Supporting Information

Electrophilic Cyclizations of Vinylcyclopropanols to Tethered Aldehydes

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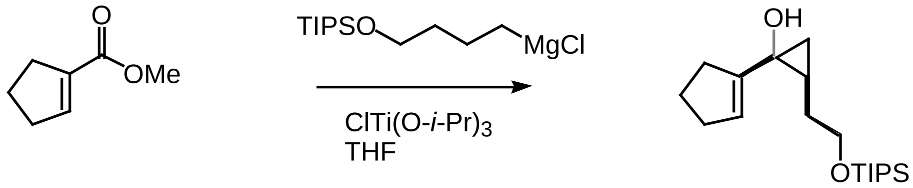
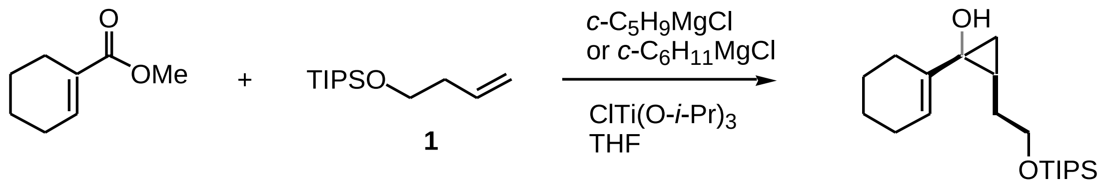
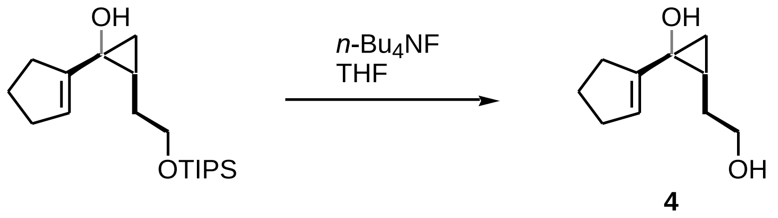


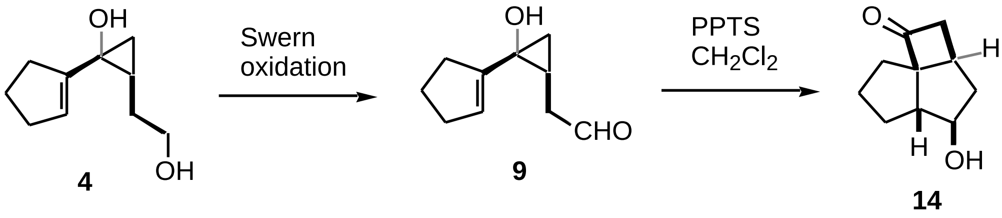
Typical Cyclopropanation Procedure; Method 1. To a solution of methyl 1-cyclopentene-1-carboxylate (0.29 g, 2.28 mmol) in THF (15 mL) was added ClTi(O-*i*-Pr)$_3$ (a 1.0 M solution in hexane, 1.15 mL, 0.5 equiv). A THF solution (25 mL) of the Grignard reagent, which had freshly been prepared from 1-triisopropylsiloxy-4-chlorobutane (11.3 mmol, 5.0 equiv), was added at room temperature over a period of 1 h (syringe pump). The reaction mixture was then stirred for an additional 2 h and poured into ice-cold 1 N HCl (20 mL). The organic layer was separated, and the aqueous layer was extracted with ether (3 x 10 mL). The combined extracts were washed with aq. NaHCO$_3$ (15 mL), followed by brine (15 mL), and dried (MgSO$_4$). Filtration and evaporation of the solvent *in vacuo* gave the crude product. Purification by silica gel column chromatography (10:1 hex–EtOAc) afforded the cyclopropanol product (0.28 g, 60%) as a colorless oil: ^{1}H NMR (360 MHz, CDCl$_3$) δ 0.67 (m, 1 H), 0.96 (dd, *J* = 5.3, 9.8 Hz, 1 H), 1.06 (m, 21 H), 1.26 (m, 2 H), 1.64 (m, 2 H), 1.92 (br t, *J* = 7.5 Hz, 2 H), 2.00 (br s, 1 H), 2.33 (m, 2 H), 2.55 (m, 1 H), 3.68 (t, *J* = 6.8 Hz, 2 H), 5.50 (m, 1 H); ^{13}C NMR (90 MHz, CDCl$_3$) δ 12.0, 17.7, 18.0, 18.4, 23.7, 24.0, 32.2, 33.2, 58.3, 63.1, 126.7, 143.7.



Typical Cyclopropanation Procedure; Method 2. To a solution of methyl 1-cyclohexene-1-carboxylate (140 mg, 1 mmol) and 1-triisopropylsiloxy-3-butene **1** (0.27 g, 1.19 mmol) in anhydrous THF (10 mL) was added ClTi(O-*i*-Pr)$_3$ (1.0 mL of a 1.0 M solution in hexane, 1.0 equiv). Freshly prepared cyclohexylmagnesium chloride (3.9 mL of a 1.0 M solution in THF, 3.9 equiv) was added at room temperature over a period of 1 h (syringe pump). The reaction mixture was stirred for an additional 0.5 h and poured into water (10 mL). The organic layer was separated, and the aqueous layer was extracted with ether (3 x 15 mL). The combined extracts were washed with brine (10 mL), and dried over $MgSO_4$, filtered, and evaporated in vacuo to give the crude product. Purification by column chromatography on silica gel using 10:1 hex-EtOAc as the eluent afforded 261 mg (77 %) of the pure cyclopropanation product (i.e., the TIPS ether of **5**) as a colorless oil: ^{1}H NMR (360 MHz, $CDCl_3$) δ 0.58 (t, *J* = 5.3 Hz, 1 H), 0.81 (dd, *J* = 5.3, 9.9 Hz, 1 H), 1.04 (m, 21 H), 1.16–1.27 (m, 1 H), 1.48–1.81 (m, 6 H), 1.82–2.12 (m, 4 H), 2.30–2.42 (m, 1 H), 3.67 (t, *J* = 6.8 Hz, 2 H), 5.63 (m, 1 H); ^{13}C NMR (90 MHz, $CDCl_3$) δ 12.2, 16.5, 17.7, 18.0, 22.4, 22.7, 25.1, 26.2, 32.2, 63.0, 63.2, 125.0, 136.4; HRMS (M^+ + H) calcd for $C_{20}H_{39}O_2Si$ 339.2719, found 339.2714.



To a mixture of the silyl ether (0.455 g, 1.40 mmol) and 4 Å molecular sieves (200 mg) in THF (10 mL) was added at 0 °C TBAF (a 1 M solution in THF, 2.2 mL, 2.2 mmol). The resulting mixture was stirred for an additional hour at the same temperature and filtered through a pad of Celite. The insolubles were washed with ether, and the combined organic filtrates were concentrated *in vacuo* to give the crude product. Purification by column chromatography (2:1 hex–EtOAc) provided the diol **4** (0.177 g, 75%): ^{1}H NMR (360 MHz, $CDCl_3$) δ 0.61 (t, *J* = 5.3 Hz, 1 H), 0.94 (dd, *J* = 5.3, 9.7 Hz, 1 H), 1.22 (m, 1 H), 1.30 (m, 1 H), 1.45 (m, 1 H), 1.86 (m, 2 H), 2.19–2.56 (m, 4 H), 3.30 (br s, 2 H, -O*H*), 3.56 (t, *J* = 6.3 Hz, 2 H), 5.43 (m, 1 H); ^{13}C NMR (90 MHz, $CDCl_3$) δ 18.2, 23.7, 23.8, 31.6, 32.2, 33.2, 57.6, 62.2, 126.3, 143.8.



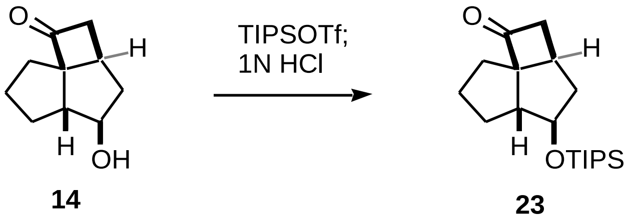
Typical Experimental Procedure for Electrophilic Cyclization of Vinylcyclopropanols. Dimethyl sulfoxide (0.30 mL, 4.24 mmol) was added dropwise to a solution of oxalyl chloride (0.28 mL, 3.18 mmol) in CH_2Cl_2 (7 mL) at –78 °C. The mixture was stirred for 15 min, followed by the addition of a solution of **4** (0.18 g, 1.06 mmol) in CH_2Cl_2 (3 mL) at –78 °C. After the reaction mixture had been stirred at the same temperature for 40 min, triethylamine (3.0 mL, 21.0 mmol) was added. The mixture was then allowed to warm to 0 °C, stirred for an additional 5 min at 0 °C, and poured quickly into a 1:1 mixture (10 mL) of water and CH_2Cl_2. The organic layer was washed with water, and dried ($MgSO_4$), and concentrated *in vacuo*. The resulting crude aldehyde **9** was used immediately for the next step without further purification.

A solution of **9** in CH_2Cl_2 (5 mL) was treated with a catalytic amount of PPTS at room temperature. After the resulting mixture had been stirred for an additional 3 h, water (5 mL) was added. The aqueous layer was extracted with CH_2Cl_2 (2 x 5 mL). The combined organic layers were washed with brine, dried ($MgSO_4$), filtered, and evaporated *in vacuo* to afford the crude cyclization product. Purification by column chromatography provided the butanone **14** (132 mg, 75% overall): IR ($CHCl_3$) 1763, 3440 cm^{-1}; ^{1}H NMR (360 MHz, $CDCl_3$) δ 1.24 (m, 1 H), 1.52–1.93 (m, 5 H), 1.94 (br s, -OH, 1 H), 2.06 (m, 1 H), 2.26 (m, 1 H), 2.50 (m, 1 H), 2.63 (m, 1 H), 3.10 (m, 2 H), 4.33 (br d, *J* = 4.6 Hz, 1 H); ^{13}C NMR (90 MHz, $CDCl_3$) δ 25.8, 30.5, 33.1, 37.7, 39.0, 40.0, 51.0, 61.4, 80.7, 216.4.

16. IR ($CHCl_3$) 1770, 3404 cm^{-1}; ^{1}H NMR (360 MHz, $CDCl_3$) δ 0.73 (dt, *J* = 3.5, 13.2 Hz, 1 H), 1.09–1.16 (m, 2 H), 1.83 (d, *J* = 14.5 Hz, 1 H), 1.55–1.90 (m, 6 H), 2.09 (dd, *J* = 6.0, 12.8 Hz, 1 H), 2.30 (ddd, *J* = 9.5, 4.2, 3.4 Hz, 1 H), 2.56 (dt, *J* = 3.4, 9.5 Hz, 1 H), 2.88 (dd, *J* = 17.8, 3.4 Hz, 1 H), 3.23 (dd, *J* = 17.8, 9.5 Hz, 1 H), 4.11 (d, *J* = 4.2 Hz, 1 H); ^{13}C NMR (90 MHz, $CDCl_3$) δ 22.1, 23.9, 27.0, 27.4, 33.7, 38.6, 51.0, 51.6, 73.6, 80.6, 218.4.

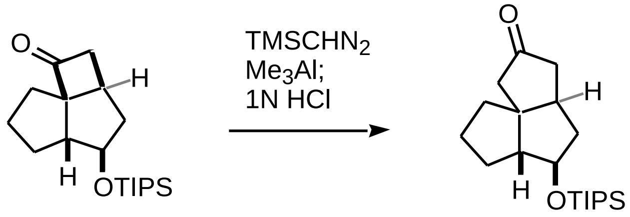
18. IR ($CHCl_3$) 1766, 3444 cm^{-1}; ^{1}H NMR (360 MHz, $CDCl_3$) δ 1.37 (m, 1 H), 1.59–1.97 (m, 1 H), 2.14 (m, 1 H), 2.31 (m, 1 H), 2.69 (dd, *J* = 16.8, 6.1 Hz, 1 H), 3.04 (dd, *J* = 16.8, 8.9 Hz, 1 H), 3.88 (ddd, *J* = 3.2, 4.6, 7.2 Hz, 1 H); ^{13}C NMR (90 MHz, $CDCl_3$) δ 22.7, 24.5, 26.6, 27.1, 28.7, 36.6, 42.9, 48.7, 68.6, 70.0, 213.9.

19. IR ($CHCl_3$) 1766, 3477 cm^{-1}; ^{1}H NMR (360 MHz, $CDCl_3$) δ 1.24–1.37 (m, 4 H), 1.61 (m, 1 H), 1.65 (m, 1 H), 1.53–1.76 (m, 5 H), 1.82 (m, 1 H), 1.92 (ddd, *J* = 4.9, 6.1, 9.2 Hz, 1 H), 2.21 (m, 1 H), 2.16–2.26 (m, 1 H), 2.63 (dd, *J* = 17.3, 5.4 Hz, 1 H), 3.14 (dd, *J* = 17.3, 8.9 Hz, 1 H), 3.94 (ddd, *J* = 3.7, 6.1, 7.0 Hz, 1 H); ^{13}C NMR (90 MHz, $CDCl_3$) δ 22.5, 23.3, 23.6, 24.2, 26.5, 28.6, 32.6, 38.9, 49.0, 66.1, 70.0, 214.9.



To a solution of **14** (39 mg, 0.237 mmol) in CH_2Cl_2 (1 mL) were added at 0 °C 2,6-lutidine (0.14 mL, 1.20 mmol) and TIPSOTf (0.19 mL, 0.71 mmol). The resulting mixture was allowed to warm to room temperature overnight, diluted with CH_2Cl_2 (3 mL), and then treated with aqueous 1 N HCl (5 mL). The organic layer was separared, and the aqeous layer was extracted with CH_2Cl_2 (2 x 3 mL). The combined organic extracts were washed with brine (5 mL), dried ($MgSO_4$), filtered, and evaporated *in vacuo* to afford the crude product. Purification by column chromatography on silica gel (30:1 hex–EtOAc) provided the TIPS ether **23** (71 mg, 93%): ^{1}H NMR (360 MHz, $CDCl_3$) δ 1.04 (m, 21 H), 1.09 (m, 1 H), 1.62 (m, 2 H), 1.83 (m, 2 H), 1.95 (d, *J* = 14.0 Hz, 1 H), 2.09 (dt, *J* = 15.3, 7.6 Hz, 1 H), 2.20 (ddd, J = 14.0, 7.6, 4.6 Hz, 1 H), 2.46 (m, 1 H), 2.71 (t, *J* = 8.9 Hz, 1 H), 3.03 (dd, *J* = 17.9, 9.3 Hz, 1 H), 3.20

(dd, *J* = 17.9, 5.5 Hz, 1 H), 4.36 (d, *J* = 4.6 Hz, 1 H).



23 **24**

To a solution of **23** (44 mg, 0.135 mmol) were added sequentially at –20 °C trimethylaluminum (a 2.0 M solution in hexane, 81 μL, 0.16 mmol) and $\mathrm{TMSCHN_2}$ (a 2.0 M solution in hexane, 75 μL, 0.15 mmol). The reaction mixture was stirred at the same temperature for 2 h, diluted with $\mathrm{CH_2Cl_2}$ (3 mL), and then treated with aqueous 1 N HCl (5 mL). The organic layer was separated, and the aqueous layer was extracted with $\mathrm{CH_2Cl_2}$ (2 x 3 mL). The combined organic extracts were washed with brine (5 mL), dried ($\mathrm{MgSO_4}$), filtered, and evaporated to give the crude product. Purification by column chromatography on silica gel (30:1 hex–EtOAc) provided **24** (30 mg, 65%): IR ($\mathrm{CHCl_3}$) 1741 cm^{-1}; ^{1}H NMR (360 MHz, $\mathrm{CDCl_3}$) δ 1.06 (m, 21 H), 1.36 (m, 1 H), 1.53–1.74 (m, 5 H), 1.90 (m, 1 H), 2.06 (m, 1 H), 2.22 (m, 1 H), 2.32 (m, 1 H), 2.38 (dd, *J* = 1.2, 14.2 Hz, 1 H), 2.50 (m, 2 H), 2.68 (br d, *J* = 14.2 Hz, 1 H), 4.07 (m, 1 H); ^{13}C NMR (90 MHz, $\mathrm{CDCl_3}$) δ 12.2, 18.0, 26.2, 31.9, 42.2, 42.3, 45.4, 45.7, 52.4, 57.2, 61.7, 82.0, 220.5.