Highly Selective Asymmetric Acetate Aldol Additions Using Mesityl Substituted Chiral Auxiliaries

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Supporting Information

Methods and Materials: Infrared (IR) spectra were obtained using a Jasco 460 Plus Fourier transform infrared spectrometer and values reported in cm^{-1} . Proton and carbon nuclear magnetic resonance (^1H and ^{13}C NMR) spectra were recorded on the Bruker 400 (^1H at 400 MHz; ^{13}C at 100 MHz). Optical rotations were determined using a Jasco P1010 polarimeter. Thin layer chromatography (TLC) was conducted on silica gel F254 TLC plates purchased from Scientific Adsorbents, Inc. Flash column chromatography was carried out using silica gel (32 to 63 μm) purchased from Scientific Adsorbents, Inc. Diethyl ether (Et_2O), tetrahydrofuran (THF), dichloromethane (CH_2Cl_2), and toluene were dried by being passed through a column of neutral alumina under nitrogen immediately prior to use. Alkylamines were distilled from calcium hydride immediately prior to use. Mesitylmagnesium bromide was synthesized using standard Grignard techniques from 2-bromomesitylene. (*R*)-(+)-2-methyl-2-propanesulfinamide and (*S*)-(-)-2-methyl-2-propanesulfinamide were prepared using Ellman's procedure.¹ All other reagents and solvents were used as received from the manufacturer. All air and water sensitive reactions were performed in flasks flame dried under positive flow argon and conducted under an argon atmosphere.

(*R,E*)-*N*-(2-(4-methoxybenzyloxy)ethylidene)-2-methylpropane-2-sulfinamide

(2): To a dry 25 mL round-bottom flask, under argon, was added (*R*)-(+)-2-methyl-2-propanesulfinamide (0.715 g, 5.90 mmol) and 12 mL of CH_2Cl_2 (0.5 M). Anhydrous CuSO_4 (2.07 g, 13.0 mmol) was added in one portion followed by (4-methoxybenzyloxy)-acetaldehyde (1.17 g, 6.49 mmol). The reaction mixture was stirred at room temperature for 24 h, filtered through a pad of celite, and concentrated under reduced pressure. The crude product was purified by flash column chromatography (25%

¹ Weix, D. J.; Ellman, J. A. *Org. Synth.*, **2005**, 82, 57.

EtOAc/Hex to 35% EtOAc/Hex) to provide the product as a pale yellow oil (1.67 g, 85%). ¹H NMR (400 MHz, CDCl₃): δ 1.17 (s, 9H), 3.76 (s, 3H), 4.33 (s, 2H), 4.52 (s, 2H), 6.85 (d, 2H, J = 8.4 Hz), 7.24 (d, 2H, J = 8.4), 8.07 (s, 1H). ¹³C NMR (100 MHz, CDCl₃): δ 22.3, 55.1, 56.8, 70.8, 72.8, 113.8, 129.1, 129.4, 159.4, 166.7. IR (film): 2959, 2866, 1633, 1613, 1514, 1363, 1249, 1175 cm⁻¹. ESI-MS: C₁₄H₂₁NO₃S [M+H] calc. 284.4, found 284.2. [α]_D²⁶ = -173° (c = 1.25, CH₂Cl₂).

(R)-N-((R)-1-mesityl-2-(4-methoxybenzyloxy)ethyl)-2-methylpropane-2-sulfonamide: To a dry 250 mL round-bottom flask, under argon, was added imine **2** (4.00 g, 14.1 mmol) and 71 mL of toluene (0.2 M) and the flask was cooled to -78 °C. To this solution was slowly added mesityl magnesium bromide (5.0 equiv), prepared from 4.30 g Mg turnings (0.18 mol), 24.0 mL 2-bromomesitylene (0.17 mol) and 80 mL of dry ether. The mixture was stirred for 2 h at -78 °C upon which the reaction was quenched with saturated ammonium chloride. The layers were separated and the aqueous layer was extracted with ethyl acetate (2x). The combined organic layers were dried over Na₂SO₄, filtered, and concentrated under reduced pressure. The crude product was purified by flash column chromatography (40% EtOAc/Hex to 70% EtOAc/Hex) to provide a single diastereomer of the product as a yellow oil (5.40 g, 95%). ¹H NMR (400 MHz, CDCl₃): δ 1.19 (s, 9H), 2.23 (s, 3H), 2.39 (s, 6H), 3.51 (dd, 1H, J = 4.0, 10.0 Hz), 3.78 (s, 3H), 3.95 (t, 1H, J = 10.4 Hz), 4.11 (s, 1H), 4.51 (AB_q, 2H, J_{AB} = 11.6 Hz, Δν_{AB} = 75.9 Hz), 5.12 (ddd, 1H, J = 10.4, 3.6, 1.2 Hz), 6.80 (s, 2H), 6.87 (d, 2H, J = 8.4 Hz), 7.26 (d, 2H, J = 8.8 Hz). ¹³C NMR (100 MHz, CDCl₃): δ 20.7, 20.9, 22.5, 52.7, 54.8, 55.1, 69.8, 72.0, 113.7, 129.3, 129.4, 129.7, 140.0, 137.2, 137.8, 159.2. IR (film): 3277, 2955, 2866, 1612, 1513, 1464, 1363, 1249, 1174 cm⁻¹. ESI-MS: C₂₃H₃₃NO₃S [M+H] calc. 404.6, found 404.2. [α]_D²⁵ = -86.1° (c = 1.65, CH₂Cl₂).

(R)-2-amino-2-mesitylethanol (3): To a dry 250 mL round-bottom flask, under argon, was added the protected amino alcohol (4.50 g, 11.2 mmol) in 23 mL of MeOH (0.5 M). To this solution was added 4 N HCl/dioxane (28.0 mL, 112.0 mmol) and the solution was stirred for 1 h at room temperature. The solution was then concentrated under reduced pressure. The residue was dissolved in ether and 4 N NaOH (200 mL) was slowly added while stirring. The layers were separated and the aqueous layer was extracted with ether (2x). The combined organic layers were dried over Na₂SO₄ and concentrated under reduced pressure. The crude product was purified by flash column chromatography (80% EtOAc/Hex to 10% MeOH/CH₂Cl₂) to provide the amino alcohol as a pale yellow solid (1.52 g, 76%). ¹H NMR (400 MHz, CDCl₃): δ 2.25 (s, 3H), 2.40 (s,

6H), 2.60 (brs, 3H), 3.62 (dd, 1H, $J = 4.0, 10.8$ Hz), 3.83 (t, 1H, $J = 12.0$ Hz), 4.47 (dd, 1H, $J = 4.8, 10.0$ Hz). 6.83 (s, 2H). ^{13}C NMR (100 MHz, CDCl_3): δ 20.6, 21.2, 53.9, 64.6, 130.3, 134.8, 136.2, 136.6. IR (film): 3364, 3300, 2954, 2920, 2867, 1610, 1455, 1378, 1249 cm^{-1} . ESI-MS: $\text{C}_{11}\text{H}_{17}\text{NO}$ $[\text{M}+\text{H}]$ calc. 180.3, found 180.2. $[\alpha]_{\text{D}}^{25} = -25.9^\circ$ ($c = 0.40$, CH_2Cl_2).

(R)-4-mesityloxazolidine-2-thione: To a dry 250 mL round-bottom flask, under argon, was added amino alcohol **3** (4.86 g, 27.1 mmol) in 97 mL of CH_2Cl_2 (0.3 M). To this solution was added triethylamine (9.4 mL, 67.8 mmol) and the solution was cooled to 0 $^\circ\text{C}$. Thiophosgene (2.1 mL, 27.1 mmol) was diluted in 2 mL of CH_2Cl_2 and added to the reaction vessel. The reaction mixture was stirred for 30 min at 0 $^\circ\text{C}$ and then quenched with 10% NaHSO_4 . After warming to room temperature, the layers were separated and the aqueous layer was extracted with CH_2Cl_2 (2x). The combined organic layers were washed with 1 M NH_4OH , followed by saturated NaCl , dried over NaSO_4 , filtered, and concentrated under reduced pressure. The crude product was purified by flash column chromatography (30% EtOAc/Hex) to provide the product as a pale yellow foam (5.1 g, 85%). The product was crystallized by triturating with hexanes. ^1H NMR (400 MHz, CDCl_3): δ 2.25 (s, 3H), 2.34 (s, 6H), 4.53 (dd, 1H, $J = 8.8, 8.8$ Hz), 4.96 (dd, 1H, $J = 9.2, 10.8$ Hz), 5.64 (dd, 1H, $J = 8.8, 10.8$ Hz), 6.87 (s, 2H). ^{13}C NMR (100 MHz, CDCl_3): δ 20.3, 20.7, 55.6, 74.9, 129.1, 131.0, 136.9, 138.7, 189.3. IR (film): 3382, 3184, 2971, 2923, 1610, 1505, 1269, 1174, 1146 cm^{-1} . ESI-MS: $\text{C}_{12}\text{H}_{15}\text{NOS}$ $[\text{M}+\text{H}]$ calc. 222.3, found 222.1, $[\text{M}+\text{Na}]$ calc. 244.3, found 244.1. $[\alpha]_{\text{D}}^{25} = -5.3^\circ$ ($c = 3.0$, CH_2Cl_2).

(R)-1-(4-mesityl-2-thioxooxazolidin-3-yl)ethanone (4): To a dry 500 mL round-bottom flask, under argon, was added oxazolidinethione (7.82 g, 35.3 mmol) and 176 mL of CH_2Cl_2 (0.2 M). The solution was cooled to 0 $^\circ\text{C}$ and triethylamine (9.8 mL, 70.6 mmol) was added. The reaction mixture was stirred for 15 min at 0 $^\circ\text{C}$ and acetyl chloride (3.8 mL, 53.0 mmol) was slowly added. The mixture was stirred for 15 min at 0 $^\circ\text{C}$, then warmed to room temperature and stirred for 20 min. The reaction was quenched with 10% NaHSO_4 and the layers were separated. The aqueous layer was extracted with CH_2Cl_2 (2x) and the combined organic layers were dried over NaSO_4 , filtered, and

concentrated under reduced pressure. The crude product was purified by flash column chromatography (15% EtOAc/Hex) to provide the product as a yellow foam (7.53 g, 81%). The foam was dissolved in CH₂Cl₂ and a crystal of the racemic *N*-acetyloxazolidinethione was used as a seed to induce crystallization. ¹H NMR (400 MHz, CDCl₃): δ 2.26 (s, 6H), 2.46 (s, 3H), 2.78 (s, 3H), 4.39 (dd, 1H, J = 7.6, 8.8 Hz), 4.86 (dd, 1H, J = 10.0, 10.8 Hz), 6.10 (dd, 1H, J = 7.2, 10.8 Hz), 6.87 (s, 2H). ¹³C NMR (100 MHz, CDCl₃): δ 19.4, 20.4, 20.6, 26.3, 57.9, 71.5, 129.6, 130.3, 131.7, 134.7, 137.2, 138.0, 170.7, 186.3. IR (film): 3009, 2971, 2920, 2867, 1707, 1611, 1483, 1415, 1372, 1341, 1311, 1239, 1181 cm⁻¹. ESI-MS: C₁₄H₁₇NO₂S [M+H] calc. 264.2, found 264.1. [α]_D²⁵ = +75.3° (c = 5.55, CH₂Cl₂).

Typical aldol procedure using *N*-acetyloxazolidinethione 4: To a dry 25 mL round-bottom flask, under argon, was added *N*-acetyloxazolidinethione (0.263 g, 1.00 mmol) and 5 mL of CH₂Cl₂ (0.2 M). The flask was cooled to -40 °C and titanium tetrachloride (neat, 0.22 mL, 2.00 mmol) was added and the reaction mixture was stirred for 5 min. Diisopropylethylamine (0.35 mL, 2.00 mmol) was then added and the solution was stirred for 2 h at -40 °C and was then cooled to -78 °C, whereupon the freshly distilled aldehyde (neat, 1.2 mmol) was added. The mixture was stirred for 4 h at -78 °C, then quenched with half saturated ammonium chloride and warmed to room temperature. The layers were separated and the aqueous layer was extracted with CH₂Cl₂ (2x). The combined organic layers were dried over NaSO₄, filtered, and concentrated under reduced pressure. The crude product was purified by flash column chromatography (20% EtOAc/Hex). Yields and diastereoselectivities are listed in Table 1.

(*R*)-3-hydroxy-1-((*R*)-4-mesityl-2-thioxooxazolidin-3-yl)pentan-1-one: ¹H NMR (400 MHz, CDCl₃): δ 0.94 (dd, 3H, J = 7.2, 7.6 Hz), 1.48-1.60 (band, 2H), 2.25 (s, 6H), 2.46 (s, 3H), 2.88 (brs, OH), 3.36 (dd, 1H, J = 2.4, 17.6 Hz), 3.51 (dd, 1H, J = 9.2, 17.6 Hz), 3.91 (m, 1H), 4.39 (dd, 1H, J = 7.2, 9.2 Hz), 4.88 (dd, 1H, J = 9.6, 10.8 Hz), 6.12 (dd, 1H, J = 7.2, 10.8 Hz), 6.86 (s, 1H), 6.87 (s, 1H). ¹³C NMR (100 MHz, CDCl₃): δ 9.73, 19.5, 20.5, 20.7, 29.2, 44.5, 58.1, 69.0, 71.8, 129.7, 130.3, 131.8, 134.7, 137.0, 138.1, 173.5, 185.9. IR (film): 3472, 2967, 2919, 2875, 1703, 1612, 1487, 1456, 1395, 1369, 1340, 1304, 1196 cm⁻¹. ESI-MS: C₁₇H₂₃NO₃S [M+H] calc. 322.4, found 322.2, [M+Na] calc. 344.4, found 344.1. [α]_D²⁵ = +21.5° (c = 3.7, CH₂Cl₂).

(R)-3-hydroxy-1-((R)-4-mesityl-2-thioxooxazolidin-3-yl)hexan-1-one: ^1H NMR (400 MHz, CDCl_3): δ 0.91 (dd, 3H, $J = 6.8, 10.8$ Hz), 1.37-1.52 (bands, 4H), 2.52 (s, 6H), 2.46 (s, 3H), 2.88 (s, 1H), 3.35 (dd, 1H, $J = 2.4, 18.0$ Hz), 3.51 (dd, 1H, $J = 9.6, 18.0$ Hz), 3.99 (s, 1H), 4.38 (dd, 1H, $J = 7.2, 9.2$ Hz), 4.88 (dd, 1H, $J = 9.2, 10.8$ Hz), 6.12 (dd, 1H, $J = 7.2, 10.8$ Hz), 6.86 (s, 1H), 6.87 (s, 1H). ^{13}C NMR (100 MHz, CDCl_3): δ 13.8, 18.5, 19.4, 20.5, 20.6, 38.3, 44.9, 58.1, 67.4, 71.7, 129.7, 130.3, 131.7, 134.7, 137.0, 138.1, 173.5, 185.9. IR (film): 3458, 2958, 2929, 2871, 1705, 1611, 1395, 1370, 1341, 1199, 1161 cm^{-1} . ESI-MS: $\text{C}_{18}\text{H}_{25}\text{NO}_3\text{S}$ $[\text{M}+\text{H}]$ calc. 336.5, found 336.2, $[\text{M}+\text{Na}]$ calc. 358.5, found 358.2. $[\alpha]_{\text{D}}^{23} = +24.3^\circ$ ($c = 3.00$, CH_2Cl_2).

(S)-3-hydroxy-1-((R)-4-mesityl-2-thioxooxazolidin-3-yl)-4-methylpentan-1-one: ^1H NMR (400 MHz, CDCl_3): δ 0.94 (dd, 6H, $J = 5.6, 6.8$ Hz), 1.71-1.76 (m, 1H), 2.25 (s, 6H), 2.46 (s, 3H), 2.75 (d, 1H, $J = 4.8$ Hz), 3.32 (dd, 1H, $J = 2.0, 17.6$ Hz), 3.56 (dd, 1H, $J = 10.0, 17.6$ Hz), 3.77 (m, 1H), 4.39 (dd, 1H, $J = 7.2, 9.2$ Hz), 4.87 (dd, 1H, $J = 9.6, 11.2$ Hz), 6.12 (dd, 1H, $J = 7.2, 11.2$ Hz), 6.86 (s, 2H). ^{13}C NMR (100 MHz, CDCl_3): δ 17.7, 18.4, 19.6, 20.6, 20.7, 33.1, 42.1, 58.2, 71.8, 72.5, 76.7, 129.8, 130.4, 131.8, 134.8, 137.1, 138.2, 174.0, 186.1. IR (film): 3473, 2962, 2923, 2875, 1704, 1611, 1482, 1465, 1394, 1370, 1341, 1308, 1198, 1161 cm^{-1} . ESI-MS: $\text{C}_{18}\text{H}_{25}\text{NO}_3\text{S}$ $[\text{M}+\text{H}]$ calc. 336.5, found 336.2, $[\text{M}+\text{Na}]$ calc. 358.5, found 358.2. $[\alpha]_{\text{D}}^{23} = +12.3^\circ$ ($c = 3.65$, CH_2Cl_2).

(R)-3-hydroxy-1-((R)-4-mesityl-2-thioxooxazolidin-3-yl)-5-methylhexan-1-one: ^1H NMR (400 MHz, CDCl_3): δ 0.89 (t, 6H, $J = 6.8$ Hz), 1.19 (ddd, 1H, $J = 4.0, 8.8, 12.8$ Hz), 1.52 (ddd, 1H, $J = 5.2, 9.2, 14.4$ Hz), 1.76-1.81 (bands, 1H), 2.26 (s, 6H), 2.47 (s, 3H), 2.83 (s, 1H), 3.32 (dd, 1H, $J = 2.0, 17.6$ Hz), 3.51 (dd, 1H, $J = 9.6, 18.0$ Hz), 4.05-

4.08 (m, 1H), 4.39 (dd, 1H, $J = 7.2, 9.2$ Hz), 4.88 (dd, 1H, $J = 9.6, 10.8$ Hz), 6.13 (dd, 1H, $J = 7.2, 11.2$ Hz), 6.87 (s, 1H), 6.88 (s, 1H). ^{13}C NMR (100 MHz, CDCl_3): δ 19.5, 20.5, 20.7, 21.8, 23.1, 24.2, 45.3, 45.4, 58.1, 65.8, 71.8, 129.7, 130.4, 131.8, 134.7, 137.0, 138.1, 173.6, 185.9. IR (film): 3448, 2955, 2923, 2869, 1704, 1611, 1487, 1466, 1395, 1370, 1340, 1199, 1161 cm^{-1} . ESI-MS: $\text{C}_{19}\text{H}_{27}\text{NO}_3\text{S}$ $[\text{M}+\text{H}]$ calc. 350.5, found 350.2, $[\text{M}+\text{Na}]$ calc. 372.5, found 372.2. $[\alpha]^{24}_{\text{D}} = +36.1^\circ$ ($c = 1.5$, CH_2Cl_2).

(S)-3-hydroxy-1-((R)-4-mesityl-2-thioxooxazolidin-3-yl)-3-phenylpropan-1-one: ^1H NMR (400 MHz, CDCl_3): δ 2.22 (s, 3H), 2.27 (s, 3H), 2.48 (s, 3H), 3.58 (dd, 1H, $J = 2.4, 17.6$ Hz), 3.93 (dd, 1H, $J = 9.6, 17.6$ Hz), 4.41 (dd, 1H, $J = 7.6, 9.6$ Hz), 4.87 (dd, 1H, $J = 9.6, 10.8$ Hz), 5.13 (dd, 1H, $J = 2.8, 10.0$ Hz), 6.13 (dd, 1H, $J = 7.2, 11.2$ Hz), 6.85 (s, 1H), 6.89 (s, 1H), 7.27-7.35 (bands, 5H). ^{13}C NMR (100 MHz, CDCl_3): δ 19.5, 20.6, 20.7, 46.6, 58.2, 70.0, 71.8, 125.8, 127.7, 128.5, 129.8, 130.2, 131.9, 138.3, 142.2, 172.8, 185.9. IR (film): 3464, 2971, 2919, 1704, 1607, 1482, 1452, 1391, 1370, 1341, 1200, 1158 cm^{-1} . ESI-MS: $\text{C}_{21}\text{H}_{23}\text{NO}_3\text{S}$ $[\text{M}+\text{H}]$ calc. 370.5, found 370.2, $[\text{M}+\text{Na}]$ calc. 392.5, found 392.2. $[\alpha]^{26}_{\text{D}} = +53.7^\circ$ ($c = 0.25$, CH_2Cl_2).

(S,E)-3-hydroxy-1-((R)-4-mesityl-2-thioxooxazolidin-3-yl)-5-phenylpent-4-en-1-one: ^1H NMR (400 MHz, CDCl_3): δ 2.24 (s, 6H), 2.45 (s, 3H), 3.04 (s, 1H), 3.53 (dd, 1H, $J = 3.2, 17.6$ Hz), 3.75 (dd, 1H, $J = 8.8, 18.0$ Hz), 4.37 (dd, 1H, $J = 7.6, 9.2$ Hz), 4.72 (m, 1H), 4.83 (dd, 1H, $J = 9.6, 10.8$ Hz), 6.09 (dd, 1H, $J = 7.2, 10.8$ Hz), 6.21 (dd, 1H, $J = 6.0, 16.0$ Hz), 6.59 (d, 1H, $J = 16.0$ Hz), 6.79 (s, 1H), 6.87 (s, 1H), 7.23-7.35 (bands, 5H). ^{13}C NMR (100 MHz, CDCl_3): δ 19.5, 20.6, 20.7, 44.9, 58.2, 68.5, 71.8, 126.5, 127.6, 128.4, 129.7, 130.2, 130.5, 131.8, 134.7, 136.3, 137.0, 138.2, 172.5, 185.8. IR (film): 3430, 3022, 2971, 2919, 2867, 1705, 1611, 1484, 1448, 1393, 1370, 1342, 1269, 1200, 1161 cm^{-1} . ESI-MS: $\text{C}_{23}\text{H}_{25}\text{NO}_3\text{S}$ $[\text{M}+\text{H}]$ calc. 396.2, found 396.2, $[\text{M}+\text{Na}]$ calc. 418.2, found 418.2. $[\alpha]^{24}_{\text{D}} = +62.5^\circ$ ($c = 1.25$, CH_2Cl_2).

(*R,E*)-*N*-(2-chloroethylidene)-2-methylpropane-2-sulfinamide (7): To a dry 3-neck 1 L round-bottom flask, equipped with a mechanical stirrer and argon inlet, was added (*R*)-(+)-2-methyl-2-propanesulfinamide (20.00 g, 165 mmol) and 330 mL of CH₂Cl₂ (0.5 M). Anhydrous CuSO₄ (165 g, 1.03 mol) was added in one portion followed by chloroacetaldehyde (198 mmol). The mixture was stirred at room temperature for 24 h. The reaction mixture was filtered through a pad of celite and the filtrate was concentrated under reduced pressure. The crude product was purified by flash column chromatography (15% EtOAc/Hex to 25% EtOAc/Hex) to provide the product as a pale yellow oil (26.14 g, 87%). ¹H NMR (400 MHz, CDCl₃): δ 1.18 (s, 1H), 4.29 (d, 2H, *J* = 4.8 Hz), 7.99 (ddd, 1H, *J* = 0.8, 4.8, 4.8 Hz). ¹³C NMR (100 MHz, CDCl₃): δ 22.2, 43.5, 57.4, 162.4. IR (film): 2979, 2963, 2928, 2903 2869, 1624, 1474, 1457, 1365, 1335, 1253, 1182, 1133 cm⁻¹. ESI-MS: C₆H₁₂ClNOS [M+H] calc. 182.7, found 182.0. [α]_D²⁷ = -295° (c = 2.90, CH₂Cl₂).

(*S*)-4-mesitylthiazolidine-2-thione (8): A dry 2 L round-bottom flask was charged with mesityl magnesium bromide (398 mmol, 5.0 equiv), prepared from 10.0 g Mg turnings (0.41 mol), 60.0 mL 2-bromomesitylene (0.40 mol) and 139 mL of dry ether. The flask was cooled to -78 °C and imine **7** (14.50 g, 79.6 mol, 1.0 equiv), dissolved in 265 mL of toluene (0.3 M), was slowly added to the solution and the reaction mixture was stirred for 3 h at -78 °C, quenched with 4 N HCl (199 mL, 796 mmol), warmed to room temperature and stirred for 3 h. The layers were separated, and the organic layer was extracted with H₂O (2x). The aqueous layers were combined and cooled to 0 °C, upon which 50% NaOH was slowly added, while stirring, until the pH reached 11. H₂O was added (approximately 500 mL, to prevent an emulsion from forming) and the solution was extracted with ether (3x). The combined organic layers were dried over Na₂SO₄, filtered, and concentrated under reduced pressure. The residue was transferred to a 1 L round-bottom flask and 1 M KOH (398 mL, 398 mmol) was added. The reaction mixture was stirred for 10 min and carbon disulfide (24.0 mL, 398 mmol) was added. The reaction mixture was stirred for 30 min at room temperature, refluxed for 16 h, cooled to room temperature and extracted with CH₂Cl₂ (3x). The combined organic layers were dried over Na₂SO₄, filtered and concentrated under reduced pressure. The crude product was purified by flash column chromatography (15% EtOAc/Hex to 100% CH₂Cl₂) to provide the product as a pale yellow solid (14.5 g, 77%). ¹H NMR (400 MHz, CDCl₃): δ 2.26 (s, 3H), 2.39 (s, 6H), 3.63 (s, 1H), 3.65 (s, 1H), 5.83 (t, 1H, *J* = 10.4 Hz), 6.87 (s, 2H), 7.75 (brs, 1H). ¹³C NMR (100 MHz, CDCl₃): δ 20.5, 20.8, 37.5, 63.6, 129.3, 130.8, 136.6, 138.6, 199.5. IR (film): 3333, 3130, 2965, 2923, 2858, 1610, 1482, 1383, 1288,

1218, 1134 cm^{-1} . ESI-MS: $\text{C}_{12}\text{H}_{15}\text{NS}_2$ $[\text{M}+\text{H}]$ calc. 238.4, found 238.0. $[\alpha]_{\text{D}}^{25} = +139^\circ$ ($c = 0.25$, CH_2Cl_2).

(S)-1-(4-mesityl-2-thioxothiazolidin-3-yl)ethanone (9): To a dry 250 mL round-bottom flask, under argon, was added thiazolidinethione **8** (2.40 g, 10.1 mmol) and 51 mL THF (0.2 M). The solution was cooled to 0 °C and 60% NaH in mineral oil (0.48 g, 12.1 mmol) was slowly added. The reaction mixture was stirred for 15 min at 0 °C, and acetyl chloride (0.86 mL, 12.1 mmol) was added dropwise. The reaction mixture was stirred for 30 min at 0 °C, upon which it was warmed to room temperature and allowed to stir for 2 h. The reaction was quenched with saturated ammonium chloride and the layers were separated. The aqueous layer was extracted with EtOAc (2x) and the combined organic layers were dried over Na_2SO_4 , filtered, and concentrated under reduced pressure. The crude product was purified by flash column chromatography (2% EtOAc/hexanes to 15% EtOAc/hexanes) to provide *N*-acetylthiazolidinethione (2.63 g, 93%) as a yellow solid. ^1H NMR (400 MHz, CDCl_3): δ 2.26 (s, 3H), 2.41 (s, 6H), 2.70 (s, 3H), 3.34 (dd, 1H, $J = 10.0, 11.2$ Hz), 3.55 (dd, 1H, $J = 10.4, 11.2$ Hz), 6.36 (t, 1H, $J = 10.4$ Hz), 6.86 (s, 2H). ^{13}C NMR (100 MHz, CDCl_3): δ 20.2, 20.8, 27.7, 32.4, 67.9, 132.6, 137.7, 171.9, 201.4. IR (film): 3009, 2967, 2919, 2867, 1712, 1610, 1453, 1409, 1371, 1326, 1266, 1217, 1136 cm^{-1} . ESI-MS: $\text{C}_{14}\text{H}_{17}\text{NOS}_2$ $[\text{M}+\text{Na}]$ calc. 302.1, found 302.2. $[\alpha]_{\text{D}}^{25} = +81.0^\circ$ ($c = 0.8$, CH_2Cl_2).

Typical aldol procedure using *N*-acetylthiazolidinethione 9: To a dry 25 mL round-bottom flask, under argon, was added *N*-acetylthiazolidinethione (0.307 g, 1.10 mmol) and 5.2 mL of CH_2Cl_2 (0.2 M). The solution was cooled to -78°C and titanium tetrachloride (neat, 0.12 mL, 1.10 mmol) was added and stirred for 5 min. Diisopropylethylamine (0.19 mL, 1.10 mmol) was added and the solution was stirred for 30 min at -78°C , whereupon the freshly distilled aldehyde (neat, 1.0 mmol) was added dropwise. The mixture was stirred for 1 h at -78°C , then quenched with half saturated ammonium chloride and warmed to room temperature. The layers were separated and the aqueous layer was extracted with CH_2Cl_2 (2x). The combined organic layers were dried over NaSO_4 , filtered, and concentrated under reduced pressure. The crude product was purified by flash column chromatography (10% EtOAc/Hex to 20% EtOAc/Hex). Yields and diastereoselectivities are listed in Table 2.

(S)-3-hydroxy-1-((S)-4-mesityl-2-thioxothiazolidin-3-yl)pentan-1-one: ^1H NMR (400 MHz, CDCl_3): δ 0.91 (dd, 3H, $J = 7.2, 7.6$ Hz), 1.41-1.54 (bands, 2H), 2.26 (s, 3H), 2.40 (s, 6H), 3.17 (dd, 1H, $J = 2.4, 17.2$ Hz), 3.33 (dd, 1H, $J = 9.6, 11.2$ Hz), 3.48-3.61 (bands, 2), 3.76-3.82 (bands, 1H), 6.38 (t, 1H, $J = 10.0$ Hz), 6.86 (s, 2H). ^{13}C NMR (100 MHz, CDCl_3): δ 9.73, 20.2, 20.8, 29.3, 32.5, 46.1, 68.0, 69.6, 132.6, 137.9, 175.0, 201.7. IR (film): 3439, 2964, 2924, 2875, 1704, 1610, 1456, 1371, 1325, 1258, 1177, 1129 cm^{-1} . ESI-MS: $\text{C}_{17}\text{H}_{23}\text{NO}_2\text{S}_2$ $[\text{M}+\text{Na}]$ calc. 360.5, found 360.2. $[\alpha]_{\text{D}}^{26} = +101^\circ$ ($c = 0.65$, CH_2Cl_2).

(S)-3-hydroxy-1-((S)-4-mesityl-2-thioxothiazolidin-3-yl)hexan-1-one: ^1H NMR (400 MHz, CDCl_3): δ 0.88 (t, 3H, $J = 7.2$ Hz), 1.28-1.50 (bands, 4H), 2.25 (s, 3H), 2.40 (s, 6H), 2.81 (d, 1H, $J = 3.2$ Hz), 3.16 (dd, 1H, $J = 2.8, 17.6$ Hz), 3.33 (dd, 1H, $J = 9.6, 11.2$ Hz), 3.48-3.61 (bands, 2H), 3.87 (m, 1H), 6.38 (t, 1H, $J = 10.0$ Hz), 6.86 (s, 2H). ^{13}C NMR (100 MHz, CDCl_3): δ 13.9, 18.6, 20.2, 20.8, 32.5, 38.6, 46.6, 67.9, 68.0, 132.6, 137.9, 175.0, 201.7. IR (film): 3460, 2957, 2927, 2862, 1705, 1456, 1371, 1322, 1259, 1175, 1128 cm^{-1} . ESI-MS: $\text{C}_{18}\text{H}_{25}\text{NO}_2\text{S}_2$ $[\text{M}+\text{H}]$ calc. 352.5, found 352.2, $[\text{M}+\text{Na}]$ calc. 374.5, found 374.2. $[\alpha]_{\text{D}}^{26} = +108^\circ$ ($c = 0.25$, CH_2Cl_2).

(R)-3-hydroxy-1-((S)-4-mesityl-2-thioxothiazolidin-3-yl)-4-methylpentan-1-one: ^1H NMR (400 MHz, CDCl_3): δ 0.90 (dd, 6H, $J = 4.0, 6.8$ Hz), 1.68 (m, 1H), 2.26 (s, 3H), 2.40 (s, 6H), 2.84 (brs, 1H), 3.13 (dd, 1H, $J = 1.6, 16.8$ Hz), 3.33 (dd, 1H, $J = 9.6, 11.6$ Hz), 3.51-3.67 (bands, 3H), 6.39 (t, 1H, $J = 10.0$ Hz), 6.86 (s, 2H). ^{13}C NMR (100 MHz, CDCl_3): δ 17.6, 18.3, 20.2, 20.8, 32.5, 33.2, 43.6, 68.1, 73.0, 132.6, 137.9, 175.4, 201.8. IR (film): 3460, 2960, 2927, 2873, 1698, 1610, 1463, 1371, 1326, 1258, 1178, 1128 cm^{-1} .

ESI-MS: C₁₈H₂₅NO₂S₂ [M+H] calc. 352.5, found 352.2, [M+Na] calc. 374.5, found 374.2. $[\alpha]^{25}_D = +102^\circ$ (c = 0.55, CH₂Cl₂).

(S)-3-hydroxy-1-((S)-4-mesityl-2-thioxothiazolidin-3-yl)-5-methylhexan-1-one:

¹H NMR (400 MHz, CDCl₃): δ 0.85 (dd, 6H, J = 6.4, 10.0 Hz), 1.10 (ddd, 1H, J = 4.4, 8.8, 13.2), 1.46 (ddd, 1H, J = 5.2, 8.8, 14.4), 1.74 (m, 1H), 2.26 (s, 3H), 2.40 (s, 6H), 2.76 (brs, 1H), 3.15 (dd, 1H, J = 2.8, 17.2 Hz), 3.33 (dd, 1H, J = 9.6, 11.6 Hz), 3.47-3.62 (bands, 2H), 3.94 (m, 1H), 6.39 (t, 1H, J = 10.0 Hz), 6.86 (s, 2H). ¹³C NMR (100 MHz, CDCl₃): δ 20.2, 20.7, 21.8, 23.2, 24.3, 32.5, 45.6, 47.1, 66.4, 68.0, 132.6, 137.8, 174.9, 201.6. IR (film): 3448, 2954, 2925, 2868, 1709, 1610, 1462, 1370, 1324, 1259, 1174, 1127 cm⁻¹. ESI-MS: C₁₉H₂₇NO₂S₂ [M+Na] calc. 388.6, found 388.3. $[\alpha]^{24}_D = +83.6^\circ$ (c = 0.90, CH₂Cl₂).

(R)-3-hydroxy-1-((S)-4-mesityl-2-thioxothiazolidin-3-yl)-3-phenylpropan-1-one:

¹H NMR (400 MHz, CDCl₃): δ 2.24 (s, 3H), 2.36 (s, 6H), 3.18 (brs, 1H), 3.27-3.38 (bands, 2H), 3.55 (dd, 1H, J = 11.2, 10.4 Hz), 3.91 (dd, 1H, J = 9.6, 17.6), 4.98 (dd, 1H, J = 2.4, 9.2 Hz), 6.36 (t, 1H, J = 10.0 Hz), 6.82 (s, 2H), 7.23-7.28 (bands, 5H). ¹³C NMR (100 MHz, CDCl₃): δ 20.3, 20.8, 32.5, 48.4, 68.1, 70.6, 125.8, 127.7, 128.5, 132.4, 137.9, 142.3, 174.0, 201.7. IR (film): 3437, 3030, 2968, 2919, 2869, 1706, 1610, 1493, 1483, 1454, 1371, 1325, 1257, 1183, 1129 cm⁻¹. ESI-MS: C₂₁H₂₃NO₂S₂ [M+H] calc. 386.6, found 386.2, [M+Na] calc. 408.6, found 408.3. $[\alpha]^{26}_D = +60.0^\circ$ (c = 0.55, CH₂Cl₂).

(R,E)-3-hydroxy-1-((S)-4-mesityl-2-thioxothiazolidin-3-yl)-5-phenylpent-4-en-1-one: ¹H NMR (400 MHz, CDCl₃): δ 2.20 (s, 3H), 2.35 (s, 6H), 2.87 (s, 6H), 3.28-3.33

(bands, 2H), 3.53 (dd, 1H, $J = 10.4, 11.2$ Hz), 3.76 (dd, 1H, $J = 8.4, 17.2$ Hz), 4.60 (m, 1H), 6.11 (dd, 1H, $J = 6.0, 16.0$ Hz), 6.35 (t, 1H, $J = 10.0$ Hz), 6.53 (d, 1H, $J = 16.0$ Hz), 6.77 (s, 2H), 7.19-7.31 (bands, 5H). ^{13}C NMR (100 MHz, CDCl_3): δ 20.3, 20.8, 32.5, 46.8, 68.1, 69.0, 126.5, 127.7, 128.5, 129.8, 130.6, 132.4, 136.4, 137.9, 173.8, 201.7. IR (film): 3027, 2962, 2917, 2867, 1705, 1607, 1448, 1374, 1326, 1260, 1190, 1129 cm^{-1} . ESI-MS: $\text{C}_{23}\text{H}_{25}\text{NO}_2\text{S}_2$ $[\text{M}+\text{H}]$ calc. 412.3, found 412.3, $[\text{M}+\text{Na}]$ calc. 434.3, found 434.3. $[\alpha]_D^{26} = +20.2^\circ$ ($c = 0.20$, CH_2Cl_2).

Aldehyde **12a** was synthesized via a 2 step sequence from the acetate aldol adduct (Table 2, entry 4), as shown in Scheme S1.

Scheme S1

(*R*)-3-(tert-butyldimethylsilyloxy)-1-((*S*)-4-mesityl-2-thioxothiazolidin-3-yl)-4-methylpentan-1-one (S1): To a dry 100 mL round-bottom flask, under argon, was added the aldol adduct (1.90 g, 5.40 mmol) in 18 mL CH_2Cl_2 (0.2 M). The flask was cooled to 0°C and 2,6-lutidine (1.3 mL, 10.8 mmol) was added followed by TBSOTf (1.49 mL, 6.48 mmol). The reaction mixture was stirred for 30 min at 0°C and reaction progress was monitored by TLC. The reaction mixture was quenched with saturated sodium bicarbonate, warmed to room temperature, and extracted with CH_2Cl_2 (3x). The combined organic layers were dried over Na_2SO_4 and concentrated under reduced pressure. The crude product was purified via flash column chromatography (2% EtOAc/Hex to 10% EtOAc/Hex) to provide the product as a yellow solid (2.48 g, 98%). ^1H NMR (400 MHz, CDCl_3): δ 0.00 (d, 6H, $J = 0.8$ Hz), 0.71 (d, 3H, $J = 6.8$ Hz), 0.76 (d, 3H, $J = 6.8$ Hz), 0.85 (s, 9H), 1.37 (m, 1H), 2.24 (s, 3H), 2.40 (s, 6H), 2.92 (dd, 1H, $J = 6.4, 10.0$ Hz), 3.30 (dd, 1H, $J = 9.2, 11.2$ Hz), 3.57 (dd, 1H, $J = 10.8, 11.2$ Hz), 3.73 (dd, 1H, $J = 6.4, 18.0$ Hz), 4.02 (ddd, 1H, $J = 3.2, 6.4, 9.2$ Hz), 6.36 (dd, 1H, $J = 8.8, 10.0$ Hz), 6.84 (s, 2H). ^{13}C NMR (100 MHz, CDCl_3): δ -4.88, -4.89, 16.4, 18.1, 18.5, 20.3, 20.8, 25.6, 32.4, 32.8, 44.1, 68.0, 72.7, 132.9, 137.8, 140.4, 173.5, 201.2. IR (film): 2956, 2927, 2849, 1713, 1616, 1469, 1371, 1327, 1254, 1175, 1127 cm^{-1} . ESI-MS: $\text{C}_{24}\text{H}_{39}\text{NO}_2\text{S}_2\text{Si}$ $[\text{M}+\text{H}]$ calc. 466.8, found 466.3, $[\text{M}+\text{Na}]$ calc. 488.6, found 488.3. $[\alpha]_D^{23} = +108^\circ$ ($c = 0.10$, CH_2Cl_2).

(R)-3-(tert-butyldimethylsilyloxy)-4-methylpentanal (12a): To a dry 100 mL round-bottom flask, under argon, was added protected aldol adduct **S1** (0.75 g, 1.61 mmol) in 16 mL CH₂Cl₂ (0.1 M). The flask was cooled to -78 °C, upon which DIBALH (1 M in hexanes) was added dropwise until the reaction mixture became colorless (~3.2 mL, 3.22 mmol). The reaction mixture was immediately quenched with saturated potassium sodium tartrate, warmed to room temperature, and vigorously stirred for 1 h. 5 mL Et₂O was added and the reaction mixture was stirred 5 min, then extracted with Et₂O (3x). The combined organic layers were dried over Na₂SO₄ and concentrated under reduced pressure. The crude product was purified via flash column chromatography (2% EtOAc/Hex) to provide the product as a pale yellow oil (0.307 g, 83%). ¹H NMR (400 MHz, CDCl₃): δ 0.03 (d, 6H, J = 10.8 Hz), 0.85-0.92 (bands, 15H), 1.77 (m, 1H), 2.41 (ddd, 1H, J = 2.0, 4.4, 15.6 Hz), 2.50 (ddd, 1H, J = 2.8, 7.2, 15.6 Hz), 4.01 (ddd, 1H, J = 4.8, 4.8, 7.2 Hz), 9.79 (dd, 1H, J = 2.0, 3.2 Hz). ¹³C NMR (100 MHz, CDCl₃): δ -4.67, -4.56, 17.2, 18.0, 25.7, 34.0, 47.2, 72.4, 202.6. IR (film): 2958, 2931, 2888, 2858, 2718, 1728, 1472, 1388, 1370, 1254, 1218 cm⁻¹. ESI-MS: C₁₂H₂₆O₂Si [M+H] calc. 231.4, found 231.2. [α]_D²² = -4.54° (c = 1.05, CH₂Cl₂).

(3S,5R)-5-(tert-butyldimethylsilyloxy)-3-hydroxy-1-((S)-4-mesityl-2-thioxothiazolidin-3-yl)-6-methylheptan-1-one (14a): See “Typical aldol procedure using *N*-acetylthiazolidinethione.” One modification made to this procedure involves quenching with half-saturated sodium bicarbonate instead of ammonium chloride. The crude product was purified by flash column chromatography (5% EtOAc/Hex to 15% EtOAc/Hex) to provide the product as a mixture of diastereomers (93% yield, 90:10 *dr*) as a yellow oil. ¹H NMR (400 MHz, CDCl₃): δ 0.03 (s, 6H), 0.64 (d, 3H, J = 6.8 Hz), 0.81 (d, 3H, J = 7.2 Hz), 0.85 (s, 9H), 1.21-1.26 (bands, 1H), 1.39-1.45 (bands, 1H), 1.70 (m, 1H), 2.21 (s, 3H), 2.38 (s, 6H), 3.15 (dd, 1H, J = 5.6, 17.6 Hz), 3.30 (dd, 1H, J = 10.0, 11.2 Hz), 3.53-3.61 (bands, 2H), 3.67 (m, 1H), 4.07 (m, 1H), 6.36 (t, 1H, J = 10.0 Hz), 6.81 (s, 2H). ¹³C NMR (100 MHz, CDCl₃): δ -4.74, -4.41, 16.6, 17.2, 17.8, 20.2, 20.6, 25.7, 25.8, 32.3, 32.5, 37.3, 47.3, 67.0, 67.8, 75.7, 75.8, 132.5, 137.6, 173.7, 201.0. IR (film): 3481, 2956, 2928, 2895, 2856, 1708, 1611, 1577, 1462, 1370, 1329, 1258, 1177, 1129 cm⁻¹. ESI-MS: C₂₆H₄₃NO₃S₂Si [M+H] calc. 510.8, found 510.4, [M+Na] calc. 532.8, found 532.4. [α]_D²¹ = +65.5° (c = 0.45, CH₂Cl₂).

(3R,5R)-5-(tert-butyldimethylsilyloxy)-3-hydroxy-1-((R)-4-mesityl-2-thioxothiazolidin-3-yl)-6-methylheptan-1-one (15a): See “Typical aldol procedure using *N*-acetylthiazolidinethione.” One modification made to this procedure involves quenching with half-saturated sodium bicarbonate instead of ammonium chloride. The crude product was purified by flash column chromatography (5% EtOAc/Hex to 15% EtOAc/Hex) to provide the product as a mixture of diastereomers (91% yield, 95:5 *dr*) as a yellow oil. ¹H NMR (400 MHz, CDCl₃): δ -0.02 (s, 3H), 0.2 (s, 3H), 0.75 (d, 3H, 6.4 Hz), 0.82-0.90 (bands, 12H), 1.26-1.45 (bands, 2H), 1.75 (m, 1H), 2.23 (s, 3H), 2.39 (s, 6H), 3.14 (dd, 1H, *J* = 5.6, 16.8 Hz), 3.30 (t, 2H, *J* = 10.0 Hz), 3.45 (dd, 1H, *J* = 8.0 Hz, 17.2 Hz), 3.53-3.64 (bands, 2H), 4.08 (m, 1H), 6.35 (t, 1H, *J* = 10.0 Hz), 6.82 (s, 2H). ¹³C NMR (100 MHz, CDCl₃): δ -4.83, -4.74, 16.9, 17.7, 18.5, 20.1, 20.5, 25.7, 32.4, 32.9, 38.2, 47.3, 65.1, 67.7, 73.8, 73.9, 132.2, 137.3, 174.3, 200.9. IR (film): 3488, 2956, 2928, 2895, 2856, 1705, 1611, 1577, 1463, 1386, 1370, 1331, 1296, 1258, 1186, 1129 cm⁻¹. ESI-MS: C₂₆H₄₃NO₃S₂Si [M+H] calc. 510.8, found 510.4, [M+Na] calc. 532.8, found 532.3, [2M+Na] calc. 1041.8, found 1041.5. [α]_D²¹ = -71.9° (c = 0.15, CH₂Cl₂).

Aldehyde **12b** was synthesized via a 2 step sequence from known compound **S2**,² as shown in Scheme S2.

(2R,3S)-1-((R)-4-benzyl-2-thioxothiazolidin-3-yl)-3-(tert-butyldimethylsilyloxy)-2,4-dimethylpentan-1-one (S3): To a dry 100 mL round-bottom flask, under argon, was added aldol adduct **S2** (2.95 g, 5.40 mmol) in 29 mL CH₂Cl₂ (0.2 M). The flask was cooled to 0 °C and 2,6-lutidine (2.0 mL, 17.5 mmol) was added followed by TBSOTf (2.41 mL, 10.5 mmol). The reaction mixture was stirred for 30 min

² Crimmins, M.T.; King, B.W.; Tabet, E.A.; Chaudhary, K. *J. Org. Chem.* **2001**, *66*, 894.

at 0 °C and reaction progress was monitored by TLC. The reaction mixture was quenched with saturated sodium bicarbonate, warmed to room temperature, and extracted with CH₂Cl₂ (3x). The combined organic layers were dried over Na₂SO₄ and concentrated under reduced pressure. The crude product was purified via flash column chromatography (2% EtOAc/Hex to 10% EtOAc/Hex) to provide the product as a yellow solid (3.66 g, 94%). ¹H NMR (400 MHz, CDCl₃): δ 0.06 (s, 3H), 0.07 (s, 3H), 0.82 (d, 3H, J = 6.8 Hz), 0.90 (s, 12H), 1.24 (d, 3H, J = 6.4 Hz), 1.63 (m, 1H), 2.87 (d, 1H, J = 11.6 Hz), 3.03 (dd, 1H, J = 4.8, 4.8 Hz), 3.21 (dd, 1H, J = 3.2, 12.8 Hz), 3.33 (dd, 1H, J = 7.2, 11.6 Hz), 3.88 (dd, 1H, J = 2.4, 7.2 Hz), 4.47 (m, 1H), 5.21 (ddd, 1H, J = 3.6, 6.4, 10.4 Hz), 7.24-7.34 (bands, 5H). ¹³C NMR (100 MHz, CDCl₃): δ -3.80, -3.73, 15.1, 17.1, 18.4, 19.8, 26.1, 32.0, 33.4, 36.5, 42.6, 69.1, 78.5, 127.2, 128.9, 129.5, 136.6, 177.5, 200.6. IR (film): 2957, 2927, 2893, 2858, 1694, 1456, 1363, 1339, 1253, 1190, 1162, 1116 cm⁻¹. ESI-MS: C₂₃H₃₇NO₂S₂Si [M+H] calc. 452.8, found 452.3, [M+Na] calc. 474.8, found 474.2. [α]_D²³ = -213° (c = 0.20, CH₂Cl₂).

(2R,3S)-3-(tert-butyldimethylsilyloxy)-2,4-dimethylpentanal (12b): To a dry 100 mL round-bottom flask, under argon, was added protected aldol adduct **S3** (0.60 g, 1.33 mmol) in 13 mL CH₂Cl₂ (0.1 M). The flask was cooled to -78 °C, upon which DIBALH (1 M in hexanes) was added dropwise until the reaction mixture became colorless (~2.7 mL, 2.66 mmol). The reaction mixture was immediately quenched with saturated potassium sodium tartrate, warmed to room temperature, and vigorously stirred for 1 h. 5 mL Et₂O was added and the reaction mixture was stirred 5 min, then extracted with Et₂O (3x). The combined organic layers were dried over Na₂SO₄ and concentrated under reduced pressure. The crude product was purified via flash column chromatography (2% EtOAc/Hex to 10% EtOAc/Hex) to provide the product as a pale yellow oil (0.268 g, 82%). ¹H NMR (400 MHz, CDCl₃): δ 0.01 (s, 3H), 0.07 (s, 3H), 0.89-0.93 (bands, 15H), 1.09 (d, 3H, J = 8.0 Hz), 1.81 (m, 1H), 2.50 (m, 1H), 3.90 (t, 1H, J = 4.4 Hz), 9.78 (s, 1H). ¹³C NMR (100 MHz, CDCl₃): δ -4.21, -4.03, 8.59, 18.3, 19.7, 25.9, 32.2, 50.6, 76.4, 205.5. IR (film): 2958, 2884, 2858, 1728, 1472, 1387, 1254, 1100 cm⁻¹. ESI-MS: C₁₃H₂₈O₂Si [M+H] calc. 245.6, found 245.2, [M+Na] calc. 267.5, found 267.2. [α]_D²² = -59.1° (c = 0.40, CH₂Cl₂).

(3R,4S,5S)-5-(tert-butyldimethylsilyloxy)-3-hydroxy-1-((S)-4-mesityl-2-thioxothiazolidin-3-yl)-4,6-dimethylheptan-1-one (14b): To a dry 25 mL round-bottom

flask, under argon, was added *N*-acetylthiazolidinethione **9** (0.474 g, 1.70 mmol) and 6 mL of CH₂Cl₂ (0.2 M). The solution was cooled to -78 °C and titanium tetrachloride (neat, 0.19 mL, 1.70 mmol) was added and stirred for 5 min. Diisopropylethylamine (0.30 mL, 1.70 mmol) was added and the solution was stirred for 30 min at -78 °C, upon which the freshly prepared aldehyde (neat, 1.13 mmol) was added dropwise. The mixture was stirred for 1 h at -78 °C, then quenched with half saturated sodium bicarbonate and warmed to room temperature. The layers were separated and the aqueous layer was extracted with CH₂Cl₂ (2x). The combined organic layers were dried over NaSO₄, filtered, and concentrated under reduced pressure. The crude product was purified by flash column chromatography (5% EtOAc/Hex to 10% EtOAc/Hex) to provide the product as a mixture of diastereomers (0.537 g, 91%, 97:3 *dr*) as a yellow oil. ¹H NMR (400 MHz, CDCl₃): δ 0.02 (d, 6H, J = 10.0 Hz), 0.75 (d, 3H, J = 6.8 Hz), 0.84-0.93 (bands, 15H), 1.49 (m, 1H), 1.76 (m, 1H), 2.25 (s, 3H), 2.40 (s, 6H), 2.68 (s, 1H), 3.13 (dd, 1H, J = 3.6, 17.6 Hz), 3.34 (dd, 1H, J = 10.0, 11.6 Hz), 3.47 (dd, 1H, J = 4.0, 4.4 Hz), 3.55-3.68 (bands, 2H), 3.96 (m, 1H), 6.39 (t, 1H, J = 10.0 Hz), 6.85 (s, 2H). ¹³C NMR (100 MHz, CDCl₃): δ -3.96, -3.65, 9.86, 17.5, 18.4, 19.4, 20.2, 20.7, 26.1, 32.2, 32.4, 40.4, 45.1, 68.0, 70.4, 78.6, 132.5, 137.9, 174.8, 201.5. IR (film): 3545, 2956, 2928, 2856, 1705, 1611, 1462, 1371, 1329, 1257, 1178, 1128 cm⁻¹. ESI-MS: C₂₇H₄₅NO₃S₂Si [M+H] calc. 524.9, found 524.3, [M+Na] calc. 546.9, found 546.3. [α]_D²² = +52.2° (c = 0.70, CH₂Cl₂).

(3*S*,4*S*,5*S*)-5-(tert-butyldimethylsilyloxy)-3-hydroxy-1-((*R*)-4-mesityl-2-thioxothiazolidin-3-yl)-4,6-dimethylheptan-1-one (15b**):** To a dry 25 mL round-bottom flask, under argon, was added *N*-acetylthiazolidinethione **13** (0.419 g, 1.50 mmol) and 5 mL of CH₂Cl₂ (0.2 M). The solution was cooled to -78 °C and titanium tetrachloride (neat, 0.16 mL, 1.50 mmol) was added and stirred for 5 min. Diisopropylethylamine (0.26 mL, 1.50 mmol) was added and the solution was stirred for 30 min at -78 °C, upon which the freshly prepared aldehyde (neat, 1.0 mmol) was added dropwise. The mixture was stirred for 1 h at -78 °C, then quenched with half saturated sodium bicarbonate and warmed to room temperature. The layers were separated and the aqueous layer was extracted with CH₂Cl₂ (2x). The combined organic layers were dried over NaSO₄, filtered, and concentrated under reduced pressure. The crude product was purified by flash column chromatography (5% EtOAc/Hex to 10% EtOAc/Hex) to provide the product as a mixture of diastereomers (0.482 g, 92%, 92:8 *dr*) as a yellow oil. ¹H NMR (400 MHz, CDCl₃): δ -0.06 (s, 3H), 0.03 (s, 3H), 0.79 (d, 3H, J = 6.8 Hz), 0.85-0.92 (bands, 15H), 1.72 (m, 2H), 2.25 (s, 3H), 2.41 (s, 6H), 3.25-3.36 (bands, 3H), 4.46 (dd, 1H, J = 9.6, 16.8 Hz), 3.58 (dd, 1H, J = 10.4, 11.2 Hz), 3.72 (m, 2H), 6.34 (t, 1H, J = 10.0 Hz), 6.85 (s, 2H). ¹³C NMR (100 MHz, CDCl₃): δ -4.26, -4.11, 10.9, 18.3, 19.5, 19.6, 20.2, 20.7, 26.1, 32.2, 32.5, 41.4, 44.4, 68.1, 70.2, 76.3, 132.4, 137.7, 175.3, 201.7. IR

(film): 3460, 2956, 2927, 2855, 1696, 1611, 1462, 1385, 1369, 1327, 1258, 1185, 1128 cm^{-1} . ESI-MS: $\text{C}_{27}\text{H}_{45}\text{NO}_3\text{S}_2\text{Si}$ $[\text{M}+\text{H}]$ calc. 524.9, found 524.3, $[\text{M}+\text{Na}]$ calc. 546.9, found 546.3. $[\alpha]_{\text{D}}^{22} = -73.4^\circ$ ($c = 0.30$, CH_2Cl_2).