An Intramolecular [2+2]-Photocycloaddition/Thermal Fragmentation Approach toward 5-8-5 Ring Systems

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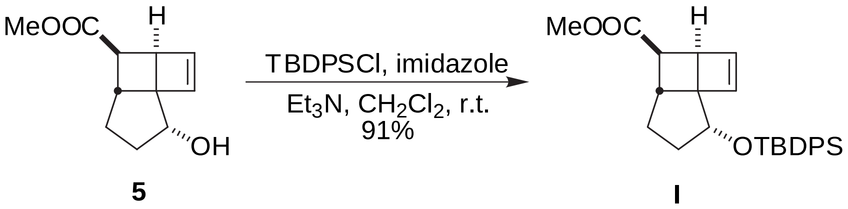
Supporting Information

Starting materials and reagents were purchased from commercial suppliers and used without further purification except the following: Benzene and Et_2O were distilled over sodium and benzophenone under N_2 atmosphere. Dichloromethane and pentane were distilled from CaH_2 under N_2 atmosphere. Hexanes, pentane, diethyl ether and dichloromethane used in chromatography were distilled before use.

All oxygen- or moisture-sensitive reactions were carried out under N_2 or Ar atmosphere in oven-dried (140 ˚C, $\geq$ 4 h) glassware. Air- or moisture-sensitive liquids were transferred by syringe or cannula and were introduced into the reaction flasks through rubber septa or through a stopcock under N_2 or Ar positive pressure. Air- or moisture-sensitive solids were transferred in a glove box. Degassing refers to a flow of dry N_2(g) bubbling through reaction solvent for 30 min. Unless otherwise stated, reactions were stirred with a PTFE-covered stir bar. Concentration refers to the removal of solvent using a Büchi rotatory evaporator followed by use of a vacuum pump at approximately 1 torr. Heavy wall sealed tubes with Teflon screw caps, purchased from Ace Glass Incorporated, were used for all thermolysis reactions. Thermolysis tubes were immersed about 50 mm into a silicone oil bath heated by a Therm-O-Watch™ sold by I^2R. Silica gel column chromatography refers to flash chromatography and was performed using Baxter brand silica gel 60Å (230-400 Mesh ASTM).

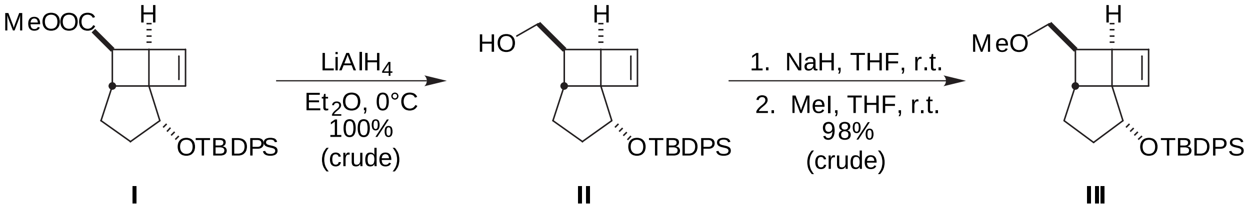
Proton nuclear magnetic resonance spectra (**^{1}H-NMR**) were measured on either a Varian Unity-300 instrument (300 MHz), a Varian Gemini-400 instrument (400 MHz), or a Varian Gemini-500 instrument (500 MHz). Chemical shifts are reported in ppm down field from tetramethylsilane with the solvent reference as the internal standard ($CHCl_3$: δ 7.26 ppm). Data is reported as follows: chemical shift, integration, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, qi = quintet, sex = sextet, br = broad, m = multiplet), and coupling constants (Hz). **^{13}C-NMR** spectra were recorded on either a Varian Unity-300 instrument (75 MHz), a Varian Gemini-400 instrument (100 MHz), or a Varian Gemini-500 instrument (125 MHz) with complete proton decoupling. Chemical shifts are reported in ppm down field from tetramethylsilane with the solvent as the internal reference ($CDCl_3$: δ 77.23 ppm). Infrared spectra (**IR**) were measured on either a Perkin Elmer 1310 Infrared spectrometer or a Nicolet 210 FT-

Infrared spectrometer and are reported in wave numbers (cm^{-1}). Some bands are characterized as broad (br), strong (s), medium (m) or weak (w). Elemental analyses (**Anal**) were performed by Robertson Microlit Laboratories, Inc., Madison, NJ and are reported in percent atomic abundance.



tert-Butylchlorodiphenylsilane (1.87 mL, 7.19 mmol) was added slowly to a solution of **5** (559 mg, 2.88 mmol), imidazole (399 mg, 5.86 mmol) and triethylamine (0.80 mL, 5.74 mmol) in CH_2Cl_2 (7.0 mL) at room temperature. The reaction mixture was stirred for 2 hours and then diluted with Et_2O (20 mL) and water (30 mL). The two layers were separated and the aqueous layer was extracted with Et_2O (2 x 20 mL). The combined organic extracts were washed with sat. NaCl (aq), dried over $MgSO_4$ and concentrated *in vacuo*. The product was purified by silica gel chromatography (3% Et_2O/pentane) to give compound **I** (1.13 g, 2.62 mmol) in 91% yield.

Protected alcohol I: **^{1}H-NMR** ($CDCl_3$, 400 MHz): δ 7.63-7.67 (4H, m), 7.33-7.44 (6H, m), 6.14 (1H, d, *J* = 2.4 Hz), 5.96 (1H, dd, *J* = 2.2, 1.4 Hz), 4.20 (1H, t, *J* = 8.0 Hz), 3.65 (3H, s), 3.56 (1H, d, *J* = 8.4 Hz), 2.80 (1H, dd, *J* = 8.6, 4.6 Hz), 2.46 (1H, dd, *J* = 7.8, 4.8 Hz), 1.78-1.84 (2H, m), 1.55-1.70 (2H, m), 1.03 (9H, s). **^{13}C-NMR** ($CDCl_3$, 100 MHz): δ 174.3, 140.5, 136.5, 136.3, 136.0, 134.8, 134.1, 129.8, 129.8, 127.7, 127.6, 73.8, 61.5, 56.3, 42.5, 41.3, 40.6, 33.4, 27.4, 27.1, 19.5. **IR** (NaCl, thin film): 3073 (w), 2962 (m), 2931 (m), 2856 (m), 1734 (s), 1433 (m), 1246 (m), 1118 (s) cm^{-1}. **Anal:** Calcd for $C_{27}H_{32}O_3Si$: C, 74.96; H, 7.46. Found: C, 74.98; H, 7.62.

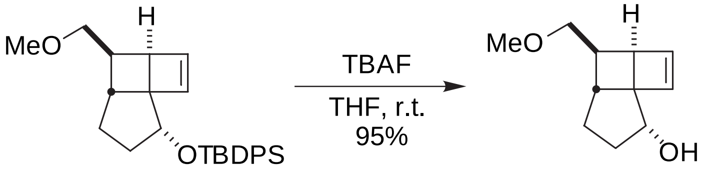


To a suspension of LiAlH$_4$ (200 mg, 5.27 mmol) in Et$_2$O (10 mL) at 0 °C, a solution of **I** (1.13 g, 2.61 mmol) in Et$_2$O (20 mL) was added slowly. The reaction mixture was stirred 0 °C for 40 minutes and then quenched cautiously by the subsequent addition of water (0.2 mL), 15% NaOH (aq) (0.2 mL) and water (0.6 mL). The resulting suspension was warmed to room temperature and stirred for one hour. The suspension was filtered through a fritted funnel and the filtrate was concentrated *in vacuo* to give alcohol **II** (1.06 g, 2.61 mmol). The product was used in the next step without purification.

Alcohol II: ^{1}**H-NMR** (CDCl$_3$, 500 MHz): δ 7.65-7.67 (4H, m), 7.40-7.44 (2H, m), 7.34-7.38 (4H, m), 6.19 (1H, d, J = 2.5 Hz), 5.96 (1H, d, J = 1.0 Hz), 4.19 (1H, dd, J = 10.0, 6.5 Hz), 3.65 (1H, dd, J = 10.3, 8.8 Hz), 3.53 (1H, dd, J = 10.5, 7.0 Hz), 3.39 (1H, d, J = 8.5 Hz), 2.11 (1H, ddd, J = 15.0, 7.5, 4.5 Hz), 1.77-1.89 (3H, m), 1.61 (1H, td, J = 13.0, 6.8 Hz), 1.54 (1H, dd, J = 13.3, 6.8 Hz), 1.19 (1H, br, s), 1.03 (9H, s). ^{13}**C-NMR** (CDCl$_3$, 125 MHz): δ 140.7, 136.4, 136.3, 136.1, 134.9, 134.4, 129.73, 129.68, 127.63, 127.59, 74.1, 64.8, 61.2, 41.5, 40.7, 38.6, 33.5, 27.7, 27.2, 19.5.

To a suspension of NaH (318 mg, 13.3 mmol) in THF (10 mL), a solution of **II** (1.06 g, 2.61 mmol) in THF (20 mL) was added slowly at room temperature. The reaction mixture was stirred for 2 hours and a solution of MeI in MTBE (2.0 M, 2.62 mL, 5.24 mmol) was added. The reaction mixture was stirred for 16 hours and then quenched cautiously with water at 0 °C. The solution was diluted with water (30 mL) and extracted with Et$_2$O (3 x 20 mL). The combined ethereal layers were washed with sat. NaCl (aq), dried over MgSO$_4$ and concentrated *in vacuo* to afford methyl ether **III** (1.07 g, 2.55 mmol) in 98% yield. The product was used in the next step without purification.

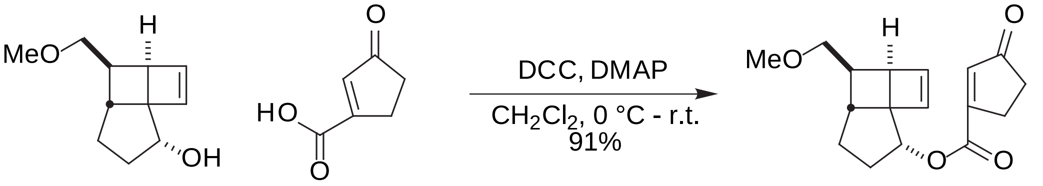
Methyl ether III: ^{1}**H-NMR** (CDCl$_3$, 400 MHz): δ 7.64-7.67 (4H, m), 7.33-7.43 (6H, m), 6.16 (1H, d, J = 2.4 Hz), 5.95 (1H, dd, J = 2.4, 1.6 Hz), 4.17 (1H, dd, J = 9.4, 6.2 Hz), 3.40 (1H, t, J = 9.2 Hz), 3.38 (1H, d, J = 7.2 Hz), 3.31 (3H, s), 3.24 (1H, dd, J = 9.4, 7.8 Hz), 2.16 (1H, ddd, J = 12.4, 7.6, 4.6 Hz), 1.75-1.90 (3H, m), 1.59 (1H, td, J = 13.2, 6.8 Hz), 1.49-1.56 (1H, m), 1.02 (9H, s). ^{13}**C-NMR** (CDCl$_3$, 100 MHz): δ 140.3, 136.6, 136.1, 135.9, 134.3, 129.6, 129.5, 127.5, 127.4, 74.7, 74.2, 61.4, 58.9, 41.1, 39.2, 39.0, 33.6, 27.9, 27.3, 19.6.



III **6**

A solution of **III** (223 mg, 0.53 mmol) and tetrabutylammonium fluoride trihydrate (830 mg, 2.63 mmol) in THF (5.0 mL) was stirred at room temperature for 16 hours. The reaction mixture was diluted with water (15 mL) and then extracted with CH_2Cl_2 (3 x 5 mL). The organic layers were combined and washed with sat. NaCl (aq), dried over $MgSO_4$ and concentrated *in vacuo*. The concentrate was purified by silica gel chromatography (20% EtOAc/pentane) to give **6** (91 mg, 0.50 mmol) in 95% isolated yield.

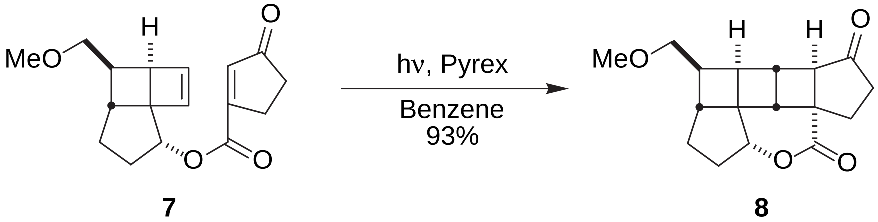
Alcohol 6: **^{1}H-NMR** ($CDCl_3$, 400 MHz): δ 6.27 (1H, dd, *J* = 2.4, 1.2 Hz), 6.25 (1H, d, *J* = 2.8 Hz), 4.22 (1H, dt, *J* = 9.6, 4.8 Hz), 3.41 (1H, t, *J* = 9.2 Hz), 3.31 (3H, s), 3.27 (1H, dd, *J* = 9.6, 7.2 Hz), 3.22 (1H, d, *J* = 7.6 Hz), 2.16 (1H, ddd, *J* = 15.6, 8.4, 4.4 Hz), 2.08 (1H, dt, *J* = 11.2, 5.6 Hz), 1.92 (1H, dd, *J* = 7.8, 4.6 Hz), 1.70-1.85 (2H, m), 1.64 (1H, dd, *J* = 11.4, 5.8 Hz), 1.37 (1H, d, *J* = 4.4 Hz). **^{13}C-NMR** ($CDCl_3$, 100 MHz): δ 139.5, 138.1, 74.3, 73.3, 61.8, 58.9, 40.5, 39.3, 38.8, 33.2, 27.9. **IR** (NaCl, thin film): 3412 (br, s), 3094 (w), 3028 (m), 2935 (s), 2856 (s), 2802 (s), 1455 (m), 1314 (m), 1102 (s) cm^{-1}. **Anal:** Calcd for $C_{11}H_{16}O_2$: C, 73.30; H, 8.95. Found: C, 73.31; H, 8.95.



6 **7**

To a solution of alcohol **6** (56 mg, 0.31 mmol), 3-oxocyclopentenecarboxylic acid (62 mg, 0.5 mmol) and 4-(dimethylamino)pyridine (8 mg, 0.066 mmol) in CH_2Cl_2 (2.5 mL), 1,3-dicyclohexylcarbodiimide (89 mg, 0.43 mmol) in CH_2Cl_2 (1.5 mL) was added at 0 °C. The reaction was warmed to room temperature and stirred for 1.5 hours. The resulting pale yellow suspension was filtered through a short column of silica gel (1.5 cm) and Celite (1.5 cm) using 50% Et_2O/CH_2Cl_2 as an eluent. The filtrate was concentrated and purified by silica gel chromatography (20% EtOAc/hexanes) to give the desired ester **7** (82 mg, 0.28 mmol) in 91% yield.

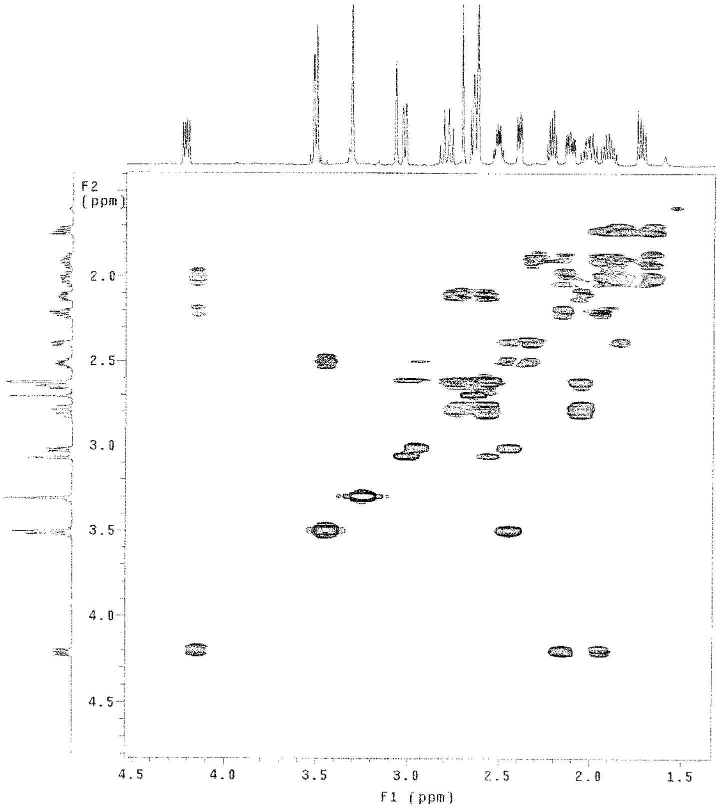
Ester 7: ^{1}**H-NMR** ($CDCl_3$, 400 MHz): δ 6.66 (1H, t, *J* = 2.2 Hz), 6.20 (1H, dd, *J* = 2.4, 1.2 Hz), 6.11 (1H, d, *J* = 2.4 Hz), 5.27 (1H, dd, *J* = 9.2, 6.4 Hz), 3.37 (1H, t, *J* = 9.0 Hz), 3.27 (3H, s), 3.24 (1H, dd, *J* = 9.4, 7.0 Hz), 3.19 (1H, d, *J* = 7.6 Hz), 2.75-2.79 (2H, m), 2.46 (2H, dd, *J* = 5.1, 4.5 Hz), 2.15-2.20 (2H, m), 1.96 (1H, dd, *J* = 7.6, 4.4 Hz), 1.85-1.92 (2H, m), 1.71-1.73 (1H, m). ^{13}**C-NMR** ($CDCl_3$, 100 MHz): δ 209.0, 164.4, 164.3, 139.5, 138.1, 137.1, 75.9, 74.2, 59.2, 59.0, 41.7, 39.2, 39.1, 35.9, 30.0, 28.1, 27.8. **IR** (NaCl, thin film): 3097 (w), 3027 (w), 2940 (s), 2861 (s), 1723 (s), 1716 (s), 1443 (m), 1224 (s), 1163 (s), 1106 (m) cm^{-1}. **Anal:** Calcd for $C_{17}H_{20}O_4$: C, 70.81; H, 6.99. Found: C, 70.77; H, 7.19.

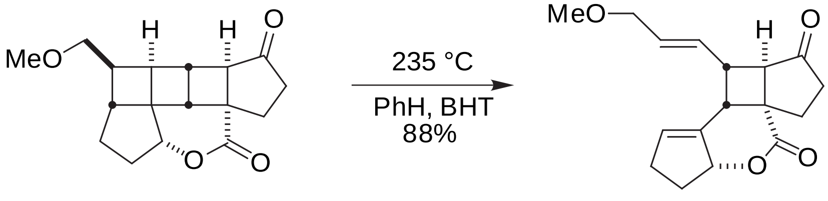


Ester **7** (100 mg, 0.35 mmol) was dissolved in benzene (70 mL) in a round bottom flask equipped with a condenser. The solution was irradiated with a 450 W Hanovia medium pressure mercury lamp through a borosilicate immersion well and 4 mm borosilicate filter for 7 hours. The solution was then concentrated *in vacuo* and the concentrate was purified by silica gel chromatography (100% Et_2O) to give photoadduct **8** in 93% yield (93 mg, 0.33 mmol).

Photoadduct 8: ^{1}**H-NMR** ($CDCl_3$, 400 MHz): δ 4.22 (1H, dd, *J* = 10.8, 6.2 Hz), 3.51 (2H, d, *J* = 7.8 Hz), 3.31 (3H, s), 3.08 (1H, t, *J* = 2.2 Hz), 3.03 (1H, d, *J* = 8.4 Hz), 2.80 (1H, dt, *J* = 12.8, 11.0 Hz), 2.72 (1H, app. s), 2.64-2.67 (1H, m), 2.62-2.63 (2H, m), 2.52 (1H, ddd, *J* = 15.2, 7.6, 3.6 Hz), 2.40 (1H, dd, *J* = 8.0, 3.6 Hz), 2.23 (1H, dt, *J* = 11.6, 6.0 Hz), 2.12 (1H, ddd, *J* = 12.8, 6.4, 4.0 Hz), 1.97-2.08 (1H, m), 1.91 (1H, tdd, *J* = 15.2, 8.4, 6.8 Hz), 1.74 (1H, dd, *J* = 13.6, 7.6 Hz). ^{13}**C-NMR** ($CDCl_3$, 125 MHz): δ 216.5, 174.3, 80.5, 72.9, 59.9, 59.1, 49.3, 47.0, 43.3, 41.9, 40.5, 38.5, 37.1, 33.8, 32.1, 29.4, 29.4. **IR** (NaCl, thin film): 2935 (m), 2869 (m), 2821 (w), 1735 (s), 1717 (s), 1149 (m), 1089 (m) cm^{-1}. **Anal:** Calcd for $C_{17}H_{20}O_4$: C, 70.81; H, 6.99. Found: C, 70.62; H, 6.92.

COSY spectrum of 8 ($CDCl_3$, 500 MHz)



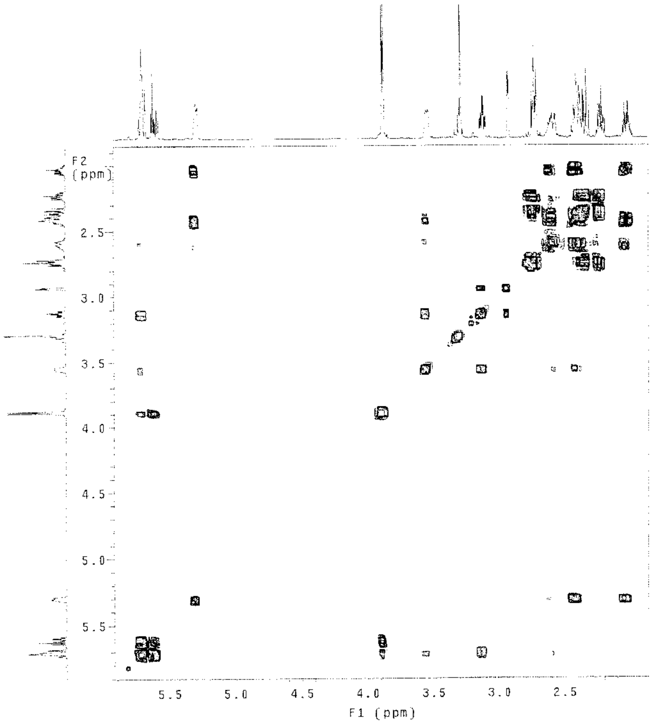


8 11

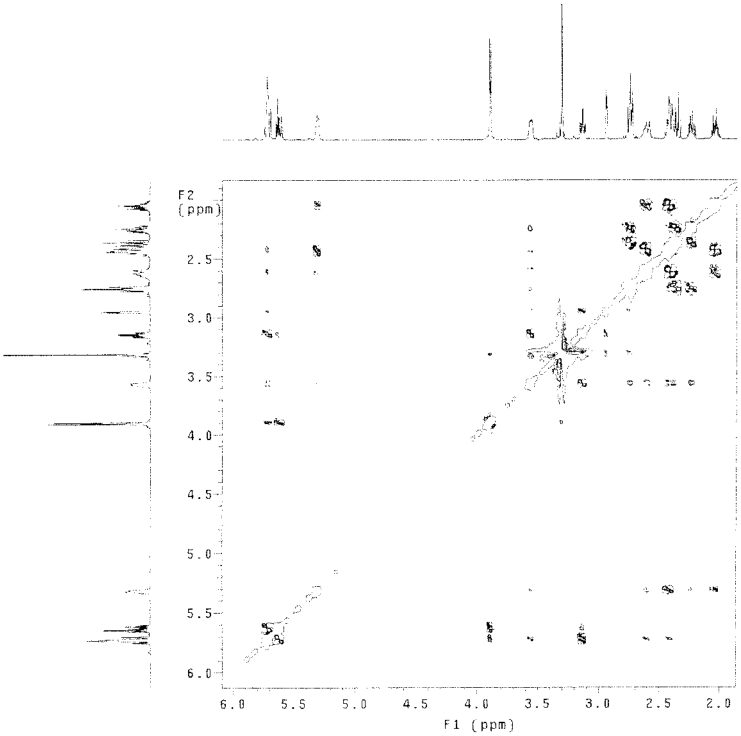
A heavy-walled reaction tube was charged a solution of photoadduct **8** (50 mg, 0.17 mmol) and 2,6-di-*tert*-butyl-4-methylphenol (BHT) (40 mg, 0.18 mmol) in benzene (29 mL). The solution was degassed and the tube was sealed quickly with a PTFE screw cap. The reaction was heated to 235 °C in a silicone oil bath for 3 hours or until the starting material was not observed by TLC (50% EtOAc/pentane). The resulting solution was cooled to room temperature and concentrated *in vacuo*. The concentrate was purified by silica gel chromatography (80% Et_2O/pentane) to afford dialkenyl cyclobutane **11** in 88% yield (44 mg, 0.15 mmol).

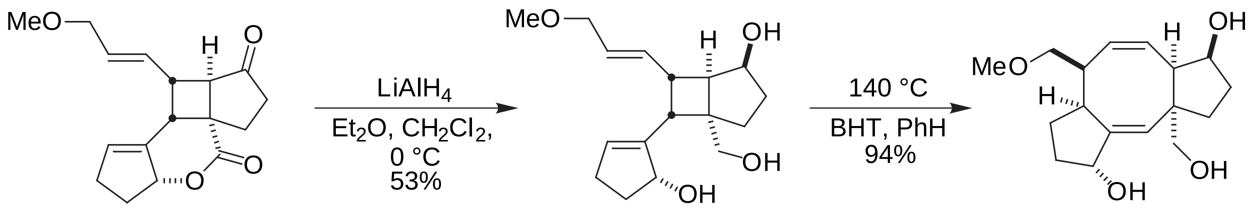
Dialkenyl cyclobutane 11: ^{1}**H-NMR** ($CDCl_3$, 400 MHz): δ 5.70 (1H, br, s), 5.69 (1H, dd, *J* = 14.8, 8.8 Hz), 5.59 (1H, dt, *J* = 15.2, 5.6 Hz), 5.28-5.30 (1H, br m), 3.87 (2H, d, *J* = 5.6 Hz), 3.54 (1H, dd, *J* = 8.8, 3.2 Hz), 3.28 (3H, s), 3.11 (1H, td, *J* = 8.8, 4.0 Hz), 2.92 (1H, d, *J* = 4.4 Hz), 2.70-2.75 (2H, m), 2.54-2.63 (1H, m), 2.40-2.43 (1H, m), 2.38 (1H, t, *J* = 9.6 Hz), 2.32 (1H, t, *J* = 9.8 Hz), 2.22 (1H, ddd, *J* = 13.0, 8.0, 4.8 Hz), 2.01 (1H, tt, *J* = 13.2, 4.4 Hz). ^{13}**C-NMR** ($CDCl_3$, 100 MHz): δ 216.3, 175.8, 134.0, 131.3, 131.1, 129.1, 86.9, 72.5, 58.2, 55.3, 47.2, 41.6, 40.7, 37.9, 31.7, 31.6, 29.6. **IR** (NaCl, thin film): 3048 (w), 2983 (m), 2931 (m), 2856 (w), 2825 (w), 1738 (s), 1732 (s), 1448 (w), 1153 (m) cm^{-1}. **Anal:** Calcd for $C_{17}H_{20}O_4$: C, 70.81; H, 6.99. Found: C, 70.53; H, 7.21.

COSY spectrum of 11 ($CDCl_3$, 500 MHz)



NOESY spectrum of 11 ($CDCl_3$, 500 MHz)



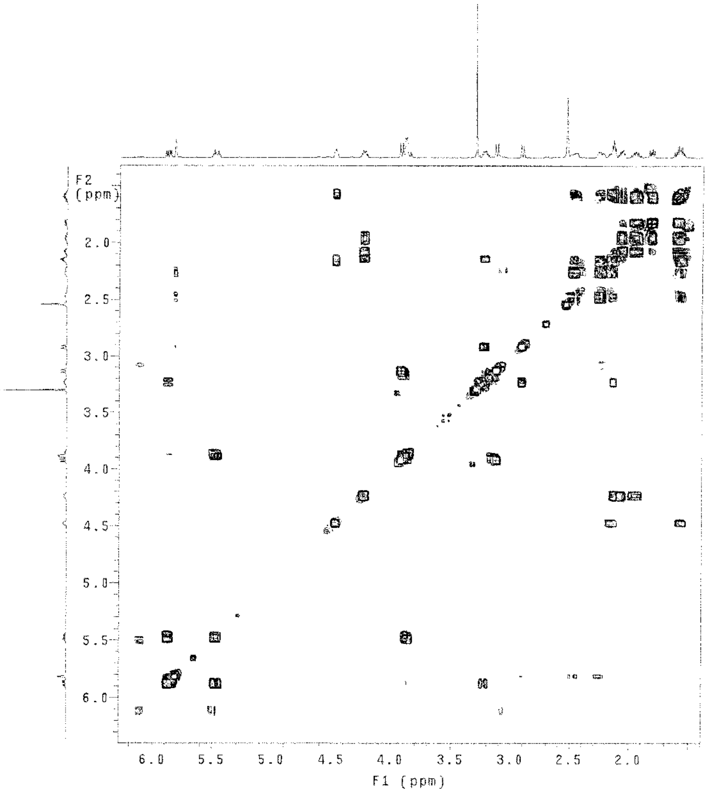


11 IV 13

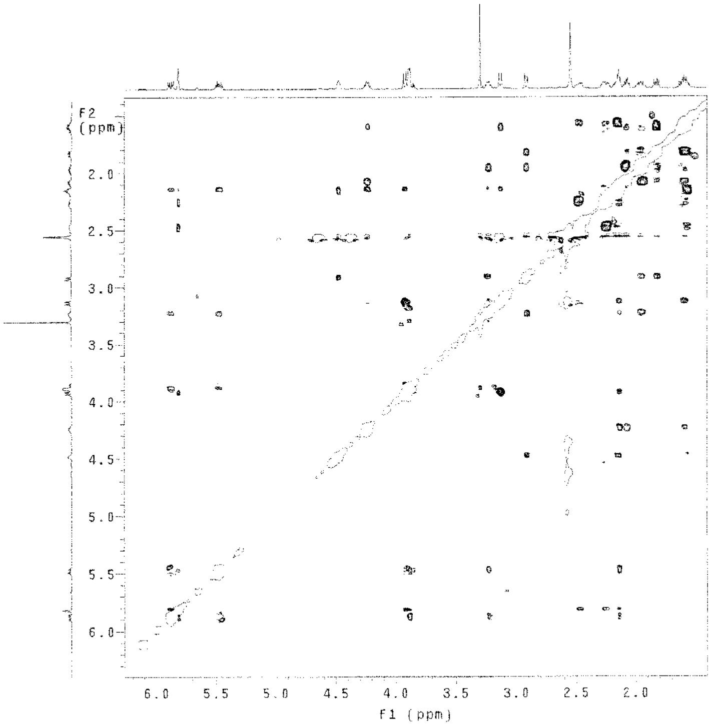
To a solution of **11** (32 mg, 0.11 mmol) in Et_2O/CH_2Cl_2 (3.0 mL/1.2 mL) at 0 °C, a solution of $LiAlH_4$ (1.0 M, 0.58 mL, 0.58 mmol) in Et_2O was added slowly. The resulting cloudy solution was stirred at 0 °C for 1.5 hours. The reaction was quenched by the subsequent addition of water (22 μL), 15% NaOH (aq) (22 μL) and water (66 μL). The suspension was stirred at room temperature for 15 minutes and was filtered. The filtrate was concentrtted *in vacuo* and purified by silica gel chromatography (80% EtOAc/pentane) to afford triol **IV** in 53% yield (18 mg, 0.06 mmol).

Triol IV: ^{1}**H-NMR** (8% $CD_3OD/CDCl_3$, 500 MHz): δ 5.86 (1H, dd, J = 15.5, 6.5 Hz), 5.79 (1H, app. s), 5.45 (1H, dtd, J = 15.0, 6.5, 1.5 Hz), 4.46 (1H, br s), 4.22 (1H, dt, J = 10.0, 7.0 Hz), 3.91 (1H, d, J = 10.5 Hz), 3.87 (1H, dd, J = 18.0, 6.5 Hz), 3.84 (1H, dd, J = 17.5, 6.5 Hz), 3.28 (3H, s), 3.21 (1H, dt, J = 10.0, 6.3 Hz), 3.11 (1H, d, J = 11.0 Hz), 2.90 (1H, d, J = 10.5 Hz), 2.51 (2H, app. s), 2.43-2.49 (1H, m), 2.21-2.27 (1H, m), 2.11-2.17 (2H, m), 2.06 (1H, dt, J = 12.5, 6.5 Hz), 1.94 (1H, dtd, J = 10.5, 12.0, 7.0 Hz), 1.81 (1H, dd, J = 13.3, 7.3 Hz), 1.60 (1H, dd, J = 13.0, 6.5 Hz), 1.55 (1H, dt, J = 13.5, 5.0 Hz). ^{13}**C-NMR** (8% $CD_3OD/CDCl_3$, 125 MHz): δ 142.8, 136.9, 131.2, 125.4, 81.7, 73.6, 73.4, 65.6, 58.0, 50.6, 47.1, 42.9, 33.4, 33.3, 33.1, 32.7, 31.3. **IR** (NaCl, thin film): 3258 (br, s), 2957 (m), 2927 (m), 2852 (m), 1458 (m), 1346 (m), 1122 (m), 1097 (s) cm^{-1}. **Anal:** Calcd for $C_{17}H_{26}O_4$: C, 69.36; H, 8.90. Found: C, 69.08; H, 8.68.

COSY spectrum of IV (8% $CD_3OD/CDCl_3$, 500 MHz)



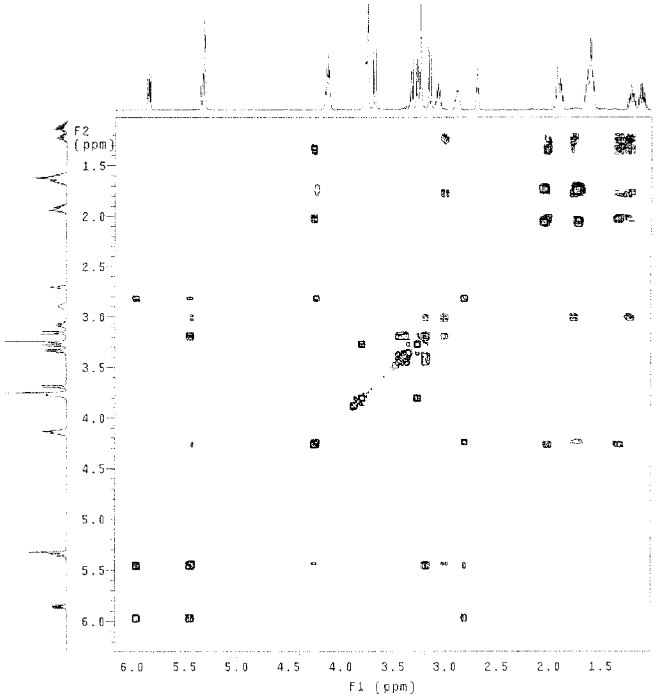
NOESY spectrum of IV (8% $CD_3OD/CDCl_3$, 500 MHz)



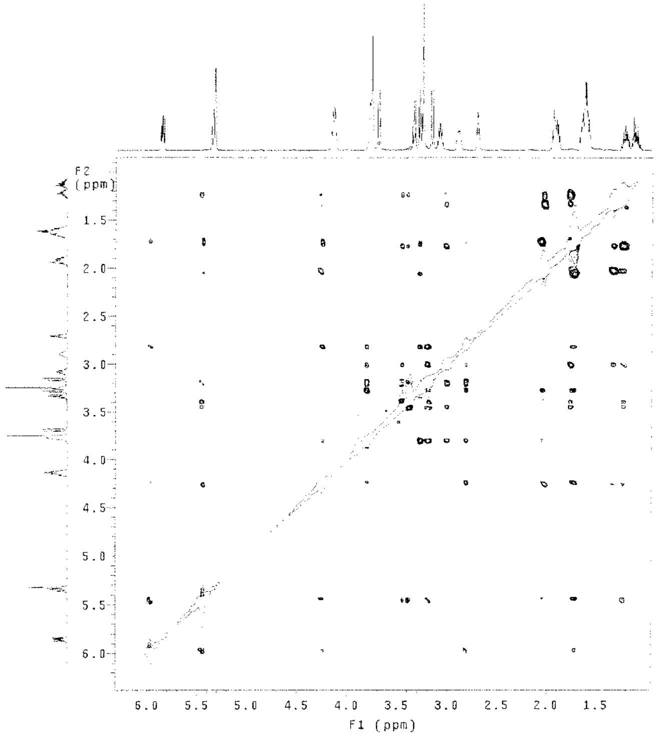
A heavy walled reaction tube was charged with a solution of triol **IV** (14 mg, 0.047 mmol) and BHT (9.7 mg, 0.044 mmol) in benzene (8 mL) under N_2 atmosphere. The tube was sealed quickly with a PTFE screw cap and the reaction mixture was heated to 140 °C in a silicone oil bath for 4 hours. The solution was concentrated *in vacuo* and purified by silica gel chromatography (5% MeOH/CH_2Cl_2)to afford cyclooctadiene triol **13** in 94% yield (13 mg, 0.044 mmol).

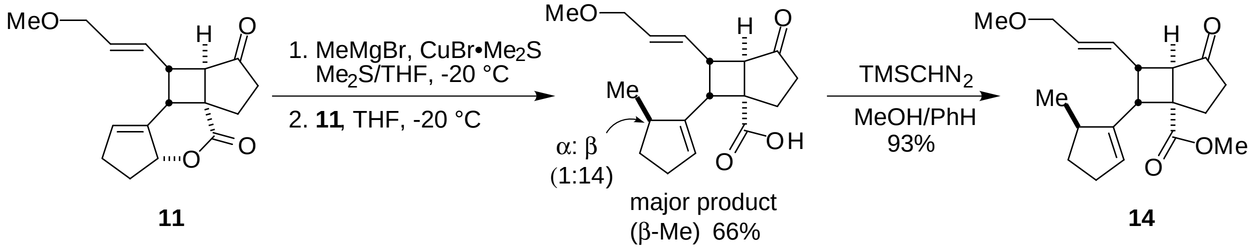
Cyclooctadiene triol 13: **^{1}H-NMR** (8% $CD_3OD/CDCl_3$, 500 MHz): δ 5.85 (1H, dd, *J* = 10.3, 6.3 Hz), 5.34 (1H, td, *J* = 10.3, 2.5 Hz), 5.32 (1H, app. s), 4.11-4.16 (2H, m), 3.72-3.77 (2H, m), 3.75 (1H, app. s), 3.69 (1H, d, *J* = 10.5 Hz), 3.34 (1H, dd, *J* = 9.0, 7.0 Hz), 3.27 (1H, t, *J* = 8.3 Hz), 3.24 (3H, s), 3.16 (1H, d, *J* = 11.0 Hz), 3.08 (1H, dt, *J* = 16.0, 7.5 Hz), 2.87-2.92 (1H, m), 2.70 (1H, td, *J* = 6.0, 1.5 Hz), 1.92-1.95 (1H, m), 1.91 (1H, dt, *J* = 11.0, 7.0 Hz), 1.58-1.68 (4H, m), 1.22 (1H, tt, *J* = 12.3, 7.3 Hz), 1.12 (1H, qd, *J* = 12.0, 6.6 Hz). **^{13}C-NMR** ($CDCl_3$, 100 MHz): δ 149.0, 131.0, 130.6, 130.3, 77.6, 75.2, 74.9, 68.0, 59.2, 53.4, 49.9, 44.1, 39.6, 36.1, 33.6, 32.9, 24.9. **IR** (NaCl, thin film): 3369 (s), 2918 (s), 2864 (s), 1634 (m), 1460 (m), 1187 (m) 1103(s), 731 (m). **Anal:** Calcd for $C_{17}H_{26}O_4$: C, 69.36; H, 8.90. Found: C,69.52; H, 8.68.

COSY spectrum of 13 (8% $CD_3OD/CDCl_3$, 500 MHz)



NOESY spectrum of 13 (8% $CD_3OD/CDCl_3$, 500 MHz)



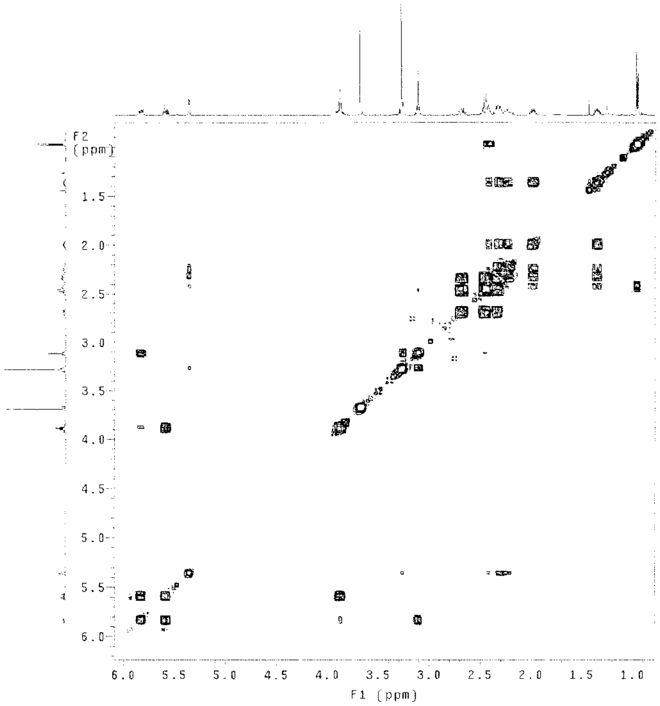


In a Schlenk flask, copper (I) bromide-dimethyl sulfide complex (140 mg, 0.68 mmol) was dissolved in a 3:7 mixture of Me_2S/THF (2.4 mL/5.6 mL) under N_2 atmosphere. The solution was cooled to -20 ℃ and then a solution of MeMgBr in toluene/THF (0.81 M, 0.84 mL) was added. The resulting bright yellow slurry was stirred at the same temperature for 1 hour. A solution of dialkenyl cyclobutane **11** (40 mg, 0.14 mmol) in THF (4.0 mL) was added slowly to the cuprate solution. The reaction was stirred at -20 °C for 16 hours and then quenched by the addition of sat. NH_4Cl solution (5 mL). The solution was warmed to room temperature and stirred vigorously in air for 4 hours. The blue biphasic solution was extracted with CH_2Cl_2 (3 x 5 mL). The combined organic layers were washed with brine, dried over Na_2SO_4 and concentrated *in vacuo*. The diastereomeric ratio of the crude products was found to be 14:1 by ^{1}H-NMR. The major product was isolated with a short silica gel column (15% Et_2O/CH_2Cl_2 with 1 drop acetic acid/100 mL of the solvent mixture) in 66% yield (28 mg, 0.092 mmol).

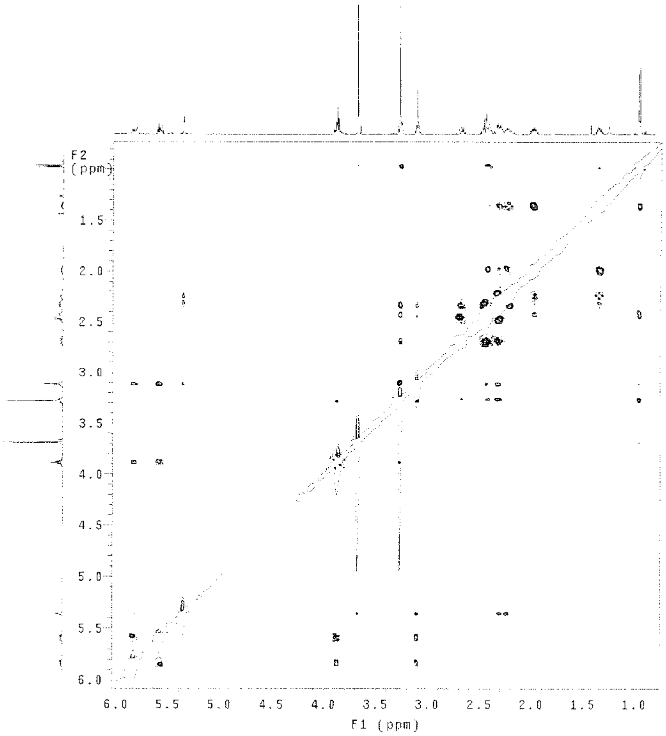
The carboxylic acid was dissolved in a 3:1 mixture of benzene/methanol (3.0 mL/1.0 mL) under N_2 atmosphere at room temperature. A 2.0 M solution of trimethylsilyldiazomethane (110 μL, 0.22 mmol) was added slowly. After the evolution of gas bubbles ceased, the solution was stirred for another 15 minutes and then concentrated *in vacuo*. The concentrate was purified by silica gel chromatography (15% EtOAc/pentane) to give methyl ester **14** in 93% yield (27.2 mg, 0.085 mmol) (61% for 2 steps from dialkenylcyclobutane **11**).

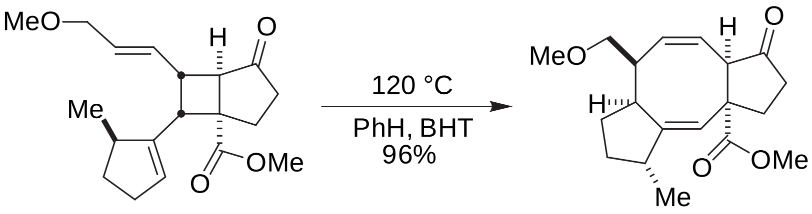
Methyl ester 14: ^{1}H-NMR ($CDCl_3$, 500 MHz): δ 5.84 (1H, dd, *J* = 15.3, 7.8 Hz), 5.59 (1H, dt, *J* = 15.5, 6.0 Hz), 5.36 (1H, app. s), 3.90 (1H, dd, *J* = 13.0, 6.0 Hz), 3.86 (1H, dd *J* = 12.5, 6.5 Hz), 3.69 (3H, s), 3.28 (3H, s), 3.25-3.27 (1H, m), 3.12 (2H, dt, *J* =12.5, 6.3 Hz), 2.65-2.72 (1H, m), 2.41-2.51 (3H, m), 2.30-2.35 (2H, m), 2.21-2.28 (1H, m), 1.99 (1H, dtd, *J* = 12.5, 8.5, 5.5 Hz), 1.36 (1H, dtd, *J* = 12.5, 9.0, 6.0 Hz), 0.97 (3H, d, *J* = 7.5 Hz). **^{13}C-NMR** ($CDCl_3$, 75 MHz): δ 217.6, 174.4, 144.8, 132.0, 129.1, 124.9, 72.8, 57.8, 52.3, 51.9, 51.8, 46.1, 42.9, 41.2, 38.5, 32.1, 32.06, 31.4, 19.2. **IR** (NaCl, thin film): 3060 (w), 2942 (s), 2874 (s), 2734 (w), 1742 (s), 1724 (s), 1469 (m), 1434 (m), 1203 (s), 1113 (s) cm^{-1}. **Anal:** Calcd for $C_{19}H_{26}O_4$: C, 71.67; H, 8.23. Found: C, 71.43; H, 8.34.

COSY spectrum of 14 ($CDCl_3$, 500 MHz)



NOESY spectrum of 14 ($CDCl_3$, 500 MHz)



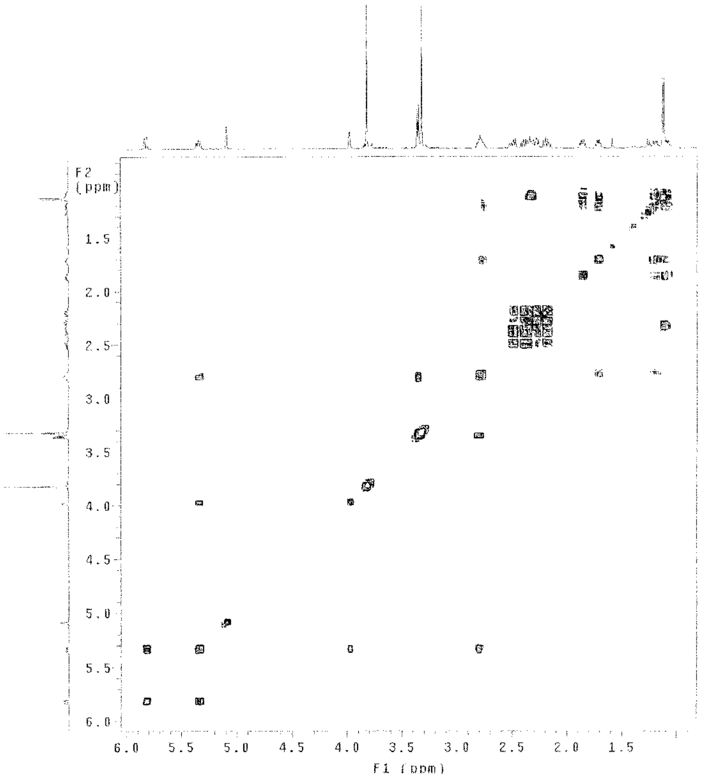


14 **15**

To a heavy walled reaction tube, a solution of methyl ester **14** (13.6 mg, 0.043 mmol) and BHT (13 mg, 0.059 mmol) in benzene (8.5 mL) was charged under N_2 atmosphere. The tube was sealed quickly with a PTFE screw cap and the reaction mixture was heated to 120 °C in a silicone oil bath for 4 hours. The solution was concentrated *in vacuo* and purified by silica gel chromatography (15% EtOAc/pentane) to afford cyclooctadiene **15** in 96% yield (13 mg, 0.041 mmol).

Cyclooctadiene 15: **^{1}H-NMR** ($CDCl_3$, 400 MHz): δ 5.79 (1H, dd, *J* = 10.6, 2.2 Hz), 5.31 (1H, ddd, *J* = 11.4, 8.2, 2.5 Hz), 5.06 (1H, t, *J* = 2.6 Hz), 3.95 (1H, app. s), 3.80 (3H, s), 3.33 (2H, d, *J* = 7.2 Hz), 3.30 (3H, s), 2.75-2.81 (2H, m), 2.48 (1H, dddd, *J* = 18.4, 9.2, 2.4, 1.4 Hz), 2.38 (1H, dd, *J* = 11.4, 8.6 Hz), 2.29-2.34 (1H, m), 2.25 (1H, dd, *J* = 8.6, 2.6 Hz), 2.16 (1H, ddd, *J* = 12.2, 11.4, 8.6 Hz), 1.83 (1H, dt, *J* = 12.4, 6.4 Hz), 1.69 (1H, dt, *J* = 11.8, 6.4 Hz), 1.18 (1H, qd, *J* = 12.4, 6.2 Hz), 1.11 (3H, d, *J* = 6.8 Hz), 1.07 (1H, qd, *J* = 12.6, 6.2 Hz). **^{13}C-NMR** ($CDCl_3$, 125 MHz): δ 215.8, 176.9, 156.1, 129.1, 127.4, 117.3, 75.2, 58.9, 58.4, 55.3, 53.1, 47.3, 40.9, 38.7, 35.4, 35.1, 33.4, 27.2, 20.9. **IR** (NaCl, thin film): 3014 (w), 2949 (s), 2968 (s), 2737 (w), 1740 (s), 1718 (s), 1439 (m), 1249 (m), 1151 (m), 1105 (m) cm^{-1}. **Anal:** Calcd for $C_{19}H_{26}O_4$: C, 71.67; H, 8.23. Found: C, 71.39; H, 8.01.

COSY spectrum of 15 ($CDCl_3$, 500 MHz)



NOESY spectrum of 15 ($CDCl_3$, 500 MHz)