SUPPORTING INFORMATION

Low-Valent Titanium-Mediated Cyclopropanation of Vinylogous Esters

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Representative Procedure for Cyclopropanation of Vinylogous Esters

A. Without Lewis acid:

To a solution of 3-methoxy-2-cyclohexen-1-one (**1**) (126 mg, 1 mmol) in 8 mL of anhydrous ether was added $Ti(O-i-Pr)_4$ (0.33 mL, 1.1 equiv). A 1.5 M solution of *n*-butylmagnesium bromide in ether (2 mL) was added at room temperature over a period of 1 h (via syringe pump). After the reaction mixture had been stirred for an additional 1 h, water (5 mL) was added to quench the reaction. The mixture was filtered to remove inorganic solids, the organic layer was separated, and the aqueous layer was extracted with ether (3 x 10 mL). The combined extracts were concentrated under reduced pressure to ca. 10 mL, and *p*-TsOH·H₂O (10 mg) was then added. The resulting mixture was stirred for 2 h to ensure complete hydrolysis of the enol ether functionality, washed with aqueous NaHCO₃ (10 mL) and also brine (10 mL), dried over MgSO₄, filtrated, and evaporated under reduced pressure. Purification of the concentrate by column chromatography on silica gel afforded 101 mg (66%) of **3a**, as a mixture of two inseparable diastereomers (a 1:2 ratio by GC-MS), as a colorless oil: IR (neat) 1713 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) (major diastereomer) δ -0.02 (t, $J = 5.0$ Hz, 1H), 0.46 (m, 1H), 0.55 (m, 1H), 0.97 (t, $J = 7.3$ Hz, 3H), 1.19–1.88 (m, 6H), 1.99 (d, $J = 14.5$ Hz, 1H), 2.27 (d, $J = 14.5$ Hz, 1H), 2.37 (t, $J = 6.5$ Hz, 2H); ¹³C NMR (125 MHz, CDCl₃) δ (14.5, 17.3, 22.4, 25.0, 25.5, 29.3, 36.3, 41.8, 52.8, 211.4), (14.6, 17.4, 22.5, 24.6, 25.5, 25.7, 36.3, 41.8, 46.0, 211.7); HRMS (M^+) calcd for C₁₀H₁₆O 152.1201, Found: 152.1199.

B. With Lewis acid:

To a solution of **1** (126 mg, 1 mmol) in 8 mL of anhydrous ether was added $\text{Ti}(\text{O}-i\text{-Pr})_4$ (0.33 mL, 1.1 equiv). A 1.0 M solution of 4-triisopropylsiloxybutylmagnesium chloride in THF (3 mL) was added at room temperature over a period of 1 h (via syringe pump). The reaction mixture was stirred for an additional 1 h and then cooled to $-78\text{ }^\circ\text{C}$, followed by addition of $\text{BF}_3\cdot\text{OEt}_2$ (0.25 mL, 2 mmol). The solution was allowed to warm up to room temperature (over a period of 1 h). An aqueous saturated NaHCO_3 solution (5 mL) was then added, and the mixture was filtrated to remove inorganic solids. The organic layer was separated, and the aqueous layer was extracted with ether (3 x 10 mL). The combined extracts were washed with aqueous NaHCO_3 (10 mL) and also brine (10 mL), dried over MgSO_4 , filtrated, and evaporated under reduced pressure. Purification of the concentrate by column chromatography on silica gel afforded 162 mg (50%) of **3e**, as a mixture of two inseparable diastereomers (a 1:2 ratio by GC-MS), as a colorless oil: IR (neat) 1716 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) (major diastereomer) δ 0.04 (t, $J = 5.2\text{ Hz}$, 1H), 0.50 (m, 1H), 0.65 (m, 1H), 1.06 (m, 21H), 1.40–1.89 (m, 6H), 1.97 (d, $J = 14.4\text{ Hz}$, 1H), 2.30 (d, $J = 14.4\text{ Hz}$, 1H), 2.37 (m, 2H), 3.73 (t, $J = 7.0\text{ Hz}$, 2H); ^{13}C NMR (100 MHz, CDCl_3) δ (12.2, 17.3, 18.3, 20.2, 24.0, 25.4, 29.5, 32.6, 41.7, 52.6, 63.6, 210.5), (12.2, 17.4, 18.3, 20.3, 24.1, 25.0, 32.6, 36.2, 41.8, 46.4, 63.7, 210.6); HRMS ($\text{M}^+ - i\text{-Pr}$) calcd for $\text{C}_{16}\text{H}_{29}\text{O}_2\text{Si}$ 281.1937, found: 281.1939.

3b: IR (neat) 1726 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) (major diastereomer) δ 0.33 (m, 4H), 1.53 (t, $J = 6.0\text{ Hz}$, 2H), 1.90 (m, 2H), 2.16 (s, 2H), 2.35 (t, $J = 6.8\text{ Hz}$, 2H); ^{13}C NMR (125 MHz, CDCl_3) δ 11.4, 20.5, 25.3, 34.3, 41.4, 50.9, 211.5.

3c: IR (neat) 1715 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) (major diastereomer) δ 0.03 (t, $J = 5.0\text{ Hz}$, 1H), 0.33 (m, 1H), 0.44 (m, 1H), 0.97 (d, $J = 6.5\text{ Hz}$, 3H), 1.01 (d, $J = 6.5\text{ Hz}$,

3H), 1.48–2.02 (m, 5H), 2.34 (m, 2H), 2.36 (d, $J = 15.5$ Hz, 1H), 2.51 (d, $J = 15.5$ Hz, 1H); ^{13}C NMR (125 MHz, CDCl_3) δ (16.8, 22.9, 23.3, 25.0, 25.5, 29.0, 29.3, 32.3, 41.8, 52.8, 211.4), (16.8, 23.0, 23.4, 24.9, 25.0, 25.1, 29.3, 32.8, 41.7, 46.2, 211.8); HRMS (M^+) calcd for $\text{C}_{11}\text{H}_{18}\text{O}$ 166.1358, found 166.1360.

3d: IR (neat) 1713 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) (major diastereomer) δ 0.85 (m, 1H), 0.97 (t, $J = 6.0$ Hz, 1H), 1.37 (m, 1H), 1.66 (m, 1H), 1.75 (m, 1H), 2.04 (m, 2H), 2.35 (m, 4H), 7.16–7.26 (m, 5H); ^{13}C NMR (100 MHz, CDCl_3) δ (15.8, 24.6, 27.6, 29.0, 35.9, 41.5, 52.5, 126.3, 128.3, 129.0, 138.4, 211.2), (16.0, 24.9, 27.0, 27.6, 28.4, 41.7, 46.2, 126.4, 128.4, 129.1, 138.1, 211.1); HRMS (M^+) calcd for $\text{C}_{14}\text{H}_{16}\text{O}$ 200.1201, found: 200.1206.

4a: IR (neat) 1670 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 0.92 (t, $J = 7.4$ Hz, 3H), 1.35 (m, 2H), 1.48 (m, 1H), 2.00 (m, 2H), 2.20 (d, $J = 7.2$ Hz, 2H), 2.28 (t, $J = 6.0$ Hz, 2H), 2.35 (t, $J = 6.2$ Hz, 2H), 5.87 (s, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ 14.1, 22.5, 23.0, 28.9 (t, $J = 15.5$ Hz), 29.9, 37.6, 37.9, 125.8, 167.0, 200.2.

4e: IR (neat) 1672 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 1.05–1.07 (m, 21H), 1.52–1.56 (m, 3H), 1.99 (m, 2H), 2.24 (d, $J = 6.8$ Hz, 2H), 2.28 (t, $J = 5.4$ Hz, 2H), 2.35 (t, $J = 6.4$ Hz, 2H), 3.69 (t, $J = 6.0$ Hz, 2H), 5.87 (s, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ 12.2, 18.3, 23.0, 23.1 (t, $J = 19.2$ Hz), 29.8, 32.6, 37.6, 38.0, 63.1, 126.0, 166.8, 200.2.

Hydroxycyclopropanation of Homoallylic Alcohols

To a solution of 3-methoxy-2-cyclohexen-1-one **1** (126 mg, 1 mmol) and homoallylic alcohol **5a** or **5b** (1 mmol) in 8 mL of anhydrous ether was added $\text{Ti}(\text{O-}i\text{-Pr})_4$ (0.33 mL, 1.1 equiv). A 2 M solution of cyclopentylmagnesium chloride in ether (2.5 mL) was

added at 0° C over a period of 1 h (via syringe pump). After the reaction mixture had been stirred for an additional 1 h, water (0.5 mL) was added to quench the reaction. The mixture was filtered through a pad of Celite to remove inorganic solids. The filter cake was washed with ether. The combined extracts were concentrated under reduced pressure to ca. 10 mL, and TsOH•H₂O (10 mg) was then added. The resulting mixture was stirred for 2 h to ensure complete hydrolysis of the enol ether functionality, washed with aqueous NaHCO₃ (10 mL) and also brine (10 mL), dried over MgSO₄, filtered, and evaporated under reduced pressure. Purification of the concentrate by column chromatography on silica gel afforded cyclopropane **6a** or **6b** as a mixture of inseparable diastereomers.

6a: IR (neat) 1709 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 0.06–0.10 (m, 1H), 0.51–0.55 (m, 1H), 0.62–0.74 (m, 1H), 1.36–1.95 (m, 7H), 1.98–2.41 (m, 4H), 3.61–3.75 (m, 2H); ¹³C NMR (100 MHz, CDCl₃) δ (16.9, 20.1, 23.6, 24.7, 31.9, 35.9, 41.5, 46.0, 62.9, 211.5), (16.8, 19.7, 23.9, 25.1, 29.2, 31.8, 41.4, 52.3, 63.0, 211.0); HRMS (M⁺) calcd for C₁₀H₁₆O₂ 168.1150, found 168.1150.

6b: IR (neat) 1706 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) (Major diastereomers) δ 0.05–0.08 (m, 1H), 0.52–0.61 (m, 1H), 0.71–0.84 (m, 1H), 1.31–2.20 (m, 8H), 2.29–2.42 (m, 3H), 2.61–2.73 (m, 1H), 2.81–2.91 (m, 1H), 3.84–3.93 (m, 1H), 7.20–7.35 (m, 5H); HRMS (M⁺ + H) calcd for C₁₇H₂₃O₂ 259.1698, found 259.1707.

Intramolecular Cyclopropanation of 7.

To a solution of **7** (90 mg, 0.5 mmol) in 4 mL of anhydrous ether was added Ti(O*i*-Pr)₄

(0.165 mL, 1.1 equiv). A 2 M solution of cyclopentylmagnesium chloride in ether (1.25 mL) was added at 0° C over a period of 1 h (via syringe pump). The reaction mixture was stirred for an additional 1 h and then cooled to -78°, followed by addition of BF₃•OEt₂ (0.31 mL, 2.5 mmol). After the solution had been allowed to warm up to room temperature (1 h), an aqueous saturated NaHCO₃ solution (5 mL) was added, and the mixture was filtered through a pad of Celite to remove inorganic solids. The organic layer was separated, and the aqueous layer was extracted with ether (3 x 10 mL). The combined extracts were washed with aqueous NaHCO₃ (10 mL) and also brine (10 mL), dried over MgSO₄, filtrated, and evaporated under reduced pressure. Purification of the concentrate by column chromatography on silica gel afforded 60 mg (80%) of **10** as a colorless oil: IR (neat) 1716 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 0.19 (dd, *J* = 4.9, 8.1 Hz, 1H), 0.49 (dd, *J* = 4.1, 8.1 Hz, 1H), 1.11 (dt, *J* = 4.1, 8.1 Hz, 1H), 1.25–1.33 (m, 1H), 1.41–1.52 (m, 2H), 1.59–1.65 (m, 1H), 1.79–1.86 (m, 1H), 1.82–1.95 (m, 1H), 1.88 (d, *J* = 15.9 Hz, 1H), 2.14–2.20 (m, 1H), 2.38–2.48 (m, 2H), 2.85 (d, *J* = 15.9 Hz, 1H); ¹³C NMR (100 MHz, CDCl₃) δ 12.3, 23.3, 25.4, 26.9, 30.4, 30.9, 38.8, 41.2, 45.8, 211.5.

8a: IR (neat) 1667 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 1.18 (d, *J* = 6.5 Hz, 3H), 1.18–1.38 (m, 2H), 1.57–1.67 (m, 1H), 2.03–2.13 (m, 2H), 2.21–2.35 (m, 2H), 2.44–2.50 (m, 1H), 2.57–2.74 (m, 2H), 5.88 (s, 1H); ¹³C NMR (100 MHz, CDCl₃) δ 19.5, 29.3, 32.2, 33.6, 37.5, 39.1, 43.0, 121.7, 180.3, 200.2.

8b: IR (neat) 1664 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 1.16 (d, *J* = 9.0 Hz, 2H), 1.27 (m, 2H), 1.62 (m, 1H), 2.06 (m, 2H), 2.24 (m, 2H), 2.45 (m, 1H), 2.64 (m, 2H), 5.88 (s, 1H); ¹³C NMR (125 MHz, CDCl₃) δ 19.5 (t, *J* = 19.5 Hz), 29.5, 32.5, 33.8, 37.7, 39.2, 43.3, 121.9, 180.5, 200.5.