# Stereoselective Synthesis of a Model C(18)-C(35) Spiroketal Fragment of Integramycin

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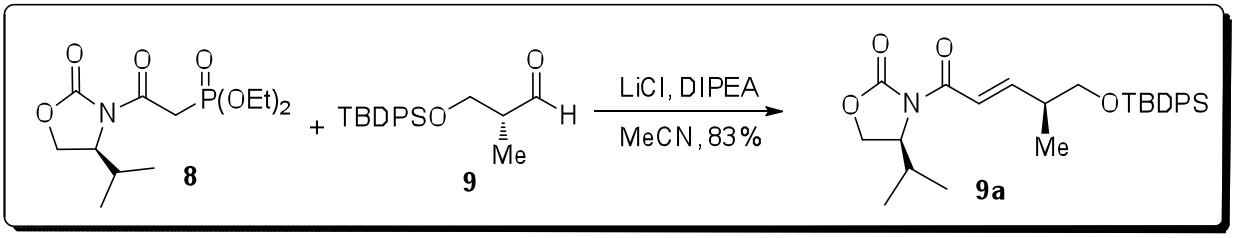
**Supporting Information Part I.**

**Experimental Procedures and Characterization Data**

**General Experimental Details**. All reactions were conducted using flame-dried or oven-dried (140 °C) glassware. All reaction solvents were purified before use. Tetrahydrofuran, dichloromethane and toluene were purified by passing through a solvent column composed of activated A-1 alumina. Triethylamine, pyridine, 2,6-lutidine and diisopropylethylamine were distilled under argon from calcium hydride. Unless indicated, all commercially available reagents were used as received without further purification. Air and moisture sensitive reagents and solutions were transferred with a syringe or cannula through rubber septa.

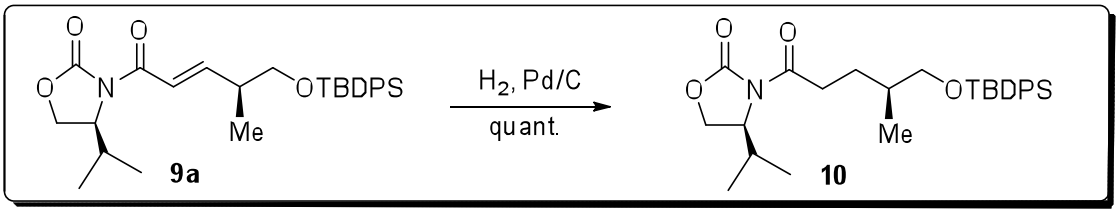
Proton nuclear magnetic resonance ($^1$H NMR) spectra and carbon-13 ($^{13}$C) NMR spectra were recorded on a commercial Bruker 400 MHz spectrometer. The proton signal of residual, non-deuterated solvent (δ: 7.26 ppm for $CHCl_3$) was used as an internal reference for $^1$H spectra. For $^{13}$C spectra, chemical shifts are reported relative to the δ 77.0 ppm resonance of $CDCl_3$. Coupling constants are reported in Hz. Infrared spectra (IR) were recorded on a commercially available FT-IR spectrometer. Optical rotations were measured using a quartz cell with 1.0 mL capacity and a 10 cm path length. High resolution mass spectra (HRMS) were recorded using an Agilent 6210 TOF mass spectrometer at the University of Florida (Gainesville).

Thin layer chromatography (TLC) was performed on Kieselgel 60 F254 glass plates (obtained from Merck) with a 0.25 mm thickness. TLC plates were visualized with UV light and/or by staining with an aqueous solution of $KMnO_4$. Column Chromatography was performed on Kieselgel 60 (230-400mesh).

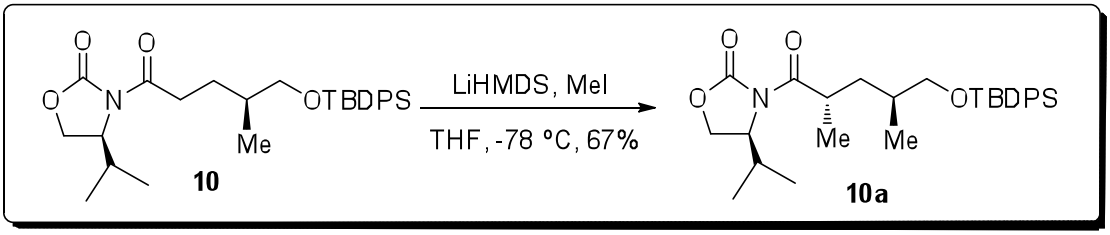



**(*S*)-3-((*S*)-5-((*tert*-butyldiphenylsilyl)oxy)-4-methylpentanoyl)-4-isopropyloxazolidin-2-one (9a)**. To a mixture of β-keto phosphonate **8** (8.17 g, 26.6 mmol, 1.2 equiv) and LiCl (3.30 g, 77.6 mmol, 3.5 equiv) in MeCN (180 mL) under Ar, was added diisopropylethyl amine (3.84 mL, 23.3 mmol, 1.05 equiv). The mixture was stirred for 30 min, the a solution of aldehyde **9** (7.23 g, 22.2 mmol, 1.0 equiv) in MeCN (50 mL) was added slowly. The resulting mixture was stirred for

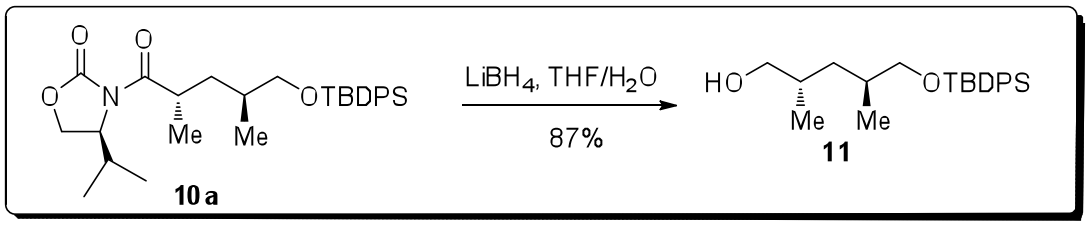
16 h. The solution was then diluted with pH 7.0 buffer (100 mL) and water (100 mL), and extracted with $Et_2O$ (200 mL x 3). The combined organic layers were dried over $Na_2SO_4$, filtered and concentrated in vacuo. The product was purified by flash chromatography (hexane-EtOAc = 6:1) to provide **9a** (8.80 g, 83%). $R_f$ = 0.65 (hexane-EtOAc = 2:1). $[\alpha]_D^{25}$ = +26.0 (*c* = 0.7, $CHCl_3$). $^1H$ NMR (400 MHz, $CDCl_3$): δ 7.68-7.65 (4H), 7.45-7.37 (6H), 7.34 (dd, *J* = 15.6 and 0.8 Hz 1H), 7.15 (dd, *J* = 15.6 and 7.6 Hz, 1H), 4.53-4.49 (1H), 4.28 (dd, *J* = 8.8 and 8.8 Hz, 1H), 4.21 (dd, *J* = 8.8 and 3.2 Hz, 1H), 3.62 (d, *J* = 6.4 Hz, 2H), 2.72-2.62 (1H), 2.46-2.38 (1H), 1.11 (d, *J* = 6.8 Hz, 3H), 1.06 (s, 9H), 0.94 (d, *J* = 7.2 Hz, 3H), 0.89 (d, *J* = 6.8 Hz, 3H). $^{13}C$ NMR (100 MHz, $CDCl_3$): δ 165.0, 154.0, 153.6, 135.6, 133.6, 133.5, 129.7, 127.7, 120.2, 67.6, 63.3, 58.5, 39.7, 28.5, 26.8, 19.3, 18.0, 15.7, 14.7. IR (neat) 3071, 2962, 2858, 1780, 1685, 1636, 1486, 1472, 1365, 1204, 1112, 703. HRMS (ESI) calcd for $[M+Na]^+$ ($C_{28}H_{37}NO_4SiNa$) 502.2390, found, 502.2409.




**(*S*)-3-((*S*,*E*)-5-((*tert*-butyldiphenylsilyl)oxy)-4-methylpent-2-enoyl)-isopropyloxazolidin-2-one (10)**. To a solution of compound **9a** (8.80g, 18.4 mmol) in ethyl acetate (300 mL), was carefully added 10% Pd/C (0.88 g). A hydrogen balloon was applied, and the reaction mixture was vigorously stirred for 24 h. The catalyst was filtered off through a pad of Celite. The filtrate was concentrated in vacuo to provide **10** (8.80 g, quantitative), which used directly in the next step without further purification: $R_f$ = 0.65 (hexane-EtOAc = 2:1). $[\alpha]_D^{25}$ = +33.2 (*c* = 1.3, $CHCl_3$). $^1H$ NMR (400 MHz, $CDCl_3$): δ 7.68-7.65 (4H), 7.44-7.36 (6H), 4.44-4.40 (1H), 4.24 (dd, *J* = 9.2 and 9.2 Hz, 1H), 4.19 (dd, *J* = 9.2 and 3.2 Hz, 1H), 3.55-3.48 (2H), 3.01-2.87 (2H), 2.41-2.33 (1H), 1.91-1.83 (1H), 1.79-1.71 (1H), 1.54-1.45 (1H), 1.06 (s, 9H), 0.95 (d, *J* = 6.0 Hz, 3H), 0.92 (d, *J* = 7.2 Hz, 3H), 0.87 (d, *J* = 7.2 Hz, 3H). $^{13}C$ NMR (100 MHz, $CDCl_3$): δ 173.5, 154.0, 135.6, 133.9, 129.5, 127.6, 68.6, 63.3, 58.4, 35.3, 33.3, 28.4, 27.9, 26.9, 19.3, 18.0, 16.6, 14.7. IR (neat) 3049, 2960, 2858, 1783, 1703, 1471, 1463, 1428, 1386, 1206, 1111, 702. HRMS (ESI) calcd for $[M+NH_4]^+$ ($C_{28}H_{43}N_2O_4Si$) 499.2992, found, 499.2991.

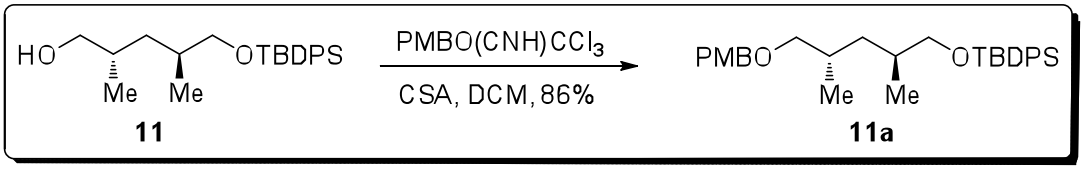



**(*S*)-3-((2*S*,4*S*)-5-((*tert*-butyldiphenylsilyl)oxy)-2,4-dimethylpentanoyl)-4-isopropyloxazolidin-2-one** (**10a**). To a solution of imide **10** (8.7 g, 18.1 mmol) and MeI (7.90 mL, 126.6 mmol, 7.0 equiv) in dry THF (70 mL) under Ar at -78 ºC, was added a solution of LiHMDS (3.32 g, 19.9 mmol, 1.1 equive.) in dry THF (30 mL) over 1.0 h. After the reaction solution was stirred at -78 ºC for 10 min, it was allowed to warm up to 0 ºC over 3.0 h, and stirred at this temperature for 2.0 h. The reaction solution was quenched with brine (100 mL), and extracted with $Et_2O$ (100 mL x 3). The combined organic layers were dried over $Na_2SO_4$, filtered and concentrated in vacuo. The product was purified by flash chromatography (hexane-EtOAc = 8:1) to provide **10a** (5.98 g, 67%). $R_f$ = 0.60 (hexane-EtOAc = 5:1). $[\alpha]_D^{25}$ = +45.3 (*c* = 1.1, $CHCl_3$). $^1$H NMR (400 MHz, $CDCl_3$): δ 7.67-7.65 (4H), 7.42-7.36 (6H), 4.43-4.39 (1H), 4.23-4.17 (2H), 3.84-3.78 (1H), 3.51-3.44 (2H), 2.38-2.33 (1H), 1.71-1.68 (1H), 1.58-1.52 (2H), 1.18 (d, *J* = 7.2 Hz, 3H), 1.06 (s, 9H), 0.94 (d, *J* = 6.4 Hz, 3H), 0.91 (d, *J* = 7.2 Hz, 3H), 0.88 (d, *J* = 6.8 Hz, 3H). $^{13}$C NMR (100 MHz, $CDCl_3$): δ 177.4, 153.5, 135.6, 134.0, 133.9, 129.5, 129.4, 127.6, 127.5, 68.9, 63.1, 58.5, 36.2, 35.5, 33.6, 28.4, 26.9, 19.3, 18.0, 17.7, 16.7, 14.7. IR (neat) 3071, 2962, 2858, 1781, 1699, 1462, 1427, 1385, 1201, 1111, 702. HRMS (ESI) calcd for $[M+H]^+$ ($C_{29}H_{42}NO_4Si$) 496.2883, found, 496.2894.

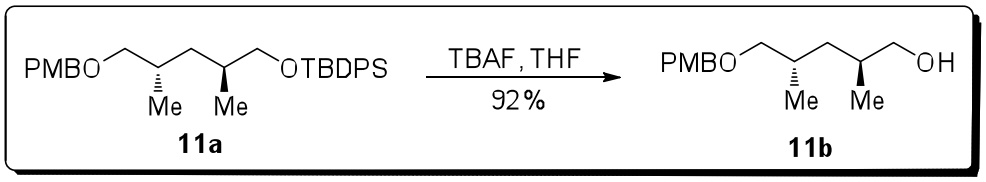



**WRR (2*S*,4*S*)-5-((*tert*-butyldiphenylsilyl)oxy)-2,4-dimethylpentan-1-ol** (**11**). To a solution of imide **10a** (5.4 g, 10.9 mmol) in THF (80 mL) and water (0.35 mL) at 0 ºC, was added $LiBH_4$ (0.38 g, 17.4 mmol, 1.6 equiv) portion-wise over 2.5 h. The reaction mixture was stirred at this temperature for 3.0 h, then additional $LiBH_4$ (0.15 g, 6.9 mmol) was added, followed by water (0.10 mL). The reaction mixture was stirred for another 3.0 h, and then was quenched with sat. $NH_4Cl$ (100 mL) at 0 ºC. The mixture was diluted with water (50 mL) and extracted with ethyl acetate (100 mL x 3). The combined organic layers were dried over $Na_2SO_4$, filtered and

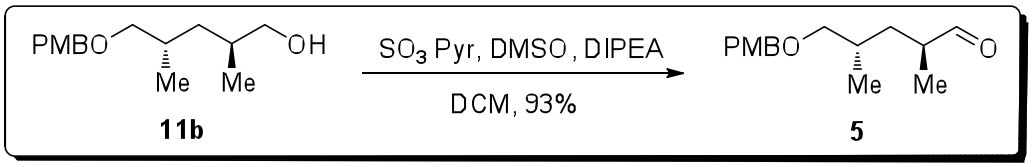
concentrated in vacuo. The product was purified by flash chromatography (hexane-EtOAc = 8:1) to provide **11** (3.46 g, 87%): $R_f$ = 0.45 (hexane-EtOAc = 5:1). $[\alpha]_D^{25}$ = -13.0 (*c* = 1.0, $CHCl_3$). $^1H$ NMR (400 MHz, $CDCl_3$): δ 7.70-7.67 (4H), 7.44-7.37 (6H), 3.53-3.38 (4H), 1.80-1.75 (1H), 1.75-1.68 (1H), 1.43 (br, 1H), 1.28-1.18 (1H), 1.17-1.10 (1H), 1.08 (s, 9H), 0.91 (d, *J* = 6.8 Hz, 3H), 0.89 (d, *J* = 6.8 Hz, 3 H). $^{13}C$ NMR (100 MHz, $CDCl_3$): δ 135.7, 134.1, 134.0, 129.5, 127.6, 69.6, 69.0, 36.8, 33.1, 33.0, 26.9, 19.3, 16.6, 16.5. IR (neat) 3338, 3070, 2957, 2857, 1472, 1427, 1111, 701. HRMS (ESI) calcd for $[M+H]^+$ ($C_{23}H_{35}O_2Si$) 371.2406, found, 371.2407.




***Tert*-butyl(((2*S*,4*S*)-5-((4-methoxybenzyl)oxy)-2,4-dimethylpentyl)oxy)diphenylsilane** (**11a**). To a solution of alcohol **11** (2.63 g, 7.11 mmol) and 4-methoxybenzyl trichloroacetimidate (3.52 g, 12.4 mmol, 1.75 equiv) in $CH_2Cl_2$ (26 mL) at room temperature was added CSA (168 mg, 0.72 mmol) in one portion. After the reaction solution was stirred for 24 h, it was quenched with sat. $NaHCO_3$ (50 mL) and extracted with 15/1 hexanes/ethyl acetate (100 mL x 3). The combined organic layers were washed with brine (50 mL), dried over $Na_2SO_4$, filtered and concentrated in vacuo. The product was purified by flash chromatography ($Et_2O$-hexane = 1:12) to provide **11a** (2.98 g, 86%: $R_f$ = 0.43 ($Et_2O$-hexane = 1:12). $[\alpha]_D^{25}$ = -6.7 (*c* = 1.2, $CHCl_3$). $^1H$ NMR (400 MHz, $CDCl_3$): δ 7.67-7.65 (4H), 7.42-7.36 (6H), 7.25 (d, *J* = 8.4 Hz, 2H), 6.87 (d, *J* = 8.4 Hz, 2H), 4.42 (s, 2H), 3.80 (s, 3H), 3.49 (dd, *J* = 9.6 and 6.0 Hz, 1H), 3.44 (dd, *J* = 9.6 and 6.0 Hz, 1H), 3.26 (dd, *J* = 9.2 and 6.0 Hz, 1H), 3.20 (dd, *J* = 9.2 and 6.8 Hz, 1H), 1.85-1.78 (1H), 1.78-1.72 (1H), 1.21-1.16 (2H), 1.06 (s, 9H), 0.90 (d, *J* = 6.4 Hz, 3H), 0.88 (d, *J* = 6.4 Hz, 3H). $^{13}C$ NMR (100 MHz, $CDCl_3$): δ 159.1, 135.7, 134.1, 134.0, 131.0, 129.5, 129.1, 127.6, 113.7, 76.4, 72.6, 69.6, 55.3, 37.2, 33.1, 30.8, 26.9, 19.3, 17.0, 16.6. IR (neat) 3049, 3071, 2956, 2930, 2856, 1614, 1587, 1514, 1471, 1455, 1427, 1389, 1361, 1246, 1110, 1038, 822, 740, 701, 614. HRMS (ESI) calcd for $[M+H]^+$ ($C_{31}H_{43}O_3Si$) 491.2981, found, 491.2978.

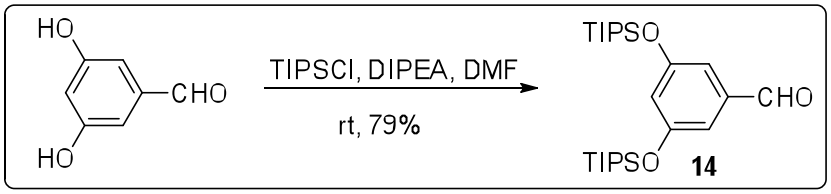



**(2*S*,4*S*)-5-((4-methoxybenzyl)oxy)-2,4-dimethylpentan-1-ol** (**11b**). To a solution of compound **11a** (2.75 g, 5.61 mmol) in dry THF (150 mL) at room temperature was added a solution of TBAF (7.3 mL, 7.3 mmol, 1.3 equiv 1.0 M in THF). The reaction mixture was stirred at room temperature for 12 h, then water (75 mL) was added followed by brine (75 mL). The resulting mixture was extracted with $Et_2O$ (100 mL x 3). The combined organic layers were washed with brine (50 mL), dried over $Na_2SO_4$, filtered and concentrated in vacuo. The product was purified by flash chromatography (hexane-EtOAc = 3:1) to provide **11b** (1.30 g, 92%): $R_f$ = 0.33 (hexane-EtOAc = 3:1). $[\alpha]_D^{25}$ = -16.9 (*c* = 1.2, $CHCl_3$). $^1$H NMR (400 MHz, $CDCl_3$): δ 7.35 (d, *J* = 8.8 Hz, 2H), 6.99 (d, *J* = 8.8 Hz, 2H), 4.43 (s, 2H), 3.81 (s, 3H), 3.48-3.40 (2H), 3.29-3.22 (2H), 1.91-1.84 (1H), 1.78-1.71 (1H), 1.54 (br, 1H), 1.28-1.14 (2H), 0.90 (d, *J* = 6.8 Hz, 3H), 0.89 (d, *J* = 6.8 Hz, 3H). $^{13}$C NMR (100 MHz, $CDCl_3$): δ 159.1, 130.7, 129.2, 113.7, 76.3, 72.7, 68.8, 55.3, 37.3, 33.0, 30.5, 17.0, 16.3. IR (neat) 3400, 2956, 2926, 2871, 1613, 1513, 1463, 1247, 1093, 1036, 820. HRMS (ESI) calcd for $[M+NH_4]^+$ ($C_{15}H_{28}NO_3$) 270.2609, found, 270.2085.

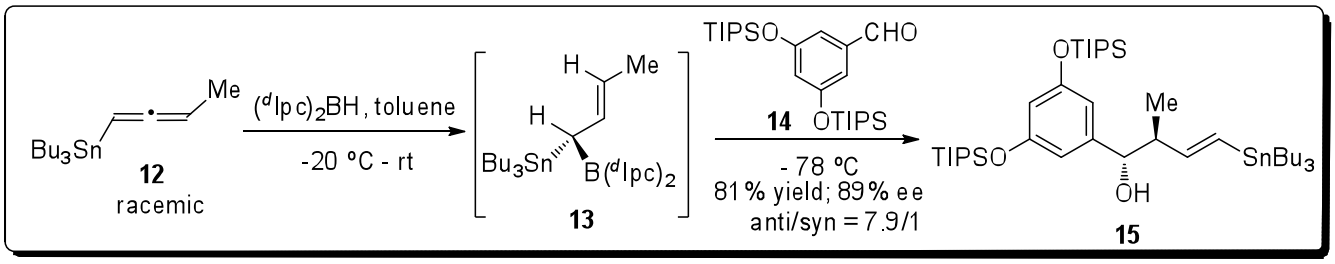



**(2*S*,4*S*)-5-((4-methoxybenzyl)oxy)-2,4-dimethylpentanal** (**5**). To a solution of alcohol **11b** (400 mg, 1.59 mmol) in $CH_2Cl_2$ (13 mL) at 0 ºC was added diisopropylethylamine (1.05 mL, 6.35 mmol, 4.0 equiv) followed by slow addition of a solution of $SO_3$·Py. (758 mg, 4.77 mmol, 3.0 equiv) in DMSO (5.0 mL). The resulting reaction solution was stirred at 0 ºC for 1.5 h, and then diluted with pH = 7 buffer (40 mL) and $Et_2O$ (40 mL). The organic layer was separated, and the aqueous layer was extracted with $Et_2O$ (20 mL). The combined organic layers were washed with sat. $CuSO_4$ (30 mL). The aqueous layer was extracted with additional $Et_2O$ (20 mL) and the combined organic extracts were washed with sat. $NH_4Cl$ (30 mL). The aqueous layer was extracted with $Et_2O$ (2 x 20 mL) and the combined organic layers were washed with pH = 7 buffer (30 mL). The combined organic extracts were washed with brine (30 mL), dried over $MgSO_4$, filtered and concentrated in vacuo. The crude product was dried under high vacuum overnight, then the

colorless aldehyde **5** (370 mg, 93% yield, >98.5 % purity) was directly used in the next step without further purification: $R_f$ = 0.59 (hexane-EtOAc = 5:1). $[\alpha]_D^{25}$ = +5.8 (*c* = 0.9, $CHCl_3$). $^1$H NMR (400 MHz, $CDCl_3$): δ 9.61 (d, *J* = 2.0 Hz, 1H), 7.24 (d, *J* = 6.8 Hz, 2H), 6.88 (d, *J* = 6.4 Hz, 2H), 4.42 (s, 2H), 3.81 (s, 3H), 3.28 (dd, *J* = 6.0 and 1.2 Hz, 2H), 2.46-2.40 (1H), 1.89-1.83 (1H), 1.58 (ddd, *J* = 14.8, 8.4 and 6.0 Hz, 1H), 1.46 (ddd, *J* = 13.6, 8.4 and 5.6 Hz, 1H), 1.10 (d, *J* = 7.2 Hz, 3H), 0.95 (d, *J* = 6.8 Hz, 3H). $^{13}$C NMR (100 MHz, $CDCl_3$): δ 205.2, 159.1, 130.6, 129.1, 113.8, 75.4, 72.7, 55.3, 44.0, 34.4, 31.0, 16.9, 13.4. IR (neat) 2960, 2931, 2853, 1721, 1612, 1513, 1459, 1247, 1090, 1035, 819. HRMS (ESI) calcd for $[M+NH_4]^+$ ($C_{15}H_{26}NO_3$) 268.1913, found, 268.1907.



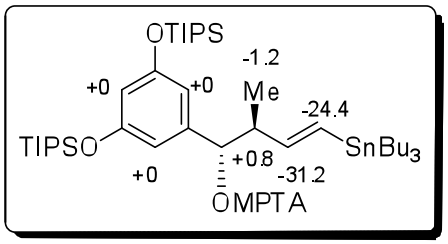

**3,5-Bis((triisopropylsilyl)oxy)benzaldehyde** (**14**). To a solution of 3,5-dihydroxybenzaldehyde (3.50 g, 25.4 mmol) in DMF (40 mL) at room temperature was added DIPEA (8.37 mL, 50.7 mmol, 2.0 equiv). This solution was stirred for 15 min, then TIPSCl (10.8 mL, 50.7 mmol, 2.0 equiv) was added and stirring was continued for 16 h. The solution was diluted with water (200 mL) and then extracted with 20% ethyl acetate in hexanes (150 mL x 3). The combined organic layers were washed with brine (50 mL x 2), dried over $Na_2SO_4$, filtered and concentrated in vacuo. The product was purified by flash chromatography (hexane-EtOAc = 25:1) to provide **14** (8.96 g, 79%): $R_f$ = 0.70 (hexane-EtOAc = 15:1). $^1$H NMR (400 MHz, $CDCl_3$): δ 9.88 (s, 1H), 7.00 (d, *J* = 2.0 Hz, 2H), 6.70 (dd, *J* = 2.4 and 2.0 Hz, 1H), 1.33-1.24 (6H), 1.13 (d, *J* = 7.2 Hz, 36 H). $^{13}$C NMR (100 MHz, $CDCl_3$): δ 192.0, 157.6, 138.3, 118.0, 114.0, 17.8, 12.6. IR (neat) 2946, 2868, 1704, 1587, 1470, 1473, 1455, 1384, 1337, 1175, 1033, 882, 831, 757, 681. HRMS (ESI) calcd for $[M+H]^+$ ($C_{55}H_{47}O_3Si_2$) 451.3064, found, 451.3060.

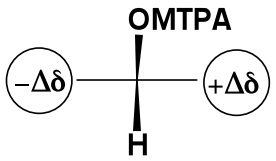



**(1*S*,2*S*,*E*)-1-(3,5-bis((triisopropylsilyl)oxy)phenyl)-2-methyl-4-(tributystannyl)but-3-en-1-ol** (**15**). To a mixture of ($^{d}$Ipc)$_2$BH (4.83 g, 16.9 mmol, 1.9 equiv) in dry toluene (75 mL) at -20 ºC under Ar, was slowly added a solution of racemic allenylstannane **12** (6.10 g, 17.8 mmol, 2.0 equiv) in dry toluene (7.5 mL) over 30 min. The resulting mixture was stirred at -20 ºC for 30 min, then was warmed to 0 ºC and stirred at this temperature for 6 h. The solution was warmed to room temperature and stirred for another 6 h. The mixture was then cooled to -78 ºC and a solution of aldehyde **14** (4.00 g, 8.89 mmol, 1.0 equiv) in dry toluene (7.5 mL) was slowly added over 30 min. The resulting reaction mixture was stirred at -78 ºC for 12 h, then sat. $NaHCO_3$ (30 mL) was added. The mixture was allowed to warm to 0 ºC over 1 h, then THF (60 mL) was added, followed by addition of a premixed solution of 3 N NaOH (30 mL) and 30% $H_2O_2$ (60 mL). The resulting mixture was stirred at room temperature for 8 h and then extracted with $Et_2O$ (80 mL x 3). The combined organic layers were washed with brine (50 mL), dried over $Na_2SO_4$, filtered and concentrated in vacuo. The product was purified by reverse phase (C18) chromatography ($CH_2Cl_2$:MeCN/1:5) to provide **15** (5.70 g, 81% yield, 89% ee, determined by Mosher ester analysis): $R_f$ = 0.50 ($CH_2Cl_2$-MeCN = 1:5, C18 TLC plate). $[\alpha]_D^{25}$ = -44.6 (*c* = 1.1, $CHCl_3$). $^1$H NMR (400 MHz, $CDCl_3$): δ 6.48 (d, *J* = 2.4 Hz, 2H), 6.34 (dd, *J* = 2.0 and 2.4 Hz, 1H), 6.15 (dd, *J* = 18.8 and 0.4 Hz, 1H), 5.90 (dd, *J* = 18.8 and 7.6 Hz, 1H), 4.16 (dd, *J* = 8.4 and 2.4 Hz, 1H), 2.42-2.37 (1H), 2.14 (d, *J* = 2.4 Hz, 1H), 1.53-1.48 (6H), 1.34-1.26 (6H), 1.24-1.10 (6H), 1.09 (d, *J* = 7.2 Hz, 36H), 0.90 (t, *J* = 7.2 Hz, 9H), 0.92-0.90 (6H), 0.83 (d, *J* = 6.8 Hz, 3H) $^{13}$C NMR (100 MHz, $CDCl_3$): δ 156.7, 151.2, 144.4, 131.1, 111.8, 110.9, 77.5, 50.5, 29.1, 27.2, 17.9, 16.6, 13.7, 12.7, 9.5. IR (neat) 3564, 2957, 2868, 2590, 1463, 1455, 1385, 1336, 1169, 1026, 882, 858, 765, 685. HRMS (ESI) calcd for $[M+H]^+$ ($C_{41}H_{81}O_3Si_2Sn$) 797.4746, found, 797.4727.

The absolute stereochemistry of **15** was assigned by application of the advanced Mosher ester analysis, as summarized in the following diagram.

**Advanced Mosher Ester Analysis of 15 (Absolute Stereochemistry)**




$\Delta\delta = \delta_S - \delta_R$

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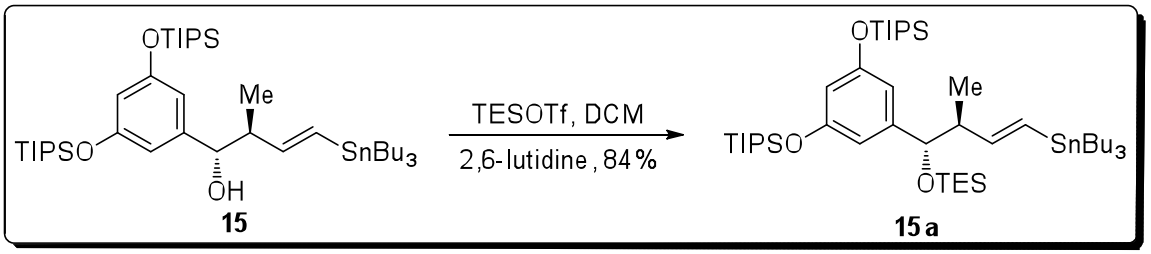
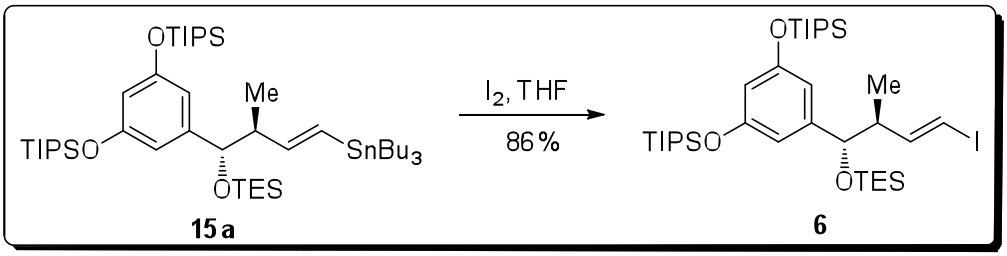
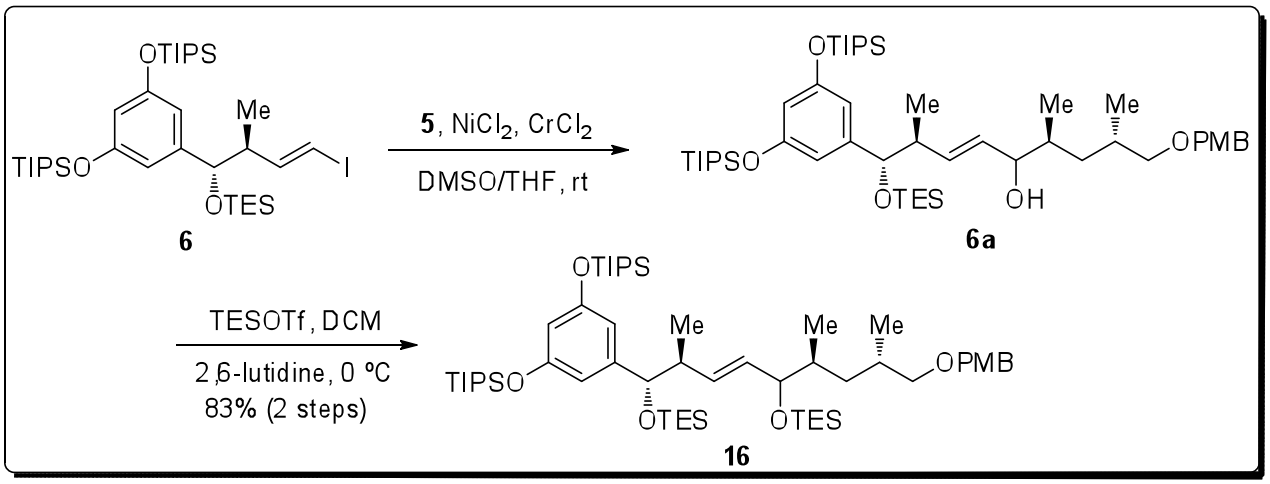



**((5-((1*S*,2*S*,*E*)-2-methyl-4-(tributylstannyl)-1-((triethylsilyl)oxy)but-3-en-1-yl)-1,3-phenylene)bis (oxy))bis(triisopropylsilane) (15a)**. To a solution of alcohol **15** (2.0 g, 2.51 mmol) and 2,6-lutidine (1.45 mL, 12.6 mmol, 5.0 equiv) in $CH_2Cl_2$ (70 mL) at 0 °C under Ar was slowly added $Et_3SiOTf$ (0.62 mL, 2.76 mmol, 1.1 equiv). The resulting solution was stirred at 0 °C for 1 h, then was warmed to room temperature over 15 min and stirred at this temperature for another 15 min. Sat. $NaHCO_3$ (60 mL) was carefully added, and the resulting mixture was extracted with hexanes (50 mL x 3). The combined organic layers were washed with brine (30 mL), dried over $Na_2SO_4$, filtered and concentrated in vacuo. The product was purified by a rapid flash chromatography (0.5% $Et_3N$ in hexanes) to provide **15a** (2.10 g, 92%): $R_f$ = 0.51 (hexanes). $[\alpha]_D^{25}$ = -29.6 (*c* = 0.9, $CHCl_3$). $^1H$ NMR (400 MHz, $CDCl_3$): δ 6.42 (d, *J* = 2.0 Hz, 2H), 6.30 (dd, *J* = 2.0 and 2.0 Hz, 1H), 6.05 (dd, *J* = 18.8 and 6.8 Hz, 1H), 5.89 (dd, *J* = 18.8 and 0.8 Hz, 1H), 4.22 (d, *J* = 7.2, 1H), 2.41-2.36 (1H), 1.55-1.42 (6H), 1.36-1.28 (6H), 1.26-1.19 (6H), 1.09 (d, *J* = 7.2 Hz, 36H), 0.89 (t, *J* = 7.2 Hz, 9H), 0.86 (t, *J* = 8.0 Hz, 9H), 0.92-0.84 (6H), 0.77 (d, *J* = 6.8 Hz, 3H), 0.49 (q, *J* = 8.0 Hz, 6H). $^{13}C$ NMR (100 MHz, $CDCl_3$): δ 156.3, 152.0, 146.3, 126.6, 111.8, 110.5, 79.4, 49.4, 29.1, 27.3, 17.9, 16.1, 13.7, 12.7, 9.3, 6.9, 5.0. IR (neat) 2956, 2928, 2869, 1590, 1450, 1333, 1169, 1029, 1008, 882, 686. HRMS (ESI) calcd for $[M+Na]^+$ ($C_{47}H_{94}NaO_3Si_3Sn$) 933.5430, found, 933.5434.

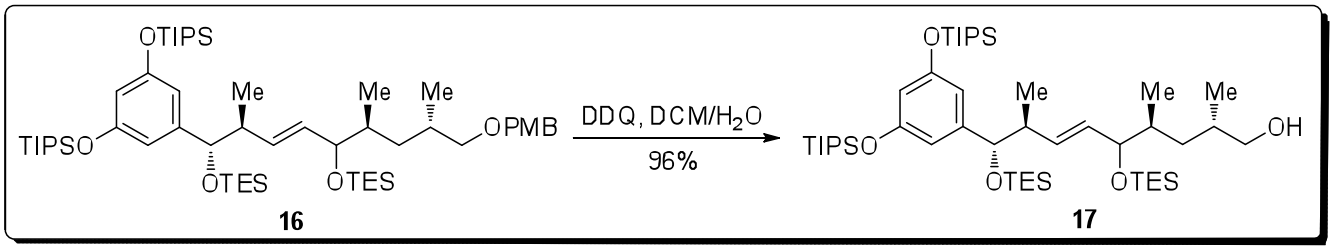



**((5-((1S,2S,E)-4-iodo-2-methyl-1-((triethylsilyl)oxy)but-3-en-1-yl)-1,3-phenylene)bis(oxy))bis (triisopropylsilane)** (**6**). To a solution of vinylstannane **15a** (1.82 g, 2.00 mmol) in THF (4.5 mL) at 0 ºC, was added a solution of iodine (0.56 g, 2.2 mmol, 1.1 equiv) in THF (4.5 mL) dropwise. The reaction mixture was stirred at 0 ºC for 0.5 h with the reaction flask covered with aluminum foil. A solution of 0.1 N $Na_2S_2O_3$ (10 mL) was added, and the resulting mixture was extracted with $Et_2O$ (15 mL x 3). The combined organic layers were washed with brine (15 mL), dried over $Na_2SO_4$, filtered and concentrated in vacuo. The product was purified by flash chromatography (hexanes) to provide **6** (1.28 g, 86%): $R_f$ = 0.33 (hexanes). $[\alpha]_D^{25}$ = -41.8 (*c* = 0.8, $CHCl_3$). $^1$H NMR (400 MHz, $CDCl_3$): δ 6.52 (dd, *J* = 14.4 and 8.4 Hz, 1H), 6.38 (d, *J* = 2.0 Hz, 2H), 6.32 (dd, *J* = 2.4 and 2.0 Hz, 1H), 5.96 (dd, *J* = 14.4 and 0.8 Hz, 1H), 4.25 (d, *J* = 6.4 Hz, 1H), 2.39-2.34 (1H), 1.28-1.20 (6H), 1.09 (d, *J* = 7.2 Hz, 36H), 0.87 (t, *J* = 8.0 Hz, 9H), 0.83 (d, *J* = 6.8 Hz, 3H), 0.50 (q, *J* = 8.0 Hz, 6H). $^{13}$C NMR (100 MHz, $CDCl_3$): δ 156.5, 148.9, 145.3, 111.5, 110.9, 78.2, 75.1, 49.0, 17.9, 15.6, 12.6, 6.8, 4.8. IR (neat) 2945, 2867, 1591, 1450, 1348, 1169, 1029, 1008, 882, 761, 686. HRMS (ESI) calcd for $[M+NH_4]^+$ ($C_{35}H_{71}INO_3Si_3$) 764.3784, found, 764.3806.

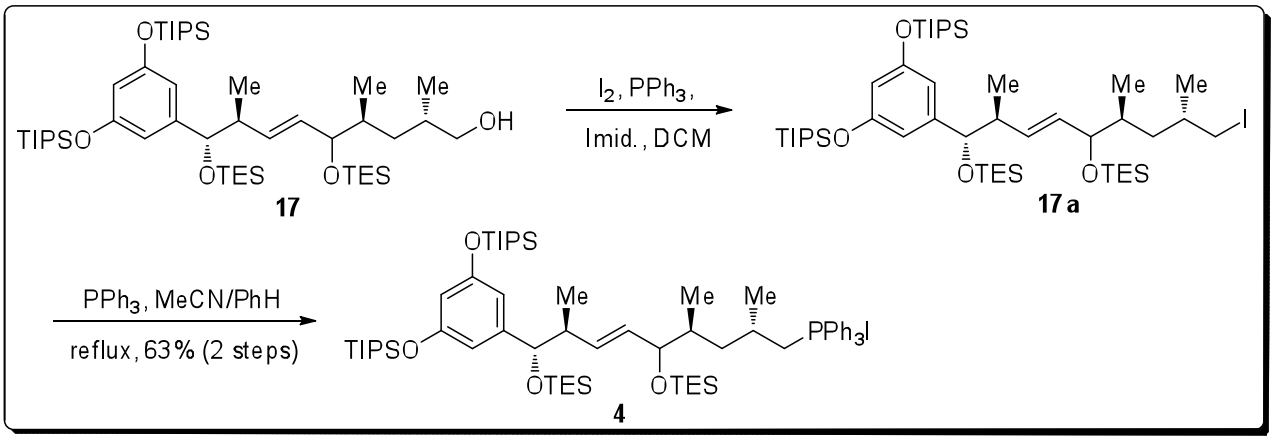


**(8*S*,9*S*,*E*)-9-(3,5-bis((triisopropylsilyl)oxy)phenyl)-3,3,11,11-tetraethyl-5-((2*S*,4*S*)-5-((4-methoxy benzyl)oxy)-4-methylpentan-2-yl)-8-methyl-4,10-dioxa-3,11-disilatridec-6-ene** (**16**). To a solution of vinyl iodide **6** (1.24g, 1.66 mmol, 1.3 equiv) and aldehyde **5** (0.32 g, 1.28 mmol) in mixture of THF (4 mL) and DMSO (7 mL) under Ar was added $CrCl_2$ (0.73 g, 5.92 mmol, 4.6 equiv) and $NiCl_2$ (10.0 mg, 77 μmol). The reaction mixture was vigorously stirred at room temperature for 12 h, then additional $NiCl_2$ (4.0 mg, 31 μmol) was added. The mixture was stirred for an additional 5 h, then was diluted with $Et_2O$ (150 mL), washed with water (40 mL x 2) and brine (40 mL). The organic phase was dried over $Na_2SO_4$, filtered and concentrated in vacuo. The residue was eluted through a short silica gel column (hexane-EtOAc = 3:1) to provide an inseparable mixture (1.01 g) of aldehyde **5** (13%) and the desired product **6a** (87%), which was used directly in the next step without further purification. $R_f$ = 0.59 (hexane-EtOAc = 5:1).

To a solution of the above product (1.01 g) and 2,6-lutidine (0.77 mL, 6.68 mmol, 6.0 equiv) in $CH_2Cl_2$ (32 mL) at 0 ºC under Ar, was slowly added $Et_3SiOTf$ (0.28 mL, 1.23 mmol, 1.1 equiv). The resulting reaction solution was stirred at 0 ºC for 1 h, then was warmed to room temperature over 30 min. Sat. $NaHCO_3$ (40 mL) was carefully added, and the resulting mixture was extracted with $Et_2O$ (40 mL x 3). The combined organic layers were washed with brine (40 mL), dried over $Na_2SO_4$, filtered and concentrated in vacuo. The product was purified by flash chromatography (6% $Et_2O$ in hexanes) to provide **16** (1.04 g, 83% over two steps) as a mixture of two diastereomers (11:10 ratio). $R_f$ = 0.40 (3% $Et_2O$ in hexanes). $^1$H NMR (400 MHz, $CDCl_3$): δ 7.26 (d, *J* = 8.4 Hz, 2H), 6.87 (d, *J* = 8.4 Hz, 2H), 6.41 (dd, *J* = 5.6 and 2.0 Hz, 2H), 6.30 (dd, *J* = 2.0 and 2.0 Hz, 1H), 5.57 (dd, *J* = 15.6 and 6.4 Hz, 0.52H), 5.50 (dd, *J* = 15.6 and 7.2 Hz, 0.48H), 5.36 (dd, *J* = 15.6 and 7.2 Hz, 1H), 4.46-4.39 (2H), 4.34 (d, *J* = 5.6 Hz, 0.52 H), 4.29 (d, *J* = 6.0 Hz, 0.48H), 3.84-3.81 (0.48H), 3.80 (s, 3H), 3.76-3.74 (0.52H), 3.32-3.27 (1H), 3.21-3.15 (1H), 2.42-2.34 (1H), 1.83-1.79 (1H), 1.61-1.55 (1H), 1.26-1.20 (8H), 1.09 (d, *J* = 7.2 Hz, 36H),, 0.93 (t, *J* = 8.0 Hz, 9H), 0.87 (t, *J*= 8.0 Hz, 9H), 0.88-0.78 (multiple doublets, 9H), 0.59-0.47 (12H). $^{13}$C NMR (100 MHz, $CDCl_3$): δ 159.0, 156.3, 156.2, 146.0, 145.9, 133.7, 133.4, 131.7, 131.4, 131.0, 131.0, 129.0, 113.7, 111.8, 110.5, 79.0, 78.7, 78.6, 78.5, 72.6, 55.2, 45.0, 44.6, 37.3, 37.2, 36.5, 36.1, 31.0, 30.9, 17.9, 16.7, 16.6, 16.0, 15.9, 15.0, 14.9, 12.7, 6.9, 6.9, 6.8, 5.1, 4.9, 4.8. HRMS (ESI) calcd for $[M+NH_4]^+$ ($C_{56}H_{108}NO_6Si_4$) 1002.7254, found, 1002.7287.



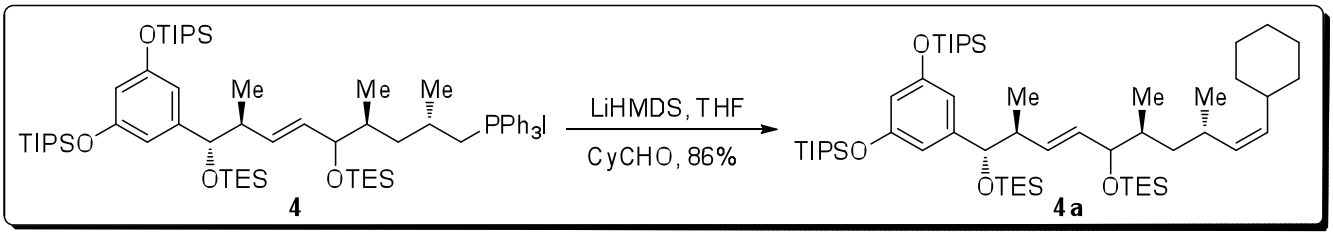

**(2*S*,4*S*,8*S*,9*S*,*E*)-9-(3,5-bis((triisopropylsilyl)oxy)phenyl)-2,4,8-trimethyl-5,9-bis((triethylsilyl)oxy) non-6-en-1-ol** (**17**). To a solution of PMB ether **16** (1.03 g, 1.05 mmol) in $CH_2Cl_2$ (23 mL) at 0 ºC, was added water (1.14 mL) followed by DDQ (0.28 g, 1.25 mmol, 1.2 equiv). The reaction mixture was vigorously stirred for 2 h, then sat. $NaHCO_3$ (45 mL) was added and the resulting mixture was extracted with $CH_2Cl_2$ (30 mL x 3). The combined organic layers were washed with water (30 mL) and brine (30 mL), dried over $Na_2SO_4$, filtered and concentrated in vacuo. The product was purified by flash chromatography (hexane-EtOAc = 10:1) to provide **17** (0.87 g, 97%) as a mixture of two diastereomers (11:10 ratio). $R_f$ = 0.46 (hexane-EtOAc = 10:1). $^1$H NMR (400 MHz, $CDCl_3$): δ 6.41 (dd, *J* = 6.8 and 2.0 Hz, 2H), 6.30 (dd, *J* = 2.0 and 2.4 Hz, 1H), 5.57 (dd, *J* = 15.6 and 6.8 Hz, 0.52H), 5.51 (dd, *J* = 15.6 and 7.2 Hz, 0.48H), 5.35 (dd, *J* = 15.6 and 7.6 Hz, 0.52H), 5.32 (dd, *J* = 15.6 and 8.0 Hz, 0.42H), 4.34 (d, *J* = 9.6 Hz, 0.52H), 4.33 (d, *J* = 10.0 Hz, 0.48H), 3.83-3.74 (1H), 3.49-3.38 (2H), 2.43-2.33 (1H), 1.73-1.65 (1H), 1.65-1.58 (br, 1H), 1.60-1.56 (0.48H), 1.51-1.45 (0.52H), 1.30-1.18 (8H), 1.09 (d, *J* = 7.2 Hz, 36H), 0.93 (t, *J* = 8.0 Hz, 9H), 0.88 (t, *J*= 8.0 Hz, 9H), 0.90-0.78 (multiple doublets, 9H), 0.59-0.50 (12H). $^{13}$C NMR (100 MHz, $CDCl_3$): δ 156.3, 146.0, 145.9, 133.9, 133.4, 131.4, 131.3, 111.8, 111.7, 110.5, 110.4, 78.9, 78.8, 78.7, 78.6, 69.2, 69.0, 45.1, 44.5, 37.1, 36.9, 36.0, 35.2, 33.4, 33.3, 17.9, 16.4, 16.1, 16.0, 15.9, 15.7, 15.5, 12.6, 6.9, 6.8, 5.1, 5.0, 4.9, 4.8. HRMS (ESI) calcd for $[M+NH_4]^+$ ($C_{48}H_{100}NO_5Si_4$) 882.6679, found, 882.6670.



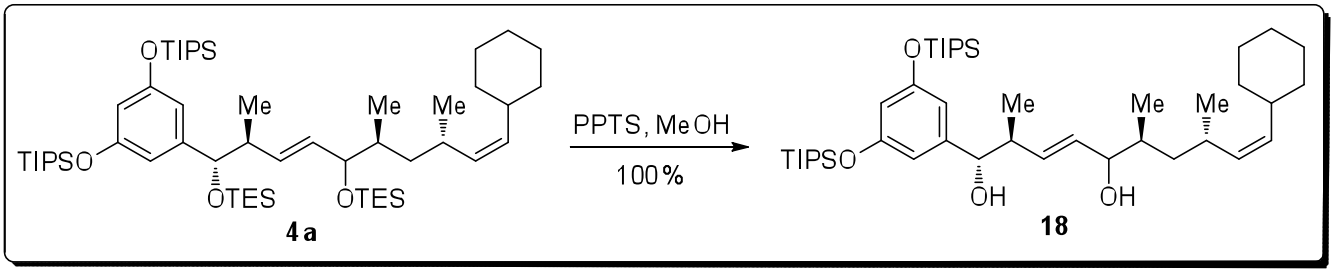

**((2S,4S,8S,9S,E)-9-(3,5-bis((triisopropylsilyl)oxy)phenyl)-2,4,8-trimethyl-5,9-bis((triethylsilyl)oxy) non-6-en-1-yl)triphenylphosphonium iodide** (**4**). To a solution of imidazole (180 mg, 2.71 mmol, 3.6 equiv) and triphenylphosphine (650 mg, 2.48 mmol, 3.3 equiv) in $Et_2O$-MeCN (3:1, 8.5 mL) with reaction flask covered with aluminum foil, was added iodine (573 mg, 2.25 mmol, 3.0 equiv). This mixture was stirred for 5 min, then a solution of alcohol **17** (650 mg, 0.75 mmol) in $Et_2O$-MeCN (3:1, 5.0 mL) was added dropwise. The resulting mixture was stirred at room temperature for 2 h, then sat. $NaHCO_3$ (20 mL) and 10% $Na_2S_2O_3$ (20 mL) were added. The resulting mixture was stirred 10 min, and then extracted with 1:10 $Et_2O$-hexanes (25 mL x 3). The combined organic layers were washed with brine (20 mL), dried over $Na_2SO_4$, filtered and concentrated in vacuo. The residue was eluted through a slica gel column (0.7% $Et_2O$ in hexanes) to provide a mixture (703 mg) of **17a**, $PPh_3$ and 1-2% of an unidentified impurity. This mixture was used directly in the next step without further purification. $R_f$ = 0.34 (0.7% $Et_2O$ in hexanes).

The above mixture (703 mg), triphenylphosphine (2.62 g, 10.0 mmol, 15.0 equiv) and $Li_2CO_3$ (1.09 g, 14.7 mmol, 22.0 equiv) in a mixture of benzene (11 mL) and MeCN (39 mL) was heated under reflux for 60 h. The precipitate was filtered off and rinsed with $CH_2Cl_2$ (20 mL x 3). The combined organic phases were concentrated in vacuo. The product was purified by flash chromatography (2% MeOH in $CH_2Cl_2$ and then 5% MeOH in $CH_2Cl_2$) to provide **4** (589 mg, 63% over two steps) as a mixture of two diastereomers. $R_f$ = 0.37 (5% MeOH in $CH_2Cl_2$). $^1$H NMR (400 MHz, $CDCl_3$): δ 7.83-7.77 (9H), 7.72-7.67 (6H), 6.38 (dd, *J* = 4.0 and 2.4 Hz, 2H), 6.28 (dd, *J* = 2.4 and 2.0 Hz, 1H), 5.48 (dd, *J* = 15.6 and 6.8 Hz, 1H), 5.13 (dd, *J* = 15.6 and 6.4 Hz, 0.52H), 5.06 (dd, *J* = 15.6 and 6.8 Hz, 0.48H), 4.30 (d, *J* = 5.6 Hz, 0.48H), 4.23 (dd, *J* = 6.0 Hz, 0.52H), 4.04-3.94 (1H), 3.70 (dd, *J* = 7.6 and 3.6 Hz, 0.52H), 3.59 (dd, *J* = 6.0 and 6.4 Hz, 0.48H), 3.25-3.18 (1H), 2.35-2.22 (1H), 2.0-1.88 (1H), 1.72-1.63 (1H), 1.53-1.40 (2H), 1.26-1.15 (6H), 1.12-1.02

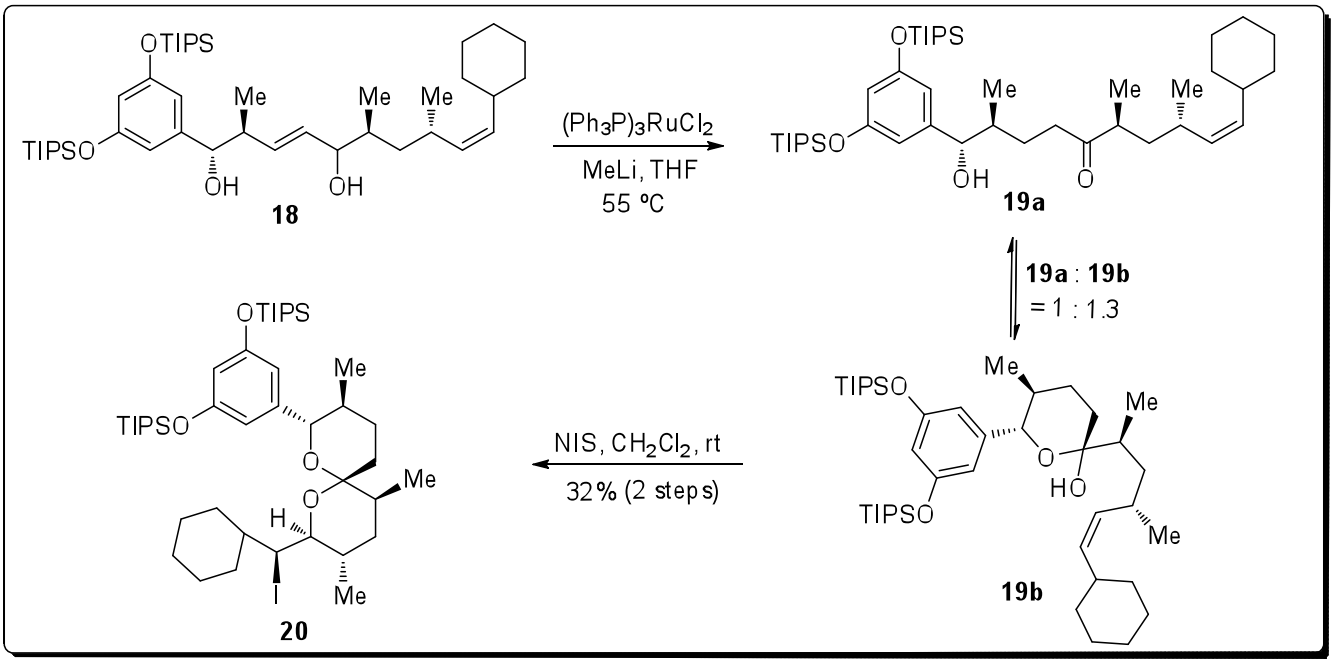
(39H), 086 (t, $J$ = 7.6 Hz, 9H), 0.84 (t, $J$= 8.0 Hz, 9H), 0.82-0.78 (3H), 0.52-0.42 (15H). $^{13}$C NMR (100 MHz, $CDCl_3$): δ 156.4, 156.3, 146.3, 145.9, 135.1, 135.0, 133.8, 133.7, 133.7, 131.1, 130.6, 130.5, 130.4, 130.3, 119.2, 118.4, 111.8, 111.7, 110.5, 44.7, 44.6, 40.7, 40.6, 37.3, 37.1, 30.7, 30.6, 30.2, 26.8, 26.7, 26.6, 21.0, 20.9, 17.9, 16.5, 16.3, 14.9, 13.8, 12.6, 7.0, 6.9, 5.0, 4.9, 4.8. HRMS (ESI) calcd for $[M-I]^+$ ($C_{66}H_{110}O_4PSi_4$) 1109.7219, found, 1109.7196.




**(8*S*,9*S*,*E*)-9-(3,5-bis((triisopropylsilyl)oxy)phenyl)-5-((2*S*,4*S*,*Z*)-6-cyclohexyl-4-methylhex-5-en-2-yl)-3,3,11,11-tetraethyl-8-methyl-4,10-dioxa-3,11-disilatridec-6-ene** (**4a**). To a – 78 ºC solution of phosphonium salt **4** (346 mg, 0.28 mmol) in anhydrous THF (3.0 mL) under Ar was added dropwise a solution of LiHMDS (49 mg, 0.29 mmol, 1.05 equiv) in toluene (0.90 mL). This mixture was stirred – 78 ºC for 1 h, then a solution of cyclohexanecarboxaldehyde (35 mg, 0.31 mmol, 1.1 equiv) in THF (0.8 mL) was slowly added, and the mixture was stirred for 15 min. The reaction temperature was increased to 0 ºC over 1 h, and the mixture was stirred at this temperature for 3 h. It was then quenched by the addition of sat. $NH_4Cl$ (5 mL) and extracted with $Et_2O$ (15 mL x 3). The combined organic layers were washed with brine (15 mL), dried over $Na_2SO_4$, filtered and concentrated in vacuo. The product was purified by flash chromatography (0.7% $Et_2O$ in hexanes) to provide **4a** (226 mg, 86%) as a mixture of two diastereomers (11:10 ratio). $R_f$ = 0.30 (0.6% $Et_2O$ in hexanes). $^1$H NMR (400 MHz, $CDCl_3$): δ 6.41 (dd, $J$ = 10.0 and 2.4 Hz, 2H), 6.31-6.29 (1H), 5.56 (dd, $J$ = 15.6 and 6.8 Hz, 0.52H), 5.48 (dd, $J$ = 15.6 and 7.6 Hz, 0.48 Hz), 5.36 (dd, $J$ = 15.6 and 6.4 Hz, 0.48H), 5.35 (dd, $J$ = 15.6 and 7.6 Hz, 0.52), 5.11-5.03 (2H), 4.34 (d, $J$ = 6.4 Hz, 0.52H), 4.29 (d, $J$ = 6.0 Hz, 0.48H), 3.86 (dd, $J$ = 7.6 and 4.4 Hz, 0.52H), 3.77 (dd, $J$ = 6.8 and 6.8 Hz, 0.48H), 2.52-2.39 (1H), 2.37-2.30 (1H), 2.28-2.21 (1H), 1.72-1.58 (5H), 1.52-1.37 (2H), 1.31-1.78 (9H), 1.09 (d, $J$ = 7.2 Hz, 36H), 1.12-1.06 (3H), 0.96-0.81 (27H), 0.59-0.47 (12H). $^{13}$C NMR (100 MHz, $CDCl_3$): δ 156.3, 146.0, 135.4, 135.2, 133.8, 133.3, 133.2, 132.3, 131.2, 111.8, 110.4, 79.0, 78.7, 78.4, 77.2, 45.0, 44.6, 41.1, 40.6, 37.9, 37.8, 36.7, 36.6, 33.8, 33.7, 33.6, 33.5, 29.8, 29.7, 26.1, 26.0, 26.0, 21.2, 21.0, 17.9, 16.1, 16.0, 15.5, 15.2, 12.7, 6.9, 6.8, 6.8, 5.1, 5.0, 4.9, 4.8. HRMS (ESI) calcd for $[M+Na]^+$ ($C_{55}H_{106}O_4NaSi_4$) 965.7066, found, 965.7061.



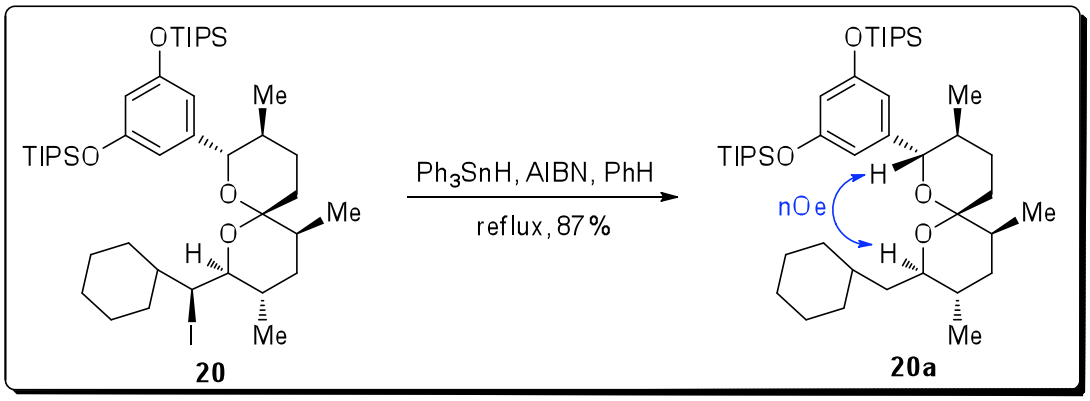

**(1*S*,2*S*,3*E*,6*S*,8*S*,9*Z*)-1-(3,5-bis((triisopropylsilyl)oxy)phenyl)-10-cyclohexyl-2,6,8-trimethyldeca-3,9-diene-1,5-diol** (**18**). A solution of **4a** (226 mg, 0.24 mmol) in a mixture of $CH_2Cl_2$ (3 mL) and MeOH (12 mL) was treated with PPTS (241 mg, 0.96 mmol, 4.0 equiv) at room temperature for 2.5 h. Water (25 mL) was added, and the resulting mixture was extracted with ethyl acetate (15 mL x 3). The combined organic layers were washed with water (15 mL) and brine (15 mL), dried over $Na_2SO_4$, filtered and concentrated in vacuo. The product was purified by flash chromatography (hexane-EtOAc = 7:1) to provide **18** (171 mg, 100%) as a mixture of two diastereomers. $R_f$ = 0.50 (hexane-EtOAc = 5:1). $^1$H NMR (400 MHz, $CDCl_3$): δ 6.45 (dd, *J* = 2.4 and 2.0 Hz, 2H), 6.34 (dd, *J* = 1.6 and 2.0 Hz, 1H), 5.63-5.59 (2H), 5.14-5.01 (2H), 4.20 (dd, *J* = 8.0 and 8.4 Hz, 1H), 4.01 (br, 0.52H), 3.92 (br, 0.48H), 2.59-2.51 (1H), 2.44-2.38 (1H), 2.27-2.22 (1H), 2.14 (br, 0.52H), 2.04 (br, 1H), 1.72-1.58 (6.5H), 1.48-1.35 (1H), 1.27-1.19 (9H), 1.09 (d, *J* = 7.6 Hz, 36H), 1.11-0.98 (3H), 0.93-0.80 (multiple doublets, 9H). $^{13}$C NMR (100 MHz, $CDCl_3$): δ 156.9, 156.8, 144.8, 144.7, 134.9, 134.8, 134.7, 134.3, 134.1, 133.6, 133.5, 132.5, 111.5, 111.0, 110.9, 78.3, 78.1, 75.6, 44.8, 44.5, 40.8, 40.7, 36.7, 36.4, 36.5, 33.7, 33.5, 33.5, 29.6, 29.5, 26.1, 26.0, 25.9, 21.4, 21.2, 17.9, 17.2, 16.9, 15.2, 14.8, 12.6. HRMS (ESI) calcd for $[M+NH_4]^+$ ($C_{43}H_{82}NO_4Si_4$) 732.5782, found, 732.5789.




**(1*S*,2*S*,6*S*,8*S*,*Z*)-1-(3,5-bis((triisopropylsilyl)oxy)phenyl)-10-cyclohexyl-1-hydroxy-2,6,8-trimethyl dec-9-en-5-one** (**19a**) and **(2*R*,5*S*,6*S*)-6-(3,5-bis((triisopropylsilyl)oxy)phenyl)-2-((2*S*,4*S*,*Z*)-6-cyclohexyl-4-methylhex-5-en-2-yl)-5-methyltetrahydro-2H-pyran-2-ol** (**19b**). To a solution of $(PPh_3)_3RuCl_2$ (54 mg, 58 μmol, 0.8 equiv) in anhydrous THF (6.1 mL, deoxygenized via the freeze-pump-thaw method three times) at room temperature under Ar, was added dropwise a solution of MeLi (70 μL, 112 μmol, 1.6 equiv, 1.6 M in $Et_2O$). The reaction solution was stirred for 15 min, with the solution turning to a red wine color. A solution of diol **18** (50 mg, 70 μmol, 1.0 equiv) in anhydrous THF (0.8 mL) was slowly added. This solution was stirred at room temperature for 10 min, then was heated to 50 °C for 3 h, and to 60 °C for 1.5 h. The reaction was cooled to ambient, solvent was evaporated, and the residue was purified by column chromatography (Davisil silica gel, $Et_2O$-hexane = 8:1). All fractions with $R_f$ = 0.30 – 0.55 were combined and concentrated. The resulting mixture was dissolved in $Et_2O$ (20 mL), washed with sat. $NaHCO_3$ (3 mL x 2) and water (3 mL), dried over $Na_2SO_4$, filtered and concentrated in vacuo. The product was purified by flash chromatography (Davisil silica gel, $Et_2O$-hexane = 1:8) to provide a mixture (40 mg) consisiting of 85% of **19a/b** (**19a**:**19b**/1:1.3, ca. 68% yield) and 15% of some inseparable impurities. $R_f$ = 0.30-0.55 ($Et_2O$-hexane = 1:8). $^1H$ NMR (400 MHz, $C_6D_6$): δ 6.95 (d, *J* = 2.0 Hz, 1H), 6.87-6.83 (2H), 5.38-5.32 (1.55H), 5.11 (dd, *J* = 10.8 and 10.8 Hz, 0.45H), 4.62 (d, *J* = 10.0 Hz, 0.55H), 4.22 (d, *J* = 11.2 and 2.4 Hz, 0.45 H), 2.79-2.72 (0.55H), 2.68-2.58 (0.45H), 2.58-2.48 (1.55H), 2.40-2.28 (1H), 2.24-2.16 (0.45H), 1.98-1.68 (9.55H), 1.63-1.52 (2H), 1.48-1.32 (10H),

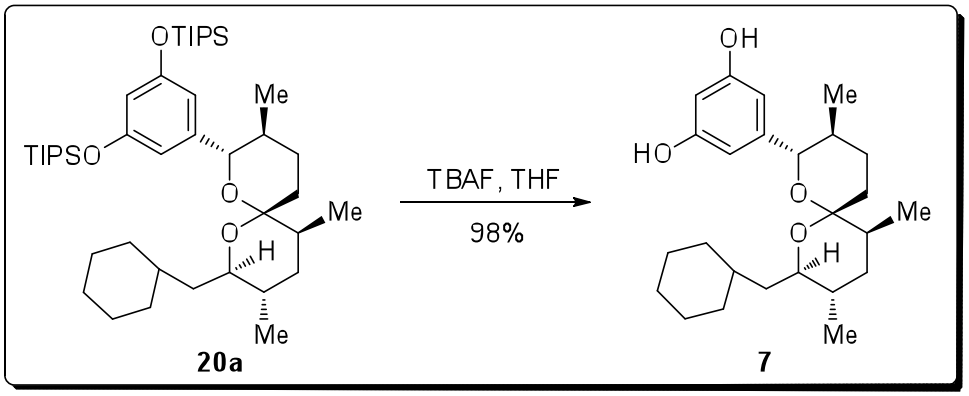
1.27 (d, *J* = 6.4, 36H), 1.30-1.15 (7H), 1.24 (d, *J* = 6.4 Hz, 0.55H), 1.09 (d, *J* = 6.4 Hz, 0.45H), 1.04 and 1.03 (two doublets, *J* = 6.8 Hz, 1H), 0.88 (d, *J* = 6.8 Hz, 0.55H), 0.85 (d, *J* = 6.4 Hz, 0.45H). $^{13}$C NMR (100 MHz, $C_6D_6$): δ 213.0, 157.3, 157.2, 146.9, 145.0, 135.7, 135.6, 134.3, 134.1, 112.9, 112.0, 111.4, 111.1, 99.0, 79.5, 78.9, 44.5, 42.9, 41.2, 40.5, 39.3, 39.1, 37.9, 37.1, 37.0, 34.2, 34.1, 33.9, 33.8, 30.6, 30.5, 30.2, 29.7, 28.5, 26.8, 26.4, 26.3, 26.2, 22.4, 21.0, 18.2, 18.0, 17.9, 16.3, 14.9, 13.1. HRMS (ESI) calcd for $[M+Na]^+$ ($C_{43}H_{78}O_4NaSi_2$) 737.5336, found, 737.5343.

**((5-((2*S*,3*S*,6*S*,8*S*,9*S*,11*S*)-8-((*S*)-cyclohexyliodomethyl)-3,9,11-trimethyl-1,7-dioxaspiro[5.5] undecan-2-yl)-1,3-phenylene)bis(oxy))bis(triisopropylsilane)** (**20**). To a solution of impure **19a/b** (40 mg, 55.7 μmol, from the preceding experiment) in $CH_2Cl_2$ (1.1 mL) at 0 ºC was added NIS (15.0 mg, 67 μmol). The reaction mixture was stirred at 0 °C for 1 h in the dark, than for 24 h at room temperature. Sat. $Na_2S_2O_3$ (2 mL) was added, followed by sat. $NaHCO_3$ (2 mL). The resulting mixture was stirred for 10 min and extracted with $Et_2O$ (5 mL x 3). The combined organic layers were washed brine (3 mL), dried over $Na_2SO_4$, filtered and concentrated in vacuo. The product was purified by preparative TLC (2% $Et_2O$ in hexanes) to provide spiroketal **20** (19 mg, 32% over two steps). $R_f$ = 0.44 (2% $Et_2O$ in hexanes). $[\alpha]_D^{25}$ = -20.1 (*c* = 0.9, $CHCl_3$). $^1$H NMR (400 MHz, $C_6D_6$): δ 6.99 (d, *J* = 2.0 Hz, 2H), 6.86 (dd, *J* = 2.0 and 2.4 Hz, 1H), 4.36 (d, *J* = 9.6 Hz, 1H), 4.27 (dd, *J* = 5.6 and 0.8 Hz, 1H), 2.75 (d, *J* = 8.0 Hz, 1H), 2.56 (d, *J* = 12.0 Hz, 1H), 2.25-2.05 (3H), 2.20-2.93 (2H), 1.93-1.2 (2H), 1.82-1.68 (4H), 1.61-1.52 (2H), 1.50-1.31 (12H), 1.26 (d, *J* = 7.2 Hz, 36H), 1.21 (d, *J* = 7.2 Hz, 3H), 0.91 (d, *J* = 6.4 Hz, 3H), 0.63 (d, *J* = 6.0 Hz, 3H). $^{13}$C NMR (100 MHz, $C_6D_6$): δ 157.3, 144.33, 113.1, 111.6, 99.2, 79.3, 76.6, 51.6, 44.5, 36.9, 36.6, 36.4, 34.5, 33.6, 33.1, 30.0, 28.9, 27.2, 27.1, 26.9, 18.1, 17.4, 15.4, 13.1. IR (neat) 2945, 2927, 2867, 1591, 1462, 1451, 1374, 1168, 1030, 972, 906, 883, 763, 685. HRMS (ESI) calcd for $[M+Na]^+$ ($C_{43}H_{81}INO_4Si_2$) 858.4749, found, 858.4752.



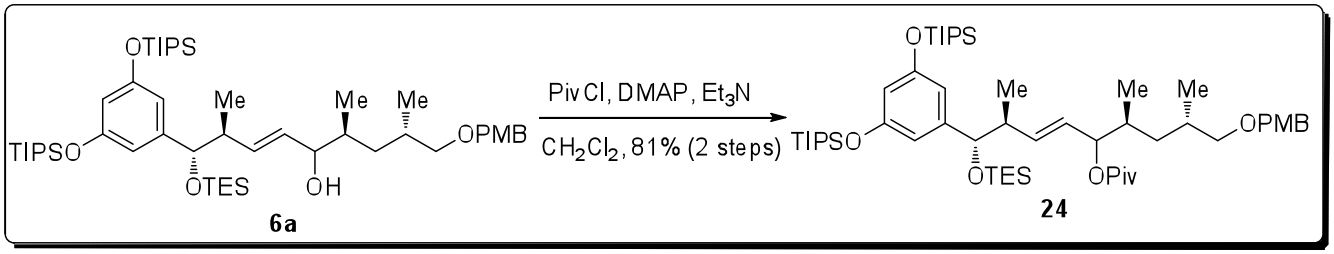
**((5-((2*S*,3*S*,6*R*,8*R*,9*S*,11*S*)-8-(cyclohexylmethyl)-3,9,11-trimethyl-1,7-dioxaspiro[5.5]undecan-2-yl)-1,3-phenylene)bis(oxy))bis(triisopropylsilane)** (**20a**). A solution of spiroketal **20** (20 mg, 24 μmol), $Ph_3SnH$ (16.5 mg, 47.1 μmol, 2.0 equiv) and AIBN (0.5 mg) in benzene (1.7) was purged with Ar for 10 min, and then heated under reflux for 15 min. The mixture was cooled and solvent was evaporated. The residue was purified by flash chromatography (2% $Et_2O$ in hexanes) to provide **20a** (15 mg, 87% yield). $R_f$ = 0.40 (2% $Et_2O$ in hexanes). $[\alpha]_D^{25}$ = +2.0 (*c* = 0.6, $CHCl_3$). $^1H$ NMR (400 MHz, $CDCl_3$): δ 6.50 (d, *J* = 2.4 Hz, 2H), 6.38 (dd, *J* = 2.4 and 2.4 Hz, 1H), 3.98 (d, *J* = 9.6 Hz, 1H), 3.27 (dt, *J* = 10.4 and 2.0 Hz, 1H), 2.02 (d, *J* = 12.8 Hz, 1H), 1.84-1.68 (8H), 1.68-1.60 (2H), 1.50-1.37 (4H), 1.34-1.18 (11H), 1.11 (d, *J* = 7.2 Hz, 36H), 1.01 (d, *J* =7.2 Hz, 3H), 0.98-0.82 (2H), 0.69 (d, *J* = 6.8 Hz, 3H), 0.68 (d, *J* = 6.4 Hz, 3H). $^{13}C$ NMR (100 MHz, $CDCl_3$): δ 156.3, 143.9, 112.8, 111.0, 97.9, 78.3, 72.1, 41.3, 36.3, 36.0, 35.3, 35.0, 33.9, 33.2, 33.1, 29.5, 28.6, 26.8, 26.7, 26.4, 18.0, 17.9, 17.8, 15.2, 12.6. IR (neat) 2925, 2867, 1590, 1449, 1374, 1168, 1030, 906, 882, 764, 685. HRMS (ESI) calcd for $[M+NH_4]^+$ ($C_{43}H_{82}NO_4Si_2$) 732.5782, found, 732.5777.

The stereochemistry of the spiroketal **20a** was assigned by the $^1H$ NOE studies summarized in the preceding equation.



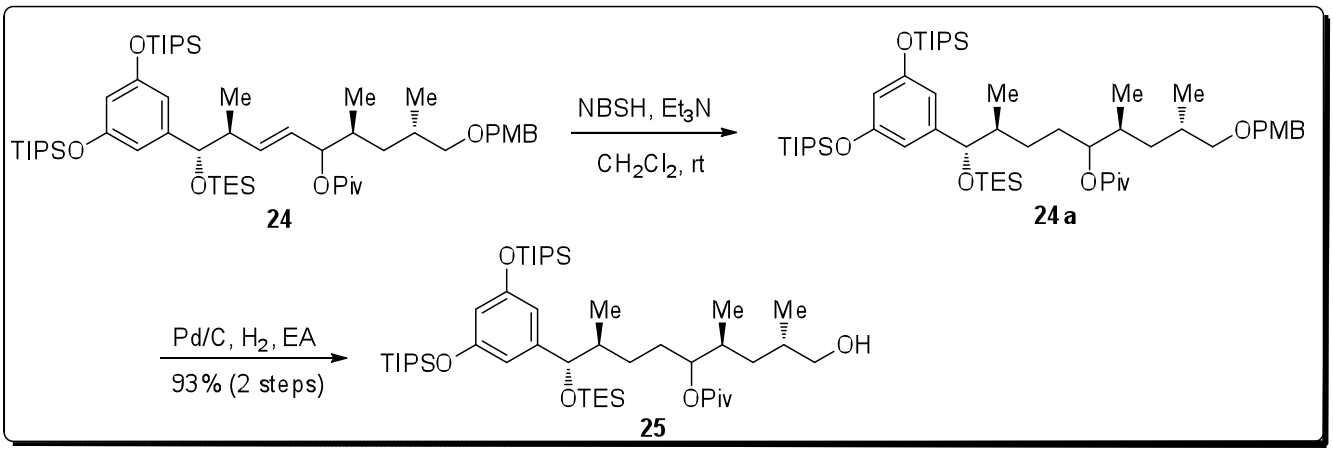

**5-((2*S*,3*S*,6*R*,8*R*,9*S*,11*S*)-8-(cyclohexylmethyl)-3,9,11-trimethyl-1,7-dioxaspiro[5.5]undecan-2-yl) benzene-1,3-diol** (**7**). To a solution of **20a** (7.3 mg, 10.2 μmol) in THF (0.4 mL), was added a solution of TBAF (40 μL, 40 μmol, 4.0 equiv 1.0 M in THF). The reaction mixture was stirred for 4 h, then ethyl acetate (4 mL) was added. The organic phase was washed with $NH_4Cl$ (1.0 mL), brine (1 mL x 2), dried over $Na_2SO_4$, filtered and concentrated in vacuo. The product was purified by flash chromatography (hexane-EtOAc = 3:1) to provide **7** (4.0 mg, 98%). $R_f$ = 0.44 (hexane-EtOAc = 3:1). $[\alpha]_D^{25}$ = +10.0 (*c* = 0.4, acetone). $^1H$ NMR (400 MHz,

$(CD_3)_2CO$): δ 8.09 (s, 2H), 6.34 (d, *J* = 2.4 Hz, 2H), 6.28 (dd, *J* = 2.4 and 2.0 Hz, 1H), 4.01 (dd, *J* = 9.6 Hz, 1H), 3.28 (dt, *J* = 10.4 and 2.0 Hz, 1H), 1.89-1.81 (1H), 1.80-1.67 (7H), 1.67-1.60 (2H), 1.59-1.40 (5H), 1.39-1.20 (5H), 1.07-1.00 (1H), 0.99 (d, *J* = 6.8 Hz, 3H), 0.94-0.85 (1H), 0.69 (d, *J* = 6.8 Hz, 3H), 0.68 (d, *J* = 7.2 Hz, 3H). $^{13}$C NMR (100 MHz, $(CD_3)_2CO$): δ 159.0, 145.3, 106.9, 102.6, 98.7, 79.5, 72.8, 42.0, 37.1, 37.0, 36.3, 35.8, 34.9, 34.0, 33.9, 27.6, 27.5, 27.3, 18.5, 18.3, 15.6. IR (neat) 3369, 2923, 2850, 1701, 1602, 1449, 1376, 1152, 1069, 1022, 973, 825, 697. HRMS (ESI) calcd for $[M+H]^+$ ($C_{25}H_{39}O_4$) 403.2848, found, 403.2848.




**(1*S*,2S,6*S*,8*S*,*E*)-1-(3,5-bis((triisopropylsilyl)oxy)phenyl)-9-((4-methoxybenzyl)oxy)-2,6,8-trimethyl -1-((triethylsilyl)oxy)non-3-en-5-yl pivalate** (**24**). To a solution of impure alcohol **6a** (0.83 g, 0.83 mmol, containing 13% of aldehyde **5**) in $CH_2Cl_2$ (15 mL) at room temperature, was added pivaloyl chloride (0.40 mL, 3.31 mmol, 4.0 equiv), $Et_3N$ (0.69 mL, 4.97 mmol, 6.0 equiv) and DMAP (100 mg, 0.83, 1.0 equiv). The reaction mixture was stirred at room temperature for 16 h, then at 43 ºC for another 16 h. The solution was then diluted with sat. $NaHCO_3$ (20 mL) and extracted with $Et_2O$ (20 mL x 3). The combined organic layers were washed with brine (15 mL x 2), dried over $Na_2SO_4$, filtered and concentrated in vacuo. The product was purified by flash chromatography (hexane-ether = 12:1) to provide **24** (0.76 g, 96%) as a mixture of two diastereomers (11:10). $R_f$ = 0.57 (hexane-ether = 6:1). $^1$H NMR (400 MHz, $CDCl_3$): δ 7.25 (d, *J* = 6.8 Hz, 2H), 6.87 (d, *J* = 6.8 Hz, 2H), 6.40 (dd, *J* = 2.4 and 2.0 Hz, 2H), 6.29 (dd, *J* = 1.6 and 2.0 Hz, 1H), 5.74-5.66 (1H), 5.36-5.30 (1H), 5.15 (dd, *J* = 4.4 and 6.4 Hz, 0.52 H), 5.03 (dd, *J* = 6.0 and 6.4 Hz, 0.48H), 4.45-4.39 (2H), 4.25 and 4.22 (two doublets, *J* = 6.4 Hz, 1H), 3.80 (s, 3H), 3.30-3.25 (1H), 3.22-3.17 (1H), 2.39-2.33 (1H), 1.82-1.76 (2H), 1.27-1.21 (6H), 1.19 and 1.18 (two singlets, 9H), 1.09 (d, *J* = 7.2 Hz, 36H), 1.15-1.08 (2H), 0.85 (dt, *J* = 8.0 and 1.2 Hz, 9H), 0.90-0.78 (9H), 0.47 (dq, *J* = 8.0 and 2.0 Hz, 6H). $^{13}$C NMR (100 MHz, $CDCl_3$): δ 177.4, 174.0, 159.0, 156.4, 156.3, 146.1, 146.0, 136.5, 136.2, 130.9, 130.8, 129.0, 126.4, 125.9, 113.7, 111.7, 111.6, 110.5, 79.1, 79.0, 78.3, 76.3, 72.6, 55.2, 45.1, 45.0, 40.2, 38.9, 38.8, 36.4, 36.2, 34.6, 34.5, 30.8, 30.7,

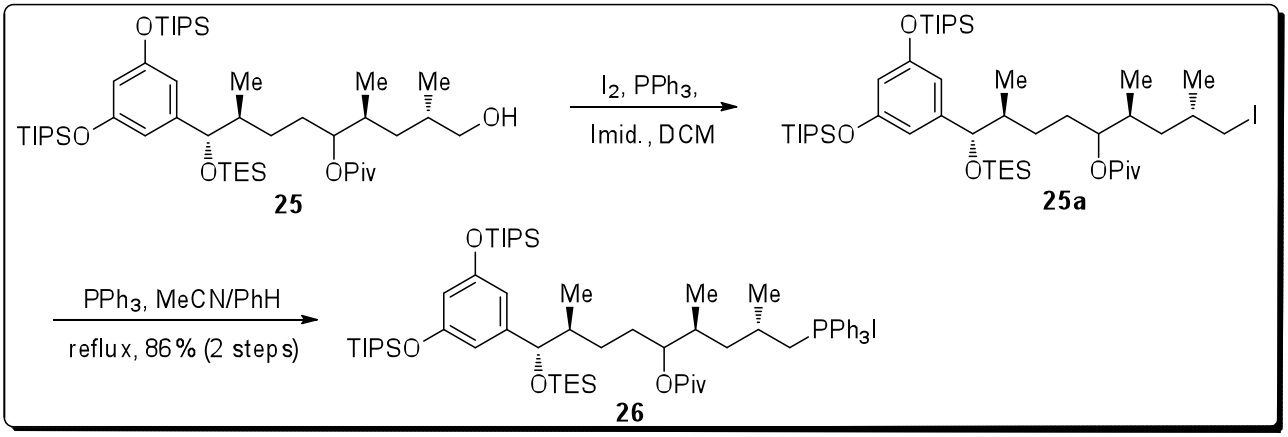
27.2, 27.2, 26.5, 17.9, 16.8, 16.7, 16.6, 16.4, 15.0, 14.6, 12.6, 6.9, 4.9. HRMS (ESI) calcd for $[M+Na]^+$ ($C_{55}H_{98}O_7NaSi_3$) 977.6518, found, 977.6516.



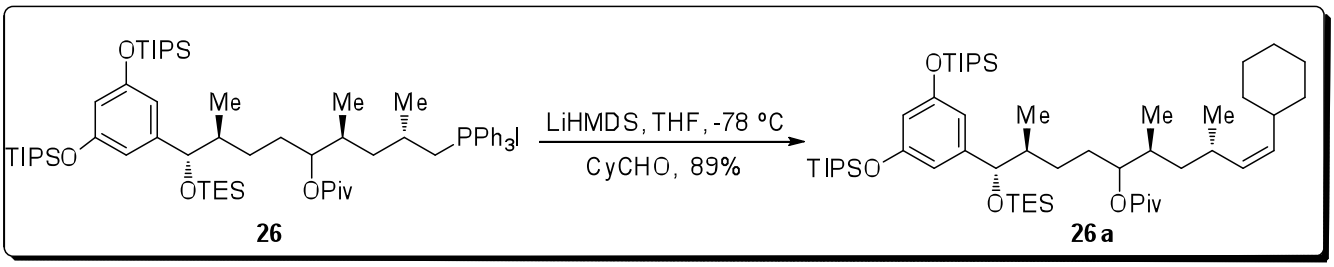

**(1*S*,2*S*,6*S*,8*S*)-1-(3,5-bis((triisopropylsilyl)oxy)phenyl)-9-hydroxy-2,6,8-trimethyl-1-((triethylsilyl) oxy)nonan-5-yl pivalate** (**25**). To a solution of compound **24** (0.66 g, 0.72 mmol) in $CH_2Cl_2$ (9 mL) was added 2-nitrobenzenesulfonyl hydrazine (1.55 g, 7.12 mmol, 10.0 equiv) and $Et_3N$ (3.18 mL). The reaction mixture was stirred at room temperature for 2 days, then additional 2-nitrobenzenesulfonyl hydrazine (1.55 g, 7.12 mmol, 10.0 equiv) and $Et_3N$ (3.18 mL) were added. The mixture was stirred for another 2 days, then $Et_2O$ (10 mL) and hexanes (100 mL) were added. The top light yellow layer was separated, and the bottom brown residue was washed with hexanes-ether (10:1, 20 mL x 2). The combined organic layers were washed with brine (20 mL), dried over $Na_2SO_4$, filtered and concentrated in vacuo. The product was purified by flash chromatography (hexane-ether = 15:1) to provide an inseparable mixture (0.64 g) of **24a** (88%) and unreacted **24** (125 mg). $R_f$ = 0.48 (hexane-ether = 6:1).

To a solution of the above mixture (0.64 g) in ethyl acetate (15 mL) was carefully added 10% Pd/C (60 mg). A hydrogen balloon was applied, and the reaction mixture was vigorously stirred for 36 h. The catalyst was filtered off through a pad of Celite and the filtrate was concentrated in vacuo. The product was purified by flash chromatography (hexane-EtOAc = 10:1) to provide **25** (0.54 g, 93% over two steps) as a mixture of two diastereomers (11:10 ratio). $R_f$ = 0.23 (hexane-EtOAc = 6:1). $^1$H NMR (400 MHz, $CDCl_3$): δ 6.39 (d, *J* = 2.0 Hz, 2H), 6.29 (dd, *J* = 2.4 and 2.0 Hz, 1H), 4.75-4.68 (1H), 4.20 and 4.16 (two doublets, *J* = 6.4 Hz, 1H), 3.49-3.40 (2H), 1.82-1.75 (1H), 1.72-1.63 (1H), 1.63-1.51 (3H), 1.46-1.28 (2H), 1.26-1.19 (7H), 1.18 (s, 9H), 1.10 and 1.08 (two singlets, 36H), 1.15-0.91 (2H), 0.86 (t, *J* = 7.6 Hz, 9H), 0.89-0.83 (6H), 0.71 and 0.68

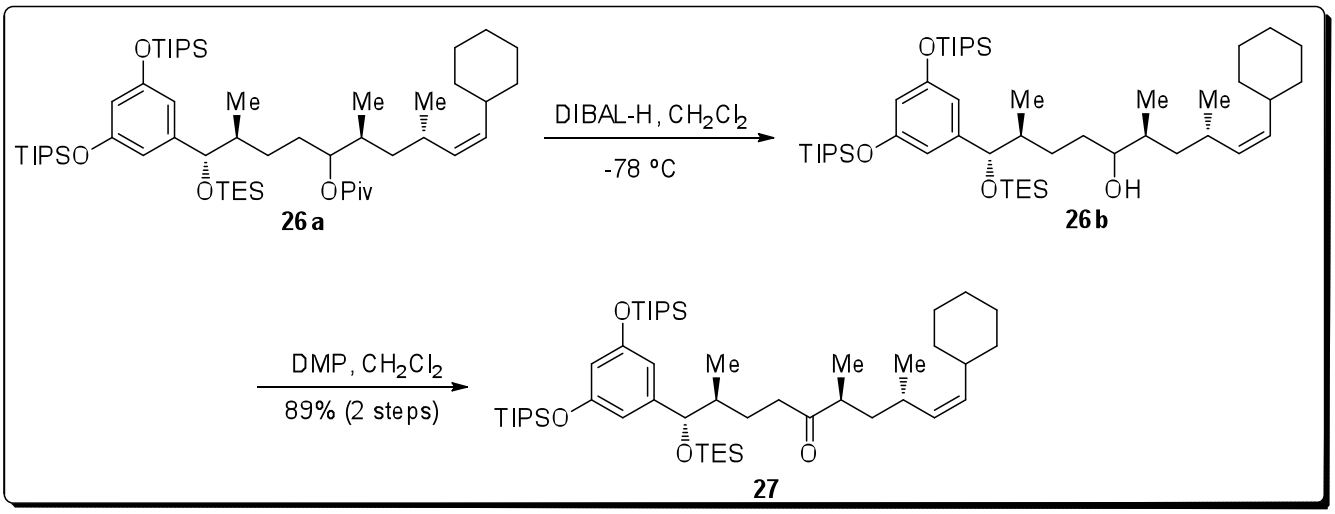
(two doublets, $J$ = 7.2 Hz, 3H), 0.48 (q, $J$ = 8.0 Hz, 6H). $^{13}$C NMR (100 MHz, $CDCl_3$): δ 178.2, 178.0, 156.3, 146.4, 146.4, 111.8, 111.7, 110.5, 110.4, 79.6, 79.4, 78.1, 75.8, 75.5, 75.2, 69.1, 69.0, 41.5, 39.0, 36.0, 35.2, 33.3, 33.2, 33.1, 33.0, 28.4, 28.3, 27.8, 27.6, 27.3, 25.8, 17.9, 16.4, 16.1, 16.0, 15.8, 15.2, 14.4, 12.6, 11.1, 6.9, 3.4, 4.9. HRMS (ESI) calcd for $[M+H]^+$ ($C_{47}H_{93}O_6Si_3$) 837.6280, found, 837.6282.




**(1*S*,2*S*,6*S*,8*S*)-1-(3,5-bis((triisopropylsilyl)oxy)phenyl)-9-(iodotriphenylphosphoranyl)-2,6,8-trimethyl-1-((triethylsilyl)oxy)nonan-5-yl pivalate** (**26**). Primary alcohol **25** (538 mg, 0.64 mmol) was converted to phosphonium salt **26** by using the procedure described for the preparation of compound **4**. The product was purified by flash chromatography (2% MeOH in $CH_2Cl_2$ and then 5% MeOH in $CH_2Cl_2$) to provide **26** (668 mg, 86% over two steps) as a mixture of two diastereomers. $R_f$ = 0.29 (5% MeOH in $CH_2Cl_2$). $^1$H NMR (400 MHz, $CDCl_3$): δ 8.15-8.08 (6H), 7.46-7.42 (9H), 6.89 (d, $J$ = 2.4 Hz, 2H), 6.81-6.79 (1H), 4.88-4.81 (1H), 4.72-4.63 and 4.48-4.41 (1H), 4.54 and 4.51 (two doublets, $J$ = 6.4 Hz, 1H), 4.20-4.10 (1H), 2.50-2.12 (6H), 1.42-1.36 (6H), 1.36 and 1.35 (two singlets, 9H), 1.29 and 1.28 (two doublets, $J$ = 6.8 Hz, 36H), 1.30-1.25 (2H), 1.19-1.16 (2H), 1.18-1.10 (13H), 1.01 and 0.99 (two doublets, $J$ = 6.4 Hz, 3H), 0.78-0.69 (9H). $^{13}$C NMR (100 MHz, $C_6D_6$): δ 177.6, 177.4, 157.1, 147.3, 147.2, 134.6, 134.5, 130.5, 130.4, 130.3, 130.2, 120.2, 120.1, 119.3, 119.2, 112.3, 110.9, 110.8, 80.3, 80.0, 77.6, 76.6, 42.3, 41.8, 41.2, 40.2, 40.1, 39.1, 39.0, 34.2, 33.7, 29.8, 29.4, 29.0, 28.9, 28.6, 28.2, 27.7, 27.2, 26.9, 21.0, 20.9, 20.8, 20.7, 18.2, 16.3, 16.0, 14.8, 14.3, 13.1, 7.3, 7.2, 6.5, 5.5, 5.4. HRMS (ESI) calcd for $[M-I]^+$ ($C_{65}H_{106}O_5Si_3P$) 1081.7086, found, 1081.7083.



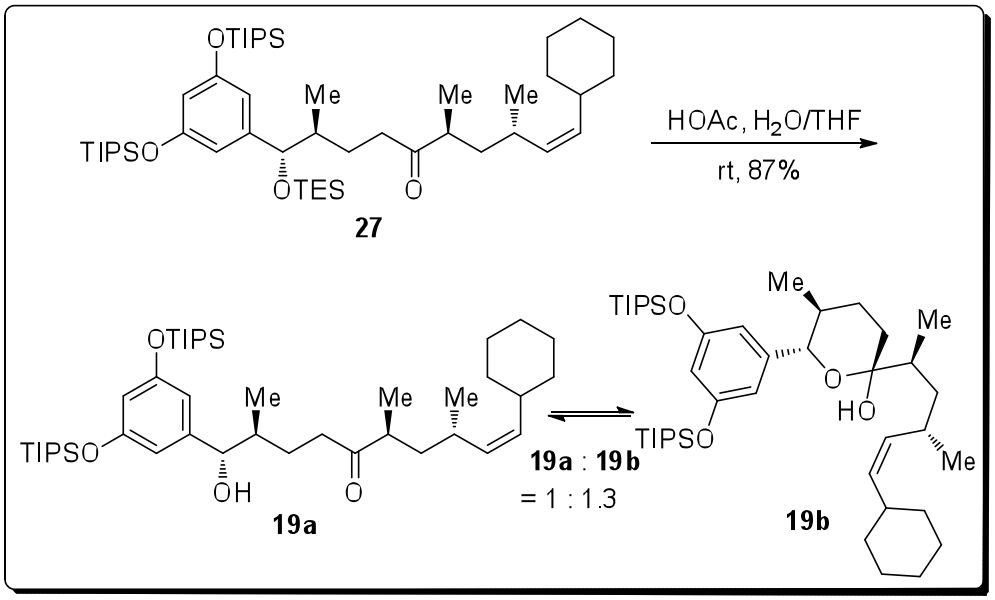

**(1*S*,2*S*,6*S*,8*S*,*Z*)-1-(3,5-bis((triisopropylsilyl)oxy)phenyl)-10-cyclohexyl-2,6,8-trimethyl-1-((triethyl silyl)oxy)dec-9-en-5-yl pivalate** (**26a**). The Wittig reaction of **26** (100 mg, 82.7 μmol) and cyclohexanecarboxaldehyde was performed by using the procedure described for the preparation of compound **4a**. The product was purified by flash chromatography (1.5% $Et_2O$ in hexanes) to provide **26a** (100.8 mg, 89%) as a mixture of two diastereomers (11:10 ratio). $R_f$ = 0.40 and 0.49 (2% $Et_2O$ in hexanes). $^1H$ NMR (400 MHz, $CDCl_3$): δ 6.41 (dd, *J* = 2.4 and 2.0 Hz, 2H), 6.31 (dd, *J* = 2.4 and 2.0 Hz, 1H), 5.16-5.00 (2H), 4.86-4.83 (0.48H), 4.74-4.71 (0.52H), 4.22 (d, *J* = 6.4 Hz, 0.52H), 4.16 (d, *J* = 6.8 Hz, 0.48), 2.60-2.50 (1H), 2.30-2.25 (1H), 1.73-1.60 (9H), 1.42-1.21 (11H), 1.21 and 1.20 (two singlets, 9H), 1.11 (d, *J* = 7.6 Hz, 36H), 1.10-0.98 (4H), 0.93-0.85 (15H), 0.73 and 0.69 (two doublets, *J* = 6.8 Hz, 3H), 0.50 (q, *J* = 8.0 Hz, 6H). $^{13}C$ NMR (100 MHz, $CDCl_3$): δ 178.0, 177.9, 156.3, 146.4, 134.9, 134.5, 134.4, 134.1, 111.8, 111.7, 110.5, 110.4, 79.6, 79.4, 78.1, 77.3, 77.0, 76.7, 76.0, 41.6, 41.5, 41.1, 39.7, 39.0, 38.9, 36.7, 36.6, 34.0, 33.8, 33.7, 33.6, 33.6, 33.5, 29.7, 29.3, 29.2, 28.5, 28.0, 27.9, 27.3, 27.2, 26.1, 26.0, 25.9, 21.5, 20.7, 17.9, 16.0, 15.8, 15.7, 14.7, 12.7, 6.9, 5.0, 4.9. HRMS (ESI) calcd for $[M+Na]^+$ ($C_{54}H_{102}O_5NaSi_3$) 937.6933, found, 937.6936.




**(1*S*,2*S*,6*S*,8*S*,*Z*)-1-(3,5-bis((triisopropylsilyl)oxy)phenyl)-10-cyclohexyl-2,6,8-trimethyl-1-((triethyl silyl)oxy)dec-9-en-5-one** (**27**). To a solution of **26a** (77.0 mg, 84.1 μmol) in $CH_2Cl_2$ (1 mL) at – 78 °C, was slowly added a solution of DIBAL-H (0.25 mL, 252 μmol, 3.0 equiv, 1.0 M in $CH_2Cl_2$). The reaction mixture was stirred at – 78 °C for 3 h, then aqueous Rochelle's salt (3.5 mL) was added. Once the reaction temperature had reached ambient, the resulting mixture was extracted with $Et_2O$ (8 mL x 3). The combined organic layers were washed with brine (6 mL x 2), dried over $Na_2SO_4$, filtered and concentrated in vacuo. The residue was eluted through a short silica gel pad (Hex:$Et_2O$/9:1) to give a mixture (63.0 mg) of **26b** and some unidentified impurities. This mixture was directly used in the next step without further purification. $R_f$ = 0.50 (hexane-ether = 9:1).

To a solution of the above mixture (63.0 mg) in $CH_2Cl_2$ (5.5 mL) was added Dess-Martin periodinane reagent (48.2 mg, 113 μmol, about 1.5 equiv). The reaction mixture was stirred for 1.5 h, then sat. $NaHCO_3$ (3 mL) and sat. $NaS_2O_3$ (3 mL) were added. The resulting two-phase mixture was stirred for 15 min, then was extracted with $CH_2Cl_2$ (5 mL x 3). The combined organic layers were washed with brine (5 mL), dried over $Na_2SO_4$, filtered and concentrated in vacuo. The product was purified by flash chromatography (hexane-ether = 30:1) to provide **27** (62 mg, 89% over two steps). $R_f$ = 0.50 (hexane-ether = 30:1). $[\alpha]_D^{25}$ = -19.0 (*c* = 1.4, THF) $^1$H NMR (400 MHz, $C_6D_6$): δ 6.89 (d, *J* = 2.4 Hz, 2H), 6.81 (dd, *J* = 2.4 and 2.0 Hz, 1H), 5.36 (dd, *J* = 10.4 and 10.4 Hz, 1H), 5.12 (ddd, *J* = 10.8, 10.0 and 0.8 Hz, 1H), 4.53 (d, *J* = 6.8 Hz, 1H), 2.65-2.54 (3H), 2.40-2.29 (3H), 2.00-1.91 (2H), 1.88-1.81 (2H), 1.77-1.73 (3H), 1.72-1.62 (1H), 1.44-1.35 (9H), 1.27 (d, *J* = 7.2 Hz, 36H), 1.23-1.14 (3H), 1.11 (t, *J* = 8.0 Hz, 9H), 1.13-.095 (1H), 1.06 (d, *J* = 7.2 Hz, 3H), 1.04 (d, *J* = 6.4 Hz, 3H), 0.95 (d, *J* = 6.8 Hz, 3H), 0.73 (dt, *J* = 7.6 and 0.8 Hz, 6H). $^{13}$C NMR (100 MHz, $C_6D_6$):

δ 212.3, 157.2, 146.8, 135.5, 134.4, 112.3, 111.1, 80.0, 44.4, 41.8, 41.3, 39.7, 37.0, 34.2, 33.9, 30.7, 26.9, 26.3, 26.2, 22.4, 18.2, 15.8, 13.1, 7.2, 5.4. IR (neat) 2946, 2868, 1715, 1590, 1449, 1331, 1169, 1030, 1011, 882, 761, 687. HRMS (ESI) calcd for $[M+Na]^+$ ($C_{49}H_{92}O_4NaSi_3$) 851.6201, found, 851.6205.




**Deprotection of Compound 27 to provide 19a/19b**. A solution of pure **27** (52 mg, 62.7 μmol) in THF (1.9 mL), water (0.5 mL) and HOAc (1.9 mL) was stirred for 24 h. The reaction was quenched by careful addition of sat. $NaHCO_3$ (15 mL), and the mixture waas extracted with $Et_2O$ (6 mL x 3). The combined organic layers were washed with brine (8 mL), dried over $Na_2SO_4$, filtered and concentrated in vacuo. The product was purified by flash chromatography (Davisil silica gel, hexane-EtOAc = 15:1) to provide **19a/b** (38.9 mg, 87%). $R_f$ = 0.25-0.50 (hexane-EtOAc = 15:1).