Ni(II) Tol-BINAP-Catalyzed Enantioselective Michael Reactions of β -Keto Esters and *N*-Acylthiazolidinethiones

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Supporting Information

General Information. Michael reactions were carried out under a nitrogen atmosphere with a septum cap and magnetic stirring; no special precautions were taken to exclude water from the reaction vessel. Toluene and CH_2Cl_2 were purified by passage through a bed of activated alumina.¹ Ethyl acetate was stored over oven dried 4Å molecular sieves. MeOH was distilled from $\text{Mg}(\text{OMe})_2$. All other reaction solvents were used as received. AgOTf and AgBF_4 were used as received from Aldrich Chemical Co. NiCl_2 was used as received from Alfa/Aesar Chemical Co. (*S*)-Tol-BINAP was used as received from Strem Chemicals. Reagents were purified prior to use unless otherwise stated following the guidelines of Perrin and Armarego.² Purification of reaction products was carried out by flash chromatography using EM Reagent silica gel 60 (230-400 mesh). Analytical thin layer chromatography was performed on EM Reagent 0.25 mm silica gel 60-F plates. Visualization was accomplished with UV light and ceric ammonium nitrate stain, followed by heating. Optical rotations were measured on a Jasco DIP-0181 digital polarimeter with a sodium lamp and are reported as follows: $[\alpha]_D^{25}$ ($c = \text{g}/100 \text{ mL}$, solvent). Infrared spectra were recorded on a Perkin Elmer 1600 series FT-IR spectrometer. ^1H NMR spectra were recorded on a Varian Inova-500 (500 MHz) spectrometer and are reported in ppm using solvent as an internal standard (CDCl_3 at 7.26 ppm). Data are reported as (a = apparent, obs = obscured, s = singlet, d = doublet, t = triplet, q = quartet, p = pentet, h = hexet, sep = septet, o = octet, m = multiplet, b = broad; coupling constant(s) in Hz; integration. Proton-decoupled ^{13}C NMR spectra were recorded on a Varian Mercury 400 (100 MHz) spectrometer and are reported in ppm using solvent as an internal standard (CDCl_3 at 77.0 ppm). Low- and high-resolution mass spectra were obtained on Jeol AX-505 or SX-102 spectrometers in the Harvard University Mass Spectrometry Laboratory.

1-(2-Thioxo-thiazolidin-3-yl)-pent-2-en-1-one (2b): Prepared in analogy to the procedure of Evans.³ To a stirred suspension of 2-mercaptothiazoline (3.6 g, 0.03 mol) in CH_2Cl_2 (50 mL) at -78°C was added triethylamine (4.6 mL, 0.033 mol) and 2-pentenoyl chloride (3.3g, 0.03 mol). The solution was allowed to warm to 0°C and stirred for 2 h

after which time the reaction was quenched with water (20 mL) and diluted with CH_2Cl_2 (200 mL). The organic layer was washed with 1.0 M HCl (100 mL), water (100 mL), brine (100 mL) and dried (Na_2SO_4). Removal of the solvent *in vacuo* followed by flash chromatography on neutral alumina using 10% EtOAc in hexanes as the eluant afforded the desired product as a yellow oil (2.0 g, 33% yield): IR (film) 2948, 1682, 1633, 1370, 1220, 1054 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 7.22 (d, 1H, $J = 15.1$ Hz), 7.08 (dt, 1H, $J = 15.1, 6.3$ Hz), 4.53 (t, 2H, $J = 7.3$ Hz), 3.33 (t, 2H, $J = 7.3$ Hz), 2.30 (p, 2H, $J = 6.8$ Hz), 1.10 (t, 3H, $J = 7.3$ Hz); ^{13}C NMR (100 MHz, CDCl_3) δ 201.6, 167.3, 151.2, 122.3, 56.0, 29.0, 25.7, 11.9; HRMS (EI+): Exact mass calcd for $\text{C}_8\text{H}_{11}\text{NOS}_2$ $[\text{M}]^+$, 201.0282. Found 201.0281.

1-(2-Thioxo-thiazolidin-3-yl)-hex-2-en-1-one (2c): 2-Mercaptothiazoline (0.03 mol) converted to the title compound by the procedure described for thione **2b**. Purification by flash chromatography on neutral alumina using 10% EtOAc in hexanes as the eluant

(1) Pangborn, A. B.; Giardello, M. A.; Grubbs, R. H.; Rosen, R. K.; Timmers, F. J. *Organometallics* **1996**, *15*, 1518-1520.

(2) Perrin, D. D. and Armarego, W. L. *Purification of Laboratory Chemicals*; 3rd ed., Pergamon Press, Oxford. 1988.

(3) Evans, D. A.; Miller, S. J.; Lectka, T.; von Matt, P. *J. Am. Chem. Soc.* **1999**, *121*, 7559-7573.

afforded the product as a yellow oil (2.8 g, 43% yield): IR (film) 2943, 1683, 1632, 1370, 1278, 1170 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) 7.19 (d, 1H, $J = 15.1$ Hz), 7.01 (m, 1H), 4.51 (t, 2H, $J = 7.3$ Hz), 3.32 (t, 2H, $J = 7.3$ Hz), 2.24 (m, 2H), 1.51 (m, 2H), 0.94 (t, 3H, $J = 7.3$ Hz); ^{13}C NMR (100 MHz, CDCl_3) δ 201.5, 167.1, 149.8, 123.2, 55.9, 34.5, 28.9, 21.1, 13.7; HRMS (ES+): Exact mass calcd for $\text{C}_9\text{H}_{14}\text{NOS}_2$ $[\text{M}+\text{H}]^+$, 216.0517. Found 216.0515.

5-Methyl-1-(2-thioxo-thiazolidin-3-yl)-hex-2-en-1-one (2d): 2-Mercaptothiazoline (0.01 mol) converted to the title compound by the procedure described for thione **2b**. Purification by flash chromatography on neutral alumina using 10% EtOAc in hexanes as the eluant afforded the product as a yellow oil (0.96 g, 38% yield): IR (film) 2956, 1682, 1634, 1465, 1369, 1278, 1227, 1172, 1068 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) 7.18 (br d, 1H, $J = 15.0$ Hz), 7.00 (dt, 1H, $J = 15.4$, 7.3 Hz), 4.52 (t, 2H, $J = 7.3$ Hz), 3.33 (t, 2H, $J = 7.7$ Hz), 2.15 (t, 2H, $J = 7.0$ Hz), 1.80 (sep, 1H, $J = 6.6$ Hz), 0.92 (d, 6H, $J = 6.6$ Hz); ^{13}C NMR (100 MHz, CDCl_3) δ 201.5, 167.1, 148.9, 124.1, 56.0, 41.8, 29.0, 28.0, 22.5; HRMS (EI+): Exact mass calcd for $\text{C}_{10}\text{H}_{15}\text{NOS}_2$ $[\text{M}]^+$, 229.0595. Found 229.0596.

4-Methyl-1-(2-thioxo-thiazolidin-3-yl)-pent-2-en-1-one (2e): 2-Mercaptothiazoline (0.044 mol) converted to the title compound by the procedure described for thione **2b**. Purification by flash chromatography on neutral alumina using 10% EtOAc in hexanes as the eluant afforded the product as a yellow oil (3.2 g, 57% yield): IR (film) 2962, 1684, 1631, 1465, 1369, 1302, 1164, 1062 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) 7.18 (d, 1H, $J = 15.4$ Hz), 6.98 (dd, 1H, $J = 15.4$, 6.2 Hz), 4.52 (t, 2H, $J = 7.3$ Hz), 3.32 (t, 2H, $J = 7.3$ Hz), 2.52 (o, 1H, $J = 6.6$ Hz), 1.08 (d, 3H, $J = 7.0$ Hz); ^{13}C NMR (100 MHz, CDCl_3) δ 201.6, 167.5, 155.7, 120.7, 56.0, 31.3, 29.0, 21.0; HRMS (ES+): Exact mass calcd for $\text{C}_9\text{H}_{14}\text{NOS}_2$ $[\text{M}+\text{H}]^+$, 216.0517. Found 216.0518.

[Ni((S)-Tol-BINAP)]Cl₂ (1a): To a stirred suspension of (S)-Tol-BINAP (1.16 g, 1.71 mmol) in acetonitrile (30 mL) was added anhydrous NiCl_2 (221 mg, 1.71 mmol) and water (30 μL). The resulting mixture was heated at reflux for 16 h after which time a deep purple solution had formed. The reaction mixture was cooled to rt, filtered through a pad of dried celite and the solvent removed *in vacuo*. Drying overnight at 100 mtorr afforded a purple solid (1.3 g, 99%) which was stored in a dry box and could be used directly without further purification: mp (decomp.) 237-240 $^{\circ}\text{C}$; IR (film) 3050, 1598, 1499, 1189, 1097, 806 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) 10.49 (br s, 4H), 9.48 (br s, 2H), 8.90 (variable br s, 4H), 8.63 (d, 2H, $J = 7.8$ Hz), 8.44 (br s, 4H), 8.03 (t, 2H, $J = 7.3$ Hz), 6.96 (br s, 4H), 4.74 (s, 2H), 4.73 (s, 2H), 4.59 (br s, 2H), 4.55 (s, 6H), 2.39 (s, 6H).

General Procedures for Fresh Preparation of Catalysts 1b and 1c:

[Ni((S)-Tol-BINAP)]OTf₂ (1b): To a dried 2 dram reaction vial in a glove box was added [Ni((S)-Tol-BINAP)] NiCl_2 (20.2 mg, 0.025 mmol). The vial was fitted with a septum and removed to ambient atmosphere. In a separate dried 2 dram reaction vial in a glove box was added AgOTf (12.8 mg, 0.050 mmol) and a stirrer bar. The vial was fitted with a septum and removed to ambient atmosphere. The nickel complex was dissolved in CH_2Cl_2 (1.0 mL) and added to the vial containing AgOTf . The resulting mixture was

stirred in the dark under an atmosphere of dry nitrogen for 3 h after which time the solution was filtered (0.45 μm) and the solvent removed under a stream of dry nitrogen to afford a dark brown residue that was used directly in the required Michael reaction.

[Ni((S)-Tol-BINAP)](BF₄)₂ (1c): To a dried 2 dram reaction vial in a glove box was added [Ni((S)-Tol-BINAP)] NiCl_2 (20.2 mg, 0.025 mmol). The vial was fitted with a septum and removed to ambient atmosphere. In a separate dried 2 dram reaction vial in a glove box was added AgBF_4 (9.7 mg, 0.050 mmol) and a stirrer bar. The vial was fitted

with a septum and removed to ambient atmosphere. The nickel complex was dissolved in CH₂Cl₂ (1.0 mL) and added to the vial containing AgBF₄. The resulting mixture was stirred in the dark under an atmosphere of dry nitrogen for 3 h after which time the solution was filtered (0.45 µm) into a dried 2 dram reaction vial containing a stirrer bar. The solvent was removed under a stream of dry nitrogen to afford a brownish orange residue that was used directly in the required Michael reaction.

General procedure for the [Ni((S)-Tol-BINAP)]OTf₂ and [Ni((S)-Tol-BINAP)](BF₄)₂ catalyzed Michael reaction of β-keto esters to N-acylthiazolidinethiones: Freshly prepared **1b** or **1c** (0.025 mmol) was dissolved in ethyl acetate (0.75 mL) and to this solution was added thione (0.25 mmol) in ethyl acetate (0.5 mL). The reaction mixture was cooled to 0 °C, β-keto ester (0.375 mmol) added and stirred for 12–72 h until the reaction was complete. The mixture was filtered through a pad of silica gel and the solvent removed *in vacuo*. The residue was purified by flash column chromatography on silica gel to give the desired product in greater than 95% purity by ¹H NMR spectroscopy, except where otherwise noted.

General procedure for the DBU catalyzed cyclization of Michael adducts into dihydropyrene derivatives: To a stirred 0.3 M solution of the thione in CH₂Cl₂ at 0 °C was added DBU (20 mol%). When the yellow color had disappeared (2–5 min) the reaction mixture was diluted with CH₂Cl₂ and washed with 1.0 M HCl. The aqueous layer was extracted twice with CH₂Cl₂ and the combined organic layers washed with brine, and dried (Na₂SO₄). Removal of the solvent *in vacuo* afforded a residue which was purified by flash column chromatography to give the desired product in greater than 95% purity by ¹H NMR spectroscopy, except where otherwise noted.

(3R)-tert-Butyl 2-acetyl-3-methyl-5-oxo-5-(2-thioxothiazolidin-3-yl)pentanoate

(4a): Prepared according to the General Procedure using complex **1b** and purified by column chromatography using 30% EtOAc in hexanes as the eluant to afford the product as a yellow oil (77 mg, 89% yield) as a 1:1 mixture of C2 epimers: $[\alpha]_D^{25} = -$

2.3° (*c* = 1.0, CHCl₃); IR (film) 2978, 1739, 1717, 1464, 1367, 1282, 1225, 1154, 1053 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 4.60–4.55 (m, 4H), 3.41 (d, 1H, *J* = 7.3 Hz), 3.38 (d, 1H, *J* = 7.8 Hz), 3.35–3.25 (m, 8H), 2.85 (m, 2H), 2.224 (s, 3H), 2.216 (s, 3H), 1.47 (s, 9H), 1.46 (s, 9H), 1.05 (d, 3H, *J* = 6.8 Hz), 1.02 (d, 3H, *J* = 6.8 Hz); ¹³C NMR (100 MHz, CDCl₃) δ 202.8, 201.5, 201.4, 173.2, 173.1, 168.0, 82.2, 82.1, 77.3, 65.4, 65.0, 56.0, 43.3, 42.9, 29.5, 29.4, 29.2, 28.2, 27.9, 18.1, 17.5; HRMS (EI⁺): Exact mass calcd for C₁₅H₂₄O₄NS₂ [M]⁺, 346.1147. Found 346.1150.

(3R)-tert-Butyl 3-methyl-5-oxo-2-propionyl-5-(2-thioxothiazolidin-3-yl)pentanoate

(4b): Prepared according to the General Procedure using complex **1b** and purified by column chromatography using 30% EtOAc in hexanes as the eluant to afford the product as a yellow oil (83 mg, 92% yield) as a 2:1 mixture of C2

epimers: $[\alpha]_D^{25} = -7.93^\circ$ (*c* = 1.0, CHCl₃); IR (film) 2977, 1733, 1711, 1460, 1368, 1282, 1225, 1155, 1053 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 4.57 (m, 4H), 3.42 (m, 2H), 3.36–3.18 (m, 8H), 2.88 (m, 2H), 2.59 (m, 4H), 2.46 (m, 4H), 1.46 (s, 9H, major), 1.45 (s, 9H, minor), 1.07 (d, 3H, *J* = 6.8 Hz), 1.05 (t, 6H, *J* = 6.8 Hz), 1.00 (d, 3H, *J* = 6.8 Hz); ¹³C NMR (100 MHz, CDCl₃) δ 205.6, 201.6, 173.2, 168.1, 82.1, 82.0, 77.3, 64.3, 64.2, 56.0, 43.4, 42.9, 35.9, 35.7, 29.6, 29.4, 28.3, 28.2, 27.9, 18.2, 17.6, 7.68, 7.64; HRMS (ES⁺): Exact mass calcd for C₁₆H₂₆O₄NS₂ [M+H]⁺, 360.1303. Found 360.1302.

tert-Butyl 3-oxo-2-((R)-4-oxo-4-(2-thioxothiazolidin-3-yl)butan-2-yl)hexanoate

(4c): Prepared according to the General Procedure using complex **1b** and purified by column chromatography using 30% EtOAc in hexanes as the eluant to afford the product as a yellow oil (80 mg, 86% yield) as a 2:1 mixture of C2 epimers:

$[\alpha]_D^{25} = -5.6^\circ$ (*c* = 1.0, CHCl₃); IR (film) 2969, 2877, 1783, 1719, 1458, 1368, 1282, 1225, 1052 cm⁻¹; ¹H NMR

(500 MHz, CDCl₃) δ 4.55 (m, 4H), 3.40 (apparent t, 2H, J = 8.4 Hz), 3.32–3.14 (m, 8H), 2.85 (sep, 2H, J = 6.6 Hz), 2.56–2.36 (m, 4H), 1.57 (m, 4H), 1.43 (s, 9H, major), 1.42 (s, 9H, minor), 1.01 (d, 3H, J = 7.0 Hz, major), 0.97 (d, 3H, J = 7.0 Hz, minor), 0.883 (t, 3H, J = 6.7 Hz, minor), 0.878 (t, 3H, J = 6.7 Hz, major); ¹³C NMR (100 MHz, CDCl₃) δ 204.9, 201.5, 201.4, 173.2, 168.0, 167.9, 82.1, 82.0, 64.5, 64.4, 56.0, 44.6, 44.3, 43.4, 42.9, 29.5, 29.3, 28.25, 28.21, 27.9, 18.2, 17.5, 16.9, 16.8, 13.6; HRMS (ES⁺): Exact mass calcd for C₁₇H₂₈O₄NS₂ [M+H]⁺, 374.1460. Found 374.1452.

tert-Butyl 5-methyl-3-oxo-2-((R)-4-oxo-4-(2-thioxothiazolidin-3-yl)butan-2-yl)hexanoate (4d): Prepared according to the General Procedure using complex **1b** and purified by column chromatography using 30% EtOAc in hexanes as the eluant to afford the product as a yellow oil (76 mg, 78% yield) as a 1:1 mixture

of C2 epimers: $[\alpha]_D^{25}$ = -21.4° (c = 1.0, CHCl₃); IR (film) 2960, 1738, 1713, 1469, 1393, 1368, 1282, 1225, 1156, 1053 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 4.55 (m, 4H), 3.41–3.16 (m, 10H), 2.85 (sep, 2H, J = 6.6 Hz), 2.42–2.30 (m, 4H), 2.14 (o, 2H, J = 6.6 Hz), 1.44 (s, 3H), 1.43 (s, 3H), 1.02 (d, 3H, J = 7.0 Hz), 0.98 (d, 3H, J = 7.0 Hz), 0.89 (m, 12H); ¹³C NMR (100 MHz, CDCl₃) δ 204.4, 201.5, 201.4, 173.21, 173.18, 167.93, 167.85, 82.1, 82.0, 77.2, 64.9, 64.8, 56.04, 56.01, 51.7, 51.5, 43.4, 43.0, 29.5, 29.2, 28.3, 28.2, 27.90, 27.88, 24.0, 23.8, 22.52, 22.47, 22.37, 18.2, 17.5; HRMS (ES⁺): Exact mass calcd for C₁₈H₃₀O₄NS₂ [M+H]⁺, 388.1616. Found 388.1609.

(3R)-tert-Butyl 2-(cyclohexanecarbonyl)-3-methyl-5-oxo-5-(2-thioxothiazolidin-3-yl)pentanoate (4e): Prepared according to the General Procedure using complex **1b** and purified by column chromatography using 30% EtOAc in hexanes as the eluant to afford the product as a yellow oil (100 mg, 97% yield) as a 1:1 mixture of

C2 epimers: $[\alpha]_D^{25}$ = -6.6° (c = 1.0, CHCl₃); IR (film) 2978, 2856, 1735, 1706, 1450, 1368, 1281, 1226, 1156, 1053 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 4.58–4.50 (m, 4H), 3.58 (m, 2H), 3.34–3.20 (m, 6H), 3.14–3.11 (m, 1H), 2.83 (m, 2H), 2.45 (m, 2H), 1.85–1.70 (m, 8H), 1.65 (br m, 2H), 1.43 (s, 9H), 1.42 (s, 9H), 1.40–1.30 (m, 2H), 1.30–1.15 (m, 4H), 1.02 (d, 3H, J = 6.6 Hz), 0.97 (d, 3H, J = 6.6 Hz); ¹³C NMR (100 MHz, CDCl₃) δ 208.8, 207.9, 201.5, 201.4, 173.3, 173.1, 197.9, 167.8, 82.04, 82.00, 77.2, 62.7, 62.5, 56.0, 51.4, 51.0, 43.6, 42.9, 29.7, 29.3, 28.7, 28.4, 28.3, 28.2, 28.0, 27.93, 27.89, 25.7, 25.6, 25.4, 25.3, 18.3, 17.5; HRMS (ES⁺): Exact mass calcd for C₂₀H₃₂O₄NS₂ [M+H]⁺, 414.1773. Found 414.1674.

(3R)-tert-Butyl 2-benzoyl-3-methyl-5-oxo-5-(2-thioxothiazolidin-3-yl)pentanoate (4f): Prepared according to the General Procedure using complex **1c** and purified by column chromatography using 30% EtOAc in hexanes as the eluant to afford the product as a yellow oil (97 mg, 95% yield) as a 2:1 mixture of C2

epimers: $[\alpha]_D^{25}$ = -5.2° (c = 0.25, CHCl₃); IR (film) 2977, 1727, 1694, 1448, 1367, 1281, 1225, 1156 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 7.96 (d, 4H, J = 7.3 Hz), 7.55 (t, 2H, J = 7.3 Hz), 7.45 (t, 4H, J = 7.3 Hz), 4.60–4.50 (m, 4H), 4.30 (d, 1H, J = 7.7 Hz), 4.27 (d, 1H, J = 8.1 Hz), 3.40–3.20 (m, 8H), 3.06 (sep, 2H, J = 5.5 Hz), 1.31 (s, 9H, minor), 1.30 (s, 9H, major), 1.12 (d, 3H, J = 6.6 Hz, minor), 1.06 (d, 3H, J = 6.6 Hz, major); ¹³C NMR (100 MHz, CDCl₃) δ 201.4, 194.8, 194.6, 173.2, 168.0, 167.9, 137.0, 136.7, 133.2, 128.5, 128.3, 94.3, 82.2, 82.1, 77.2, 59.55, 59.51, 56.02, 55.98, 43.5, 43.0, 29.9, 29.5, 28.3, 28.2, 27.6, 27.4, 18.5, 17.5; HRMS (EI⁺): Exact mass calcd for C₂₀H₂₅O₄NS₂ [M+H]⁺, 408.1303. Found 408.1306.

(R)-tert-Butyl 2,4-dimethyl-6-oxo-5,6-dihydro-4H-pyran-3-carboxylate (5a): Prepared from **4a** (0.3 mmol) according to the General Procedure for dihydropyrone formation and purified by column chromatography using 10% EtOAc in hexanes as the eluant to afford the product as a colorless oil (55 mg, 84% yield): $[\alpha]_D^{25}$ = +27.9° (c = 1.0, CHCl₃); IR (film) 2977, 1789, 1708, 1650, 1301, 1254, 1132, 1086 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 2.99 (br p, 1H, J = 6.6 Hz), 2.64 (dd, 1H, J = 15.7, 6.6 Hz), 2.51 (dd, 1H, J = 15.7, 2.2 Hz), 2.28 (s, 3H), 1.50 (s, 9H), 1.09 (d, 3H, J = 7.0

Hz); ^{13}C NMR (100 MHz, CDCl_3) δ 167.4, 165.5, 159.0, 113.6, 81.2, 35.7, 28.2, 27.3, 19.2, 18.7; HRMS (CI, NH_3): Exact mass calcd for $\text{C}_{12}\text{H}_{22}\text{O}_4\text{N}$ $[\text{M}+\text{NH}_4]^+$, 244.1548. Found 244.1549. Enantioselectivity determined by HPLC (Chiralcel ODH column, 5% *i*-PrOH/hexanes, 0.8 mL/min, 235 nm), $t_{\text{major}} = 6.5$ min, $t_{\text{minor}} = 9.7$ min; ee = 93%.

(R)-tert-Butyl 2-ethyl-4-dimethyl-6-oxo-5,6-dihydro-4H-pyran-3-carboxylate (5b):

Prepared from **4b** (0.3 mmol) according to the General Procedure for dihydropyrone formation and purified by column chromatography using 10% EtOAc in hexanes as the eluant to afford the product as a colorless oil (54 mg, 80% yield): $[\alpha]_{\text{D}}^{25} = +23.7^\circ$ ($c = 1.0$, CHCl_3); IR (film) 2977, 1789, 1710, 1645, 1460, 1369, 1298, 1253, 1130 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 3.11 (pd, 1H, $J = 6.8, 1.5$ Hz), 2.84–2.73 (m, 3H), 2.63 (dd, 1H, $J = 15.6, 2.0$ Hz), 1.63 (s, 9H), 1.28 (t, 3H, $J = 7.3$ Hz), 1.22 (d, 3H, $J = 6.8$ Hz); ^{13}C NMR (100 MHz, CDCl_3) δ 167.6, 165.4, 163.4, 113.0, 81.2, 35.7, 28.1, 27.4, 25.2, 19.2, 11.7; HRMS (ES+): Exact mass calcd for $\text{C}_{13}\text{H}_{21}\text{O}_4$ $[\text{M}+\text{H}]^+$, 241.1440. Found 241.1445. Enantioselectivity determined by HPLC (Chiralcel ODH column, 1% *i*-PrOH/hexanes, 0.7 mL/min, 235 nm), $t_{\text{major}} = 8.1$ min, $t_{\text{minor}} = 13.7$ min; ee = 94%.

(R)-tert-Butyl 4-methyl-6-oxo-2-propyl-5,6-dihydro-4H-pyran-3-carboxylate (5c):

Prepared from **4c** (0.3 mmol) according to the General Procedure for dihydropyrone formation and purified by column chromatography using 10% EtOAc in hexanes as the eluant to afford the product as a colorless oil (58 mg, 85% yield): $[\alpha]_{\text{D}}^{25} = +26.8^\circ$ ($c = 1.0$, CHCl_3); IR (film) 2967, 1768, 1708, 1697, 1644, 1462, 1368, 1252, 1130 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 2.97 (pd, 1H, $J = 7.0, 2.2$ Hz), 2.66–2.58 (m, 3H), 2.49 (dd, 1H, $J = 13.5, 2.2$ Hz), 1.59 (h, 2H, $J = 7.4$ Hz), 1.49 (s, 9H), 1.08 (d, 3H, $J = 7.0$ Hz), 0.92 (t, 3H, $J = 7.3$ Hz); ^{13}C NMR (100 MHz, CDCl_3) δ 167.6, 165.4, 162.1, 113.8, 81.2, 35.7, 33.3, 28.1, 27.4, 20.6, 19.2, 13.5; HRMS (ES+): Exact mass calcd for $\text{C}_{14}\text{H}_{23}\text{O}_4$ $[\text{M}+\text{H}]^+$, 255.1596. Found 255.1602. Enantioselectivity determined by HPLC (Chiralcel ODH column, 1% *i*-PrOH/hexanes, 0.7 mL/min, 235 nm), $t_{\text{major}} = 7.4$ min, $t_{\text{minor}} = 9.5$ min; ee = 93%.

(R)-tert-Butyl 2-isobutyl-4-methyl-6-oxo-5,6-dihydro-4H-pyran-3-carboxylate (5d):

Prepared from **4d** (0.36 mmol) according to the General Procedure for dihydropyrone formation and purified by column chromatography using 10% EtOAc in hexanes as the eluant to afford the product as a colorless oil (70 mg, 72% yield): $[\alpha]_{\text{D}}^{25} = +24.0^\circ$ ($c = 1.0$, CHCl_3); IR (film) 2961, 1788, 1711, 1694, 1644, 1463, 1302, 1252, 1129 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 2.98 (pd, 1H, $J = 7.0, 2.2$ Hz), 2.60 (a dd, 1H, $J = 15.7, 6.2$ Hz), 2.56 (d, 2H, $J = 7.3$ Hz), 2.48 (dd, 1H, $J = 15.7, 2.2$ Hz), 1.99 (sep, 1H, $J = 6.6$ Hz), 1.48 (s, 9H), 1.08 (d, 3H, $J = 7.0$ Hz), 0.91 (d, 3H, $J = 6.6$ Hz), 0.90 (d, 3H, $J = 6.6$ Hz); ^{13}C NMR (100 MHz, CDCl_3) δ 167.5, 165.4, 161.2, 114.7, 81.2, 39.5, 35.7, 28.1, 27.6, 26.8, 22.2, 21.9, 19.2; HRMS (CI, NH_3): Exact mass calcd for $\text{C}_{15}\text{H}_{28}\text{O}_4\text{N}$ $[\text{M}+\text{NH}_4]^+$, 286.2019. Found 286.2018. Enantioselectivity determined by HPLC (Chiralcel ODH column, 1% *i*-PrOH/hexanes, 0.7 mL/min, 235 nm), $t_{\text{major}} = 6.9$ min, $t_{\text{minor}} = 7.6$ min; ee = 91%.

(R)-tert-Butyl 2-cyclohexyl-4-methyl-6-oxo-5,6-dihydro-4H-pyran-3-carboxylate (5e):

Prepared from **4e** (0.08 mmol) according to the General Procedure for dihydropyrone formation and purified by column chromatography using 10% EtOAc in hexanes as the eluant to afford the product as a colorless oil (20 mg, 94% yield): $[\alpha]_{\text{D}}^{25} = +15.1^\circ$ ($c = 1.0$, CHCl_3); IR (film) 2930, 1785, 1703, 1636, 1250, 1133, 1085 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 3.31 (tt, 1H, $J = 11.7, 3.3$ Hz), 2.97 (pd, 1H, $J = 6.6, 2.2$ Hz), 2.59 (dd, 1H, $J = 15.7, 6.2$ Hz), 2.47 (dd, 1H, $J = 15.7, 2.6$ Hz), 1.80–1.52 (m, 7H), 1.51 (s, 9H), 1.35–1.15 (m, 3H), 1.07 (d, 3H, $J = 7.3$ Hz); ^{13}C NMR (100 MHz, CDCl_3) δ 167.8, 165.7, 164.9, 112.6, 81.2, 39.5, 35.7, 29.4, 29.0, 28.2, 27.5, 26.1, 26.0, 25.6, 19.2; HRMS (EI+): Exact mass calcd for $\text{C}_{17}\text{H}_{26}\text{O}_4$ $[\text{M}]^+$, 294.1831. Found 294.1828.

Enantioselectivity determined by HPLC (Chiralcel ODH column, 1% *i*-PrOH/hexanes, 0.7 mL/min, 235 nm), $t_{\text{major}} = 6.8$ min, $t_{\text{minor}} = 7.7$ min; ee = 90%.

(R)-tert-Butyl 4-methyl-6-oxo-2-phenyl-5,6-dihydro-4H-pyran-3-carboxylate (5f):

Prepared from **4f** (0.12 mmol) according to the General Procedure for dihydropyran formation and purified by column chromatography using 10% EtOAc in hexanes as the eluant to afford the product as a colorless solid (32 mg, 94% yield): mp 101–102 °C; $[\alpha]_{\text{D}}^{25} = +8.2^\circ$ ($c = 1.0$, CHCl_3); IR (film) 2980, 1779, 1686, 1349, 1307, 1132, 1066 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 7.41–7.37 (m, 5H), 3.15 (pd, 1H, $J = 7.0, 2.6$ Hz), 2.82 (dd, 1H, $J = 16.1, 7.0$ Hz), 2.62 (dd, 1H, $J = 15.7, 2.2$ Hz), 1.22 (obs d, 3H), 1.21 (s, 9H); ^{13}C NMR (100 MHz, CDCl_3) δ 167.1, 165.9, 156.5, 133.6, 129.6, 128.6, 127.9, 115.4, 81.5, 35.6, 28.3, 27.5, 19.1; HRMS (EI+): Exact mass calcd for $\text{C}_{17}\text{H}_{20}\text{O}_4$ $[\text{M}]^+$, 289.1440. Found 289.1438. Enantioselectivity determined by HPLC (Chiralcel ODH column, 1% *i*-PrOH/hexanes, 0.7 mL/min, 235 nm), $t_{\text{major}} = 22.0$ min, $t_{\text{minor}} = 26.3$ min; ee = 91%.

(3R)-tert-Butyl 2-acetyl-3-ethyl-5-oxo-5-(2-thioxothiazolidin-3-yl)pentanoate (6b):

Prepared according to the General Procedure using complex **1c** and purified by column chromatography using 30% EtOAc in hexanes as the eluant to afford the product as a yellow oil (79 mg, 88% yield) as a 1:1 mixture of C2 epimers: $[\alpha]_{\text{D}}^{25} = -15.2^\circ$ ($c = 1.0$, CHCl_3); IR (film) 2970, 1726, 1705, 1462, 1368, 1280, 1224, 1152, 1053 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 4.60–4.48 (m, 4H), 3.52 (t, 2H, $J = 7.3$ Hz), 3.42–3.20 (m, 8H), 2.78–2.70 (m, 2H), 2.22 (s, 3H), 2.21 (s, 3H), 1.45 (s, 18H), 0.91 (t, 23H, $J = 7.7$ Hz), 0.90 (t, 3H, $J = 7.7$ Hz); ^{13}C NMR (100 MHz, CDCl_3) δ 203.3, 201.5, 201.3, 173.9, 173.9, 173.8, 168.4, 168.2, 82.2, 82.1, 77.3, 63.6, 62.7, 56.2, 56.1, 40.09, 40.06, 35.4, 29.52, 29.47, 28.4, 28.3, 27.92, 27.89, 25.3, 24.5, 11.2; HRMS (EI+): Exact mass calcd for $\text{C}_{16}\text{H}_{26}\text{O}_4\text{NS}_2$ $[\text{M}+\text{H}]^+$, 360.1303. Found 360.1304.

(3R)-tert-Butyl 2-acetyl-3-(2-oxo-2-(2-thioxothiazolidin-3-yl)ethyl)hexanoate (6c):

Prepared according to the General Procedure using complex **1c** and purified by column chromatography using 30% EtOAc in hexanes as the eluant to afford the product as a yellow oil (85 mg, 91% yield) as a 1:1 mixture of C2 epimers: $[\alpha]_{\text{D}}^{25} = -17.8^\circ$ ($c = 1.0$, CHCl_3); IR (film) 2945, 1710, 1456, 1368, 1281, 1224, 1154, 1052 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 4.59–4.50 (m, 4H), 3.51 (t, 2H, $J = 7.0$ Hz), 3.45–3.26 (m, 8H), 2.79 (m, 2H), 2.21 (s, 3H), 2.20 (s, 3H), 1.45 (s, 18H), 1.50–1.20 (m, 8H), 0.88 (a t, 6H, $J = 7.0$ Hz); ^{13}C NMR (100 MHz, CDCl_3) δ 203.33, 203.28, 201.5, 201.3, 173.9, 173.8, 168.4, 168.2, 82.2, 82.1, 77.3, 63.8, 62.9, 56.15, 56.08, 40.8, 40.5, 34.8, 34.0, 33.9, 33.8, 29.6, 29.5, 28.4, 28.3, 27.90, 27.87, 20.0, 14.1, 14.0; HRMS (EI+): Exact mass calcd for $\text{C}_{17}\text{H}_{28}\text{O}_4\text{NS}_2$ $[\text{M}+\text{H}]^+$, 374.1460. Found 374.1462.

(3R)-tert-Butyl 2-acetyl-5-methyl-3-(2-oxo-2-(2-thioxothiazolidin-3-yl)ethyl)hexanoate (6d):

Prepared according to the General Procedure using complex **1c** and purified by column chromatography using 30% EtOAc in hexanes as the eluant to afford the product as a yellow oil (65 mg, 67% yield) as a 1:1 mixture of C2 epimers: $[\alpha]_{\text{D}}^{25} = -17.1^\circ$ ($c = 1.0$, CHCl_3); IR (film) 2957, 1713, 1683, 1469, 1368, 1281, 1225, 1146, 1053 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 4.60–4.42 (m, 4H), 3.50 (m, 2H), 3.40–3.20 (m, 5H), 2.83 (m, 4H), 2.20 (s, 3H), 2.19 (s, 3H), 1.58 (m, 2H), 1.45 (s, 9H), 1.44 (s, 9H), 1.43–1.14 (m, 6H), 0.90–0.84 (m, 12 H); ^{13}C NMR (100 MHz, CDCl_3) δ 203.4, 203.3, 201.5, 201.3, 173.93, 173.85, 168.5, 168.2, 82.2, 82.1, 63.9, 62.6, 56.1, 56.0, 41.9, 41.0, 40.5, 32.1, 31.8, 29.7, 29.6, 28.3, 27.90, 27.87, 25.4, 25.2, 23.6, 22.4, 22.5, 21.6; HRMS (ES+): Exact mass calcd for $\text{C}_{18}\text{H}_{29}\text{O}_4\text{NS}_2$ $[\text{M}+\text{H}]^+$, 388.1616. Found 388.1614.

(3R)-tert-Butyl 4-ethyl 2-acetyl-3-(2-oxo-2-(2-thioxothiazolidin-3-yl)ethyl)succinate (6f):

Prepared according to the General Procedure using

complex **1c** and purified by column chromatography using 30% EtOAc in hexanes as the eluant to afford the product as a yellow oil (88 mg, 87% yield) as a 2:1 mixture of C2 epimers: $[\alpha]_D^{25} = -36.6^\circ$ ($c = 1.0$, CHCl_3); IR (film) 2953, 1732, 1719, 1642, 1368, 1281, 1226, 1156, 1054 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 4.64–4.46 (m, 4H), 4.18–4.19 (m, 4H), 3.95 (d, 1H, $J = 7.3$ Hz), 3.81 (d, 1H, $J = 7.0$ Hz), 3.79–3.60 (m, 4H), 3.52–3.40 (m, 2H), 3.39–3.20 (m, 4H), 2.29 (s, 3H), 2.26 (s, 3H), 1.44 (s, 9H), 1.43 (s, 9H), 1.21 (a t, 6H, $J = 7.3$ Hz); ^{13}C NMR (100 MHz, CDCl_3) δ 201.9, 201.4, 201.2, 172.6, 172.5, 172.3, 172.0, 167.3, 166.8, 83.0, 82.5, 61.2, 60.0, 55.9, 55.8, 40.5, 40.2, 39.9, 38.2, 38.0, 29.7, 29.5, 28.5, 28.4, 28.1, 27.8, 14.0, 13.9; HRMS (ES+): Exact mass calcd for $\text{C}_{17}\text{H}_{26}\text{O}_6\text{NS}_2$ $[\text{M}+\text{H}]^+$, 404.1201. Found 404.1194.

(R)-tert-Butyl 4-ethyl-2-methyl-6-oxo-5,6-dihydro-4H-pyran-3-carboxylate (7b):

Prepared from **6b** (0.13 mmol) according to the General Procedure for dihydropyrrone formation and purified by column chromatography using 10% EtOAc in hexanes as the eluant to afford the product as a colorless oil (28 mg, 94% yield): $[\alpha]_D^{25} = +11.3^\circ$ ($c = 1.0$, CHCl_3); IR (film) 2971, 1768, 1705, 1650, 1368, 1251, 1134 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 2.82 (br d, 1H, $J = 7.0$ Hz), 2.66 (dd, 1H, $J = 16.1, 1.5$ Hz), 2.57 (dd, 1H, 16.1, 6.6 Hz), 2.29 (s, 3H), 1.52 (m, 1H), 1.50 (s, 9H), 1.36–1.28 (m, 1H), 0.90 (t, 3H, $J = 7.7$ Hz); ^{13}C NMR (100 MHz, CDCl_3) δ 167.6, 165.7, 159.1, 112.8, 81.2, 33.4, 32.9, 28.1, 26.5, 18.7, 11.1; HRMS (CI, NH_3): Exact mass calcd for $\text{C}_{13}\text{H}_{24}\text{O}_4\text{N}$ $[\text{M}+\text{NH}_4]^+$, 258.1703. Found 258.1703. Enantioselectivity determined by HPLC (Chiralcel ODH column, 2% *i*-PrOH/hexanes, 0.8 mL/min, 235 nm), $t_{\text{major}} = 6.8$ min, $t_{\text{minor}} = 9.3$ min; ee = 95%.

(R)-tert-Butyl 2-methyl-6-oxo-4-propyl-5,6-dihydro-4H-pyran-3-carboxylate (7c):

Prepared from **6c** (0.13 mmol) according to the General Procedure for dihydropyrrone formation and purified by column chromatography using 10% EtOAc in hexanes as the eluant to afford the product as a colorless oil (30 mg, 89% yield): $[\alpha]_D^{25} = +16.3^\circ$ ($c = 1.0$, CHCl_3); IR (film) 2962, 1788, 1709, 1650, 1458, 1368, 1314, 1253, 1132, 1023 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 2.90 (br q, 1H, $J = 6.2$ Hz), 2.65 (dd, 1H, $J = 15.7, 2.2$ Hz), 2.56 (dd, 1H, $J = 15.7, 6.6$ Hz), 2.28 (s, 3H), 1.50 (s, 9H), 1.48–1.21 (m, 4H), 0.88 (t, 3H, $J = 7.0$ Hz); ^{13}C NMR (100 MHz, CDCl_3) δ 167.7, 165.6, 159.1, 113.1, 81.2, 35.5, 33.1, 31.5, 28.1, 19.7, 18.7, 13.9; HRMS (ES+): Exact mass calcd for $\text{C}_{14}\text{H}_{23}\text{O}_4$ $[\text{M}+\text{H}]^+$, 255.1596. Found 255.1605. Enantioselectivity determined by HPLC (Chiralcel ODH column, 2% *i*-PrOH/hexanes, 0.8 mL/min, 235 nm), $t_{\text{major}} = 6.1$ min, $t_{\text{minor}} = 8.2$ min; ee = 95%.

(R)-tert-Butyl 4-isobutyl-2-methyl-6-oxo-5,6-dihydro-4H-pyran-3-carboxylate (7d):

Prepared from **6d** (0.15 mmol) according to the General Procedure for dihydropyrrone formation and purified by column chromatography using 10% EtOAc in hexanes as the eluant to afford the product as a colorless oil (35 mg, 72% yield): $[\alpha]_D^{25} = +17.3^\circ$ ($c = 1.0$, CHCl_3); IR (film) 2959, 1768, 1711, 1650, 1368, 1310, 1254, 1134, 1108, 1072 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 2.96 (m, 1H), 2.65 (dd, 1H, $J = 15.7, 1.8$ Hz), 2.55 (dd, 1H, $J = 16.1, 6.6$ Hz), 2.28 (s, 3H), 1.63–1.56 (m, 1H), 1.50 (s, 9H), 1.33–1.15 (m, 2H), 0.90 (d, 3H, $J = 6.6$ Hz), 0.88 (d, 3H, $J = 6.6$ Hz); ^{13}C NMR (100 MHz, CDCl_3) δ 167.6, 165.5, 159.2, 113.6, 81.3, 42.1, 32.9, 29.7, 28.2, 24.9, 23.4, 21.5, 18.7; HRMS (CI, NH_3): Exact mass calcd for $\text{C}_{15}\text{H}_{28}\text{O}_4\text{N}$ $[\text{M}+\text{NH}_4]^+$, 286.2018. Found 286.2019. Enantioselectivity determined by HPLC (Chiralcel ODH column, 1% *i*-PrOH/hexanes, 0.7 mL/min, 235 nm), $t_{\text{major}} = 7.8$ min, $t_{\text{minor}} = 9.1$ min; ee = 84%.

(S)-tert-Butyl 4-isopropyl-2-methyl-6-oxo-5,6-dihydro-4H-pyran-3-carboxylate (7e):

Prepared from **2e** (0.25 mmol) using complex **1c** followed by treatment of the unpurified reaction mixture with to the General Procedure for dihydropyrrone formation. Purification by column chromatography using 10% EtOAc in hexanes as the eluant afforded the product as a colorless oil (6 mg, 10% yield): $[\alpha]_D^{25} = +9.3^\circ$ ($c = 0.12$, CHCl_3); IR (film) 2926, 1783, 1642, 1363, 1256, 1130, 1102, 1068; ^1H NMR (500 MHz, CDCl_3) δ 2.79 (br t, 1H, $J = 7.0$ Hz), 2.73 (dd, 1H, J

= 16.5, 1.5 Hz), 2.52 (dd, 1H, J = 16.1, 7.3 Hz), 2.30 (s, 3H), 1.73 (o, 1H, J = 7.0 Hz), 1.51 (s, 3H), 0.92 (d, 3H, J = 7.0 Hz), 0.86 (d, 3H, J = 7.0 Hz); ^{13}C NMR (100 MHz, CDCl_3) δ 168.2, 166.0, 158.9, 112.1, 81.3, 38.0, 31.6, 30.7, 28.2, 20.1, 18.8, 18.7; Exact mass calcd for $\text{C}_{14}\text{H}_{26}\text{O}_4\text{N}$ $[\text{M}+\text{NH}_4]^+$, 272.1859. Found 272.1862. Enantioselectivity determined by HPLC (Chiralcel ODH column, 1% *i*-PrOH/hexanes, 0.7 mL/min, 235 nm), t_{major} = 8.4 min, t_{minor} = 10.6 min; ee = 70%.

(R)-3-tert-Butyl 4-ethyl 2-methyl-6-oxo-5,6-dihydro-4H-pyran-3,4-dicarboxylate (7f):

Prepared from **6f** (0.12 mmol) according to the General Procedure for dihydropyrene formation and purified by column chromatography using 30% EtOAc in hexanes as the eluant to afford the product as a colorless oil (34 mg, 97% yield): $[\alpha]_{\text{D}}^{25}$ = +92.0° (c = 0.75, CHCl_3); IR (film) 2981, 1793, 1733, 1652, 1370, 1255, 1185, 1127, 1034 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 4.15 (q, 2H, J = 7.0 Hz), 2.96 (dd, 1H, J = 16.1, 2.6 Hz), 2.84 (br d, 1H, J = 7.3 Hz), 2.68 (dd, 1H, J = 16.5, 7.3 Hz), 2.34 (s, 3H), 1.50 (s, 9H), 1.24 (t, 3H, J = 7.0 Hz); ^{13}C NMR (100 MHz, CDCl_3) δ 171.2, 165.1, 164.6, 161.4, 106.8, 81.9, 61.7, 38.3, 30.7, 28.1, 18.8, 14.0; HRMS (ES+): Exact mass calcd for $\text{C}_{14}\text{H}_{21}\text{O}_6$ $[\text{M}+\text{H}]^+$, 285.1338. Found 285.1329. Enantioselectivity determined by HPLC (Chiralcel ODH column, 10% *i*-PrOH/hexanes, 0.8 mL/min, 235 nm), t_{major} = 9.9 min, t_{minor} = 12.8 min; ee = 97%.

(3R)-Methyl 2-acetyl-3-methyl-5-oxo-5-(2-thioxothiazolidin-3-yl)pentanoate:

Prepared according to the General Procedure using complex **1b** and purified by column chromatography using 30% EtOAc in hexanes as the eluant to afford the product as a yellow oil (58 mg, 76% yield) as a 1:1 mixture of C2 epimers: $[\alpha]_{\text{D}}^{25}$ = -3.0° (c = 1.0, CHCl_3); IR (film) 2952, 1738, 1714, 1463, 1363, 1281, 1224, 1155 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 4.56–4.52 (m, 4H), 3.71 (s, 3H), 3.70 (s, 3H), 3.55 (d, 1H, J = 7.7 Hz), 3.49 (d, 1H, J = 8.4 Hz), 3.40–3.20 (m, 8H), 2.88 (sep, 2H, J = 6.6 Hz), 2.22 (s, 3H), 1.01 (d, 6H, J = 7.0 Hz); ^{13}C NMR (100 MHz, CDCl_3) δ 202.6, 202.5, 201.64, 201.55, 173.0, 169.33, 169.28, 124.8, 77.2, 63.9, 63.7, 56.0, 52.4, 52.3, 43.0, 42.7, 29.8, 29.76, 29.66, 29.5, 28.2, 18.1, 17.6; HRMS (ES+): Exact mass calcd for $\text{C}_{12}\text{H}_{18}\text{O}_4\text{NS}_2$ $[\text{M}+\text{H}]^+$, 304.0677. Found 304.0676.

(3R)-Ethyl 2-acetyl-3-methyl-5-oxo-5-(2-thioxothiazolidin-3-yl)pentanoate:

Prepared according to the General Procedure using complex **1b** and purified by column chromatography using 30% EtOAc in hexanes as the eluant to afford the product as a yellow oil (55 mg, 69% yield) as a 1:1 mixture of C2 epimers: $[\alpha]_{\text{D}}^{25}$ = -2.4° (c = 1.0, CHCl_3); IR (film) 2980, 1732, 1714, 1464, 1366, 1280, 1224, 1157, 1051 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 4.54 (m, 4H), 4.17 (m, 4H), 3.52 (d, 1H, J = 7.7 Hz), 3.46 (d, 1H, J = 8.1 Hz), 3.40–3.20 (m, 8H), 2.88 (sep, 2H, J = 7.0 Hz), 2.21 (s, 3H), 2.20 (s, 3H), 1.27–1.23 (m, 6H), 1.02 (d, 3H, J = 6.6 Hz), 1.01 (d, 3H, J = 6.6 Hz); ^{13}C NMR (100 MHz, CDCl_3) δ 202.7, 202.6, 201.6, 201.5, 173.1, 168.9, 168.8, 124.8, 72.2, 64.2, 63.9, 61.4, 61.3, 56.0, 43.1, 42.8, 29.7, 29.6, 29.4, 28.2, 18.2, 17.5, 14.1, 14.0; HRMS (ES+): Exact mass calcd for $\text{C}_{13}\text{H}_{20}\text{O}_4\text{NS}_2$ $[\text{M}+\text{H}]^+$, 318.0834. Found 318.0841.

(3R)-Benzyl 2-acetyl-3-methyl-5-oxo-5-(2-thioxothiazolidin-3-yl)pentanoate:

Prepared according to the General Procedure using complex **1b** and purified by column chromatography using 30% EtOAc in hexanes as the eluant to afford the product as a yellow oil (66 mg, 70% yield) as a 1:1 mixture of C2 epimers: $[\alpha]_{\text{D}}^{25}$ = -3.3° (c = 1.0, CHCl_3); IR (film) 2966, 1738, 1713, 1455, 1366, 1281, 1224, 1155, 1052 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 7.40–7.30 (m, 10H), 5.16 (m, 4H), 4.51 (m, 4H), 3.60 (d, 1H, J = 7.3 Hz), 3.55 (d, 1H, J = 8.4 Hz), 3.40–3.20 (m, 8H), 2.91 (sep, 2H, J = 6.6 Hz), 2.18 (s, 9H), 2.17 (s, 9H), 1.02 (d, 3H, J = 6.6 Hz), 1.01 (d, 3H, J = 6.6 Hz); ^{13}C NMR (100 MHz, CDCl_3) δ 202.41, 202.37, 201.4, 173.0, 172.9, 168.7, 135.1, 128.6, 128.5, 128.4, 128.3, 124.8, 77.2, 67.12, 67.06, 64.1, 63.7, 55.9, 43.1, 42.8, 29.8, 29.7, 29.6, 29.5, 28.2, 18.2, 17.5; HRMS (ES+): Exact mass calcd for $\text{C}_{18}\text{H}_{22}\text{O}_4\text{NS}_2$ $[\text{M}+\text{H}]^+$, 380.0990. Found 380.0994.

(R)-Methyl 2,4-dimethyl-6-oxo-5,6-dihydro-4H-pyran-3-carboxylate: Prepared from the acyclic adduct (0.16 mmol) according to the General Procedure for dihydropyrone formation and purified by column chromatography using 30% EtOAc in hexanes as the eluant to afford the product as a colorless oil (23 mg, 78% yield): $[\alpha]_D^{25} = +28.0^\circ$ ($c = 0.5$, CHCl_3); IR (film) 2955, 1788, 1714, 1436, 1298, 1252, 1132, 1083 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 3.77 (s, 3H), 3.06 (br p, 1H, $J = 6.2$ Hz), 2.65 (dd, 1H, $J = 16.1, 6.2$ Hz), 2.54 (dd, 1H, $J = 15.7, 1.8$ Hz), 2.33 (s, 3H), 1.10 (d, 3H, $J = 7.0$ Hz); ^{13}C NMR (100 MHz, CDCl_3) δ 167.1, 166.7, 160.5, 112.1, 51.8, 35.6, 27.1, 19.3, 18.8; HRMS (EI⁺): Exact mass calcd for $\text{C}_9\text{H}_{12}\text{O}_4$ $[\text{M}]^+$, 185.0814. Found 185.0813. Enantioselectivity determined by HPLC (Chiralcel ODH column, 10% *i*-PrOH/hexanes, 0.8 mL/min, 235 nm), $t_{\text{major}} = 8.2$ min, $t_{\text{minor}} = 12.8$ min; ee = 86%.

(R)-Ethyl 2,4-dimethyl-6-oxo-5,6-dihydro-4H-pyran-3-carboxylate: Prepared from the acyclic adduct (0.16 mmol) according to the General Procedure for dihydropyrone formation and purified by column chromatography using 30% EtOAc in hexanes as the eluant to afford the product as a colorless oil (28 mg, 88% yield): $[\alpha]_D^{25} = +19.3^\circ$ ($c = 1.0$, CHCl_3); IR (film) 2979, 1788, 1702, 1648, 1297, 1250, 1132, 1082 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 4.22 (m, 2H), 3.06 (br p, 1H, $J = 7.3$ Hz), 2.65 (dd, 1H, $J = 15.7, 6.7$ Hz), 2.54 (dd, 1H, $J = 15.7, 2.2$ Hz), 2.32 (s, 3H), 1.31 (t, 3H, $J = 7.3$ Hz), 1.10 (d, 3H, $J = 7.0$ Hz); ^{13}C NMR (100 MHz, CDCl_3) δ 167.2, 166.2, 160.2, 112.3, 60.7, 35.6, 27.1, 19.3, 18.7, 14.2; HRMS (EI⁺): Exact mass calcd for $\text{C}_{10}\text{H}_{14}\text{O}_4$ $[\text{M}]^+$, 199.0970. Found 199.0976. Enantioselectivity determined by HPLC (Chiralcel ODH column, 5% *i*-PrOH/hexanes, 0.8 mL/min, 235 nm), $t_{\text{major}} = 8.3$ min, $t_{\text{minor}} = 12.5$ min; ee = 91%.

(R)-Benzyl 2,4-dimethyl-6-oxo-5,6-dihydro-4H-pyran-3-carboxylate: Prepared from the acyclic adduct (0.16 mmol) according to the General Procedure for dihydropyrone formation and purified by column chromatography using 30% EtOAc in hexanes as the eluant to afford the product as a colorless oil (40 mg, 95% yield): $[\alpha]_D^{25} = +17.4^\circ$ ($c = 0.5$, CHCl_3); IR (film) 2962, 1789, 1713, 1650, 1382, 1296, 1248, 1131, 1083 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 7.40–7.32 (m, 5H), 5.22 (s, 2H), 3.10 (br p, 1H, $J = 6.2$ Hz), 2.65 (dd, 1H, $J = 9.2, 6.6$ Hz), 2.54 (dd, 1H, $J = 9.2, 1.8$ Hz), 2.34 (s, 3H), 1.12 (d, 3H, $J = 7.0$ Hz); ^{13}C NMR (100 MHz, CDCl_3) δ 167.0, 166.0, 160.8, 135.8, 128.6, 128.3, 128.1, 112.0, 66.5, 35.6, 27.1, 19.3, 18.9; HRMS (ES⁺): Exact mass calcd for $\text{C}_{15}\text{H}_{17}\text{O}_4$ $[\text{M}+\text{H}]^+$, 261.1127. Found 261.1134. Enantioselectivity determined by HPLC (Chiralcel ODH column, 10% *i*-PrOH/hexanes, 0.8 mL/min, 235 nm), $t_{\text{major}} = 10.5$ min, $t_{\text{minor}} = 15.0$ min; ee = 93%.

(S)-Methyl 3-methyl-5-oxoheptanoate (8b):⁴ To a stirred solution of **4b** (815 mg, 2.27 mmol) in MeOH (25 mL) was added K_2CO_3 (1 spatula tip). After the yellow color had faded the reaction was diluted with EtOAc (150 mL) and washed with 1.0 M HCl (50 mL). The aqueous layer was extracted with EtOAc (100 mL) and the combined organic layers washed with brine and dried (Na_2SO_4). Removal of the solvent *in vacuo* and purification by column chromatography using 10% EtOAc in hexanes as the eluant afforded a mixture of epimers as a colorless oil. The epimers and TsOH (200 mg) were heated at reflux in benzene (5 mL) for 2 h. After cooling to rt, the reaction mixture was diluted with saturated aqueous NaHCO_3 (40 mL) and extracted with EtOAc (1 $\times$ 50 mL, 2 $\times$ 25 mL). The combined organic layers were washed with brine (40 mL) and dried (Na_2SO_4). Removal the solvent removed *in vacuo* and purification by flash column chromatography on silica gel using 10% EtOAc in hexanes as the eluant afforded the product as a colorless oil (328 mg, 84% yield): $[\alpha]_D^{25} = +1.71^\circ$ (neat), lit. for (*R*) $[\alpha]_D^{25} = -2.8^\circ$ (neat); IR (film) 2958, 1737, 1715, 1438, 1371, 1260, 1172 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 3.65 (s, 3H), 2.52–2.45 (m, 2H), 2.42 (br d, 1H, $J = 7.3$ Hz), 2.39 (br d, 1H, $J = 7.3$ Hz), 2.35–2.28 (m, 2H), 2.22 (dd, 1H, $J = 15.0, 7.0$ Hz), 1.03 (t, 3H, $J =$

(4) Enders, D.; Papadopoulos, K. *Tetrahedron Lett.* **1983**, 45, 4967–4970.

7.3 Hz), 0.96 (d, 3H, $J = 6.6$ Hz); ^{13}C NMR (100 MHz, CDCl_3) δ 210.4, 173.0, 51.4, 48.5, 40.7, 36.3, 26.3, 20.0, 7.7; HRMS (CI, NH_3): Exact mass calcd for $\text{C}_9\text{H}_{20}\text{O}_3\text{N}$ $[\text{M}+\text{NH}_4]^+$, 190.1443. Found 190.1437.

(S)-Methyl 3-methyl-5-oxo-5-phenylpentanoate (8f):⁵ Prepared from **4f** (200 mg, 0.49 mmol) in an analogous fashion to **8b** as described above. Purification by column chromatography using 10% EtOAc in hexanes as the eluant afforded the product as a colorless oil (95 mg, 86% yield): $[\alpha]_{\text{D}}^{25} = -2.7^\circ$ (c 2.71, benzene), lit. for (*S*) $[\alpha]_{\text{D}}^{25} = -5.65^\circ$ (c 1.24, benzene); IR (film) 2957, 1732, 1683, 1449, 1286, 1215, 1003 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 7.96 (d, 2H, $J = 7.7$ Hz), 7.55 (t, 1H, $J = 7.3$ Hz), 7.45 (t, 2H, $J = 7.7$ Hz), 3.66 (s, 3H), 3.09 (dd, 1H, $J = 16.1$, 5.9 Hz), 2.83 (dd, 1H, $J = 16.1$, 7.7 Hz), 2.67 (o, 1H, $J = 7.0$ Hz), 2.43 (dd, 1H, $J = 15.4$, 6.6 Hz), 2.31 (dd, 1H, $J = 15.4$, 7.0 Hz), 1.04 (d, 3H, $J = 7.0$ Hz); ^{13}C NMR (100 MHz, CDCl_3) δ 199.2, 173.0, 137.0, 133.0, 128.6, 128.1, 51.4, 44.8, 40.8, 26.8, 20.1; HRMS (CI, NH_3): Exact mass calcd for $\text{C}_{13}\text{H}_{20}\text{O}_3\text{N}$ $[\text{M}+\text{NH}_4]^+$, 238.1440. Found 248.1443.

3-[(1R,2R,3S,4S)-3-Methylbicyclo[2.2.1]hept-5-en-2-yl]carbonyl]-2-thiazolidine-thione (9a):³ Freshly prepared **1b** (0.01 mmol) was dissolved in toluene (0.3 mL) and to this solution was added thione **2a** (37.5 mg, 0.2 mmol) in toluene (0.2 mL), followed by freshly distilled cyclopentadiene (83 μL , 1 mmol). The mixture was allowed to stir overnight. Purification by silica gel flash chromatography using 100% hexanes, increasing to 30% EtOAc in hexanes, afforded the desired product (42 mg, 83% yield). The product was identical in all respects to that reported in the literature, but with opposite sign of optical rotation: $[\alpha]_{\text{D}}^{25} = +263^\circ$ (c 1.4, CHCl_3), lit. for (1*S*,2*R*,3*R*,4*S*) $[\alpha]_{\text{D}}^{25} = -285^\circ$ (c 0.85, CHCl_3). Enantioselectivity determined by HPLC (Chiralcel OJH column, 5% *i*-PrOH/hexanes, 0.7 mL/min, 265 nm), $t_{\text{minor}} = 25.1$ min, $t_{\text{major}} = 27.1$ min; ee = 97%.

(4R,5R)-tert-Butyl 5-benzyl-2-ethyl-4-methyl-6-oxo-5,6-dihydro-4H-pyran-3-carboxylate (11): To a stirred solution of **5b** (126 mg, 0.52 mmol) in THF (2.6 mL) at -78°C under an atmosphere of nitrogen was added LiHMDS (1.0 M in THF, 0.54 mL, 0.54 mmol). After 30 min, BnBr (311 μL , 2.6 mmol) was added and the mixture stirred at -50°C for 4 h. The reaction mixture was quenched with sat. NH_4Cl (1.0 mL), diluted with EtOAc (50 mL) and washed with 1.0 M HCl (20 mL). The organic layer was washed with brine (20 mL), dried (Na_2SO_4) and the solvent removed under reduced pressure. Purification by silica gel flash chromatography using 4% EtOAc in hexanes, afforded the desired product (138 mg, 80%) as a mixture of stereoisomers (15:1): $[\alpha]_{\text{D}}^{25} = +60.1^\circ$ ($c = 1.0$, CHCl_3); IR (film) 2974, 1784, 1706, 1644, 1455, 1367, 1251 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 7.32-7.11 (m, 5H), 2.89 (dd, 1H, $J = 12.6$, 5.3 Hz), 2.83-2.77 (m, 1H), 2.73-2.57 (m, 4H), 1.50 (s, 9H), 1.21 (t, 3H, $J = 7.8$ Hz), 1.01 (d, 3H, $J = 7.3$ Hz); ^{13}C NMR (100 MHz, CDCl_3) δ 169.5, 165.5, 162.8, 137.1, 129.0, 128.8, 128.6, 126.9, 110.7, 81.1, 47.9, 35.8, 30.8, 28.1, 25.0, 19.6, 11.6; HRMS (ES+): Exact mass calcd for $\text{C}_{20}\text{H}_{27}\text{O}_4$ $[\text{M}+\text{H}]^+$, 331.1909. Found 331.1910.

(2R,3S)-2-Benzyl-N-methoxy-N,3-dimethyl-5-oxoheptanamide (12): To a stirred suspension of $\text{Me}(\text{OMe})\text{NH}\cdot\text{HCl}$ (203 mg, 2.1 mmol) and lactone **11** (138 mg, 0.42 mmol) in THF (8.0 mL) at -20°C was added *i*-PrMgCl (2.0 M in THF, 1.87 mL, 3.7 mmol). After 15 min the reaction was quenched by the careful addition of sat. NH_4Cl (1.0 mL) and allowed to warm to rt. The mixture was diluted with EtOAc (50 mL) and washed with 1.0 M HCl (25 mL) and brine (25 mL). The organic layer was dried (Na_2SO_4) and the solvent removed under reduced pressure. Purification by silica gel flash chromatography using 20% EtOAc in hexanes afforded a mixture of keto esters (157 mg). The keto esters (157 mg) were stirred in a mixture of CH_2Cl_2 (6.3 mL), TFA (3.1 mL) and DMS (294 μL) at room temperature until all starting material was consumed by tlc. The solvent was removed

under a stream of nitrogen and the residue dissolved in benzene (8.0 mL). Gentle heating at 60 °C affected decarboxylation over a period of 1 h. The reaction mixture was diluted with NaHCO₃ (10 mL) and extracted with EtOAc (3 × 20 mL). The combined organic layers were washed with brine (10 mL) and dried (Na₂SO₄). Removal of the solvent under reduced pressure, followed by purification by silica gel flash chromatography using 15% EtOAc in hexanes, afforded the desired product (96 mg, 76%): $[\alpha]_D^{25} = +30.2^\circ$ ($c = 1.0$, CHCl₃); IR (film) 2970, 1712, 1652, 1495, 1455, 1380, 1116, 997 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 7.23-7.11 (m, 5H), 3.07 (s, 3H), 3.06 (ob s, 1H), 3.02 (s, 3H), 2.93 (t, 1H, $J = 12.6$ Hz), 2.72 (d, 1H, $J = 10.2$ Hz), 2.55 (d, 1H, $J = 14.6$ Hz), 2.41-2.32 (m, 4H), 1.02 (t, 3H, $J = 7.3$ Hz), 0.99 (d, 3H, $J = 6.3$ Hz); ¹³C NMR (100 MHz, CDCl₃) δ 210.9, 175.0, 140.2, 129.0, 128.9, 128.8, 128.2, 126.0, 60.8, 48.0, 46.5, 36.2, 35.6, 32.0, 31.8, 31.6, 17.8, 7.7; HRMS (ES⁺): Exact mass calcd for C₁₇H₂₆O₃N [M+H]⁺, 292.1912. Found 292.1906.

(*R,E*)-tert-Butyl 5-benzylidene-2-ethyl-4-methyl-6-oxo-5,6-dihydro-4H-pyran-3-carboxylate (13):

To a stirred solution of **5b** (200 mg, 0.83 mmol) in THF (4.2 mL) at –78 °C under an atmosphere of nitrogen was added LiHMDS (1.0 M in THF, 1.25 mL, 1.25 mmol). After 30 min, benzaldehyde (127 μ L, 1.25 mmol) was added dropwise and the reaction stirred for a further 1 h at –78 °C. Saturated aqueous ammonium chloride (1.0 mL) was added and the mixture allowed to warm to room temperature. The reaction mixture was diluted with 1.0 M HCl (20 mL) and extracted with EtOAc (3 × 20 mL). The combined organic layers were washed with brine (20 mL) and dried (Na₂SO₄). Removal of the solvent under reduced pressure, followed by flash chromatography on silica gel using 5% EtOAc in hexanes, increasing to 30% EtOAc gave the aldol adduct (268 mg, 93%) as a 1:1 mixture of stereoisomers. The mixture was dissolved in CH₂Cl₂ (2.0 mL), cooled to 0 °C, and Et₃N (268 μ L, 1.93 mmol) followed by MsCl (120 μ L, 1.54 mmol) was added. The mixture was allowed to warm to room temperature. After 1 h the mixture was diluted with 1.0 M HCl (20 mL) and extracted with CH₂Cl₂ (2 × 20 mL). The combined organic layers were washed with brine (20 mL), dried (Na₂SO₄) and the solvent removed under reduced pressure. The residue was dissolved in toluene (5 mL) and DBU (230 μ L, 1.54 mmol) added. After 30 min the solution was diluted with 1.0 M HCl (20 mL) and extracted with EtOAc (2 × 15 mL). The combined organic layers were washed with brine (10 mL) and dried (Na₂SO₄). Removal of the solvent under reduced pressure, followed by flash chromatography on silica gel using 10% EtOAc in hexanes gave **13** (220 mg, 81% over three steps) as a 10:1 mixture of olefin isomers: $[\alpha]_D^{25} = +168.4^\circ$ ($c = 1.0$, CHCl₃); IR (film) 2976, 1748, 1695, 1656, 1369, 1157, 1113, 1074 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 7.68 (s, 1H), 7.46-7.38 (m, 5H), 4.14 (q, 1H, $J = 6.8$ Hz), 2.75 (m, 1H), 2.65 (m, 1H), 1.50 (s, 9H), 1.35 (d, 3H, $J = 6.8$ Hz), 1.19 (t, 3H, $J = 7.8$ Hz); ¹³C NMR (100 MHz, CDCl₃) δ 165.1, 164.5, 162.4, 140.8, 134.2, 129.9, 129.6, 128.3, 112.4, 81.4, 30.3, 28.1, 25.6, 21.2, 11.7; HRMS (ES⁺): Exact mass calcd for C₂₀H₂₅O₄ [M+H]⁺, 329.1753. Found 329.1747.

(*4R,5S*)-tert-Butyl 5-benzyl-2-ethyl-4-methyl-6-oxo-5,6-dihydro-4H-pyran-3-carboxylate (14):

10% Pd/C (20 mg) was added to a stirred solution of lactone **13** (100 mg, 0.3 mmol) in toluene (3.0 mL). The atmosphere was purged with hydrogen (balloon) and stirred at ambient pressure for 3 h. The atmosphere was flushed with nitrogen, and the reaction mixture filtered through a short plug of silica gel. Removal of the solvent afforded the product (100 mg, 100%) as a single stereoisomer (dr 25:1): $[\alpha]_D^{25} = +31.7^\circ$ ($c = 1.0$, CHCl₃); IR (film) 2976, 1779, 1700, 1645, 1456, 1368, 1250, 1105 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 7.33-7.23 (m, 5H), 3.35 (AB d, 1H, $J = 14.6, 5.9$ Hz), 2.87 (dt, 1H, $J = 8.3, 5.9$ Hz), 2.79-2.67 (m, 3H), 2.58 (m, 1H), 1.46 (s, 9H), 1.15 (t, 3H, $J = 7.3$ Hz), 1.04 (d, 3H, $J = 6.8$ Hz); ¹³C NMR (100 MHz, CDCl₃) δ 170.2, 165.3, 163.3, 138.7, 128.8, 128.6, 126.6, 114.8, 81.3, 45.4, 32.3, 30.3, 28.1, 25.2, 13.9, 11.8; HRMS (ES⁺): Exact mass calcd for C₂₀H₂₇O₄ [M+H]⁺, 331.1909. Found 331.1905.

(*2S,3S*)-2-Benzyl-N-methoxy-N,3-dimethyl-5-oxoheptanamide (15): To a stirred suspension of Me(OMe)NH•HCl (74 mg, 0.75 mmol) and lactone **14** (50 mg, 0.15

mmol) in THF (1.5 mL) at $-20\text{ }^{\circ}\text{C}$ was added *i*-PrMgCl (2.0 M in THF, 680 μL , 1.35 mmol). After 15 min the reaction was quenched by the careful addition of 1.0 M HCl (1.0 mL) and allowed to warm to rt. The mixture was diluted with 1.0 M HCl (15 mL) and extracted with EtOAc ($2 \times 20\text{ mL}$). The combined organic layers were washed with brine (20 mL) and dried (Na_2SO_4). Removal of the solvent under reduced pressure, followed by purification by silica gel flash chromatography using 20% EtOAc in hexanes, increasing to 40% EtOAc, afforded a mixture of keto esters (59 mg, 100%).

The keto esters (30 mg, 77 μmol) were stirred in a mixture of CH_2Cl_2 (1.0 mL), TFA (0.5 mL) and DMS (56 μL) at room temperature until all starting material was consumed by tlc. The solvent was removed under a stream of nitrogen and the residue dissolved in benzene (2.0 mL). Gentle heating at $60\text{ }^{\circ}\text{C}$ affected decarboxylation over a period of 1 h. The reaction mixture was diluted with NaHCO_3 (10 mL) and extracted with EtOAc ($3 \times 20\text{ mL}$). The combined organic layers were washed with brine (10 mL) and dried (Na_2SO_4). Removal of the solvent under reduced pressure, followed by purification by silica gel flash chromatography using 15% EtOAc in hexanes, afforded the desired product (18 mg, 80%): $[\alpha]_{\text{D}}^{25} = -30.3^{\circ}$ ($c = 0.4$, CHCl_3); IR (film) 2970, 2936, 1714, 1654, 1456, 1415, 1379, 1176 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 7.25-7.14 (m, 5H), 3.12 (s, 3H), 3.11 (br s, 1H), 3.05 (s, 3H), 3.01 (ob d, 1H), 2.70 (m, 2H), 2.48-2.32 (m, 3H), 2.28 (dd, 1H, $J = 16.6, 7.8\text{ Hz}$), 1.04 (t, 3H, $J = 7.3\text{ Hz}$), 1.01 (d, 3H, $J = 6.8\text{ Hz}$); ^{13}C NMR (100 MHz, CDCl_3) δ 210.6, 174.8, 140.4, 129.0, 128.8, 128.2, 126.0, 60.9, 47.2, 46.3, 36.3, 35.4, 31.6, 17.5, 7.7; HRMS (ES $^{+}$): Exact mass calcd for $\text{C}_{17}\text{H}_{26}\text{O}_3\text{N}$ $[\text{M}+\text{H}]^{+}$, 292.1912. Found 292.1910.

(2R,3S)-2-Benzyl-3-methyl-5-oxoheptanoic acid (16): To a stirred solution of **11** (107 mg, 0.32 mmol) in THF:water (2:1, 7.5 mL) at $0\text{ }^{\circ}\text{C}$ was added LiOH (8 mg, 0.32 mmol). After 1 h the reaction mixture was carefully quenched with 1.0 M HCl (10 mL) and extracted with EtOAc ($2 \times 20\text{ mL}$). The combined organic layers were washed with brine (20 mL) and dried (Na_2SO_4). The solvent was removed under reduced pressure, and the

resulting residue dissolved in CH_2Cl_2 (5 mL), TFA (2.5 mL) and dimethylsulfide (240 μL). After stirring at rt for 1.5 h the solvent was removed under a stream of nitrogen. The residue was then gently heated at $60\text{ }^{\circ}\text{C}$ in benzene (5 mL) to induce decarboxylation. The reaction mixture was diluted with 1.0 M HCl (10 mL) and extracted with EtOAc ($2 \times 20\text{ mL}$). The combined organic layers were washed with brine (20 mL) and dried (Na_2SO_4). Removal of the solvent under reduced pressure followed by purification by flash chromatography on silican gel using 30% EtOAc in hexanes as the eluant afforded the desired product (67 mg, 84%): $[\alpha]_{\text{D}}^{25} = +10.7^{\circ}$ ($c = 1.0$, CHCl_3); IR (film) 3029 (br), 2974, 2938, 1731, 1707, 1456, 1412, 1245, 1163 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 7.27-7.15 (m, 5H), 2.90 (dd, 1H, $J = 13.6, 10.2\text{ Hz}$), 2.78 (dd, 1H, $J = 13.6, 4.8\text{ Hz}$), 2.57 (dd, 1H, $J = 16.1, 3.9\text{ Hz}$), 2.41 (m, 4H), 1.05 (t, 3H, $J = 7.3\text{ Hz}$), 1.03 (d, 3H, $J = 6.8\text{ Hz}$); ^{13}C NMR (100 MHz, CDCl_3) δ 210.4, 180.2, 139.1, 128.7, 128.4, 126.3, 52.2, 46.1, 36.4, 34.8, 31.0, 17.8, 7.6; HRMS (ES $^{+}$): Exact mass calcd for $\text{C}_{15}\text{H}_{21}\text{O}_3$ $[\text{M}+\text{H}]^{+}$, 249.1490. Found 249.1488.

(2R,3S)-Methyl 2-benzyl-3-methyl-5-oxoheptanoate (17): To a stirred solution of **11** (100 mg, 0.30 mmol) in MeOH (3.0 mL) at rt was added NaOMe (82 mg, 1.5 mmol). After 20 min the reaction was carefully quenched by the dropwise addition of 1.0 M HCl (2.0 mL). The mixture was diluted with 1.0 HCl (20 mL) and extracted with EtOAc ($3 \times$

20 mL). The combined organic layers were washed with brine (20 mL) and dried (Na_2SO_4). The solvent was removed under reduced pressure and the residue dissolved in CH_2Cl_2 (2.0 mL) and TFA (1.0 mL). After stirring at rt for 2 h the solvent was removed under a stream of nitrogen, dissolved in benzene and heated at $60\text{ }^{\circ}\text{C}$ for 3 h to affect decarboxylation. Concentration in vacuo, followed by purification by silica gel flash chromatography using 5% EtOAc in hexanes, increasing to 10% EtOAc in hexanes afforded the desired product (60 mg, 93%) as a colorless oil: $[\alpha]_{\text{D}}^{25} = +12.9^{\circ}$ ($c = 1.0$, CHCl_3); IR (film) 2964, 1732, 1715, 1456, 1368, 1261, 1165, 1030 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 7.27-7.12 (m, 5H), 3.53 (s, 3H), 2.89 (dd, 1H, $J = 13.5, 10.6\text{ Hz}$), 2.78 (dd, 1H, $J = 13.5, 4.8\text{ Hz}$), 2.64 (dt, 1H, $J = 10.6, 4.8\text{ Hz}$), 2.55 (dd, 1H, $J = 16.1, 4.0\text{ Hz}$), 2.48-2.29 (m, 5H), 1.04 (t, 3H, $J = 7.3\text{ Hz}$), 0.99 (d, 3H, $J = 7.0\text{ Hz}$); ^{13}C NMR (100 MHz, CDCl_3) δ 210.3, 174.8, 139.4,

128.7, 128.4, 126.3, 52.7, 51.2, 46.3, 36.4, 35.4, 31.2, 18.0, 7.7; HRMS (ES⁺): Exact mass calcd for C₁₆H₂₃O₃ [M+H]⁺, 263.1647. Found 263.1651.

X-Ray Crystal Structure: [Ni((*S*)-BINAP)]Cl₂ (1a, X-ray)

Table 2. Crystal data and structure refinement for [Ni((*S*)-BINAP)]Cl₂ (**1a**).

Identification code	[Ni((<i>S</i>)-BINAP)]Cl ₂	
Empirical formula	C ₄₄ H ₃₂ Cl ₂ Ni P ₂	
Formula weight	752.25	
Temperature	213(2) K	
Wavelength	0.71073 Å	
Crystal system	Tetragonal	
Space group	P4(3)2(1)2	
Unit cell dimensions	a = 11.647(3) Å	a = 90°.
	b = 11.647(3) Å	b = 90°.
	c = 26.381(8) Å	g = 90°.
Volume	3578.5(15) Å ³	
Z	4	
Density (calculated)	1.396 Mg/m ³	
Absorption coefficient	0.813 mm ⁻¹	
F(000)	1552	
Crystal size	0.2 x 0.2 x 0.3 mm ³	
Theta range for data collection	1.91 to 27.74°.	
Index ranges	-15 ≤ h ≤ 14, -15 ≤ k ≤ 14, -12 ≤ l ≤ 34	
Reflections collected	22367	
Independent reflections	3907 [R(int) = 0.0539]	
Completeness to theta = 27.74°	94.1 %	
Absorption correction	Empirical	
Max. and min. transmission	1.000000 and 0.639095	

Refinement method	Full-matrix least-squares on F ²
Data / restraints / parameters	3907 / 0 / 222
Goodness-of-fit on F ²	1.014
Final R indices [I>2sigma(I)]	R1 = 0.0343, wR2 = 0.0686
R indices (all data)	R1 = 0.0502, wR2 = 0.0732
Absolute structure parameter	-0.009(13)
Largest diff. peak and hole	0.236 and -0.239 e.Å ⁻³

Table 8. Atomic coordinates (x 10⁴) and equivalent isotropic displacement parameters (Å²x 10³)
For **5**. U(eq) is defined as one third of the trace of the orthogonalized U_{ij} tensor.

	x	y	z	U(eq)
Ni(1)	5278(1)	5278(1)	0	30(1)
P(1)	3673(1)	5075(1)	407(1)	26(1)
Cl(1)	7160(1)	5177(1)	-70(1)	52(1)
C(1)	2343(2)	6133(2)	-332(1)	40(1)
C(2)	3456(2)	3582(2)	606(1)	24(1)
C(3)	2801(2)	6395(2)	1216(1)	42(1)
C(4)	3760(2)	5869(2)	1001(1)	35(1)
C(5)	2337(2)	5502(2)	114(1)	31(1)
C(6)	3802(2)	3236(2)	1099(1)	35(1)
C(7)	1291(2)	5156(2)	320(1)	38(1)
C(8)	3004(2)	1574(2)	416(1)	33(1)
C(9)	3072(2)	2748(2)	266(1)	25(1)
C(10)	2897(3)	7007(2)	1667(1)	59(1)
C(11)	3368(2)	1256(2)	915(1)	44(1)
C(12)	3751(3)	2115(2)	1245(1)	44(1)
C(13)	4817(3)	5971(3)	1243(1)	57(1)
C(14)	283(3)	6034(3)	-365(1)	58(1)
C(15)	1307(3)	6396(3)	-571(1)	58(1)
C(16)	272(2)	5435(2)	83(1)	50(1)
C(17)	3352(3)	80(3)	1052(1)	67(1)
C(18)	2662(3)	-434(2)	234(1)	66(1)
C(19)	4885(4)	6590(3)	1699(1)	78(1)
C(20)	3026(4)	-737(3)	718(1)	78(1)
C(22)	2646(3)	685(2)	85(1)	45(1)
C(25)	3921(4)	7090(3)	1904(1)	72(1)

Table 9. Bond lengths [$\text{\AA}$] and angles [$^\circ$] for $[\text{Ni}((S)\text{-BINAP})]\text{Cl}_2$ (**1a**).

Ni(1)-P(1)#1	2.1697(7)
Ni(1)-P(1)	2.1697(7)
Ni(1)-Cl(1)#1	2.2022(8)
Ni(1)-Cl(1)	2.2022(8)
P(1)-C(5)	1.807(2)
P(1)-C(4)	1.822(2)
P(1)-C(2)	1.834(2)
C(1)-C(5)	1.388(3)
C(1)-C(15)	1.395(4)
C(2)-C(9)	1.394(3)
C(2)-C(6)	1.420(3)
C(3)-C(10)	1.390(3)
C(3)-C(4)	1.395(4)
C(4)-C(13)	1.391(4)
C(5)-C(7)	1.393(3)
C(6)-C(12)	1.363(3)
C(7)-C(16)	1.380(3)
C(8)-C(22)	1.417(3)
C(8)-C(9)	1.426(3)
C(8)-C(11)	1.433(3)
C(9)-C(9)#1	1.502(4)
C(10)-C(25)	1.350(5)
C(11)-C(12)	1.398(4)
C(11)-C(17)	1.417(4)
C(13)-C(19)	1.406(4)
C(14)-C(16)	1.371(4)
C(14)-C(15)	1.377(4)
C(17)-C(20)	1.353(4)
C(18)-C(22)	1.362(4)
C(18)-C(20)	1.391(5)
C(19)-C(25)	1.374(5)
P(1)#1-Ni(1)-P(1)	93.28(3)
P(1)#1-Ni(1)-Cl(1)#1	153.27(3)
P(1)-Ni(1)-Cl(1)#1	91.20(2)
P(1)#1-Ni(1)-Cl(1)	91.19(2)

P(1)-Ni(1)-Cl(1)	153.27(3)
Cl(1)#1-Ni(1)-Cl(1)	96.55(4)
C(5)-P(1)-C(4)	106.04(11)
C(5)-P(1)-C(2)	105.34(10)
C(4)-P(1)-C(2)	104.06(10)
C(5)-P(1)-Ni(1)	120.04(8)
C(4)-P(1)-Ni(1)	108.81(9)
C(2)-P(1)-Ni(1)	111.31(7)
C(5)-C(1)-C(15)	119.6(3)
C(9)-C(2)-C(6)	118.8(2)
C(9)-C(2)-P(1)	121.39(15)
C(6)-C(2)-P(1)	119.42(17)
C(10)-C(3)-C(4)	120.5(3)
C(13)-C(4)-C(3)	119.0(2)
C(13)-C(4)-P(1)	119.2(2)
C(3)-C(4)-P(1)	121.9(2)
C(1)-C(5)-C(7)	119.3(2)
C(1)-C(5)-P(1)	120.24(19)
C(7)-C(5)-P(1)	120.43(17)
C(12)-C(6)-C(2)	121.2(2)
C(16)-C(7)-C(5)	120.4(2)
C(22)-C(8)-C(9)	123.1(2)
C(22)-C(8)-C(11)	117.7(2)
C(9)-C(8)-C(11)	119.1(2)
C(2)-C(9)-C(8)	120.51(19)
C(2)-C(9)-C(9)#1	120.43(16)
C(8)-C(9)-C(9)#1	119.05(17)
C(25)-C(10)-C(3)	120.3(3)
C(12)-C(11)-C(17)	122.5(2)
C(12)-C(11)-C(8)	118.8(2)
C(17)-C(11)-C(8)	118.7(3)
C(6)-C(12)-C(11)	121.6(2)
C(4)-C(13)-C(19)	119.1(3)
C(16)-C(14)-C(15)	120.2(3)
C(14)-C(15)-C(1)	120.3(3)
C(14)-C(16)-C(7)	120.2(3)
C(20)-C(17)-C(11)	121.1(3)
C(22)-C(18)-C(20)	120.8(3)

C(25)-C(19)-C(13)	120.5(3)
C(17)-C(20)-C(18)	120.4(3)
C(18)-C(22)-C(8)	121.2(3)
C(10)-C(25)-C(19)	120.6(3)

Symmetry transformations used to generate equivalent atoms:

#1 y,x,-z

Table 10. Anisotropic displacement parameters ($\text{\AA}^2 \times 10^3$) for $[\text{Ni}((S)\text{-BINAP})]\text{Cl}_2$ (**1a**). The anisotropic displacement factor exponent takes the form: $-2p^2[h^2 a^{*2}U^{11} + \dots + 2 h k a^* b^* U^{12}]$

	U ¹¹	U ²²	U ³³	U ²³	U ¹³	U ¹²
<hr/>						
Ni(1)	26(1)	26(1)	38(1)	-4(1)	4(1)	-5(1)
P(1)	25(1)	23(1)	30(1)	-2(1)	1(1)	0(1)
Cl(1)	26(1)	58(1)	71(1)	-10(1)	6(1)	-10(1)
C(1)	45(2)	29(1)	46(1)	6(1)	0(1)	3(1)
C(2)	21(1)	26(1)	26(1)	1(1)	2(1)	3(1)
C(3)	58(2)	25(1)	43(1)	-4(1)	16(1)	-5(1)
C(4)	44(2)	27(1)	34(1)	-5(1)	5(1)	-10(1)
C(5)	32(1)	24(1)	36(1)	-1(1)	1(1)	7(1)
C(6)	42(2)	36(1)	26(1)	-2(1)	-7(1)	6(1)
C(7)	32(1)	38(1)	44(1)	1(1)	4(1)	9(1)
C(8)	37(2)	27(1)	35(1)	0(1)	9(1)	-3(1)
C(9)	21(1)	26(1)	29(1)	0(1)	3(1)	3(1)
C(10)	94(3)	34(2)	49(2)	-11(1)	32(2)	-17(2)
C(11)	61(2)	31(1)	40(1)	10(1)	9(1)	8(1)
C(12)	60(2)	43(2)	30(1)	8(1)	-6(1)	13(2)
C(13)	55(2)	67(2)	49(2)	-16(1)	-1(2)	-13(2)
C(14)	46(2)	59(2)	71(2)	4(2)	-11(2)	26(2)
C(15)	71(2)	47(2)	56(2)	17(1)	-11(2)	13(2)
C(16)	30(1)	54(2)	66(2)	-3(2)	2(1)	14(1)
C(17)	111(3)	38(2)	50(2)	16(2)	11(2)	8(2)
C(18)	109(3)	27(2)	61(2)	-4(1)	24(2)	-18(2)
C(19)	90(3)	92(3)	54(2)	-19(2)	-17(2)	-43(2)
C(20)	137(4)	26(2)	70(2)	13(2)	31(2)	-1(2)
C(22)	61(2)	32(1)	42(1)	-2(1)	10(1)	-11(1)
C(25)	113(3)	61(2)	42(2)	-21(2)	20(2)	-41(2)

Table 11. Hydrogen coordinates ($\times 10^4$) and isotropic displacement parameters ($\text{\AA}^2 \times 10^{-3}$) for $[\text{Ni}((S)\text{-BINAP})]\text{Cl}_2$ (**1a**).

	x	y	z	U(eq)
H(1A)	3042	6383	-473	48
H(3A)	2083	6336	1055	51
H(6A)	4072	3791	1328	41
H(7A)	1279	4730	623	46
H(10A)	2247	7365	1807	71
H(12A)	3979	1914	1575	53
H(13A)	5476	5630	1103	69
H(14A)	-411	6197	-531	70
H(15A)	1308	6821	-873	70
H(16A)	-430	5214	228	60
H(17A)	3571	-136	1382	80
H(18A)	2423	-1009	7	79
H(19A)	5595	6663	1866	94
H(20A)	3047	-1515	812	94
H(22A)	2394	872	-244	54
H(25A)	3976	7493	2212	86