SUPPORTING INFORMATION

Tuning Reactivity and Chemoselectivity in Electron Transfer Initiated Cyclization Reactions: Applications to Carbon-Carbon Bond Formation

John R. Seiders, II, Lijun Wang, and Paul E. Floreancig

Department of Chemistry

University of Pittsburgh

Pittsburgh, PA 15260

General Procedures. THF and Et₂O were dried by distillation over Na/benzophenone under N₂. Toluene, 1,2-dichloroethane, and CH₂Cl₂ were dried by distillation over CaH₂. Photoirradiations were performed with a Hanovia 450 W medium pressure mercury lamp through Pyrex filtration. Samples were held 4 cm away from the lamp. Reagents were used as purchased without further purification unless noted. Chemical shifts (δ) are reported in ppm.

Reagents and Conditions

a) Vinylmagnesium bromide, CuI, THF. b) NaH, DMF, then C₈H₁₇I. c) BH₃•THF, THF, then NaOOH.

Scheme 1.

1-(4-Methoxyphenyl)but-3-en-2-ol

To a suspension of CuI (140 mg, 0.736 mmol) in THF (10 mL) at -78 °C was added vinyl magnesium bromide (1.0 M in THF, 25.7 mL, 25.7 mmol). The mixture was stirred for 20 min and 2-(4-methoxybenzyl)oxirane¹ (1.21 g, 7.36 mmol) was added. The reaction was stirred at -78 °C for 2 h and then slowly warmed to room temperature. The reaction was then quenched by adding saturated aqueous NH₄Cl. Air was then gently bubbled through the mixture for 2 h. The mixture was extracted with ethyl acetate (2 x). The organic layers were then combined and washed with water and brine. The organic layer was then dried (Na₂SO₄), filtered and concentrated under reduced pressure. The resulting residue was then purified by flash column chromatography (25% EtOAc in hexanes) to provide the desired product (1.36 g, 96%): ¹H NMR (300 MHz, CDCl₃) δ 7.14 (d, *J* = 8.6 Hz, 2H), 6.88 (d, *J* = 8.6, 2H), 5.92-5.80 (m, 1H), 5.20-5.16 (m, 1H), 5.14-5.13 (m, 1H), 3.86-3.82 (m, 1H), 3.80 (s, 3H), 2.77 (dd, *J* = 13.7, 4.9 Hz, 1H), 2.67 (dd, *J* = 13.7, 7.8 Hz, 1H), 2.38-2.31 (m, 1H), 2.27-2.21 (m, 1H), 1.70 (br s, 1H); ¹³C NMR (75 MHz, CDCl₃) δ 158.6, 135.0, 130.7, 118.3, 114.3, 72.0, 55.6, 42.7, 41.4; IR (neat)

3421, 2933, 2835, 1612, 1512, 1246, 807 cm^{-1} ; HRMS (EI): m/z calcd for $\text{C}_{12}\text{H}_{16}\text{O}_2$ (M^+) 192.1150, found 192.1151.

1-Methoxy-4-(2-oxyloxybut-3-enyl)benzene

To alcohol 1-(4-methoxyphenyl)but-3-en-2-ol (1.30 g, 6.76 mmol) in DMF (20 mL) at 0 °C was added sodium hydride (1.02 g, 25.4 mmol). The mixture was stirred for 15 min and octyl iodide (7.64 g, 31.8 mmol) was added. The reaction was slowly warmed to room temperature and stirred overnight. The reaction was then quenched by the addition of water at 0 °C. The mixture was extracted with hexanes (2 x), and the organic layers were combined and washed with water and brine. The organic layer was then dried (Na_2SO_4), filtered and concentrated under reduced pressure. The resulting residue was purified by flash column chromatography (5% EtOAc in hexanes) to provide the desired product (1.32 g, 64%): ^1H NMR (300 MHz, CDCl_3) δ 7.10 (d, J = 8.5 Hz, 2H), 6.83 (d, J = 8.5 Hz, 2H), 5.90-5.84 (m, 1H), 5.10-5.04 (m, 2H), 3.79 (s, 3H), 3.50-3.30 (m, 3H), 2.76 (dd, J = 13.8, 6.5 Hz, 1H), 2.69 (dd, J = 13.8, 5.9 Hz, 1H), 2.25-2.23 (m, 2H), 1.50 (p, J = 6.5 Hz, 2H), 1.24 (br s, 10H), 0.88 (t, J = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, CDCl_3) δ 158.3, 135.5, 131.6, 130.7, 117.1, 113.9, 80.9, 69.9, 63.3, 55.5, 39.9, 38.5, 32.1, 30.8, 29.7, 29.6, 26.5, 22.9, 14.4; IR (neat) 2927, 2855, 1512, 1247, 1039 cm^{-1} ; HRMS (EI): m/z calcd for $\text{C}_{20}\text{H}_{32}\text{O}_2$ (M^+) 304.2402, found 304.2407.

4-(4-Methoxyphenyl)-3-oxyloxybutan-1-ol

To 1-methoxy-4-(2-oxyloxybut-3-enyl)benzene (1.30 g, 4.03 mmol) in THF (5 mL) at 0 °C was added $\text{BH}_3 \cdot \text{THF}$ (1.0 M in THF, 12.1 mL, 12.1 mmol). The reaction was stirred for 10 min and quenched by adding water (1 mL) dropwise followed by 20% aqueous NaOH (1 mL), 30% aqueous hydrogen peroxide (1 mL) and saturated aqueous Na_2SO_3 (2 mL). The mixture was stirred for an additional 45 min. The mixture was extracted with ethyl acetate (2 x), and the organic layers were combined and washed with water and brine. The organic layer was dried (Na_2SO_4), filtered and concentrated under reduced pressure. The resulting residue was purified by flash column chromatography (20% EtOAc in hexanes) to provide the desired product (448 mg, 34%): ^1H NMR (300 MHz, CDCl_3) δ 7.10 (d, J = 8.5 Hz, 2H), 6.8 (d, J = 8.5 Hz, 2H), 3.78 (s, 3H), 3.61 (t, J = 5.8 Hz, 2H), 3.49-3.37 (m, 3H), 2.85 (dd, J = 13.7, 5.8 Hz, 1H), 2.64 (dd, J = 13.7, 6.7 Hz, 1H), 2.10 (s, 1H), 1.70-1.60 (m, 2H), 1.59-1.43 (m, 4H), 1.25 (br s, 10H), 0.88 (t, J = 6.4 Hz, 3H); ^{13}C NMR (75 MHz, CDCl_3) δ 158.29, 131.28, 130.63, 113.99, 81.30, 69.95, 55.53, 39.71, 32.14, 30.84, 30.35, 29.73, 29.57, 29.13, 26.48, 22.96, 14.41; IR (neat) 3445, 2928, 2855, 1612, 1512, 1247, 819 cm^{-1} ; HRMS (ESI): m/z calcd for $\text{C}_{20}\text{H}_{34}\text{O}_{16}\text{Na}$ ($\text{M}+\text{Na}$) 345.2406, found 345.2410.

Reagents and Conditions

a) KO^tBu, MeI, THF.² b) Allylmagnesium bromide, THF. c) NaH, DMF, then C₈H₁₇I.
d) BH₃•THF, THF, then NaOOH.

Scheme 2.

2-(4-Methoxyphenyl)-2-methylpropionaldehyde

To (4-methoxyphenyl)acetaldehyde³ (582 mg, 3.87 mmol) in THF (5 mL) at -78 °C was added potassium *tert*-butoxide (957 mg, 8.52 mmol) and methyl iodide (1.21 g, 8.52 mmol). The reaction was stirred at -78 °C for 4 h and slowly warmed to room temperature. The reaction mixture was then quenched by the addition of saturated aqueous NH₄Cl. The mixture was extracted with ethyl acetate (2 x), and the organic layers were combined and washed with water and brine. The organic layer was then dried (Na₂SO₄), filtered and concentrated under reduced pressure. The resulting residue was purified by flash column chromatography (10% EtOAc in hexanes) to provide the desired product (146 mg, 21%): ¹H NMR (300 MHz, CDCl₃) δ 9.45 (s, 1H), 7.20 (d, *J* = 8.7 Hz, 2H), 6.92 (d, *J* = 8.8 Hz, 2H), 3.80 (s, 3H), 1.46 (s, 6H); ¹³C NMR (75 MHz, CDCl₃) δ 202.0, 168.9, 158.6, 132.9, 127.7, 114.1, 55.1, 49.6, 22.4; IR (neat) 2971, 2935, 2836, 1723, 1609, 1513, 1465, 1252, 1185, 1034, 909, 829, 796 cm⁻¹; HRMS (EI): *m/z* calcd for C₁₁H₁₄O₂ (M⁺) 178.0994, found 178.0994.

2-(4-Methoxyphenyl)-2-methylhex-5-en-3-ol

To 2-(4-methoxyphenyl)-2-methylpropionaldehyde (146 mg, 0.82 mmol) in THF (5 mL) at -78 °C was added allyl magnesium bromide (1.0 M in THF, 4.08 mL, 4.08 mmol). The mixture was then slowly warmed to room temperature over 30 min, and stirred at room temperature for an additional 2 h. The reaction was then quenched by the addition of saturated aqueous NH₄Cl at 0 °C. The mixture was extracted with ethyl acetate (2 x), and the organic layers were combined and washed with water and brine. The organic layer was then dried (Na₂SO₄), filtered and concentrated under reduced pressure. The resulting residue was purified by flash column chromatography (20% EtOAc in hexanes) to provide the desired product (150 mg, 83%): ¹H NMR (300 MHz, CDCl₃) δ 7.15 (d, *J* = 8.9 Hz, 2H), 6.88 (d, *J* = 8.9 Hz, 2H), 5.88-5.74 (m, 1H), 5.11-5.08 (m, 1H), 5.05-5.03 (m, 1H), 3.81 (s, 3H), 3.63 (dd, *J* = 10.4, 2.1 Hz, 1H), 2.24-2.17 (m, 2H), 1.35 (s, 3H), 1.33 (s, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 158.1, 136.7, 127.9, 117.5, 113.9, 78.7, 55.5, 41.9, 36.9, 24.7, 24.3; IR (neat) 3481, 2970, 1610, 1513, 1251, 1185, 1035, 829 cm⁻¹; HRMS (EI): *m/z* calcd for C₁₄H₂₀O₂ (M⁺) 220.1463, found 220.1465.

1-(1,1-Dimethyl-2-octyloxypent-4-enyl)-4-methoxybenzene

To 2-(4-methoxyphenyl)-2-methylhex-5-en-3-ol (171.6 mg, 0.778 mmol) in DMF (5 mL) at 0 °C was added NaH (125 mg, 3.11 mmol). The mixture was stirred for 15 min and octyl iodide (935 mg, 3.89 mmol) was added. The mixture was then slowly warmed to room temperature and stirred for 18 h. The reaction was quenched by the addition of water. The mixture was then

5-(4-Methoxyphenyl)-5-methyl-4-octyloxyhexan-1-ol

To **3** (100 mg, 0.29 mmol) in dichloroethane (6 mL) in a borosilicate flask at 20 °C were added *N*-methylquinolinium hexafluorophosphate (7 mg, 0.025 mmol), sodium acetate (200 mg, 2.4 mmol), anhydrous sodium thiosulfate (200 mg, 1.3 mmol) and toluene (1 mL). The mixture was stirred at room temperature while bubbling air gently and irradiating for 3 hours. The reaction

mixture was filtered through a small plug of silica gel and the filtrate was concentrated. The resulting residue was purified by flash column chromatography (5% EtOAc in hexanes) to provide **2⁴** (35.2 mg, 61.7%): ¹H NMR (300 MHz, CDCl₃) δ 5.11 (dd, *J* = 3.9, 1.5 Hz, 1H), 3.93-3.82 (m, 2H), 3.65 (dt, *J* = 9.5, 6.8 Hz, 1H), 3.37 (dt, *J* = 9.5, 6.7 Hz, 1H), 2.04-1.79 (m, 4H), 1.58-1.51 (m, 2H), 1.31-1.28 (m, 10H), 0.88 (t, *J* = 6.4 Hz, 3H).

Reagents and Conditions

a) Vinylmagnesium bromide, THF, -78 °C. b) SnCl₂, (PhCN)₂PdCl₂, 4-Pivaloxybutanal, *N,N*-dimethylimidazolone.⁵ c) NaH, DMF, C₈H₁₇I. d) LiAlH₄, THF.

Scheme 3.

1-(4-Methoxyphenyl)prop-2-en-1-ol

To *p*-anisaldehyde (2.00 g, 14.6 mmol) in THF (20 mL) at -78 °C was added vinyl magnesium bromide (1.0 M in THF, 29.4 mmol, 29.4 mL). The reaction was then slowly warmed to room temperature over 8 h and quenched by the addition of saturated aqueous NH₄Cl. The mixture was extracted with ethyl acetate (2 x), and the organic layers were combined and washed with water and brine. The organic layer was then dried (Na₂SO₄), filtered and concentrated under reduced pressure. The residue was purified by flash column chromatography (20% EtOAc in hexanes) to provide the desired product (1.99 g, 83%): ¹H NMR (300 MHz, CDCl₃) δ 7.30 (d, *J* = 8.6 Hz, 2H), 6.88 (d, *J* = 8.7 Hz, 2H), 6.08-6.00 (m, 1H), 5.34 (d, *J* = 16.8 Hz, 1H), 5.21-5.19 (m, 2H), 3.81 (s, 3H), 1.93 (d, *J* = 3.8 Hz, 1H).⁶

2,2-Dimethylpropionic acid 4-hydroxy-5-(4-methoxyphenyl)hept-6-enyl ester

To 2,2-dimethylpropionic acid-4-oxo-butyl ester⁷ (1.31 g, 7.63 mmol), 1-(4-methoxyphenyl)prop-2-en-1-ol (1.88 g, 11.4 mmol) and SnCl₂ (4.33 g, 22.8 mmol) in DMI (30 mL) was added PdCl₂(CNPh)₂ (58.5 mg, 0.152 mmol). The reaction was then stirred for 24 h and diluted with 240 mL of ether:CH₂Cl₂ (2:1). The mixture was then washed with 10% HCl, saturated aqueous NaHCO₃, water and brine. The organic layer was then dried (Na₂SO₄), filtered and concentrated under reduced pressure. The residue was then purified by flash column chromatography (10% EtOAc in hexanes) to provide the desired product in a greater than 10:1 anti:syn ratio (875 mg, 36%): ¹H NMR (300 MHz, CDCl₃) δ 7.11 (d, *J* = 8.7 Hz, 2H), 6.87, (d, *J* = 8.7 Hz, 2H), 6.10 (ddd, *J* = 19.6, 10.5, 9.1 Hz, 1H), 5.18 (d, *J* = 19.3 Hz, 1H), 5.14 (d, *J* = 10.5 Hz, 2H), 4.12 (t, *J* = 6.5 Hz, 2H), 3.84-3.74 (m, 2H), 3.79 (s, 3H), 1.89 (br s, 1H), 1.88-1.78 (m, 1H), 1.77-1.61 (m, 1H), 1.45-1.28 (m, 2H), 1.12 (s, 9H); ¹³C NMR (75 MHz, CDCl₃) δ 178.8, 158.7, 138.8, 133.6, 129.2, 117.9, 114.6, 73.9, 64.5, 56.7, 55.5, 38.9, 30.8, 27.4, 25.3; IR (neat) 3501, 2959, 1724,

1610, 1511, 1246, 1160, 1035 cm^{-1} ; HRMS (EI): m/z calcd for $\text{C}_{19}\text{H}_{26}\text{O}_3$ ($\text{M}^+ - \text{H}_2\text{O}$) 302.1882, found 302.1887.

2.2-Dimethylpropionic acid 5-(4-methoxyphenyl)-4-octyloxyhept-6-enyl ester

To 2.2-dimethylpropionic acid-4-hydroxy-5-(4-methoxyphenyl)hept-6-enyl ester (800 mg, 2.49 mmol) in DMF (10 mL) at 0 °C was added NaH (399 mg, 9.98 mmol). The mixture was stirred at 0 °C for 10 min and octyl iodide (2.99 g, 12.5 mmol) was added. The reaction was then slowly warmed to room temperature over 12 h and quenched by the addition of water. The mixture was then extracted with hexanes (2 x) and the organic layers were combined and washed with water and brine. The organic layer was then dried (Na_2SO_4), filtered and concentrated under reduced pressure. The desired product was obtained as an impure mixture that could not be separated.

5-(4-Methoxyphenyl)-4-octyloxyhept-6-en-1-ol

To 2,2-dimethylpropionic acid-5-(4-methoxyphenyl)-4-octyloxyhept-6-enyl ester (400 g, 0.92 mmol) in THF (5 mL) at 0 °C was added LAH (42.1 mg, 1.10 mmol). The reaction was then slowly warmed to room temperature over 4 h and quenched by the addition of 10% NaOH. The mixture was then extracted with EtOAc (3 x) and the organic layers were combined and washed with water and brine. The organic layer was then dried (Na_2SO_4), filtered and concentrated under reduced pressure. The residue was purified by flash column chromatography (30% EtOAc in hexanes) to provide the desired product with a ratio of greater than 10:1 anti:syn isomers (11.1 mg, 3%): ^1H NMR (300 MHz, CDCl_3) δ 7.13 (d, $J = 8.6$ Hz, 2H), 6.85 (d, $J = 8.6$ Hz, 2H), 6.15 (ddd, $J = 17.1, 9.9, 2.7$ Hz, 1H), 5.10 (d, $J = 10.0$ Hz, 1H), 5.02 (d, $J = 17.4$ Hz, 1H), 3.79 (s, 3H), 3.58 (t, $J = 5.0$ Hz, 2H), 3.51-3.41 (m, 4H), 1.93 (br s, 1H), 1.67-1.47 (m, 4H), 1.35-1.28 (m, 12H), 0.89 (t, $J = 6.4$ Hz, 3H); ^{13}C NMR (75 MHz, CDCl_3) δ 158.1, 139.1, 134.0, 129.2, 116.0, 113.8, 83.0, 70.63, 63.0, 55.2, 53.0, 31.8, 30.0, 29.4, 29.3, 28.6, 26.2, 22.6, 14.0; IR (neat) 3386, 2928, 2856, 1610, 1511, 1465, 1246, 1178, 1098, 1038, 914, 829 cm^{-1} ; HRMS (EI): m/z calcd for $\text{C}_{22}\text{H}_{34}\text{O}_2$ ($\text{M}^+ - \text{H}_2\text{O}$) 330.2558, found 330.2565.

Cyclization of 4

To **4** (37 mg, 0.11 mmol) in dichloroethane (6 mL) in a borosilicate flask at 20 °C were added *N*-methylquinolinium hexafluorophosphate (1.5 mg, 0.005 mmol), sodium acetate (74 mg, 0.9 mmol), anhydrous sodium thiosulfate (74 mg, 0.5 mmol) and toluene (1 mL). The mixture was stirred at room temperature while bubbling air gently and irradiating for 4 hours. The reaction

mixture was filtered through a small plug of silica gel and the filtrate was concentrated. The resulting residue was purified by flash column chromatography (5% EtOAc in hexanes) to provide **2** (13.3 mg, 61.6%).

Reagents and Conditions

a) 1-Pentynol, Pd(PPh₃)₄, CuI, *i*-Pr₂NH, THF. b) LiAlH₄, THF. c) TBDMSCl, imidazole, CH₂Cl₂. d) *m*-CPBA, NaHCO₃, CH₂Cl₂. e) (*p*-MeOC₆H₄)₂MgI, CuI, Et₂O. f) NaH, DMF, then C₈H₁₇I. g) B₄NF, THF.

Scheme 4.

5-Phenylpent-4-yn-1-ol

To a suspension of Pd(PPh₃)₄ (549.2 mg, 0.475 mmol) in THF (50 mL) were added 4-pentyn-1-ol (2.00 g, 23.7 mmol), iodobenzene (9.69 g, 47.5 mmol) and diisopropylamine (20 mL). The mixture was stirred at room temperature for 20 min and CuI (45.3 mg, 0.237 mmol) was added. The reaction was allowed to stir for 12 h. The solvent was then removed under reduced pressure and the resulting residue was dissolved in hexanes. The mixture was then passed through a pad of Celite and the filtrate was concentrated under reduced pressure. The resulting residue was purified by flash column chromatography (20% EtOAc in hexanes) to provide the desired product (3.74 g, 99%): ¹H NMR (300 MHz, CDCl₃) δ 7.37-7.41 (m 2H), 7.26-7.29 (m, 3H), 3.82 (t, *J* = 6.1 Hz, 2H), 2.54 (t, *J* = 6.9 Hz, 2H), 1.86 (p, *J* = 6.5 Hz, 2H), 1.59 (s, 1H); ¹³C NMR (75 MHz, CDCl₃) δ 137.9, 131.8, 128.6, 128.5, 127.9, 124.0, 89.6, 85.9, 81.5, 62.1, 31.7, 16.3, 12.7; IR (neat) 3351, 3079, 2947, 2878, 2390, 2200, 1597, 1489, 1441, 1060, 914, 756, 691 cm⁻¹; HRMS (EI): *m/z* calcd for C₁₁H₁₂O (M⁺) 160.0888, found 160.0890.

(*E*)-5-Phenylpent-4-en-1-ol

To a suspension of LAH (3.10 g, 81.9 mmol) in THF (40 mL) at 0 °C was added 5-phenylpent-4-yn-1-ol (3.74 g, 23.4 mmol). The mixture was stirred at 0 °C for 20 min and slowly warmed to reflux. The reaction was then stirred at reflux for 20 h. The reaction was then cooled to 0 °C and quenched by the addition of saturated aqueous Na⁺, K⁺ tartrate. The reaction mixture was extracted with ethyl acetate (2 x), and the organic layers were combined and washed with water and brine. The organic layers were then dried (Na₂SO₄), filtered and concentrated under reduced pressure. The resulting residue was purified by flash column chromatography (20% EtOAc in hexanes) to provide the desired product (3.76 g, 99%): ¹H NMR (300 MHz, CDCl₃) δ 7.29 – 7.36 (m, 5H), 6.45 (d, *J* = 15.8 Hz, 1H), 6.23 (dt *J* = 15.8, 6.7 Hz, 1H), 3.71 (t, *J* = 6.4 Hz, 2H), 2.30 (q, *J* = 6.8 Hz, 2H), 1.73 (p, *J* = 6.9 Hz, 2H), 1.40 (s, 1H); ¹³C NMR (75 MHz, CDCl₃) δ 137.6, 130.3, 130.0, 128.5, 126.9, 125.9, 62.4, 32.2, 29.3; IR (neat) 3342, 3024, 2935, 2875,

1494, 1447, 1057, 965, 741, 692 cm^{-1} ; HRMS (EI): m/z calcd for $\text{C}_{11}\text{H}_{14}\text{O}$ (M^+) 162.1045, found 162.1050.

***tert*-Butyldimethyl-(*E*)-(5-phenylpent-4-enyloxy)silane**

To (*E*)-5-phenylpent-4-en-1-ol (3.76 g, 23.2 mmol) in DMF (40 mL) at 0 °C was added imidazole (3.47g, 51.1 mmol) with stirring. The mixture was stirred for 10 min and TBSCl (3.84 g, 25.5 mmol) was added. The reaction was slowly warmed to room temperature overnight. The reaction mixture was quenched with water. The reaction mixture was extracted with diethyl ether (2 x), and then the organic layers were combined and washed with aqueous NaHCO_3 , water and brine. The organic layers were then dried (Na_2SO_4), filtered and concentrated under reduced pressure. The desired product was obtained without further purification (6.06 g, 95%): ^1H NMR (300 MHz, CDCl_3) δ 7.20-7.57 (m, 4H), 7.17-7.19 (m, 1H), 6.41 (d, J = 15.8 Hz, 1H), 6.21 (dt, J = 15.8, 6.7 Hz, 1H), 3.65 (t, J = 6.3 Hz, 2H), 2.25 (q, J = 6.9 Hz, 2H), 1.64 (p, J = 6.4 Hz, 2H), 0.90 (s, 9H), 0.05 (s, 6H); ^{13}C NMR (75 MHz, CDCl_3) δ 138.2, 130.8, 130.4, 128.8, 127.1, 126.2, 62.8, 32.7, 29.7, 26.3, 25.4, 18.6, - 4.9; HRMS (EI): m/z calcd for $\text{C}_{17}\text{H}_{28}\text{OSi}$ (M^+) 276.1909, found 276.1907.

***tert*-Butyldimethyl-[3-(3-phenyloxiranyl)propoxy]silane**

To *tert*-butyldimethyl-(*E*)-(5-phenylpent-4-enyloxy) silane (6.06 g, 21.9 mmol) in CH_2Cl_2 (90 mL) at 0 °C was added NaOAc (18.0 g, 219 mmol). The mixture was stirred for 10 min and *m*-CPBA (5.67 g, 32.9 mmol) was added. The reaction was slowly warmed to room temperature and stirred for 6 h. The reaction was then quenched by the addition of saturated aqueous $\text{Na}_2\text{S}_2\text{O}_3$. The mixture was stirred vigorously for 45 min and extracted with diethyl ether (2 x). The organic layers were then combined and washed with aqueous NaHCO_3 , water and brine. The organic layer was then dried (Na_2SO_4), filtered and concentrated under reduced pressure. The resulting residue was purified by flash column chromatography (10% EtOAc in hexanes) to provide the desired product (4.63 g, 72%): ^1H NMR (300 MHz, CDCl_3) δ 7.24-7.44 (m, 5H), 3.68 (m, 2H), 3.62 (br s, 1H), 2.99 (br s, 1H), 1.75 (m, 4H), 0.89 (s, 9H), 0.07 (s, 6H); ^{13}C NMR (75 MHz, CDCl_3) δ 138.1, 128.7, 128.3, 125.8, 63.2, 62.8, 59.4, 58.9, 29.3, 29.1, 26.2, - 5.0; IR (neat) 2954, 2929, 2885, 1471, 1462, 1255, 1099, 1005, 966, 835 cm^{-1} ; HRMS (EI): m/z calcd for $\text{C}_{17}\text{H}_{28}\text{O}_2\text{Si}$ (M^+) 292.1859, found 292.1848.

5-(*tert*-Butyldimethyl silyloxy)-1-(4-methoxyphenyl)-1-phenylpentan-2-ol

To a suspension of CuI (602.3 mg, 3.17 mmol) in THF (50 mL) at -40 °C was added 4-methoxyphenyl magnesium bromide (1.5 M in THF, 42.2 mL, 63.4 mmol). The mixture was stirred for 15 min and *tert*-butyldimethyl-[3-(3-phenyloxiranyl)propoxy]silane (4.63 g, 15.8 mmol) was added. The reaction was slowly warmed to room temperature and stirred for 6 h. The reaction mixture was then quenched by the addition of saturated aqueous NH_4Cl and bubbling air through the mixture overnight. The mixture was then extracted with ethyl acetate (2 x), and the combined organic layers were washed with water and brine. The organic layer was

then dried (Na₂SO₄), filtered and concentrated under reduced pressure. The resulting residue was purified by flash column chromatography (20% EtOAc in hexanes) to provide the desired product (4.50 g, 71%): ¹H NMR (300 MHz, CDCl₃) δ 7.25-7.38 (m, 5H), 7.20 (d, *J* = 8.7 Hz, 1H), 6.78 (d, *J* = 8.6 Hz, 2H), 4.32 (t, *J* = 7.8 Hz, 1H), 3.80 (d, *J* = 8.3 Hz, 1H), 3.75 (s, 3H), 3.59 (m, 2H), 2.13 (br s, 1H), 1.64 (m, 4H), 0.87 (s, 9H), 0.01 (s, 6H); ¹³C NMR (75 MHz, CDCl₃) δ 142.3, 135.2, 129.7, 129.5, 129.0, 128.9, 126.8, 120.9, 114.3, 114.2, 73.9, 63.5, 58.2, 55.5, 32.2, 29.4, 26.2, 18.6, -5.0; IR (neat) 3445, 3028, 2999, 2953, 2856, 1610, 1511, 1463, 1249, 1178, 1037, 835, 700 cm⁻¹; HRMS (EI): *m/z* calcd for C₂₄H₃₇O₃Si (M⁺ + H) 401.2512, found 401.2505.

***tert*-Butyl[5-(4-methoxyphenyl)-4-octyloxy-5-phenylpentyl]dimethylsilane**

To 5-(*tert*-butyldimethylsilyloxy)-1-(4-methoxyphenyl)-1-phenylpentan-2-ol (4.50 g, 11.2 mmol) in DMF (50 mL) at 0 °C was added sodium hydride (1.79 g, 44.9 mmol). The mixture was stirred for 15 min and octyl iodide (13.5 g, 56.2 mmol) was added. The reaction mixture was slowly warmed to room temperature and stirred for 5 h. The reaction was quenched by the addition of water and extracted with hexanes (2 x). The organic layers were then combined and washed with water and brine. The organic layer was then dried (Na₂SO₄), filtered and concentrated under reduced pressure. The resulting residue was purified by flash column chromatography (5% EtOAc in hexanes to 20% EtOAc in hexanes) to provide the starting material (1.11 g, 2.78 mmol) and the desired product (2.33 g, 40% isolated): ¹H NMR (300 MHz, CDCl₃) δ 7.36 (d, *J* = 8.5 Hz, 2H), 7.28-7.23 (m, 2H), 7.19-7.15 (m, 3H), 6.80 (d, *J* = 8.7 Hz, 2H), 3.94-3.91 (m, 2H), 3.77 (s, 3H), 3.57-3.51 (m, 2H), 3.37 (dt, *J* = 8.7, 6.4 Hz, 1H), 3.04 (dt, *J* = 8.7, 6.7 Hz, 1H), 1.63-1.54 (m, 4H), 1.39-1.06 (m, 12H), 0.88-0.85 (m, 12H), 0.008 (s, 3H), 0.001 (s, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 158.3, 143.3, 135.5, 129.7, 129.2, 128.3, 126.3, 114.1, 82.6, 70.6, 63.5, 55.9, 55.5, 32.1, 30.4, 29.7, 29.5, 29.3, 28.9, 24.2, 22.9, 18.6, 14.4; IR (neat) 2928, 2855, 1511, 1463, 1249, 1098, 1039, 835, 775 cm⁻¹; HRMS (EI): *m/z* calcd for C₂₈H₄₃O₃Si (M⁺ - C₄H₉) 455.2981, found 455.2981.

5-(4-Methoxyphenyl)-4-octyloxy-5-phenylpentan-1-ol

To *tert*-butyl[5-(4-methoxyphenyl)-4-octyloxy-5-phenylpentyl]dimethylsilane (2.33 g, 4.57 mmol) in THF (5 mL) was added acetic acid (15 mL) and water (5 mL). The mixture was stirred overnight and neutralized with saturated aqueous NaHCO₃. The mixture was extracted with ethyl acetate (2 x). The organic layers were then combined and washed with saturated aqueous NaHCO₃, water and brine. The organic layer was then dried (Na₂SO₄), filtered and concentrated under reduced pressure. The resulting residue was purified by flash column chromatography (20% EtOAc in hexanes) to provide the desired product (1.61 g, 89%): ¹H NMR (300 MHz, CDCl₃) δ 7.34 (d, *J* = 7.2 Hz, 2H), 7.24 (t, *J* = 7.0 Hz, 3H), 7.17 (d, *J* = 8.6 Hz, 2H), 6.80 (d, *J* = 8.6 Hz, 2H), 4.00 (d, *J* = 8.8 Hz, 1H), 3.98-3.93 (m, 1H), 3.75 (s, 3H), 3.63-3.47 (m, 2H), 3.38 (dt, *J* = 15.0, 6.3 Hz, 1H), 3.02 (dt, *J* = 15.4, 6.7 Hz, 1H), 2.07 (br s, 1H), 1.71-1.61 (m, 3H),

Chemical reaction scheme showing the conversion of a diol to a monomer. The starting material is 1-(4-methoxyphenyl)-2-phenyl-3-(octyloxy)propan-1-ol. It reacts with conditions 'a-c' to form the monomer 1-(4-methoxyphenyl)-2-phenyl-3-(octyloxy)-4-(trimethylsilyl)but-3-en-1-yl methoxymethyl ether.

S10

5-(4-Methoxyphenyl)-4-octyloxy-5-phenylpentanal

To a stirring mixture of 5-(4-methoxyphenyl)-4-octyloxy-5-phenylpentan-1-ol (445 mg, 1.12 mmol) and NaHCO₃ (235 mg, 2.8 mmol) in CH₂Cl₂ (10 mL) at 0 °C was added Dess-Martin periodinane (458 mg, 1.35 mmol). The ice bath was removed and the reaction mixture was stirred at room temperature for 1 h. Saturated NaHCO₃ (3 mL) and saturated Na₂S₂O₃ (3 mL) were added to the reaction mixture. The resulting cloudy mixture was stirred for 0.5 h at room temperature. The organic layer was separated, and the aqueous layer was extracted with CH₂Cl₂ (3 × 10 mL). The organic layers were combined, washed with H₂O and brine, then were dried over Na₂SO₄, filtered and concentrated under reduced pressure. The resulting residue was purified by flash chromatography (10% EtOAc in hexanes) to provide the desired product as 2 diastereomers (380 mg, 88%): ¹H NMR (300 MHz, CDCl₃) δ 9.70 (s, 1H), 7.18-7.43 (m, 7H), 6.85 (d, *J* = 8.2 Hz, 2H), 3.99 (br s, 2H), 3.76 (2 singlets, 3H), 3.29 (dt, *J* = 8.3, 6.4 Hz, 1H), 2.99 (dt, *J* = 8.3, 6.4 Hz, 1H), 2.38-2.42 (m, 2H), 1.93-2.00 (m, 1H), 1.69-1.77 (m, 1H), 1.17-1.38 (m, 12H), 0.93 (t, *J* = 7.0 Hz, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 202.0, 158.2, 158.2, 142.6, 134.3, 134.2, 129.8, 129.3, 128.7, 128.5, 128.3, 128.1, 126.3, 126.2, 113.0, 113.5, 81.5, 81.4, 70.7, 70.6, 55.8, 54.9, 39.8, 39.7, 31.8, 29.9, 29.3, 29.2, 25.9, 25.7, 25.6, 22.6, 14.1; IR (neat) 3061, 3028, 2999, 2926, 2855, 1723, 1610, 1510, 1455, 1301, 1248, 1178, 700 cm⁻¹; LRMS (EI): *m/z* 378, 199, 197; LRMS (CI): *m/z* 397, 379, 267, 268.

7-(4-Methoxyphenyl)-6-octyloxy-7-phenyl-2-trimethylsilylmethyl-hept-1-en-3-ol

To a stirring solution of 2-bromo-3-(trimethylsilyl)propene (88 mg, 0.45 mmol) in THF (1 mL) at -78 °C was added *tert*-butyllithium (1.35 M in pentane, 0.71 mL, 0.96 mmol) dropwise. The resulting mixture was stirred for 45 min at -78 °C and then at -20 °C for 30 min. A solution of MgBr₂ (0.45 mmol, in 1 mL of Et₂O) was added and the cloudy mixture was allowed to warm to room temperature over 2 h. The resulting clear solution was added to a solution of 5-(4-methoxyphenyl)-4-octyloxy-5-phenylpentanal (100 mg, 0.25 mmol) in THF (1 mL) at -78 °C. After 15 min, the reaction mixture was poured into a mixture of ether (20 mL) and saturated NH₄Cl (10 mL). The organic layer was separated and the aqueous layer was extracted with ether (3 × 10 mL). The combined organic layers were washed with H₂O and brine, then were dried over Na₂SO₄, filtered and concentrated under reduced pressure. The crude product was used directly in the next step.

[3-Methoxymethoxy-7-(4-methoxyphenyl)-2-methylene-6-octyloxy-7-phenylheptyl]trimethylsilane

To the crude 7-(4-methoxyphenyl)-6-octyloxy-7-phenyl-2-trimethylsilylmethyl-hept-1-en-3-ol in diisopropylethylamine (1.5 mL) at 0 °C was added methoxymethyl chloride (0.1 mL, 1.3 mmol), followed by a small crystal of DMAP. The resulting mixture was warmed to 35 °C and was stirred for 5 h at that temperature. Saturated NH₄Cl (1 mL) was added to the reaction mixture. The organic layer was separated and the aqueous layer was extracted with diethyl ether (3 × 5

mL). The organic layers were combined, washed with H₂O (5 mL) and brine (5 mL), then were dried over Na₂SO₄, filtered and concentrated under reduced pressure. The resulting residue was purified by flash chromatography (EtOAc/CH₂Cl₂/hexanes = 3/10/87) to afford the desired product (55 mg, 40% over 2 steps): ¹H NMR (300 MHz, CDCl₃) δ 7.18-7.38 (m, 7H), 6.80-6.84 (m, 2H), 4.84 (s, 1H), 4.71 (s, 1H), 4.56-4.59 (m, 1H), 4.41-4.46 (m, 1H), 3.92-3.98 (m, 2H), 3.76-3.78 (m, 4H), 3.36-3.40 (m, 1H), 3.28 (d, *J* = 2.2 Hz, 50% of 3H), 3.20 (d, *J* = 7.0 Hz, 50% of 3H), 3.04-3.07 (m, 1H), 1.47-1.62 (m, 4H), 1.15-1.40 (m, 14H), 0.89, (t, *J* = 6.7 Hz, 3H), 0.01 (s, 9H); ¹³C NMR (75 MHz, CDCl₃) δ 158.1, 146.1, 146.0, 143.4, 143.1, 142.9, 135.2, 134.9, 134.6, 130.3, 130.1, 129.6, 129.2, 128.9, 128.7, 128.6, 128.2, 126.3, 126.2, 113.9, 113.6, 110.4, 93.9, 82.7, 80.3, 80.1, 70.7, 70.4, 56.1, 55.6, 55.3, 32.0, 30.3, 29.6, 29.5, 29.0, 26.3, 22.9, 21.2, 14.3, -0.8; IR (neat) 2928, 2855, 1511, 1464, 1248, 1098, 1035, 841, 698 cm⁻¹; HRMS (EI): *m/z* calcd for C₃₂H₄₉O₂Si (M⁺ - OCH₂OCH₃) 493.3502, found 493.3523.

Cyclization of **6**

To **6** (41 mg, 0.07 mmol) in dichloroethane (3.0 mL) were added NaHCO₃ (82 mg, 1.0 mmol) and 4Å molecular sieves (82 mg). The stirring mixture was warmed to 40 °C, then ceric ammonium nitrate (101 mg, 0.19 mmol) in acetonitrile (0.9 mL) was added dropwise. After 10 min, the reaction mixture was filtered through a short pad of silica gel to remove the solid component. The filtrate was concentrated under vacuum, and the resulting residue was purified by flash chromatography (3% EtOAc in hexanes) to afford **7** (16.6 mg, 71.2%) as 2 diastereomers (~1.7 : 1): ¹H NMR (300 MHz, CDCl₃) δ 4.98 (app s, 1H, 63% of 1H), 4.94 (m, 37% of 1H), 4.92 (m, 37% of 1H), 4.86 (m, 63% of 1H), 4.68 (d, *J* = 6.6 Hz, 63% of 1H), 4.63 (d, *J* = 6.6 Hz, 63% of 1H), 4.65 (d, *J* = 6.6 Hz, 37% of 1H), 4.54 (d, *J* = 6.6 Hz, 37% of 1H), 4.03 (m, 63% of 1H), 3.21-3.50 (m, 3H), 3.24-3.36 (m, 37% of 1H), 3.38 (s, 3H, 63% of 3H), 3.40 (s, 3H, 37% of 3H), 2.57 (dd, *J* = 3.7, 13.1 Hz, 63% of 1H), 2.41 (dd, *J* = 4.5, 11.3 Hz, 37% of 1H), 2.22-2.30 (m, 37% of 1H), 2.10-2.14 (m, 63% of 1H), 1.94-2.07 (m, 2H), 1.69-1.83 (m, 1H), 1.46-1.59 (m, 4H), 1.26 (m, 10H), 0.86 (t, *J* = 6.6 Hz, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 144.9, 144.8, 112.8, 109.9, 94.7, 93.7, 77.4, 76.2, 74.3, 68.6, 68.4, 55.6, 55.5, 38.6, 37.7, 32.1, 30.4, 30.3, 30.1, 30.0, 29.9, 29.7, 29.5, 28.6, 27.2, 26.4, 22.9, 14.3; IR (neat) 2927, 2855, 1449, 1156, 1106, 1038 cm⁻¹; HRMS (EI) calcd for C₁₇H₃₂O₃ (M⁺) 284.2351, found 284.2346.

Reagents and Conditions

a) TsCl, pyridine, then NaI, acetone. b) 2,4-pentanedione, K_2CO_3 , acetone. c) CH_2O , K_2CO_3 , *p*-dioxane, H_2O .⁹ d) $(TMSO)_2$, $SnCl_4$, 1,2-cyclohexanediamine, 4 Å mol. sieves, CH_2Cl_2 .¹⁰

Scheme 6.

1-(5-Iodo-2-octyloxy-1-phenylpentyl)-4-methoxybenzene

To a stirring mixture of alcohol 5-(4-methoxyphenyl)-4-octyloxy-5-phenylpentan-1-ol (1.53 g, 3.83 mmol) and triethylamine (1.55 g, 15.31 mmol) in CH_2Cl_2 (20 mL) at 0 °C was added methanesulfonyl chloride (0.66 g, 5.74 mmol) dropwise. After 0.5 h, water was added to the reaction mixture. The organic layer was separated and the aqueous layer was extracted with CH_2Cl_2 . The organic layers were combined, washed with water, saturated $NaHCO_3$ and brine, then were dried over Na_2SO_4 , filtered and concentrated under reduce pressure. The resulting residue was dissolved in 20 mL of acetone and NaI (2.87 g, 19.14 mmol) was added. The resulting mixture was heated at reflux for 1.5 h. The reaction mixture was cooled to room temperature and concentrated under reduced pressure. The resulting residue was dissolved in water and ethyl acetate, the organic layer was separated and the aqueous layer was extracted with ether. The organic layers were combined, washed with water and brine, then were dried over Na_2SO_4 , filtered and concentrated under reduced pressure. The resulting residue was purified by flash chromatography (8% EtOAc in hexanes) to provide the desired product (1.79 g, 92%): 1H NMR (300 MHz, $CDCl_3$) δ 7.16-7.34 (m, 7H), 6.80 (d, J = 8.6 Hz, 2H), 3.91 (br s, 2H), 3.77 (s, 3H), 3.32 (dt, J = 8.6, 6.5 Hz, 1H), 3.10 (t, J = 7.0 Hz, 2H), 3.04 (dt, J = 8.6, 6.5 Hz, 1H), 1.92-1.96 (m, 2H), 1.57-1.65 (m, 2H), 1.02-1.34 (m, 12H), 0.88 (t, J = 6.9 Hz, 3H).

3-[5-(4-Methoxyphenyl)-4-octyloxy-5-phenylpentyl]-pentane-2,4-dione

To a stirring mixture of 1-(5-iodo-2-octyloxy-1-phenylpentyl)-4-methoxybenzene (969 mg, 1.91 mmol) and 2,4-pentanedione (385 mg, 2.86 mmol) in anhydrous acetone (1 mL) was added potassium carbonate (403 mg, 2.02 mmol). The resulting mixture was heated at reflux for 22 h. The reaction mixture was cooled to room temperature and filtered through Celite. The filtrate was concentrated under reduced pressure. The resulting residue was purified by flash chromatography (7-10% EtOAc in hexanes) to provide 514 mg of the desired product (56%) and 389 mg of the starting material (40%). 1H NMR (300 MHz, $CDCl_3$) δ 7.17-7.37 (m, 7H), 6.80 (d, J = 8.5 Hz, 2H), 3.87-3.95 (m, 2H), 3.77 (s, 3H), 3.54 (t, J = 7.7 Hz, 50% of 1H, enone C-H), 3.30 (dt, J = 8.7, 6.7 Hz, 1H), 3.01 (dt, J = 8.7, 6.7 Hz, 1H), 2.06 (s, 3H), 2.05 (s, 3H), 1.17-1.76 (m, 18H), 0.86 (t, J = 6.7 Hz, 3H); IR (neat) 3466, 2924, 2851, 1698, 1608, 1509, 1458, 1359, 1247, 1174, 1359, 1032, 722, 688 cm^{-1} ; LRMS (EI): m/z 351, 283, 197.

8-(4-Methoxyphenyl)-3-methylene-7-octyloxy-8-phenyloctan-2-one

To a stirring mixture of 3-[5-(4-methoxyphenyl)-4-octyloxy-5-phenylpentyl]-pentane-2,4-dione (637 mg, 1.32 mmol) and formaldehyde (37% aqueous solution, 0.33 mL, 4.1 mmol) in 1,4-dioxane (1 mL) was added K_2CO_3 (500 mg, 3.6 mmol) in water (0.33 mL). The resulting mixture was stirred for 12 h at 35 °C. Water was added and the resulting mixture was extracted with ethyl acetate. The combined organic layers were washed with water and brine, then were dried over Na_2SO_4 , filtered and concentrated under reduced pressure. The resulting residue was purified by flash chromatography (7-30% ethyl acetate in hexanes) to give the desired product (348 mg, 58%): 1H NMR (300 MHz, $CDCl_3$) δ 7.17-7.39 (m, 7H), 6.80 (d, J = 8.6 Hz, 2H), 5.96 (s, 1H), 5.70 (s, 1H), 3.91-3.97 (m, 2H), 3.77 (s, 3H), 3.35 (dt, J = 8.7, 6.7 Hz, 1H), 3.01 (dt, J = 8.7, 6.7 Hz, 1H), 2.30 (s, 3H), 2.16-2.30 (m, 2H), 1.47-1.57 (m, 4H), 1.13-1.44 (m, 12H), 0.87 (t, J = 6.8 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 199.8, 158.1, 149.2, 143.0, 135.2, 129.5, 129.0, 128.6, 128.5, 128.2, 126.1, 124.8, 113.9, 82.4, 70.6, 32.5, 31.9, 30.6, 30.2, 29.8, 29.5, 29.3, 26.2, 26.0, 24.0, 22.8, 14.2; IR (neat) 2927, 2855, 1678, 1610, 1454, 1248, 1100, 1035, 699 cm^{-1} ; LRMS (ESI): m/z 473.3 ($M + Na^+$).

Acetic acid 6-(4-methoxyphenyl)-1-methylene-5-octyloxy-6-phenylhexyl ester

To a stirring mixture of 4 Å molecular sieves (100 mg, flame dried under vacuum before using) and CH_2Cl_2 (4 mL) were added racemic *trans*-1,2-(diamino)cyclohexane (0.572 M in CH_2Cl_2 , 0.50 mL, 0.29 mmol) and $SnCl_4$ (1 M in CH_2Cl_2 , 0.29 mL, 0.29 mmol). After the reaction temperature was decreased to 0 °C, bis(trimethylsilyl)peroxide (211 mg, 1.0 mmol) was added into the reaction mixture, followed by a solution of 8-(4-methoxyphenyl)-3-methylene-7-octyloxy-8-phenyloctan-2-one (117 mg, 0.26 mmol) in CH_2Cl_2 (4 mL) after 7 min. The reaction mixture was stirred at room temperature for 40 h. Solid $Na_2S_2O_3$ (~100 mg) was added and the resulting mixture was stirred for another 3 h. The reaction mixture was filtered through a short pad of Celite, and the filtrate was concentrated under reduced pressure. The resulting residue was purified by flash chromatography (5-10% EtOAc in hexanes) to provide the desired product (87 mg, 71%): 1H NMR (300 MHz, $CDCl_3$) δ 7.24-7.34 (m, 7H), 6.87 (d, J = 8.7 Hz, 2H), 4.75-4.77 (m, 2H), 3.98-4.04 (m, 2H), 3.84 (s, 3H), 3.41 (dt, J = 8.7, 6.4 Hz, 1H), 3.09 (dt, J = 8.7, 6.6 Hz, 1H), 2.21-2.29 (m, 2H), 2.18 (s, 3H), 1.59-1.66 (m, 4H), 1.26-1.50 (m, 12H), 0.94 (t, J = 6.9 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.3, 158.1, 156.4, 143.0, 135.1, 129.5, 129.0, 128.2, 126.2, 114.0, 101.4, 82.3, 70.6, 55.7, 55.3, 33.5, 32.2, 32.0, 30.2, 29.5, 29.4, 26.2, 22.8, 22.2, 21.2, 14.3; IR (neat) 2927, 2854, 1756, 1511, 1248, 1199, 1178, 1101, 698 cm^{-1} ; LRMS (ESI): m/z 489.3 ($M + Na^+$).

Cyclization of **8**

To **8** (100 mg, 0.22 mmol) in dichloroethane (8.0 ml) were added NaHCO₃ (200mg, 2.38 mmol) and molecular sieves (200 mg). The mixture was heated to 50 °C, then ceric ammonium nitrate (294 mg, 0.54mmol) in acetonitrile (2.6 ml) was added dropwise. After 5 min the reaction mixture was cooled to room temperature and was filtered through a short pad of silica gel. The filtrate was concentrated under reduced pressure, and the residue was purified by flash chromatography (4% EtOAc in hexanes) to afford **9** (46 mg, 94.0%): ¹H NMR (300 MHz, CDCl₃) δ 3.65-3.75 (m, 1H), 3.38 (app t, *J* = 6.6 Hz, 2H), 2.57 (dd, *J* = 14.0, 3.8 Hz, 1H), 2.41 (dd, *J* = 14.0, 7.3 Hz, 1H), 2.28 (app t, *J* = 6.4 Hz, 2H), 1.93-2.05 (m, 2H), 1.78-1.82 (m, 1H), 1.65-1.69 (m, 1H), 1.48-1.55 (m, 2H), 1.26 (br s, 10H), 0.85 (t, *J* = 6.3 Hz, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 210.1, 68.7, 47.9, 41.3, 32.0, 30.3, 30.1, 29.6, 29.5, 26.4, 22.9, 20.9, 14.3; IR (neat) 2925, 2849, 1715, 1453, 1099 cm⁻¹; HRMS (EI) calcd for C₁₄H₂₆O₂ (M⁺) 226.1932, found 226.1923.

Reagents and Conditions

a) Mg, THF, then CeCl₃, then phenyl-*p*-methoxyphenylacetaldehyde. b) NaH, C₈H₁₇I, Δ.
c) CF₃CO₂H, CHCl₃, H₂O. d) Lithium trimethylsilylacetylide, THF. e) *o*-NO₂PhSO₂NHNH₂, Ph₃P, DEAD, THF.¹¹

Scheme 7.

1-Methoxy-4-(2-methoxy-1-phenylvinyl)benzene

11.64 g (34.0 mmol) of (methoxymethyl)triphenylphosphonium chloride was suspended in toluene (40 mL), and then the solvent was removed under reduced pressure. The resulting solid residue was dried under high vacuum for 2 h. To this solid suspended in THF (100 mL) at -78 °C was added LDA [34.0 mmol, prepared from diisopropylamine (6.8 mL, 48 mmol) and *n*-BuLi (1.37 M in hexanes, 25 mL, 34.0 mmol) in 50 mL of THF]. The color of the reaction changed to deep orange. After 0.5 h 4-methoxybenzophenone (5.15 g, 24.3 mmol) in THF (50 mL) was added and the reaction mixture was allowed to warm up to room temperature slowly. After 2 h, aqueous NH₄Cl (5 mL) was added to the reaction mixture. The organic layer was separated,

washed with water (10mL) and brine (10 mL), then was dried over Na₂SO₄, filtered and concentrated under reduced pressure. The resulting residue was dissolved in EtOAc (30 mL) and the solution was added into 200 mL of stirring hexanes dropwise. A precipitate formed and the suspension was filter through a pad of Celite. The filtrate was concentrated under reduced pressure and the resulting residue was purified by flash chromatography (4% EtOAc in Hexanes) to give the desired product as a clear oil (3.83 g, 66%): ¹H NMR (300 MHz, CDCl₃) δ 7.22-7.40 (m, 6H), 7.14 (d, *J* = 8.2 Hz, 1H), 6.86 (d, *J* = 9.2 Hz, 1H), 6.83 (d, *J* = 9.2 Hz, 1H), 6.41 (s, 50% of 1H), 6.39 (s, 50% of 1H), 3.82 (s, 3H), 3.77 (s, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 158.6, 158.3, 145.8, 140.8, 138.1, 133.0, 131.1, 130.2, 129.9, 129.5, 128.3, 128.0, 126.6, 126.5, 120.2, 120.1, 113.8, 113.5, 60.5, 55.3, 55.2; IR (neat) 3030, 2999, 2931, 2834, 1631, 1606, 1510, 1493, 1441, 1286, 1229, 1172, 1104, 1035, 832, 765, 698 cm⁻¹; HRMS (EI): *m/z* calcd for C₁₆H₁₆O₂ (M⁺) 240.1150, found 240.1154.

(4-Methoxyphenyl)phenylacetaldehyde

To 1-methoxy-4-(2-methoxy-1-phenylvinyl)benzene (1.6 g, 6.7 mmol) in 1,4-dioxane (50 mL) were added NaI (7.6 g, 50.9 mmol) and H₂SO₄ (2 M solution, 6 mL). The resulting mixture was heated to 50 °C and was stirred overnight at 50 °C. The reaction mixture was concentrated on a rotary evaporator to remove most of the dioxane, and then the mixture was extracted with EtOAc (3 × 30 mL). The organic layers were combined and washed with water (10 mL), aqueous NaHCO₃ (10 mL) and brine (10 mL), then were dried over Na₂SO₄, filtered and concentrated under reduced pressure. The resulting residue was purified by flash chromatography (10% EtOAc in hexanes) to afford the desired product (1.29 g, 90%) as a colorless oil: ¹H NMR (300 MHz, CDCl₃) δ 9.93 (s, 1H), 7.14-7.39 (m, 7H), 6.91 (d, *J* = 8.7 Hz, 2H), 4.85 (d, *J* = 2.2 Hz, 1H), 3.82 (s, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 198.6, 159.0, 136.7, 130.2, 129.0, 128.9, 128.2, 127.4, 114.4, 63.2, 55.1; IR (neat) 2933, 2835, 1720, 1608, 1509, 1421, 1251, 1179, 1033, 828, 699 cm⁻¹; HRMS (EI): *m/z* calcd for C₁₅H₁₄O₂ (M⁺) 226.0993, found 226.1001.

7,7-Diethoxy-1-(4-methoxyphenyl)-1-phenylheptan-2-ol

CeCl₃ (0.68 g, 2.76 mmol) was dried at 145 °C under vacuum for 1 h, then was cooled to 0 °C slowly after N₂ was introduced into the flask. THF (4.6 mL) was added dropwise at 0 °C with stirring. A suspension formed and it was subjected to sonication for 1 h. Grignard solution [made from 5-bromo-1,1-diethoxypentane (0.76 g, 3.17 mmol) and magnesium ribbon (76 mg, 3.17 mmol) in 5 mL of THF] was added into the CeCl₃ suspension dropwise at 0 °C. The reaction turned yellow. After 1.5 h, a solution of (4-methoxyphenyl)phenylacetaldehyde (0.5 g, 2.4 mmol) in THF (2 mL) was added into the reaction mixture dropwise at 0 °C. After 50 min, 10 mL of 10% acetic acid was added into the reaction mixture. The organic layer was separated and the aqueous layer was extracted with EtOAc. The organic layers were combined, washed with H₂O, saturated NaHCO₃ and brine, then were dried over Na₂SO₄, filtered and concentrated under reduced pressure. Purification of the resulting residue by flash chromatography (20-25% EtOAc

in hexanes) provided the desired product (612 mg, 66%) as 2 diastereomers: ^1H NMR (300 MHz, CDCl_3) δ 7.19-7.38 (m, 7H), 6.81 (d, J = 6.6 Hz, 50% of 2H), 6.82 (d, J = 6.6 Hz, 50% of 2H), 4.43 (t, J = 5.7 Hz, 1H), 4.28-4.32 (m, 1H), 3.81 (d, J = 8.3 Hz, 1H), 3.77 (s, 3H), 3.57-3.65 (m, 2H), 3.42-3.52 (m, 2H), 1.40-1.61 (m, 4H), 1.30-1.40 (m, 4H), 1.17 (t, J = 7.0 Hz, 6H); ^{13}C NMR (75 MHz, CDCl_3) δ 158.4, 142.0, 134.8, 129.36, 129.0, 128.9, 128.4, 128.0, 126.6, 114.0, 103.1, 74.0, 61.1, 61.0, 58.1, 55.4, 35.1, 33.8, 25.9, 24.9, 15.6; IR (neat) 3462, 2973, 2934, 1610, 1511, 1248, 1177, 1036, 700 cm^{-1} ; LRMS (EI): m/z 341, 340, 197; HRMS (EI): m/z calcd for $\text{C}_{22}\text{H}_{28}\text{O}_3$ (M^+ - HOC_2H_5) 340.2038, found 340.2021.

1-(7,7-Diethoxy-2-octyloxy-1-phenylheptyl)-4-methoxybenzene

To 7,7-diethoxy-1-(4-methoxyphenyl)-1-phenylheptan-2-ol (0.3 g, 0.78 mmol) at room temperature were added NaH (60% in mineral oil, 123 mg, 3.11 mmol) and 1-iodooctane (1.43 g, 6.21 mmol). The resulting mixture was heated to 120 $^\circ\text{C}$ and stirred overnight at that temperature. The reaction mixture was cooled to room temperature and diluted with hexanes (5 mL). Water (2 mL) was added slowly to the resulting mixture. The organic layer was separated and the aqueous layer was extracted with EtOAc. The combined organic layers were washed with water and brine, then were dried over Na_2SO_4 , filtered and concentrated under reduced pressure. The resulting residue was purified by flash chromatography (5% EtOAc in hexanes) to provide the desired product as 2 diastereomers (220 mg, 57%): ^1H NMR (300 MHz, CDCl_3) δ 7.17-7.40 (m, 7H), 6.81 (d, J = 8.6 Hz, 50% of 2H), 6.82 (d, J = 8.6 Hz, 50% of 2H), 4.41 (t, J = 5.6 Hz, 1H), 3.95 (d, J = 7.9 Hz, 1H), 3.90-3.94 (m, 1H), 3.76 (2 singlets, 3H), 3.61-3.67 (m, 2H), 3.45-3.51 (m, 2H), 3.32-3.40 (m, 1H), 3.00-3.06 (m, 1H), 1.17-1.60 (m, 20H), 1.21 (t, J = 6.7 Hz, 6H), 0.88 (t, J = 6.8 Hz, 3H); ^{13}C NMR (75 MHz, CDCl_3) δ 158.0, 143.5, 143.0, 135.2, 134.6, 130.1, 129.4, 128.9, 128.5, 128.4, 128.1, 126.2, 126.1, 113.8, 113.5, 102.9, 82.6, 82.5, 70.5, 60.9, 55.7, 55.1, 33.6, 32.9, 32.8, 31.9, 30.2, 29.4, 29.3, 26.2, 25.30, 25.1, 24.9, 22.7, 15.4, 14.2; IR (neat) 2924, 2847, 1705, 1506, 1239 cm^{-1} ; LRMS (CI): m/z 411, 339, 197.

7-(4-Methoxyphenyl)-6-octyloxy-7-phenyl-heptanal

To 1-(7,7-diethoxy-2-octyloxy-1-phenylheptyl)-4-methoxybenzene (0.22 g, 0.44 mmol) in CHCl_3 (8 mL) at 0 $^\circ\text{C}$ was added 50% aqueous trifluoroacetic acid (4 mL). After 1.5 h, saturated NaHCO_3 was added to the reaction mixture until no gas formation was seen. The organic layer was separated and the aqueous layer was extracted with EtOAc. The combined organic layers were washed with water and brine, then were dried over Na_2SO_4 , filtered and concentrated under reduced pressure. The resulting residue (0.19 g, ~100%) was sufficiently pure to be used in the next step.

9-(4-Methoxyphenyl)-8-octyloxy-9-phenyl-1-trimethylsilylnon-1-yn-3-ol

To a stirring solution of trimethylsilyl acetylene (0.22 g, 2.25 mmol) in THF (5 mL) at 0 $^\circ\text{C}$ was added $n\text{-BuLi}$ (1.6 M in hexanes, 1.26 mL, 2.0 mmol) dropwise. The reaction mixture was stirred at 0 $^\circ\text{C}$ for 45 min. The resulting solution was added into a solution of 7-(4-methoxyphenyl)-6-

octyloxy-7-phenyl-heptanal (190 mg, 0.44 mmol) in THF (3 mL) at 0 °C. After stirring for 1 h at 0 °C, saturated NH₄Cl was added to the reaction mixture. The organic layer was separated and the aqueous layer was extracted with EtOAc. The combined organic layers were washed with water and brine, then were dried over Na₂SO₄, filtered and concentrated under reduced pressure. The resulting residue was purified by flash chromatography (10% EtOAc in hexanes) to afford the desired product (172 mg, 75%): ¹H NMR (300 MHz, CDCl₃) δ 7.18-7.40 (m, 7H), 6.81 (d, *J* = 8.6 Hz, 2H), 4.32 (t, *J* = 6.2 Hz, 1H), 3.97 (d, *J* = 8.1 Hz, 1H), 3.90 (br s, 1H), 3.77 (s, 3H), 3.35 (dt, *J* = 8.6, 6.7 Hz, 1H), 3.01 (dt, *J* = 8.6, 6.7 Hz, 1H), 1.89 (br s, 1H, OH), 1.60-1.68 (m, 2H), 1.14-1.5 (m, 18H), 0.90 (t, *J* = 6.7 Hz, 3H), 0.18 (s, 9H); ¹³C NMR (75 MHz, CDCl₃) δ 158.1, 143.5, 143.0, 135.3, 134.7, 130.1, 129.5, 129.0, 128.6, 128.5, 128.2, 126.2, 113.9, 113.6, 107.0, 89.4, 82.5, 70.7, 62.9, 62.9, 55.9, 55.3, 37.8, 32.9, 32.0, 30.2, 29.5, 29.4, 26.2, 25.4, 25.3, 25.1, 22.8, 14.3, 0.1; IR (neat) 3429, 2926, 2855, 2170, 1512, 1033, 1243, 835 cm⁻¹; HRMS (EI): *m/z* calcd for C₃₂H₄₇O₃ (M⁺ - CH₃) 507.3294, found 507.3302.

[9-(4-Methoxyphenyl)-8-octyloxy-9-phenylnona-1,2-dienyl]-trimethylsilane

To a stirring solution of PPh₃ (0.13 g, 0.49 mmol) in THF (2.5 mL) at -10 °C was added DEAD (86 mg, 0.49 mmol). The reaction turned yellow. After stirring at -10 °C for 10 min, a solution of 9-(4-methoxyphenyl)-8-octyloxy-9-phenyl-1-trimethylsilylnon-1-yn-3-ol (172 mg, 0.33 mmol) in THF (2 mL) was added to the reaction mixture at the same temperature. After another 10 min, a solution of *o*-nitrobenzenesulfonylhydrazine (208 mg, 0.82 mmol) in 2 mL of THF was added. The reaction temperature was allowed to increase to room temperature slowly. After 2.5 h, the reaction mixture was concentrated under reduced pressure. The resulting residue was dissolved in 2 mL of EtOAc, and the resulting solution was added into hexanes (50 mL) with stirring dropwise. A precipitate formed and the resulting suspension was filtered through a thin silica gel plug using 5% EtOAc in hexanes as eluant. The filtrate was concentrated under reduced pressure, and the resulting residue was purified by flash chromatography (5% EtOAc in hexanes) to afford the desired product (140 mg, 84%): ¹H NMR (300 MHz, CDCl₃) δ 7.18-7.37 (m, 7H), 6.7 (d, *J* = 8.5 Hz, 2H), 4.84 (dt, *J* = 6.8, 3.5 Hz, 1H), 4.69 (ddd, *J* = 0.8, 6.8, 13.6 Hz, 1H), 3.93 (d, *J* = 7.8 Hz, 1H), 3.86 (br s, 1H), 3.77 (2 singlets, 3H), 3.31 (dt, *J* = 8.7, 6.6 Hz, 1H), 2.97 (dt, *J* = 8.7, 6.6 Hz, 1H), 1.90 (br s, 1H), 1.12-1.55 (m, 18H), 0.86 (t, *J* = 6.9 Hz, 3H), 0.08 (s, 9H); ¹³C NMR (75 MHz, CDCl₃) δ 210.1, 158.0, 143.6, 135.4, 134.7, 130.2, 129.5, 129.1, 128.6, 128.4, 128.1, 126.2, 113.9, 113.5, 83.4, 82.6, 70.6, 55.7, 55.3, 33.0, 31.9, 31.7, 30.2, 30.0, 29.5, 29.4, 28.0, 26.2, 25.1, 22.8, 14.2, -0.7; IR (neat) 2922, 2851, 1936, 1611, 1508, 1449, 1251, 1097, 1104, 851 cm⁻¹; HRMS (EI): *m/z* calcd for C₃₃H₅₀O₂ (M⁺) 506.3580, found 506.3590.

Cyclization of **10**

To **10** (73 mg, 0.145 mmol) in dichloroethane (4.0 ml) were added NaHCO_3 (140 mg, 1.7 mmol) and 4 Å molecular sieves (140 mg). The mixture was heated to 40 °C, then ceric ammonium nitrate (198 mg, 0.362 mmol) in acetonitrile (1.2 ml) was added dropwise. After 10 min the reaction mixture was filtered through a short pad of silica gel. The filtrate was concentrated under reduced pressure, and the resulting residue was purified by flash chromatography (20% toluene in hexanes) to afford the desired alkyne as 2 diastereomers in 1.2:1 ratio (27.9 mg, 81.5%) and the trimethylsilylacetylenes (4.4 mg, 9.8%). The latter were desilylated with Bu_4NF , which gave a 91% overall yield: Faster eluting (*cis*)¹² isomer: ^1H NMR (300 MHz, CDCl_3) δ 3.49-3.57 (m, 2H), 3.19-3.26 (m, 1H), 2.38-2.45 (m, 1H), 2.06 (d, $J = 2.4$ Hz, 1H), 1.96-1.99 (m, 2H), 1.47-1.69 (m, 6H), 1.27 (br, 12H), 0.86 (t, $J = 6.7$ Hz, 3H); ^{13}C NMR (75 MHz, CDCl_3) δ 87.0, 79.7, 69.6, 69.1, 35.0, 32.0, 30.5, 30.2, 29.8, 29.6, 29.4, 26.3, 24.1, 23.4, 22.8, 14.2; IR (neat) 3306, 2926, 2855, 2166, 2114, 1449, 1362, 1104, 839 cm^{-1} ; HRMS (EI) calcd for $\text{C}_{16}\text{H}_{28}\text{O}$ (M^+) 236.2140, found 236.2149. Slower eluting (*trans*)¹² diastereomer: ^1H NMR (300 MHz, CDCl_3) δ 3.50 (dt, $J = 9.2, 6.7$ Hz, 1H), 3.37 (dt, $J = 9.2, 6.7$ Hz, 1H), 3.22 (app dt, $J = 8.5, 4.1$ Hz, 1H), 2.97 (br s, 1H), 2.07 (d, $J = 2.4$ Hz, 1H), 1.70-1.75 (m, 1H), 1.26-1.70 (m, 19H), 0.86 (t, $J = 6.6$ Hz, 3H); ^{13}C NMR (75 MHz, CDCl_3) δ 85.0, 78.0, 70.6, 68.7, 32.8, 32.1, 30.2, 29.6, 29.5, 28.7, 26.4, 23.9, 22.9, 22.1, 14.3; IR (neat) 3310, 2930, 2847, 2114, 1457, 1366, 1100 cm^{-1} ; HRMS (EI) calcd for $\text{C}_{16}\text{H}_{28}\text{O}$ (M^+) 236.2140, found 236.2141.

Reagents and Conditions

- a) Me_3Al , Cp_2ZrCl_2 , dichloroethane, then allyl bromide, $\text{Pd}(\text{PPh}_3)_4$, THF.¹³ b) I_2 , Ph_3P , CH_2Cl_2 .
 c) $t\text{-BuLi}$, THF, -78 °C,¹⁴ then CeCl_3 , then 2-phenyl-*p*-methoxyphenylacetaldehyde. d) NaH , $\text{C}_8\text{H}_{17}\text{I}$, Δ . e) $(\text{Sia})_2\text{BH}$, THF, then NaOOH .

Scheme 8.

(E)-4-Methylocta-4,7-dien-1-ol

To a stirring solution of Cp_2ZrCl_2 (0.69 g, 2.37 mmol) in CH_2Cl_2 (20 mL) at $-23\text{ }^\circ\text{C}$ was added AlMe_3 (2 M in hexanes, 8.91 mL, 17.8 mmol) dropwise, followed by the addition of water (107 mg, 5.94 mmol) with caution. After 10 min, a mixture of 4-pentyn-1-ol (0.5 g, 5.94 mmol) and AlMe_3 (0.98 mL, 2 mmol) in 5 mL of CH_2Cl_2 (made by adding AlMe_3 solution slowly into the pentynol solution at $0\text{ }^\circ\text{C}$, the resulting mixture was then stirred at room temperature for 20 min.) was added slowly at $-23\text{ }^\circ\text{C}$. The cold bath was removed and the reaction mixture was allowed to warm up to room temperature slowly. After 5 h, a mixture of $\text{Pd}(\text{PPh}_3)_4$ (0.2 g, 0.178 mmol) and allyl bromide (0.72 g, 5.94 mmol) in 10 mL of THF (made by adding allyl bromide into the $\text{Pd}(\text{PPh}_3)_4$ solution slowly) was added to the reaction mixture at room temperature. After 12 h, saturated aqueous K_2CO_3 (5 mL) was added to the reaction mixture at $0\text{ }^\circ\text{C}$ cautiously. Some Na_2SO_4 solid was then added. The resulting thick mixture was stirred for 5 min and was filtered through a Celite pad. The filtrate was concentrated under reduced pressure. The resulting residue was purified by flash chromatography (15% EtOAc in hexanes) to afford the desired product (625 mg, 75%): ^1H NMR (300 MHz, CDCl_3) δ 5.72-5.86 (m, 1H), 5.18-5.23 (m, 1H), 4.92-5.04 (m, 2H), 3.53 (dt, $J = 1.5, 6.6\text{ Hz}$, 2H), 2.73 (t, $J = 6.7\text{ Hz}$, 2H), 2.06 (t, $J = 7.5\text{ Hz}$, 2H), 1.63-1.73 (m, 2H), 1.62 (s, 3H); ^{13}C NMR (75 MHz, CDCl_3) δ 137.3, 136.1, 121.76, 114.2, 62.5, 35.9, 32.3, 30.8, 15.9; IR (neat) 3331, 2937, 1635, 1437, 1061, 908 cm^{-1} ; HRMS (EI): m/z calcd for $\text{C}_9\text{H}_{16}\text{O}$ (M^+) 140.1201, found 140.1203.

(E)-8-Iodo-5-methylocta-1,4-diene

To a stirring mixture of (*E*)-4-methylocta-4,7-dien-1-ol (2.12 g, 15.16 mmol), PPh_3 (5.57 g, 21.22 mmol), imidazole (1.44 g, 21.22 mmol) and CH_2Cl_2 (50 mL) at $0\text{ }^\circ\text{C}$ was added iodine (5.39 g, 21.22 mmol). After 30 min, saturated aqueous Na_2SO_3 was added to the reaction mixture. The organic layer was separated and the aqueous layer was extracted with CH_2Cl_2 . The organic layers were combined, washed with H_2O and brine, then were dried over Na_2SO_4 , filtered and concentrated under reduced pressure. The resulting residue was purified by flash chromatography (straight hexanes) to provide the desired product (3.29 g, 87%): ^1H NMR (300 MHz, CDCl_3) δ 5.71-5.85 (m, 1H), 5.20 (dt, $J = 0.9, 7.2\text{ Hz}$, 1H), 4.93-5.08 (m, 2H), 3.11 (t, $J = 6.9\text{ Hz}$, 2H), 2.72-2.77 (m, 2H), 2.08 (t, $J = 6.8\text{ Hz}$, 2H), 1.88-1.95 (m, 2H), 1.60 (s, 3H); ^{13}C NMR (75 MHz, CDCl_3) δ 137.0, 134.2, 122.8, 114.3, 40.0, 32.2, 31.6, 15.9, 6.5; IR (neat) 2975, 2932, 2842, 1637, 1429, 1217, 1166, 992, 909 cm^{-1} ; HRMS (EI): m/z calcd for $\text{C}_9\text{H}_{15}\text{I}$ (M^+) 250.0218, found 250.0219.

(E)-1-(4-Methoxyphenyl)-6-methyl-1-phenyldeca-6,9-dien-2-ol

To (*E*)-8-iodo-5-methylocta-1,4-diene (3.29 g, 13.16 mmol) in 200 mL of mixed solvents of *n*-pentane/ether (3:2 by volume) at $-78\text{ }^\circ\text{C}$ was added *t*-BuLi (1.18 M in hexanes, 14.4 mL, 17.0 mmol) dropwise. The reaction turned cloudy. After 5 min, the reaction mixture was allowed to warm up to $0\text{ }^\circ\text{C}$. The reaction mixture was stirred at $0\text{ }^\circ\text{C}$ for 1.5 h and then at room temperature

for another 1.5 h. The resulting solution was cannulated into a suspension of anhydrous CeCl_3 (3.244 g, 13.16 mmol) in THF (43 mL) at $-78\text{ }^\circ\text{C}$. The reaction turned yellow brown. The reaction mixture was warmed up to $0\text{ }^\circ\text{C}$ and was stirred at $0\text{ }^\circ\text{C}$ for 40 min. A solution of (4-methoxyphenyl)phenylacetaldehyde (1.98 g, 8.77 mmol) in THF (10 mL) was then added into the reaction mixture dropwise at $0\text{ }^\circ\text{C}$. After 10 min, the cold bath was removed and the reaction mixture was stirred for another 30 min. 10% acetic acid (30 mL) was added into the reaction mixture. The organic layer was separated and the aqueous layer was extracted with EtOAc. The organic layers were combined, washed with H_2O , saturated NaHCO_3 and brine, then were dried over Na_2SO_4 , filtered and concentrated under reduced pressure. The resulting residue was purified by flash chromatography (13% EtOAc in hexanes) to provide the desired product (1.99 g, 65%): ^1H NMR (300 MHz, CDCl_3) δ 7.18-7.32 (m, 7H), 6.86 (d, $J = 6.6$ Hz, 50% of 2H), 6.85 (d, $J = 6.6$ Hz, 50% of 2H), 5.69-5.82 (m, 1H), 5.07-5.13 (m, 1H), 4.90-5.01 (m, 2H), 4.28-4.33 (m, 1H), 3.81 (d, $J = 8.2$ Hz, 1H), 3.77 (s, 3H), 2.68 (t, $J = 6.4$ Hz, 2H), 1.94 (t, $J = 5.7$ Hz, 2H), 1.55 (s, 3H), 1.41-1.67 (m, 4H); ^{13}C NMR (75 MHz, CDCl_3) δ 158.6, 143.0, 137.6, 136.6, 133.6, 130.0, 128.8, 128.3, 126.6, 121.6, 114.4, 114.3, 73.9, 58.1, 55.4, 39.6, 34.8, 32.4, 29.5, 24.2, 16.0; IR (neat) 3559, 3446, 2933, 1610, 1510, 1452, 1249, 1178, 1034, 700 cm^{-1} ; HRMS (EI): m/z calcd for $\text{C}_{24}\text{H}_{30}\text{O}_2$ (M^+) 350.2245, found 350.2236.

(E)-1-Methoxy-4-(6-methyl-2-octyloxy-1-phenyldeca-6,9-dienyl)benzene

To (E)-1-(4-methoxyphenyl)-6-methyl-1-phenyldeca-6,9-dien-2-ol (1.98 g, 5.68 mmol) at room temperature was added NaH (60% in mineral oil, 0.8 g, 21 mmol). After 5 min, 1-iodooctane (6.82 g, 28.4 mmol) was added. The reaction mixture was heated to $120\text{ }^\circ\text{C}$ and was stirred overnight at $120\text{ }^\circ\text{C}$. The reaction mixture was cooled to room temperature and diluted with hexanes, followed by the addition of an ice chunk. The organic layer was separated and the aqueous layer was extracted with ether. The combined organic layers were washed with water and brine, then were dried over Na_2SO_4 , filtered and concentrated under reduced pressure. The resulting residue was purified by flash chromatography (5% EtOAc in hexanes) to provide the desired product (2.35 g, 90%): ^1H NMR (300 MHz, CDCl_3) δ 7.16-7.40 (m, 7H), 6.80 (d, $J = 7.5$ Hz, 2H), 5.70-5.83 (m, 1H), 5.07-5.12 (m, 1H), 4.92-5.02 (m, 2H), 3.93 (d, $J = 7.9$, 1H), 3.86-3.90 (m, 1H), 3.77 (2 singlets, 3H), 3.31 (dt, $J = 8.6, 6.5$ Hz, 1H), 2.99 (dt, $J = 8.5, 6.5$ Hz, 1H), 2.69 (t, $J = 6.7$ Hz, 2H), 1.90 (t, $J = 6.9$ Hz, 2H), 1.54 (s, 3H), 1.13-1.54 (m, 16H), 0.85 (t, $J = 6.9$ Hz, 3H); ^{13}C NMR (75 MHz, CDCl_3) δ 158.0, 143.5, 143.1, 137.6, 136.5, 135.3, 134.8, 130.1, 129.5, 129.0, 128.6, 128.4, 128.1, 126.2, 126.1, 121.48, 114.2, 113.8, 113.5, 82.5, 82.4, 70.6, 70.5, 55.7, 55.6, 55.2, 39.7, 32.5, 32.3, 31.9, 30.2, 29.8, 29.5, 26.3, 26.2, 23.6, 22.8, 15.9, 14.2; IR (neat) 2928, 2855, 1510, 1510, 1463, 1248, 1178, 1101, 1038, 699 cm^{-1} ; HRMS (EI): m/z calcd for $\text{C}_{32}\text{H}_{46}\text{O}_2$ (M^+) 462.3497, found 462.3491.

(E)-10-(4-Methoxyphenyl)-5-methyl-9-octyloxy-10-phenyldec-4-en-1-ol

To a stirring solution of 2-methylbutene (1.28 mL, 12.12 mmol) in THF (12 mL) at $-5\text{ }^{\circ}\text{C}$ was added $\text{BH}_3\cdot\text{THF}$ (1M in THF, 6.1 mL, 6.1 mmol) dropwise. The reaction mixture was stirred for 45 min at $-5\text{ }^{\circ}\text{C}$. The resulting solution was added to a solution of (*E*)-1-methoxy-4-(6-methyl-2-octyloxy-1-phenyldeca-6,9-dienyl)benzene (1.4 g, 3.03 mmol) in THF (12 mL) at $0\text{ }^{\circ}\text{C}$. The reaction mixture was stirred for 1.5 h at $0\text{ }^{\circ}\text{C}$, followed by the addition of water (1 mL), NaOH (3 mL, 10%) and H_2O_2 (3 mL, 30%). After stirring for 2 h, the organic layer was separated and the aqueous layer was extracted with EtOAc. The combined organic layers were washed with water and brine, and then were dried over Na_2SO_4 , filtered and concentration under reduced pressure. The resulting residue was purified by flash chromatography (15% EtOAc in hexanes) to afford the desired product (670 mg, 46%): ^1H NMR (300 MHz, CDCl_3) δ 7.18-7.29 (m, 7H), 6.81 (d, $J = 8.6$ Hz, 2H), 5.05 (t, $J = 7.1$ Hz, 1H), 3.95 (d, $J = 9.5$ Hz, 1H), 3.89-3.92 (m, 1H), 3.78 (2 singlets, 3H), 3.59 (t, $J = 6.3$ Hz, 2H), 3.36 (dt, $J = 8.3, 6.5$ Hz, 1H), 3.03 (dt, $J = 8.6, 6.5$ Hz, 1H), 2.01 (q, $J = 7.2$ Hz, 2H), 1.90 (t, $J = 6.8$ Hz, 2H), 1.55 (s, 3H), 1.15-1.70 (br m, 18H), 0.85 (t, $J = 6.9$ Hz, 3H); ^{13}C NMR (75 MHz, CDCl_3) δ 158.1, 143.2, 135.9, 135.5, 129.6, 129.1, 128.3, 126.2, 123.9, 144.0, 113.6, 82.5, 70.6, 62.9, 55.8, 55.4, 39.8, 32.9, 32.3, 32.0, 30.3, 29.6, 29.4, 26.3, 24.3, 23.4, 22.9, 16.0, 14.3; IR (neat) 3368 (br), 2928, 2855, 1510, 1457, 1248, 1177, 1100, 1036, 698 cm^{-1} ; LRMS (CI): m/z 481($\text{M}^+ + 1$), 351, 197; LRMS (ESI): m/z 503.5($\text{M} + \text{Na}^+$).

Cyclization of 12

To **12** (100 mg, 0.208 mmol) in dichloroethane (6.0 mL) were added *N*-methylquinolinium hexafluorophosphate (3.0 mg, 0.01 mmol), NaOAc (200 mg, 2.4 mmol), $\text{Na}_2\text{S}_2\text{O}_3$ (200 mg, 1.3 mmol), 4Å molecular sieves (200 mg) and toluene (1 mL). The mixture was stirred at room temperature while bubbling air gently and irradiating. After 80 min, 1 mg (0.0035 mmol) of *N*-methylquinolinium hexafluorophosphate was added and the reaction was allowed to proceed for another 20 min. The reaction mixture was filtered through a short pad of silica gel, and the filtrate was concentrated under reduced pressure. The resulting residue was purified by flash chromatography on silica gel (3% ethyl acetate in hexanes) to afford the desired product (29 mg, 49%): ^1H NMR (300 MHz, CDCl_3) δ 3.77-3.86 (dt, $J = 3.5, 11.9$ Hz, 1H), 3.62-3.68 (app ddt, $J = 11.8, 5.2, 1.4$ Hz, 1H), 3.40 (dt, $J = 9.0, 6.3$ Hz, 1H), 3.30 (app dd, $J = 2.5, 2.7$ Hz, 1H), 3.10 (dt, $J = 9.0, 6.3$ Hz, 1H), 1.83-1.91 (m, 2H), 1.59-1.71 (m, 4H), 1.45-1.56 (m, 4H), 1.20-1.39 (m, 13H),

1.35 (s, 3H), 0.87 (t, $J = 6.7$ Hz, 3H); ^{13}C NMR (75 MHz, CDCl_3) δ 79.2, 74.9, 69.6, 61.3, 49.1, 40.7, 32.1, 30.4, 29.6, 29.5, 29.3, 27.8, 26.6, 23.4, 22.9, 19.5, 18.3, 14.3; IR (neat) 2928, 2858, 1454, 1082 cm^{-1} ; HRMS (EI) calcd for $\text{C}_{18}\text{H}_{34}\text{O}_2$ (M^+) 282.2558, found 282.2563.

Reagents and Conditions

a) 1-lithio-1-decyne, THF. b) LiAlH_4 , THF. c) NaH, DMF, then allyl bromide.
d) SiA_2BH , THF, then NaOOH.

Scheme 9.

1-(4-Methoxyphenyl)dodec-3-yn-2-ol

To 1-decyne (2.71 g, 19.6 mmol) in THF (20 mL) at -78°C was added *n*-butyl lithium (1.6 M in hexanes, 22.3 mmol, 13.9 mL). The mixture was stirred for 20 min and (4-methoxyphenyl)acetaldehyde (1.96 g, 13.1 mmol) was added dropwise. The reaction was then slowly warmed to room temperature overnight. The reaction was quenched by the addition of saturated aqueous NH_4Cl and extracted with ethyl acetate (2 x). The organic layers were then combined and washed with water and brine. The organic layer was then dried (Na_2SO_4), filtered and concentrated under reduced pressure. The resulting residue was purified by flash column chromatography (15% EtOAc in hexanes) to provide the desired product (2.59 g, 69%): ^1H NMR (300 MHz, CDCl_3) δ 7.20 (d, $J = 8.6$ Hz, 2H), 6.85 (d, $J = 8.6$ Hz, 2H), 4.53 (tt, $J = 6.3$, 1.8 Hz, 1H), 3.80 (s, 3H), 2.95 (dd, $J = 13.6$, 6.1 Hz, 1H), 2.90 (dd, $J = 13.5$, 6.1 Hz, 1H), 2.20 (td, $J = 6.9$, 1.9 Hz, 2H), 1.90 (s, 1H), 1.49 (app p, $J = 7.5$ Hz, 2H), 1.36-1.28 (m, 12H), 0.90 (t, $J = 6.5$ Hz, 3H); ^{13}C NMR (75 MHz, CDCl_3) δ 158.5, 130.7, 128.7, 86.5, 80.6, 63.5, 55.2, 43.5, 31.8, 29.3, 29.0, 28.8, 28.6, 22.6, 18.6, 14.0; IR (neat) 3418, 2927, 2855, 1613, 1512, 1464, 1246, 1177, 1036, 819, 760 cm^{-1} ; HRMS (EI): m/z calcd for $\text{C}_{19}\text{H}_{28}\text{O}_2$ (M^+) 288.2089, found 288.2088.

1-(4-Methoxyphenyl)dodec-3-en-2-ol

To a suspension of LAH (786.2 mg, 20.72 mmol) in THF (20 mL) at 0°C was slowly added 1-(4-methoxyphenyl)dodec-3-yn-2-ol (1.99 g, 6.90 mmol). The mixture was then warmed to reflux and stirred for 18 h. The reaction was then cooled to 0°C and quenched by the addition of NaOH (10% aq). The mixture was then extracted with ethyl acetate (2 x) and the organic layers were combined and washed with water and brine. The organic layer was then dried (Na_2SO_4), filtered and concentrated under reduced pressure. The resulting residue was purified by column chromatography (15% EtOAc in hexanes) to provide the desired product (1.74 g, 87%): ^1H NMR (300 MHz, CDCl_3) δ 7.14 (d, $J = 8.6$ Hz, 2H), 6.84 (d, $J = 8.6$ Hz, 2H), 5.64 (dt, $J = 15.4$, 6.5 Hz, 1H), 5.51 (dd, $J = 15.4$, 6.5 Hz, 1H), 4.25 (app q, $J = 6.2$ Hz, 1H), 3.80 (s, 3H), 2.80 (dd, $J = 13.6$, 5.3 Hz, 1H), 2.72 (dd, $J = 13.6$, 7.6 Hz, 1H), 2.02 (app q, $J = 6.6$ Hz, 2H), 1.56 (s, 1H),

1.38-1.27 (m, 12H), 0.89 (t, $J = 6.5$ Hz, 3H); ^{13}C NMR (75 MHz, CDCl_3) δ 158.6, 132.6, 132.2, 130.8, 130.3, 114.2, 73.9, 55.5, 43.5, 32.5, 32.2, 29.7, 29.5, 29.4, 22.9, 14.3; IR (neat) 3396, 2924, 2853, 1612, 1512, 1464, 1300, 1246, 1177, 1038, 969, 820 cm^{-1} ; HRMS (EI) m/z calcd for $\text{C}_{19}\text{H}_{30}\text{O}_2$ (M^+) 290.2245, found 290.2259.

1-(2-Allyloxydodec-3-enyl)-4-methoxybenzene

To 1-(4-methoxyphenyl)dodec-3-en-2-ol (330 mg, 1.14 mmol) in DMF (5 mL) at 0 °C was added NaH (136.4 mg, 3.41 mmol). The mixture was stirred for 20 min and allyl bromide (412 mg, 3.41 mmol) was added. The mixture was then slowly warmed to room temperature and stirred for 12 h. The reaction was quenched by the addition of water. The mixture was extracted with hexanes (2 x) and the organic layers were combined and washed with water and brine. The organic layer was then dried (Na_2SO_4), filtered and concentrated under reduced pressure. The resulting residue was purified by flash column chromatography (5% EtOAc in hexanes) to provide the desired product (291 mg, 77%): ^1H NMR (300 MHz, CDCl_3) δ 7.12 (d, $J = 8.57$ Hz, 2H), 6.81 (d, 8.59 Hz, 2H), 5.85 (ddd, $J = 17.2, 10.4, 5.2$ Hz, 1H), 5.47 (dt, $J = 15.4, 6.7$ Hz, 1H), 5.24 (dd $J = 15.3, 8.0$, Hz, 1H), 5.19 (dd, $J = 17.2, 1.7$ Hz, 1H), 5.10 (dd, $J = 10.38, 1.4$ Hz, 1H), 4.01 (dd, $J = 12.9, 7.7$ Hz, 1H), 3.85 – 3.77 (m, 2H), 3.77 (s, 3H), 2.87 (dd $J = 13.7, 6.7$ Hz, 1H), 2.70 (dd, $J = 13.7, 6.4$ Hz, 1H), 2.00 (q, $J = 6.7$ Hz, 2H), 1.30-1.24 (m, 12H), 0.88 (t, $J = 6.5$ Hz, 3H); ^{13}C NMR (75 MHz, CDCl_3) δ 157.9, 135.3, 134.4, 130.7, 130.6, 130.0, 116.2, 113.4, 81.3, 68.9, 55.2, 41.6, 32.2, 31.8, 29.7, 29.4, 29.3, 29.2, 29.0, 22.6, 14.0; IR (neat) 2927, 2854, 1613, 1513, 1464, 1300, 1247, 1177, 1109, 1074, 1039, 970, 821, 734 cm^{-1} ; HRMS (EI): m/z calcd for $\text{C}_{19}\text{H}_{29}\text{O}_1$ ($\text{M}^+ - \text{C}_4\text{H}_9$) 273.2218, found 273.2206.

3-[1-(4-Methoxybenzyl)undec-2-enyloxy]propan-1-ol

To a stirred solution of 2-methylbutene (247 mg, 3.52 mmol) in THF (10 mL) at -10 °C was added $\text{BH}_3 \cdot \text{THF}$ (1.0 M in THF, 1.76 mmol, 1.76 mL) drop wise. The mixture was stirred for 45 min and 1-(2-allyloxydodec-3-enyl)-4-methoxybenzene (291 mg, 0.882 mmol) was added. The reaction was stirred for 3 h and quenched by the addition of water (1 mL), 10 % aqueous NaOH (1 mL) and 30% H_2O_2 (1 mL). The mixture was then vigorously stirred overnight and extracted with ethyl acetate (2 x). The organic layers were then combined and washed with water and brine. The organic layer was then dried (Na_2SO_4), filtered and concentrated under reduced pressure. The resulting residue was purified by flash column chromatography (10% EtOAc in hexanes) to provide the desired product (169 mg, 55%): ^1H NMR (300 MHz, CDCl_3) δ 7.08 (d, $J = 8.6$ Hz, 2H), 6.81 (d, $J = 8.6$ Hz, 2H), 5.53 (dt, $J = 15.4, 6.7$ Hz, 1H), 5.26 (dd, $J = 15.4, 8.0$ Hz, 1H), 3.79-3.75 (m, 1H), 3.78 (s, 3H), 3.70-3.63 (m, 3H), 3.35 (dt, $J = 11.4, 5.7$ Hz, 1H), 2.79 (dd, $J = 13.8, 7.2$ Hz, 1H), 2.69 (dd, $J = 13.8, 5.8$ Hz, 1H), 2.01 (app q, $J = 6.7$ Hz, 2H), 1.75 (app p, $J = 5.5$ Hz, 2H), 1.35-1.25 (m, 12H), 0.88 (t, $J = 6.4$ Hz, 3H); ^{13}C NMR (75 MHz, CDCl_3) δ 158.0, 134.4, 130.5, 130.4, 129.9, 113.6, 82.5, 67.7, 62.3, 55.2, 41.7, 32.1, 32.0, 31.8, 29.4, 29.2, 29.1, 29.0, 22.6, 14.0; IR (neat) 3388, 2955, 2925, 2854, 1512, 1464, 1442, 1300, 1247,

1087, 1040, 970 cm^{-1} ; HRMS (EI): m/z calcd for $\text{C}_{22}\text{H}_{36}\text{O}_3$ ($\text{M}^+ - \text{C}_3\text{H}_8\text{O}_2$) 272.2140, found 272.2145.

Cyclization of **14**

To **14** (101 mg, 0.29 mmol) in dichloroethane (6 mL) in a borosilicate flask at 20 °C were added *N*-methylquinolinium hexafluorophosphate (7 mg, 0.025 mmol), sodium acetate (200 mg, 2.4 mmol), anhydrous sodium thiosulfate (200 mg, 1.3 mmol) and toluene (1 mL). The mixture was stirred at room temperature while bubbling air gently and irradiating for 4 hours. The reaction mixture was filtered through a small plug of silica and the filtrate was concentrated. The resulting residue was purified by flash column chromatography (5% EtOAc in hexanes) to provide **15** (50 mg, 77%): ^1H NMR (300 MHz, CDCl_3) δ 5.91 (dt, $J = 15.7, 6.6$ Hz, 1H), 5.50 (ddt, $J = 15.7, 5.1, 1.3$ Hz, 1H), 4.93 (d, $J = 5.1$ Hz, 1H), 4.14 (dd, $J = 10.6, 4.9$ Hz, 2H), 3.83 (td, $J = 12.3, 2.4$ Hz, 2H), 2.20-2.02 (m, 4H), 1.41-1.26 (m, 12 H), 0.88 (t, $J = 6.4$ Hz, 3H); ^{13}C NMR (75 MHz, CDCl_3) δ 135.7, 126.8, 101.2, 66.9, 32.0, 31.9, 29.4, 29.2, 28.6, 25.7, 22.6, 14.0; IR (neat) 2955, 2924, 2852, 1377, 1237, 1142, 1087, 996, 967 cm^{-1} ; HRMS (EI) calcd for $\text{C}_{14}\text{H}_{25}\text{O}_2$ ($\text{M}-1$) 225.1855, found 225.1854.

Reagents and Conditions

a) Dess-Martin periodinane, CH_2Cl_2 . b) $(\text{MeO})_2\text{P}(\text{O})\text{C}(\text{N}_2)\text{Ac}$, K_2CO_3 , MeOH.¹⁵
c) HOAc, $\text{Ph}_3\text{PRu}(p\text{-cymene})\text{Cl}$, PhMe.¹⁶

Scheme 10.

3-[1-(4-Methoxybenzyl)undec-2-enyloxy]propionaldehyde

To 3-[1-(4-methoxybenzyl)undec-2-enyloxy]propan-1-ol (500 mg, 1.43 mmol) in CH_2Cl_2 (5 mL) at 0 °C was added NaHCO_3 (1.20 g, 14.3 mmol). The mixture was stirred at 0 °C for 5 min and Dess-Martin periodinane (915 mg, 2.15 mmol) was added. The reaction was then slowly warmed to room temperature and stirred for 2 h. The reaction was then quenched by the addition of water and saturated aqueous $\text{Na}_2\text{S}_2\text{O}_3$. The mixture was then filtered through a pad of Celite and the organic layer was washed with water and brine. The organic layer was then dried (Na_2SO_4), filtered and concentrated under reduced pressure. The aldehyde was used without further purification.

1-(2-But-3-ynyloxydodec-3-enyl)-4-methoxybenzene

To dimethyl(1-diazo-2-oxopropyl)phosphonate⁵ (533 mg, 2.77 mmol) in methanol (3 mL) at 0 °C was added K_2CO_3 (193 mg, 1.39 mmol). The mixture was stirred at 0 °C for 30 minutes and 3-

[1-(4-methoxybenzyl)undec-2-enyloxy]propionaldehyde (481 mg, 1.39 mmol) was added in methanol. The reaction was then slowly warmed to room temperature over 12 h, and the solvent was removed under reduced pressure. The resulting residue was purified by flash column chromatography (5% EtOAc in hexanes) to provide the desired product (134 mg, 28%): ^1H NMR (300 MHz, CDCl_3) δ 7.12 (d, J = 8.6 Hz, 2H), 6.81 (d, J = 8.6 Hz, 2H), 5.51 (dt, J = 15.4, 6.6 Hz, 1H), 5.30 (dd, J = 15.4, 7.9 Hz), 3.80-3.77 (m, 1H), 3.79 (s, 3H), 3.59 (dt, J = 9.3, 7.2 Hz, 1H), 3.36 (dt, J = 9.4, 7.1 Hz), 2.86 (dd, J = 13.7, 6.8 Hz, 1H), 2.67 (dd, J = 13.7, 6.2 Hz, 1H), 2.38 (td, J = 7.2, 2.6 Hz, 2H), 2.02 (app q, J = 6.7 Hz, 2H), 1.95 (t, J = 2.6 Hz, 1H), 1.35-1.25 (m, 12H), 0.89 (t, J = 6.5 Hz, 3H); ^{13}C NMR (75 MHz, CDCl_3) δ 157.9, 134.3, 130.7, 130.5, 129.9, 113.5, 82.3, 81.6, 69.0, 66.4, 55.2, 41.6, 32.1, 31.9, 29.4, 29.3, 29.1, 29.0, 22.6, 19.9, 14.0; IR (neat) 3311, 2925, 2854, 1740, 1512, 1246, 1092, 1040 cm^{-1} ; HRMS (EI): m/z calcd for $\text{C}_{23}\text{H}_{34}\text{O}_2$ (M^+) 342.2559, found 342.2549.

Acetic acid 3-[1-(4-methoxybenzyl)undec-2-enyloxy]-1-methylenepropyl ester

To 1-(2-but-3-ynyloxydodec-3-enyl)-4-methoxybenzene (134 mg, 0.39 mmol) in toluene (5 mL) was added $\text{Ru}(p\text{-cymene})\text{PPh}_3\text{Cl}$ (2.2 mg, 0.004 mmol) and acetic acid (23.4 mg, 0.39 mmol). The mixture was then warmed to 80 $^\circ\text{C}$ and stirred for 12 h. The reaction was then cooled to room temperature and the solvent was removed under reduced pressure. The resulting residue was purified by flash column chromatography (10% EtOAc in hexanes) to provide the desired product (61.7 mg, 58 % (based on recovered SM)): ^1H NMR (300 MHz, CDCl_3) δ 7.10 (d, J = 8.6 Hz, 2H), 6.81 (d, J = 8.6 Hz, 2H), 5.48 (dt, J = 15.4, 6.7 Hz, 1H), 5.30 (ddt, J = 15.4, 8.0, 1.1 Hz, 1H), 4.71 (d, J = 1.3 Hz, 1H), 4.68 (d, J = 1.5 Hz, 1H), 3.79-3.74 (m, 1H), 3.78 (s, 3H), 3.62 (dt, J = 9.5, 6.6 Hz, 1H), 3.35 (dt, J = 9.5, 6.6 Hz, 1H), 2.84 (dd, J = 13.7, 6.8 Hz, 1H), 2.62 (dd, J = 13.7, 6.1 Hz, 1H), 2.43 (app t, J = 6.2 Hz, 2H), 2.11 (s, 3H), 2.08 (app q, J = 6.8 Hz, 2H), 1.37-1.27 (m, 12H), 0.89 (t, J = 6.5 Hz); ^{13}C NMR (75 MHz, CDCl_3) δ 168.9, 157.9, 153.7, 134.8, 130.7, 130.6, 130.0, 113.3, 102.4, 65.0, 55.1, 41.6, 34.0, 32.1, 29.5, 29.3, 29.1, 28.9, 22.6, 20.9, 14.0; IR (neat) 2925, 2854, 1758, 1667, 1612, 1441, 1465, 1370, 1300, 1246, 1179, 1090, 1039, 1020, 970, 880, 827, 733 cm^{-1} ; HRMS (ESI): m/z calcd for $\text{C}_{25}\text{H}_{38}\text{O}_4\text{Na}$ ($\text{M}+\text{Na}^+$) 425.2668, found 425.2668.

Cyclization 16

To **16** (62 mg, 0.15 mmol) in dichloroethane (3.5 mL) were added 4 Å molecular sieves (120 mg) and NaHCO_3 (120 mg, 1.4 mmol). The mixture was then warmed to 40 $^\circ\text{C}$ and stirred for 15

minutes. Ceric ammonium nitrate (168 mg, 0.31 mmol) in CH₃CN (1.5 mL) was added dropwise and the reaction was stirred at 40 °C for 1 hour. The reaction mixture was filtered through silica and the filtrate was concentrated. The resulting residue was purified by flash column chromatography (5% EtOAc in hexanes) to provide the desired product (33.1 mg, 90.8%): ¹H NMR (300 MHz, CDCl₃) δ 5.75 (dt, *J* = 15.5, 6.6 Hz, 1H), 5.55 (ddt, *J* = 15.5, 6.3, 1.3 Hz, 1H), 4.31 (ddd, *J* = 11.5, 7.2, 1.8 Hz), 4.10 (m, 1H), 3.72 (td, *J* = 11.6, 3.0 Hz, 1H) 2.61 (m, 1H), 2.45 (s, 1H), 2.43 (m, 1H), 2.37 (m, 1H), 2.05 (app q, 2H), 1.38-1.26 (m, 12H), 0.88 (t, *J* = 6.5 Hz, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 206.5, 134.1, 128.8, 78.3, 66.1, 48.3, 42.2, 32.2, 31.8, 31.6, 29.7, 29.4, 29.2, 29.1, 28.9, 22.6, 14.0; IR (neat) 2925, 2853, 1721, 1466, 1369, 1247, 1156, 1082, 969 cm⁻¹; HRMS (EI) calcd for C₁₅H₂₆O₂ 238.1933, found 238.1940.

References

- (1) Efange, S. M. N.; Michelson, R. H.; Dutta, A. K.; Parson, S. M. *J. Med. Chem.* **1991**, *34*, 2638.
- (2) Fevig, J. M.; Buriak, J., Jr.; Caciola, J.; Alexaner, R. S.; Kettner, C. A.; Knabb, R. M.; Pruitt, J. R.; Weber, P. C.; Wexler, R. R. *Bioorg. Med. Chem. Lett.* **1998**, *8*, 301.
- (3) Rivero, A.; Somanathan, R.; Hellberg, L. H. *Oppi. Briefs* **1992**, *24*, 363.
- (4) Kumar, V. S.; Floreancig, P. E. *J. Am. Chem. Soc.* **2001**, *123*, 3842.
- (5) Takahara, J. P.; Masuyama, Y.; Kurusu, Y. *J. Am. Chem. Soc.* **1992**, *114*, 2577.
- (6) Takahova, J. P.; Masayama, Y.; Kurusu, Y. *J. Am. Chem. Soc.* **1992**, *114*, 2577.
- (7) Rozema, M. J.; Sidduri, A.; Knochel, P. *J. Org. Chem.* **1992**, *57*, 1956.
- (8) Trost, B. M.; Grese, T. A.; Chan, D. M. T. *J. Am. Chem. Soc.* **1991**, *113*, 7350.
- (9) Ayed, T. B.; Amri, H. *Synth. Commun.* **1995**, *25*, 3813.
- (10) Göttlich, R.; Yamakoshi, K.; Sasai, H.; Shibasaki, M. *Synlett* **1997**, 971.
- (11) Myers, A. G.; Zheng, B. *J. Am. Chem. Soc.* **1996**, *118*, 4492.
- (12) Stereochemistry was assigned based on literature analogy. See: Wille, U.; Lietzau, L. *Tetrahedron* **1999**, *55*, 10119-10134.
- (13) Negishi, E.-i.; Matsushita, H.; Okukado, N. *Tetrahedron Lett.* **1981**, *22*, 2715.
- (14) (a) Bailey, W. F.; Punzalan, E. R. *J. Org. Chem.* **1990**, *55*, 5404. (b) Takeda, N.; Imamoto, T. *Org. Synth.* **1999**, *76*, 228.
- (15) Ohira, S. *Synth. Commun.* **1989**, *19*, 561.
- (16) Neveux, M.; Bruneau, C.; Dixneuf, P. H. *J. Chem. Soc., Perkin Trans 1* **1991**, 1197.