Carboxylate-Directed Highly Stereoselective Homogeneous Hydrogenation of Cyclic Olefins with Wilkinson's Catalyst

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Supporting Information

General. ^{1}H NMR spectra were measured with a Varian NMR spectrometer (300 MHz) with either Me_4Si (0.00) or residual protonated solvent ($CHCl_3$ 7.26; MeOH 3.30; DMSO 2.49) as standard. ^{13}C NMR spectra were measured with a Varian NMR spectrometer (75 MHz) with solvent ($CDCl_3$ 77.0; MeOD-d_3 49.0; DMSO-d_6 39.5) as standard. Coupling constants are reported in Hertz (Hz). All solvents and reagents were purchased from EM Science, Lancaster and Aldrich Chemicals and used without further purification. Elemental analyses were performed by Robertson Microlit Labs.

2-(6-Methoxy-1*H*-inden-3-yl)butanoic acid (1). An oven dried, 5-L, four-necked, round-bottomed flask was fitted with a thermometer, a condenser, an addition funnel and a mechanic stirrer. Under argon protection, a suspension of 5-methoxy-1-indanone **3** (80.0 g, 494 mmol), zinc powder from Lancaster (56.2 g, 865 mmol) in 2 L of anhydrous THF was stirred at 60^{o}C (internal temperature), while a solution of methyl bromobutyrate (134.1 g, 741 mmol) in 400 mL of anhydrous THF was added slowly through an addition funnel. After completion of the addition, the reaction mixture was stirred at 60 ^{o}C (internal temperature) for 1 hour. The reaction was followed by TLC analysis of aliquots after 1N aqueous HCl work-up. After the reaction was complete, it was cooled in an ice-water bath followed by slow addition of 3 L of 1N HCl solution. The pot temperature was kept below 20 ^{o}C. The mixture was then extracted with 1 L of ethyl acetate. The organic layer was washed with water until pH 6.0-7.0, saturated NaCl solution, and then dried over Na_2SO_4. The methyl ester of **1** was obtained as a yellow oil (127g, >99%) after solvent removal and drying under vacuum. The crude ester exhibited satisfactory ^{1}H and ^{13}C NMR spectra and was used directly for saponification: ^{1}H NMR (DMSO-d_6) 7.28 (d, J = 8, 1H), 7.05 (d, J = 2, 1H), 6.82 (dd, J = 8, J = 3, 1H), 6.22 (s,

1H), 3.72 (s, 3H), 3.60 (m, 1H), 3.58 (s, 3H), 3.28 (s, 2H), 1.95 (m, 1H), 1.80 (m, 1H), 0.88 (t, *J* = 7, 3H); ^{13}C NMR (DMSO-d_6) 13.429, 25.354, 38.509, 46.994, 52.740, 56.281, 110.903, 112.417, 120.147, 128.380, 137.087, 141.119, 146.297, 157.918, 173.523. HRMS (ES) *m/z* 247.1328 ([M +H]$^+$, calcd. for [$C_{15}H_{18}O_3$ + H], 247.1329.

To a solution of the methyl ester (200.0 g, 813 mmol) in 2 L of methanol, was added a solution of potassium hydroxide (91.0 g, 1.63 mol) in 200 mL of water. The reaction mixture was stirred at 60 ^{o}C (pot temperature) for 2 hours. TLC analysis showed 70% conversion. Additional solution of potassium hydroxide (45.0 g, 0.81 mol) in 100 mL of water was then added slowly to the pot. The reaction was completed in an hour. After the reaction mixture was cooled to room temperature, solvents were removed *in vacuo*. The residue was dissolved in 3 L of water and washed with ethyl acetate (2 x 1 L). The aqueous layer was cooled in an ice-water bath and acidified with concentrated HCl to pH < 3.0. The product was extracted into 3 L of CH_2Cl_2, washed with water (2 x 1 L), and dried over Na_2SO_4. The title compound **1** was obtained as a light brown solid (175 g, 93%) after solvent removal and vacuum drying: ^{1}H NMR (DMSO-d_6) 12.20 (s, 1H), 7.30 (d, *J* = 8, 1H), 7.06 (d, *J* = 2, 1H), 6.82 (dd, *J* = 8, *J* = 3, 1H), 6.22 (s, 1H), 3.75 (s, 3H), 3.45 (t, *J* = 7, 1H), 3.30 (s, 2H), 1.90 (m, 1H), 1.78 (m, 1H), 0.90 (t, *J* = 7, 3H); ^{13}C NMR (DMSO-d_6) 13.606, 25.271, 38.482, 47.377, 56.292, 110.803, 112.346, 120.349, 127.991, 137.380, 141.702, 146.281, 157.834, 174.562. HRMS (ES) *m/z* 231.1021 ([M-H]$^-$, calcd. for [$C_{14}H_{16}O_3$ - H], 231.1026.

2-(6-Methoxy-1*H*-inden-3-yl) propanoic acid (2). This substrate was prepared using the same procedure as described for **1** starting with 5-methoxyl-1 indanone and methyl 2-bromopropionate in 68% yield: ^{1}H NMR (CD_2Cl_2) 7.34 (d, *J* = 9, 1H), 7.07 (d, *J* = 2, 1H), 6.85 (dd, *J* = 9, *J* = 2, 1H), 6.32 (m, 1H), 3.82 (m, 4H), 3.36 (m, 2H), 1.56 (d, *J* = 7, 3H); ^{13}C NMR (CD_2Cl_2) 16.896, 38.453, 39.344, 56.041, 110.489, 111.765, 119.787, 127.806, 136.758, 141.900, 146.140, 157.928, 178.097 HRMS (ES) *m/z* 217.0865 ([M-H]$^-$, calcd. for [$C_{13}H_{14}O_3$ - H], 217.0866.

(3Z)-3-(4-Methoxy-2-methylphenyl)-2-methyl-3-hexenoic acid (3). This substrate was prepared using the same procedure as described for **1** starting with 6-methoxy tetralone and methyl 2-bromopropionate in 27% yield: ^{1}H NMR (CD_2Cl_2)

7.21 (m, 1H), 6.72 (m, 1H), 5.95 (t, J = 5, 1H), 3.79 (s, 3H), 3.74 (m, 1H), 2.72 (m, 2H), 2.28 (m, 2H), 1.44 (d, J = 7, 3H); ^{13}C NMR (CD_2Cl_2) 17.357, 23.850, 29.302, 41.886, 55.756, 110.946, 114.101, 123.596, 123.981, 126.947, 135.071, 138.645, 158.378, 179.084. Anal. Calcd. for $C_{14}H_{16}O_3$: C, 72.39; H, 6.94. Found: C, 72.12; H, 6.77.

Typical procedure for directed homogeneous hydrogenation: a solution of compound **1** (105 g, 453 mmol), $ClRh(PPh_3)_3$ (21.0 g, 5 mol%) and triethylamine (68.8 g, 679.5 mmol) in EtOH (945 mL) and THF (105 mL) was shaken in a 2 L pressure bottle under 60 psi hydrogen for 12 hours. NMR analysis showed completion of the reaction. The solvents were removed at reduced pressure, and the resulting mixture was stirred in 1.5 L of 1N HCl solution and 1.5 L of CH_2Cl_2. The aqueous layer was extracted with CH_2Cl_2 (2 x 250 mL). The combined CH_2Cl_2 layers were washed with 1 L of 1N HCl solution and stirred with 1 L of 1N NaOH solution. The organic layer was extracted with 1N NaOH solution (2 X 0.5 L). The combined aqueous layer was washed with CH_2Cl_2 (2 x 250 mL), and acidified (pH 2.0-3.0) by a slow addition of concentrated HCl solution at below 15^{o}C. The acid mixture was extracted with CH_2Cl_2 (2 x1.5 L), and washed with water (2 x 0.5 L) until pH5.0-6.0. After washing with brine and drying over anhydrous Na_2SO_4, solvent was evaporated under a reduced pressure. The product **1a** was obtained as a light yellow oil (101.0 g, 95% yield, >99 % *de*): ^{1}H NMR (DMSO-d_6) 12.20 (s, 1H), 7.03 (d, J = 8, 1H), 6.78 (d, J = 3, 1H), 6.66 (dd, J_1 = 8, J_2 = 3, 1H), 3.70 (s, 3H), 3.28 (m, 1H), 2.72 (m, 2H), 2.32 (m, 1H), 2.06 (m, 1H), 1.80 (m, 1H), 1.50 (m, 1H), 1.36 (m, 1H), 0.82 (t, J = 7, 3H); ^{13}C NMR (DMSO-d_6) 12.095, 21.557, 28.612, 30.967, 45.516, 50.867, 55.033, 109.592, 112.068, 124.254, 136.584, 145.394, 158.499, 176.202. HRMS (ES) *m/z* 233.1178 ([M-H]$^-$, calcd. for [$C_{14}H_{18}O_3$ - H], 233.1176.

Compound **2a** was prepared in 71% yield and >99% *de* using the same procedure as described for **1a** starting with **2**: ^{1}H NMR (DMSO-d_6) 12.18 (s, 1H), 7.03 (d, J = 8, 1H), 6.75 (d, J = 2, 1H), 6.67 (dd, J_1 = 8, J_2 = 2, 1H), 3.68 (s, 3H), 3.37 (m, 1H), 2.72 (m, 3H), 2.03 (m, 1H), 1.75 (m, 1H), 0.89 (d, J = 7, 3H); ^{13}C NMR (CD_2Cl_2) 12.626, 28.228, 31.950, 43.300, 46.445, 55.607, 110.054, 112.510, 124.552, 136.702, 146.411, 159.464, 182.330. Anal. Calcd. for $C_{13}H_{16}O_3$: C, 70.89; H, 7.32; Found: C, 70.83; H, 7.10.

Compound **3a** was prepared in 84% yield and >99% *de* using the same procedure as described for **1a** starting with **3**: ^{1}H NMR (DMSO-d_6) 12.15 (s, 1H), 7.12 (d, J = 8, 1H), 6.67 (dd, J_1 = 8, J_2 = 2, 1H), 6.60 (d, J = 2, 1H), 3.68 (s, 3H), 3.16 (m, 1H), 2.97 (m, 1H), 2.64 (m, 2H), 1.79 (m, 1H), 1.56 (m, 3H), 0.81 (d, J = 7, 3H); ^{13}C NMR (CD_2Cl_2) 11.638, 21.370, 24.631, 30.351, 39.510, 43.704, 55.399, 112.269, 113.971, 128.790, 130.177, 139.840, 157.986, 181.156. Anal. Calcd. for $C_{14}H_{18}O_3$: C, 71.77; H, 7.74; Found: C, 71.58; H, 7.61.

Heterogeneous hydrogenation of methyl 2-(5-methoxy-2,3-dihydro-1*H*-inden-1-yl)butanoate (**the methyl ester of 1**). A suspension of the indene methyl ester (1.0 g, 4.1 mmol), pearlman's catalyst (0.72 g, 7.0 wt. %), ammonium formate (4.92 g, 78 mmol), in ethanol (200 mL) was heated at 60^{o}C (inside) for 30 minutes. ^{1}H NMR analysis showed absence of the starting material. After cooling to room temperature, the reaction mixture was filtered through a pad of celite, and the filter cake was washed with ethyl acetate (50 mL). The filtrate was concentrated *in vacuuo*. To the resulting mixture was added ethyl acetate (50 mL) and water (50 mL). The organic layer was washed with water (2x20 mL), and dried over Na_2SO_4. Removal of solvent afforded the product (a 1:3 diastereomeric mixture) as a light yellow oil (1.0 g, 95% yield): ^{1}H NMR (DMSO-d_6): 7.08(d, *peri*-ArH from the Me ester of **1b**, integrated as 3H), 6.90(d, *peri*-ArH from the Me ester of **1a**, integrated as 1H), 6.75(m), 6.65(dd), 3.67(s), 3.60(s), 3.50(s), 3.20(m), 2.80(m), 2.70(m), 2.40(m), 2.05(m), 1.84(m), 1.53(m), 0.80(t).

Heterogeneous hydrogenation of 1. The indene acid **1** was hydrogenated in the same fashion as described for its methyl ester above to afford the corresponding indane acid as a mixture of **1a** and **1b** (1:2 based ^{1}H NMR) in 95% yield: ^{1}H NMR (DMSO-d_6): 7.10(d, *peri*-ArH from **1b,** integrated as 2H), 7.03(d, *peri*-ArH from **1a,** integrated as

1H), 6.74(m), 6.63(dd), 3.55(m), 3.42(m), 3.27(m), 3.15(m), 2.80(m), 2.68(m), 2.30(m), 2.05(m), 1.92(m), 1.76(m), 1.50(m), 1.36(m), 0.8(t).