Supplementary Materials

Diastereoselective Reduction of Cyclopropenylcarbinol: New Access to *anti*-Cyclopropylcarbinol Derivatives

Elinor Zohar and Ilan Marek*

General: All reactions involving organometallic compounds were carried out under a positive pressure of Ar using standard Schlenk techniques. THF and Et₂O were distilled over benzophenone under an argon atmosphere. LiAlH₄ (1 M solution in Et₂O) *n*-butyllithium (1.6M solution in hexane) were purchased from Aldrich Chemical CO. 1,1,2-trihalogenocyclopropanes and cyclopropenylcarbinols were prepared according to literature procedures.¹

¹H and ¹³C NMR spectra were recorded for CDCl₃ solution with external standard on Bruker NMR spectrometers.

General procedure for the preparation of Cyclopropenylcarbinols:

1-(2-Phenethylcyclopropene-1-yl)-1-propanol 1a *n*-BuLi (7.1 mL, 1.18 M solution in hexane, 8.38 mmol) was added over 5 min to a stirred solution of 1-chloro-2,2-dibromo-1-phenethylcyclopropane (1.23 g, 3.64 mmol) in Et₂O (20 mL) at -80 °C. The mixture was allowed to reach -10 °C and after 1 hour was cooled down to -50 °C. Propionaldehyde (0.4 mL, 5.58 mmol) was added and the mixture was stirred for 15 min at -50 °C, then warmed to 25 °C and stirred for 3h. Water (10 mL) was added, the aqueous layer was extracted with Et₂O (3×20 mL) and the combined organic layers were washed with water (2×20 mL), dried over MgSO₄, and the solvent was removed under reduced pressure. Purification by column chromatography on silica gel (eluent: hexane/ethyl acetate 10:1), gave **1a** (0.400 g, 56%). ¹H NMR (300 MHz, CDCl₃) δ : 0.85 (t, *J* = 7.5Hz, 3H), 0.96 (s, 2H), 1.55-1.63 (m, 2H), 2.80-2.76 (m, 2H), 2.9-2.85 (m, 2H), 4.4 (t, *J* = 4Hz, 1H), 7.15-7.26 (m, 5H).

1-(2-Methylcyclopropen-1-yl)-1-propanol 1b The reaction was performed according to the general procedure. *n*-BuLi (39 mL, 1.27 M solution in hexane, 49.5 mmol), 1,1,2-tribromo-2-methylcyclopropane (6.25 g, 21.33 mmol), propionaldehyde (2.3 mL, 32.0 mmol) in Et₂O (100 mL). Chromatography on silica gel (eluent: hexane/ethyl acetate 10:1) gave **1b** (2.03 g, 85%). ¹H NMR (300 MHz, CDCl₃) δ : 0.85-0.95 (m, 2H), 0.92 (t, *J* = 8.7 Hz, 3H), 1.65-1.75 (m, 2H), 2.08 (s, 3H), 4.51 (t, *J* = 6.3 Hz, 1H); ¹³C NMR (75 MHz, CDCl₃) δ : 8.1, 9.4, 11.5, 28.8, 30.1, 69.2, 108.6, 110.9.

1-(2,3,3-Trimethylcyclopropen-1-yl)-1-propanol 1c The reaction was performed according to the general procedure. *n*-BuLi (30 mL, 1.2 M solution in hexane, 36.0 mmol), 1,1,2-tribromo-2,3,3-trimethylcyclopropane (5.0 g, 15.57 mmol), propionaldehyde (1.7 mL, 23.7 mmol), Et₂O (80 mL). Chromatography on silica gel (eluent: hexane/ethyl

¹ (a) Baird, M.S.; Hussain, H.H.; Nethercott, W. *J. Chem. Soc., Perkin Trans. 1*. **1986**, 1845. (b) Baird, M.S.; Nethercott, W. *Tetrahedron Lett.* **1983**, 24, 605 (c) Baird, M.S.; Hussain, H.H. *Tetrahedron* **1987**, 43, 215 (d) Al-Dulayymi, J.R.; Baird, M.S. *Tetrahedron Lett.* **1988**, 29, 6147 (e) Al-Dulayymi, J.R.; Baird, M.S. *Tetrahedron* **1989**, 45, 7601 (f) Al-Dulayymi, A.R.; Baird, M.S. *J. Chem. Soc. Perkin Trans. 1*. **1994**, 1547.

acetate 10:1) gave **1c** (1.92 g, 88 %). ^1H NMR (200 MHz, CDCl_3) δ : 0.93 (t, $J = 7.44$ Hz, 3H), 1.08 (s, 6H), 1.64 (q, $J = 7.14$ Hz, 2H), 1.97 (s, 3H), 4.5 (t, $J = 6.27$ Hz, 1H); ^{13}C NMR (50 MHz, CDCl_3) δ : 8.8, 9.7, 21.3, 25.9, 26.1, 29.6, 70.2, 122.3, 125.2.

1-(2,3,3-Trimethylcyclopropen-1-yl)-1-ethanol 1d The reaction was performed according to the general procedure. *n*-BuLi (18 mL, 1.33 M solution in hexane, 23.9 mmol), 1,1,2-tribromo-2,3,3-trimethylcyclopropane (3.5 g, 10.9 mmol), acetaldehyde (1 mL, 17.7 mmol) in Et_2O (55 mL). Chromatography on silica gel (eluent: hexane/ethyl acetate 15:1) gave **1d** (965mg, 70%). ^1H NMR (300 MHz, CDCl_3) δ : 1.04 (s, 6H), 1.2 (d, $J = 5.1$ Hz, 3H), 1.91 (s, 3H), 2.42 (s, 1H), 4.7 (q, $J = 5.1$ Hz, 1H); ^{13}C NMR (75 MHz, CDCl_3) δ : 8.4, 21.1, 22.4, 25.6, 25.7, 64.5, 121.0, 125.9.

1-(3,3-Dimethylcycloprope-1-yl)-1-propanol 1e The reaction was performed according to the general procedure. *n*-BuLi (25 mL, 1.4 M solution in hexane, 35.0 mmol), 1,1,2-tribromo-3,3-dimethylcyclopropane (3.63 g, 13.8 mmol), propionaldehyde (1.5 mL, 21.0 mmol) in Et_2O (40 mL). Chromatography on silica gel (eluent: hexane/ethyl acetate 10:1), gave **1e** (1.13 g, 65%). ^1H NMR (200 MHz, CDCl_3) δ : 0.9 (t, $J = 6.7$ Hz, 3H), 1.15 (s, 6H), 1.63 (m, 2H), 4.55 (t, $J = 6.2$ Hz, 1H), 6.99 (s, 1H); ^{13}C NMR (50 MHz, CDCl_3) δ : 8.8, 21.3, 25.9, 26.1, 29.6, 71.0, 115.3, 136.2.

Cyclohexyl-(3,3-dimethylcyclopropen-1-yl)-1-methanol 1f The reaction was performed according to the general procedure. *n*-BuLi (37 mL, 1.18 M solution in hexane, 43.66 mmol), 1,1,2-tribromo-3,3-dimethylcyclopropane (5.0 g, 19.08 mmol), cyclohexane carboxaldehyde (3.5 mL, 28.5 mmol) in Et_2O (100 mL). Chromatography on silica gel (eluent: hexane/ethyl acetate 15:1) gave **1f** (3.15 g, 92%). ^1H NMR (200 MHz, CDCl_3) δ : 1.14 (s, 3H), 1.18 (s, 3H), 1.25-1.13 (m, 10H), 1.72-1.75 (m, 1H), 4.4 (d, $J = 5.5$ Hz, 1H), 7.04 (s, 1H); ^{13}C NMR (75 MHz, CDCl_3) δ : 22.8, 26.2, 26.4, 26.5, 27.7, 28.1, 29.2, 33.8, 43.6, 76.2, 115.3, 136.2.

1-(2,3,3-Trimethylcyclopropene-1-yl)-3E-hexen-1-ol 1g *n*-BuLi (5.7 mL, 1.27 M solution in hexane, 7.15 mmol) was added over 5 min to a stirred solution of 1,1,2-tribromo-2,3,3-trimethylcyclopropane (1.0 g, 3.11 mmol) in Et_2O (15 mL) at -80°C . The mixture was allowed to reach -10°C and after 1h was cooled down to -20°C and MgBr_2 (0.69 g, 3.73 mmol) was added. The reaction mixture was then allowed to warm to room temperature and stirred for 50 min. Hex-3*E*-enal (4.66 mmol, prepared by reduction of *trans*-ethylhexanoate with DIBAL-H at -80°C) was added at -80°C . After 30 min the reaction was warmed to room temperature and stirred for 7 h. Water (20 mL) was added, the aqueous layer was extracted with Et_2O (3 $\times$ 20 mL), the combined organic layers were washed with water (2 $\times$ 20 mL), dried over MgSO_4 , and the solvent was removed under reduced pressure. Column chromatography on silica gel (eluent: hexane/ethyl acetate 10:1) gave **1g** (0.28 g, 50%). ^1H NMR (300 MHz, CDCl_3) δ : 0.97 (t, $J = 7.5$ Hz, 3H), 1.1 (s, 6H), 1.98 (s, 3H), 2.03 (t, $J = 6$ Hz, 2H), 2.33-2.35 (m, 2H), 4.61 (t, $J = 6$ Hz, 1H), 5.44-5.34 (m, 1H), 5.63-5.55 (m, 1H); ^{13}C NMR (75 MHz, CDCl_3) δ : 8.9, 13.8, 14.1, 22.6, 25.7, 25.8, 26.0, 31.6, 39.7, 68.2, 124.0, 136.2.

1-(3,3-Dimethyl-2-trimethylsilylcyclopropene-1-yl)-1-propanol 1h The reaction was performed according to the general procedure. *n*-BuLi (2.5 mL, 1.18 M solution in hexane, 2.95 mmol), 1-chloro-2,2-dibromo-3,3-dimethyl-1-trimethylsilylcyclopropane (0.404 g, 1.2 mmol), propionaldehyde (0.15 mL, 2.10 mmol) in Et_2O (10 mL).

Chromatography on silica gel (eluent: hexane/ethyl acetate 15:1) gave **1h** (0.098 g, 41%). ¹H NMR (300 MHz, CDCl₃) δ : 0.148 (s, 9H), 0.98 (t, *J* = 6 Hz, 3H), 1.15 (s, 3H), 1.16 (s, 3H), 1.59-1.69 (m, 2H), 4.6 (t, *J* = 6 Hz, 1H); ¹³C NMR (75 MHz, CDCl₃) δ : -0.3, 9.9, 22.7, 28.1, 28.4, 29.5, 71.9, 124.0, 150.3.

General procedure for the hydroalumination reaction of **1a-h**:

(1R*)-1-[(1S*, 2R*)-2-Phenethylcyclopropyl]-propanol 2a LiAlH₄ (1.4 mL, 1.0 M solution in Et₂O, 1.4 mmol) was added to a stirred solution of **1a** (0.28 g, 1.386 mmol) in Et₂O (7 mL) at 0 °C. The reaction mixture was heated to +40 °C for 4.5 h and then quenched with 1M aqueous solution of HCl (5 mL). The aqueous layer was extracted with Et₂O (3 $\times$ 10 mL) and the combined organic layers were dried over MgSO₄, filtered and the solvent was removed under reduced pressure. Chromatography on silica gel (eluent: hexane/ethyl acetate 10:1), gave **2a** (0.24 g, 85% for the two diastereoisomers). ¹H NMR of the major isomer isolated after purification (300 MHz, CDCl₃) δ : -0.06 (q, *J* = 6 Hz, 1H), 0.71-0.85 (m, 1H), 0.88-0.96 (m, 2H), 0.93 (t, *J* = 9 Hz, 3H), 1.54-1.65 (m, 3H), 1.88-1.90 (m, 1H), 2.77 (t, *J* = 9 Hz, 2H), 3.09-3.12 (m, 1H), 7.16-7.30 (m, 5H); ¹³C NMR (75 MHz, CDCl₃) δ : 9.6, 10.1, 15.2, 22.6, 30.6, 30.7, 36.4, 74.2, 125.7, 128.3, 128.4, 142.4.

(1R*)-1-[(1S*, 2R*)-2-Methylcyclopropyl]-propanol 2b The reaction was performed according to the general procedure. LiAlH₄ (12.5 mL, 1.0 M solution in Et₂O, 12.5 mmol), **1b** (1.39 g, 12.4 mmol) in Et₂O (50 mL). The reaction mixture was heated to 40 °C for 19h. Chromatography on silica gel (eluent: hexane/ethyl acetate 10:1) gave **2b** (0.7 g, 50% for the two diastereoisomers). ¹H NMR of the major isomer isolated after purification (200 MHz, CDCl₃) δ : -0.16-0.1 (m, 1H), 0.61-0.67 (m, 1H), 0.78-0.81 (m, 2H), 0.92 (t, *J* = 7.4 Hz, 3H), 1.08 (d, *J* = 6 Hz, 3H), 1.55-1.6 (m, 2H), 3.05-3.12 (m, 1H); ¹³C NMR (75 MHz, CDCl₃) δ : 9.0, 10.2, 10.9, 13.4, 22.4, 30.5, 74.3.

(1R*)-1-[(1S*, 2R*)-2,3,3-Trimethylcyclopropyl]-propanol 2c The reaction was performed according to the general procedure. LiAlH₄ (4.4 mL, 1.0 M solution in Et₂O, 4.4 mmol), **1c** (0.63 g, 4.5 mmol) in Et₂O (20 mL). The reaction mixture was heated to 40 °C for 70h. Chromatography on silica gel (eluent: hexane/ethyl acetate 10:1) gave **2c** (0.55 g, 86%). ¹H NMR (300 MHz, CDCl₃) δ : 0.51 (dd, *J* = 9.6 Hz, 1H), 0.63-0.68 (m, 1H), 0.9 (s, 3H), 0.93 (t, *J* = 7.5 Hz, 3H), 0.99 (s, 3H), 1.04 (d, *J* = 6.3 Hz, 3H), 1.49-1.57 (m, 2H), 3.27-3.33 (m, 1H); ¹³C NMR (50 MHz, CDCl₃) δ : 8.8, 9.8, 15.3, 20.3, 29.0, 30.9, 33.0, 36.6, 70.7.

(1R*)-1-[(1S*, 2R*)-2,3,3-Trimethylcyclopropyl]-ethanol 2d The reaction was performed according to the general procedure. LiAlH₄ (0.9 mL, 1.0 M solution in Et₂O, 0.9 mmol), **1d** (115 mg, 0.9 mmol) in Et₂O (20 mL). The reaction mixture was heated to 30 °C for 24 h. Chromatography on silica gel (eluent: hexane/ethyl acetate 10:1) gave **2d** (83 mg, 74%). ¹H NMR (300 MHz, CDCl₃) δ : 0.5 (dd, *J* = 8.7, 10.2 Hz, 1H), 0.55-0.65 (m, 1H), 0.91 (s, 3H), 0.99 (s, 3H), 1.03 (d, *J* = 6.6 Hz, 3H), 1.21 (d, *J* = 4.8 Hz, 3H), 3.52-3.57 (m, 1H). ¹³C NMR (75 MHz, CDCl₃) δ : 8.7, 14.8, 20.6, 23.7, 29.1, 30.5, 34.5, 65.8.

(1R*)-1-[(1S*, 2R*)-3,3-dimethylcyclopropyl]-propanol 2e The reaction was performed according to the general procedure. LiAlH₄ (2.5 mL, 1.0 M solution in Et₂O,

2.5 mmol), **1e** (0.31 g, 2.46 mmol) in Et₂O (10 mL). The reaction mixture was heated to 40 °C for 20 h. Chromatography on silica gel (eluent: hexane/ethyl acetate 10:1) gave **2e** (0.25 g, 80%). ¹H NMR (200 MHz, CDCl₃) δ : 0.19 (t, *J* = 4.7 Hz, 1H), 0.44 (dd, *J* = 4.12, 6.24 Hz, 1H), 0.6 (m, 1H), 0.93 (t, *J* = 7.5 Hz, 3H), 1.00 (s, 3H), 1.02 (s, 3H), 1.51-1.61 (m, 2H), 3-3 (m, 1H).

(1R*)-[(1S*, 2S*)-3,3-Dimethylcyclopropen-1-yl]-cyclohexyl methanol 2f The reaction was performed according to the general procedure. LiAlH₄ (2.5 mL, 1.0 M solution in Et₂O, 2.5 mmol), **1f** (0.447 g, 2.48 mmol) in Et₂O (10 mL). The reaction mixture was heated to 40 °C for 19 h. Chromatography on silica gel (eluent: hexane/ethyl acetate 10:1) gave **2f** (0.34 g, 75%). ¹H NMR (300 MHz, CDCl₃) δ : 0.16 (dd, *J* = 5.4, 4Hz, 1H), 0.43 (dd, *J* = 8.7, 4Hz, 1H), 0.63-0.68 (m, 1H), 1.0 (s, 6H), 1.15-1.21 (m, 4H), 1.32-1.38 (m, 2H), 1.70-1.72 (m, 4H), 1 (m, 1H), 2.84-2.90 (m, 1H); ¹³C NMR (75 MHz, CDCl₃) δ : 17.4, 17.6, 21.3, 26.1, 26.4, 26.5, 27.0, 28.7, 29.0, 30.5, 44.7, 76.8.

(1R*)-[(1S*, 2S*)-2,3,3-Trimethylcyclopropyl]-3(E)-hexen-1-ol 2g The reaction was performed according to the general procedure. LiAlH₄ (0.85 mL, 1.0 M solution in Et₂O, 0.85 mmol), **1g** (0.149 g, 0.828 mmol) in Et₂O (5 mL). The reaction mixture was heated to 40°C for 26h. Chromatography on silica gel (eluent: hexane/ethyl acetate 10:1) gave **2g** (0.12 g, 80%). ¹H NMR (300 MHz, CDCl₃) δ : 0.5 (dd, *J* = 10,9 Hz, 1H), 0.63-0.69 (m, 1H), 0.90 (s, 3H), 0.97 (t, *J* = 5.5 Hz, 3H), 0.98 (s, 3H), 1.02 (d, *J* = 6.6 Hz, 3H), 1.96-2.04 (m, 2H), 2.19 (t, *J* = 6.6 Hz, 2H), 3.31-3.39 (m, 1H), 5.35-5.44 (m, 1H), 5.51-5.60 (m, 1H); ¹³C NMR (75 MHz, CDCl₃) δ : 9.1, 14.0, 15.6, 18.6, 20.8, 25.9, 29.4, 32.9, 41.8, 69.3, 125.2, 135.8.

(1R*)-[(1R*, 2S*)-3,3-Dimethyl-2-trimethylsilacyclopropyl]-propanol 2h The reaction was performed according to the general procedure. LiAlH₄ (0.5 ml, 1M solution in Et₂O, 0.5 mmol), **1h** (0.1 g, 0.5 mmol) in benzene (4 ml). The reaction mixture was heated to 40°C for 75h. Chromatography on silica gel (eluent: hexane/ethyl acetate 10:1) gave **2h** (0.064 g, 64% for both diastereoisomers). ¹H NMR of the major product isolated after purification (300 MHz, CDCl₃) δ : -0.6 (d, *J* = 6 Hz, 1H), 0.03 (s, 9H), 0.67 (dd, *J* = 9, 6 Hz, 1H), 0.93 (t, *J* = 9 Hz, 3H), 1.05 (s, 3H), 1.08 (s, 3H), 1.52-1.64 (m, 2H), 3.09-3.12 (m, 1H); ¹³C NMR (75 MHz, CDCl₃) δ : -0.2, 9.9, 17.9, 23.2, 24.0, 25.0, 30.5, 37.2, 75.3.

1-(1-deutero-2,3,3-trimethylcyclopropyl)-1-propanol [2c(d₁)] The reaction was performed according to the general procedure. LiAlD₄ (4.5 ml, 1.0 M solution in Et₂O, 4.5 mmol), **1c** (0.62 g, 4.43 mmol) in Et₂O (25 ml). The reaction mixture was heated to 40°C for 70h. Chromatography on silica gel (eluent: hexane/ethyl acetate 10:1) gave **2c(d₁)** (0.45 g, 72%). ¹H NMR (200 MHz, CDCl₃) δ : 0.63 (q, *J* = 6.5 Hz, 1H), 0.92 (t, *J* = 4.6 Hz, 3H), 0.99 (s, 6H), 1.03 (d, *J* = 6.5 Hz, 3H), 1.45-1.61 (m, 2H), 3.31 (t, *J* = 6 Hz, 1H).

1-(2-deutero-2,3,3-trimethylcyclopropyl)-1-propanol [2c(d₂)] The reaction was performed according to the general procedure. LiAlH₄ (7 ml, 1.0 M solution in Et₂O, 7 mmol), **1c** (1.009 g, 7.2 mmol) in Et₂O (30 ml). The reaction mixture was heated to 40°C for 72h and then quenched with CD₃OD (1 ml) at 0 °C followed by 1M HCl solution (10 ml). Chromatography on silica gel (eluent: hexane/ethyl acetate 10:1) gave **2c(d₂)** (0.72 g, 70%). ¹H NMR (300 MHz, CDCl₃) δ : 0.52 (d, *J* = 6.9 Hz, 1H), 0.92 (t, *J* = 4.5 Hz, 3H),

0.992 (s, 6H), 1.04 (s, 3H), 1.48-1.57 (m, 2H), 3.27-3.34 (m, 1H); ^{13}C NMR (75 MHz, CDCl_3) δ : 8.7, 9.8, 15.3, 18.4, 20.3, 29.0, 30.9, 32.9, 70.8.

1-(1-deutero-,3,3-trimethylcyclopropyl)-1-propanol [2e(d₁)] The reaction was performed according to the general procedure. LiAlD_4 (12 mL, 1.0 M solution in Et_2O , 12 mmol), **1e** (1.5 g, 11.9 mmol) in Et_2O (45 mL). The reaction mixture was heated to 40 °C for 22 h. Chromatography on silica gel (eluent: hexane/ethyl acetate 10:1) gave **2e(d₁)** (1.23g, 80%). ^1H NMR (300 MHz, CDCl_3) δ : 0.16 (d, $J = 4.2$ Hz, 1H), 0.42 (d, $J = 4.2$ Hz, 1H), 0.91 (t, $J = 7.5$ Hz, 3H), 0.97 (s, 3H), 1.0 (s, 3H), 1.5-1.58 (m, 2H), 3.05-3.09 (m, 1H); ^{13}C NMR (75 MHz, CDCl_3) δ : 9.7, 16.6, 17.8, 20.7, 27.1, 29.6, 30.7, 74.2.