Supporting Information to Accompany:

Transition Metal-Catalyzed [5+2] Cycloadditions of 2-Substituted-1-Vinylcyclopropanes: Catalyst Control and Reversal of Regioselectivity.

Paul A. Wender,* Alaric J. Dyckman

Department of Chemistry, Stanford University

Stanford, California 94305

General methods. Air- and moisture-sensitive reactions were carried out in oven-dried glassware sealed with rubber septa under a positive pressure of dry nitrogen or argon from a manifold or balloon, unless otherwise indicated. Similarly sensitive liquids and solutions were transferred via syringe or stainless steel cannula. Reactions were stirred using Teflon-coated magnetic stir bars. Elevated temperatures were maintained using Thermowatch-controlled silicone oil baths. Organic solutions were concentrated using a Buchi rotary evaporator with a water aspirator or recirculating aspirator pump. Tetrahydrofuran and diethyl ether were distilled from sodium benzophenone prior to use. Toluene was distilled from sodium prior to use. Wilkinson's catalyst ($RhCl(PPh_3)_3$) and silver triflate (AgOTf) were purchased through Aldrich and $[Rh(CO)_2Cl]_2$ was purchased through Pressure Chemicals. Analytical TLC was performed with 0.25 mm silica gel 60F plates with 254 nm fluorescent indicator from Merck. Plates were visualized by ultraviolet light and treatment with acidic *p*-anisaldehyde stain followed by gentle heating. Chromatographic purification of products was accomplished by flash column chromatography.

NMR spectra were measured on a Varian INOVA 500 (^{1}H at 500 MHz, ^{13}C at 125 MHz), Varian XL-400 (^{1}H at 400 MHz, ^{13}C at 100 MHz), Varian Gem-300 (^{1}H at 300 MHz, ^{13}C at 75 MHz), or Varian Gem-200 (^{1}H at 200 MHz, ^{13}C at 50 MHz) magnetic resonance spectrometer. Data for ^{1}H NMR spectra are reported as follows: chemical shift (δ ppm), multiplicity (s = singlet, br s = broad singlet, d = doublet, t = triplet, q = quartet, dd = doublet of doublets, dt = doublet of triplets, ddd = doublet of doublet of doublets, dddd = doublet of doublet of doublet of doublets, ddt = doublet of doublet of triplets, m = multiplet, dm = doublet of multiplets), coupling constant (Hz), and integration. Data for ^{13}C are reported in terms of chemical shift relative to residual solvent peak. Infrared spectra were recorded on a Perkin-Elmer 1600 Series Fourier transform spectrometer (FTIR) and are reported in wavenumbers (cm^{-1}). High-resolution mass spectra (HRMS) were recorded at the NIH regional mass spectrometry facility at the University of California, San Francisco and at the University of California, Riverside. Reported mass values are with error limits of ±13 millimass units. Elemental analyses (%C, %H) were determined by Desert Analytics, Tucson, Arizona. Reported atomic percentages are within error limits of ±0.4%.

General Cycloaddition Procedure **A** $RhCl(PPh_3)_3$, AgOTf :

Tris(triphenylphosphine)rhodium(I) chloride (X mol%) was added in one batch to a base-washed, oven-dried Schlenk flask containing freshly distilled, oxygen-free toluene (100 ml/mmol substrate) under an argon atmosphere. Silver triflate (AgOTf) (X mol%) was added in one portion and the solution was degassed by bubbling through with argon for 2-5 min during which time the solution turned from reddish-brown to pale yellow in color with the appearance of a white precipitate. The solution was stirred for 5 min at room temperature, after which yne-vinylcyclopropane (1.0 equiv) in toluene (1 ml/mmol) was added over 10 s and the resultant solution was heated at 110°C. After cooling, the reaction mixture was filtered through a plug of alumina and concentrated *in vacuo*. Purification by flash chromatography (ethyl acetate in hexane) afforded the cycloadduct.

General Cycloaddition Procedure **B** $[Rh(CO)_2Cl]_2$:

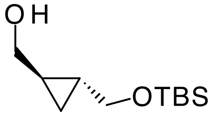
The dimeric rhodium(I) catalyst $[Rh(CO)_2Cl]_2$ (X mol%) was added in one batch to a base-washed, oven-dried Schlenk flask containing freshly distilled, oxygen-free toluene (100 ml/mmol substrate) under an argon atmosphere. The solution was stirred for 5 min at room temperature, after which yne-vinylcyclopropane (1.0 equiv) in toluene (1 ml/mmol) was added over 10 s and the resultant solution was heated at 110°C. After cooling, the reaction mixture was filtered through a plug of alumina and concentrated *in vacuo*. Purification by flash chromatography (ethyl acetate in hexane) afforded the cycloadduct.

***trans*-1,2-Disubstituted Cyclopropanes**

Procedure for the preparation of 23t:

To a 100 ml R.B. flask charged with Et_2Zn (1 M, 12.11 ml, 12.11 mmol) and CH_2Cl_2 (50 ml) at 0°C was added CH_2I_2 (1.951 ml, 24.22 mmol) dropwise. The mixture was stirred at 0°C for 10 min, followed by dropwise addition of a solution of *trans*-4-*tert*-butyldimethylsiloxy-2-butene-1-ol (1.1866 g, 5.86 mmol) in CH_2Cl_2 (5 ml). After 4 h at room temperature the reaction was quenched with sat. aq. NH_4Cl, extracted with Et_2O, dried over $MgSO_4$, and evaporated to yield a crude reddish-yellow oil that was purified by flash column chromatography to give the desired product **23t** as a colorless oil (574.6 mg, 2.637 mmol, 45%). Also recovered was the *O*-methylated compound as a yellow oil (556.9 mg, 2.403 mmol, 41%).

Physical Data for Substrate 23t:



^{1}H-NMR (500MHz, $CDCl_3$/TMS):

δ = 3.63 (dd, J = 10.6 Hz, J = 5.9 Hz, 1H), 3.51 (dd, J = 11.2 Hz, J = 7.0 Hz, 1H), 3.44-3.47 (m, 2H), 1.65 (br s, 1H), 1.01-1.06 (m, 1H), 0.98-0.92 (m, 1H), 0.91 (s, 9H), 0.51 (ddd, J = 7.9 Hz, J = 4.9 Hz, J = 4.9 Hz, 1H), 0.46 (ddd, J = 8.6 Hz, J = 4.9 Hz, J = 4.9 Hz, 1H), 0.07 (s, 6H) ppm.

^{13}C-NMR (125 MHz, $CDCl_3$):

δ = 66.18, 65.99, 25.9, 19.28, 19.22, 18.33, 7.61, -5.25 ppm.

IR (FT-IR, film):

ν = 3360.1 (br), 3002.3 (w), 2954.6 (m), 2929.4 (m), 2857.9 (m), 1471.9 (m), 1388.2 (w), 1361.4 (w), 1255.1 (m), 1090.7 (s), 1040.8 (m), 1006.2 (m), 836.1 (s), 775.1 (m), 664.6 (w) cm^{-1}

HRMS:

Calculated for $C_7H_{15}O_2Si$: 160.08815 (loss of C_4H_9) Found: 160.085778

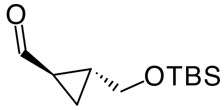
Elemental Analysis:

Calculated for $C_{11}H_{24}O_2Si$: C, 61.06: H, 11.18 Found: C, 60.76; H, 11.26.

Procedure for the preparation of 24t:

To a 50 ml R.B. flask charged with PCC (0.807 g, 3.742 mmol), 4Å molecular sieves (0.5 g), and CH_2Cl_2 (25 ml) at 0°C was added a solution of alcohol **23t** (540 mg, 2.50 mmol) in CH_2Cl_2 (5 ml) dropwise over 10 min The solution was stirred overnight at room temperature, then filtered through silica gel and concentrated to give aldehyde **24t** as a colorless oil (444 mg, 2.05 mmol, 82%).

Physical Data for Substrate 24t:



^{1}H-NMR (300 MHz, $CDCl_3$/TMS):

δ = 9.09 (d, *J* = 5.4 Hz, 1H), 3.62-3.74 (m, 2H), 1.81-1.89 (m, 1H), 1.70-1.76 (m, 1H), 1.27 (m, 1H), 1.09-1.16 (m, 1H), 0.88 (s, 9H), 0.05 (s, 6H) ppm.

^{13}C-NMR (75 MHz, $CDCl_3$):

δ = 200.85, 62.52, 27.16, 25.64, 23.65, 18.04, 11.35, -5.60 ppm.

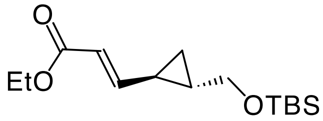
IR (FT-IR, film):

ν = 3008.0 (w), 2955.2 (m), 2930.2 (m), 2886.1 (m), 2857.9 (m), 2728.3 (w), 1711.9 (s), 1472.0 (m), 1390.0 (w), 1361.6 (w), 1254.9 (m), 1134.7 (m), 1098.0 (s), 1006.5 (m), 867.2 (m), 837.3 (s), 777.5 (s), 666.3 (w) cm^{-1}.

Procedure for the preparation of 25t:

To a 50 ml R.B. flask containing NaH (95%, 65.6 mg, 2.589 mmol) and THF (20 ml) at 0ºC was added triethyl phosphonoacetate (0.534 ml, 2.692 mmol) dropwise. After 40 min at room temperature, aldehyde **24t** (444 mg, 2.071 mmol) was added dropwise and the reaction was allowed to stir overnight. After quenching with brine, extraction with Et_2O, drying over $MgSO_4$, and concentration *in vacuo* gave a crude oil that was further purified by flash column chromatography. Ester **25t** was obtained as a clear, colorless oil (478 mg, 1.680 mmol, 81%).

Physical Data for Substrate 25t:



^{1}H-NMR (300 MHz, $CDCl_3$/TMS):

δ = 6.49 (dd, *J* = 15.5 Hz, *J* = 10.1 Hz, 1H), 5.85 (d, *J* = 15.5 Hz, 1H), 4.17 (q, *J* = 7.1 Hz, 2H), 3.56-3.66 (m, 2H), 1.46-1.58 (m, 1H), 1.28 (t, *J* = 7.1 Hz, 1H), 1.25-1.33 (m, 1H), 0.90-0.97 (m, 1H), 0.88 (s, 9H), 0.77-0.85 (m, 1H), 0.05 (s, 6H) ppm.

^{13}C-NMR (75 MHz, $CDCl_3$):

δ = 166.78, 152.67, 118.26, 64.28, 59.87, 25.74, 24.43, 19.20, 18.15, 14.12, 12.75, -5.46 ppm.

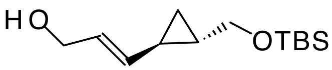
IR (FT-IR, film):

ν = 2955.3 (m), 2886.4 (w), 2857.6 (m), 1718.2 (s), 1646.5 (m), 1471.9 (m), 1464.0 (m), 1411.4 (w), 1388.9 (w), 1364.5 (w), 1326.9 (m), 1302.5 (w), 1251.5 (s), 1206.5 (m), 1144.6 (s), 1093.5 (s), 1050.0 (m), 1006.1 (m) 978.6 (m), 836.5 (s), 776.2 (m), 666.2 (w) cm^{-1}.

Procedure for the preparation of 26t:

To a 50 ml R.B. flask charged with ester **25t** (478.2 mg, 1.681 mmol) and THF (30 ml) at -78°C was added DIBAl (1 M, 5.04 ml, 5.04 mmol) dropwise. The reaction was warmed to room temperature overnight and was quenched with water (5 ml) and 10% aq. NaOH (15 ml). Extraction with Et_2O, drying over $MgSO_4$, and evaporation provided alcohol **26t** (403.6 mg, 1.675 mmol, 99%).

Physical Data for Substrate 26t:



^{1}H-NMR (500MHz, $CDCl_3$/TMS):

δ = 5.70 (dt, *J* = 15.2 Hz, *J* = 6.2 Hz, 1H), 5.29 (dd, *J* = 15.2 Hz, *J* = 8.8 Hz, 1H), 4.07 (d, *J* = 6.2 Hz, 1H), 3.60 (dd, *J* = 10.8 Hz, *J* = 5.9 Hz, 1H), 3.52 (dd, *J* = 10.9 Hz, *J* = 6.0 Hz, 1H), 1.30-1.35 (m, 1H), 1.26 (br s, 1H), 1.01-1.10 (m, 1H), 0.89 (s, 9H), 0.68-0.72 (m, 1H), 0.58-0.69 (m, 1H), 0.06 (s, 6H) ppm.

^{13}C-NMR (125 MHz, $CDCl_3$):

δ = 135.73, 126.71, 65.49, 63.45, 25.91, 22.79, 18.70, 18.33, 11.45, -5.20 ppm.

IR (FT-IR, film):

ν = 3354.2 (br), 3002.5 (w), 2954.9 (m), 2885.3 (m), 2857.6 (m), 1668.6 (w), 1471.9 (m), 1410.0 (w), 1361.4 (w), 1255.2 (m), 1167.8 (w), 1091.3 (s), 1006.1 (m), 962.9 (m), 836.3 (s), 775.5 (m), 665.8 (w) cm^{-1}.

HRMS:

Calculated for $C_{13}H_{26}O_2Si$: 242.170209 Found: 242.169895

Elemental Analysis:

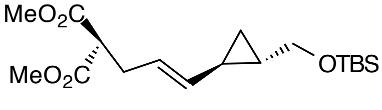
Calculated for $C_{13}H_{26}O_2Si$: C, 64.41: H, 10.81 Found: C, 64.49: H, 11.03.

Procedure for the preparation of 27t:

To a 250 ml R.B. flask containing alcohol **26t** (5.033 g, 20.64 mmol) and THF (100 ml) at -78°C was added n-BuLi (2.5 M, 9.1 ml, 2.7 mmol), followed 10 min later by methane sulfonyl chloride (1.76 ml, 22.7 mmol), and then immediately by lithium bromide (9 g, 100 mmol) in one portion. After stirring for 30 min this solution was transferred to the malonate anion via cannula.

To a second R.B. flask charged with NaH (95%, 1.8036 g, 71.36 mmol) and THF (100 ml) was added dimethyl malonate (8.25 ml, 72.2 mmol) dropwise. After 30 min at room temperature, the solution was cooled to -78°C and the bromide was introduced via cannula. The reaction was stirred for 2 h at -78°C, followed by 4 h at room temperature. Quenching with water, extraction with Et_2O, drying over $MgSO_4$, and evaporation gave a crude mixture. After removal of excess dimethyl malonate via Kugel Rohr, the malonate derivative **27t** was obtained as a colorless oil (6.3861 g, 17.91 mmol, 87%).

Physical Data for Substrate 27t:



^{1}H-NMR (500MHz, $CDCl_3$/TMS):

δ = 5.39 (dt, J = 15.2 Hz, J = 7.1 Hz, 1H), 5.13 (dd, J = 15.2 Hz, J = 8.4 Hz, 1H), 3.72 (s, 6H), 3.55 (dd, J = 10.8 Hz, J = 5.9 Hz, 1H), 3.49 (dd, J = 10.8 Hz, J = 6.1 Hz, 1H), 3.39 (t, J = 7.5 Hz, 1H), 2.55 (t, J = 7.5 Hz, 2H), 1.21-1.24 (m, 1H), 0.95-1.01 (m, 1H), 0.87 (s, 9H), 0.60-0.63 (m, 1H), 0.49-0.53 (m, 1H), 0.04 (s, 6H) ppm.

^{13}C-NMR (125 MHz, $CDCl_3$):

δ = 169.31, 136.27, 122.90, 65.54, 52.34, 51.98, 31.77, 25.90, 22.62, 18.90, 18.30, 11.22, -5.20 ppm.

IR (FT-IR, film):

ν = 3001.1 (w), 2951.5 (m), 2888.0 (m), 2857.1 (m), 1755.8 (m), 1739.1 (s), 1471.9 (m), 1436.1 (m), 1344.7 (m), 1252.9 (m), 1198.3 (m), 1151.4 (m), 1090.5 (m), 1006.3 (m), 963.9 (m), 836.9 (s), 776.3 (m), 666.0 (w) cm^{-1}.

MS (EI, 70 ev):

m/z (%) = 299 (55), 267 (11), 198 (11), 190 (14), 189 (100), 161 (15), 133 (10), 119 (13), 115 (7), 105 (14), 102 (11), 101 (98), 93 (42), 91 (12), 89 (55), 79 (17), 77 (11), 75 (64), 73 (71), 69 (11), 67 (39), 59 (18).

HRMS:

Calculated for $C_{14}H_{23}O_5Si$: 299.131478(loss of C_4H_9) Found: 299.131733

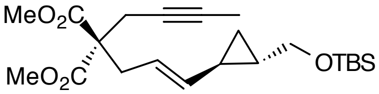
Elemental Analysis:

Calculated for $C_{18}H_{32}O_5Si$: C, 60.64: H, 9.05 Found: C, 60.68: H, 9.25.

Procedure for the preparation of 7:

To a 50 ml R.B. flask charged with NaH (95%, 15 mg, 0.593 mmol) and THF (25 ml) was added malonate derivative **27t** (192 mg, 0.539 mmol) dropwise. After 30 min at room temperature and 1 h at 50°C, 1-bromo-but-2-yne (0.052 ml, 0.593 mmol) was added dropwise. After stirring overnight at room temperature, the reaction was quenched with brine, extracted with Et_2O, dried over $MgSO_4$, and evaporated to give compound **7** (209.4 mg, 0.512 mmol, 95%) as a colorless oil.

Physical Data for Substrate 7:



^{1}H-NMR (500MHz, $CDCl_3$/TMS):

δ = 5.26 (dt, *J* = 15.0 Hz, *J* = 7.5 Hz, 1H), 5.16 (dd, *J* = 15.0 Hz, *J* = 8.4 Hz, 1H), 3.72 (s, 6H), 3.57 (dd, *J* = 10.8 Hz, *J* = 5.7 Hz, 1H), 3.49 (dd, *J* = 10.8 Hz, *J* = 6.1 Hz, 1H), 2.72 (q, *J* = 2.6 Hz, 2H), 2.69 (d, *J* = 7.3 Hz, 2H), 1.75 (t, *J* = 2.6 Hz, 3H), 1.25 (dddd, *J* = 12.8 Hz, *J* = 8.6 Hz, *J* = 4.6 Hz, *J* = 4.6 Hz, 1H), 0.98-1.00 (m, 1H), 0.89 (s, 9H), 0.62 (ddd, *J* = 10.1 Hz, *J* = 4.9 Hz, *J* = 4.9 Hz, 1H), 0.52 (ddd, *J* = 8.4 Hz, *J* = 4.8, Hz *J* = 4.8 Hz, 1H), 0.04 (s, 6H) ppm.

^{13}C-NMR (125 MHz, $CDCl_3$):

δ = 170.60, 137.95, 120.78, 78.71, 73.39, 65.60, 57.56, 52.55, 52.52, 35.92, 25.94, 22.93, 22.76, 19.02, 18.36, 11.40, 3.48, -5.16 ppm.

IR (FT-IR, film):

ν = 3000.3 (w), 2953.7 (m), 2856.9 (m), 1740.6 (s), 1472.1 (w), 1437.6 (m), 1289.0(m), 1252.2 (m) 1211.3 (m), 1089.9 (m), 965.8 (w), 836.6 (m), 776.2 (m) cm^{-1}.

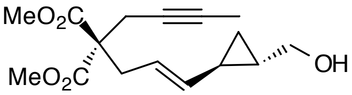
Elemental Analysis:

Calculated for : $C_{22}H_{36}O_5Si$: C, 64.67: H 8.88 Found: C, 64.27: H, 8.70

Procedure for the preparation of 3:

TBS ether **7** (209.4 mg, 0.512 mmol) was placed in THF (50 ml) and stirred with TBAF/silica gel (excess) to afford alcohol **3** as a clear colorless oil after flash column purification (134.8 mg, 0.458 mmol, 89%).

Physical Data for Substrate 3:



^{1}H-NMR (300 MHz, $CDCl_3$/TMS):

δ = 5.30 (dt, *J* = 15.1 Hz, *J* = 7.3 Hz, 1H), 5.18 (dd, *J* = 15.1 Hz, *J* = 8.3 Hz, 1H), 3.72 (s, 6H), 3.42-3.54 (m, 2H), 2.69-2.73 (m, 4H), 1.75 (t, *J* = 2.4 Hz, 3H), 1.32 (br s, 1H), 1.24-1.33 (m, 1H), 1.08-1.14 (m, 1H), 0.56-0.67 (m, 2H) ppm.

^{13}C-NMR (75 MHz, $CDCl_3$):

δ = 170.53, 127.33, 121.25, 78.75, 73.25, 66.13, 57.46, 52.52, 35.16, 22.90, 22.80, 19.37, 11.47, 3.39 ppm.

IR (FT-IR, film):

ν = 3396.0 (br), 3002.0 (m),.2954.0 (m), 2871.1 (w), 1737.6 (s), 1438.2 (m), 1290.4 (m), 1211.3 (s), 1055.9 (m), 967.2 (m), 868.1 (w) cm^{-1}.

HRMS:

Calculated for $C_{16}H_{23}O_5$: (MH^+) 295.154549 Found: 295.155600

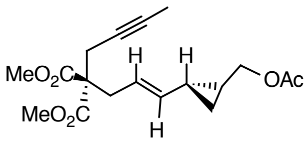
Elemental Analysis:

Calculated for: $C_{16}H_{22}O_5$: C, 65.29: H, 7.53 Found: C, 64.78: H, 7.34

Procedure for the preparation of 5:

To a stirred solution of alcohol **3** (77.7 mg, 0.264 mmol), DMAP (10 mg, 0.082 mmol) and pyridine (31 mg, 0.396 mmol) in CH_2Cl_2 (10 ml) at room temperature was added acetic anhydride (0.0374 ml, 0.386 mmol). After stirring for 2 h at room temperature, water (5 ml) was added and the aqueous phase was extracted with ethyl acetate (3x10ml). The combined organics were washed with saturated aqueous $CuSO_4$ (3x5 ml), and brine (3x 5 ml). After drying over $MgSO_4$, concentration of the organic phase afforded **5** (84.8 mg, 0.252 mmol, 96%) as a clear, colorless oil.

Physical Data for Substrate 5:



^{1}H-NMR (500 MHz, $CDCl_3$/TMS):

δ = 5.31 (ddd, *J* = 15.1 Hz, *J* = 7.5 Hz, *J* = 7.5 Hz, 1H), 5.15 (dd, *J* = 15.1 Hz, *J* = 8.2 Hz, 1H), 3.95 (dd, *J* = 11.5 Hz, *J* = 7.1 Hz, 1H), 3.89 (dd, *J* = 11.5 Hz, *J* = 7.1 Hz, 1H), 3.72 (s, 6H), 2.69-2.73 (m, 4H), 2.06 (s, 3H), 1.75 (t, *J* = 2.6 Hz, 3H), 1.30-1.35 (m, 1H), 1.10-1.15 (m, 1H), 0.64-0.70 (m, 1H), 0.61-0.64 (m, 1H) ppm.

^{13}C-NMR (125 MHz, $CDCl_3$):

δ = 171.13, 170.53, 136.78, 121.82, 78.80, 73.30, 67.70, 57.49, 52.56, 52.53, 35.24, 22.99, 20.98, 19.79, 19.07, 11.91, 3.45 ppm.

IR (FT-IR, film):

ν = 3008.3 (w), 2942.9 (w), 2855.7 (w), 1735.1 (s), 1437.4 (m), 1364.4 (w), 1283.6 (w), 1236.0 (m), 1028.0 (m), 967.2 (w), 875.0 (w), 804.2 (w) cm^{-1}.

MS (EI, 70 ev):

m/z (%) = 336 (0.3), 306 (3), 277 (3), 276 (2), 261 (2), 245 (3), 244 (2), 235 (2), 217 (29), 216 (35), 201 (10), 191 (10), 188 (7), 176 (10), 159 (10), 153 (22), 143 (10), 129 (17), 117 (12), 93(36), 91 (26), 79 (19), 77 (22), 67 (11), 59 (20), 53 (15), 42 (100).

Elemental Analysis:

Calculated for: $C_{18}H_{24}O_6$: C, 64.27 : H, 7.19 Found: C, 64.36 : H, 7.18

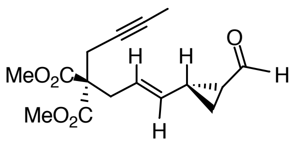
HRMS:

Calculated for $C_{18}H_{24}O_6$: (M^+) 336.157289 Found: 336.157383

Procedure for the preparation of 9:

To a solution of oxalyl chloride (237.2 mg, 1.869 mmol) in CH_2Cl_2 (30 ml) at -78°C was added dimethyl sulfoxide (292.0 mg, 3.74 mmol) dropwise. After stirring for 10 min, a solution of alcohol **3** (503.2 mg, 1.70 mmol) in CH_2Cl_2 (5 ml) was introduced, followed 30 min later by the addition of triethylamine (515 mg, 5.1 mmol). The reaction was allowed to stir for 6 h at -78°C, quenched by the addition of water (10 ml), and extracted with CH_2Cl_2 (3x20 ml). After washing with saturated aqueous $CuSO_4$ (2x10 ml), and brine (1x10 ml), the organics were dried over $MgSO_4$, concentrated, and purified by flash column chromatography (silica gel, 30% ethyl acetate/hexane) to afford aldehyde **9** (347.1 mg, 70%) as a colorless oil along with recovered starting material (55.7 mg, 11%).

Physical Data for Substrate 9:



^{1}**H-NMR** (300 MHz, $CDCl_3$/TMS):

δ = 9.13 (d, *J* = 5.1 Hz, 1H), 5.45 (dt, *J* = 15.1 Hz, *J* = 7.6 Hz, 1H), 5.19 (dd, *J* = 15.1 Hz, *J* = 8.1 Hz, 1H), 3.73 (s, 6H), 2.71-2.78 (m, 4H), 2.03-2.12 (m, 1H), 1.83-1.90 (m, 1H), 1.76 (t, *J* = 2.4 Hz, 3H), 1.45-1.59 (m, 1H), 1.11-1.18 (m, 1H) ppm.

^{13}**C-NMR** (125 MHz, $CDCl_3$):

δ = 199.61, 170.37, 133.62, 124.92, 78.99, 73.09, 57.25, 52.66, 35.16, 31.48, 24.77, 23.04, 15.07, 3.46 ppm.

IR (FT-IR, film):

ν = 304.2 (w), 2954.8 (w), 2923.1 (w), 2844.1 (w), 2734.9 (w), 1736.7 (s), 1706.4 (s), 1438.0 (m), 1400.6 (w), 1288.0 (m), 1213.1 (s), 1055.6 (m), 968.5 (m), 917.6 (w), 860.4 (w) cm^{-1}.

MS (EI, 70 ev):

m/z (%) = 291 (5), 277 (15), 261 (5), 232 (20), 217 (15), 203 (50), 189 (40), 176 (55), 143 (80), 129 (70), 105 (45), 79 (100), 59 (76), 53 (79).

HRMS:

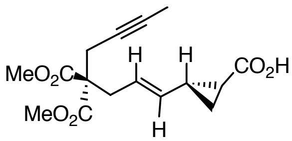
Calculated for $C_{16}H_{19}O_5$: (M-H^+) 291.12325 Found: 291.12428

Procedure for the preparation of 11:

To a solution of alcohol **3** (399.0 mg, 1.36 mmol) in wet DMF (10 ml) was added pyridinium dichromate (1.825 g, 4.85 mmol) in several portions. The mixture was allowed to stir overnight, diluted with water (20 ml) and extracted with ethyl acetate. The organic extracts were washed with brine, concentrated, and taken up in water (20 ml). Sodium hydroxide (aq.) was added, and the solution was extracted with Et_2O. Concentration and purification of these extracts afforded aldehyde **9**

(98.5 mg, 25%). The aqueous phase was acidified with HCl (1 M) until ~pH 3, then extracted with Et_2O. Drying of the organic extracts ($MgSO_4$) and concentration afforded carboxylic acid **11** (145.0 mg, 34%) as a white semi-solid.

Physical Data for Substrate 11:



^{1}H-NMR (500 MHz, $CDCl_3$/TMS):

δ = 10.6-11.6 (brs), 5.44 (dt, *J* = 15.2 Hz, *J* = 7.7 Hz, 1H), 5.17 (dd, *J* = 15.2 Hz, *J* = 8.2 Hz, 1H), 3.73 (s, 6H), 2.71-2.76 (m, 4H), 2.00-2.06 (m, 1H), 1.75 (t, *J* = 2.4 Hz, 3H), 1.59 (ddd, *J* = 8.8 Hz, *J* = 4.9 Hz, *J* = 3.5 Hz, 1H), 1.40 (ddd, *J* = 9.2 Hz, *J* = 4.8 Hz, *J* = 4.6 Hz, 1H), 1.01 (ddd, *J* = 8.2 Hz, *J* = 6.4 Hz, *J* = 4.6 Hz, 1H) ppm.

^{13}C-NMR (50 MHz, $CDCl_3$):

δ = 178.88, 170.57, 134.37, 124.72, 78.99, 73.16, 57.31, 52.65, 35.15, 25.49, 23.00, 21.48, 16.13, 3.40, ppm.

IR (FT-IR, film):

ν = 3005.3 (w), 2953.0 (w), 2911.1 (w), 2858.8 (w), 1736.1 (s), 1695.1 (s), 1437.9 (m), 1289.8 (m), 1212.8 (s), 1089.2 (w), 1056.1 (m), 1031.6 (w), 967.4 (w), 869.3 (w), 811.8 (w) cm^{-1}.

HRMS:

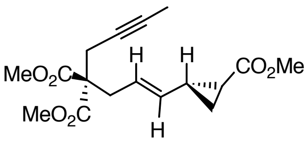
Calculated for: $C_{16}H_{21}O_6$: (MH^+) 309.133814 Found: 309.133243

Procedure for the preparation of 13:

One test tube was charged with acid **11** (124.4 mg, 0.40 mmol) and Et_2O (2 ml).

To a second test tube containing a vigorously stirred biphasic solution of KOH (135 mg, 2.4 mmol) in water (1 ml) and Et_2O (2 ml) at 0°C was added N-nitroso-N-methylurea (123.6 mg, 1.2 mmol). The resulting yellow ether layer (containing diazomethane) was transferred dropwise via a **Flame Polished** pipette to the solution of **11** until TLC analysis indicated the presence of no additional starting material. The esterified material was carefully quenched with acetic acid (5%), extracted with Et_2O, washed with saturated aqueous $NaHCO_3$, dried over $MgSO_4$, and evaporated to yield ester **13** (127.8 mg, 0.3965 mmol, 98%) as a clear, colorless oil.

Physical Data for Substrate 13:



^{1}H-NMR (300 MHz, $CDCl_3$/TMS):

δ = 5.41 (dt, *J* = 15.1 Hz, *J* = 7.7 Hz, 1H), 5.16 (dd, *J* = 15.1 Hz, *J* = 8.4 Hz, 1H), 3.73 (s, 6H), 3.67 (s, 3H), 2.70-2.72 (m, 4H), 1.92-2.01 (m, 1H), 1.75 (t, *J* = 2.5 Hz, 3H), 1.55-1.61 (m, 1H), 1.34 (dt, *J* = 8.9 Hz, *J* = 4.5 Hz, 1H), 0.90-0.96 (m, 1H) ppm.

^{13}C-NMR (75 MHz, $CDCl_3$):

δ = 173.75, 170.42, 134.71, 124.13, 78.89, 73.17, 57.29, 52.62, 51.76, 35.15, 24.68, 22.98, 21.59, 15.57, 3.43 ppm.

IR (FT-IR, film):

ν = 3005.0 (w), 2954.1 (w), 2911.1 (w), 2850.0 (w), 1735.6 (s), 1438.3 (m), 1400.5 (w), 1351.8 (w), 2850.0 (w), 1735.6 (s), 1438.2 (m), 1400.5 (w), 1351.8 (w), 1325.9 (w), 1289.4 (w), 1204.5 (s), 1173.9 (s), 1087.9 (w), 1055.8 (w), 1037.5 (w), 968.5 (w), 928.2 (w), 869.3 (w), 837.9 (w), 748.9 (w) cm^{-1}.

HRMS:

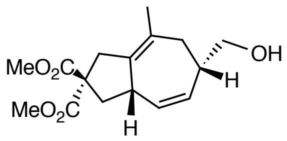
Calculated for: $C_{16}H_{19}O_5$: (M-OCH_3^+) 291.123249 Found: 291.123695

Procedure for the preparation of 4A/4B:

General cycloaddition procedure **A** (10 mol% catalyst) was followed for substrate **3** (24.1 mg, 81.8 μmol) leading after 1.5 h to the isolation of 23.1 mg (78.4 μmol, 96%) of **4A** as a clear colorless oil.

General cycloaddition procedure **B** (10 mol% catalyst) was followed for substrate **3** (23.4 mg, 79.5 μmol) leading after 0.5 h to the isolation of 20.0 mg (68.0 μmol, 85.5%) of a mixture of cycloadducts. **4A**:**4B** = 2.3:1. Separation of the regioisomers was achieved utilizing silver nitrate impregnated silica gel flash column chromatography (20-50% ethyl acetate in hexanes).

Physical Data for Substrate 4A:



^{1}H-NMR (500 MHz, $CDCl_3$/TMS):

δ = 5.62 (ddd, *J* = 10.6 Hz, *J* = 1.8 Hz, *J* = 1.8 Hz, 1H), 5.53 (ddd, *J* = 10.6 Hz, *J* = 5.5 Hz, *J* = 2.8 Hz, 1H), 3.74 (s, 3H), 3.73 (s, 3H), 3.52-3.61 (m, 3H), 3.00 (d, *J* = 16.6 Hz, 1H), 2.87 (d, *J* = 16.6 Hz, 1H), 2.67 (ddd, *J* = 11.8 Hz, *J* = 8.1 Hz, *J* = 1.3 Hz, 2H), 2.49 (d, *J* = 15.4 Hz, 1H), 2.00 (dd, *J* = 11.9 Hz, *J* = 11.9 Hz, 1H), 1.95-2.00 (m, 1H), 1.67 (s, 3H), 1.43 (br s, 1H) ppm.

^{13}C-NMR (75 MHz, $CDCl_3$):

δ = 172.20, 134.96, 133.85, 130.73, 127.38, 65.86, 58.24, 52.67, 52.62, 41.39, 39.69, 39.47, 39.19, 34.46, 22.32 ppm.

IR (FT-IR, film):

ν = 3416.9 (br), 2953.4 (m), 2916.8 (m), 2874.5 (m), 1732.0 (s), 1434.0 (m), 1273.5 (s), 1202.3 (m), 1166.7 (m), 1070.4 (m), 1044.2 (m), 953.6 (w), 887.1 (w), 743.9 (w) cm^{-1}.

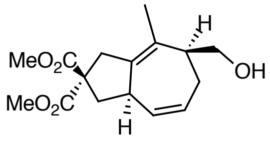
MS (EI, 70 ev):

m/z (%) = 294 (1), 264 (5), 234 (4), 216 (5), 204 (10), 203 (10), 188 (2), 175 (5), 157 (8), 143 (8), 129 (5), 105 (2), 91 (2).

HRMS:

Calculated for $C_{16}H_{22}O_5$: 294.146724 Found: 294.146843

Physical Data for Substrate 4B:



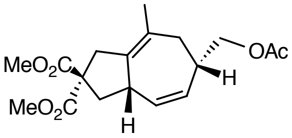
^{1}H-NMR (500 MHz, $CDCl_3$/TMS):

δ = 5.66-5.71 (m,1H), 5.55 (dt, *J* = 10.6 Hz, *J* = 1.8 Hz, 1H), 3.71-3.76 (m, 1H), 3.74 (s, 3H), 3.72 (s, 3H), 3.57-3.72 (m, 2H), 3.02 (d, *J* = 16.9 Hz, 1H), 2.89 (d, *J* = 16.9 Hz, 1H), 2.67 (ddd, *J* = 12.8 Hz, *J* = 8.2 Hz, *J* = 1.8 Hz, 2H), 2.62-2.68 (m, 1H) 2.38-2.42 (dm, *J* = 15.9 Hz, 1H), 2.07-2.13 (m,1H), 2.00 (dd, *J* = 11.5 Hz, *J* = 11.5 Hz, 1H), 1.66 (s, 3H), 1.38 (br s, 1H) ppm.

Procedure for the preparation of 6:

General cycloaddition procedure **A** (10 mol% catalyst) was followed for substrate **5** (17.0 mg, 50.5 μmol) leading after 2 h to the isolation of 15.6 mg (46.4 μmol, 92%) of **6A** as a clear colorless oil. Comparison to **4A** was possible after hydrolysis (K_2CO_3/MeOH).

General cycloaddition procedure **B** (10 mol% catalyst) was followed for substrate **5** (16.8 mg, 49.9 μmol) leading after 1.5 h to the isolation of 14.3 mg (42.5 μmol, 85%) of a mixture of cycloadducts **6A**:**6B** = 2.5:1. Comparison to **6A** and **6B** was possible after hydrolysis (K_2CO_3/MeOH)



Physical Data for Substrate 6A:

^{1}H-NMR (300 MHz, $CDCl_3$/TMS):

δ = 5.61 (dt, *J* = 10.7 Hz, *J* = 2.4 Hz, 1H), 5.50 (ddd, *J* = 10.7 Hz, *J* = 5.4 Hz, *J* = 2.4 Hz, 1H), 4.03 (dd, *J* = 10.7 Hz, *J* = 6.3 Hz, 1H), 3.91 (dd, *J* = 10.7 Hz, *J* = 7.8 Hz, 1H), 3.74 (s, 3H), 3.73 (s, 3H), 3.54-3.62 (m, 1H), 3.02 (d, *J* = 16.4 Hz, 1H), 2.85 (d, *J* = 16.4 Hz, 1H), 2.82-2.89 (m, 1H), 2.67 (ddd, *J* = 12.7 Hz, *J* = 8.1 Hz, *J* = 1.7 Hz, 1H), 2.45 (d, *J* = 15.4 Hz, 1H), 2.06 (s, 3H), 1.91-2.00 (m, 2H), 1.64 (s, 3H), ppm.

^{13}C-NMR (75 MHz, $CDCl_3$):

δ = 172.02, 171.94, 171.05, 135.05, 133.89, 129.83, 126.74, 66.79, 58.23, 52.76, 52.70, 41.42, 38.79, 39.29, 36.12, 34.53, 22.35, 20.92 ppm.

IR (FT-IR, film):

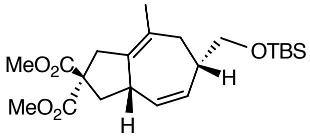
ν = 3012.2 (w), 2953.7 (w), 2901.6 (w), 2850.0 (w), 1736.3 (s), 1435.2 (m), 1364.7 (w), 1235.6 (m), 1166.3 (m), 1071.2 (w), 1038.2 (m) cm^{-1}.

Procedure for the preparation of 8A:

General cycloaddition procedure **A** (10 mol% catalyst) was followed for substrate **7** (41.2 mg, 101 μmol) leading after 1 h to the isolation of 39.2 mg (95.0 μmol, 95%) of **8A** as a clear colorless oil. Analysis was completed by removal of the TBS group with TBAF/THF and comparison to **4A**.

General cycloaddition procedure **B** (10 mol% catalyst) was followed for substrate **7** (41.2 mg, 101 μmol) leading after 1 h to the isolation of 35.4 mg (86.6 μmol, 86%) of a mixture of cycloadducts. **8A**:**8B** = 3.5:1. Analysis was completed by removal of the TBS group with TBAF/THF and comparison to **4A/4B**.

Physical Data for Substrate 8A:



^{1}H-NMR (500 MHz, $CDCl_3$/TMS):

δ = 5.47-5.60 (m, 2H), 3.74 (s 3H), 3.73 (s, 3H), 3.54-3.60 (m, 1H), 3.51 (dd, *J* = 9.8 Hz, *J* = 5.9 Hz, 1H), 3.44 (dd, *J* = 9.5 Hz, *J* = 8.1 Hz, 1H), 3.01 (d, *J* = 16.8 Hz, 1H), 2.85 (d, *J* = 16.8 Hz, 1H), 2.61-2.71 (m, 2 H), 2.40 (d, *J* = 15.6 Hz, 1H), 1.98 (dd, *J* = 12.0 Hz, *J* = 12.0 Hz, 1H), 1.64 (s, 3H), 0.89 (s, 9H), 0.04 (s, 6H) ppm.

^{13}C-NMR (125 MHz, $CDCl_3$):

δ = 172.11, 134.31, 133.00, 131.22, 127.50, 65.74, 58.30, 52.72, 52.65, 41.52, 39.77, 39.63, 39.30, 34.45, 25.89, 22.40, 18.25, -5.4 ppm.

IR (FT-IR, film):

ν = 2953.4 (m), 2929.2 (m), 2895.2 (w), 2856.5 (m), 1737.3 (s), 1434.8 (m), 1255.6 (m), 1201.1 (m), 1166.0 (m), 1107.1 (m), 1081.8 (m), 1005.8 (w), 939.0 (w), 837.2 (m), 776.2 (m) cm^{-1}.

MS (EI, 70 ev):

m/z (%) = 351 (loss of C_4H_9), 318, 291, 261, 240, 216

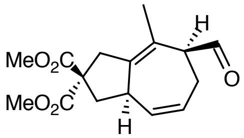
HRMS:

Calculated for $C_{18}H_{27}O_5Si$: 351.162778 (loss of C_4H_9) Found: 351.162675

Procedure for the preparation of 10B:

General cycloaddition procedure **B** (10 mol% catalyst), modified by reducing the reaction temperature to 55°C, was followed for substrate **9** (12.7 mg, 43.4 μmol) leading after 8 h to the isolation of 12.5 mg (42.7 μmol, 98%) of **10B** as a clear colorless oil.

Physical Data for Substrate 10B:



^{1}H-NMR (500 MHz, $CDCl_3$/TMS):

δ = 9.69 (d, *J* = 1.8 Hz, 1H), 5.71-5.76 (m, 1H), 5.63 (dt, *J* = 10.4 Hz, *J* = 2.0 Hz, 1H), 3.76 (s, 3H), 3.75 (s, 3H), 3.60-3.65 (m, 1H), 3.20-3.21 (m, 1H), 3.09 (d, *J* = 17.0 Hz, 1H), 2.94 (dd, *J* = 17.0 Hz, *J* = 2.0, 1H), 2.67-2.73 (m, 2H), 2.52 (dt, *J* = 16.0 Hz, , *J* = 7.0 Hz, 1H), 2.07 (t, *J* = 12.3 Hz, 1H) 1.75 (t, *J* = 2.5 Hz, 1H) ppm.

^{13}C-NMR (125 MHz, $CDCl_3$):

δ = 202.79, 172.00, 171.78, 138.40, 134.48, 127.71, 124.27, 58.03, 55.00, 52.90, 52.81, 41.16, 40.11, 39.69, 25.97, 19.94 ppm.

IR (FT-IR, film):

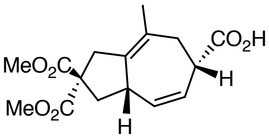
ν = 2954.7 (w), 2850.0 (w), 2084.0 (w), 2011.9 (w), 1731.9 (s), 1435.1 (m), 1258.7 (s), 1201.5 (m), 1163.3 (m), 1078.0 (m), 951.5 (w), 885.5 (w) cm^{-1}.

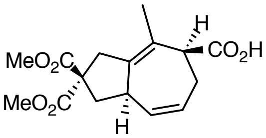
Chemical Correlation: Treatment of **10B** with $NaBH_4$/MeOH resulted in the formation of **4B**, as evidenced by ^{1}H-NMR and GC analysis.

Procedure for the preparation of 12A and 12B:

General cycloaddition procedure **A** (10 mol% catalyst) was followed for substrate **11** (15.0 mg, 48.2 μmol) leading after 2 h to the isolation of 10.4 mg (33.4 μmol, 69%) of a mixture of cycloadducts. **12A**:**12B**:**12X** = 4:1:1. (**12X** referring to an unidentified reaction product)

General cycloaddition procedure **B** (10 mol% catalyst) was followed for substrate **11** (15.2 mg, 48.8 μmol) leading after 2 h to the isolation of 11.1 mg (35.7 μmol, 73%) of a mixture of cycloadducts. **12A**:**12B** = 1:22.





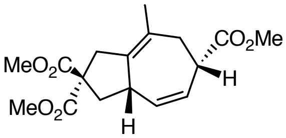
Carboxylic acids **12A** and **12B** were characterized by brief exposure to CH_2N_2 and analysis as their corresponding methyl esters (**14A** and **14B**)

Procedure for the preparation of 14A and 14B:

General cycloaddition procedure **A** (10 mol% catalyst) was followed for substrate **13** (19.9 mg, 61.7 μmol) leading after 2 h to the isolation of 16.1 mg (49.9 μmol, 81%) of a mixture of cycloadducts. **14A**:**14B** = 20:1.

General cycloaddition procedure **B** (10 mol% catalyst) was followed for substrate **13** (20.0 mg, 62.0 μmol) leading after 2 h to the isolation of 18.5 mg (57.4 μmol, 93%) of a mixture of cycloadducts. **14A**:**14B** = 1:11. Separation of the regioisomers was achieved utilizing silver nitrate impregnated silica gel flash column chromatography (20-50% ethyl acetate in hexanes).

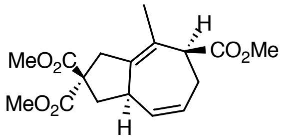
Physical Data for Substrate 14A:



^{1}H-NMR (500 MHz, $CDCl_3$/TMS):

δ = 5.83 (ddd, *J* = 10.7 Hz, *J* = 6.1 Hz, *J* = 2.9 Hz, 1H), 5.68 (ddd, *J* = 10.7 Hz, *J* = 2.7 Hz, *J* = 2.0 Hz, 1H), 3.73 (s, 6H), 3.70 (s, 3H), 3.53-3.60 (m, 2H), 3.02 (d, *J* = 16.8 Hz, 1H), 2.85 (d, *J* = 16.8 Hz, 1H), 2.68 (ddd, *J* = 12.6 Hz, *J* = 7.9 Hz, *J* = 2.0 Hz, 1H), 2.57 (d, *J* = 16.1 Hz, 1H), 2.27 (dd, *J* = 15.6 Hz, *J* = 10.1 Hz, 1H), 2.02 (t, *J* = 12.4 Hz, 1H), 1.65 (s, 3H), ppm.

Physical Data for Substrate 14B:



^{1}H-NMR (500 MHz, $CDCl_3$/TMS):

δ = 5.56-5.60 (m, 1H), 5.48 (dq, *J* = 11.0 Hz, *J* = 1.8 Hz, 1H), 3.75 (s, 3H), 3.73 (s, 3H), 3.70 (s, 3H), 3.62-3.66 (m, 1H), 3.60 (d, *J* = 9.7 Hz, 1H), 3.02 (d, *J* = 16.8 Hz, 1H) 2.95 (d, *J* = 16.8 Hz, 1H), 2.70 (ddd, *J* = 12.8 Hz, *J* = 8.4 Hz, *J* = 1.5 Hz, 1H), 2.47 (dm, *J* = 15.8 Hz, 1H), 2.34-2.41 (m, 1H), 2.02 (dd, *J* = 12.8 Hz, *J* = 10.8 Hz, 1H), 2.02 (t, *J* = 12.4 Hz, 1H), 1.61 (d, *J* = 1.5 Hz, 3H), ppm.

HRMS:

Calculated for $C_{17}H_{22}O_6$: 322.141639 Found: 322.141358

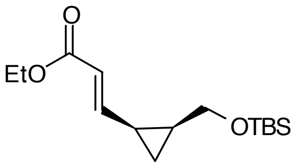
cis-1,2-Disubstituted Cyclopropanes

Procedure for the preparation of 25c:

(*cis*-1-carboxaldehyde-2-*tert*-butyldimethylsiloxymethyl-cyclopropane was prepared in a manner analogous to the preparation described for **24t**, starting with the corresponding *cis*-olefin).

To a 250 ml R.B. flask containing NaH (95%, 591 mg, 23.4 mmol) and THF (150 ml) at 0°C was added triethyl phosphonoacetate (4.81 ml, 24.23 mmol) dropwise. After 30 min at room temperature, *cis*-1-carboxaldehyde-2-*tert*-butyldimethylsiloxymethyl-cyclopropane (4.155 g, 19.38 mmol) was added dropwise and the reaction was allowed to stir overnight. After quenching with brine, extraction with Et_2O, drying over $MgSO_4$, and concentration *in vacuo* gave a crude oil that was further purified by flash column chromatography. Ester **25c** was obtained as a clear, colorless oil (3.987 g, 72%).

Physical Data for Substrate 25c:



^{1}H-NMR (300 MHz, $CDCl_3$/TMS):

δ = 6.72 (dd, *J* = 15.4 Hz, *J* = 10.3 Hz, 1H), 5.92 (d, *J* = 15.4 Hz, 1H), 4.17 (q, *J* = 7.1 Hz, 2H), 3.82 (dd, *J* = 11.0 Hz, *J* = 5.6 Hz, 1H), (dd, *J* = 11.0 Hz, *J* = 7.3 Hz, 1H), 1.67-1.78 (m, 1H), 1.49-1.58 (m, 1H), 1.28 (t, *J* = 7.1 Hz, 1H), 1.09-1.16 (m, 1H), 0.89 (s, 9H), 0.68-0.75 (m, 1H), 0.06 (s, 3H), 0.05 (s, 3H) ppm.

^{13}C-NMR (75 MHz, $CDCl_3$):

δ = 166.29, 149.74, 120.25, 62.41, 59.82, 25.79, 23.14, 19.16, 18.19, 14.23, 12.72, -5.42, -5.50 ppm.

IR (FT-IR, film):

ν = 2955.5 (m), 2925.0 (m), 2886.1 (m), 2857.6 (m), 1717.7 (s), 1645.6 (m), 1471.9 (m), 1390.0 (w), 1362.4 (w), 1307.5 (w), 1260.1 (s), 1185.6 (m), 1143.1 (m), 1087.4 (m), 1043.5 (m), 984.1 (m), 926.5 (w), 837.2 (s), 776.5 (m), 667.3 (w) cm^{-1}.

HRMS:

Calculated for $C_{11}H_{19}O_3Si$: 227.109616 (loss of C_4H_9) Found: 227.112536

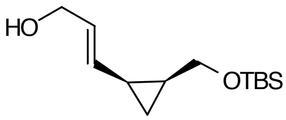
Elemental Analysis:

Calculated for $C_{15}H_{28}O_3Si$: C, 63.33: H, 9.92 Found: C, 63.35: H, 10.00

Procedure for the preparation of 26c:

To a 500 ml R.B. flask charged with ester **25c** (3.494 g, 12.3 mmol) and THF (150 ml) at 0°C was added DIBAl (1.5 M, 20.5 ml, 30.75 mmol) dropwise. The reaction was warmed to room temperature overnight and was quenched with water (30 ml) and 10% aq. NaOH (100 ml). Extraction with Et_2O, drying over $MgSO_4$, and evaporation provided alcohol **26c** (2.8605 g, 11.8 mmol, 96%) as a clear, colorless oil.

Physical Data for Substrate 26c:



^{1}H-NMR (300 MHz, $CDCl_3$/TMS):

δ = 5.77 (dt, *J* = 15.1 Hz, *J* = 6.1 Hz, 1H), 5.50 (dd, *J* = 15.1 Hz, *J* = 8.5 Hz, 1H), 4.09 (t, *J* = 11.0 Hz, 2H), 3.70 (dd, *J* = 11.0 Hz, *J* = 6.3 Hz, 1H), 3.56 (dd, *J* = 11.0 Hz, *J* = 7.6 Hz, 1H), 1.54-1.56 (m, 1H), 1.25-1.33 (m, 1H), 1.21 (br s, 1H), 0.91-0.98 (m, 1H), 0.89 (s, 9H), 0.39-0.45 (m, 1H), 0.06 (s, 3H), 0.05 (s, 3H) ppm.

^{13}C-NMR (75 MHz, $CDCl_3$):

δ = 132.19, 129.21, 63.67, 63.13, 25.94, 20.71, 18.34, 18.30, 10.70, -5.16, -5.21 ppm.

IR (FT-IR, film):

ν = 3355.1 (br), 3002.5 (w), 2954.6 (m), 2929.0 (m), 2857.3 (m), 1664.6 (w), 1471.9 (m), 1406.4 (w), 1389.1 (w), 1361.1 (w), 1255.4 (m), 1160.6 (w), 1086.3 (s), 1006.1 (m), 966.4 (m), 836.9 (s), 775.5 (m), 665.6 (w) cm^{-1}.

HRMS:

Calculated for $C_9H_{17}O_2Si$: 185.099783 (loss of C_4H_9) Found: 185.100163

Elemental Analysis:

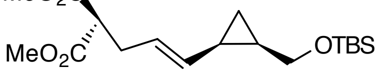
Calculated for $C_{13}H_{26}O_2Si$: C, 64.41: H, 10.81 Found: C, 64.19: H, 10.98

Procedure for the preparation of 27c:

To a 250 ml R.B. flask containing alcohol **26c** (2.8605 g, 11.8 mmol) and THF (50 ml) at -78°C was added BuLi (2.5 M, 5.2 ml, 13.0 mmol), followed 10 min later by methane sulfonyl chloride (1.01 ml, 13.0 mmol), and then immediately by lithium bromide (4 g, 49 mmol) in one portion. After stirring for 30 min this solution was transferred to the malonate anion solution via cannula.

To a second R.B. flask charged with NaH (95%, 1.03 g, 40.7 mmol) and THF (50 ml) was added dimethyl malonate (4.72 ml, 41.3 mmol) dropwise. After 30 min at room temperature, the solution was cooled to -78°C and the bromide was introduced via cannula. The reaction was stirred for 2 h at -78°C, then allowed to warm to room temperature. Quenching with water, extraction with Et_2O, drying over $MgSO_4$, and evaporation gave a crude mixture. After removal of excess dimethyl malonate via Kugel Rohr and flash column chromatography, the malonate derivative **27c** was obtained as a colorless oil (1.2652 g, 30%).

Physical Data for Substrate 27c:



^{1}H-NMR (500MHz, $CDCl_3$/TMS):

δ = 5.47 (dt, *J* = 15.2 Hz, *J* = 7.1 Hz, 1H), 5.35 (dd, *J* = 15.2 Hz, *J* = 8.2 Hz, 1H), 3.73 (s, 6H), 3.62 (dd, *J* = 11.0 Hz, *J* = 6.6 Hz, 1H), 3.55 (dd, *J* = 11.0 Hz, *J* = 7.3 Hz, 1H), 3.40 (t, *J* = 7.7 Hz, 1H), 2.60 (t, *J* = 7.3 Hz, 2H), 1.52 (ddd, *J* =14.1 Hz, *J* = 5.9 Hz, *J* = 5.9 Hz 1H), 1.22 (ddd, *J* = 21.0 Hz, *J* = 7.0 Hz, *J* = 7.0 Hz 1H), 0.90 (s, 9H), 0.84-0.89 (m, 1H), 0.34 (dd, *J* = 21.0 Hz, *J* = 7.0 Hz, 1H), 0.04 (s, 6H) ppm.

^{13}C-NMR (125 MHz, $CDCl_3$):

δ = 169.32, 169.30, 132.51, 125.51, 63.14, 52.40, 51.99, 51.97, 31.94, 25.93, 20.46, 18.39, 18.34, 10.48, -5.17, -5.22 ppm.

IR (FT-IR, film):

ν = 2953.5 (m), 2856.8 (m), 1736.3 (m), 1473.5 (s), 1437.6 (w), 1340.6 (w), 1250.9 (m), 1157.0 (w), 1083.5 (m), 967.6 (w), 837.1 (m), 775.3 (m) cm^{-1}.

HRMS:

Calculated for $C_{14}H_{23}O_5Si$: 299.13148 (loss of C_4H_9) Found: 299.13068

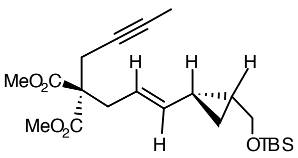
Elemental Analysis:

Calculated for $C_{18}H_{32}O_5Si$: C, 60.64: H, 9.05 Found: C, 60.62: H, 9.30

Procedure for the preparation of 17:

To a 100 ml R.B. flask charged with NaH (95%, 101 mg, 3.99 mmol) and THF (50 ml) was added malonate derivative **26c** (1.1859 g, 3.326 mmol) dropwise. After 30 min at room temperature and 1 h at 50°C, 1-bromo-but-2-yne (0.4368 ml, 4.99 mmol) was added at room temperature. After stirring overnight at room temperature, the reaction was quenched with brine, extracted with Et_2O, dried over $MgSO_4$, and evaporated to give TBS ether **17** (1.2661g, 3.09 mmol, 93%) as a colorless oil.

Physical Data for Substrate 17:



^{1}**H-NMR** (300 MHz, $CDCl_3$/TMS):

δ = 5.26-5.42 (m, 2H), 3.73 (s, 6H), 3.59 (d, *J* = 6.8 Hz, 2H), 2.72-2.74 (m, 4H), 1.75 (t, *J* = 2.7 Hz, 3H), 1.47-1.54 (m, 1H), 1.00-1.27 (m, 1H), 0.90 (s, 9H), 0.83-0.89 (m, 1H), 0.32-0.38 (m, 1H), 0.06 (s, 6H) ppm.

^{13}**C-NMR** (125 MHz, $CDCl_3$):

δ = 170.56, 134.24, 123.42, 78.66, 73.35, 63.18, 57.37, 52.55, 52.52, 35.30, 25.95, 22.83, 20.50, 18.48, 18.36, 10.61, 3.43, -5.20 ppm.

IR (FT-IR, film):

ν = 2999.2 (w), 2953.8 (m), 2856.9 (m), 1740.7 (s), 1462.7 (w), 1437.6 (m), 1291.2 (m), 1250.9 (m), 1207.0 (s), 1082.5 (s), 968.8 (w), 836.3 (s), 776.0 (m), 665.5 (w) cm^{-1}.

HRMS:

Calculated for $C_{18}H_{27}O_5Si$: 351.162778 (loss of C_4H_9) Found: 351.162146

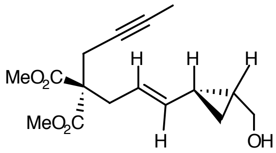
Elemental Analysis:

Calculated for : $C_{22}H_{36}O_5Si$: C, 64.67: H, 8.88 Found: C, 64.17: H, 8.90

Procedure for the preparation of 15:

TBS ether **17** (946.2 mg, 2.32 mmol) was placed in THF (50 ml) and stirred with TBAF/silica gel (excess) at room temperature to afford alcohol **15** as a clear colorless oil after flash column purification (581.1 mg, 1.974 mmol, 85%).

Physical Data for Substrate 15:



^{1}**H-NMR** (500 MHz, $CDCl_3$/TMS):

δ = 5.34-5.50 (m, 2H), 3.73-3.81 (m, 1H), 3.74 (m, 6H), 3.37 (t, J = 10.3 Hz, 1H), 2.69-2.81 (m, 4H), 1.76 (t, J = 2.5 Hz, 3H), 1.64 (br s, 1H), 1.53-1.63 (m, 1H), 1.25-1.40 (m, 1H), 0.92 (ddd, *J* = 13.2 Hz, *J* = 5.1 Hz, *J* = 5.1 Hz, 1H), 0.40 (dd, *J* = 10.7 Hz, J = 5.4 Hz, 1H) ppm.

^{13}**C-NMR** (125 MHz, $CDCl_3$):

δ = 170.58, 133.58, 124.42, 78.91, 73.23, 63.04, 57.47, 52.60, 35.44, 23.03, 20.89, 18.08, 10.65, 3.40 ppm.

IR (FT-IR, film):

ν = 3406.1 (br), 3001.1 (w), 2954.3 (w), 2869.2 (w), 1735.9 (s), 1437.9 (m), 1329.0 (w), 1292.4 (m), 1206.7 (s), 1146.8 (w), 1039.6 (m), 968.7 (w), 858.9 (w), 822.2 (w) cm^{-1}.

HRMS:

Calculated for $C_{16}H_{22}O_5$: 263.12668 (loss of CH_2OH) Found: 263.128334

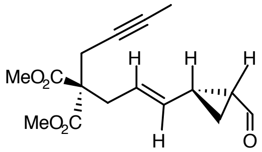
Elemental Analysis:

Calculated for: $C_{16}H_{22}O_5$: C, 65.26 : H, 7.53 Found: C, 65.14: H, 7.42

Procedure for the preparation of 19:

To a solution of PCC (30 mg, 0.139 mmol) and celite (30 mg) in CH_2Cl_2 (1 ml) was added alcohol **15** (20 mg, 67.9 μmol) in CH_2Cl_2 (.5 ml). The solution was stirred at room temperature for 2 h, layered with Et_2O (4 ml) and stirred vigorously for an additional hour. The solution was filtered through florisil and evaporated to give aldehyde **19** (16.3 mg, 55.8 μmol, 82%).

Physical Data for Substrate 19:



^{1}**H-NMR** (300 MHz, $CDCl_3$/TMS):

δ = 9.30 (d, *J* = 4.9 Hz, 1H), 5.53-5.58 (m, 2H), 3.73 (s, 3H), 3.72 (s, 3H), 2.74-2.75 (m, 2H), 2.71 (q, *J* = 2.6 H, 2H), 2.10-2.14 (m, 1H), 2.04-2.10 (m, 1H), 1.76 (t, *J* = 2.6 Hz, 3H), 1.46 (ddd, *J* = 6.9 Hz, *J* = 5.5 Hz, *J* = 5.3 Hz, 1H), 1.38 (ddd, *J* = 8.1 Hz, *J* = 8.1 Hz, *J* = 5.1 Hz, 1H) ppm.

^{13}**C-NMR** (125 MHz, $CDCl_3$):

δ = 200.69, 170.41, 131.01, 126.46, 79.05, 73.05, 73.06, 57.30, 52.69, 35.21, 29.80, 25.91, 23.08, 14.45, 3.48 ppm.

IR (FT-IR, film):

ν = 3002.8 (w), 2955.0 (w), 2923.3 (w), 2846.5 (w), 2763.9 (w), 1736.6 (s), 1703.0 (s) 1437.9 (m), 1328.9 (w), 1291.2 (m), 1205.6 (s), 1146.1 (w), 1055.6 (m), 1030.4 (w), 972.1 (m), 937.4 (w), 859.4 (w) cm^{-1}.

MS (EI, 70 ev):

m/z (%) = 292 (4), 264 (33), 232 (16), 214 (7), 204 (61), 203 (65), 189 (8), 173 (22), 155 (9), 145 (100), 128 (60), 115 (37), 105 (26), 91 (32), 77 (25), 65 (18), 59 (47).

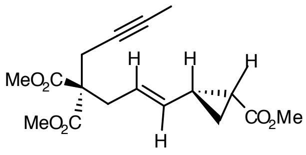
Procedure for the preparation of 21 :

Ester **21** was prepared through a three step procedure involving TPAP oxidation of alcohol **15**, Lingren oxidation of the resulting aldehyde, and esterification with diazomethane.

To a solution of alcohol **15** (223.6 mg, 0.76 mmol), *N*-methylmorpholine-*N*-oxide (120 mg, 1.02 mmol), and molecular sieves (400 mg) in CH_2Cl_2 (15 ml) was added TPAP (15 mg, 0.042 mmol, 5%). After stirring for 3 h at room temperature, the solution was filtered through a plug of silica gel, and evaporated to give aldehyde **19** which was oxidized without further purification. Aldehyde **19** and 2-methyl-2-butene (8 ml) were dissolved in *tert*-butanol (20 ml). To this was added a solution of

$NaClO_2$ (80%, 860 mg, 7.6 mmol) and NaH_2PO_4 (910 mg, 7.6 mmol) in water (10 ml). After stirring at room temperature for 3 h, the *tert*-butanol was removed *in vacuo* and the resulting slurry was diluted with water (20 ml) and extracted with ethyl acetate. The organics were extracted with 1 M NaOH, with the combined aqueous phase being acidified with 1 M HCl until pH 3 and extracted with ethyl acetate. The organic phases were washed with brine, dried over $MgSO_4$, and concentrated to afford the crude carboxylic acid. This acid was taken up in Et_2O (5 ml) and placed in a test tube. To a second test tube containing a vigorously stirred biphasic solution of KOH (340 mg, 6 mmol) in water (5 ml) and Et_2O (10 ml) at 0°C was added N-nitroso-N-methylurea (627 mg, 6 mmol). The resulting yellow ether layer (containing diazomethane) was transferred dropwise via a **Flame Polished** pipette to the solution of **11** until TLC analysis indicated the presence of no additional starting material. The esterified material was carefully quenched with acetic acid (5%), extracted with Et_2O, washed with saturated aqueous $NaHCO_3$, dried over $MgSO_4$, and purified by flash column chromatography (silica gel, 20-50% ethyl acetate/hexane) to yield ester **21** (108 mg, 0.335 mmol, 44% over 3 steps) as a colorless oil.

Physical Data for Substrate 21:



^{1}H-NMR (500MHz, $CDCl_3$/TMS):

δ = 5.47-5.55 (m, 2H), 3.72 (s, 3H), 3.71 (s, 3H), 3.68 (s, 3H), 2.77 (dd, *J* = 5.7 Hz, *J* = 1.3 Hz, 2H), 2.74 (dd, *J* = 5.1 Hz, *J* = 2.6 Hz, 2H), 1.88-1.93 (m, 2H), 1.78 (t, *J* = 2.4 Hz, 3H), 1.19-1.30 (m, 2H) ppm.

^{13}C-NMR (75 MHz, $CDCl_3$):

δ = 172.25, 170.52, 170.47, 132.11, 125.26, 78.86, 73.17, 57.44, 52.57, 51.58, 23.72, 22.90, 20.70, 14.14, 3.45 ppm.

IR (FT-IR, film):

ν = 3005.3 (w), 2955.0 (w), 2921.6 (w), 2848.3 (w), 1734.1 (s), 1438.1 (m), 1385.4 (w), 1272.4 (w), 1202.8 (s), 1054.4 (m), 957.5 (m), 858.1 (w), 832.7 (w) cm^{-1}.

HRMS:

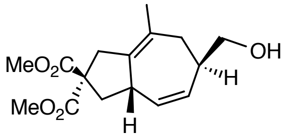
Calculated for $C_{17}H_{19}O_6$:(M-CH_3^+) 307.116 Found: 307.11683

Procedure for the preparation of 16C and 16D:

General cycloaddition procedure **A** (10 mol% catalyst) was followed for substrate **15** (9.0 mg, 30.6 μmol) leading after 1 h to the isolation of 7.6 mg (25.8 μmol, 84%) of a mixture of cycloadducts. **16C**:**16D** = 3.5:1.

General cycloaddition procedure **B** (10 mol% catalyst) was followed for substrate **15** (12 mg, 40.8 μmol) leading after 1 h to the isolation of 11.2 mg (38.1 μmol, 93%) of a mixture of cycloadducts. **16C**:**16D** = 9:1.

Physical Data for Substrate 16C:



^{1}H-NMR (500MHz, $CDCl_3$/TMS):

δ = 5.56 (dt, *J* = 11.7 Hz, *J* = 2.2 Hz, 1H), 5.41 (ddd, *J* = 11.7 Hz, *J* = 4.2 Hz, *J* = 2.0 Hz, 1H), 3.73 (s, 3H), 3.72 (s, 3H), 3.49-3.70 (m, 3H), 2.99 (d, *J* = 16.5 Hz, 1H), 2.87 (dd, *J* = 16.5 Hz, *J* = 2.2 Hz, 1H), 2.71 (ddd, *J* = 12.8 Hz, *J* = 8.9 Hz, *J* = 1.8 Hz, 2H), 2.53 (dd, *J* = 13.0 Hz, *J* = 12.6 Hz, 1H), 2.27-2.35 (m,1H), 1.88-2.00 (m, 1H), 1.74 (s, 3H), 1.65 (br s, 1H) ppm.

^{13}C-NMR (125 MHz, $CDCl_3$):

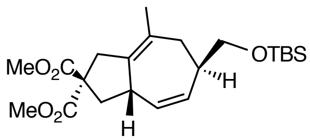
δ = 171.94, 132.78, 130.31, 129.83, 128.55, 67.98, 58.45, 52.70, 41.90, 40.00, 39.15, 38.81, 35.49, 20.94 ppm.

Procedure for the preparation of 18C:

General cycloaddition procedure **A** was followed for substrate **17** (10.4 mg, 25.5 μmol) leading after 1 h to the isolation of 8.4 mg (20.7 μmol, 81%) of **18C**.

General cycloaddition procedure **B** was followed for substrate **17** (11.4 mg, 27.9 μmol) leading after 1 h to the isolation of 10.9 mg (26.7 μmol, 96%) of **18C**.

Physical Data for Substrate 18C:



^{1}H-NMR (500 MHz, $CDCl_3$/TMS):

δ = 5.42 (s, 2H), 3.73 (s 3H), 3.72 (s, 3H), 3.51-3.72 (m, 1H), 3.46 (dd, *J* = 9.7 Hz, , *J* = 6.0 Hz, 1H), 3.36 (dd, *J* = 9.7 Hz, , *J* = 7.5 Hz, 1H), 2.99 (d, *J* = 16.3 Hz, 1H), 2.88 (dd, *J* = 16.3 Hz, *J* = 2.0 Hz, 1H), 2.70 (ddd, *J* = 12.6 Hz, *J* = 8.4 Hz, *J* = 1.8 Hz, 1H), 2.36 (t, *J* = 12.6 Hz, 1H), 2.22-2.26 (m, 1H), 1.90-1.95 (m, 2H), 1.72 (s, 3H), 0.89 (s, 9H), 0.04 (s, 6H) ppm.

^{13}C-NMR (125 MHz, $CDCl_3$):

δ = 171.99, 136.52, 131.20, 130.38, 128.92, 67.75, 58.42, 52.76, 52.70, 41.95, 40.13, 39.17, 38.80, 35.52, 25.89, 20.89, 18.28, -5.32 ppm.

IR (FT-IR, film):

ν = 2953.4 (m), 2928.7 (m), 2856.2 (m), 1737.4 (s), 1466.1 (m), 1435.1 (m), 1378.2 (w), 1361.1 (w), 1256.3 (s), 1203.0 (m), 1164.9 (m), 1106.6 (s), 1063.4 (m), 1006.0 (w), 938.5 (w), 836.3 (s), 776.2 9 (m), 666.4 (w) cm^{-1}.

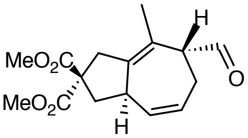
HRMS:

Calculated for $C_{18}H_{27}O_5Si$: 351.162778 (loss of C_4H_9) Found: 351.159517

Procedure for the preparation of 20D:

General cycloaddition procedure **B** (10 mol% catalyst), modified by lowering the reaction temperature to 55°C, was followed for substrate **19** (11.0 mg, 37.6 μmol) leading after 15 h to the isolation of **20D** (10.1 mg, 34.6 μmol, 92%) of as a clear colorless oil.

Physical Data for Substrate 20B:



^{1}H-NMR (500 MHz, $CDCl_3$/TMS):

δ = 9.63 (d, *J* = *2* Hz, 1H), 5.54-5.59 (m, 1H), 5.38 (dm, *J* = 12 Hz, 1H), 3.76 (s, 3H), 3.75 (s, 3H), 3.60-3.65 (m, 1H), 3.20-3.21 (m, 1H), 3.09 (d, *J* = 17.0 Hz, 1H), 2.94 (dd, *J* = 17.0 Hz, *J* = 2.0, 1H), 2.67-2.73 (m, 2H), 2.52 (dt, *J* = 16.0 Hz, *J* = 7.0 Hz, 1H), 2.07 (t, *J* = 12.3 Hz, 1H) 1.75 (t, *J* = 2.5 Hz, 1H) ppm.

^{13}C-NMR (125 MHz, $CDCl_3$):

δ = 199.79, 171.74, 140.62, 129.75, 126.10, 125.04, 57.83, 56.13, 52.87, 52.79, 41.81, 41.70, 40.09, 39.89, 25.42, 22.49 ppm.

IR (FT-IR, film):

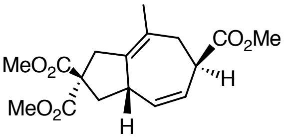
ν = 3015.8 (w), 2945.5 (w), 2900.6 (w), 2848.3 (w), 1733.9 (s), 1435.6 (m), 1259.3 (m), 1202.5 (m), 1165.5 (m), 1069.4 (w), 953.1 (w) cm^{-1}.

Procedure for the preparation of 22C and 22D:

General cycloaddition procedure **A** (10 mol% catalyst) was followed for substrate **21** (14.6 mg, 45.3 μmol) leading after 2 h to the isolation of 13.9 mg (43.1 μmol, 95%) of a mixture of cycloadducts. **22C**:**22D** = 6.4:1.

General cycloaddition procedure **B** (10 mol% catalyst) was followed for substrate **21** (14.4 mg, 44.7 μmol) leading after 2 h to the isolation of 14.1 mg (43.7 μmol, 98%) of a mixture of cycloadducts. **22C**:**22D** = 1.5:1. Separation of the regioisomers was achieved utilizing silver nitrate impregnated silica gel flash column chromatography (20-50% ethyl acetate in hexanes).

Physical Data for Substrate 22C:



^{1}H-NMR (500 MHz, $CDCl_3$/TMS):

δ = 5.61 (ddd, *J* = 11.7 Hz, *J* = 4.4 Hz, *J* = 2.4 Hz, 1H), 5.52 (ddd, *J* = 11.7 Hz, *J* = 2.4 Hz, *J* = 2.3 Hz, 1H), 3.73 (s, 3H), 3.73 (s, 3H), 3.70 (s, 3H), 3.55-3.60 (m, 1H), 3.14 (dm, *J* = 12.5 Hz, 1H), 2.98 (d, *J* = 16.3 Hz, 1H), 2.86 (d, *J* = 16.3 Hz, 1H), 2.82 (t, *J* = 13.0 Hz, 1H), 2.73 (ddd, *J* = 12.6 Hz, *J* = 8.4 Hz, *J* = 1.4 Hz, 1H), 2.15 (dt, *J* = 13.6 Hz, *J* = 2.2 Hz, 1H), 1.95 (dd, *J* = 12.8 Hz, *J* = 10.8 Hz, 1H), 1.75 (s, 3H), ppm.

^{13}C-NMR (125 MHz, $CDCl_3$):

δ = 174.33, 171.84, 137.78, 132.51, 127.53, 126.29, 58.41, 52.80, 52.73, 52.03, 42.21, 41.74, 39.93, 38.79, 34.96, 20.74 ppm.

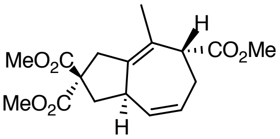
IR (FT-IR, film):

ν = 2963.5 (w), 2924.4 (w), 2858.8 (w), 1734.0 (s), 1437.3 (w), 1260.6 (m), 1204.4 (w), 1167.7 (w), 1089.2 (w), 1026.4 (w), 796.0 (w) cm^{-1}.

HRMS:

Calculated for $C_{17}H_{22}O_6$: 322.14164 Found: 322.14119

Physical Data for Substrate 22D:



^{1}H-NMR (500 MHz, $CDCl_3$/TMS):

δ = 5.60-5.65 (m, 1H), 5.36 (dd, *J* = 9.7 Hz, *J* = 1.1 Hz, 1H), 3.75 (s, 3H), 3.73 (s, 3H), 3.67 (s, 3H), 3.47-3.53 (m, 1H), 3.03 (d, *J* = 16.8 Hz, 1H), 2.98-3.05 (m, 1H), 2.95 (d, *J* = 16.8 Hz, 1H), 2.64-2.73 (m, 2H), 2.31 (ddd, *J* = 16.1 Hz, *J* = 7.0 Hz, *J* = 2.9 Hz, 1H), 1.98 (dd, *J* = 12.5 Hz, *J* = 11.4 Hz, 1H), 1.59 (s, 3H), ppm.

^{13}C-NMR (125 MHz, $CDCl_3$):

δ = 173.94, 171.99, 171.84, 137.67, 132.17, 126.74, 125.96, 57.96, 52.79, 52.76, 51.87, 48.55, 41.62, 40.14, 40.00, 28.38, 21.86 ppm.

IR (FT-IR, film):

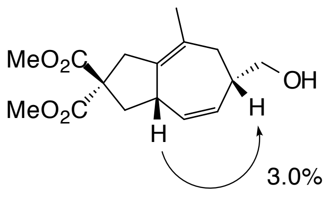
ν = 3005.3 (w), 2955.8 (w), 2921.6 (w), 2848.3 (w), 1735.2 (s), 1437.5 (m), 1260.6 (m), 1204.4 (m), 1167.7 (m), 1073.5 (w), 1026.4 (w), 963.6 (w), 801.3 (w) cm^{-1}.

HRMS:

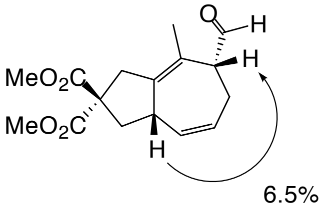
Calculated for $C_{17}H_{22}O_6$: 322.14164 Found: 322.14079

Regio- and Stereochemical Assignments

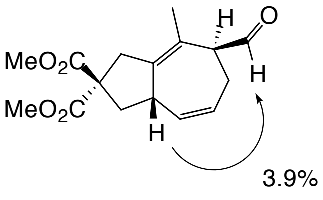
The regiochemistries of the cycloadducts were assigned on the basis of decoupling experiments and 2-dimensional NMR experiments (COSY). Stereochemical assignments are based on extensive NOESY experiments and/or 1D nOe experiments, as indicated below. Compound **16C** was assigned as the diastereomer of **4A**, while chemical correlation was able to relate **4A** to **6A** and **8A**; **4B** to **6B** and **10B**; **12A/B** to **14A/B**; **16C** to **18C**, and **16D** to **20D**.



4A

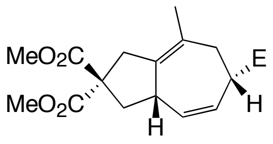


10B

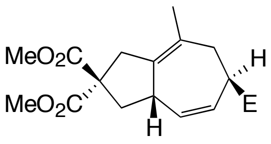


20D

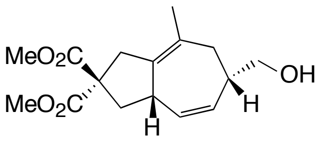
Compounds for n.O.e. experiments:



14A

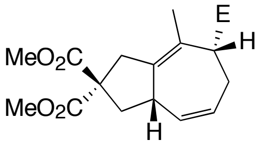


22C

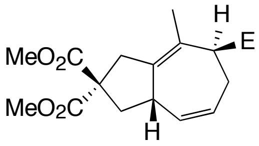


4A

E = COOMe
or COOEt



14B



22D

Compounds for NOESY experiments: