neat Film, NaCl) 3084, 3062, 3029, 2924, 1713, 1657, 1495, 1454, 1432, 1378, 1364, 1329, 1311, 1275, 1262, 1230, 1190, 1132, 1117, 1092, 1076, 1046, 1032, 965, 912, 810, 771, 741, 702 cm^{-1}; HRMS (FAB+) *m/z* calc'd for $C_{17}H_{21}O_3S$ $[M+H]^+$: 305.1211, found 305.1220.



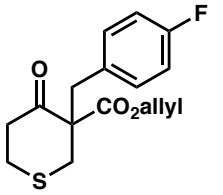
Allyl 3-(4-methylbenzyl)-4-oxotetrahydro-2*H*-thiopyran-3-carboxylate (1i)

Purified by column chromatography (15% Et_2O in hexanes) to provide a white solid (299.4 mg, 49% yield); ^1H NMR (500 MHz, $CDCl_3$) δ 7.09 – 6.95 (m, 4H), 5.83 (ddt, *J* = 17.1, 10.4, 5.9 Hz, 1H), 5.29 (dq, *J* = 17.2, 1.5 Hz, 1H), 5.24 (dq, *J* = 10.4, 1.2 Hz, 1H), 4.64–4.54 (m, 2H), 3.33–3.22 (m, 2H), 3.08 (d, *J* = 13.8 Hz, 1H), 2.97–2.78 (m, 4H), 2.75 (d, *J* = 13.9 Hz, 1H), 2.31 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 205.0, 170.0, 136.7, 132.5, 131.5, 130.5, 129.0, 119.3, 66.3, 64.3, 43.6, 39.4, 38.0, 30.7, 21.12; IR (Neat Film, NaCl) 2922, 1710, 1514, 1422, 1359, 1272, 1229, 1181, 1112, 1048, 967, 931, 828 cm^{-1}; HRMS (FAB+) *m/z* calc'd for $C_{17}H_{21}O_3S$ $[M+H]^+$: 305.1211, found 305.1208.;



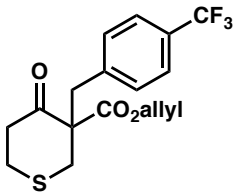
Allyl 3-(4-bromobenzyl)-4-oxotetrahydro-2*H*-thiopyran-3-carboxylate (1j)

Purified by column chromatography (15% Et_2O in hexanes) to provide a white solid (502.0 mg, 68% yield); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.39–7.31 (m, 2H), 7.09–7.02 (m, 2H), 5.79 (ddt, *J* = 17.2, 10.4, 5.9 Hz, 1H), 5.32–5.16 (m, 2H), 4.61–4.49 (m, 2H), 3.33–3.22 (m, 2H), 3.01 (d, *J* = 13.7 Hz, 1H), 2.98–2.78 (m, 4H), 2.73 (d, *J* = 13.8 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 204.7, 169.8, 134.8, 132.4, 131.4, 131.2, 121.2, 119.5, 66.4, 64.2, 43.6, 39.2, 38.3, 30.8; IR (Neat Film, NaCl) 2926, 1711, 1488, 1426, 1359, 1311, 1295, 1271, 1230, 1190, 1108, 1072, 1048, 1012, 968, 937, 832, 792, 711, 682, 624 cm^{-1}; HRMS (FAB+) *m/z* calc'd for $C_{16}H_{16}O_3S^{81}Br$ $[(M+H)-H_2]^+$: 368.9983, found 368.9967.



Allyl 3-(4-fluorobenzyl)-4-oxotetrahydro-2*H*-thiopyran-3-carboxylate (1k)

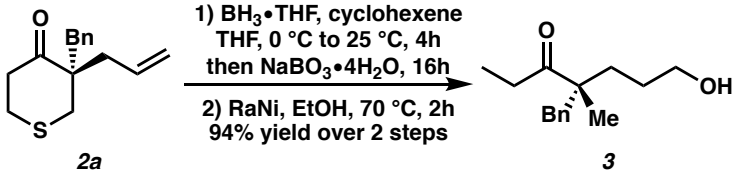
Purified by column chromatography (15% Et_2O in hexanes) to provide a colorless oil (383.7.5 mg, 62% yield); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.18 – 7.10 (m, 2H), 6.97 – 6.88 (m, 2H), 5.79 (ddt, *J* = 17.2, 10.4, 5.9 Hz, 1H), 5.31–5.19 (m, 2H), 4.61–4.49 (m, 2H), 3.33 (d, *J* = 13.8 Hz, 1H), 3.26 (dd, *J* = 13.9, 2.7 Hz, 1H), 3.03 (d, *J* = 13.8 Hz, 1H), 2.99–2.77 (m, 4H), 2.74 (d, *J* = 13.9 Hz, 1H); ^{19}F NMR (282 MHz, $CDCl_3$) δ –115.82 (tt, *J* = 8.6, 5.4 Hz); ^{13}C NMR (101 MHz, $CDCl_3$) δ 204.9, 169.8, 163.3, 160.8, 132.2 (d, *J* = 7.9 Hz), 131.5 (d, *J* = 3.3 Hz), 115.1 (d, *J* = 20.9 Hz), 66.3, 64.4 (2C), 43.6, 39.0, 38.3, 30.8; IR (Neat Film, NaCl) 2928, 1709, 1601, 1508, 1421, 1273, 1221, 1185, 1158, 1116, 1100, 1048, 1016, 934, 840 cm^{-1}; HRMS (FAB+) *m/z* calc'd for $C_{16}H_{18}O_3SF$ $[M+H]^+$: 309.0961, found 309.0958.



Allyl 4-oxo-3-(4-(trifluoromethyl)benzyl)tetrahydro-2*H*-thiopyran-3-carboxylate (1l)

Purified by column chromatography (15% Et_2O in hexanes) to provide a white solid (481.9 mg, 67% yield); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.55–7.43 (m, 2H), 7.34–7.27 (m, 2H), 5.74 (ddt, *J* = 17.2, 10.4, 6.0 Hz, 1H), 5.29–5.14 (m, 2H), 4.53 (dq, *J* = 6.0, 1.5 Hz, 2H), 3.41 (d, *J* = 13.6 Hz, 1H), 3.27 (dd, *J* = 13.8, 2.7 Hz, 1H), 3.07 (d, *J* = 13.6 Hz, 1H), 3.02–2.77 (m, 4H), 2.75 (d, *J* = 13.8 Hz, 1H); ^{19}F NMR (282 MHz, $CDCl_3$) δ –62.57; ^{13}C NMR (101 MHz, $CDCl_3$) δ 204.6, 169.7, 140.1 (d, *J* = 1.5 Hz), 131.0 (2C), 129.4 (q, *J* = 32.3 Hz), 125.1 (q, *J* = 3.8 Hz), 122.9 (q, *J* = 272.7 Hz) 119.5, 66.4, 64.3, 43.6, 39.6, 38.5, 30.8; IR (Neat Film, NaCl) 2929, 1715, 1618, 1420, 1326, 1293, 1276, 1232, 1191, 1165, 1114, 1068, 1020, 969, 939, 855, 732, 684, 630, 607 cm^{-1}; HRMS (FAB+) *m/z* calc'd for $C_{17}H_{18}O_3SF_3$ $[M+H]^+$: 359.0929, found 359.0939.

Derivatization of Alkylation Products

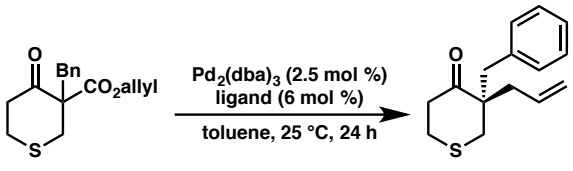


(*R*)-4-benzyl-7-hydroxy-4-methylheptan-3-one (3)

To an oven dried vial was added a 1 M solution of BH_3•THF (0.25 mmol, 250 μL) and the vial cooled to 0 °C. Cyclohexene (0.5 mmol, 50.6 μL) was then added neat dropwise and the mixture stirred for 1 h at 0 °C. A solution of ***2a*** (0.2 mmol, 49.2 mg) in 1.0 mL THF was then added, the cooling bath removed, and the reaction continued at room temperature for 4h. Water (500 μL) was then added followed by $NaBO_3$•$4H_2O$ (1.0 mmol, 153.9 mg), and the reaction continued at room temperature for 12h at which point the reaction was diluted with water and extracted with Et_2O. The combined organic layers were dried with Na_2SO_4 and concentrated. The crude reaction mixture was then dissolved in 3 mL of EtOH, treated with a suspension of Raney Ni (1.0 mL settled volume) and to 70 °C for 2h. The reaction was then allowed to settle, and the

supernatant removed via pipette and filtered through a plug of Celite®. Additional EtOH was added to the reaction vial and stirred for ~5 mins before again being allowed to settle and the supernatant removed. This process was repeated an additional two times, and the combined filtrates concentrated. The crude residue was purified by column chromatography (30% EtOAc in hexanes) to afford the desired linear alcohol (43.9 mg, 94% yield over two steps); $[\alpha]_D^{25}$ -20.4 (*c* 1.39, $CHCl_3$);^{1}H NMR (500 MHz, $CDCl_3$) δ 7.27–7.16 (m, 3H), 7.05 (d, *J* = 7.0 Hz, 2H), 3.59 (h, *J* = 4.5 Hz, 2H), 2.95 (d, *J* = 13.3 Hz, 1H), 2.66 (d, *J* = 13.3 Hz, 1H), 2.42 (dq, *J* = 18.5, 7.1 Hz, 1H), 2.26 (dq, *J* = 18.4, 7.1 Hz, 1H), 1.82 (td, *J* = 11.3, 10.5, 2.9 Hz, 1H), 1.61 (s, 1H), 1.55 – 1.36 (m, 3H), 1.13 (s, 3H), 0.97 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 216.3, 137.6, 130.3, 128.2, 126.5, 63.1, 51.8, 45.3, 34.9, 32.2, 28.0, 20.7, 7.8; IR (Neat Film, NaCl) 3421 (br), 3029, 2972, 2938, 1701, 1496, 1454, 1409, 1378, 1352, 1097, 1059, 1031, 1019, 973, 753, 703 cm^{-1}; HRMS (MM) *m/z* calc'd for $C_{15}H_{23}O_2$ $[M+H]^+$: 235.1693, found 235.1685.

Additional Ligand Screen Results



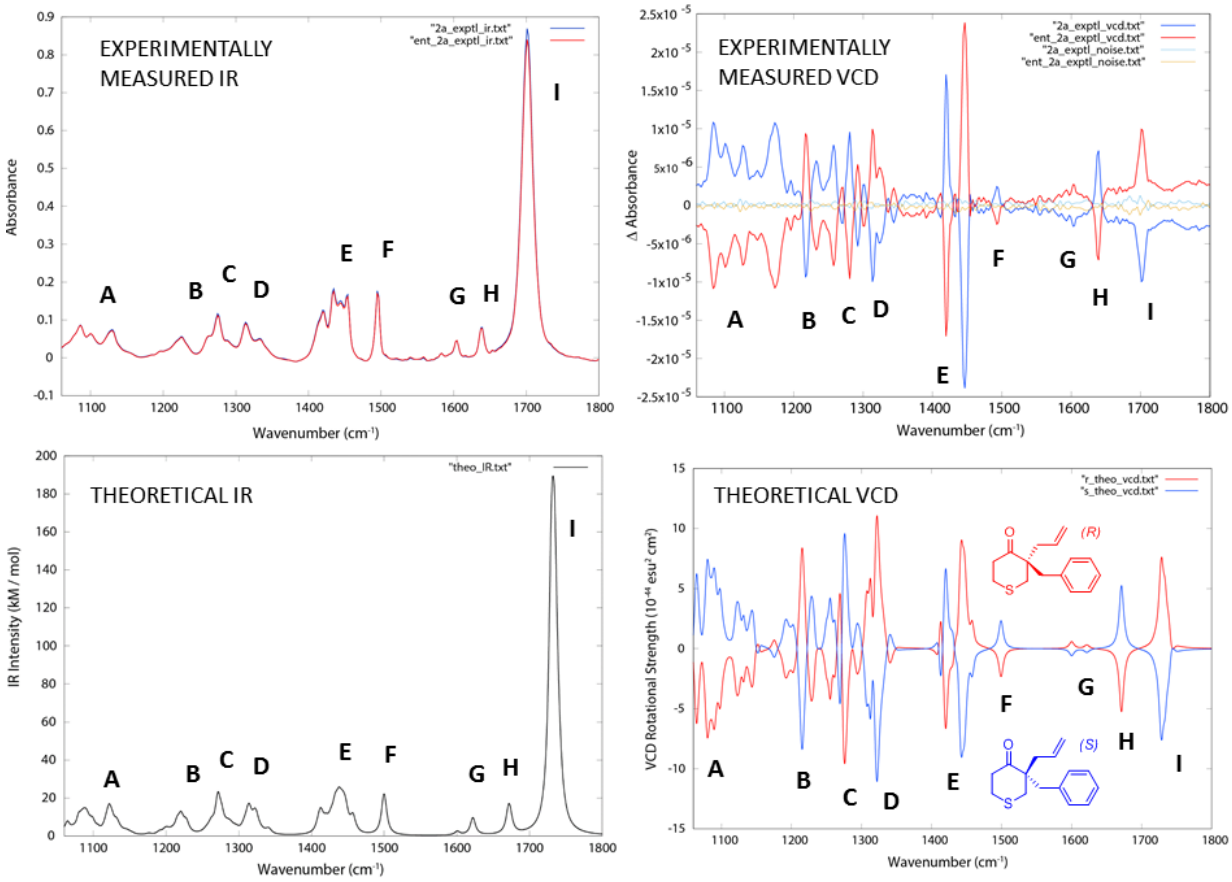
entry	ligand	e.e
1	(*R*)-BINAP	9
2	(*S*)-DTBM-BIPHEP	22
3	(*R*)-BTFM-Garphos	NR
4	(*S*)-C3-TunePhos	19
5	(*R*)-SEGPHOS	–17
6	(*R*)-bis(Diisopropylphosphino)-SEGPHOS	low conv
7	(*R*)-P-Phos	–16
8	(*R*)-PhanePhos	–7
9	(*R*)-SDP	–3
10	(*S*,*S*,*S*)-(-)-Ph-SKP	25
11	(*R*,*R*)-Chiraphos	low conv
12	(*S*,*S*)-BDPP	27
13	catASium D(*R*)	28
14	(*S*,*S*)-BPPM	12
15	(*R*,*R*)-Norphos	10
16	(*S*,*S*)-Et-BPE	23
17	R,R-Me_2NXyl^{F}R	NR
18	(*S*,*S*)-Me-Ferrocelane	–1
19	(*R*,*R*)-Me-DuPhos	low conv
20	(*S*,*S*)-Et-Ferrotane	–6
21	(1*R*,1'*R*,2*S*,2'*S*)– DuanPhos	29
22	(*S*)–BINAPINE	–15

entry	ligand	e.e
23	(*R*)-(*S*)-Ph, Cy Josiphos (J-001-1)	–6
24	(*R*)-(*S*)-$MeOMe_2C_6H_2$, Cy Josiphos (SL-J007-1)	–13.6
25	(*R*)-(*R*)-Ph, Ph Walphos (W-002-1)	10
26	(*R*)-(*R*)-Ph, Xyl^F Walphos (W-001-1)	low conv
27	(*R*)-(*R*)-Ph, Norbornyl Walphos (W-022-1)	8
28	(*S*)-(*R*)-Ph Mandyphos (M-001-2)	19
29	(*S*)-(*R*)-Xyl^F Mandyphos (M-003-2)	NR
30	(*R*)-(*R*)-Ph, Ph Taniaphos (T-001-1)	–17
31	(*R*,*R*)–ChenPHOS	6
32	(*S*)-Quinap	low conv
33	(*S*,*S*)-CpFe(4-^{i}Pr-oxazolinyl)$C_5H_3PPh_2$	38
34	(*R*)-Difluorphos	–16
35	(*R*)-Synphos	–12
36	Josiphos (SL-J212-1)	1

Determination of Absolute Configuration of Alkylation Product *2a*

Experimental Protocol. Samples (15.2 mg each) of **2a** (generated from the reaction of **1a** and (*R,R*)-**L5**; Scheme 1, entry 5) and ***ent*-2a** (generated from **1a** and (*S,S*)-**L5**) were subjected to absolute configuration determination via vibrational circular dichroism (VCD) using a ChiralIR-2X spectrometer (BioTools, Inc) at 4 cm^{-1} resolution and optimized at 1400 cm^{-1}. Each sample was dissolved in 280 μL of $CDCl_3$ (54 mg/mL), loaded into an SL-4 cell (International Crystal Laboratories) with BaF_2 windows and 100 μm path length, and infrared (IR) and VCD spectra acquired in 24 one-hour blocks which were averaged at the completion of the run. A 15-minute acquisition of neat (+)-α-pinene control yielded a VCD spectrum in agreement with literature spectra. IR and VCD spectra were background-corrected using a 5-minute block acquisition of the empty instrument chamber. IR spectra of **2a** and ***ent*-2a** were solvent corrected utilizing a 1-hour block acquisition of $CDCl_3$. VCD spectra of **2a** and ***ent*-2a** were enantiomer subtracted (half-difference).

Computational Protocol. The arbitrarily chosen (*S*) enantiomer of **2a** was subjected to an exhaustive initial molecular mechanics-based conformational search (MMFF94 force field, 0.08 Å geometric RMSD cutoff, and 30 kcal/mol energy window) as implemented in MOE (Chemical Computing Group, Montreal, CA). All conformers retained the (*S*) configuration. All MMFF94 conformers were then subjected to geometry optimization, harmonic frequency calculation, and VCD rotational strength evaluation with density functional theory. All quantum mechanical calculations utilized the B3PW91 functional, cc-pVTZ basis, and implicit IEFPCM chloroform solvation model as implemented in the *Gaussian 09* program system (Rev. E.01; Frisch *et al*., Gaussian, Inc., Wallingford, CT). Resultant harmonic frequencies were scaled by 0.98. All structurally unique conformers were Boltzmann weighted by relative free energy at 298.15 K. The predicted IR and VCD frequencies and intensities were convolved using Lorentzian line shapes (γ = 4 cm^{-1}) and summed using the respective Boltzmann weights to yield the final predicted IR and VCD spectra of the (*S*) enantiomer of **2a**. The predicted VCD of the corresponding (*R*) enantiomer was generated by inversion of sign. From the excellent agreement between the predicted and measured IR and VCD spectra (see below) the absolute configuration of **2a** was unambiguously established as (*S*).



Experimental (top) and computed (bottom) IR and VCD spectra for **2a** and ***ent*-2a.**

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