Asymmetric Conjugate Addition of Copper Reagents to α,β -Unsaturated *tert*-Butanesulfinyl Imines

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Supporting Information

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Experimental

General Methods. 1-Phenylbut-2-en-1-one was prepared according to a previously reported method.¹ All other ketones and crotonaldehyde were purchased from commercial suppliers and were used without further purification. Ti(OEt)₄ was purchased from Strem (containing 5-15% isopropanol) and was used without further purification. All copper salts were purchased from commercial suppliers and were stored in a glovebox. PBu₃ was purchased from Aldrich and was stored in a glovebox prior to use. Tetrahydrofuran and diethyl ether were distilled from Na/benzophenone ketyl immediately prior to use. All reactions were carried out in flame- or oven-dried glassware under an inert N₂ atmosphere. NMR spectra were obtained in CDCl₃ at room temperature. Chemical shifts in NMR spectra are expressed in ppm, and all coupling constants are expressed in Hz.

General procedure for condensation of α,β -unsaturated ketones and aldehydes with *tert*-butanesulfinamide. To a 0.5 M solution of ketone (1.2 equiv) in THF under a N₂ atmosphere is added Ti(OEt)₄ (~4 equiv). *tert*-Butanesulfinamide (1 equiv) is then added and the resulting mixture is heated and monitored by TLC. The reaction mixture is then poured into an equal volume of saturated aqueous NaHCO₃ with rapid stirring and immediately filtered through celite. The filter cake is washed with EtOAc and the aqueous layer is separated and washed once with EtOAc. The combined organic layer is dried over MgSO₄, filtered, and reduced under vacuum to give the crude product. The crude product is then purified by silica gel chromatography. The product imines were stored by placing a vial of the product into a container of drierite within a -20 °C freezer.

(*R*)-*N*-((*E*)-1-methyl-but-2-en-ylidene)-*tert*-butanesulfinamide (1a). The general procedure was followed using 0.291 mL (2.98 mmol) of 3-penten-2-one, 2.08 mL (9.90 mmol) of Ti(OEt)₄, 300 mg (2.48 mmol) (*R*)-*tert*-butanesulfinamide, and 4.96 mL of tetrahydrofuran. The reaction mixture was stirred at reflux overnight. Chromatography

¹ Pitts, M. R.; Harrison, J. R.; Moody, C. J. *J. Chem. Soc., Perkin Trans. I*, **2001**, 955-977.

(7:3 hexanes:EtOAc) provided 344 mg (74%) of a yellow oil. As determined by NMR, product **1a** existed as a 2:1 mixture of imine isomers. ^1H NMR (500 MHz) δ 7.09 (d, J = 15.3 Hz, 0.33H), 6.57-6.47 (m, 1H), 6.18 (d, J = 15.9 Hz, 0.67H), 2.37 (s, 2H), 2.23 (s, 1H), 1.88 (d, J = 6.7 Hz, 3H), 1.20 (s, 9H); ^{13}C NMR (125 MHz) δ 176.9, 175.2, 141.5, 138.8, 134.7, 127.2, 57.0, 56.8, 24.6, 22.5, 22.4, 19.1, 18.9, 18.7. HRMS calcd. for $\text{C}_9\text{H}_{18}\text{NOS}$ 188.1109, found 188.1105.

(*R*)-*N*-((*E*)-1-phenyl-but-2-en-ylidene)-*tert*-butanesulfinamide (1b). The general procedure was followed using 289 mg (1.98 mmol) of phenyl propenyl ketone, 1.63 mL (6.6 mmol) of $\text{Ti}(\text{OEt})_4$, 200 mg (1.65 mmol) of (*R*)-*tert*-butanesulfinamide, and 3.3 mL of tetrahydrofuran. The reaction mixture was stirred at reflux for 4 h. Chromatography (80:20 hexanes:EtOAc) provided 306 mg (74%) of **1b** as a clear oil. ^1H NMR (500 MHz) δ 7.56 (m, 2H), 7.44-7.37 (m, 3H), 7.23 (d, J = 15.0 Hz, 1H), 6.20 (m, 1H), 1.92 (d, J = 5 Hz, 3H), 1.30 (s, 9H); ^{13}C NMR (125 MHz) δ 176.3, 144.6, 139.1, 130.8, 129.4, 128.3, 126.8, 57.8, 22.7, 19.23. HRMS calcd. for $\text{C}_{14}\text{H}_{20}\text{NOS}$ 250.1266, found 250.1264.

(*R*)-*N*-((*E*)-1-methyl-3-phenyl-prop-2-en-ylidene)-*tert*-butanesulfinamide (1c). The general procedure was followed using 290 mg (1.98 mmol) of benzylideneacetone, 1.63 mL (6.6 mmol) of $\text{Ti}(\text{OEt})_4$, 200 mg (1.65 mmol) of *tert*-butanesulfinamide, and 4.0 mL of THF. The reaction mixture was stirred at reflux overnight. Chromatography (8:2 hexanes:EtOAc) provided 334 mg (81%) of **1c** as a yellow solid. As determined by NMR, product **1c** existed as a 2:1 mixture of imine isomers. ^1H NMR (400 MHz) δ 7.94 (d, J = 16.1 Hz, 0.3 H), 7.52 (d, J = 6.5 Hz, 2H), 7.39-7.33 (m, 3H), 7.27 (d, J = 16.5 Hz, 0.7 H), 7.16 (d, J = 16.0 Hz, 0.3H), 6.84 (d, J = 16.4 Hz, 0.7 H), 2.55 (s, 2.1H), 2.41 (s, 0.9H), 1.28 (s, 9H); ^{13}C NMR (100 MHz) δ 176.5, 174.2, 141.1, 139.3, 135.2, 130.4, 130.1, 129.9, 129.0, 128.2, 127.9, 122.4, 57.6, 57.2, 24.5, 22.6, 22.4, 19.0. HRMS calcd. for $\text{C}_{14}\text{H}_{20}\text{NOS}$ 250.1266, found 250.12164.

(*R*)-*N*-((*E*)-1,3-diphenyl-prop-2-en-ylidene)-*tert*-butanesulfinamide (1d). The general procedure was followed using 620 mg (2.98 mmol) of chalcone, 2.08 mL (9.92 mmol) of $\text{Ti}(\text{OEt})_4$, 300 mg (2.48 mmol) of (*R*)-*tert*-butanesulfinamide, and 5 mL of

tetrahydrofuran. The solution was heated to reflux overnight. Chromatography (9:1 to 85:15 hexanes:EtOAc) provided 585 mg (77%) of **1d** as a yellow solid. ¹H NMR (500 MHz) δ 8.07 (d, J = 16.1 Hz, 1H), 7.65 (m, 2H), 7.53-7.43 (m, 5H), 7.38-7.33 (m, 3H), 6.91 (d, J = 16.1 Hz, 1H), 1.35 (s, 9H); ¹³C NMR (125 MHz) δ 175.6, 144.1, 138.9, 135.4, 130.9, 130.2, 129.5, 129.0, 128.5, 128.3, 122.6, 58.5, 22.9. HRMS calcd. for C₁₉H₂₂NOS 312.1422, found 312.1426.

(*R*)-*N*-(cyclohex-2-en-ylidene)-*tert*-butanesulfinamide (1e**).**

The general procedure was followed using 0.288 mL (2.98 mmol) of 2-cyclohexen-1-one, 2.08 mL (9.92 mmol) of Ti(OEt)₄, 300 mg (2.48 mmol) of (*R*)-*tert*-butanesulfinamide, and 5 mL of tetrahydrofuran. The solution was heated to reflux overnight.

Chromatography (7:3 hexanes:EtOAc) provided 425 mg (86%) of **1e** as a yellow oil. As determined by NMR, product **1e** existed as a 6:4 mixture of imine isomers. ¹H NMR (400 MHz) δ 7.05 (d, J = 10.2 Hz, 0.4H), 6.66-6.58 (m, 1H), 6.16 (d, J = 10.0 Hz, 0.6H), 3.03-2.95 (m, 0.6H), 2.81-2.74 (m, 0.6H), 2.52 (apparent triplet, 0.8H), 2.29-2.21 (m, 2H), 1.93-1.75 (m, 2H), 1.19 (s, 9H); ¹³C NMR (100 MHz) δ 178.0, 175.8, 146.1, 145.0, 130.5, 123.2, 57.0, 56.6, 36.2, 31.0, 26.1, 25.3, 22.6, 22.4, 22.3, 22.0. HRMS calcd. for C₁₀H₁₈NOS 200.1109, found 200.1108.

(*R*)-*N*-((*E*)-but-2-en-ylidene)-*tert*-butanesulfinamide (1f**).** The general procedure was followed using 0.752 mL (9.08 mmol) of crotonaldehyde, 6.92 mL (33 mmol) of Ti(OEt)₄, 1.00 g (8.25 mmol) of (*R*)-*tert*-butanesulfinamide, and 16.5 mL of tetrahydrofuran. The reaction mixture was stirred at room temperature overnight. Chromatography (9:1 to 8:2 hexanes:EtOAc) provided 1.173 g (82%) of **1f** as a pale yellow oil. ¹H NMR (500 MHz) δ 8.11 (d, J = 9.18 Hz, 1H), 6.53-6.46 (m, 1H), 6.41-6.35 (m, 1H), 1.91 (dd, J = 1.4, 6.7 Hz, 3H), 1.13 (s, 9H); ¹³C NMR (125 MHz) δ 164.0, 146.6, 130.4, 57.2, 22.5, 18.9. HRMS calcd. for C₈H₁₆NOS 174.0953, found 174.0955.

(*R*)-*N*-(1,3-dimethyl-heptylidene)-*tert*-butanesulfinamide (2a**).** To a round-bottom flask containing 37 mg of anhydrous CuCN (0.41 mmol, 1.5 equiv) was added 0.45 mL of THF. This solution was cooled to 0 °C and 0.373 mL of *n*-BuLi in hexanes (2.2M,

0.82 mmol, 3 equiv) was added to form a 0.5 M solution. The solution was stirred for 15 min at 0 °C and then was cooled to -78 °C. BF₃·OEt₂ (0.052 mL, 0.41 mmol, 1.5 equiv) was added, and the solution was stirred for 10 min. A precooled -78 °C solution of 50 mg of sulfinyl imine **1a** (0.27 mmol, 1 equiv) in 0.54 mL of THF was then added via canula. The flask containing the imine solution was rinsed once with 0.100 mL of THF and the resulting solution was added by cannula to the reaction flask. The reaction solution was then stirred at -78 °C for 5 h. The reaction was quenched by addition of 1M AcOH in THF (3 equiv), and the solution was then filtered through a plug of basic alumina and concentrated to give the crude product. HPLC analysis (250 mm x 4.6 mm Chiralcel AS column, detection at 254 nm, 1 mL/min, 98:2 hexanes:iPrOH) on the unpurified material established a 93 (*t_R* = 6.7 min) to 7 (*t_R* = 7.7 min) ratio of diastereomers. The crude product was purified by silica gel chromatography (9:1 hexanes:EtOAc) to provide 89.1 mg (68%) of **2a** as a clear oil. As determined by NMR, product **2a** existed as a 85:15 mixture of imine isomers. ¹H NMR (500 MHz) δ 2.76-2.70 (m, 0.15H), 2.60-2.54 (m, 0.15H), 2.38 (dd, *J* = 6.0, 15.0 Hz, 0.85H), 2.30 (s, 2.55H), 2.20 (dd, *J* = 7.9, 14.9Hz, 0.85H), 2.15 (s, 0.45H), 1.95 (m, 1H), 1.36-1.12 (m, 6H), 1.24 (s, 9H), 0.95-0.67 (m, 6H); ¹³C NMR (125 MHz) δ 185.6, 56.4, 51.2, 36.8, 30.6, 29.4, 23.5, 23.1, 22.4, 19.9, 14.3 [in the ¹³C NMR spectra only the peaks corresponding to the major isomer are listed]. HRMS calcd. for C₁₃H₂₈NOS 246.1892, found 246.1895.

(*R*)-*N*-(3-methyl-1-phenyl-heptylidene)-*tert*-butanesulfinamide (2b). To a round-bottom flask containing 54 mg of anhydrous CuCN (0.60 mmol, 1.5 equiv) was added 0.900 mL of THF. This solution was cooled to 0 °C, and 0.600 mL of *n*-BuLi in hexanes (2.0 M, 1.20 mmol, 3 equiv) was added to form a 0.5 M solution, which was stirred for 15 min at 0 °C and then was cooled to -78 °C. BF₃·OEt₂ (0.076 mL, 0.60 mmol, 1.5 equiv) was added, and the solution was stirred for 10 min. A precooled -78 °C solution of 100 mg of sulfinyl imine **1b** (0.40 mmol, 1 equiv) in 0.800 mL of THF was then added via canula. The flask containing the imine solution was rinsed once with 0.150 mL of THF, and the resulting solution was added via cannula to the reaction flask. The reaction solution was then stirred at -78 °C for 5 h. The reaction was then quenched by addition of 1M AcOH in THF (3 equiv), and the solution was then filtered through a plug

of basic alumina and concentrated to give the crude product. HPLC analysis (250 mm x 4.6 mm Chiralcel AD column, detection at 254 nm, 1 mL/min, 99:1 hexanes:iPrOH) on the unpurified material established a 92 (t_R = 12.4 min) to 8 (t_R = 13.4 min) ratio of diastereomers. The crude product was then purified by silica gel chromatography (9:1 hexanes:EtOAc) to provide 93.4 mg (76%) of **2b** as a clear oil. ^1H NMR (500 MHz) δ 7.79 (bs, 2H), 7.48-7.45 (m, 1H), 7.44-7.39 (m, 2H), 3.36-3.28 (m, 1H), 3.10-3.02 (m, 1H), 1.93-1.85 (m, 1H), 1.37-1.30 (m, 6H), 1.31 (s, 9H), 0.90 (d, J = 6.7 Hz, 3H), 0.86 (t, J = 6.8 Hz, 3H); ^{13}C NMR (125 MHz) δ 180.5, 138.8, 131.4, 128.6, 127.8, 57.7, 39.2, 36.9, 32.8, 29.3, 23.0, 22.9, 19.9, 14.2. Anal. Calcd for $\text{C}_{18}\text{H}_{29}\text{NOS}$: C, 70.31; H, 9.51; N, 4.56. Found: C, 70.16; H, 9.60; N, 4.46.

(*R*)-*N*-(1-methyl-3-phenyl-butyldiene)-*tert*-butanesulfinamide (2c). To a round-bottom flask containing 103 mg of anhydrous CuI (0.54 mmol, 1.5 equiv) was added 0.405 mL of THF. This solution was cooled to 0 °C and 0.675 mL of MeLi in Et₂O (1.6 M, 1.1 mmol, 3 equiv) was added to form a 0.5 M solution. This solution was stirred for 15 min at 0 °C and then was cooled to -78 °C. A precooled -78 °C solution of 90 mg of sulfinyl imine **1c** (0.36 mmol, 1 equiv) in 0.720 mL of THF was then added via canula. The flask containing the imine solution was rinsed once with 0.150 mL of THF, and this rinse solution was added by cannula to the reaction flask. The reaction solution was warmed over 1.75 h to -48 °C and then was stirred at -48 °C for 3.5 h. The reaction was quenched by addition of 1M AcOH in THF (3 equiv), and the solution was then filtered through a plug of basic alumina and concentrated to give the crude product. HPLC analysis (250 mm x 4.6 mm Chiralcel AD column, detection at 254 nm, 1 mL/min, 99:1 hexanes:iPrOH) on the unpurified material established a 85 (t_R = 20.1 min) to 15 (t_R = 16.7 min) ratio of diastereomers. The crude product was then purified by silica gel chromatography (75:25 hexanes:EtOAc) to give 66.8 mg (70%) of **2c** as a clear oil. ^1H NMR (500 MHz) δ 7.30-7.26 (m, 2H), 7.20-7.17 (m, 3H), 3.26 (m, 1H), 2.80 (dd, J = 7.6, 15.3 Hz, 1H), 2.64 (dd, J = 7.3, 15.2 Hz, 1H), 2.26 (s, 3H), 1.30 (d, J = 6.9 Hz, 3H), 1.09 (s, 9H); ^{13}C NMR (125 MHz) δ 184.1, 146.0, 128.8, 127.1, 126.6, 56.4, 51.7, 37.2, 22.4, 22.8, 22.1. HRMS calcd. for $\text{C}_{15}\text{H}_{24}\text{NOS}$ 266.1579, found 266.1583.

(*R*)-*N*-(1,3-diphenyl-butylidene)-*tert*-butanesulfinamide (2d). To a round-bottom flask containing 78 mg of anhydrous CuI (0.41 mmol, 1.5 equiv) was added 0.307 mL of THF. This solution was cooled to 0 °C and 0.513 mL of MeLi in Et₂O (1.6M, 0.82 mmol, 3 equiv) was added to form a 0.5 M solution, which was stirred for 15 min at 0 °C and then was cooled to -78 °C. A precooled -78 °C 0.5 M solution of 80 mg of sulfinyl imine **1d** (0.27 mmol, 1 equiv) in 0.540 mL of THF was then added via canula. The flask containing the imine solution was rinsed once with 0.150 mL of THF and this rinse solution was added by cannula to the reaction solution. The reaction solution was then stirred at -78 °C for 5 h. The reaction was quenched by addition of 1M AcOH in THF (3 equiv), and the solution was then filtered through a plug of basic alumina and concentrated to give the crude product. HPLC analysis (250 mm x 4.6 mm Chiralcel AD column, detection at 254 nm, 1 mL/min, 99:1 hexanes:iPrOH) on the unpurified material established a 96 (*t_R* = 19.7 min) to 4 (*t_R* = 26.8 min) ratio of diastereomers. The crude product was then purified by silica gel chromatography (85:15 hexanes:EtOAc) to give 76.8 mg (91%) of **2d** as a white solid. ¹H NMR (500 MHz) δ 7.71 (m, 2H), 7.45 (t, *J* = 7.0Hz, 1H), 7.40-7.37 (m, 2H), 7.28-7.21 (m, 4H), 7.19-7.15 (m, 1H), 3.93 (m, 1H), 3.30-3.16 (m, 2H), 1.33-1.30 (m, 12H); ¹³C NMR (125 MHz) δ 178.5, 145.9, 138.6, 131.4, 128.7, 128.7, 127.7, 127.1, 126.7, 58.3, 39.6, 39.5, 23.1, 21.2. HRMS calcd. for C₂₀H₂₆NOS 328.1735, found 328.1740.

(*R*)-*N*-(3-methyl-cyclohexylidene)-*tert*-butanesulfinamide (2e). To a round-bottom flask containing 143 mg of anhydrous CuI (0.75 mmol, 1.5 equiv) was added 0.500 mL of Et₂O. This solution was cooled to 0 °C and 1.00 mL of MeLi in Et₂O (1.5M, 1.5 mmol, 3 equiv) was added to form a 0.5 M solution, which was stirred for 15 min at 0 °C and then was cooled to -78 °C. A precooled -78 °C solution of 100 mg of sulfinyl imine **1e** (0.50 mmol, 1 equiv) in 1.00 mL of Et₂O was then added via canula. The flask containing the imine solution was rinsed once with 0.200 mL of Et₂O, and this rinse solution was added by cannula to the reaction solution. The reaction solution was then stirred at -78 °C for 3 h. The reaction was quenched by addition of 1M AcOH in THF (3 equiv), and the solution was then filtered through a plug of basic alumina and

concentrated to give the crude product. HPLC analysis (250 mm x 4.6 mm Chiralcel AS column, detection at 254 nm, 1 mL/min, 95:5 hexanes:iPrOH) on the unpurified material established a 87 (t_R = 10.3 min) to 13 (t_R = 16.2 min) ratio of diastereomers. The crude product was then purified by silica gel chromatography (8:2 hexanes:EtOAc) to deliver 59.3 mg (55%) of product **2e** as a clear oil. As determined by NMR, product **2e** existed as a 1:1 mixture of imine isomers. ^1H NMR (500 MHz) δ 3.37-3.24 (m, 1H), 2.52-2.47 (m, 1H), 2.31-2.21 (m, 1H), 2.10-1.95 (m, 2H), 1.87-1.75 (m, 3H), 1.67-1.55 (m, 0.5H), 1.55-1.45 (m, 0.5H), 1.21 (s, 4.5H) 1.21 (s, 4.5H), 1.01-0.98 (m, 3H); ^{13}C NMR (125 MHz) δ 188.6, 188.4, 56.3, 55.9, 48.7, 42.3, 40.3, 35.0, 34.7, 33.9, 33.9, 33.8, 33.7, 26.6, 26.1, 22.3, 22.2, 22.2. HRMS calcd. for $\text{C}_{11}\text{H}_{22}\text{NOS}$ 216.1422, found 216.1416.

(R)-N-(3-methyl-heptylidene)-tert-butanefulfonamide (2f). Method A: To a round-bottom flask containing 104 mg of anhydrous CuCN (1.16 mmol, 2.0 equiv) was added 1.79 mL of THF. This solution was cooled to 0 °C, and 0.527 mL of *n*-BuLi in hexanes (2.2M, 1.16 mmol, 2.0 equiv) was added to form a 0.5 M solution. This solution was stirred for 15 min at 0 °C and then was cooled to -78 °C. PBU_3 (0.289 mL, 1.16 mmol, 2.0 equiv) was added, and the solution was stirred for 45 min at -78 °C. A precooled -78 °C solution of 100 mg of sulfinyl imine **1f** (1 equiv) in 1.16 mL of THF was then added via cannula. The flask containing the imine solution was rinsed once with 0.200 mL of THF, and this rinse solution was added by cannula to the reaction solution. The reaction solution was then stirred at -78 °C for 7 h. The reaction was then quenched by addition of 1M AcOH in THF (3 equiv), and the solution was then filtered through a plug of basic alumina and concentrated to give the crude product. HPLC analysis (250 mm x 4.6 mm Chiralcel AS column, detection at 254 nm, 1 mL/min, 99:1 hexanes:iPrOH) on the unpurified material established an 85 (t_R = 7.0 min) to 15 (t_R = 7.5 min) ratio of diastereomers. The crude product was then purified by silica gel chromatography (9:1 hexanes:EtOAc) to provide 98 mg (73%) of **2f** as a clear oil. ^1H NMR (500 MHz) δ 8.03 (t, J = 5.1 Hz, 1H), 2.50-2.45 (m, 1H), 2.37-2.30 (m, 1H), 1.92-1.84 (m, 1H), 1.36-1.15 (m, 6H), 1.18 (s, 9H), 0.93 (d, J = 6.7 Hz, 3H) 0.88-0.84 (t, J = 6.3 Hz, 3H); ^{13}C NMR (125 MHz) δ 169.8, 56.7, 43.5, 36.7, 31.0, 29.3, 23.0, 22.6, 20.0, 14.2. HRMS calcd. for $\text{C}_{12}\text{H}_{26}\text{NOS}$ 232.1735, found 232.1734.

Method B: To a round-bottom flask containing 72 mg anhydrous of Cu(OAc) (0.59 mmol, 2.0 equiv) was added 0.912 mL of THF. This solution was cooled to 0 °C, and 0.268 mL of *n*-BuLi in hexanes (2.2M, 0.59 mmol, 2.0 equiv) was added to form a 0.5 M solution. This solution was stirred for 15 min at 0 °C and then was cooled to -78 °C. PBu₃ (0.147 mL, 0.59 mmol, 2.0 equiv) was added, and the solution was stirred for 45 min at -78 °C. A precooled -78 °C solution of 50 mg of sulfinyl imine **1f** (1 equiv) in 0.58 mL of THF was then added via cannula. The flask containing the imine solution was rinsed once with 0.100 mL of THF, and this rinse solution was added by cannula to the reaction solution. The reaction solution was then stirred at -78 °C for x h and then was slowly allowed to warm to -20 °C overnight. The reaction was quenched by addition of 1M AcOH in THF (3 equiv), and the solution was then filtered through a plug of basic alumina and concentrated to give the crude product. HPLC analysis (250 mm x 4.6 mm Chiralcel AS column, detection at 254 nm, 1 mL/min, 99:1 hexanes:iPrOH) on the unpurified material established an 15 (*t_R* = 7.0 min) to 85 (*t_R* = 7.5 min) ratio of diastereomers. Addition of 2,6-dimethoxytoluene as an internal standard shows an NMR yield of 55%. ¹H NMR (500MHz) δ 8.05 (t, *J* = 5.1 Hz, 1H), 2.53-2.48 (m, 1H), 2.37-2.32 (m, 1H), 1.92-1.88 (m, 1H), 1.36-1.15 (m, 6H), 1.19 (s, 9H), 0.95 (d, *J* = 6.7 Hz, 3H) 0.88 (t, *J* = 6.3 Hz, 3H); ¹³C NMR (125 MHz) δ 169.9, 56.8, 43.6, 36.7, 31.1, 29.4, 23.0, 22.6, 20.2, 14.3.

Hydrolysis of compound 2a. To a solution of **2a** (114 mg, 0.46 mmol) in 23 mL of methanol was added 9.2 mL of 1 M AcOH in water. The resulting solution was stirred at room temperature for 24 h, then concentrated by half, and brine was added. This solution was extracted three times with 2:8 dichloromethane:pentane. The combined organic layers were washed once with 0.1 M Na₂CO₃, dried over MgSO₄ and filtered. The solvent was removed by Kugelrohr distillation. Column chromatography (9:1 pentane:Et₂O) provided 60.0 mg (92%) of (*R*)-4-methyloctan-2-one. Spectroscopic data matched those reported in the literature. [α]_D²⁵ = +7.8° (c 1.0, CHCl₃) 86%ee (*R*) (lit.² [α]_D²⁰ = +8.3° (*R*)).

² Yamaguchi, M.; Igarashi, Y.; Reddy, R. S.; Shiraishi, T.; Hiram, M. *Tetrahedron* **1997**, 53, 11223-11236.

Hydrolysis of compound 2c. To a solution of **2c** (62 mg, 0.23 mmol) in 11 mL of methanol was added 4.7 mL of 1 M AcOH in water, and the resulting solution was stirred at room temperature for 24 h. The solution was then concentrated half. Brine was added, and the aqueous layer was extracted three times with ethyl acetate. The combined organic layers were dried over MgSO₄, filtered and concentrated. Column chromatography (9:1 hexanes:EtOAc) provided 28.7 mg (77%) of (*R*)-4-phenylpentan-2-one. Spectroscopic data matched those reported in the literature. $[\alpha]_{\text{D}}^{24} = -26.3^{\circ}$ (c 1.44, CHCl₃) 70%ee (*R*) (lit.³ $[\alpha]_{\text{D}}^{20} = +40^{\circ}$ (c 0.5, CHCl₃)(*S*)).

Hydrolysis of compound 2d. To a solution of **2d** (40 mg, 0.12 mmol) in 6 mL of methanol was added 2.4 mL of 1 M AcOH in water, and the resulting solution was stirred at 40 °C for 15 h. The solution was then concentrated by half. Brine was added, and the aqueous layer was extracted three times with ethyl acetate. The combined organic layers were dried over NaSO₄, filtered and concentrated. Column chromatography (8:2 hexanes:EtOAc) provided 24.9 mg (91%) of (*R*)-1,3-diphenylbutan-1-one. Spectroscopic data matched those reported in the literature. $[\alpha]_{\text{D}}^{25} = -14.5^{\circ}$ (c 1.22, CCl₄) 92%ee (*R*) (lit.³ $[\alpha]_{\text{D}}^{20} = -14.8^{\circ}$ (c 1.2, CCl₄)(*R*)).

Hydrolysis of compound 2f. To a solution of **2f** (114 mg, 0.49 mmol) in 2 mL of THF was added 2.0 mL of glacial AcOH and 1.0 mL of water, and this was stirred at 70° C for 48 h. Brine was added and the solution was extracted 3 times with 2:8 dichloromethane:pentane. The organic was washed once with 0.1 M Na₂CO₃, dried over MgSO₄ and filtered. The solvent was carefully Kugelrohr distilled off the crude. Column chromatography (95:5 pentane:Et₂O) provided 44.2 mg (70%) of (*R*)-3-methylheptanal. Spectroscopic data matched those reported in the literature. $[\alpha]_{\text{D}}^{25} = +4.7^{\circ}$ (c 0.9, CHCl₃) 70%ee (*R*) (lit.⁴ $[\alpha]_{\text{D}}^{22} = +8.1^{\circ}$ (c 1.0, CHCl₃)(*R*)).

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