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Intramolecular Ketene – Allene Cycloadditions

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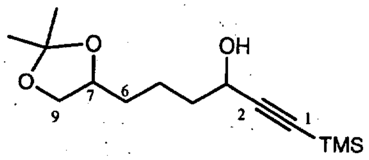
Supporting Information

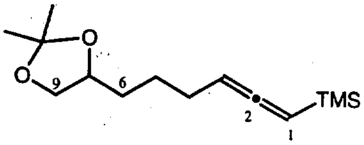
General Methods. ^{1}H and ^{13}C spectra were recorded on either a Varian Unity INOVA-500, a Brucker AM-400 or a Varian VXR-300S spectrometer. ^{1}H NMR spectra are reported in parts per million (δ) relative to residual solvent peaks (7.26 ppm for $CDCl_3$). ^{1}H assignments were made on the basis of ^{1}H-^{1}H coupling constants, ^{1}H-^{1}H correlated spectroscopy (COSY), nuclear Overhauser effect difference spectroscopy (NOE) and distortionless enhancement by polarization transfer (DEPT). ^{13}C NMR spectra are reported in parts per million (δ) relative to residual solvent peaks (77.1 ppm for $CDCl_3$). Infrared spectra were obtained using a Nicolet Impact 410 FTIR. Electon ionization (EI) mass spectra were obtained at 70 eV. Chemical ionization (CI) mass spectra were performed with *iso*-butane, methane or ammonia. Electrospray ionization (ESI) mass spectra were performed with methanol. Ultraviolet spectra (UV) were recorded using an HP 8452A diode array spectrophotometer.

Commercially available reagents were used as purchased without further purification unless noted. THF and Et_2O were distilled from sodium / benzophenone ketyl prior to use under an N_2 atmosphere. Dichloromethane was distilled from CaH_2 under an N_2 atmosphere prior to use. Benzene, toluene and acetonitrile were purified by distillation from CaH_2 under an N_2 atmosphere, and stored over 3Å molecular sieves. All reactions were performed under an atmosphere of dry N_2 unless otherwise noted. All aqueous solutions used for work-up were saturated unless otherwise noted. All flash chromatograpy was performed with silica gel (32-63 microns, 250-450 mesh) which was purched from Scientific Adsorbents, Inc.

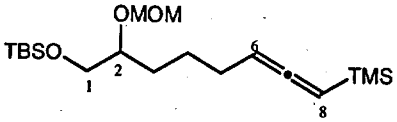
Analytical thin-layer chromatography (TLC) was performed on E. Merck silica gel 60 F_{254} plates (0.25 mm). Compounds were visualized with UV, or by staining with cerium ammonium molybdate, *p*-anisaldehyde or $KMnO_4$ and heating. Gas chromatography analyses (GC) were performed on a HP6890 series GC equipped with an HP-5 column. High perfomance liquid chromatograpy (HPLC) was performed with a Varian HPLC solvent delivery system and a Varian UV-1 absorbance detector. All samples were eluted through a Dynamax 100Å prep silica column at a flow rate of 1 mL per minute.



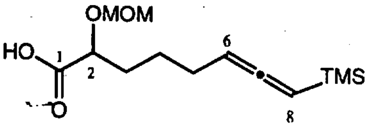
6-(2,2-Dimethyl-[1,3]-dioxolan-4-yl)-1-trimethylsilyl-hex-1-yn-3-ol (8). Trimethylsilyl acetylene (4.5 mL, 32.05 mmol, 1.1 equiv) was dissolved in THF (100 mL), cooled to 0 °C, and treated with *n*-BuLi (19.7 mL of a 1.62 M solution in hexanes, 32.05 mmol, 1.1 equiv). The yellow solution was stirred at 0 °C for 30 min before addition of the aldehyde **18** (5.02 g, 29.14 mmol, 1 equiv) in THF (40 mL), dropwise over 1 h. The bright yellow solution was allowed to warm to rt overnight. The reaction was quenched by addition of 75 mL of 5% H_3PO_4 (aq) and extracted with EtOAc (4 × 100 mL). The combined organic extracts were washed with saturated NH_4Cl (3 × 150 mL), with brine (150 mL), dried ($MgSO_4$), filtered and concentrated on a rotary evaporator. The product **8**, a 1:1 mixture of diastereomers, was isolated as a colorless oil (7.51 g , 27.87 mmol, 95%). $R_f = 0.27$ (SiO_2, 4:1 hexanes:EtOAc); IR (thin film) 3449 (br), 2983, 2171, 1744 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 4.37 (m, 1H, H-3), 4.08 (br m, 2H, H-9 and H-7), 3.51 (dd, 1H, $J = 7, 7$ Hz, H-9), 1.67 (br m, 6H, 2 × H-4, 2 × H-5 and 2 × H-6), 1.41 (m, 3H, CH_3), 1.35 (s, 3H, CH_3), 0.17 (s, 9H, TMS); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 109.4, 107.5, 89.8, 76.5, 70.0, 63.0, 38.1, 33.7, 27.6, 26.4, 22.0, 0.56; HRMS-EI (*m / z*): $[M - CH_3]^+$ calcd for $C_{13}H_{23}O_3Si$, 255.1416; found, 255.1401.



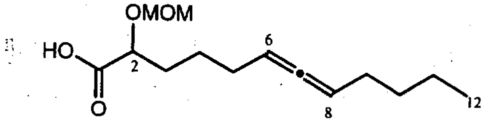
6-(2,2-Dimethyl-[1,3]-dioxolan-4-yl)-hexa-1,2-dienyl-1-trimethylsilane (10). Triphenylphosphine (9.76 g, 37.24 mmol, 1.3 equiv) in THF (100 mL) was cooled −10 °C and treated with diethylazodicarboxylate (5.86 mL, 37.24 mmol, 1.3 equiv). The bright orange solution was stirred at −10 °C for 10 min before addition of the alcohol **8** (7.75 g, 28.65 mmol, 1 equiv) in THF (40 mL) via cannula. After another 10 min at −10 °C, *o*-nitrobenzenesulfonyl hydrazide (10.85 g, 42.97 mmol, 1.5 equiv) in THF (70 mL) was cannulated into the dark orange solution. The reaction was allowed to warm to rt overnight. The solvent was removed on a rotary evaporator. The orange solids were dissolved in EtOAc (200 mL) and added to a stirred solution of hexanes (800 mL). The mixture was filtered through a pad of silica, and the filtrate was concentrated on a rotary evaporator to give the desired product, a 1:1 mixture of diastereomers, as a yellow oil (6.95 g , 27.31 mmol, 95%). The product allene **10** was of sufficient purity for use in the next reaction. $R_f = 0.71$ (SiO_2, 4:1 hexanes:EtOAc); IR (thin film) 2986, 2175, 1942, 1748 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 4.90 (m, 1H, H-1), 4.76 (m, 1H, H-3), 4.05 (br m, 2H, H-7 and H-9), 3.50 (dd, 1H, $J = 7, 7$ Hz, H-9), 2.00 (m, 2H, 2 × H-4), 1.55 (br m, 4H, 2 × H-5 and 2 × H-6), 1.40 (s, 3H, CH_3), 1.35 (s, 3H, CH_3), 0.09 (s, 9H, TMS); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 210.7, 109.2, 83.5, 83.3, 76.6, 70.1, 33.7, 28.4, 27.6, 26.5, 26.4, 0.24; HRMS-EI (*m / z*): $[M]^+$ calcd for $C_{14}H_{26}O_2Si$, 254.1702; found, 254.1695.



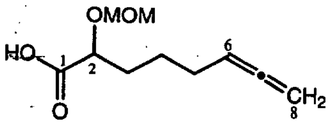
8-(Trimethylsilyl)-1-(*tert*-butyldimethylsilyloxy)-2-methoxymethoxy-octa-6,7-diene (11). The secondary alcohol **20** (8.51 g, 25.88 mmol, 1 equiv) in CH_2Cl_2 (130 mL) was treated with diisopropylethylamine (49.6 mL, 284.7 mmol, 10 equiv) and chloromethyl methyl ether (9.8 mL, 129.4 mmol, 5 equiv). After 16 h at rt, the reaction was quenched with saturated NH_4Cl (75 mL), extracted with CH_2Cl_2 (3 × 200 mL), washed with saturated NH_4Cl (175 mL), with H_2O (175 mL), dried ($MgSO_4$), filtered and concentrated on a rotary evaporator. The product **11** was isolated as a yellow oil (9.36 g, 25.10 mmol, 97%) of sufficient purity for use in the next reaction. $R_f = 0.85$ (SiO_2, 4:1 hexanes:EtOAc); IR (thin film) 2955, 1938 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 4.89 (m, 1H, H-8), 4.78 (br m, 2H, O-CH_2-O and H-6), 4.65 (d, 1H, $J = 7$ Hz, O-CH_2-O), 3.60 (m, 3H, 2 × H-1 and H-2), 3.38 (s, 3H, -OCH_3), 2.05 (m, 2H, 2 × H-5), 1.56 (br m, 4H, 2 × H-3 and 2 × H-4), 0.89 (s, 9H, *t*-Bu), 0.08 (s, 9H, TMS), 0.05 (s, 6H, Si-CH_3); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 210.7, 96.9, 83.8, 83.2, 78.7, 66.5, 56.1, 32.0, 28.6, 26.6, 26.2, 18.9, -0.21; HRMS-EI (*m / z*): $[M - OCH_3]^+$ calcd for $C_{18}H_{37}O_2Si$, 341.2332; found, 341.2307.



2-Methoxymethoxy-8-(trimethylsilyl)-octa-6,7-dienoic acid (12a). The starting material **21** (4.4 g, 17.02 mmol, 1 equiv) was dissolved in DMF (100 mL) and treated with PDC (32.3 g, 85.85 mmol, 5 equiv) and the dark orange solution was stirred at rt. After 18 h, the solution was poured into H_2O (100 mL) and extracted with Et_2O (2 × 250 mL). The aqueous layer was NaCl-saturated and extracted again with Et_2O (2 × 250 mL). The combined organic extracts were washed with brine (300 mL), dried ($MgSO_4$), filtered and concentrated on a rotary evaporator. Purification by flash chromatography (1:1:0.05 hexanes:EtOAc:AcOH) gave the desired product **12a** as a yellow oil (3.13 g, 11.5 mmol, 65%). $R_f = 0.10$ (SiO_2, 4:1 hexanes:EtOAc); IR (thin film) 3172 (br), 2959, 1941, 1728 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 4.91 (m, 1H, H-8), 4.75 (m, 2H, O-CH_2-O and H-6), 4.70 (d, 1H, *J* = 7 Hz, O-CH_2-O), 4.18 (dd, 1H, *J* = 7, 7 Hz, H-2), 3.42 (s, 3H, -OCH_3), 2.00 (m, 2H, 2 × H-5), 1.86 (m, 2H, 2 × H-3), 1.56 (m, 2H, 2 × H-4), 0.08 (s, 9H, TMS); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 210.6, 178.6, 96.9, 83.6, 83.3, 75.8, 56.8, 32.8, 28.1, 25.9, -0.23; HRMS-CI$^-$ (*m* / *z*): $[M - H]^+$ calcd for $C_{13}H_{23}O_4Si$, 271.1366; found, 271.1367.

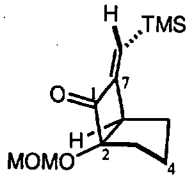


2-Methoxymethoxydodeca-6,7-dienoic acid (12b). The starting material **28** (2.48 g, 10.25 mmol, 1 equiv) was dissolved in DMF (50 mL) and treated with PDC (18.6 g, 49.44 mmol, 5 equiv) and the dark orange solution was stirred at rt. After 20 h, the solution was poured into H_2O (200 mL) and extracted with EtOAc (2 × 250 mL). The aqueous layer was NaCl-saturated and extracted again with EtOAc (2 × 250 mL). The combined organic extracts were washed with brine (250 mL), dried ($MgSO_4$), filtered and concentrated on a rotary evaporator. Purification be flash chromatography (1:1:0.05 hexanes:EtOAc:AcOH) gave the desired product **12b** as a yellow oil (2.11 g, 8.22 mmol, 79%). R_f = 0.10 (SiO_2, 4:1 hexanes:EtOAc); IR (thin film) 3211 (br), 2963, 1961, 1720 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 5.07 (m, 2H, H-6 and H-8), 4.73 (d, 1H, *J* = 7 Hz, O-CH_2-O), 4.69 (d, 1H, *J* = 7 Hz, O-CH_2-O), 4.18 (dd, 1H, *J* = 5, 5 Hz, H-2), 3.42 (s, 3H, OCH_3), 2.00 (m, 4H, 2 × H-5 and 2 × H-9), 1.96 (m, 2H, 2 × H-3), 1.57 (m, 2H, 2 × H-4), 1.35 (m, 4H, 2 × H-10 and 2 × H-11), 0.98 (t, 3H, *J* = 7 Hz, 3 × H-12); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 204.6, 178.8, 96.8, 91.8, 90.7, 75.6, 56.6, 32.7, 32.0, 29.3, 29.1, 25.4, 22.8, 14.5; HRMS-CI$^-$ (*m* / *z*): $[M - H]^+$ calcd for $C_{14}H_{23}O_4$, 255.1596; found, 255.1582.

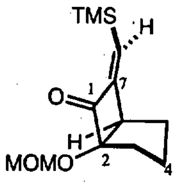


2-Methoxymethoxy-octa-6,7-dienoic acid (12c). The alcohol **22** (2.58 g, 13.85 mmol, 1 equiv) was dissolved in DMF (100 mL) and treated with PDC (25.1 g, 66.71 mmol, 5 equiv). After 24 h at rt, the dark brown solution was poured into H_2O (200 mL) and extracted with EtOAc (2 × 250 mL). The aqueous layer was NaCl-saturated and extracted again with EtOAc (2 × 250 mL). The combined organic extracts were washed with brine (350 mL), and dried ($MgSO_4$), filtered and concentrated on a rotary evaporator. Purification by flash chromatography (2:1:0.05 hexanes:EtOAc:AcOH) gave the desired carboxylic acid **12c** (1.65 g, 8.23 mmol, 59%) as a yellow oil. R_f = 0.10

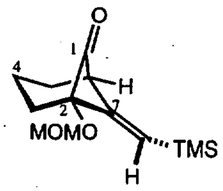
(SiO_2, 1:1 hexanes:EtOAc); IR (thin film) 3060 (br), 2951, 1953, 1732 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 5.08 (quin, 1H, J = 6.75 Hz, H-6), 4.73 (d, 1H, J = 7 Hz, O-CH_2-O), 4.67 (m, 3H, O-CH_2-O and 2 × H-8), 4.19 (dd, 1H, J = 5, 7 Hz, H-2), 3.42 (s, 3H, OCH_3), 2.05 (m, 2H, 2 × H-5), 1.87 (m, 2H, 2 × H-3), 1.59 (m, 2H, 2 × H-4); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 209.2, 178.6, 96.8, 89.9, 75.7, 75.6, 56.7, 32.6, 28.3, 25.2; HRMS–CI$^-$ (m/z): $[M - H]^+$ calcd for $C_{10}H_{15}O_4$, 199.0970; found, 199.0969.



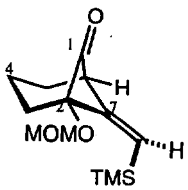
***E*-15a**



***Z*-15a**



***E*-16a**



***Z*-16a**

(*E*)- and (*Z*)-2-(Methoxymethoxy)-7-(trimethylsilyl)-methylidine-bicyclo[3.2.0]heptan-1-one (15a); (*E*)- and (*Z*)-2-(Methoxymethoxy)-7-(trimethylsilyl)-methylidine-bicyclo[3.1.1]heptan-1-one (16a).

Method A: 2-Chloro-*N*-methyl pyridinium iodide (1.74 g, 6.79 mmol, 4 equiv) in CH_3CN (34 mL) was treated with Et_3N (1.94 mL, 13.59 mmol, 8 equiv) and the solution was heated to reflux. The solution gradually turned dark red. The carboxylic acid **12a** (463.1 mg, 1.699 mmol, 1 equiv) in CH_3CN (17 mL) was added over 1 h to the refluxing mixture using an addition funnel. The solution was heated at 67-68 °C overnight. After 24 h at reflux, the solution was cooled to rt and poured into EtOAc (250 mL). The organic layer was washed with saturated $NaHCO_3$ (3 × 125 mL), with brine (2 × 125 mL), dried ($MgSO_4$), filtered and concentrated on a rotary evaporator to give 564.7 mg of crude orange oil. Purification by flash chromatography (SiO_2, 4:1 hexanes:EtOAc) afforded **15a** and **16a** in a 1:3.5 ratio, 253.1 mg (0.994 mmol, 59%).

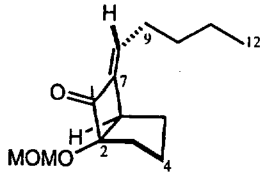
Method B: The carboxylic acid **12a** (11.0 mg, 0.0405 mmol, 1 equiv) was dissolved in benzene (2 mL) and treated with oxalyl chloride (10.5 μL, 0.121 mmol, 3 equiv). After 22 h at rt, the solvent was removed on a rotary evaporator, giving the acid chloride, 11.7 mg (0.040 mmol, 99%) as an orange oil. The acid chloride (11.7 mg, 0.0402 mmol, 1 equiv) was dissolved in benzene (0.4 mL) and treated with Et_3N (14 μL, 0.100 mmol, 2.5 equiv). The solution turned yellow as it was heated to reflux. After 12 h, the solution was cooled to rt and saturated NH_4Cl (2 mL) was added. The resulting mixture was extracted with EtOAc (3 × 8 mL), washed with NH_4Cl (4 mL), with brine (4 mL), dried ($MgSO_4$), filtered and concentrated on a rotary evaporator to give 18.4 mg brown oil. Purification by flash chromatography (SiO_2, 19:1 hexanes:EtOAc) gave 7.1 mg (0.028 mmol, 70%) of **15a** and **16a** in a ratio of 1:3.

Data for **(*E*)-15a**: $R_f = 0.67$ (SiO_2, 4:1 hexanes:EtOAc); ^1H NMR ($CDCl_3$, 500 MHz) δ 6.57 (d, 1H, $J = 2.75$ Hz, H-8), 4.81 (d, 1H, $J = 6$ Hz, O-CH_2-O), 4.77 (d, 1H, $J = 6$ Hz, O-CH_2-O), 3.51 (m, 1H, H-6), 3.36 (s, 3H, OCH_3), 2.26 (m, 1H, H-3), 2.02 (m, 2H, 2 × H-5), 1.83 (m, 2H, H-4 and H-3), 1.57 (m, 1H, H-4), 0.19 (s, 9H, TMS).

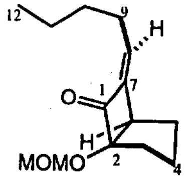
Data for **(*Z*)-15a**: $R_f = 0.67$ (SiO_2, 4:1 hexanes:EtOAc); ^1H NMR ($CDCl_3$, 500 MHz) δ 6.14 (m, 1H, $J = 2.75$ Hz, H-8), 5.01 (d, 1H, $J = 6$ Hz, O-CH_2-O), 4.77 (d, 1H, $J = 6$ Hz, O-CH_2-O), 3.45 (m, 1H, H-6), 3.35 (s, 3H, OCH_3), 1.95 (br m, 6H, 2 × H-3, 2 × H-4 and 2 × H-5), 0.17 (s, 9H, TMS).

Data for (*E*)-**16a**: R_f = 0.67 (SiO_2, 4:1 hexanes:EtOAc); IR (thin film) 2959, 1798, 1658; ^1H NMR ($CDCl_3$, 500 MHz) δ 5.82 (d, 1H *J* = 1.8 Hz, H-8), 4.86 (d, 1H, *J* = 6 Hz, O-CH_2-O), 3.44 (s, 3H, OCH_3), 3.22 (m, 1H, H-6), 2.36 (m, 4H, 2 × H-5 and 2 × H-3), 1.80 (m, 1H, H-4), 1.71 (m, 1H, H-4), 0.12 (s, 9H, TMS); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 206.7, 150.3, 119.1, 94.8, 93.7, 56.9, 56.8, 43.1, 37.0, 19.4, 0.2; UV (CH_3CN) λ_{max}, nm (ε): 242 (107); HRMS-CI^+ (*m* / *z*): $[M]^+$ calcd for $C_{13}H_{22}O_3Si$, 254.1338; found, 254.1349.

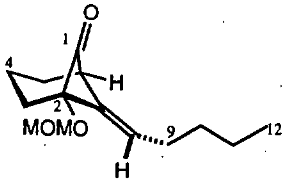
Data for (**Z**)-**16a**: R_f = 0.67 (SiO_2, 4:1 hexanes:EtOAc); ^1H NMR ($CDCl_3$, 500 MHz) δ 5.82 (d, 1H, *J* = 2 Hz, H-8), 4.81 (d, 1H, *J* = 6 Hz, O-CH_2-O), 4.74 (d, 1H, *J* = 6 Hz, O-CH_2-O), 3.45 (s, 3H, OCH_3), 3.11 (m, 1H, H-6), 2.36 (m, 4H, 2 × H-5 and 2 × H-3), 1.76 (m, 2H, 2 × H-4), 0.61 (s, 9H, TMS).



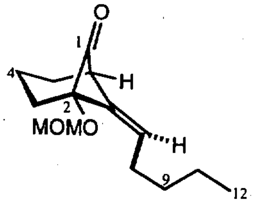
***E*-15b**



***Z*-15b**



***E*-16b**



***Z*-16b**

(*E*)- and (Z)-2-(Methoxymethoxy)-7-pentylidine-bicyclo[3.2.0]heptan-1-one (15b); (*E*)- and (Z)-2-(Methoxymethoxy)-7-pentylidine-bicyclo[3.1.1]heptan-1-one (16b).

Method A: 2-Chloro-*N*-methyl pyridinium iodide (2.34 g, 9.17 mmol, 4 equiv) in CH_3CN (62 mL) was treated with Et_3N (2.55 mL, 18.35 mmol, 8 equiv) and the solution was heated to reflux. The solution gradually turned dark red. The carboxylic acid **12b** (588.2 mg, 2.29 mmol, 1 equiv) in CH_3CN (23 mL) was added over 1 h to the refluxing mixture using a syringe pump. The solution was heated at reflux overnight. After 24 h at reflux, the solution was cooled to rt and poured into EtOAc (250 mL). The organic layer was washed with saturated $NaHCO_3$ (3 × 120 mL), with brine (2 × 120 mL), dried ($MgSO_4$), filtered and concentrated on a rotary evaporator to give 858.1 mg crude brown oil. Purification by flash chromatography (SiO_2, 4:1 hexanes:EtOAc) afforded **15b** and **16b** in a 3:1 ratio, 326.1 mg (1.368 mmol, 60%).

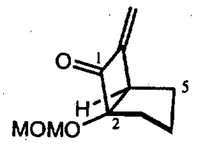
Method B: The carboxylic acid **12b** (160.4 mg, 0.625 mmol, 1 equiv) was dissolved in benzene (5 mL) and treated with oxalyl chloride (0.16 mL, 1.876 mmol, 3 equiv). After 4 h at rt, the solvent was removed on a rotary evaporator, giving the acid chloride, 161.2 mg (0.586 mmol, 94%) as an orange oil. The acid chloride (161.2 mg, 0.586 mmol, 1 equiv) was dissolved in benzene (5.8 mL) and treated with Et_3N (0.20 mL, 1.466 mmol, 2.5 equiv). The solution turned yellow as it was heated to reflux. After 13 h, the solution was cooled to rt and saturated NH_4Cl (10 mL) was added. The resulting mixture was extracted with EtOAc (3 × 35 mL), washed with NH_4Cl (40 mL), with brine (40 mL), dried ($MgSO_4$), filtered and concentrated on a rotary evaporator to give 139.4 mg orange oil. Purification by flash chromatography (SiO_2, 19:1 hexanes:EtOAc) gave 108.4 mg (0.455 mmol, 78%) of **15b** and **16b** in a ratio of 3:1.

Data for **(*E*)-15b**: $R_f = 0.35$ (SiO_2, 4:1 hexanes:EtOAc); IR (thin film) 2963, 1745, 1667 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 6.45 (dt, 1H, $J = 2.5$, 8 Hz, H-8), 4.77 (s, 2H, O-CH_2-O), 3.45 (m, 1H, H-6), 3.36 (s, 3H, OCH_3), 2.22 (m, 1H, H-3), 2.13 (m, 2H, 2 × H-9), 1.96 (m, 2H, 2 × H-5), 1.77 (m, 2H, H-4 and H-3), 1.55 (m, 1H, H-4), 1.44 (m, 2H, 2 × H-10), 1.34 (m, 2H, 2 × H-11), 0.92 (t, 3H, $J = 7$ Hz, 3 × H-12); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 202.4, 146.0, 135.8, 101.4, 94.5, 56.3, 46.4, 35.7, 32.3, 31.7, 28.9, 24.3, 22.9, 14.3; UV (CH_3CN) λ_{max}, nm (ε): 278 (565), 372 (81); HRMS-ESI$^+$ (m/z): $[M]^+$ calcd for $C_{14}H_{22}O_3$, 238.1569; found, 238.1553.

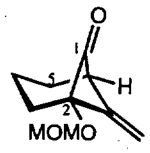
Data for (*Z*)-**15b**: R_f = 0.35 (SiO_2, 4:1 hexanes:EtOAc); IR (thin film) 2957, 1741, 1659 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 5.68 (dt, 1H *J* = 2.5, 8 Hz, H-8), 4.82 (s, 2H, O-CH_2-O), 3.36 (m, 4H, OCH_3 and H-6), 2.50 (m, 2H, H-9), 2.21 (m, 1H, H-3), 1.96 (m, 2H, H-5), 1.86 (m, 2H, H-3 and H-4), 1.59 (m, 1H, H-4), 1.34 (m, 4H, 2 × H-10 and 2 × H-11), 0.91 (t, 3H, *J* = 7 Hz, 3 × H-12); UV (CH_3CN) λ_{max}, nm (ε): 272 (1083), 374 (28).

Data for (*E*)-**16b**: R_f = 0.35 (SiO_2, 4:1 hexanes:EtOAc); ^1H NMR ($CDCl_3$, 500 MHz) δ 5.67 (m, 1H, H-8), 4.84 (d, 1H, *J* = 6 Hz, O-CH_2-O), 4.74, (d, 1H, *J* = 6 Hz, O-CH_2-O), 3.43 (s, 3H, OCH_3), 3.26 (m, 1H, H-6), 2.32 (br m, 6H, 2 × H-3, 2 × H-5 and 2 × H-9), 1.73 (m, 2H, 2 × H-4), 1.39 (m, 4H, 2 × H-10 and 2 × H-11), 0.93 (m, 3H, 3 × H-12); UV (CH_3CN) λ_{max}, nm (ε): 241 (141); GC-MS *m / z* (% relative intensity, ion): 193 (3, M - CH_2OCH_3), 45 (100, CH_2OCH_3).

Data for (*Z*)-**16b**: R_f = 0.35 (SiO_2, 4:1 hexanes:EtOAc); IR (thin film) 2962, 1790 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 5.68 (t, 1H, *J* = 8 Hz, H-8), 4.86 (d, 1H, *J* = 6 Hz, O-CH_2-O), 4.72 (d, 1H, *J* = 6 Hz, O-CH_2-O), 3.47 (s, 3H, OCH_3), 3.11 (m, 1H, H-6), 2.42 (m, 2H, 2 × H-3), 2.22 (m, 4H, 2 × H-5 and 2 × H-9), 1.82 (m, 1H, H-4), 1.67 (m, 1H, H-4), 1.38 (m, 4H, 2 × H-10 and 2 × H-11), 0.92 (m, 3H, 3 × H-12); UV (CH_3CN) λ_{max}, nm (ε): 230 (151); GC-MS *m / z* (% relative intensity, ion): 207 (1, M - OCH_3), 193 (10, M - CH_2OCH_3), 45 (87, CH_2OCH_3).



15c



16c

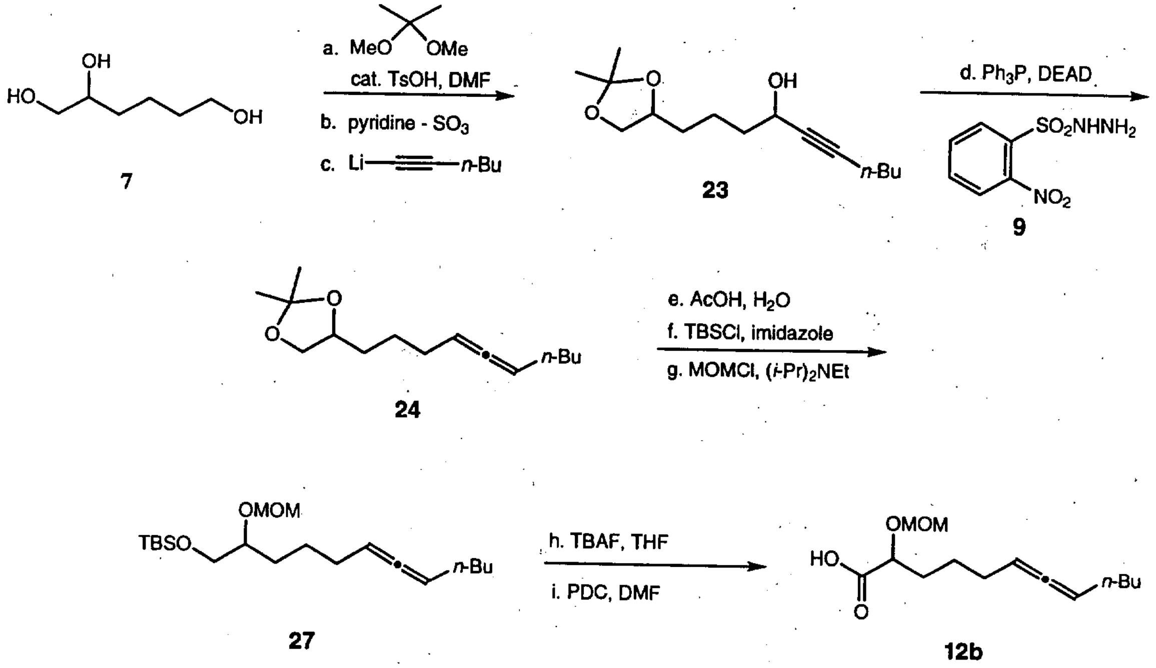
2-(Methoxymethoxy)-7-methylidine-bicyclo[3.2.0]heptan-1-one (15c), and **2-(Methoxymethoxy)-7-methylidine-bicyclo[3.1.1]heptan-1-one (16c).**

Method A: 2-Chloro-*N*-methyl pyridinium iodide (562.8 mg, 2.203 mmol, 4 equiv) in CH_3CN (15 mL) was treated with Et_3N (0.61 mL, 4.406 mmol, 8 equiv) and the solution was heated to reflux. The yellow solution gradually turned dark red. The carboxylic acid **12c** (110.3 mg, 0.550 mmol, 1equiv) in CH_3CN (5.5 mL) was added over 1.5 h to the refluxing mixture using a syringe pump. The solution was heated at reflux overnight. After 20 h at reflux, the solution was cooled to rt and poured into EtOAc (150 mL). The organic layer was washed with saturated $NaHCO_3$ (3 × 50 mL), with H_2O (3 × 50 mL), with saturated $NaHCO_3$ (50 mL), with brine (50 mL), dried ($MgSO_4$), filtered and concentrated on a rotary evaporator to give 225.7 mg crude brown oil. Purification by flash chromatography (SiO_2, 19:1 hexanes:EtOAc) afforded **15c** and **16c** in a 5:1 ratio, 57.6 mg (0.316 mmol, 57%).

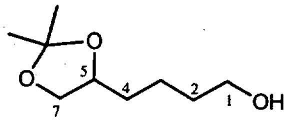
Method B: The carboxylic acid **12c** (29.3 mg, 0.146 mmol, 1 equiv) was dissolved in benzene (4 mL) and treated with oxalyl chloride (38.2 μL, 0.438 mmol, 3 equiv). After 10 h at rt, the solvent was removed on a rotary evaporator, giving the acid chloride, 25.3 mg (0.115 mmol, 79%) as a yellow oil. The acid chloride (25.3 mg, 0.115 mmol, 1 equiv) was dissolved in benzene (1.1 mL) and treated with Et_3N (40.3 μL, 0.289 mmol, 2.5 equiv). The solution turned yellow as it was heated to reflux. After 12 h, the solution was cooled to rt and saturated NH_4Cl was added. The resulting mixture was extracted with EtOAc (3 × 15 mL), dried ($MgSO_4$), filtered and concentrated on a rotary evaporator to give 26.1 mg orange oil. Purification by flash chromatography (SiO_2, 19:1 hexanes:EtOAc) gave 9.2 mg (0.050 mmol, 45%) of **15c** and **16c** in a ratio of 5:1.

Data for **15c**: $R_f = 0.55$ (SiO_2, 4:1 hexanes:EtOAc); IR (thin film) 2959, 1759, 1654 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 5.92 (d, 1H, $J = 3$ Hz, H-8), 5.17 (d, 1H, $J = 3$ Hz, H-8), 4.80 (d, 1H, $J = 7$ Hz, O-CH_2-O), 4.78 (d, 1H, $J = 7$ Hz, O-CH_2-O), 3.48 (m, 1H, H-6), 3.37 (s, 3H, OCH_3), 2.25 (m, 1H, H-3), 2.00 (m, 2H, H-3 and H-4), 1.57 (m, 1H, H-4); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 203.4, 154.9, 116.1, 102.3, 94.6, 56.5, 48.0, 36.5, 34.0, 24.4; UV (CH_3CN) λ_{max}, nm (ε): 288 (495), 380 (30); GC-MS *m / z* (% relative intensity, ion): 167 (2, M - CH_3), 150 (11, M – CH_3OH), 137 (67, M-CH_2OCH_3), 45 (100, CH_2OCH_3).

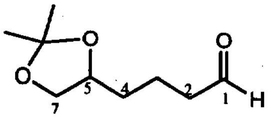
Data for **16c**: $R_f = 0.55$ (SiO_2, 4:1 hexanes:EtOAc); IR (thin film) 2955, 1794, 1685 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 5.35 (d, 1H, $J = 1$ Hz, H-8), 5.31 (d, 1H, $J = 1$ Hz, H-8), 4.86 (d, 1H, $J = 6$ Hz, O-CH_2-O), 4.78 (d, 1H, $J = 6$ Hz, O-CH_2-O), 3.46 (s, 3H, OCH_3), 3.21 (m, 1H, H-6), 2.44 (t, 2H, $J = 7$ Hz, 2 × H-3), 2.29 (m, 2H, 2 × H-5), 1.79 (m, 1H, H-4), 1.64 (m, 1H, H-4); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 206.7, 143.5, 105.1, 93.8, 92.6, 57.2, 56.8, 43.0, 36.8, 19.3; UV (CH_3CN) λ_{max}, nm (ε): 286 (56); GC-MS m/z (% relative intensity, ion): 167 (2, M - CH_3), 122 (20, [M + H] – OCH_2OCH_3), 45 (100, CH_2OCH_3).



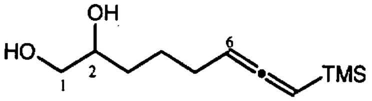
Synthesis of Dialkylallene Substrates



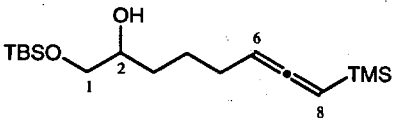
4-(2,2-Dimethyl-[1,3]-dioxolan-4-yl)-butan-1-ol (17). 1,2,6-Trihydroxyhexane (25.2 g, 188.2 mmol, 1 equiv) was dissolved in DMF (90 mL) and 2,2-dimethoxypropane (23.1 mL, 188.2 mmol, 1 equiv). The solution was treated with TsOH (7.2 g, 37.6 mmol, 0.2 equiv) and stirred at rt for 3 h. To the reaction mixture was added H_2O (75 mL), and the resulting mixture was extracted with EtOAc (3 × 225 mL). The combined organic extracts were washed with saturated $NaHCO_3$ (2 × 100 mL), with H_2O (4 × 100 mL), with brine (150 mL), dried ($MgSO_4$), filtered and concentrated on a rotary evaporator. Residual DMF was removed by azeotropic distillation with toluene on a rotary evaporator. The acetonide (18.9 g, 108.7 mmol, 57%) was isolated in sufficient purity for use in the next reaction. $R_f = 0.38$ (SiO_2, 1:1 hexanes:EtOAc); IR (thin film) 3425 (br), 2986 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 4.05 (br m, 2H, H-7 and H-5), 3.65 (t, 2H, $J = 6.5$ Hz, 2 × H-1), 3.51 (dd, 1H, $J = 7, 7$ Hz, H-7), 1.51 (m, 6H, 2 × H-2, 2 × H-3 and 2 × H-4), 1.40 (s, 3H, CH_3), 1.35 (s, 3H, CH_3); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 109.2, 76.6, 69.9, 62.7, 33.8, 33.7, 27.5, 26.3, 22.6; HRMS-CI$^+$ (m/z): $[M + H]^+$ calcd for $C_9H_{19}O_3$, 175.1334; found, 175.1325.



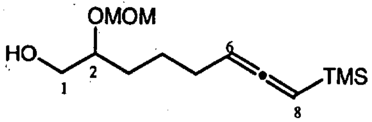
4-(2,2-Dimethyl-[1,3]-dioxolan-4-yl)-butyraldehyde (18). The primary alcohol **17** was dissolved in CH_2Cl_2 (100 mL), cooled to 0 °C and treated with DMSO (12.5 mL, 176.5 mmol, 4 equiv), with Et_3N (18.4 mL, 132.3 mmol, 3 equiv), and pyr-SO_3 (14.0 g, 88.2 mmol, 2 equiv). The cloudy yellow solution was stirred at 0 °C for 4 h, then saturated NH_4Cl (70 mL) was added, the mixture stirred at rt for 45 min and extracted with CH_2Cl_2 (3 × 150 mL). The combined organic extracts were washed with saturated NH_4Cl (200 mL), with saturated $CuSO_4$ (2 × 200 mL), with H_2O (200 mL), dried ($MgSO_4$), filtered and concentrated on a rotary evaporator. The crude oil was taken up in EtOAc and filtered through a pad of silica to remove copper salts. The solution was concentrated on a rotary evaporator to give the desired aldehyde **17** (6.98 g, 40.5 mmol, 91%) which was used without further purification. $R_f = 0.29$ (SiO_2, 4:1 hexanes:EtOAc); IR (thin film) 2990, 1730 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 9.77 (t, 1H, $J = 1$ Hz, H-1), 4.05 (br m, 2H, H-7 and H-5), 3.51 (dd, 1H, $J = 7, 7$ Hz, H-7), 2.49 (dt, 2H, $J = 1, 7$ Hz, 2 × 2-H), 1.66 (br m, 4H, 2 × H-3 and 2 × H-4), 1.39 (s, 3H, CH_3), 1.34 (s, 3H, CH_3); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 202.6, 109.4, 76.2, 69.8, 44.2, 33.5, 27.5, 26.2, 19.0.



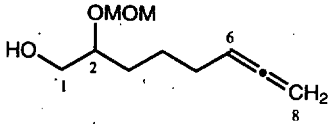
8-Trimethylsilylocta-6,7-diene-1,2-diol (19). The acetonide **10** (4.66 g, 18.31 mmol) was dissolved in 3:1 AcOH:H_2O (150 mL). The pale yellow solution was stirred at rt for 3.5 h. The yellow solution was added to 300 mL EtOAc, washed with H_2O (4 × 100 mL), with saturated $NaHCO_3$ (4 × 150 mL), with H_2O (150 mL), dried ($MgSO_4$), filtered, and concentrated on a rotary evaporator. The product **19** was isolated as a yellow oil . Purification by flash chromatography (SiO_2, gradient from 9:1 hexanes:EtOAc, to 1:1 hexanes:EtOAc) afforded the desired diol **19** as a colorless oil (2.63 g, 12.26 mmol, 67%). R_f = 0.12 (SiO_2, 4:1 hexanes:EtOAc); IR (thin film) 3371 (br), 2951, 2175, 1942, 1709 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 4.90 (m, 1H, H-8), 4.77 (q, 1H, J = 7, 6.8 Hz, H-6), 3.73 (m, 1H, H-2), 3.66 (dd, 1H, J = 3, 11 Hz, H-1), 3.44 (dd, 1H, J = 7, 11 Hz, H-1), 2.00 (m, 2H, 2 × H-5), 1.49 (br m, 4H, 2 × H-3 and 2 × H-4), 0.09 (s, 9H, TMS); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 210.6, 83.6, 83.4, 72.9, 67.4, 33.2, 28.5, -0.21; HRMS-EI (m/z): $[M - CH_3]^+$ calcd for $C_{10}H_{19}O_2Si$, 119.1154; found, 119.1101.



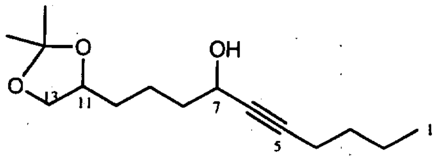
8-(Trimethylsilyl)-1-(*tert*-butyldimethylsilyloxy)-octa-6,7-dien-2-ol (20). The diol **19** (4.44 g, 20.07 mmol, 1 equiv) in DMF (75 mL) was treated with imidazole (2.11 g, 31.06 mmol, 1.5 equiv) and *tert*-butyldimethylsilyl chloride (3.12 g, 20.70 mmol, 1 equiv), and the resulting yellow solution was stirred at rt. After 1.5 h, saturated NH_4Cl (70 mL) was added, and the mixture was poured into EtOAc (350 mL). The phases were separated and the aqueous phase was extracted with EtOAc (150 mL). The combined organic extracts were washed with saturated NH_4Cl (100 mL), with H_2O (3 × 100 mL), with brine (100 mL), dried ($MgSO_4$), filtered, and concentrated on a rotary evaporator. Residual DMF was removed by azeotropic distillation with toluene on a rotary evaporator. The product **20** (6.31 g, 19.19 mmol, 93%) was isolated as a yellow oil of sufficient purity for use in the next reaction. R_f = 0.07 (SiO_2, 4:1 hexanes:EtOAc); IR (thin film) 3437 (br), 2959, 2179, 1938, 1751 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 4.89 (m, 1H, H-8), 4.76 (m, 1H, H–6), 3.62 (m, 2H, H-1 and H-2), 3.39 (dd, 1H, J = 7, 7 Hz, H-1), 2.00 (m, 2H, 2 × H-5), 1.45 (br m, 4H, 2 × H-3 and 2 × H-4), 0.90 (s, 9H, t-Bu), 0.07 (s, 6H, TMS), 0.07 (s, 6H, Si-CH_3); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 210.6, 83.7, 83.2, 72.4, 67.9, 32.9, 28.5, 26.5, 26.3, 18.9, 0.56, -0.22; HRMS-EI (*m* / *z*): [M - *t*Bu]$^+$ calcd for $C_{13}H_{27}O_2Si_2$, 271.1550; found, 271.1523.



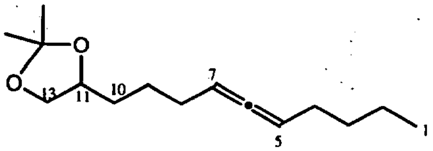
2-Methoxymethoxy-8-(trimethylsilyl)-octa-6,7-diene-1-ol (21). The TBS ether **11** (6.60 g, 17.70 mmol, 1 equiv) in THF (50 mL) was treated with 3:1 AcOH:H_2O (200 mL) and the yellow solution was stirred at rt. After 36 h, the solution was added to 450 mL EtOAc, washed with H_2O (3 × 100 mL), with saturated $NaHCO_3$ (5 × 100 mL), dried ($MgSO_4$), filtered and concentrated on a rotary evaporator. Purification by flash chromatography (1:1 hexanes:EtOAc) gave the product alcohol **21** (4.4 g, 17.02 mmol, 96%) as a yellow oil. R_f = 0.72 (SiO_2, 1:1 hexanes: EtOAc); IR (thin film) 3460 (br), 2959, 2179, 1938, 1728 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 4.90 (m, 1H, H-8), 4.75 (m, 2H, O-CH_2-O and H-6), 4.68 (d, 1H, J = 7 Hz, O-CH_2-O), 3.50 (br m, 3H, 2 × H-1 and 2 × H-2), 3.43 (s, 3H, -OCH_3), 1.97 (m, 2H, 2 × H-5), 1.49 (br m, 4H, 2 × H-3 and 2 × H-4), 0.08 (s, 9H, TMS); ^{13}C NMR ($CDCl_3$, 125 MHz)
δ 210.6, 97.5, 83.6, 83.4, 82.5, 66.3, 56.2, 31.8, 28.4, 26.2, –0.23; HRMS-CI$^+$ (*m* / *z*): [M - OH]$^+$ calcd for $C_{13}H_{25}O_3Si$, 241.1624; found, 241.1255.



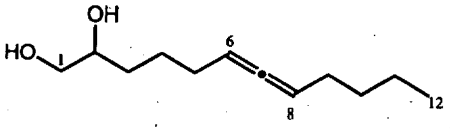
2-Methoxymethoxy-octa-6,7-dien-1-ol (22). The TBS ether **11** (5.12 g, 13.73 mmol, 1 equiv) in THF (50 mL) was treated with *n*-Bu_4NF (41.2 mL of a 1M solution in THF, 41.20 mmol, 3 equiv). After 1 h at rt, the brown solution was treated with H_2O (35 mL), extracted with EtOAc (3 × 75 mL), washed with saturated NH_4Cl (3 × 100 mL), with H_2O (100 mL), washed with brine (100 mL), dried ($MgSO_4$), filtered and concentrated on a rotary evaporator to give a yellow oil. Purification by flash chromatography (4:1 hexanes:EtOAc) gave the primary alcohol **22** (2.51 g, 13.47 mmol, 98%). R_f = 0.26 (SiO_2, 2:1 hexanes:EtOAc); IR (thin film) 3433(br), 2959, 2361, 1739 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 5.08 (quin, 1H, J = 6.75 Hz, H-6), 4.73 (d, 1H, J = 7 Hz, O-CH_2-O), 4.67 (m, 3H, O-CH_2-O and 2 × H-8), 3.52 (m, 3H, 2 × H-1 and H-2), 3.43 (s, 3H, -OCH_3), 2.02 (m, 2H, 2 × H-5), 1.53 (m, 4H, 2 × H-3 and 2 × H-4); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 209.7, 97.7, 90.3, 82.8, 75.6, 66.3, 56.3, 31.7, 28.8, 25.7; HRMS–EI (*m* / *z*): [M - OCH_2CH_3]$^+$ calcd for $C_8H_{13}O$, 125.0966; found, 125.0969.



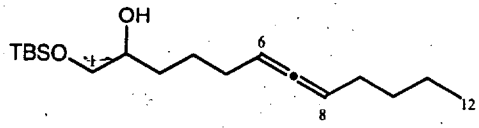
10-(2,2-Dimethyl-[1,3]-dioxolan-4-yl)-non-5-yn-7-ol (23). 1-Hexyne (5.42 mL, 47.18 mmol, 1.1 equiv) was dissolved in THF (150 mL), cooled to 0 °C, and treated with *n*-BuLi (29.1 mL of a 1.62 M solution in hexanes, 47.18 mmol, 1.1 equiv). The yellow solution was stirred at 0 °C for 30 min, after which the aldehyde **18** (7.38 g, 42.89 mmol, 1 equiv) in THF (80 mL), was added dropwise over 40 min. The pale yellow solution was allowed to warm to rt overnight. The reaction was quenched by addition of 100 mL of 5% H_3PO_4 (aq) and extracted with EtOAc (4 × 150 mL). The combined organic extracts were washed with saturated NH_4Cl (4 × 100 mL), with brine (150 mL), dried ($MgSO_4$), filtered and concentrated on a rotary evaporator. The product, a 1:1 mixture of diastereomers, was isolated as a yellow oil. Purification by flash chromatography (SiO_2, gradient from 4:1 Hex:EtOAc to 1:1 Hex:EtOAc) gave the desired alcohol **23** (6.55 g, 25.78 mmol, 60%) as a pale yellow oil. $R_f = 0.13$ (SiO_2, 4:1 hexanes:EtOAc); IR (thin film) 3445 (br), 2979, 2229, 1736 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 4.29 (dd, 1H, J = 7, 7 Hz, H-7), 3.99 (m, 2H, H-11 and H-13), 3.46 (dd, 1H, J = 7, 7 Hz, H-13), 2.40 (br s, 1H, OH), 2.15 (m, 2H, 2 × H-4), 1.59 (br m, 16H, 2 × CH_3, 2 × H-10, 2 × H-9, 2 × H-8, 2 × H-3 and 2 × H-2), 0.85 (t, 3H, J = 7 Hz, 3 × 1-H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 109.3, 86.0, 81.8, 76.6, 70.0, 62.9, 38.6, 33.8, 31.4, 27.5, 26.4, 22.5, 22.2, 19.0, 14.2; HRMS–EI (m/z): $[M - CH_3]^+$ calcd for $C_{14}H_{23}O_3$, 239.1647; found, 239.1646.



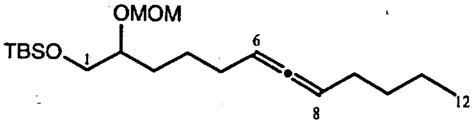
10-(2,2-Dimethyl-[1,3]-dioxolan-4-yl)-nona-5,6-diene (24). Triphenylphosphine (8.79 g, 33.51 mmol, 1.3 equiv) in THF (95 mL) was cooled –10 °C and treated with diethylazodicarboxylate (5.27 mL, 33.51 mmol, 1.3 equiv). The bright orange solution was stirred at –10 °C for 10 min, after which the alcohol **23** (6.55 g, 25.78 mmol, 1 equiv) in THF (30 mL) was added by cannula. After another 10 min at –10 °C, *o*-nitrobenzenesulfonyl hydrazide (9.77 g, 38.67 mmol, 1.5 equiv) in THF (60 mL) was added to the dark orange solution. The reaction was allowed to warm to rt overnight. The solvent was removed on a rotary evaporator. The orange solids were dissolved in EtOAc (250 mL) and added to a stirred solution of hexanes (800 mL). The mixture was filtered through a pad of silica, and the filtrate was concentrated on a rotary evaporator to give the desired product, a 1:1 mixture of diastereomers, as a yellow oil (5.38 g, 22.59 mmol, 88%). The product allene **24** was of sufficient purity for use in the next reaction. R_f = 0.85 (SiO_2, 4:1 hexanes:EtOAc); IR (thin film) 2990, 1968 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 5.07 (m, 2H, H-5 and H-7), 4.05 (m, 2H, H-11 and H-13), 3.51 (dd, 1H, J = 7, 7 Hz, H-13), 2.09 (m, 4H, 2 × H-4 and 2 × H-8), 1.53 (m, 4H, 2 × H-9 and 2 × H-3), 1.31 (br m, 10H, 2 × CH_3, 2 × H-10 and 2 × H-2), 0.90 (m, 3H, 3 × H-1); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 204.6, 109.3, 91.9, 91.0, 76.6, 70.1, 32.3, 32.0, 29.6, 29.3, 27.6, 26.4, 25.9, 23.3, 14.8; HRMS-EI (*m* / *z*): $[M]^+$ calcd for $C_{15}H_{26}O_2$, 238.1933; found, 238.1930.



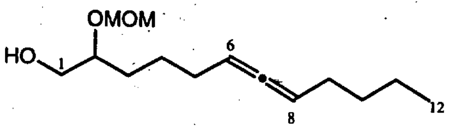
Dodeca-6,7-diene-1,2-diol (25). The acetonide **24** (5.35 g, 22.46 mmol) was dissolved in 3:1 AcOH:H_2O (220 mL). The yellow solution was stirred at rt for 8 h. The solution was added to 450 mL EtOAc, washed with H_2O (2 × 200 mL), with saturated $NaHCO_3$ (3 × 150 mL), with H_2O (150 mL), dried ($MgSO_4$), filtered, and concentrated on a rotary evaporator. The product **25** was isolated as a yellow oil (3.52 g, 17.75 mmol, 79%). R_f = 0.10 (SiO_2, 4:1 hexanes:EtOAc); IR (thin film) 3375 (br), 2959, 2249, 1965, 1744 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 5.06 (m, 2H, H-6 and H-8), 3.72 (m, 1H, H-2), 3.65 (dd, 1H, J = 3, 11 Hz, H-1), 3.43 (dd, 1H, J = 7, 11 Hz, H-1), 1.99 (m, 4H, 2 × H-5 and 2 × H-9), 1.42 (m, 8H, 2 × H-3, 2 × H-4, 2 × H-10 and 2 × H-11), 0.89 (t, 3H, J = 7 Hz, 3 × H-12); ^{13}C NMR ($CDCl_3$, 125 MHz)
δ 204.6, 91.9, 91.0, 72.8, 67.5, 33.2, 32.1, 29.5, 29.3, 25.7, 22.8, 14.6; HRMS-EI (*m* / *z*): $[M - H_2O]^+$ calcd for $C_{12}H_{20}O$, 180.1514; found, 180.1496.



1-(*tert*-Butyldimethylsilyloxy)-dodeca-6,7-diene-2-ol (26). The diol **25** (3.52 g, 17.75 mmol, 1 equiv) in DMF (75 mL) was treated with imidazole (1.81 g, 26.63 mmol, 1.5 equiv) and *tert*-butyldimethylsilyl chloride (2.68 g, 17.75 mmol, 1 equiv) and the yellow solution stirred at rt. After 1 h, saturated NH_4Cl (75 mL) was added, and the mixture was poured into to EtOAc (300 mL). The phases were separated and the aqueous phase was extracted with EtOAc (150 mL). The combined organic extracts were washed with saturated NH_4Cl (3 × 100 mL), with H_2O (3 × 100 mL), dried ($MgSO_4$), filtered, and concentrated on a rotary evaporator. Residual DMF was removed by azeotropic distillation with toluene on a rotary evaporator. The product **26** (5.19 g, 16.60 mmol, 94%) was isolated as a yellow oil of sufficient purity for use in the next reaction. R_f = 0.60 (SiO_2, 4:1 hexanes:EtOAc); IR (thin film) 3464 (br), 2963, 1961, 1744 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 5.06 (m, 2H, H-6 and H-8), 3.61 (m, 2H, H-1 and H-2), 3.38 (dd, 1H, *J* = 9, 9 Hz, H-1), 1.99 (m, 4H, 2 × H-5 and 2 × H-9), 1.42 (m, 8H, 2 × H-3, 2 × H-4, 2 × H-10 and 2 × H-11), 0.90 (m, 12H, 3 × H-12 and *t*-Bu), 0.07 (s, 6H, Si-CH_3); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 204.6, 91.8, 91.2, 72.4, 68.0, 32.9, 32.3, 29.7, 26.6, 25.9, 23.3, 22.8, 19.0, 14.8, 14.6; HRMS-EI (*m / z*): $[M]^+$ calcd for $C_{18}H_{36}O_2Si$, 312.2485; found, 312.2480.



1-(*tert*-Butyldimethylsilyloxy)-2-methoxymethoxy-dodeca-6,7-diene (27). The secondary alcohol **26** (4.86 g, 15.54 mmol, 1 equiv) in CH_2Cl_2 (100 mL) was treated with diisopropylethylamine (29.7 mL, 171.0 mmol, 11 equiv) and chloromethyl methyl ether (8.27 mL, 108.8 mmol, 7 equiv). After 12 h at rt, the reaction was quenched with saturated NH_4Cl (100 mL), extracted with CH_2Cl_2 (3 × 250 mL), washed with saturated NH_4Cl (3 × 150 mL), with H_2O (2 × 150 mL), dried ($MgSO_4$), filtered and concentrated on a rotary evaporator. The product **27** was isolated as a yellow oil (5.14 g, 14.41 mmol, 93%) of sufficient purity for use in the next reaction. R_f = 0.71 (SiO_2, 4:1 hexanes:EtOAc); IR (thin film) 2959, 1961, 1736 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 5.09 (m, 2H, H-6 and H-8), 4.81 (d, 1H, *J* = 7 Hz, O-CH_2-O), 4.68 (d, 1H, *J* = 7 Hz, O-CH_2-O), 3.63 (m, 3H, 2 × H-1 and H-2), 3.41 (s, 3H, OCH_3), 2.01 (m, 4H, 2 × H-5 and 2 × H-9), 1.39 (br m, 8H, 2 × H-3, 2 × H-4, 2 × H-10 and 2 × H-11), 0.92 (m, 15H, 3 × H-12 and *t*-Bu), 0.08 (s, 6H, Si-CH_3); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 204.6, 96.9, 91.7, 91.2, 78.7, 66.6, 56.1, 32.0, 31.9, 29.7, 29.3, 26.6, 26.5, 25.7, 22.8, 18.9, 14.5; HRMS-EI (*m / z*): $[M - OCH_3]^+$ calcd for $C_{19}H_{37}O_2Si$, 325.2563; found, 325.2624.



2-Methoxymethoxy-dodeca-6,7-diene-1-ol (28). The TBS ether **27** (4.99 g, 13.99 mmol, 1 equiv) in THF (65 mL) was treated with 3:1 AcOH:H_2O (260 mL) and the yellow solution was stirred at rt. After 18 h, the solution was added to 250 mL EtOAc, washed with H_2O (2 × 200 mL), with saturated $NaHCO_3$ (3 × 100 mL), with H_2O (100 mL), dried ($MgSO_4$), filtered and concentrated on a rotary evaporator. Purification by flash chromatography (1:1 hexanes:EtOAc) gave the alcohol **28** (2.48 g, 10.25 mmol, 73%) as a yellow oil. $R_f = 0.67$ (SiO_2, 1:1 hexanes: EtOAc); IR (thin film) 3456 (br), 2955, 1961, 1744 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 5.07 (m, 2H, H-6 and H-8), 4.73 (d, 1H, $J = 7$ Hz, O-CH_2-O), 4.68 (d, 1H, $J = 7$Hz, O-CH_2-O), 3.53 (m, 3H, 2 × H-1 and H-2), 3.43 (s, 3H, OCH_3), 1.98 (br m, 4H, 2 × H-5 and 2 × H-9), 1.43 (br m, 8H, 2 × H-3, 2 × H-4, 2 × H-10 and 2 × H-11), 0.90 (t, 3H, $J = 7$ Hz, 3 × H-12); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 204.6, 97.5, 91.8, 91.0, 82.4, 66.2, 56.2, 32.0, 31.8, 29.5, 29.3, 25.7, 22.8, 14.5; HRMS-EI (m / z): $[M]^+$ calcd for $C_{14}H_{26}O_3$, 242.1882; found, 242.1869.