Total Synthesis of Papulacandin D

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SUPPORTING INFORMATION

Table of Contents *Page*

General Experimental *S1*

Literature Preparations *S4*

Experimental Procedures *S6*

Preparation of Aromatic Iodide **4** *S6*

Preparation of Spirocyclic Arylglycoside **20** *S12*

Preparation of Acid **2** *S33*

Acylation and Global Deprotection *S51*

References *S59*

^{1}H and ^{13}C NMR Spectra *S60*

General Experimental

All reactions were performed in oven (120 °C) and/or flame dried glassware under an atmosphere of dry nitrogen or argon, unless noted. Syringes and needles were dried (120 °C) for at least 12 hours. All reaction temperatures correspond to internal temperatures measured by Teflon-coated thermocouples unless otherwise noted. Reaction solvents including dichloromethane (Fisher, HPLC Grade), diethyl ether (Fisher, BHT stabilized HPLC Grade) and tetrahydrofuran (Fisher, HPLC Grade), toluene (Fisher, ACS Grade) were dried by percolation through a column packed with neutral alumina and a column packed with Q5 reactant, a supported copper catalyst for scavenging oxygen, under a positive pressure of argon. Reaction solvent acetonitrile (Fisher, HPLC grade) was distilled from sodium, *N,N*-dimethylformamide (Aldrich, ACS Grade) and dimethyl sulfoxide (Fisher, ACS Grade) were distilled from CaH_2 and dried sequentially over two batches of activated 4Å molecular sieves. Benzene (Aldrich ACS Grade) was distilled from sodium and benzophenone, dichloroethane (Aldrich ACS Grade) was distilled from CaH_2, methanol (Aldrich ACS Grade) was distilled from MgOMe and

chloroform (Aldrich ACS Grade) was distilled from P_2O_5 and deacidfied by percolating through basic Bockmann Act I grade alumina and stored over freshly activated 3Å sieves. Pyridine (Aldrich ACS Grade) and 2,6-lutidine (Aldrich ACS Grade) were freshly distilled from CaH_2 prior to use. Acetone (Fisher, ACS Grade) was used without further purification.

Solvents for chromatography were: hexanes (Fisher, ACS Grade), ethyl acetate (Aldrich, ACS Grade), diethyl ether (Fisher, ACS Grade), dichloromethane (Aldrich, ACS Grade), toluene (Aldrich, ACS Grade), methanol (Aldrich ACS Grade) and chloroform (Aldrich ACS Grade).

Analytical thin-layer chromatography was preformed on Merck silica or aluminum oxide, basic gel plates with QF-254 indicator. Visualization was accomplished with UV (254 nm), iodine, potassium permanganate ($KMnO_4$), vanillin solution, ceric ammonium molybdate (CAM), *p*-anisaldehyde staining solutions.

Column chromatography was performed using Silicycle Silaflash P60 (40-63 μ, 60 Å pore size) silica gel. Geraniol (Aldrich) was enriched by spinning band distillation prior to use. 3,5-Dihydroxyrobenzoic acid (Aldrich) was recrystallized from H_2O. Tris(dibenzylideneacetone)-dipalladium chloroform ($Pd_2(dba)_3 \cdot CHCl_3$) was prepared by recrystallization of $Pd_2(dba)_3$ from chloroform.[1,2] Triethylsilyl chloride (TESCl, Gelest), 2-(Trimethylsilyl)ethanol (TMS ethanol) (Gelest) were freshly distilled prior to use. 4-Dimethylaminopyridine (DMAP) (Aldrich) was recrystallized from ethyl acetate prior to use. Diisopropylethylamine (*i*-Pr_2NEt) (Aldrich) and triethylamine (Et_3N) (Aldrich) were freshly distilled from CaH_2 prior to use. 2,4,6-Trichlorobenzoyl chloride (Aldrich), acrolein (Fluka) were distilled prior to use

(1,3-Bis-(2,4,6-trimethylphenyl)-2-imidazolidinylidene)dichloro(phenylmethylene)-(tricyclohexylphosphine)ruthenium (Grubb's 2nd Generation Catalysts) (Materia), di-*tert*-butylchlorosilane (Gelest), pivalolyl chloride (Fluka, 99%+), *N*-iodosuccinimide (NIS) (Aldrich, 95%), dimethyl sulfide (DMS) (Aldrich, 99%+), citric acid monohydrate (Fisher), lithium hydroxide monohydrate (Fisher), sodium thiosulfate pentahydrate (Aldrich, ACS Grade), pyridium-*p*-toluenesulfonate (PPTS) (Avocado, 98%), *p*-toluenesulfonyl chloride (TsCl) (99%+, Acros), di-chlorobis[(*p*-cymene)chlororuthenium(II)] (Strem, 98%), triphosgene (TCI, 98%), ethanol (absolute, Aaper), potassium trimethylsilanoate (TMSOK) (Gelest, 95%), sodium *tert*-butoxide (NaO*t*-Bu) (Strem, 97%), hydrofluoric acid (HF) (Fisher, 49%), thionyl chloride ($SOCl_2$) (Aldrich, 97%), and (*S*)-(+)- and (*R*)-(-)-α-methoxy-α-trifluoromethylphenylacetyl

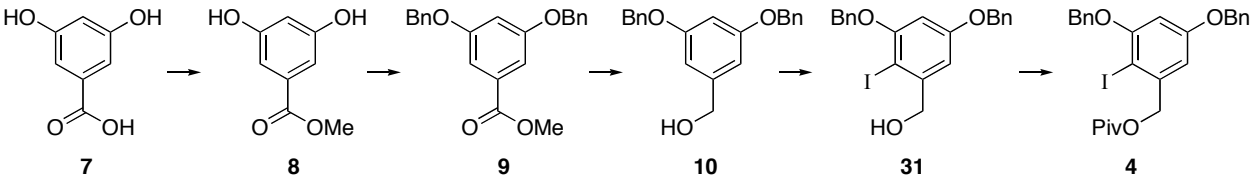
chloride (MPTACl) (Fluka, ChiralSelect, ≥99.0%) were used without further purification. The following were titrated according to the representative reference and by ^{1}H-NMR titration according to Hoye et. al:[3] *tert*-butyllithium (*t*-BuLi),[4] 3-chloroperbenzoic acid washed (*m*-CPBA),[5] diisobutylaluminum hydride (DIBAL-H),[6] Lithium triethylborohydride (super hydride),[6,7] a solution of lithium aluminum hydride in tetrahydrofuran was prepared and titrated according Brown et al.[7]

^{1}H NMR, ^{13}C NMR, ^{19}F NMR were recorded on Varian Unity 400 (400 MHz, ^{1}H; 100 MHz, ^{13}C), Varian Inova 500 (500 MHz, ^{1}H), and Varian VXR 500 (499 MHz, ^{1}H; 125 MHz ^{13}C; 470 MHz, ^{19}F) spectrometer. Spectra were referenced to residual chloroform (7.26 ppm, ^{1}H; 77.00 ppm, ^{13}C), dimethyl sulfoxide (2.50 ppm, ^{1}H; 39.51 ppm ^{13}C) and methanol (4.87 ppm, 3.31 ppm ^{1}H; 49.15 ppm ^{13}C). Chemical shifts are reported in ppm, multiplicities are indicated by s (singlet), d (doublet), t (triplet), q (quartet), sep (septet), m (multiplet), dd (doublet of doublets), ddd (doublet of doublet of doublets) dddd (doublet of doublet of doublet of doublets), tq (triplet of quartet), dt (doublet of triplet), td (triplet of doublets), nofoddd (non first order doublet of doublet of doublets), and br (broad). Coupling constants, *J*, are reported in Hertz. The University of Illinois Mass Spectrometer Center performed Mass spectroscopy. EI and CI mass spectra were performed on a 70-VSE spectrometer. ESI mass spectra were performed on a Micromass Quattro spectrometer. Data are reported in the form of (m/z). Infrared spectra (IR) were recorded on a Mattson Galaxy 5020 spectrophotometer in NaCl cells. Peaks are reported in cm^{-1} with indicated relative intensities: s (strong, 67-100%); m (medium, 34-66%); w (weak, 0-33%). The University of Illinois Microanalytical Service Laboratory performed elemental analyses. Optical rotation data was obtained on a JASCO DIP-360 digital polarimeter and are reported as follows: concentration (c = g/100 mL), and solvent. Analytical supercritical fluid chromatography (CSP-SFC) was performed on a Berger Instruments packed-column SFC with built-in photometric detector (220 nm) using Daicel Chiralpak OD, OJ, OB, AD and AS columns as well as a Regis Whelk-O1 column. Melting points (mp) were determined on a Thomas-Hoover capillary melting point apparatus in sealed tubes and are corrected. Ozonolyses were performed with a Welsbach Model T-816 Ozonator set at 55 W/90 V with a 1 lpm flow rate. Kugelrohr distillations were performed on a Büchi GKR-50 Kugelrohr and temperatures reported are air bath temperatures (ABT).

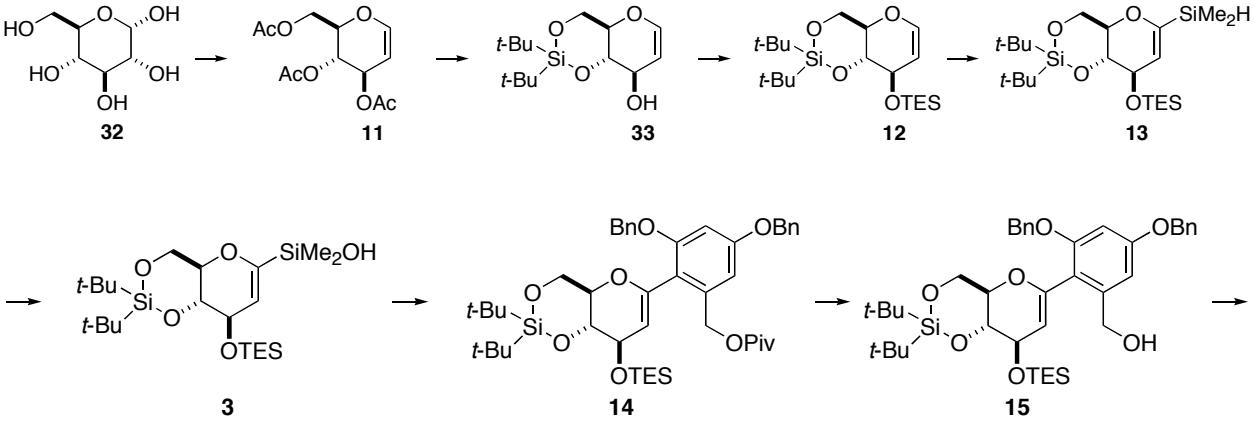
Literature Preparations

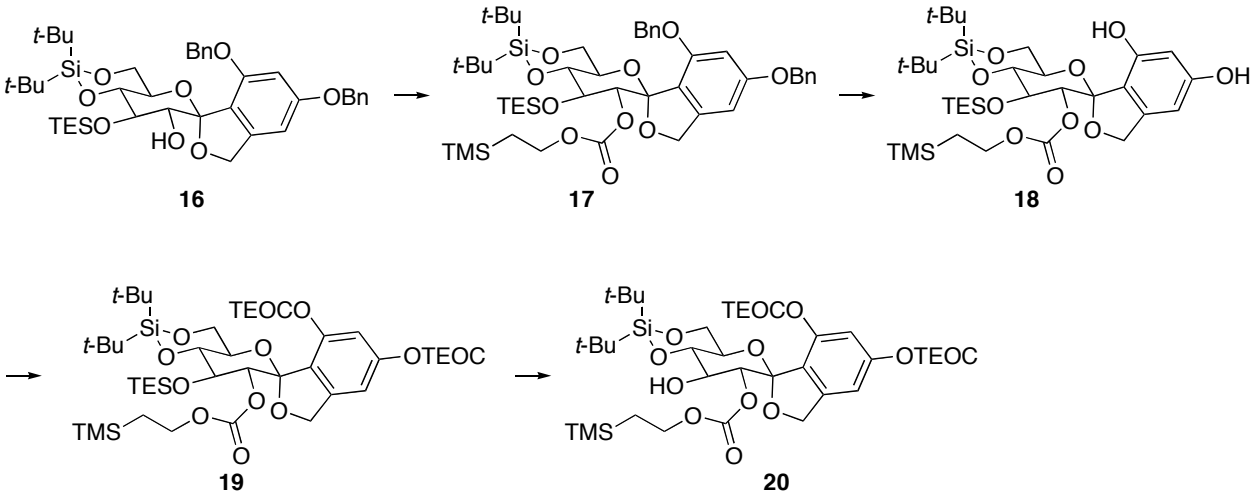
Ethyl 4-(diethoxyphosphinyl) tiglate was prepared according to Kibayashi et. al.[8] (*S*)-(-)-Citronellol was prepared following the procedure described by Noyori and co-workers.[9] Allyltrichlorosilane was prepared following the procedure of Sakurai and co-workers.[10] *N*, *N*'-Dimethyl-*N,N*'-bis-((3'a*R*,4'a*R*)-7'-oxooctahydro-6'a,7'a-diaza-7'-phospha-cyclopenta[a]-apentalene-7'-yl)-pentane-1,5-diamine (*R,R*-**26**) was prepared according to Denmark and Fu.[11] Di(*tert*-butyl)silyl ditriflate was prepared according to the method of Corey and Hopkins.[12] Methyl (triphenylphosphoranylidene)acetate was prepared according to Hesse and Li.[13] Trimethylsilylethoxy chlorocarbonate (TEOC-Cl) was prepared following the procedure of Gioeli and co-workers.[14] Tri-*O*-acetyl-D-glucal was prepared in accord with Roth and Pigman.[15]

Scheme 1

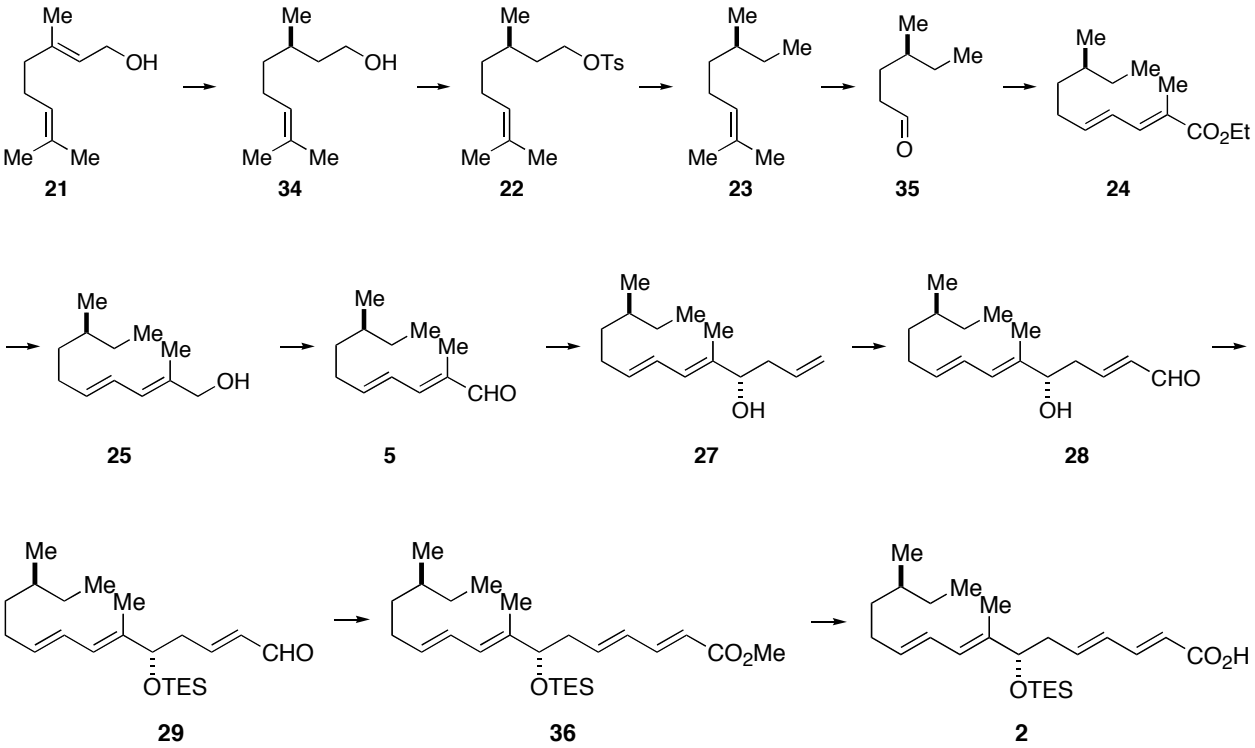


Scheme 2

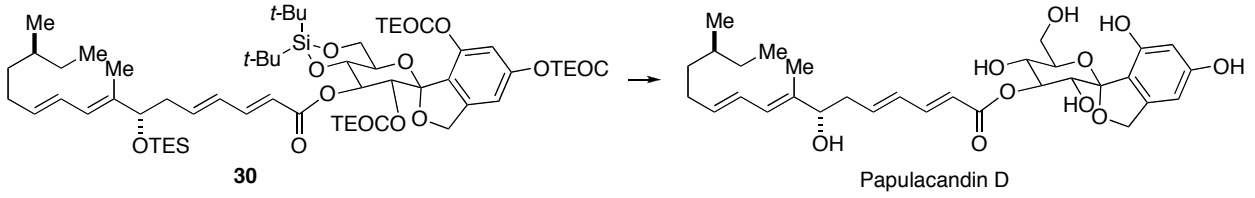




Scheme 3

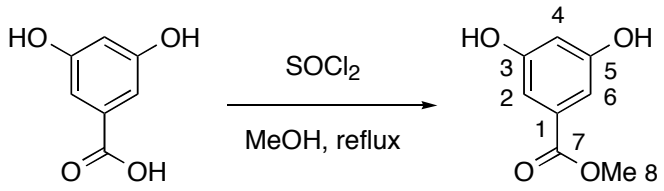


Scheme 4



Preparation of Aromatic Iodide 4

Preparation of Methyl 3,5-Dihydroxybenzoate (8)[16] [CSR-IV-89]



7 **8**

A 500-mL, three-necked, round-bottom flask, equipped with a Teflon-coated blade attached to an over-head stirrer, nitrogen inlet, reflux condenser bearing a drying tube, and a rubber septum which contains a needle vented to a mineral oil bubbler, was purged with nitrogen and charged with 3,5-dihydrobenzoic acid (**7**, 20 g, 130 mmol, 1.0 equiv), followed by the addition of freshly distilled MeOH (300 mL). Thionyl chloride (11.4 mL, 157 mmol, 1.2 equiv) was added cautiously by syringe over 25 min. to the rapidly stirring solution at room temperature. The nitrogen inlet was removed after the addition was complete and the nitrogen inlet was replaced with a rubber septum. The resulting solution was stirred at reflux (oil bath temperature 97 ºC) for 2 h. The contents were then transferred to a 500-mL, one-neck, round-bottom flask, and the MeOH was removed under reduced pressure by rotary evaporation. The resulting beige solid was dissolved in MeOH (50 mL) and once again concentrated under reduced pressure by rotary evaporation, this procedure was repeated two more times and remaining volatiles were removed under high-vacuum (0.03 mmHg) to afford 22.0 g (99%) of **8** as a powdery, beige solid.

Data for **8**:

mp: 168 - 169 °C (MeOH)

^{1}H NMR: (400 MHz, DMSO)
9.64 (br, 1H, (OH)), 6.80 (d, J = 2.2 Hz, 2H, HC(2)), 6.43 (t, J = 2.2 Hz, 1H, HC(4)), 3.77 (s, 3H, H_3C(6))

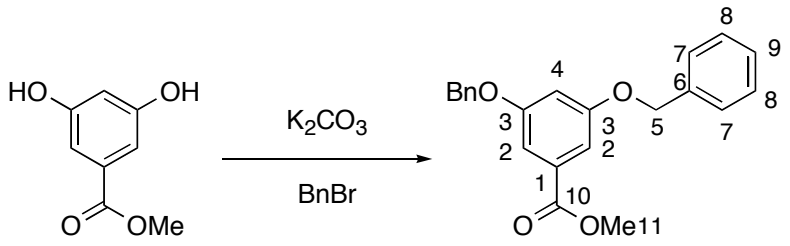
^{13}C NMR: (126 MHz, DMSO)
166.3 (C(5)), 158.6 (C(3)), 131.3 (C(1)), 107.2 (C(4)), 107.1 (C(2)), 52.0 (C(6))

IR: (KBr)
3560 (s), 3050 (s), 2910 (s), 1710 (s), 1590 (s), 1320 (m), 1280 (m)

MS: (EI, 70 eV)
168 (M^+, 73), 137 (100), 109 (39), 81 (17), 69 (27)

TLC: R_f 0.43 (hexanes/EtOAc, 1/1) [SiO_2, UV, CAM]

Preparation of Methyl 3,5-Bis(phenylmethoxy)benzoate (9)[16] [CSR-V-2]



8 **9**

A 500-mL, single-necked, round-bottom flask, equipped with a large magnetic stir-bar and nitrogen inlet was purged with nitrogen and charged with **8** (15.0 g, 89.2 mmol, 1.0 equiv) and acetone (100 mL). Potassium carbonate (37.0 g, 267.6 mmol, 3.0 equiv) was added and a brown mixture was observed. Then, benzyl bromide (32 mL, 267.6 mmol, 3.0 equiv) was added by syringe to the mixture at room temperature, the resulting mixture was stirred continuously at room temperature for 24 h (the mixture became a thick slurry over time, due to precipitation of KBr, and for lager scale preparation an over-head stirrer was used). The contents were diluted with EtOAc (150 mL) and H_2O (175 mL). The aqueous layer was separated and extracted with EtOAc (4 x 150 mL). The combined organic layers were washed with brine (75 mL), dried over anhydrous magnesium sulfate, filtered, and concentrated under reduced pressure to afford a brown solid which was recrystallized from *tert*-butyl methyl ether (60 mL) to provide 31 g (99%) of **9** as a white crystalline powder.

Data for **9**:

mp: 70 - 71 ^{o}C (TBME)

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

7.45 (d, J = 7.1 Hz, 2H, HC(7)), 7.41 (t, J = 7.1 Hz, 2H, HC(8)), 7.37 (d, J = 7.1 Hz, 2H, HC(9)), 7.34 (d, J =2.2 Hz, 2H, HC(2)), 6.834 (t, J = 2.4 Hz, 1H, HC(4)), 5.09 (s, 4H, HC(5)), 3.92 (s, 3H, HC(11))

^{13}C NMR: (126 MHz, $CDCl_3$)

166.2 (C(10)), 159.7 (C(3)), 136.4 (C(6)), 132.0 (C(1)), 128.6 (C(8)), 128.1 (C(9)), 127.5 (C(7)), 108.3 (C(2)), 107.2 (C(4)), 70.2 (C(5)), 52.2 (C(11))

IR: (KBr)

1714 (s), 1724 (s), 1597 (s), 1439 (s), 1378 (s), 1252 (s), 1083 (s), 966 (w), 868

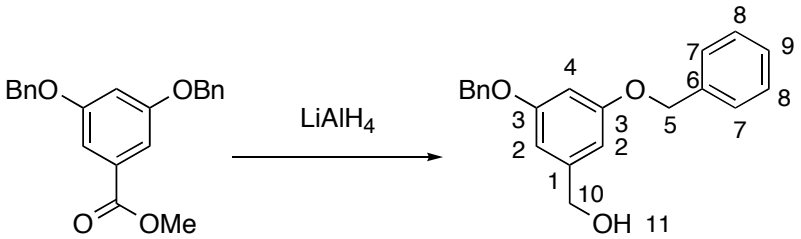
(w), 763 (s)

MS: (EI, 70 eV)

348 (M^+, 13), 100 (100), 62 (3)

TLC: R_f 0.39 (hexanes/EtOAc, 3/1) [SiO_2, UV, CAM]

Preparation of 3,5-Bis(phenylmethoxy)benzenemethanol (10)[16] [CSR-IV-95]



9 **10**

A 250-mL, two-necked, round-bottom flask, equipped with a magnetic stir-bar, argon inlet and a rubber septum was purged with argon and charged with **9** (10.0 g, 28.7 mmol, 1.0 equiv) followed by THF (20 mL). The solution was then cooled to 0 °C using an ice bath. Lithium aluminum hydride in THF (0.9 M, 70 mL, 63.1 mmol, 2.2 equiv)[7] was added cautiously by syringe over 30 min (maintaining the internal temperature between 10 to 15 °C). After the addition was complete the resulting solution was stirred at room temperature for 3 h, whereupon the solution was once again cooled to 0 °C and H_2O (2.5 mL), 15% NaOH (2.5 mL), H_2O (7.5 mL) were added sequentially. Upon warming to room temperature, the white suspension was filtered through Celite (5 g) and the Celite pad was washed with THF (40 mL). The filtrate was concentrated under reduced pressure by rotary evaporation. The resulting white suspension was dissolved in toluene (20 mL) and once again concentrated under reduced pressure by rotary evaporation, this procedure was repeated two more times and remaining volatiles were removed under high vacuum (0.06 mmHg) to afford a white solid. The solid was recrystallized from hot absolute ethanol (60 mL) to afford 9.0 g (98%) of **10** as white needles.

Data for **10**:

mp: 79 - 80 °C (EtOH)

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

7.34 (m, 10H, HC(7, 8, 9)), 6.63 (d, J = 2.2 Hz, 2 H, H C(2)), 6.56 (t, J = 2.3 Hz, 1H, HC(4)), 5.04 (s, 4 H, HC(5)), 4.62 (d, J = 5.2 Hz, 2H, HC(10)), 1.90 (t, J = 5.2 Hz, 1H, (OH))

^{13}C NMR: (126 MHz, $CDCl_3$)

160.1 (C(3)), 143.4 (C(6)), 136.7 (C(1)), 128.6 (C(8)), 127.9 (C(9)), 127.5 (C(7)), 105.6 (C(2)), 101.2 (C(4)), 69.9 (C(5)), 65.2 (C(10))

IR: (KBr)

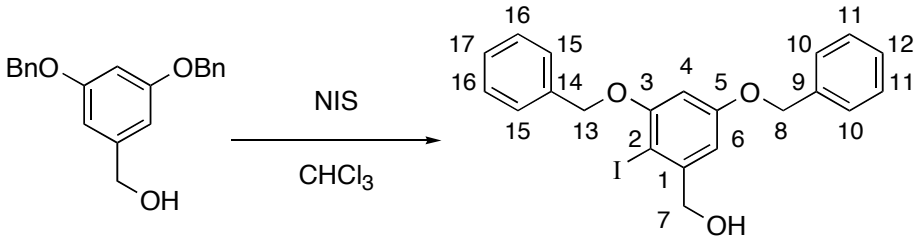
3303 (br), 3325 (m), 2923 (s), 1593 (m), 1497 (m), 1352 (m), 1285 (m), 1159 (s), 833 (m)

MS: (EI, 70 eV)

320 (M^+, 17), 181 (11), 91 (100)

TLC: R_f 0.30 (hexanes/EtOAc, 3/1) [SiO_2, UV, *p*-anisaldehyde]

Preparation of 2-Iodo-3,5-bis(phenylmethoxy)benzenemethanol (31) [CSR-V-1]



10 **31**

A 250-mL, single-necked, round-bottom flask, equipped with a magnetic stir-bar, argon inlet, was purged with argon and charged with **10** (5.0 g, 15.6 mmol, 1.0 equiv) followed by freshly distilled chloroform (34 mL). To this solution, *N*-iodosuccinimide (4.21 g, 18.7 mmol, 1.2 equiv) was added. The flask was wrapped in aluminum foil and stirred at room temperature for 18 h. The mixture was diluted with EtOAc (50 mL) and the pink suspension was eluted through Celite (5 g) washing the Celite pad with EtOAc (100 mL). Then H_2O (20 mL) was added and the aqueous layer was separated and extracted with EtOAc (2 x 15 mL). The combined organic layers were washed with saturated, aqueous sodium thiosulfate (30 mL) and brine (40 mL), dried over anhydrous magnesium sulfate, filtered, and concentrated under reduced pressure by rotary evaporation. The white residue was recrystallized from isopropyl acetate (20 mL) adding hot heptane (80 mL), until the solution became turbid and then cooled in an ice bath for 2 h, to provide 6.3 g (91%) of **31**, as a white crystalline powder.

Data for **31**:

mp: 113-114 °C (4/1 heptane/isopropyl acetate)

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

7.49 (d, J = 7.5 Hz, 2H, HC(16, 11)), 7.41 - 7.31 (m, 8H, HC(15, 17, 12, 10)), 6.84 (d, J = 2.6 Hz, 1H, HC(6)), 6.50 (d, J = 2.6 Hz, 1H, HC(4)), 5.10 (s, 2H, HC(13)), 5.05 (s, 2H, HC(8)), 4.69 (d, J = 6.2 Hz, 2H, HC (7)), 2.12 (t J = 6.2 Hz, 1H, (OH))

^{13}C NMR: (126 MHz, $CDCl_3$)

160.4 (C(3)), 157.7 (C(5)), 144.8 (C(1)), 136.5 (C(14)), 136.3 (C(9)), 128.7 (C(16), 128.6 (C(11)), 128.2 (C(15), 127.9 (C(17)), 127.6 (C(10)), 126.9 (C(12)), 106.6 (C(6)), 100.3 (C(4)), 78.8 (C(2)), 70.9 (C(13)), 70.3 (C(8)), 69.6 (C(7))

IR: (KBr)

3305 (br), 1580 (s), 1498 (m), 1424 (m), 1279 (m), 1169 (s), 1055 (s), 1010 (s), 732 (m)

MS: (EI, 70 eV)

446 (M^+, 12), 181 (10), 91 (100), 65 (10)

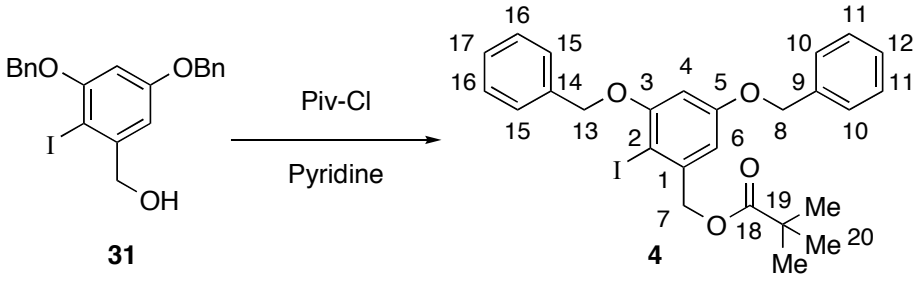
TLC: R_f 0.24 (hexanes/EtOAc, 10/1) [SiO_2, UV]

Analysis: $C_{21}H_{19}IO_3$ (446.23)

Calcd: C, 56.52 %; H, 4.29 %; I, 28.44 %

Found: C, 56.43 %; H, 4.24 %; I, 28.09 %

Preparation of 2-Iodo-3,5-bis(phenylmethoxy-2',2'-dimethylpropanoate)benzenemethanol (4) [CSR-V-27]



31 **4**

A 100-mL, two-necked, round-bottom flask, equipped with a magnetic stir-bar, argon inlet, and a rubber septum, was purged with argon and charged with **31** (4.0 g, 8.9 mmol, 1.0 equiv) followed by CH_2Cl_2 (35 mL). To this solution, pyridine (1.08 mL, 13.4 mmol, 1.5 equiv) and pivaloyl chloride (1.3 mL, 10.6 mmol, 1.2 equiv) were added sequentially. The light-yellow solution was stirred at room temperature for 3 h. The solution was diluted with H_2O (60 mL) and

the aqueous layer was separated and extracted with CH_2Cl_2 (3 x 40 mL). The combined organic layers were washed with saturated, aqueous sodium bicarbonate (30 mL) and brine (40 mL), dried over anhydrous magnesium sulfate, filtered, and concentrated under reduced pressure by rotary evaporation. The oily residue was purified by column chromatography (SiO_2 (40 x 180 mm), hexanes/EtOAc, 3/1). Further purification by recrystallization from hexane (15 mL) afforded 4.5 g (94%) of **4** as white crystalline rhombuses.

Data for **4**:

mp: 50-51 ^{o}C (hexane)

^{1}H NMR: (500 MHz, $CDCl_3$)
7.49 (d, J = 7.6 Hz, 2H, HC(16, 11)), 7.41 - 7.28 (m, 8H, HC(15, 17, 12, 10)), 6.69 (d, J = 2.7 Hz, 1H, HC(6)), 6.52 (d, J = 2.4 Hz, 1H, HC(4)), 5.13 (s, 2H, HC(13)), 5.12 (s, 2 , HC(8)), 5.04 (s, 2 H, HC (7)), 1.25 (s, 9H, HC(20))

^{13}C NMR: (126 MHz, $CDCl_3$)
177.9 (C(18)), 160.1 (C(3)), 157.9 (C(5)), 140.8 (C(1)), 136.4 (C(14)), 136.3 (C(9), 128.7 (C(16)), 128.6 (C(11), 128.2 (C(15)), 127.9 (C(17)), 127.5 (C(10)), 127.0 (C(12)), 107.2 (C(6)), 100.5 (C(4)), 79.8 (C(11)), 71.0 (C(13)), 70.3 (C(8)), 70.2 (C(7)), 38.9 (C(19)), 27.3 (C(20))

IR: (KBr)
3075 (w), 2927 (w), 1720 (s), 1584 (2), 1496 (m), 1465 (m), 1281 (s), 1158 (s), 732 (s)

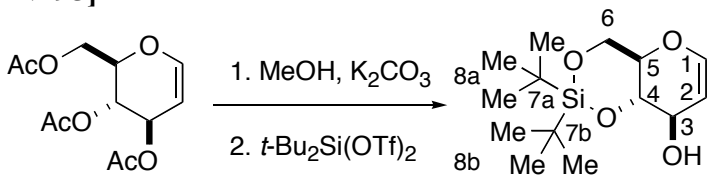
MS: (EI, 70 eV)
530 (M^+, 6), 446 (9), 404 (2), 348 (100), 181 (11), 91 (100)

TLC: R_f 0.50 (hexanes/EtOAc, 10/1) [SiO_2, $KMnO_4$]

Analysis: $C_{26}H_{27}IO_4$ (530.39)
Calcd: C, 58.88 %; H, 5.13 %; I, 23.93 %
Found: C, 58.96 %; H, 5.15 %; I, 23.79 %

Preparation of Spirocyclic *C*-Arylglycoside 20

Preparation of 1,5-Anhydro-4,6-O-[bis(1,1-dimethylethyl)silylene]-2-deoxy-*D*-arabino-1-hexenitol (33) [CSR-V-95][18]



11 **33**

To a 500-mL, two-necked, round-bottom flask, fitted with a nitrogen inlet, a septum, and magnetic stir-bar was added triacetoxyglucal **11** (10.0 g, 36.6 mmol, 1.0 equiv) followed by dry MeOH (37 mL). Then K_2CO_3 (0.051 g, 0.369 mmol, 0.01 equiv) was added. The light-yellow solution was stirred at room temperature for 1 h. The volatiles were removed under reduced pressures using rotary evaporation. The resulting yellow viscous reside was dissolved in $CHCl_3$ (100 mL) and once again concentrated under reduced pressure by rotary evaporation. This procedure was repeated two more times and the remaining volatiles were removed under high vacuum (0.06 mmHg) for approximately 2 h. Then dry dimethylformamide (37 mL) was added to the crude yellow syrup, followed by 2,6-lutidine (12.9 mL, 110.8 mmol, 3.0 equiv) was added and the solution was cooled to -15 °C using an acetone/ice bath. Di(*tert*-butyl)silyl ditriflate[12] (14.8 mL, 40.6 mmol, 1.1 equiv) was added. The contents were warmed to room temperature and stirred for 1.5 h. This solution was diluted with H_2O (200 mL) and extracted with Et_2O (3 x 100 mL). The combined organic extracts were washed with brine (100 mL), dried over Na_2SO_4 and filtered. The solvent was removed by rotary evaporation to afford a light-yellow oil. The crude reside was purified by column chromatography (SiO_2 (60 x 220 mm), hexanes/EtOAc, 15/1)), which afforded 9.4 g (89%) of **33** as a white powder.

Data for **33**:

mp: 67-69 ºC (hexanes/EtOAc, 15/1)

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

6.27 (dd, *J* = 6.5, 2.0 Hz, 1H, CH(1)); 4.76 (dd, *J* = 6.5, 2.0 Hz, 1H, CH(2)); 4.30 (d, *J* = 6.5 Hz, 1H, CH(3)); 4.18 (dd, *J* = 10.7, 5.4 Hz, 1H, CHe(6)); 3.96 (t, *J* = 10.7 Hz, 1H, CHa(6)); 3.92 (dd, *J* = 10.7, 6.5 Hz, 1H, CH(4)); 3.84 (dt, *J* = 10.7, 5.4 Hz, 1H, CH(5)); 2.41 (s, 1H, (OH)); 1.08 (s, 9H, $C(CH_3)_3$(8a or 8b)); 1.00(s, 9H, $C(CH_3)_3$(8a or 8b))

^{13}C NMR: (126 MHz, $CDCl_3$)

143.9 (C(1)); 103.2 (C(2)); 77.6 (C(4)); 72.5 (C(5)); 70.4 (C(3)); 65.9 (C(6)); 27.6 (C(8a or 8b)); 27.1 (C(8a or 8b)); 22.9 (C(7a or 7b)); 20.0 (C(7a or 7b))

IR: (film)

3430 (m); 2963 (s); 2891(s); 1647 (m); 1473 (m); 1388 (w); 1364 (w); 1233 (m); 1159 (m); 1121 (s); 1098 (s); 1031 (w); 1012 (w); 994 (w); 871 (s); 826 (s); 767 (s); 653 (s)

MS: (EI, 70 eV)

286 (M^+ (13)); 230 (17); 229 (100); 199 (12); 157 (41); 119 (15); 115 (14); 103 (11); 91(11); 81(26); 77 (32); 57 (12)

Opt. Rot.: $[\alpha]_D^{24}$ -12.31 (c = 0.79, EtOH)

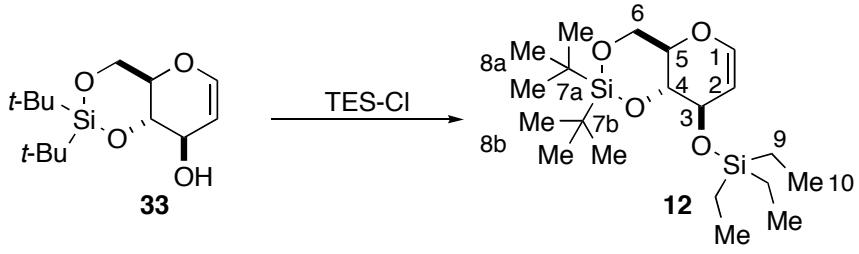
TLC: R_f 0.16 (hexanes/EtOAc, 20/1) [SiO_2, UV, $KMnO_4$]

HRMS: $C_{14}H_{26}O_4Si$ (286.44)

Calcd: 286.1600

Found: 286.1599

Preparation of 1,5-Anhydro-4,6-O-[bis(1,1-dimethylethyl)silylene]-2-deoxy-3-O-(triethylsilyl)-*D*-arabino-1-hexenitol (12) [CSR-V-96]



To a 500-mL, two-necked, round-bottom flask fitted with a nitrogen inlet, septum, and magnetic stir-bar was added alcohol **33** (8.9 g, 31.1 mmol, 1.0 equiv) followed by CH_2Cl_2 (100 mL). Pyridine (3.77 mL, 46.7 mmol, 1.2 equiv) was added along with triethylchlorosilane (6.27 mL, 37.4 mmol, 1.2 equiv) and the colorless solution was stirred at room temperature for 4 h. To this solution was added saturated, aqueous $NaHCO_3$ (300 mL). The aqueous layer was extracted with CH_2Cl_2 (3 x 50 mL). The combined organic layers were washed with brine (100 mL), dried over Na_2SO_4, filtered and concentrated under reduced pressure using rotary evaporation. The

crude yellow oil was purified by column chromatography (SiO_2 (60 x 220 mm), hexanes/EtOAc, 15/1)) to afford 11.5 g (92%) of **12** as a colorless oil.

Data for **12**:

bp: 145 ºC ($6.5x10^{-5}$ mmHg, ABT)

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

6.23 (dd, *J* = 6.0, 2.0 Hz, 1H, CH(1)); 4.61 (dd, *J* = 6.0, 2.0 Hz, 1H, CH(2)); 4.28 (dd, *J* = 7.0, 2.0 Hz, 1H, CH(3)); 4.15 (dd, *J* = 10.5, 5.0 Hz, 1H, CH(6e)); 3.96 (dd, *J* = 10.4, 7.0 Hz, 1H, CH(4)); 3.95 (t, *J* =10.5 Hz 1H, CH(6a)); 3.80 (dt, *J* = 10.4, 5.0 Hz, 1H, CH(5)); 1.07 (s, 9H, $C(CH_3)_3$(8a or 8b)); 1.00 (s, 9H, $C(CH_3)_3$(8a or 8b)); 0.99 (t, *J* = 8.0 Hz, 9H, CH_3(10)); 0.66 (dq, *J* = 15.0, 8.0 Hz, 6H, CH_2(9))

^{13}C NMR: (126 MHz, $CDCl_3$)

142.97 (C(1)); 105.13 (C(2)); 77.13 (C(4)); 72.77 (C(5)); 70.51 (C(3)); 65.84 (C(6)); 27.36 (C(8a or 8b)); 26.08 (C(8a or 8b)); 22.67 (C(7a or 7b)); 19.74 (C(7a or 7b)); 6.75 (C(9)); 4.76 (C(10))

IR: (film)

2957 (s); 2935 (s); 2860 (s); 2878 (s); 1649 (m); 1473 (m); 1414 (w); 1391 (m); 1364 (w); 1234 (s); 1162 (s); 1123 (s); 1109 (s); 1002 (s); 969 (w); 880 (s); 826 (s); 735 (s); 653 (s)

MS: (CI, 130 eV)

401 ($(M^+$+1) (10)); 371 (14); 341 (18); 289 (13); 270 (18); 269 (76); 267 (15); 217 (22); 201 (15); 187 (30); 103 (10); 81 (100)

Opt. Rot.: $[\alpha]_D^{24}$ -46.80 (c = 1.23, $CHCl_3$)

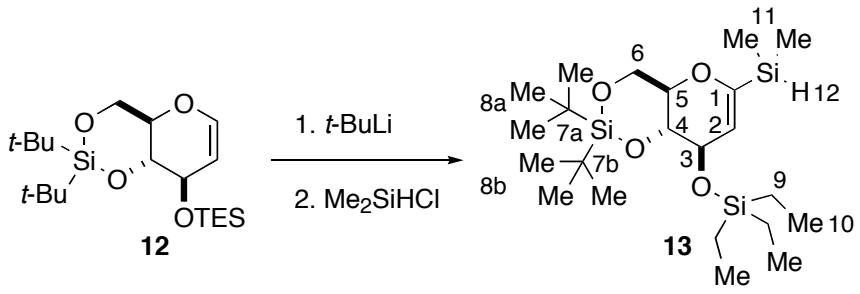
TLC: R_f 0.60 (hexanes/EtOAc, 10/1) [SiO_2, CAM]

Analysis: $C_{20}H_{40}O_4Si_2$ (400.70)

Calcd: C, 59.87%; H, 10.35%

Found: C, 59.95%; H, 10.06%

Preparation of 1,5-Anhydro-4,6-*O*-[bis(1,1-dimethylethyl)silylene]-2-deoxy-1-*C*-(dimethyl(hydrido))-3-*O*-(triethylsilyl)-*D*-arabino-1-hexenitol (13) [CSR-V-66]



To a 25-mL, one-necked, round-bottom flask fitted with an argon inlet adaptor with septum, and magnetic stir-bar was charged with **12** (1.90 g, 4.7 mmol, 1.0 equiv), followed by THF (3.8 mL). The contents were cooled to -78 ºC using a 2-propanol/dry-ice bath. Then *tert*-butyllithium (1.51 M in pentane, 3.77 mL, 5.69 mmol, 1.2 equiv) was added drop wise. The solution turned bright yellow and became heterogeneous after the addition. The resulting solution was warmed to -50 ºC and was stirred for 30 min., until the contents became homogenous. To a separate 50-mL, round-bottom flask, equipped with a magnetic stir-bar and an argon inlet with septum, dimethylchlorosilane (672 μL, 6.16 mmol, 1.3 equiv) was added and the contents were cooled to -72 ^{o}C. The solution of metalated **12** added into the solution of dimethylchlorosilane via cannula. The white mixture was warmed to room temperature with stirring for 1 h. The suspension was then cooled to 0 ºC (ice-bath) and quenched with saturated sodium bicarbonate (20 mL). The aqueous layer was extracted with EtOAc (3 x 10 mL). The combined organic extracts were washed with brine (15 mL), dried and concentrated to a colorless oil. The crude contents were purified by column chromatography (SiO_2 (40 x 180 mm), hexanes/EtOAc, 15/1), which afforded 2.1 g (94%) of **13** as a colorless. Further purification by diffusion pump distillation (140 ^{o}C, at 7.0 x 10^{-5} mmHg) afforded 1.90 g (4.23 mmol, 89%) of analytically pure **13** as a colorless oil.

Data for **13**:

bp: 140 ºC (7.0x10^{-5} mmHg, ABT)

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

4.88 (d, *J* = 2.0 Hz, 1H, CH(2)); 4.25 (dd, *J* = 7.3, 2.0 Hz, 1H, CH(3)); 4.15 (dd, *J* = 10.3, 5.1 Hz, 1H, (CHe(6)); 3.97 (sept, *J* = 3.7 Hz, 1H, (SiH(12)); 3.94 (t, *J* = 10.3 Hz, 1H, (CHa(6)); 3.93 (dd, *J* = 10.1, 7.0 Hz, 1H, CH(4)); 3.74 (dt, *J* = 10.3,

5.1 Hz, 1H, CH(5)); 1.06 (s, 9H, $(CH_3)_3C$ (8a or 8b)); 1.00 (s, 9H, $(CH_3)_3C$ (8a or 8b)); 0.99 (t, *J* = 8.0 Hz, 9H, CH_3(10)); 0.69 (dq, *J* = 8.0, 2.0 Hz, 6H, CH_2(9)); 0.158 (d, *J* = 3.7 Hz, 6H, $Si(CH_3)_2$ (11))

^{13}C NMR: (126 MHz, $CDCl_3$)

157.56 (C(1)); 115.49 (C(2)); 77.21 (C(4)); 73.11 (C(5)); 71.14 (C(3)); 66.12 (C(6)); 27.44 (C(8a or 8b)); 26.94 (C(8a or 8b)); 22.72 (C(7a or 7b)); 19.82 (C(7a or 7b)); 6.84 (C(9)); 4.83 (C(10)); -5.47 (C(11))

IR: (neat)

2959 (s); 2935 (s); 2860 (s); 2136 (m); 1620 (w); 1473 (m); 1441 (w); 1386 (w); 1249 (m); 1162 (s); 1130 (s); 1060 (s); 1016 (s); 897 (s); 872 (s); 826 (s); 796 (s); 770 (s); 653 (m)

MS: (EI, 70 eV)

458 (M^+ (1)); 446 (6); 245 (17); 244 (39); 147 (30); 139 (100); 133 (14); 95 (11); 75 (14); 59 (28); 57 (15)

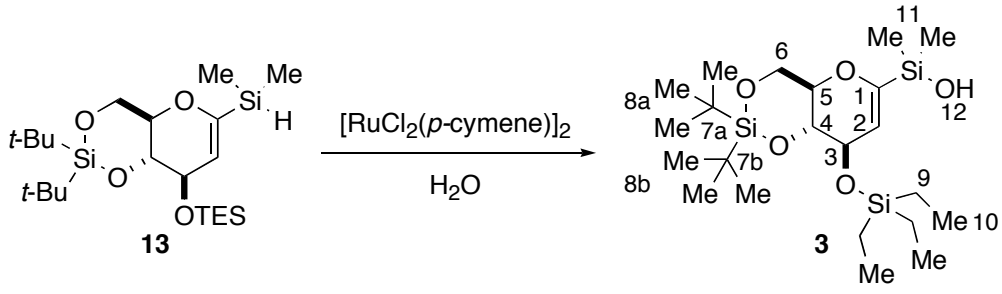
Opt. Rot.: $[\alpha]_D^{24}$ -37.8 (c = 4.62, CH_3Cl)

TLC: R_f 0.61 (hexanes/EtOAc, 20/1) [SiO_2, CAM]

Analysis: $C_{22}H_{46}O_4Si_3$ (458.85)

Calcd:	C, 57.59%;	H, 10.10%
Found:	C, 57.76%;	H, 10.29%

Preparation 1,5-Anhydro-4,6-*O*-[bis(1,1-dimethylethyl)silylene]-2-deoxy-1-*C*-(hydroxydimethylsilyl))-3-*O*-(triethylsilyl)-*D*-arabino-1-hexenitol (3) [CSR-V-60]



To a 10-mL, one-necked round-bottom flask, equipped with a magnetic stir-bar was charged with silane **13** (0.715 g, 1.56 mmol, 1.0 equiv) and benzene (4.0 mL). To another 50-mL, round-bottom flask, equipped with a magnetic stir-bar was added di-μ-chlorobis[(*p*-

cymene)chlororuthenium(II)] (0.027 g, 0.047 mmol, 0.03 equiv) along with CH_3CN (6.0 mL) and benzene 2.0 mL) followed by H_2O (56 μL, 3.12 mmol, 2.0 equiv). The solution of **13** was added drop wise by pipette and bubbling was observed. After the addition, the orange solution was stirred open to air for 1 h at room temperature. Over the course of the reaction the contents darkened from red to a final blood-red color. The red solution was diluted with H_2O (30 mL). The aqueous layer was extracted with EtOAc (3 x 30 mL) and the combined organic extracts were washed with brine (30 mL). The contents were concentrated and immediately subjected to column chromatography ((SiO_2, 40 x 200 mm), hexanes/EtOAc, 15/1), which afforded 0.622 g (84%) of **3** as colorless viscous oil.

Data for **3**:

bp: 145 ºC ($2.0x10^{-5}$ mmHg, ABT)

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

4.94 (d, *J* = 2.1 Hz, 1H, CH(2)); 4.26 (dd, *J* = 7.3, 2.0 Hz, 1H, CH(3)); 4.16 (dd, *J* = 10.1, 4.8 Hz, 1H, CHe(6)); 3.94 (t, *J* = 10.1 Hz, 1H, CHa(6)); 3.93 (dd, *J* = 10.1, 7.0 Hz, 1H, CH(4)); 3.75 (dt, *J* = 10.1, 5.4 Hz, 1H, CH(5)); 1.76 (s, 1H, SiOH(12)); 1.06 (s, 9H, $(CH_3)_3$C(8a or 8b)); 1.00 (s, 9H, $(CH_3)_3$C(8a or 8b)); 0.99 (t, *J* = 7.7 Hz, 9H, CH_3(10)); 0.69 (dq, *J* = 7.7, 2.0 Hz, 6H, CH_2(9)); 0.22 (s, 6H, $Si(CH_3)_2$(11))

^{13}C NMR: (126 MHz, $CDCl_3$)

158.28 (C(1)); 114.84 (C(2)); 76.97 (C(4)); 73.07 (C(5)); 71.01 (C(3)); 66.13 (C(6)); 27.44 (C(8a or 8b)); 26.94 (C(8a or 8b)); 22.73 (C(7a or 7b)); 6.84 (C(9)); 4.85 (C(10)); -1.32 (C(11))

IR: (neat)

3401 (s); 2994 (s); 2956 (s); 2877 (s); 1613 (m); 1459 (m); 1382 (s); 1370 (s); 1251 (s); 1168 (s); 943 (w); 891 (s); 828 (s); 782 (s); 744 (s)

MS: (EI, 70 eV)

474 (M^+ (2)); 261 (13); 260 (41); 213 (13); 177 (26); 156 (14); 155 (100); 133 (12); 115 (10)

Opt. Rot.: $[\alpha]_D^{24}$ -40.55 (c = 0.512, CH_3Cl)

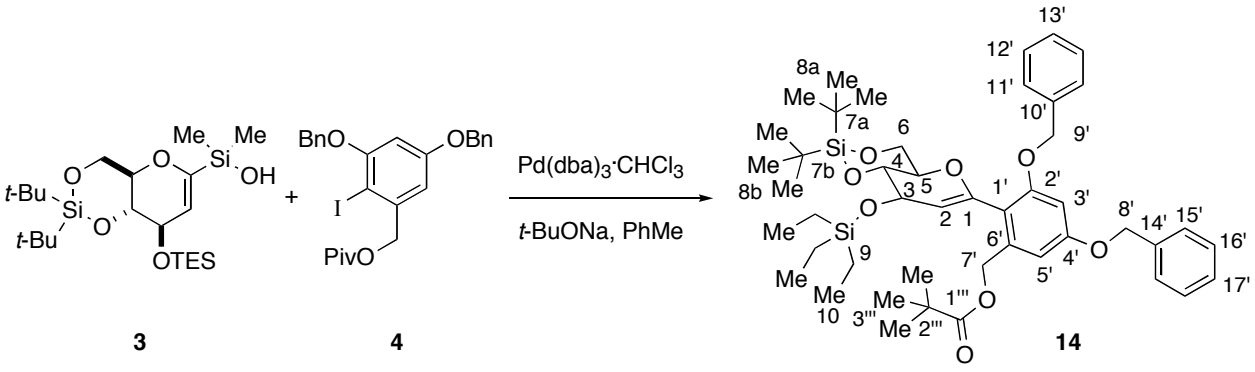
TLC: R_f 0.22 (hexanes/EtOAc, 10/1) [SiO_2, CAM]

Analysis: $C_{22}H_{46}O_5Si_3$ (474.85)

Calcd: C, 55.65 %; H, 9.76 %

Found: C, 55.52 %; H, 9.99 %

Preparation of 1,5-Anhydro-4,6-O-[bis(1,1-dimethylethyl)silylene]-1-C-[2',4'-bis(phenylmethoxy)-6'-[(2'',2''-dimethylpropanoyl)methoxy]phenyl]-2-deoxy-3-O-triethylsilyl-*D*-arabino-1-hexenitol (14) [CSR-VI-44]



3 **4** **14**

A 25-mL, one-necked, round-bottom flask containing a magnetic stir-bar was charged with aryl iodide **4** (0.559 g, 1.05 mmol, 1.0 equiv), sodium *tert*-butoxide (0.202 g, 2.11 mmol, 2.0 equiv) and $Pd_2(dba)_3$•$CHCl_3$ (0.0052 g, 0.052 mmol, 0.05 equiv). A water condenser fitted with an argon inlet with a rubber septum was attached and the contents of the flask were placed under an atmosphere of argon. Toluene (3 mL) was added and a red-purple suspension was observed. To this suspension a solution of silanol **3** (0.500 mg, 1.05 mmol, 1.0 equiv) in toluene (3 mL) under argon was added *via* syringe. Then the contents were stirred and heated under argon at 50 ˚C for 5h. The reaction mixture was diluted with EtOAc (10 mL) and H_2O (20 mL), transferred to a 125-mL separatory funnel and the aqueous layer was removed. The organic layer was washed with 10% aqueous solution of 2-dimethylaminoethanethiol (10 mL). The aqueous extract was back-extracted with EtOAc (3 × 10 mL). Then the combined organic layers were washed with brine (15 mL), dried (Na_2SO_4), filtered and concentrated, initially by rotary evaporation and then by high vacuum (0.08 mmHg), to afford a brown oil. The crude material was loaded directly onto a silica column and purified twice by column chromatography ((SiO_2, 40 x 200), hexanes/EtOAc, 10/1), then ((SiO_2, 40 x 200), CH_2Cl_2/hexanes 2/1) to afford 0.693 g (82%) of **14** as a colorless wax.

Data for **14**:

mp: 95-97 °C (CH_2Cl_2/hexanes, 2/1)

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

7.28-7.45 (m, 10 H, CH(15', 16', 17', 11', 12', 13')); 6.66 (d, *J* = 2.1 Hz, 1 H, CH(3' or 5')); 6.56 (d, *J* = 2.1 Hz, 1 H, CH(3' or 5')); 5.16 (d, *J* = 13.0 Hz, 1 H, CH (7'a)); 5.11 (d, *J* = 13.0 Hz, 1 H, CH (7'b)); 5.04 (s, 2 H, CH_2(8' or 9')); 5.02 (s, 2 H, CH_2 (8' or 9')); 4.74 (d, *J* = 2.1 Hz, 1 H, CH(2)); 4.39 (dd, *J* = 7.0, 2.1 Hz, 1H, CH(3)); 4.04 - 4.17 (m, 2H, CH(4),CHe(6)); 3.97 (t, *J* = 10.5 Hz, 1H, CHa(6)); 3.94 (dt, *J* = 10.5 4.4 Hz, 1H, HC(5)); 1.21 (s, 9H, HC(3'")); 1.18 (s, 9H, $(CH_3)_3$C(8a or 8b)); 1.10 (s, 9H, $(CH_3)_3$C(8a or 8b)); 0.98 (t, *J* = 8.0 Hz, 9H, CH_3(10)); 0.67 (dq, *J* = 8.0 2.0 Hz, 6H, CH_2(9))

^{13}C NMR: (126 MHz, $CDCl_3$)

178.17 (C(1'")); 159.99 (C(2')); 157.90 (C(4')); 146.64 (C(1')); 137.58 (C(1)); 136.90 (C(10' or 14')); 136.56 (C(10' or 14')); 128.65 (C(6' or 11' or 12' or 13' or 15' or 16' or 17')); 128.40 (C(6' or 11' or 12' or 13' or 15' or 16' or 17')); 128.10 (C(6' or 11' or 12' or 13' or 15' or 16' or 17')); 127.76 (C(6' or 11' or 12' or 13' or 15' or 16' or 17')); 127.44 (C(6' or 11' or 12' or 13' or 15' or 16' or 17')); 126.93 (C(6' or 11' or 12' or 13' or 15' or 16' or 17')); 117.50 (C(2'")); 107.39 (C(2)); 105.51 (C(3' or 5')); 100.47 (C(3' or 5')); 73.18 (C(5)); 71.41 (C(3)); 70.32 (C(8' or 9')); 70.06 (C(8' or 9')); 66.00 (C(7')); 63.71 (C(6)); 38.78 (C(4)); 27.43 (C(8a or 8b)); 27.20 (C(3'")); 26.94 (C(8a or 8b)); 22.70 (C(7a or 7b)); 19.91 (C(7a or 7b)); 6.85 (C(9)); 4.84 (C(10))

IR: (film)

2958 (m); 2876 (m); 1730 (m); 1670 (w); 1604 (m); 1473 (w); 1374 (w); 1322 (w); 1281 (m); 1157 (s); 1107 (s); 1058 (m); 1014 (m); 890 (m); 844 (m); 770 (w); 696 (w); 652 (w)

MS: (ESI)

826 ((M^++Na) 14)); 803 (M^+ (51)); 673 (15); 672 (44); 671 (100); 569 (24)

Opt. rot.: $[\alpha]_D^{24}$ -8.47 (EtOH, c = 0.74)

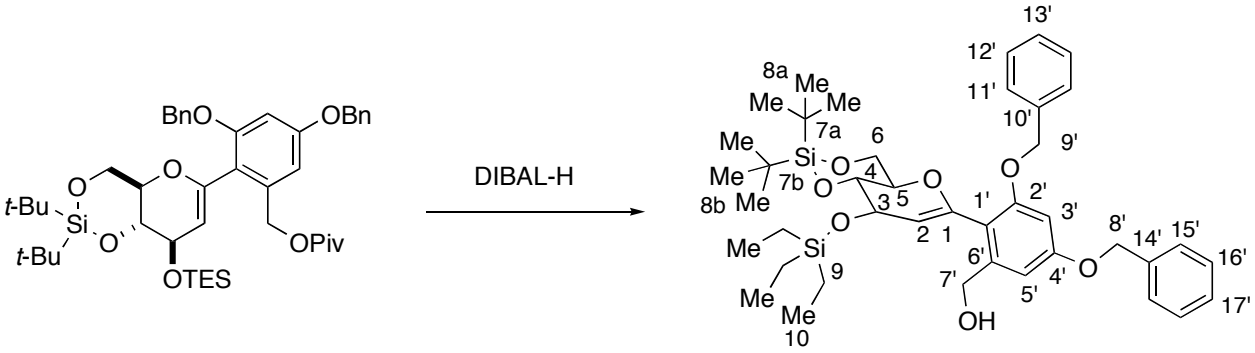
TLC: R_f 0.63 (3:1 hexanes/EtOAc) [SiO_2, CAM]

Analysis: $C_{46}H_{66}O_8Si_2$ (803.18)

Calcd: C, 68.79%; H, 8.28%

Found: C, 68.49%; H, 8.44%

Preparation of 1,5-anhydro-4,6-O-[bis(1,1-dimethylethyl)silylene]-1-C-[2',4'-bis(phenylmethoxy)-6'-(methoxy)phenyl-2-deoxy-3-O-triethylsilyl-*D*-arabino-1-hexenitol (15) [CSR-VI-59]



14 **15**

A 100-mL, one-necked, round-bottom flask fitted with an argon inlet with a septum, and a magnetic stir-bar was charged with aryl glucal **14** (0.955 mg, 1.18 mmol, 1.0 equiv) and CH_2Cl_2 (19 mL). The solution was cooled to -78 ºC using a 2-propanol/dry ice bath. Then DIBAL-H (1.0 M hexane, 2.5 mL, 2.48 mmol, 2.1 equiv) was added and the contents were warmed to room temperature with stirring for 0.5 h. The solution was cooled to 0 ºC (ice bath) and Celite (4 g) was added along with CH_2Cl_2 (5 mL). Water (1.2 mL) was added very slowly (~20 min) until the contents became gelatinous. The ice bath was removed and the contents were stirred vigorously (~10 min) to break up the gelatinous solid. The suspension was filtered through Celite (2 g) and the pad was washed with EtOAc (25 mL). The filtrate was dried (Na_2SO_4) decanted and concentrated to a white foam. The foam was dissolved in hexane (3.0 mL) and concentrated to afford 0.832 g of **15** (98%) as a white solid.

Data for **15**:

mp: 50-51 °C (hexanes)

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

7.31-7.43 (m, 10H, CH(15', 16', 17', 11', 12', 13')); 6.74 (d, *J* = 2.2 Hz, 1H, CH(3' or 5')); 6.55 (d, *J* = 2.2 Hz, 1H, CH(3' or 5')); 5.07 (s, 2H, CH_2(8' or 9')); 5.03 (s,

2H, CH_2(8' or 9')); 4.76 (s, *J* = 2.2 Hz, 1H, CH(7')); 4.65 (d, *J* = 6.6 Hz, 2H, CH_2(2)); 4.40 (dd, *J* = 7.0, 2.2 Hz, 1H, CH(3)); 4.15 (dd, *J* = 9.3, 3.7 Hz, 1H, CHe(6)); 4.08 (dd, *J* = 7.0 Hz, 2.4 Hz, 1H, CH(4)); 3.97 (t, *J* = 9.3 Hz, 1H, CHa(6)); 3.97 (dt, *J* = 9.3, 3.7 Hz, 1H, CH(5)); 1.90 (t, *J* = 6.6 Hz, 1H, br(OH)); 1.08 (s, 9H, $(CH_3)_3$C(8a or 8b)); 1.02 (s, 9H, $(CH_3)_3$C(8a or 8b)); 0.98 (t, *J* = 8.0 Hz, 9H, CH_3(10)); 0.66 (dq, *J* = 8.0, 2.0 Hz, 6H, CH_2(9))

^{13}C NMR: (126 MHz, $CDCl_3$)

160.29 C(2')); 157.72 C(4')); 147.24 C(1')); 136.93 C(1)); 136.59 C(10' or 14')); 128.61 C(10' or 14')); 128.39 C(11' or 12' or 13' or 15' or 16' or 17')); 128.61 C(11' or 12' or 13' or 15' or 16' or 17')); 128.08 C(11' or 12' or 13' or 15' or 16' or 17')); 127.74 C(11' or 12' or 13' or 15' or 16' or 17')); 127.53 C(11' or 12' or 13' or 15' or 16' or 17')); 126.87 C(11' or 12' or 13' or 15' or 16' or 17')); 116.79 C(6')); 107.46 C(2)); 105.50 C(3' or 5')); 100.31 C(3' or 5')); 77.18 C(4)); 73.28 C(3)); 71.43 C(5)); 70.35 C(8' or 9')); 70.11 C(8' or 9')); 65.95 C(6)); 63.41 C(7')); 27.42 C(8a or 8b)); 26.94 C(8a or 8b)); 22.73 C(7a or 7b)); 26.94 C(7a or 7b)); 6.85 C(10)); 4.84 C(9))

IR: (film)

3436 (w); 2934 (s); 2877 (s); 2860 (w); 1670 (w); 1603 (s); 1472 (m); 1322 (m); 1157 (s); 1107 (s); 1077(s); 890 (m); 826 (m); 736 (m)

MS: (ESI)

719 (M^+ (27)); 588 (40); 587 (100)

Opt. rot.: $[\alpha]_D^{24}$ -9.67 (EtOH, c = 1.00)

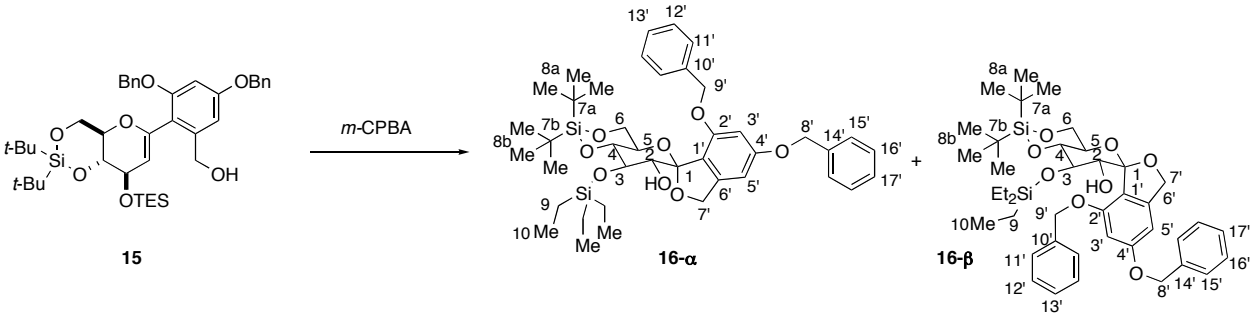
TLC: R_f 0.15 (10:1 hexanes/EtOAc) [SiO_2, UV]

Analysis: $C_{41}H_{58}O_7Si_2$ (719.07)

Calcd: C, 68.48%; H, 8.13%

Found: C, 68.17%; H, 8.02%

Preparation of (1*S*,4'a*R*,7'*R*,8'*R*,8'a*R*)-Spiro[isobenzofuran-1(3H),6'(4'H)-pyrano[3,2-d][1,3,2]dioxasilin]-7'-ol, 2',2'-bis(1,1-dimethylethyl)-4'a,7',8',8'a-tetrahydro-5,7,-bis(phenylmethoxy)-8'- triethylsilyl (16-α) and (1*R*,4'a*R*,7'*R*,8'*R*,8'a*R*)-Spiro[isobenzofuran-1(3H),6'(4'H)-pyrano[3,2-d][1,3,2]dioxasilin]-7'-ol, 2',2'-bis(1,1-dimethylethyl)-4'a,7',8',8'a-tetrahydro-5,7,- bis(phenylmethoxy)-8'- triethylsilyl (16-β) [CSR-VIII-76]



A 250-mL, one-necked, round-bottom flask fitted with an argon inlet with a septum, and a magnetic stir-bar was charged with **15** (0.930 mg, 1.29 mmol, 1.0 equiv), CH_2Cl_2 (31 mL), and $NaHCO_3$ (0.325 g, 3.87 mmol, 3.0 equiv). Then the solution was cooled to 0 ºC using an ice bath. To a separate 25-mL, one-necked, conical flask, fitted with an argon inlet with a septum and magnetic stir-bar was added washed *m*-CPBA (98%, 0.267 g, 1.55 mmol, 1.2 equiv) along with CH_2Cl_2 (10 mL). This solution was transferred via cannula into the solution of **15**. The contents were stirred at 0 ºC for 5 min, and warmed to room temperature and stirred at this temperature for 3 h. To the cloudy mixture was added H_2O (20 mL) and the aqueous extract was back-extracted with CH_2Cl_2 (3 × 15 mL), the organic layers combined, washed with brine (15 mL), dried (Na_2SO_4), filtered and concentrated to afford a white foam. The crude reaction mixture was analyzed by ^{1}H-NMR to afford a 5:1 ratio of anomers (**16-α**:**16-β**). The sample was analyzed using dry and non-acidic $CDCl_3$ (freshly percolated through Brockmann Act I basic alumina and stored over 3 Å molecular sieves prior to use). The crude material was purified by column chromatography ((SiO_2, 40 x 180), hexanes/EtOAc, 7/1) to afford a colorless wax (m.p. 56 – 61 ºC for **16-α**) of separated isomers. The separated isomers were recrystallized from hexanes (15 mL for **16-α**, 5 mL for **16-β**) to afford 0.733 g (77%) of **16-α** as a white, cubic solid and 0.142 g (15%) of **16-β** as a white powder.

Data for **16-α**:

mp: 130-131 °C (hexane)

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

7.29-7.39 (m, 10H, CH(15', 16', 17', 11', 12', 13')); 6.47 (d, *J* = 1.7 Hz, 1H, CH(3')); 6.40 (d, *J* = 1.7 Hz, 1H, CH(5')); 5.16 (d, *J* = 12.4 Hz, 1H, CH(7'a)); 5.11 (s, 2H, CH_2(8' or 9')); 5.07 (d, *J* = 12.4 Hz, 1H, CH(7'b)); 5.00 (s, 2H, CH_2(8' or 9')); 4.32 (dd, *J* =10.2, 7.3 Hz, 1H, CH(2)); 4.13 (dd, *J* = 10.2, 4.4 Hz, 1H, CH(6e)); 3.96 (dd, *J* = 10.2, 4.4 Hz, 1H, CH(5)); 3.88 (t, *J* = 10.2 Hz, 1H, CH(4)); 3.84 (t, *J* = 9.8 Hz, 1H, CH(3)); 3.78 (t, *J* = 10.2 Hz, 1H, CH(6a)); 1.84 (d, *J* = 7.3 Hz, 1H,br(OH)); 1.08 (s, 9H, $(CH_3)_3$C(8a or 8b)); 1.04 (s, 9H, $(CH_3)_3$C(8a or 8b)); 0.99 (t, *J* = 8.0 Hz, 9H, CH_3(10)); 0.70 (dq, *J* = 8.0, 2.0 Hz, 6H, CH_2(9))

^{13}C NMR: (126 MHz, $CDCl_3$)

162.06 C(2')); 154.73 C(4')); 143.41 C(1')); 136.79 C(10' or14')); 136.59 C(10' or 14')); 128.65 C(11' or 12' or 13' or 15' or 16' or 17')); 128.46 C(11' or 12' or 13' or 15' or 16' or 17')); 128.09 C(11' or 12' or 13' or 15' or 16' or 17')); 127.77 C(11' or 12' or 13' or 15' or 16' or 17')); 127.41 C(11' or 12' or 13' or 15' or 16' or 17')); 126.67 C(11' or 12' or 13' or 15' or 16' or 17')); 118.17 C(6')); 110.85 C(1)); 100.48 C(3')); 98.36 C(5')); 77.78 C(4)); 76.64 C(2)); 73.22 C(5)); 73.16 C(3)); 70.37 C(8' or 9')); 69.69 C(8' or 9')); 68.97 C(7')); 67.13 C(6)); 27.58 C(8a or 8b)); 27.06 C(8a or 8b)); 22.82 C(7a or 7b)); 19.93 C(7a or 7b)); 6.95 C(10)); 5.16 C(9))

IR: (film)

3569 (w); 3033 (w); 2950 (s); 2934 (s); 2875 (s); 2860 (s); 1728 (w); 1610 (s); 1498 (m); 1444 (m); 1378 (m); 1300 (m); 1160 (s); 1073 (s); 1021 (s); 965 (m); 828 (s); 736 (s); 696 (m)

MS: (ESI)

735 (M^+ (25); 604 (27); 603 (100); 357 (21); 213 (15); 201 (14); 177 (28)

Opt. rot. : $[\alpha]_D^{24}$ -10.09 (EtOH, c = 0.85)

TLC: R_f 0.31 (7:1 hexanes/EtOAc) [SiO_2, CAM]

Analysis: $C_{41}H_{58}O_8Si_2$ (735.07)

Calcd: C, 66.99%; H, 7.95%

Found: C, 67.02%; H, 8.17%

Data for **16-β**:

mp: 120-122 °C (hexane)

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

7.26-7.38 (m, 10H, CH(15', 16', 17', 11', 12', 13')); 6.42 (d, *J* = 2.0 Hz, 1H, CH(3')); 6.32 (d, *J* = 2.0 Hz, 1H, CH(5')); 5.31 (d, *J* = 14.2 Hz, 1H, CH(8'a or 9'a)); 5.26 (d, *J* = 14.2 Hz, 1H, CH(8'a or 9'a)); 5.14 (d, *J* = 12.8 Hz, 1H, CH(7'a)); 4.92 (d, *J* = 12.8 Hz, 1H, CH(7'b)); 4.90 (s, 2H, CH_2(8' or 9')); 4.51 (t, *J* = 8.2 Hz, 1H, CH(3)); 4.10 (dt, *J* = 9.4, 4.3 Hz, 1H, CH(5)); 4.06 (dd, *J* = 9.4, 4.3 Hz, 1H, CH(6e)); 3.97 (dd, *J* = 9.4, 8.2 Hz, 1H, CH(4)); 3.92 (t, *J* = 8.2, 3.1 Hz, 1H, CH(2)); 3.86 (t (br), *J* = 9.4 Hz, 1H, CH(6a)); 2.56 (d, 3.1 Hz 1H, (brOH)); 1.06 (s, 9H, $(CH_3)_3$C(8a or 8b)); 0.98 (s, 9H, $(CH_3)_3$C(8a or 8b)); 0.94 (t, *J* = 8.1 Hz, 9H, CH_3(10)); 0.58-0.75 (m, 6H, CH_2(9))

^{13}C NMR: (126 MHz, $CDCl_3$)

161.36 (C(2')); 153.79 (C(4')); 145.60 (C(1')); 136.37 (C(10' or14')); 136.15 (C(10' or 14')); 128.74 (C(11' or 12' or 13' or 15' or 16' or 17')); 128.64 (C(11' or 12' or 13' or 15' or 16' or 17')); 128.15 (C(11' or 12' or 13' or 15' or 16' or 17')); 127.73 (C(11' or 12' or 13' or 15' or 16' or 17')); 127.47 (C(11' or 12' or 13' or 15' or 16' or 17')); 125.92 (C(11' or 12' or 13' or 15' or 16' or 17')); 118.48 (C(6')); 113.03 (C(1)); 100.59 (C(3')); 99.33 (C(5')); 78.01 (C(4)); 77.80 (C(2)); 76.91 (C(5)); 71.31 (C(3)); 70.30 (C(8' or 9')); 69.64 (C(8' or 9')); 68.77 (C(7')); 67.22 (C(6)); 27.57 (C(8a or 8b)); 26.99 (C(8a or 8b)); 22.74 (C(7a or 7b)); 19.81 (C(7a or 7b)); 6.89 (C(10)); 5.07 (C(9))

IR: (film)

3480 (w); 3065 (w); 2934 (s); 2875 (s); 2860 (s); 1612 (s); 1597 (s); 1471 (m); 1385 (w); 1339 (w); 1296 (w); 1210 (w); 1148 (s); 1089 (s); 1043 (s); 836 (s); 773 (s); 736 (s)

MS: (ESI)

735 (M^+ (22)); 621 (100); 603 (5); 460 (3)

Opt. rot.: $[\alpha]_D^{24}$ 6.80 (EtOH, c = 0.10)

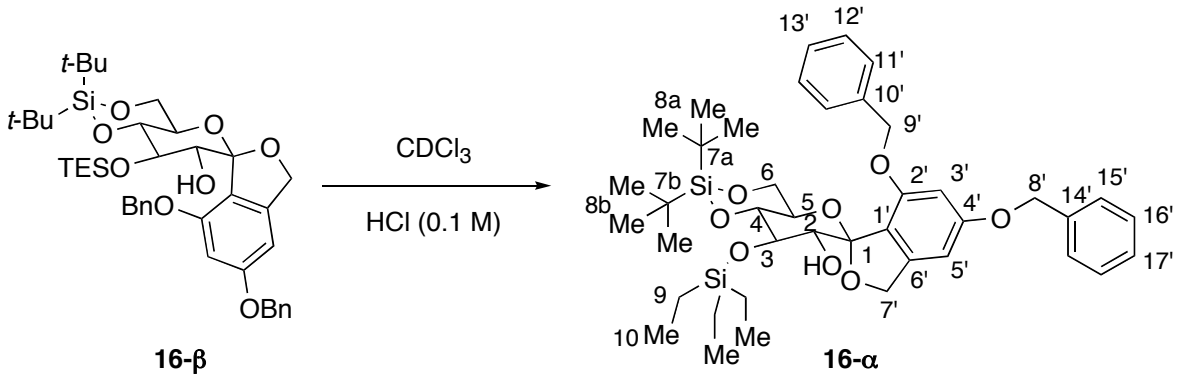
TLC: R_f 0.15 (10:1 hexanes/EtOAc) [SiO_2, CAM]

HRMS: $C_{41}H_{58}O_8Si_2$ (735.07)

Calcd: 735.3749

Found: 735.3782

Isomerization of 16-β to 16-α [CSR-IX-p13]



16-β **16-α**

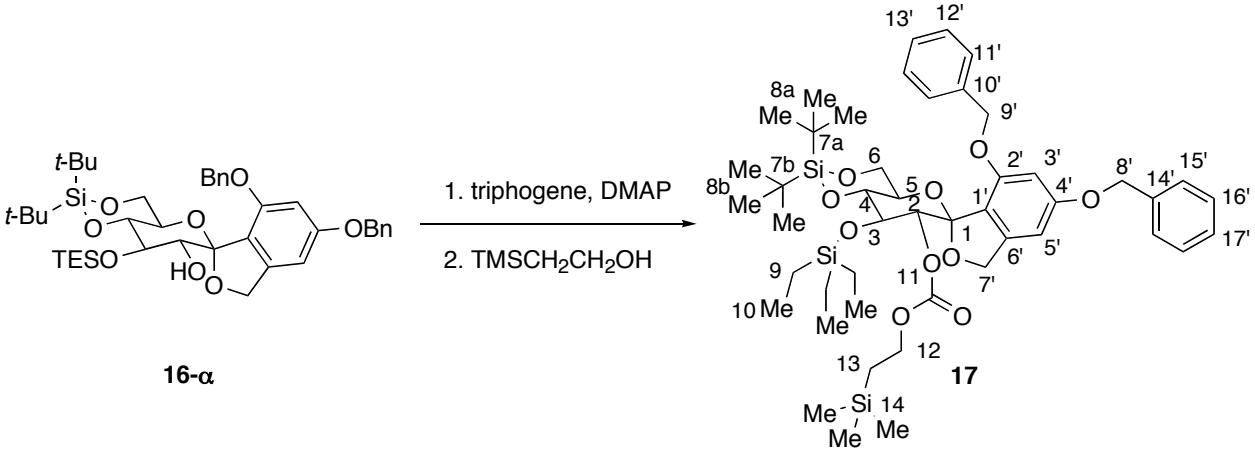
A solution of **16-β** (0.026 g, 0.035 mmol) in $CDCl_3$ (0.7 mL, containing HCl (0.1 M, titrated)) was analyzed by ^{1}H-NMR. Complete epimerization to **16-α** was observed after 12 h at 20 °C. After NMR analysis the contents were diluted with CH_2Cl_2 (0.1 mL) and subjected to column chromatography ((SiO_2, 10 x 50 mm), hexanes/EtOAc, 7/1) to afford 0.025 g (96%) of **16-α**.

Data for **16-α**:

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

7.29-7.39 (m, 10H, CH(15', 16', 17', 11', 12', 13')); 6.47 (d, *J* = 1.7 Hz, 1H, CH(3')); 6.40 (d, *J* = 1.7 Hz, 1H, CH(5')); 5.16 (d, *J* = 12.4 Hz, 1H, CH(7'a)); 5.11 (s, 2H, CH_2(8' or 9')); 5.07 (d, *J* = 12.4 Hz, 1H, CH(7'b)); 5.00 (s, 2H, CH_2(8' or 9')); 4.32 (dd, *J* =10.2, 7.3 Hz, 1H, CH(2)); 4.13 (dd, *J* = 10.2, 4.4 Hz, 1H, CH(6e)); 3.96 (dd, *J* = 10.2, 4.4 Hz, 1H, CH(5)); 3.88 (t, *J* = 10.2 Hz, 1H, CH(4)); 3.84 (t, *J* = 9.8 Hz, 1H, CH(3)); 3.78 (t, *J* = 10.2 Hz, 1H, CH(6a)); 1.84 (d, *J* = 7.3 Hz, 1H,br(OH)); 1.08 (s, 9H, $(CH_3)_3$C(8a or 8b)); 1.04 (s, 9H, $(CH_3)_3$C(8a or 8b)); 0.99 (t, *J* = 8.0 Hz, 9H, CH_3(10)); 0.70 (dq, *J* = 8.0, 2.0 Hz, 6H, CH_2(9))

Preparation of (1*R*,4'a*R*,7'*R*,8'*R*,8'a*R*)-Spiro[isobenzofuran-1(3H),6'(4'H)-pyrano[3,2-d][1,3,2]dioxasilin]-7'-ol, 2',2'-bis(1,1-dimethylethyl)-4'a,7',8',8'a-tetrahydro-5,7,-bis(phenylmethoxy)-8'- triethylsilyl-9'-(2-trimethylsilylethoxycarbonyl) (17) [CSR-VIII-35]



To a 25-mL Schlenk flask, equipped with a magnetic stir-bar was added triphosgene (0.197 g, 0.73 mmol, 0.67 equiv) and the flask was sealed with a septum and purged with argon. Then $CHCl_3$ (1.0 mL) was added and the contents were cooled in a 2-propanol bath to -56 °C using a Cryocool to maintain the temperature. Then to a 5-mL conical flask, equipped with a magnetic stir-bar, argon inlet with septum, DMAP (0.266 g, 2.18 mmol, 2.0 equiv) was added and dissolved in $CHCl_3$ (1.0 mL). The solution of DMAP was also cooled to -56 °C. The DMAP solution was added drop wise (~3 min) to the solution of triphosgene. A light-yellow precipitate formed upon the addition of DMAP. The contents were warmed to room temperature and stirred at this temperature for 1 h, where a light yellow solution was observed. To a separate 10-mL conical flask, equipped with a magnetic stir-bar and an argon inlet with a septum, spiroketal **16-α** (0.803 g, 1.09 mmol, 1.0 equiv) was added, followed by $CHCl_3$ (2.5 mL) and *i*-Pr_2NEt (1.33 mL, 7.63 mmol, 7.0 equiv). The Schlenk flask was once again cooled to -56 °C and the solution of **16-α** was added drop wise via cannula into the Schlenk flask. The flask containing **16-α** was then rinsed with $CHCl_3$ (900 μL). After the addition the yellow mixture was stirred for 10 min at -56 °C and then warmed to room temperature. Upon warming the contents became a yellow solution, which eventually became a yellow mixture. The mixture was stirred at room temperature for an additional 2 h. Then 2-(trimethylsilyl)ethanol (641 μL, 4.45 mmol, 4.1 equiv) was added and the mixture became a yellow solution. This solution was stirred for 12 h at room

temperature. Then water (30 mL) was and the contents were transferred to a 125-mL separatory funnel and the aqueous layer was extracted. The aqueous layer was extracted with EtOAc (3 x 30 mL). The combined organic extracts were washed with brine (1 x 30 mL), dried (Na_2SO_4), filtered and concentrated to a light yellow oil. The crude product was purified by column chromatography ((SiO_2, 50 x 120 mm), hexanes/EtOAc, 20/1 to 10/1) to afford 0.879 g (92%) of **17** as a white foam.

Data for **17**:

mp: 53-55 °C (10/1 hexanes/EtOAc)

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

7.29-7.47 (m, 10H, CH(15', 16', 17', 11', 12', 13')); 6.43 (d, *J* = 1.7 Hz, 1H, CH(3')); 6.35 (d, *J* = 1.7 Hz, 1H, CH(5')); 5.47 (d, *J* = 10.0 Hz, 1H, CH(2)); 5.13 (d, *J* = 12.0 Hz, 2H, CH_2(7a')); 5.12 (d, *J* = 12.0 Hz, 1H, CH(8a' or 9a')); 5.09 (d, *J* = 12.0 Hz, 1H, CH(8b' or 9b')); 5.08 (d, *J* = 12.0 Hz, 1H, CH(7b')); 4.98 (s, 2H, CH_2(8b' or 9b')); 4.32 (dd, *J* =10.2, 7.3 Hz, 1H, CH(5)); 4.14 (dd, *J* = 10.0, 5.0 Hz, 1H, CH(6e)); 4.04 (t, *J* = 9.0 Hz, 1H, CH(4)); 3.98 (dt, *J* = 7.8, 1.2 Hz, 2H, CH_2(12)); 3.85 (t, *J* = 10.0 Hz, 1H, CH(6a)); 3.82 (t, *J* = 9.5 Hz, 1H, CH(3)); 1.07 (s, 9H, $C(CH_3)_3$(8a or 8b)); 1.03 (s, 9H, $C(CH_3)_3$ (8a or 8b)); 0.96 (t, *J* = 8.0 Hz, 9H, CH_3(10)); 0.82 (dt, *J* = 8.0, 2.6 Hz, 2H, CH_2(13)); 0.66 (dq, *J* = 8.0, 2.0 Hz, 6H, CH_2(9)); -0.04 (s, 9H, CH_3(14))

^{13}C NMR: (126 MHz, $CDCl_3$)

162.45 (C(2')); 155.76 (C(11)); 154.63 (C(4')); 143.66 (C(1')); 137.33 (C(10' or 14')); 136.78 (C(10' or 14')); 128.85 (C(15', 16', 7', 11', 12', 13')); 128.58 (C(15', 16', 17', 11', 12', 13')); 128.33 (C(15', 16', 17', 11', 12', 13')); 127.84 (C(15', 16', 17', 11', 12', 13')); 127.67 (C(15', 16', 17', 11', 12', 13')); 127.02 (C(15', 16', 17', 11', 12', 13')); 117.17 (C(6')); 109.66 (C(1)); 100.43 (C(3')); 98.20 (C(5')); 78.10 (C(4)); 77.50 (C(2)); 74.24 (C(5)); 73.76 (C(3)); 70.55 (C(8' or 9')); 70.27 (C(8' or 9')); 68.97 (C(6)); 67.25 (C(7')); 66.21 (C(12)); 27.84 (C(8a or 8b)); 27.31 (C(8a or 8b)); 23.09 (C(7a or 7b)); 20.20 (C(7a or 7b)); 17.48 (C(13)); 7.15 (C(10)); 5.29 (C(9)); -1.36 (C(14))

IR: (film)

2952 (s); 2935 (s); 2861 (s); 1750 (s); 1611 (s); 1445 (w); 1456 (w); 1385 (w);

1253 (s); 1263 (s); 1163 (m); 1094 (m); 1070 (m); 1023 (m); 836 (s); 740 (m)

MS: (ESI)

879 (M^+ (80)); 873 (15); 854 (2); 852 (24); 851 (100)

Opt. rot.: $[\alpha]_D^{24}$ -35.30 (EtOH, c = 0.90)

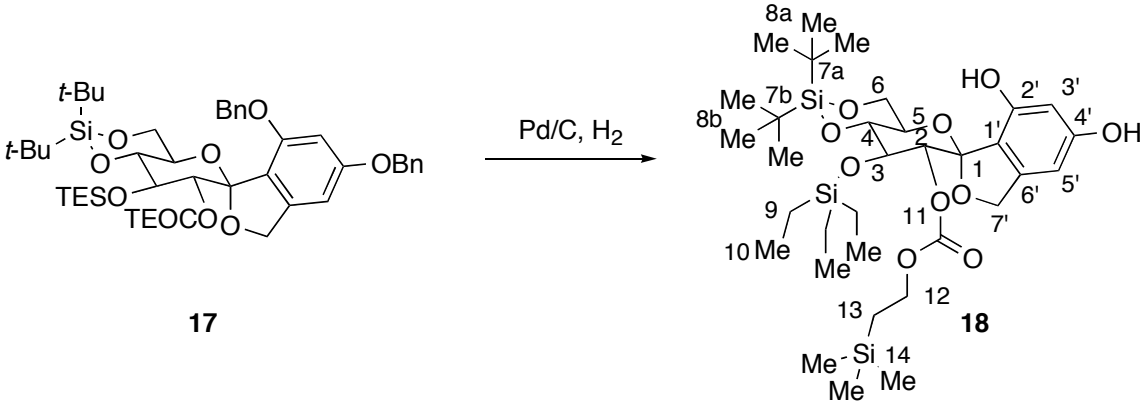
TLC: R_f 0.22 (10:1 hexanes/EtOAc) [SiO_2, CAM]

Analysis: $C_{47}H_{70}O_{10}Si_3$ (879.31)

Calcd: C, 64.20%; H, 8.02%

Found: C, 63.85%; H, 8.04%

Preparation of (1*R*,4'a*R*,7'*R*,8'*R*,8'a*R*)-Spiro[isobenzofuran-1(3H),6'(4'H)-pyrano[3,2-d][1,3,2]dioxasilin]-7'-ol, 2',2'-bis(1,1-dimethylethyl)-4'a,7',8',8'a-tetrahydro-5,7,-bis(hydroxy)-8'- triethylsilyl-9'-(2-trimethylsilylethoxycarbonyl) (18) [CSR-VIII-79]



To a 100-mL, one-necked, round-bottom flask, equipped with a magnetic stir-bar was added **17** (0.731 g, 0.831 mmol, 1.0 equiv) followed by THF (50 mL). Then $NaHCO_3$ (0.451 g, 5.37 mmol, 6.5 equiv) was added along with 5% palladium on carbon (451 mg, 0.211 mmol, 0.25 equiv). The flask was attached to hydrogen manifold and the flask was purged with hydrogen (3x) and stirred at room temperature under 1 atm of H_2 for 5 h. The flask and manifold were flushed with nitrogen and the contents were filtered through Celite (1 g) and the filter pad was washed with Et_2O (30 mL). The colorless filtrate was concentrated to a foamy solid using rotary evaporation. The solid was further dried overnight at 30 °C (6 h) under high vacuum (0.06 mmHg) to afford 0.581 g (quantitative) of **18** as a powdery, white solid.

Data for **18**:

mp: 106-108 °C (THF)

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

6.35 (d, *J* = 2.0 Hz, 1H, CH(3')); 6.22 (d, *J* = 2.0 Hz, 1H, CH(5')); 6.20 (s, 1H, br(OH)); 6.09 (s, 1H, br(OH)); 5.26 (d, *J* = 9.0 Hz, 1H, CH(2)); 5.08 (d, *J* = 11.8 Hz, 1H, CH(7a')); 5.05 (d, *J* = 11.8 Hz, 1H, CH(7b')); 4.15 (dd, *J* = 10.0, 4.6 Hz, 1H, CH(6e)); 4.11 (t, *J* = 8.8 Hz, 1H, CH(3)); 4.01 (t, *J* = 8.5 Hz, 2H, CH_2(12)); 4.07-4.00 (m, 1H, CH(5)); 3.95 (t, *J* = 8.8 Hz, 1H, CH(4)); 3.90 (t, *J* = 10.0 Hz, 1H, CH(6a)); 1.08 (s, 9H, $C(CH_3)_3$(8a or 8b)); 1.04 (s, 9H, $C(CH_3)_3$(8a or 8b)); 0.97 (t, *J* = 8.1 Hz, 9H, CH_3(10)); 0.84 (dt, *J* = 8.5, 2.0 Hz, 2H, CH_2(13)); 0.68 (dq, *J* = 8.1, 2.0 Hz, 2H, CH_2(9)); -0.04 (s, 9H, $Si(CH_3)_3$(14))

^{13}C NMR: (126 MHz, $CDCl_3$)

159.49 (C(2')); 155.42 (C(11)); 151.89 (C(4')); 143.57 (C(1')); 115.02 (C(6')); 108.80 (C(1)); 103.60 (C(3')); 100.51 (C(5')); 78.31 (C(4)); 77.78 (C(2)); 73.98 (C(5)); 73.61 (C(3)); 68.85 (C(6)); 66.95 (C(7')); 66.75 (C(12)); 27.60 (C(8a or 8b)); 27.06 (C(8a or 8b)); 22.74 (C(7a or 7b)); 19.99 (C(7a or 7b)); 17.77 (C(13)); 6.87 (C(10)); 5.05 (C(9)); -1.68 (C(14))

IR: (film)

3413 (m); 2954 (s); 2936 (s); 2878 (s); 2913 (m); 2861 (m); 1727 (m); 1612 (m); 1473 (m); 1388 (m); 1341 (w); 1278 (s); 1252 (s); 1167 (m); 1094 (m); 1066 (s) 979 (m)

MS: (ESI)

699 (M^+ (55)); 609 (5); 402 (3); 383 (5); 372 (2)

Opt. rot. : $[\alpha]_D^{24}$ -23.80 (EtOH, c = 0.50)

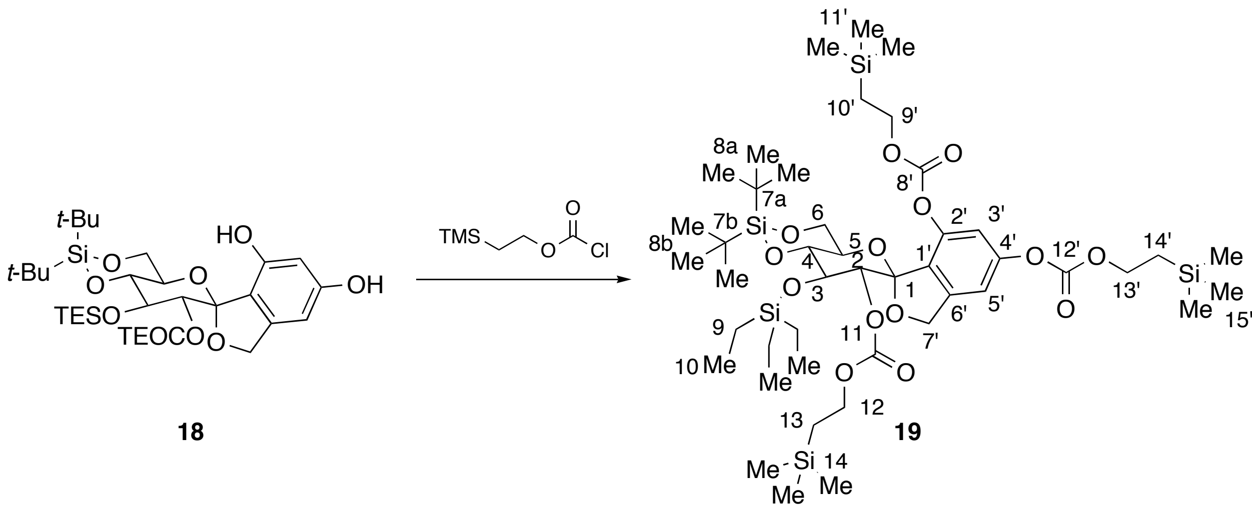
TLC: R_f 0.20 (10:1 hexanes/EtOAc) [SiO_2, CAM]

Analysis: $C_{33}H_{58}O_{10}Si_3$ (699.06)

Calcd: C, 56.70%; H, 8.36%

Found: C, 56.50%; H, 8.11%

Preparation of (1*R*,4'a*R*,7'*R*,8'*R*,8'a*R*)-Spiro[isobenzofuran-1(3H),6'(4'H)-pyrano[3,2-d][1,3,2]dioxasilin]-7'-ol, 2',2'-bis(1,1-dimethylethyl)-4'a,7',8',8'a-tetrahydro-5,7,- bis(2-trimethylsilylethoxycarbonyl)-8'-triethylsilyl-9'-(2-trimethylsilylethoxycarbonyl) (19) [CSR-VII-62]



To a 25-mL Schlenk flask, equipped with a magnetic stir-bar and an argon inlet with a septum was added **18** (0.273 g, 0.391 mmol, 1.0 equiv) and the flask was charged with argon. Then CH_2Cl_2 (5.0 mL) was added along with *i*-Pr_2NEt (681 μL, 3.91 mmol, 10 equiv). Trimethylsilylethoxy chlorocarbonate (0.354 g, 1.96 mmol, 5.0 equiv) was added drop wise to the colorless solution, which turned light-yellow after the addition. The solution was stirred at room temperature 10 h. Then H_2O (30 mL) was added and the contents were transferred to a 125-mL separatory funnel and the aqueous was extracted. The aqueous extracted was extracted with EtOAc (3 x 15 mL). The combined organic extracts were washed with brine (1 x 15 mL), dried (Na_2SO_4), filtered and concentrated to a light-yellow wax. The crude product was purified using column chromatography ((SiO_2, 30 x 80 mm), hexanes/EtOAc, 15/1 to 10/1). The purified product was isolated as a viscous oil that was dried at 50 °C for 18 h to afford 0.371 g (96%) of **19** as a colorless glassy solid.

Data for **19**:

mp: 40-42 °C (10/1 hexanes/EtOAc)

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

7.10 (d, *J* = 2.0 Hz, 1H, CH(3' or 5')); 6.95 (d, *J* = 2.0 Hz, 1H, CH(3' or 5')); 5.35 (d, *J* = 9.5 Hz, 1H, CH(2)); 5.16 (s, 2H, CH_2(7')); 4.27 4.38 (m, 4H, CH_2(9') and 13')); 4.09 (dd, *J* = 9.8, 4.8 Hz, 1H, CH(6e)); 4.07 (t, *J* = 9.2 Hz, 1H, CH(3));

3.94-4.03 (m, 3H, CH_2(12) and CH(5)); 3.88 (t, J = 9.2 Hz, 1H, CH(4)); 3.77 (t, J = 9.8 Hz, 1H, CH(6a)); 1.09-1.15 (m, 4H, CH_2(10' and 14')); 1.08 (s, 9H, $C(CH_3)_3$(8a or 8b)); 1.03 (s, 9H, $C(CH_3)_3$(8a or 8b)); 0.97 (t, J = 8.1 Hz, 9H, CH_3(10)); 0.81-0.86 (m, 2H, CH_2(13)); 0.66 (q, J = 8.1 Hz, 6H, CH_2(9)); 0.08 (s, 9H, CH(11' or 15')); 0.07 (s, 9H, CH(11' or 15')); -0.05 (s, 9H, CH(14))

^{13}C NMR: (126 MHz, $CDCl_3$)

154.23 (C(11)); 153.06 (C(2')); 152.83 (C(8' or 12')); 152.56 (C(8' or 12')); 146.82 (C(4')); 143.16 (C(1')); 124.93 (C(6')); 115.25 (C(3')); 111.35 (C(5')); 108.83 (C(1)); 77.72 (C(4)); 76.69 (C(2)); 73.69 (C(5)); 73.16 (C(3)); 68.89 (C(6)); 67.64 (C(9' or 13')); 67.57 (C(9' or 13')); 66.74 (C(7')); 66.36 (C(12)); 27.55 (C(8a or 8b)); 27.02 (C(8a or 8b)); 22.76 (C(7a or 7b)); 19.95 (C(7a or 7b)); 17.51 (C(10' or 14')); 17.47 (C(10' or 14')); 17.17 (C(13)); 6.87 (C(10)); 4.99 (C(9)); -1.53 (C(11' or 15')); -1.58 (C(11' or 15')); -1.70 (C(14))

IR: (film)

2954 (s); 2878 (m); 1766 (s); 1694 (w); 1628 (w); 1473 (w); 1383 (w); 1228 (s); 1175 (s); 1066 (s); 1032 (m); 971 (m); 936 (m); 859 (s)

MS: (ESI)

1009 (M^+ + Na (100)); 904 (40); 903 (50); 485 (100); 469 (20)

Opt. rot.: $[\alpha]_D^{24}$ -19.07 (EtOH, c = 0.30)

TLC: R_f 0.20 (15:1 hexanes/EtOAc) [SiO_2, CAM]

HRMS: $C_{45}H_{82}O_{14}Si_5Na$ (1009.44)

Calcd: 1009.4449

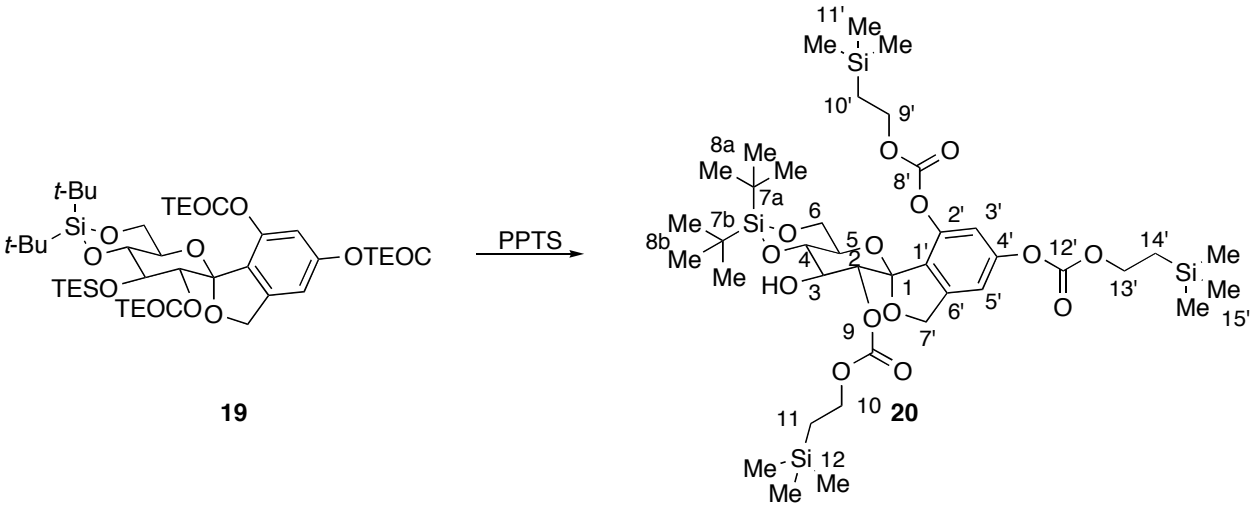
Found: 1009.4443

Analysis: $C_{45}H_{82}O_{14}Si_5$ (987.55)

Calcd: C, 54.73%; H, 8.37%

Found: C, 54.61%; H, 8.58%

Preparation of (1*R*,4'a*R*,7'*R*,8'*R*,8'a*R*)-Spiro[isobenzofuran-1(3H),6'(4'H)-pyrano[3,2-d][1,3,2]dioxasilin]-7'-ol, 2',2'-bis(1,1-dimethylethyl)-4'a,7',8',8'a-tetrahydro-5,7,- bis(2-trimethylsilylethoxycarbonyl)-9'-(2-trimethylsilylethoxycarbonyl) (20) [CSR-IX-1]



To a 35-mL, one-necked, round-bottom flask, equipped with a magnetic stir-bar and an argon inlet with a septum was added **19** (0.622 mg, 0.639 mg, 1.0 equiv) followed by absolute EtOH (17 mL). Then pyridium-*p*-toluenesulfonate (1.1 g, 1.26 mmol, 2.0 equiv) was added and the contents were stirred at room temperature for 24 h. The colorless solution was transferred to a 250-mL separatory funnel and H_2O (30 mL) was added along with EtOAc (100 mL). The aqueous extract was extracted with EtOAc (5 x 25 mL). The combined organic extracts were washed with brine (1 x 20 mL), dried (Na_2SO_4), filtered and concentrated to a viscous colorless oil. The crude product was purified using column chromatography ((SiO_2, 40 x 150 mm), hexanes/EtOAc, 7/1). The purified product was isolated as a viscous oil that was dried at 70 °C for 8 h to afford 0.497 g (93%) of **20** as a colorless, glassy solid.

Data for **20**:

mp: 51-54 °C (7/1 hexanes/EtOAc)

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

7.11 (d, *J* = 1.7 Hz, 1H, CH(3' or 5')); 6.97 (d, *J* = 1.7 Hz, 1H, CH(3' or 5')); 5.48 (d, *J* = 10.0 Hz, 1H, CH(2)); 5.20 (d, *J* = 5.2 Hz, 1H, CH(7'a)); 5.17 (d, *J* = 5.2 Hz, 1H, CH(7'b)); 4.28-4.38 (m, 4H, CH_2(9' and 13')); 4.07-4.13 (m, 2H, CH(6e and 3)); 3.99-4.08 (m, 4H, CH_2(10) and CH(6a) and CH(4)); 2.63 (d, *J* = 2.4 Hz, 1H, (OH)); 1.12-1.15 (m, 4H, CH_2(10' and 14')); 1.10 (s, 9H, $C(CH_3)_3$(8a or 8b));

1.02 (s, 9H, $C(CH_3)_3$(8a or 8b)); 0.97 (t, J = 8.8 Hz, 2H, CH_2(11)); 0.07 (s, 9H, CH_3(11' or 15')); 0.07 (s, 9H, CH_3(11' or 15')); -0.05 (s, 9H, CH_3(12))

^{13}C NMR: (126 MHz, $CDCl_3$)

154.51 (C(9)); 153.16 (C (2')); 152.86 (C(8' or 12')); 152.52 (C(8' or 12')); 146.69 (C(4')); 143.26 (C(1')); 124.75 (C(6')); 115.31 (C(3')); 111.52 (C(5')); 108.59 (C(1)); 77.36 (C(4)); 75.94 (C(2)); 72.98 (C(5)); 68.44(C(3)); 67.75 (C(9' or 13')); 67.72 (C(9' or 13')); 66.90 (C(6)); 66.77 (C(7')); 66.54 (C(10)); 27.44 (C(8a or 8b)); 27.01 (C(8a or 8b)); 22.71 (C(7a or 7b)); 19.98 (C(7a or 7b)); 17.54 (C(10' or 14')); 17.50 (C(10' or 14')); 17.12 (C(11)); -1.53 (C(11' or 15')); -1.57 (C(11' or 15')); -1.64 (C(12))

IR: (film)

2954 (s); 2878 (m); 1766 (s); 1694 (w); 1628 (w); 1473 (w); 1383 (w); 1228 (s); 1175 (s); 1066 (s); 1032 (m); 971 (m); 936 (m); 859 (s)

MS: (ESI)

1009 (M^+ + Na (100)); 904 (40); 903 (50); 485 (100); 469 (20)

Opt. rot. : $[\alpha]_D^{24}$ -19.07 (EtOH, c = 0.30)

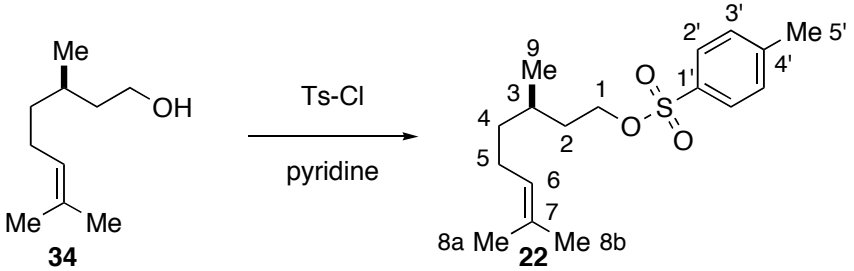
TLC: R_f0.20 (15:1 hexanes/EtOAc) [SiO_2, CAM]

Analysis: $C_{39}H_{68}O_{14}Si_4$ (873.29)

Calcd:	C, 53.64%;	H, 7.85%
Found:	C, 53.68%;	H, 8.05%

Preparation of Acid 2

Preparation of (*S*)- 2,6-Dimethyl-, 6-octene-1-ol, 4'-methylbenzenesulfonate (22)[16] [CSR-VII-63]



A 50-mL, two-necked, round-bottom flask, containing a magnetic stir-bar, glass stopcock, and nitrogen inlet was charged with **34** (6.0 g, 38.9 mmol, 1.0 equiv), pyridine (4.72 mL, 58.4 mmol, 1.5 equiv). To this solution finely ground *p*-toluenesulfonyl chloride (8.9 g,

46.7 mmol, 1.2 equiv) was added in three portions of approximately 3 g each. The internal temperature rose to 52 ºC and a white suspension formed upon cooling to room temperature. The thick, white suspension was stirred at room temperature for 10 h. The reaction mixture was diluted with EtOAc (20 mL) and 2N HCl (10 mL), and stirred until the biphasic contents were homogenous (~3 min.). The contents were transferred to a 250-mL separatory funnel and the aqueous layer was extracted. The aqueous phase was back-extracted with EtOAc (2 × 15 mL), the organic layers combined, washed with water (3 x 10 mL) and brine (20 mL). The organic layer was dried (Na_2SO_4), filtered and concentrated under reduced pressure using rotary evaporation to afford a colorless oil. The crude material was purified by column chromatography ((SiO_2, 60 x 120 mm), hexanes/EtOAc, 7/1) to afford 10.7 g (89%) of **22** as a colorless oil.

Data for **22**:

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

7.79 (d, *J* = 8.3 Hz, 2H, CH(2')); 7.34 (d, *J* = 8.3 Hz, 2H, CH(3')); 5.02 (t, *J* = 7.3 Hz, 1 H, CH(6)); 4.02-4.10 (m, 2 H, CH_2(1)); 2.45 (s, 3 H, CH_3(5')); 1.83-1.98 (m, 2H, CH_2(5)); 1.71-1.64 (m, 2H, CH_2(3)); 1.67 (s, 3H, CH_3(8a or 8b)); 1.57 (s, 3H, CH_3 (8a or 8b)); 1.56-1.49 (m, 1H, CH(2a)); 1.39-1.46 (m, 1H, CH(2b)); 1.21-1.27 (m, 1H, CH(4a)); 1.06-1.13 (m, 1H, CH(4b)); 0.82 (d, *J* = 6.6 Hz, 3H, CH_3(9))

^{13}C NMR: (126 MHz, $CDCl_3$)

144.87 (C(4')); 133.45 (C(7)); 131.73 (C(1')); 130.04 (C(2')); 128.13 (C(3')); 124.55 (C(6)); 69.29 (C(1)); 36.94 (C(4)); 35.89 (C(2)); 29.08 (C(3)); 25.94 (C(8a or 8b)); 25.49 (C(5)); 21.88 (C(5')); 19.27 (C(9)); 17.87 (C(8a or 8b))

IR: (neat)

2963 (s); 2925 (s); 2873 (s); 2856 (s); 2730 (w); 2345 (w); 1920 (w); 1805 (w); 1654 (w); 1598 (m); 1495 (w); 1454 (m); 1361 (s); 1307 (w); 1291 (w); 1189 (s); 1177 (s); 1038 (w); 1020 (w); 945 (s); 889 (s); 815 (s); 764 (m); 665 (s)

MS: (EI, 70 eV)

310 (M^+ (3)); 173 (11); 155 (34); 138 (61); 123 (59); 109 (32); 95 (54); 92 (14); 91(100); 89 (20); 81 (49); 79 (12); 69 (73); 68 (33); 67 (40); 65 (70); 63 (17); 55 (37); 53 (18)

Opt. rot. : $[\alpha]_D^{24}$ 2.68 (EtOH, c = 1.00)

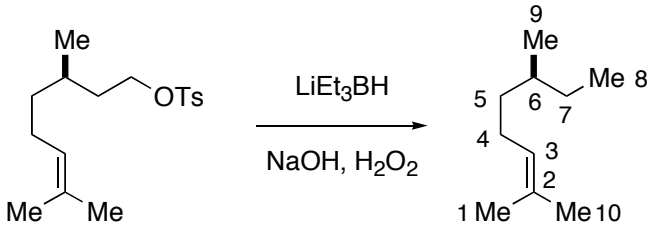
TLC: R_f 0.30 (10:1 hexanes/EtOAc) [SiO_2, UV]

HRMS: for $C_{17}H_{26}O_3S$

Calcd: 310.1603

Found: 310.1605

Preparation of (*S*)- 2,6-Dimethyl-2-octene (23)[7] [CSR-VII-88]



22 **23**

A 250-mL, two-necked, round-bottom flask, containing a magnetic stir-bar, septum, and argon inlet was charged with **22** (6.9 g, 22.1 mmol, 1.0 equiv), THF (22 mL). The solution was cooled to 0 ºC using an ice bath. To this solution was added a solution of lithium triethylborohydride (44.2 mL, 44.2 mmol, 1.0 M in THF, 2.0 equiv) slowly over 15 min. The colorless solution was stirred at room 0 ºC for 3 h. Then H_2O (3.0 mL) was added drop wise at 0 ºC, followed by 3 N NaOH (30 mL). Then 30% H_2O_2 (30 mL) was added slowly, at a rate that the internal temperature did not rise above 40 ºC (~2.5 h). After the quench, the biphasic reaction mixture was diluted with pentane (50 mL) and transferred to a 500-mL separatory funnel and the aqueous layer was extracted. The aqueous phase was back-extracted with pentane (5 × 30 mL), the organic layers were combined, washed with water (4 x 20 mL) and brine (20 mL). The organic layer was dried (Na_2SO_4), filtered and the pentane was removed by atmospheric distillation. The residue was purified by distillation first at 100 mmHg (oil bath 50 ºC) to remove the THF and then at 30 mmHg to afford 2.7 g (87%) of **23** as a colorless liquid.

Data for **23**:

bp: 76-80 °C at 30 mmHg

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

5.11 (tq, J = 7.3, 1.5 Hz, 1H, CH(3)); 1.87-2.06 (m, 2H, CH_2(4)); 1.69 (s, 3H, CH_3(1 or 10)); 1.61 (s, 3H, CH_3(1 or 10)); 1.28-1.38 (m, 3H, CH_2(5), CH(6)); 1.08-1.18 (m, 2H, CH_2(7)); 0.86 (t, J = 7.2 Hz, 3H, CH_3(8)); 0.86 (d, J = 6.4 Hz, 3H, CH_3(9))

^{13}C NMR: (126 MHz, $CDCl_3$)

130.97 (C(2)); 125.07 (C(3)); 36.70 (7)); 34.00 (4)); 29.39 (6)); 25.74 (5)); 25.57 (1 or 10)); 19.08 (9)); 17.61 (1 or 10)); 11.38 (C(8))

IR: (neat)

2964 (s); 2916 (s); 2875 (s); 2857 (s); 1461 (m); 1377 (m); 1155 (w); 1116 (w); 1090 (w); 948 (w)

MS: (EI)

140 ((M^+) 30); 84 (17); 83 (21); 70 (64); 69 (100); 57 (27); 56 (39); 55 (48)

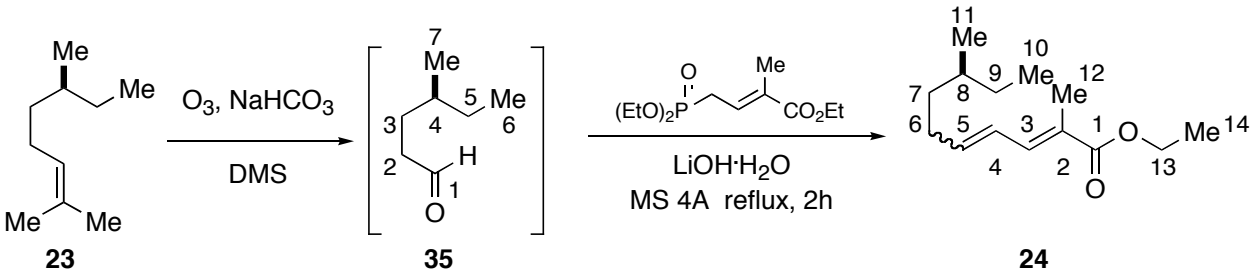
Opt. rot.: $[\alpha]_D^{24}$ 10.8 ($CHCl_3$, c = 2.00)

Analysis: $C_{10}H_{20}$ (140.27)

Calcd: C, 85.63%; H, 14.37%

Found: C, 85.67%; H, 14.33%

Preparation of Ethyl (*S*)-2,8-Dimethyl-2(*E*),4(*E,Z*)-decadienoate (24) [CSR-VIII-5]



A 25-mL, round-bottomed flask, containing a stir-bar, Teflon thermometer adaptor and gas dispersion tube through the Teflon adaptor was charged with **23** (1.36 g, 9.7 mmol, 1.0 equiv), CH_2Cl_2 (5 mL) and MeOH (1.2 mL). To this solution was added $NaHCO_3$ (162 mg, 1.9 mmol, 0.2 equiv). The contents were cooled to -78 ºC in a 2-propanol/dry ice bath whereupon ozone was bubbled through the solution for 20 min or until the contents turned deep blue. Then, oxygen was bubbled through the solution until the blue color dissipated. While still at -78 ºC (under an argon atmosphere) dimethyl sulfide (1.2 mL, 16.5 mmol, 1.7 equiv) was added and the solution was stirred at this temperature for 40 min. The 2-propanol/dry ice bath was removed and the contents were allowed to warm to room temperature over 2.5 h. The colorless solution was filtered though Celite (2 g) washing the pad with $CHCl_3$ (5 mL) and pentane (20 mL). The solvent was removed using rotary evaporation with the water bath cooled to 0 ºC. The colorless

oil was used in the next step without further purification.

The above oil (1.12 g, 9.7 mmol, 1.0 equiv, assuming quantitative yield in the first step) was transferred to a 50-mL, one-necked, round-bottomed flask and then THF (10 mL) and a magnetic stir-bar were added. To this solution was added 3 Å molecular sieves (9 g, 1g/mmol) and lithium hydroxide monohydrate (448 mg, 10.7 mmol, 1.1 equiv). The flask was equipped with a water condenser and an argon inlet with a rubber septum. The apparatus was then flushed with argon. To a separate 25-mL, one-necked, conical-flask sealed with a septum and flushed with argon, ethyl 4-(diethoxyphosphinyl)tiglate (2.82 g, 10.7 mmol, 1.1 equiv) was added along with THF (8 mL). The phosphonate solution was transferred via cannula into the mixture of aldehyde **35** rinsing the flask with THF (0.5 mL). The contents were heated to reflux (oil bath temperature 75 ˚C) and stirred for 2.5 h. The contents became yellow and turbid as the reaction progressed. Upon cooling to room temperature the mixture was filtered thorough Celite (2.5 g) washing the pad with 1:1 hexane/EtOAc (40 mL). The crude product was analyzed by ^{1}H-NMR to reveal a 91:9 ratio of (*E*,*E*)-**24** and (*E*,*Z*)-**24** isomers. The orange slurry was purified by column chromatography ((SiO_2, 40 x 220 mm), hexane/EtOAc, 15/1) to afford 1.69 g (78%) of an inseparable mixture of esters **24** as a colorless oil.

Data for **24**:

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

9.77 (d, J = 1.7 Hz, 1H, CH(1)); 2.48-2.36 (m, 2H, CH_2(2)); 1.70-1.63 (m, 1H, CH_2(3a or 3b)); 1.47-1.40 (m, 1H, CH_2(3a or 3b)); 1.40-1.31(m, 2H, CH_2(5a or 5b, 4)); 1.20-1.12 (m, 1H, CH_2(5a or 5b)); 0.87 (t, J = 7.4 Hz, 3H, CH_3(6)); 0.86 (d, J = 6.5 Hz, 3H, CH_3(7))

^{13}C NMR: (126 MHz, $CDCl_3$)

203.27 (C(1)); 41.71 (C(2)); 33.96 (C(4)); 29.13 (C(5)); 28.45 (C(3)); 18.84 (C(7));11.26 (C(6))

IR: (neat)

2867 (s); 2700 (s); 1725 (s)

MS: (ESI)

114 ((M^+) 2); 86 (65); 70 (100); 67 (14); 58 (19); 57 (42); 55 (55)

Opt. rot. : $[\alpha]_D^{24}$ 7.61 (heptane, c = 1.29)

HRMS: (for $C_{17}H_{14}O$)

Calcd: 114.1045

Found: 114.1043

Data for **24**:

bp: 100 °C at $1x10^{-5}$ mmHg (ABT)

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

7.50 (dt, *J* = 11.9, 1.2 Hz, 1H, CH(3), (*Z*-isomer)); 7.16 (d, *J* = 11.5 Hz, 1H, CH(3), (*E*-isomer)); 6.34 (ddt, *J* = 14.4, 11.6, and 1.4 Hz, 1H, CH(4), (*E*-isomer)); 6.27 (ddt, *J* = 11.6, 11.2, and 1.4 Hz, 1H, CH(4), (*Z*-isomer)); 6.08 (dt, *J* = 14.4, 7.2 Hz, 2H, CH_2(5), (*E*-isomer)); 5.83 (dt, *J* = 11.2, 7.2 Hz, 1H, CH(5), (*Z*-isomer)); 4.22 (q, *J* = 7.2 Hz, 2H, CH_2(13), (*Z*-isomer)); 4.20 (q, *J* = 7.2 Hz, 2H, CH_2(13), (*E*-isomer)); 2.34-2.10 (m, 2H, CH_2(6), (*Z* and *E*- isomer)); 1.93 (d, *J* = 0.8 Hz, 3H, CH_3(12), (*Z*-isomer)); 1.92 (d, *J* = 0.8 Hz, 3H, CH_3(12), (*E*-isomer)); 1.30 (t, *J* = 7.0 Hz, 3H, CH_3(14), (*E*-isomer)); 1.49-1.10 (m, 5H, CH_2(7,9) and CH(8), (*Z* and *E*- isomer)); 0.88 (d, *J* = 6.0 Hz, 3H, CH(11), (*E*-isomer)); 0.87 (t, *J* = 8.0 Hz, 3H, CH(10), (*E*-isomer))

^{13}C NMR: (126 MHz, $CDCl_3$)

168.66 (C(1), (*E*-isomer)); 143.42 (C(5), (*E*-isomer)); 140.21 (C(3), (*Z*-isomer)); 138.58 (C(3), (*E*-isomer)); 132.81 (C(5), (*Z*-isomer)); 125.77 (C(4), (*E*-isomer)); 124.98 (C(2), (*E*-isomer)); 123.63 (C(4), (*Z*-isomer)); 60.50 (C(13), (*Z*-isomer)); 60.40 (C(13), (*E*-isomer)); 36.24 (C(7), (*Z*-isomer)); 35.72 (C(7), (*E*-isomer)); 33.94 (C(8), (*E*-isomer)); 30.89 (C(6), (*E*-isomer)); 29.32 (C(9), (*E*-isomer)); 18.98 (C(11), (*E*-isomer)); 14.32 (C(12), (*E*-isomer)); 12.53 (C(14), (*E*-isomer)); 11.29 (C(10), (*E*-isomer))

IR: (neat)

3032 (w); 2961(s); 2922 (s); 2856 (m); 1706 (s); 1639 (s); 1610 (w); 1462 (m); 1367 (m); 1284 (m); 1241 (s); 1166 (w); 1105 (s); 972 (s)

MS: (EI, 70 eV)

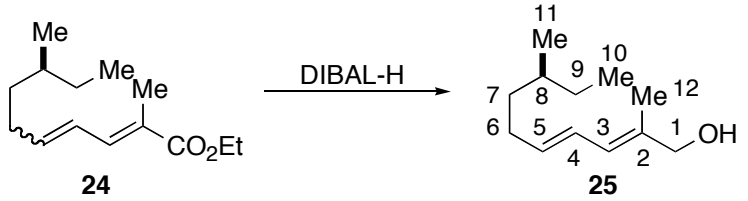
224 ((M^+ (95); 195 (11); 180 (12); 179 (80); 168 (25); 167 (32); 150 (16); 149 (20); 141 (96); 140 (60); 139 (100); 128 (54); 126 (22); 125 (36); 122 (28); 113 (61); 111 (95); 110 (54); 102 (21); 100 (20); 97 (36); 91 (30); 79 (61); 69 (25); 57 (33)

TLC: R_f 0.39 (10:1 hexanes/EtOAc) [SiO_2, UV]

Analysis: $C_{14}H_{24}O_2$ (224.43)

Calcd:	C, 74.95%;	H, 10.78%
Found:	C, 75.00%;	H, 10.79%

Preparation of (*S*)-2,8-Dimethyldeca-2*E*,4*E*-dien-ol (25)[18] [CSR-VIII-8]



24 **25**

A 100-mL, one-necked, recovery-flask, containing a magnetic stir-bar and an argon inlet with a septum, was charged with ester **24** (1.54 g, 6.86 mmol, 1.0 equiv) and THF (15 mL). The solution was cooled to 0 °C using an ice bath. Once at 0 °C, a solution of DIBAL-H (15.1 mL, 15.1mmol, 1.0 M in hexane, 2.2 equiv) was added drop wise over 15 min. The yellow solution quickly became colorless with each drop of DIBAL-H. After the addition (~15 min) Celite (3 g) and Et_2O (15 mL) were added and then H_2O (~1.2 mL) was added slowly until a gelatinous solid formed. Diethyl ether (10 mL) was added and the contents were stirred vigorously to break up the gelatinous solid. The contents were filtered through Celite (1 g) washing the pad with Et_2O (100 mL), and the filtrate was concentrated to a light-yellow oil. The crude product was purified by column chromatography ((SiO_2, 40 x 220 mm), hexanes/EtOAc, 10/1) to afford 1.06 g (85%, (*E*,*E*)-**25**) and 0.013 g (11%, (*E*,*Z*)-**25**) as colorless oils.

Data for **(*E*,*E*)-25**:

bp: 95 °C ($8.5X10^{-5}$ mmHg, ABT)

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

6.25 (ddt, *J* = 10.7, 15.1, and 1.5 Hz, 1H, CH(4)); 6.02 (d, *J* = 11.0 Hz, 1H, CH(3)); 5.70 (dt, *J* = 15.0, 7.1 Hz, 1H, CH(5)); 4.01(s, 2H, CH_2(1)); 2.18-2.05 (nfoddd, *J* = 15, 9.0, and 7.3 Hz, 2H, CH_2(6)); 1.78 (s, 3H, CH_3(12)); 1.61(s, 1H, br (OH); 1.29-1.45 (m, 3H, CH(8), CH_2(9)); 1.11-1.24 (m, 2H, CH_2(7)); 0.86 (t, *J* = 7.3 Hz, 3H, CH_3(10)); 0.86 (d, *J* = 6.8 Hz, 3H, CH_3(11))

^{13}C NMR: (126 MHz, $CDCl_3$)

135.58 (C(5)); 134.60 (C(2)); 125.60 (C(4)); 125.41 (C(3)); 68.75 (C(1)); 36.23 (C(7)); 33.92 (C(8)); 30.54 (C(6)); 29.36 (C(9)); 19.03 (C(11)); 14.08 (C(12)); 11.33 (C(10))

IR: (neat)

3325 (s); 2961(s); 2916 (s); 2873 (s); 1461(m); 1377 (m); 1210 (w); 1144 (w); 1067 (w); 1008 (m); 967 (s); 882 (w)

MS: (EI, 70 eV)

182((M^+) 100); 111(40); 98(75); 96(67); 95(24); 93(25); 86(33); 85(70); 84(38); 83(67); 82(19); 81(55); 79(34); 71(34); 70(46); 69(67); 67(21); 56 (14); 55(43); 54(29); 53(69); 50(27)

Opt. rot. : $[\alpha]_D^{24}$ 8.17 (EtOH, c = 1.00)

TLC: R_f0.20 (CH_2Cl_2) [SiO_2, UV]

HRMS: for ($C_{12}H_{22}O$)

Calcd: 182.1667

Found: 182.1671

Data for **(*E*,*E*)-25**:

bp: 95 °C ($8.5X10^{-5}$ mmHg, ABT)

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

6.33 (dt, *J* = 11.2, 1.5 Hz, 1H, CH(3)); 6.02 (d, *J* = 11.0, 1.5 Hz, 1H, CH(4)); 5.48 (dt, *J* = 10.7, 7.3 Hz, 1H, CH(5)); 4.10 (d, *J* = 5.6 Hz, 2H, CH_2(1)); 2.16-2.23 (m, 2H, CH_2(6)); 1.79 (s, 3H, CH_3(12)); 1.32-1.43 (m, 3H, CH(8), CH_2(9)); 1.25 (s, 1H, (br(OH)); 1.13-1.22 (m, 2H, CH_2(7)); 0.87 (t, *J* = 7.3 Hz, 3H, CH_3(10)); 0.87 (d, *J* = 6.1 Hz, 3H, CH_3(11))

^{13}C NMR: (126 MHz, $CDCl_3$)

137.00 (C(2)); 133.17 (C(5)); 123.78 (C(4)); 120.40 (C(3)); 69.12 (C(1)); 36.71 (C(7)); 34.31 (C(8)); 29.61 (C(9)); 25.51 (C(6)); 19.31 (C(11)); 14.21 (C(12)); 11.60 (C(10))

IR: (neat)

3308(s); 3020(w); 2961(s); 2916(s); 2873(s); 1461(m); 1378(m); 1211(w); 1067(w); 1009(m); 877(w)

MS: (EI, 70 eV)

182((M$^+$) 100); 135(29); 123(15); 98(84); 95(59); 85(75); 83(93); 81(64); 79(37); 70(49); 69(86); 67(67); 55(53); 53(96); 50(31)

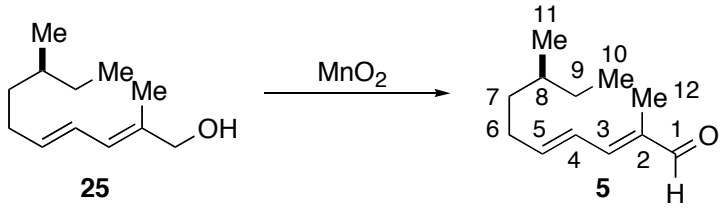
TLC: R_f0.18 (CH_2Cl_2) [SiO_2, UV]

HRMS: for ($C_{12}H_{22}O$)

Calcd: 182.1667

Found: 182.1671

Preparation of (*S*)-2,8-Dimethyldeca-2*E*,4*E*-dienal (5)[18] [CSR-VIII-18]



A 100-mL, one-necked, recovery-flask, containing a magnetic stir-bar, water condenser, and an argon inlet with a septum was charged with alcohol **25** (1.07 g, 5.87 mmol, 1.0 equiv), $CHCl_3$ (23 mL), and manganese dioxide (2.04 g, 23.5 mmol, 4.0 equiv). The flask contents were flushed with argon and heated to reflux (oil bath 80 °C) with stirring for 4 h. The black suspension was cooled to room temperature and filtered through Celite (2 g) washing the pad with CH_2Cl_2 (50 mL) to afford a yellow filtrate. The yellow solution was concentrated to a yellow oil which was purified by column chromatography ((SiO_2, 50 x 180 mm), hexane/EtOAc, 20/1) to afford 0.943 g (89%) of aldehyde **5** as a light-yellow oil.

Data for **5**:

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

9.41(s, 1H, CH(1)); 6.83 (d, J = 11.2 Hz, 1H, CH(3)); 6.52 (ddt, J = 15.0, 11.1, and 1.5 Hz, 1H, CH(4)); 6.24 (dt, J = 15.0, 7.1 Hz, 1H, CH(5)); 2.10-2.33 (m, 2H, CH_2(6)); 1.83 (s, 3H, CH_3(12)); 1.43-1.50 (m, 1H, CH(9a or 9b)); 1.32-1.39 (m, 2H, CH(9a or 9b), CH(8)); 1.24-1.30 (m, 1H, CH(7a or 7b)); 1.13-1.21 (m, 1H, CH(7a or 7b)); 0.89 (d, J = 6.4 Hz, 3H, CH_3(11)); 0.88 (t, J = 7.3 Hz, 3H, CH_3(10))

^{13}C NMR: (126 MHz, $CDCl_3$)

195.23 (C(1)); 149.51 (C(3)); 146.33 (C(5)); 135.83 (C(2)); 125.65 (C(4)); 35.48

(C(7)); 33.98 (C(8)); 31.10 (C(6)); 29.28 (C(9)); 18.97 (C(11)); 11.32 (C(10)); 9.38 (C(12))

IR: (neat)

3342 (w); 2960 (s); 2926 (s); 2874 (s); 2856 (m); 2709 (w); 2764 (w); 1685 (s); 1636 (s); 1462 (m); 1405 (w); 1378 (w); 1212 (m); 1008 (m); 967 (m); 835 (w); 683 (w)

MS: (EI, 70 eV)

180 ((M^+) 9); 110 (16); 97 (21); 95 (100); 81 (15); 79 (10); 67 (11)

Opt. rot. : $[\alpha]_D^{24}$ 13.58 (EtOH; c = 0.55)

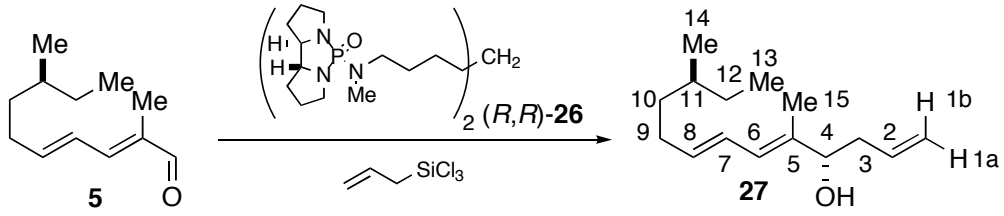
TLC: R_f 0.36 (10:1 hexanes/EtOAc) [SiO_2, UV]

HRMS: (for $C_{12}H_{20}O$)

Calcd: 180.1515

Found: 180.1514

Preparation of (4*S*, 11*S*)-4-Hydroxy-5,11-Dimethyltrideca-1,5*E*,7*E*-triene (27) [CSR-VIII-43]



In a 5-mL, round-bottomed flask were placed a magnetic stir-bar, phosphoramide (*R,R*)-**26** (40 mg, 0.1 mmol, 0.01 equiv), CH_2Cl_2 (1 mL), and *i*-Pr_2NEt (1 mL). The solution was cooled to –70 °C using a 2-propanol/dry ice bath. To the reaction mixture was added allyltrichlorosilane (290 μL, 2.0 mmol, 2.0 equiv) followed by aldehyde **5** (180 mg, 1.0 mmol, 1.0 equiv) drop wise. The reaction mixture was stirred at –70 °C for 8 h. Then the reaction mixture was transferred via cannula into 50-mL Erlenmeyer flask, containing a vigorously stirring solution of a 1:1 mixture of saturated, aqueous $NaHCO_3$ and saturated, aqueous KF solution (20 mL), at room temperature. Then the reaction flask was rinsed with CH_2Cl_2 (10 mL) and this wash was transferred via cannula into the Erlenmeyer. The resulting yellow biphasic mixture was stirred vigorously for 12 h at room temperature. The solution was filtered through a

layer of Celite (1 g), and the filtrate was transferred into a 250-mL separatory funnel. The aqueous layer was extracted with EtOAc (3 x 20 mL), and the combined organic layers were washed with brine (20 mL). The organic solution was dried over Na_2SO_4 and concentrated under reduced pressure to afford a yellow oil. The crude product was purified using column chromatography ((SiO_2, 30 x 200 mm), hexanes/EtOAc, 20/1 to 10/1) to afford 0.195 g (88%) of **27** as a clear, colorless oil.

Data for **27**:

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

6.24 (ddt, *J* = 15.0, 10.9, and 1.5 Hz, 1H, CH(7)); 6.02 (d, *J* = 10.9 Hz, 1H, CH(6)); 5.78 (ddt, *J* = 17.1, 10.3, and 7.3 Hz, 1H, CH(2)); 5.68 (dt, *J* = 16.8, 7.3 Hz, 1H, CH(8)); 5.14 (dd, *J* = 10.3, 1.7 Hz, 1H, CH(1a)); 5.10 (dq, *J* = 16.8, 1.5 Hz, 1H, CH(1b)); 4.08 (t, *J* = 6.8 Hz, 1H, CH(4)); 2.27-2.40 (m, 2H, CH_2(3)); 2.02-2.20 (m, 2H, CH_2(9)); 1.75 (s, 3H, CH_3(15)); 1.62 (d, *J* = 6.8 Hz, 1H, (br(OH)); 1.30-1.44 (m, 3H, CH(11), CH_2(12)); 1.12-1.23 (m, 2H, CH_2(10)); 0.86 (d, *J* = 6.8 Hz, 3H, CH_3(14)); 0.86 (t, *J* = 7.1 Hz, 3H, CH_3(13))

^{13}C NMR: (126 MHz, $CDCl_3$)

136.30 (C(5)); 135.70 (C(8)); 134.71 (C(2)); 125.63 (C(7)); 125.53 (C(6)); 117.81 (C(1)); 76.20 (C(4)); 39.86 (C(3)); 36.18 (C(10)); 33.19 (C(11)); 30.54 (C(9)); 29.33 (C(12)); 19.02 (C(14)); 12.28 (C(15)); 11.32 (C(13))

IR: (neat)

3368 (m); 2961 (s); 2917 (s); 2874 (s); 1641 (w); 1461 (w); 1378 (w); 997 (w); 964 (w); 911 (m)

MS: (EI, 70 eV)

222 ((M^+) 4); 181(100); 163 (22); 121 (10); 111 (30); 97 (42); 95 (19); 93 (62); 91 (13); 83 (63); 81 (35); 79 (16); 71(18); 69 (26); 67 (21); 57 (19); 55 (39)

Opt. Rot.: $[\alpha]_D^{24}$ 23.22 (c = 0.50, EtOH)

TLC: R_f 0.22 (hexanes/EtOAc, 10/1) [SiO_2, CAM]

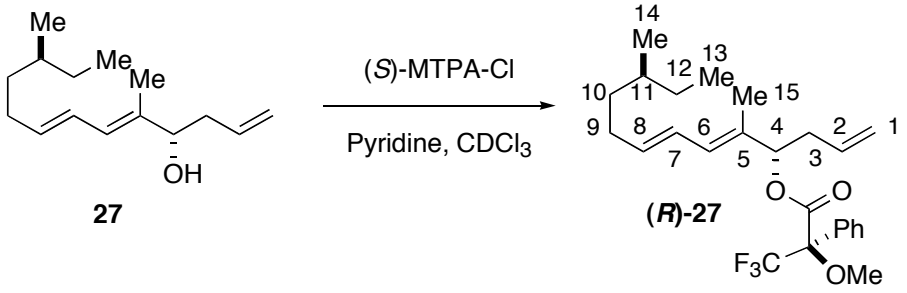
SFC: (Chiralpak-AD, 3.0 mL/min, 3.0% MeOH, 150 bar);

(4*R*)-**27**: 3.22 min (4.1%); (4*S*)-**27**: 3.50 min (95.9%)

Analysis: $C_{15}H_{26}O$ (222.37)

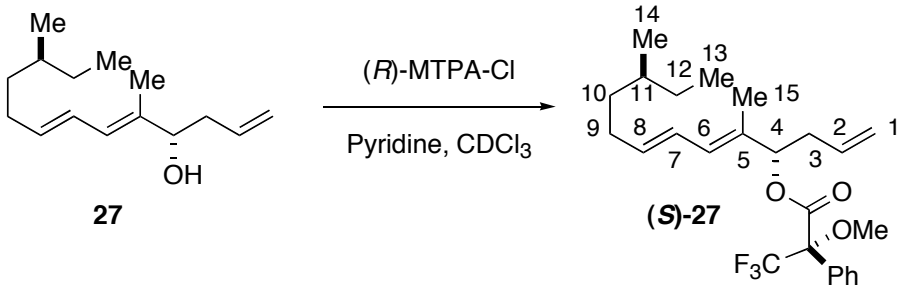
Calcd:	C, 81.02%;	H, 11.79%
Found:	C, 80.94%;	H, 11.81%

Determination of the C(4) Configuration of (4*S*,11*S*)-4-Hydroxy-5,11-Dimethyltrideca-1,5*E*,7*E*-triene (27) [CSR-VIII-29]



In a 5-mm NMR tube was placed a solution of allyl alcohol **27** (4.0 mg, 0.0180 mmol) in $CDCl_3$ (0.5 mL). To the solution was added sequentially pyridine (0.2 mL, 0.196 mmol, 11 equiv) and (*S*)-α-mehoxy-α-trifluoromethyl-phenylacetyl chloride (8.4 μL, 0.045 mmol, 2.5 equiv). The reaction mixture was thoroughly mixed and stood for 2 h at room temperature. The crude Mosher ester (*R*)-**27** was analyzed by ^{1}H-NMR (Table 1).

Determination of the C(4) Configuration of (4*S*,11*S*)-4-Hydroxy-5,11-Dimethyltrideca-1,5*E*,7*E*-triene (27) [CSR-VIII-30]



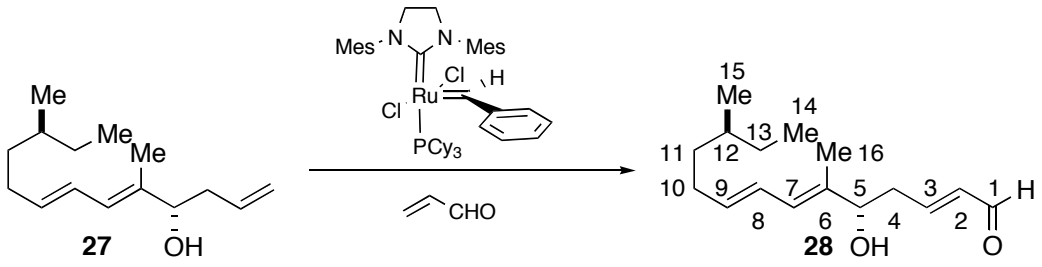
In a 5-mm NMR tube was placed a solution of allyl alcohol **27** (4.0 mg, 0.0180 mmol) in $CDCl_3$ (0.5 mL). To the solution was added sequentially pyridine (0.2 mL, 0.196 mmol, 11 equiv) and (*R*)-α-mehoxy-α-trifluoromethyl-phenylacetyl chloride (8.4 μL, 0.045 mmol, 2.5 equiv). The reaction mixture was thoroughly mixed and was stood for 2 h at room temperature.

The crude Mosher ester (*S*)-**27** was analyzed by ^{1}H-NMR (Table 1).

Table 1: Mosher Ester Analysis. Assignment of C(4) Stereocenter of **27**

Assignment	δ-**27**	δ (*S*-ester)	δ (*R*-ester)	Δδ-(*S*-*R*)
7	6.243	6.154	6.108	0.046
6	6.02	6.047	5.941	0.106
2	5.78	5.54	5.65	-0.11
8	5.68	5.683	5.615	0.068
1	5.14	4.952	5.04	-0.088
4	4.08	3.686	3.692	-0.006
3	2.27-2.40	2.363	2.414	-0.051
9	2.02-2.20	2.057	2.048	0.009
15	1.75	1.679	1.533	0.146
12,11	1.30-1.44	1.317	1.317	0
10	1.12-1.23	1.121	1.121	0
14	0.86	0.805	0.811	-0.006

Preparation of (5*S*,12*S*)-5-Hydroxy-6,12-Dimethyltetradeca-2*E*,6*E*,8*E*-trienal (28) [CSR-VIII-31]



To a 5-mL Schlenk flask, purged with argon, were placed a magnetic stir-bar, Grubbs 2nd generation catalyst (42 mg, 0.05 mmol, 0.05 equiv), CH_2Cl_2 (1 mL) and acrolein (868 μL, 13 mmol, 13 equiv). To a 5-mL conical-flask, flushed with argon and equipped with a magnetic stir-bar and a septum was placed allyl alcohol **27** (222.3 mg, 1.0 mmol, 1.0 equiv) along with CH_2Cl_2 (1 mL). The solution of **27** was transferred via cannula into the flask. Bubbling was observed and the contents were stirred at room temperature for 2 h. The resulting mixture was diluted with hexanes/EtOAc (3/1, 10 mL) and immediately subjected to column chromatography ((SiO_2, 40 x 200), hexanes/EtOAc, 3/1) to afford 0.223 g (90%) of **28** as a clear, yellow oil.

Data for **28**:

bp: 120 ºC (3.0×10^{-5} mmHg, ABT)

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

9.49 (d, *J* = 8.1 Hz, 1H, CH(1)); 6.83 (dt, *J* = 15.6, 7.2 Hz, 1H, CH(3)); 6.22 (dd, *J* = 15.0, 10.7 Hz, 1H, CH(8)); 6.17 (dd, *J* = 15.6, 7.3 Hz, 1H, CH(2)); 6.04 (d, *J* = 10.7 Hz, 1H, CH(7)); 5.72 (dt, *J* = 15.0, 7.3 Hz, 1H, CH(9)); 4.22 (t, *J* = 6.4 Hz, 1H, CH(5)); 2.54-2.65 (m, 2H, CH_2(4)); 2.05-2.20 (m, 2H, CH_2(10)); 1.78 (s, 1H, (br(OH)); 1.75 (s, 3H, CH_3(16)); 1.29-1.43 (m, 3H, CH(12), CH_2(13)); 1.11-1.23 (m, 2H, CH_2(11)); 0.86 (d, *J* = 6.4 Hz, 3H, CH_3(15)); 0.86 (t, *J* = 7.6 Hz, 3H, CH_3(14))

^{13}C NMR: (126 MHz, $CDCl_3$)

194.34 (C(1)); 154.95 (C(3)); 137.01 (C(9)); 135.73 (C(6)); 134.84 (C(2)); 126.71 (C(7)); 125.44 (C(8)); 76.15 (C(5)); 38.44 (C(4)); 36.31 (C(13)); 34.14 (C(12)); 30.77 (C(10)); 29.54 (C(11)); 19.23 (C(15)); 12.33 (C(16)); 11.53 (C(14))

IR: (neat)

3429 (w); 2960 (m); 2922 (m); 2874 (m); 1691 (s); 1637 (w); 1461 (w); 1378 (w); 1129 (w);1040 (w); 1012 (w); 967 (m)

MS: (EI, 70 eV)

250 (M^+ (2)); 239 (19); 232 (10); 205 (2); 181 (100); 163 (72); 148 (17); 135 (4); 121 (12); 107 (24); 95 (56); 83 (52); 69 (23); 55 (38)

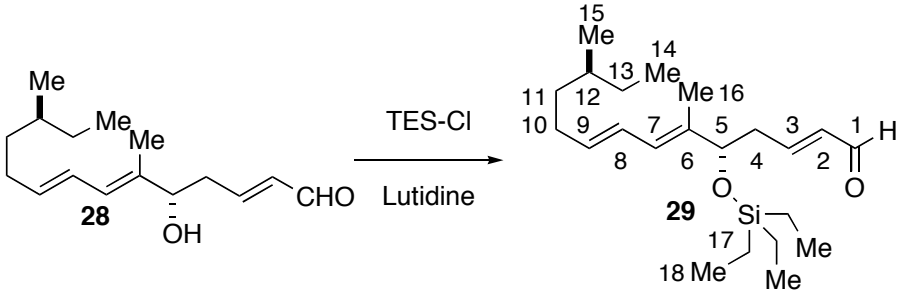
Opt. Rot.: $[\alpha]_D^{24}$ 10.55 (c = 0.485, EtOH)

TLC: R_f 0.20 (hexanes/EtOAc, 10/1) [SiO_2, CAM]

Analysis: $C_{16}H_{26}O_2$ (250.38)

Calcd:	C, 76.75%;	H, 10.47%
Found:	C, 76.86%;	H, 10.74%

Preparation of (5*S*,12*S*)-6,12-Dimethyl-5-(triethylsilyloxy)tetradeca-2*E*,6*E*,8*E*-trienal (29) [CSR-VIII-68]



To a 35-mL, one-neck, round-bottom flask, equipped with an argon inlet with a septum, were placed aldehyde **28** (258 mg, 1.03 mmol, 1.0 equiv), CH_2Cl_2 (12 mL), lutidine (360 μL, 6.0 mmol, 6.0 equiv), and triethylsilyl chloride (519 μL, 3.0 mmol, 3.0 equiv). The yellow solution was stirred for 7 h. The contents were quenched with saturated, aqueous sodium bicarbonate (20 mL) and transferred into a 250-mL separatory funnel. The aqueous layer was extracted with CH_2Cl_2 (3 x 10 mL), and the combined organic extracts were washed with water (3 x 20 mL) and brine (20 mL). The organic extracts was dried over Na_2SO_4 and concentrated to a yellow oil. The crude product was purified using column chromatography ((SiO_2, 30 x 200 mm), hexanes/EtOAc, 10/1 to 3/1) to afford 0.342 g (92%) of **29** as a clear, yellow oil.

Data for **29**:

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

9.48 (d, *J* = 7.8 Hz, 1H, CH(1)); 6.80 (dt, *J* = 15.6, 8.1 Hz, 1H, CH(3)); 6.20 (dd, *J* = 15.0, 10.7 Hz, 1H, CH(8)); 6.13 (dd, *J* = 15.6, 8.0 Hz,1H, CH(2)); 5.96 (d, *J* = 10.8 Hz,1H, CH(7)); 5.67 (dt, *J* = 15.0, 7.3 Hz, 1H, CH(9)); 4.16 (t, *J* = 5.4 Hz, 1H, CH(5)); 2.46-2.61 (m, 2H, CH_2(4)); 2.04-2.18 (m, 2H, CH_2(10)); 1.71 (s, 3H, CH_3(16)); 1.29-1.45 (m, 3H, CH(12), CH_2(13)); 1.12-1.25 (m, 3H, CH_3(11)); 0.93 (t, *J* = 8.0 Hz, 3H CH_3(18)); 0.86 (d, *J* = 6.0 Hz, 3H CH_3(15)); 0.86 (t, *J* = 7.3 Hz, 3H, CH_3(14)); 0.57 (q, *J* = 8.0 Hz, 2H, CH_2(17))

^{13}C NMR: (126 MHz, $CDCl_3$)

194.31 (C(1)); 155.75 (C(3)); 136.19 (C(6)); 135.99 (C(7)); 134.66 (C(9)); 126.12 (C(2)); 125.66 (C(8)); 76.87 (C(5)); 40.25 (C(4)); 36.40 (C(13)); 34.27 (C(12)); 30.83 (C(10)); 29.60 (C(11)); 19.31 (C(15)); 12.18 (C(16)); 11.58 (C(14)); 7.06 (C(18)); 4.97 (C(17))

IR: (neat)

2957 (s); 2913 (s); 2876 (s); 1697 (s); 1638 (s); 1460 (m); 1378 (w); 1333 (w); 1239 (w); 1128 (w); 1069 (m); 1006 (s); 971(s); 743 (s)

MS: (EI, 70 eV)

364 (M^+) 1)); 295 (100); 225 (8); 211 (3); 185 (3); 157 (10); 115 (53); 103 (14); 87 (59); 59 (20)

Opt. Rot.: $[\alpha]_D^{24}$ 9.49 (c = 0.575, EtOH)

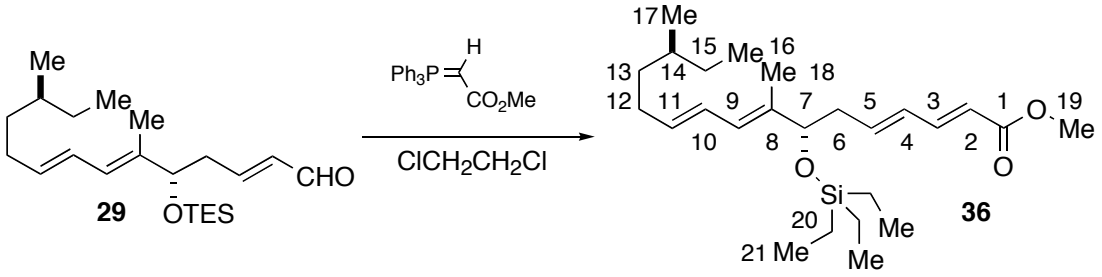
TLC: R_f 0.44 (hexanes/EtOAc, 10/1) [SiO_2, CAM]

Analysis: $C_{22}H_{40}O_2Si$ (318.48)

Calcd: C, 72.47%; H, 11.06%

Found: C, 72.63%; H, 8.41%

Preparation of Methyl (7*S*,14*S*)-8,14-Dimethyl-7-(triethylsilyloxy)hexadeca-2*E*,4*E*,8*E*,10*E*-tetraenoate (36) [CSR-VIII-77]



To a 50-mL, one-necked, round-bottom flask, equipped with a magnetic stir-bar, argon inlet with a septum, and water condenser, were placed aldehyde **29** (365 mg, 1.00 mmol, 1.0 equiv), 1,2-dichloroethane (5 mL). To a 5-mL one-necked, conical-flask, sealed with a septum, methyl (triphenylphosphoranylidene)acetate (501 mg, 1.5 mmol, 1.5 equiv) was added along with dichloroethane (4 mL). The solution of ylide was transferred via cannula into the solution of aldehyde using dichloroethane (1 mL) to rinse. The contents were heated to reflux (oil bath temperature was 95 ºC) and stirred for 18 h. Upon cooling to room temperature the orange solution was transferred to a 125-mL separatory funnel containing 30 mL of water. The aqueous layer was extracted with CH_2Cl_2 (3 x 15 mL), and the combined organic extracts were washed with brine (10 mL). The organic extracts was dried over Na_2SO_4, filtered, and concentrated to an orange syrup. The crude product was analyzed by ^{1}HNMR to reveal a 90:10 ratio of (*E,E,E,E*)-**36** to (*E,E,E,Z*)-**36** isomers. The crude product was purified with column chromatography ((SiO_2, 40 x 200 mm), hexane/CH_2Cl_2, 2/1 to 1/1) to afford 0.379 g (90%) of 2(*E*)-**36**) and 0.029 g (7%) of 2(*Z*)-**36** as a clear, yellow oils.

Data for (*E,E,E,E*)-**36**:

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

7.25 (dd, *J* = 15.4, 10.7 Hz, 1H, CH(3)); 6.20 (dd, *J* = 14.9, 10.7 Hz, 1H, CH(10)); 6.18 (dd, *J* = 15.3, 11.0 Hz, 1H, CH(4)); 6.06 (dt, *J* = 15.3, 7.6 Hz, 1H, CH(5)); 5.91 (d, *J* = 15.4 Hz, 1H, CH(9)); 5.79 (d, *J* = 15.4 Hz, 1H, CH(2)); 5.65 (dt, *J* = 14.9, 7.0 Hz, 1H, CH(11)); 4.05 (t, *J* = 5.9 Hz, 1H, CH(7)); 3.76 (s, 3H,

CH_3(19)); 2.30-2.43 (m, 2H, CH_2(6)); 2.20-2.02 (m, 2H, CH_2(12)); 1.69 (s, 3H, CH_3(18)); 1.45-1.30 (m, 3H, CH(14), CH_2(15)); 1.25-1.12 (m, 2H, CH_2(13)); 0.90 (t, J = 8.1 Hz, 9H, CH_3(21)); 0.86 (d, J = 7.0 Hz, 3H, CH_3(17)); 0.86 (t, J = 6.8 Hz, 3H, CH_3(16)); 0.55 (q, J = 8.1 Hz, 6H, CH_2(20))

^{13}C NMR: (126 MHz, $CDCl_3$)

168.01 (C(1)); 145.43 (C(3)); 141.48 (C(5)); 136.93 (C(8)); 135.49 (C(11)); 130.24 (C(4)); 125.84 (C(10)); 125.74 (C(9)); 119.27 (C(2)); 77.68 (C(7)); 51.72 (C(19)); 40.68 (C(6)); 36.45 (C(13)); 34.28 (C(14)); 30.84 (C(12)); 29.61 (C(15)); 19.33 (C(17)); 12.12 (C(18)); 11.59 (C(16)); 7.07 (C(21)); 4.75 (C(20))

IR: (neat)

2956 (s); 2913 (s); 2876 (s); 1723 (s); 1645 (s); 1617 (w); 1459 (m); 1435 (w); 1345 (w); 1302 (w); 1262 (s); 1208 (m); 1135 (m); 1067 (s); 1002 (s); 965 (m); 743 (m)

MS: (EI, 70 eV)

390 (M^+-OMe, 1); 295 (100); 281(2); 225 (4); 171 (4); 115 (28); 87 (36); 59 (14)

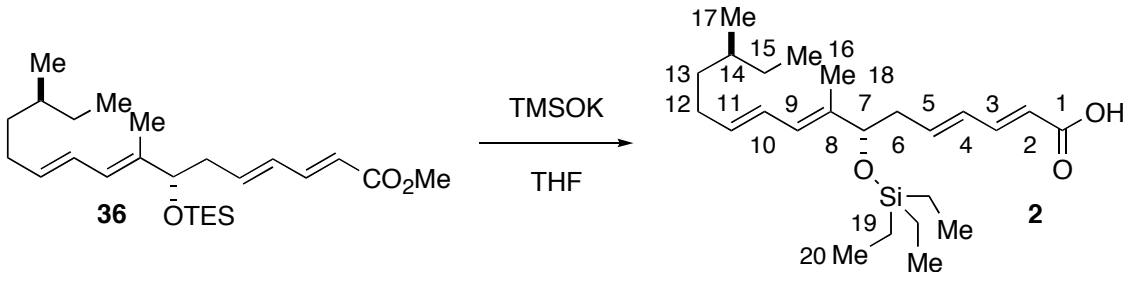
Opt. Rot.: $[\alpha]_D^{24}$ 12.62 (c = 0.530, $CHCl_3$)

TLC: R_f 0.47 (hexanes/EtOAc, 10/1) [SiO_2, UV]

Analysis: $C_{25}H_{44}O_3Si$ (420.70)

Calcd:	C, 71.37%;	H, 10.54%
Found:	C, 71.45%;	H, 10.90%

Preparation of (7*S*,14*S*)-8,14-Dimethyl-7-(triethylsilyloxy)hexadeca-2*E*,4*E*,8*E*,10*E*-tetraenoic Acid (2) [CSR-IX-57][18]



To a 25-mL, one-necked, round-bottom flask, equipped with a magnetic stir-bar, and an argon inlet with a septum were placed ester **36** (57.9 mg, 0.138 mmol, 1.0 equiv) and THF (1

mL). To a 5-mL, one-necked, conical-flask, sealed with a septum was added potassium trimethylsilanoate (177 mg, 1.38 mmol, 10 equiv) along with THF (1.5 mL). The solution of TMSOK was transferred via cannula into the solution of **36** using THF (0.5 mL) to rinse the flask. The reaction solution turned orange/yellow upon addition of TMSOK. The solution was stirred for 4 h at room temperature, then the reaction was quenched with an aqueous solution of citric acid (0.5 M, 2 mL) and the mixture was stirred for 10 min. The solution turned bright-yellow upon addition of citric acid. The mixture was transferred to 125-mL separatory funnel containing water (25 mL) and the aqueous layer was extracted with Et_2O (3 x 15 mL), and the combined organic layers were washed with brine (10 mL) and concentrated to a yellow oil. The crude product was purified by column chromatography ((SiO_2, 40 x 50 mm), hexane/EtOAc, 1/1) to afford 56 mg (99%) of **2** as a yellow film.

Data for **2**:

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

7.32 (dd, *J* = 15.8, 10.5 Hz, 1H, CH(3)); 6.25-6.18 (m, 2H, CH(10) and CH(4)); 6.12 (dt, *J* = 15.3, 7.5 Hz, 1H, CH(5)); 5.92 (d, *J* = 10.5 Hz, 1H, CH(9)); 5.78 (d, *J* = 15.8 Hz, 1H, CH(2)); 5.66 (dt, *J* = 14.5, 7.2 Hz, 1H, CH(11)); 4.06 (t, *J* = 6.4 Hz, 1H, CH(7)); 2.46-2.30 (m, 2H, CH(6)); 2.24-2.00 (m, 2H, CH(12)); 1.88 (s, 3H, CH(18)); 1.48-1.08 (m, 5H, CH_2(13) and CH_2(15) and CH(14)); 0.92 (t, *J* = 7.9 Hz, 9H, CH(20)); 0.86 (d, *J* = 6.8 Hz, 3H, CH(17)); 0.86 (t, *J* = 7.2 Hz, 3H, CH_3(16)); 0.55 (q, *J* = 7.9 Hz, 6H, CH(19))

^{13}C NMR: (126 MHz, $CDCl_3$)

172.21 (C(1)); 147.26 (C(3)); 142.47 (C(5)); 136.59 (C(8)); 135.30 (C(11)); 129.91 (C(4)); 125.58 (C(10)); 125.56 (C(9)); 118.54 (C(2)); 77.37 (C(7)); 40.49 (C(6)); 36.20 (C(13)); 34.04 (C(14)); 30.60 (C(12)); 29.36 (C(15)); 19.08 (C(17)); 11.90 (C(18)); 11.33 (C(16)); 6.82 (C(19)); 4.78 (C(20))

IR: (film)

3025 (m); 2958 (s); 2914 (s); 2876 (s); 2360 (w); 2342 (w); 1689 (s); 1639 (m); 1616 (m); 1458 (w); 1417 (m); 1378 (w); 1303 (w); 1272 (m); 1241 (w); 1149 (w); 1067 (m); 1002 (s); 965 (m); 742 (m)

MS: (ESI)

429 ((M^+ + Na (32)); 360 (28); 338 (100); 275 (71); 261(25)

Opt. Rot.: $[\alpha]_D^{24}$ 6.90 (c = 0.63, $CHCl_3$)

TLC: R_f 0.29 (hexanes/EtOAc, 7/1) [SiO_2, CAM]

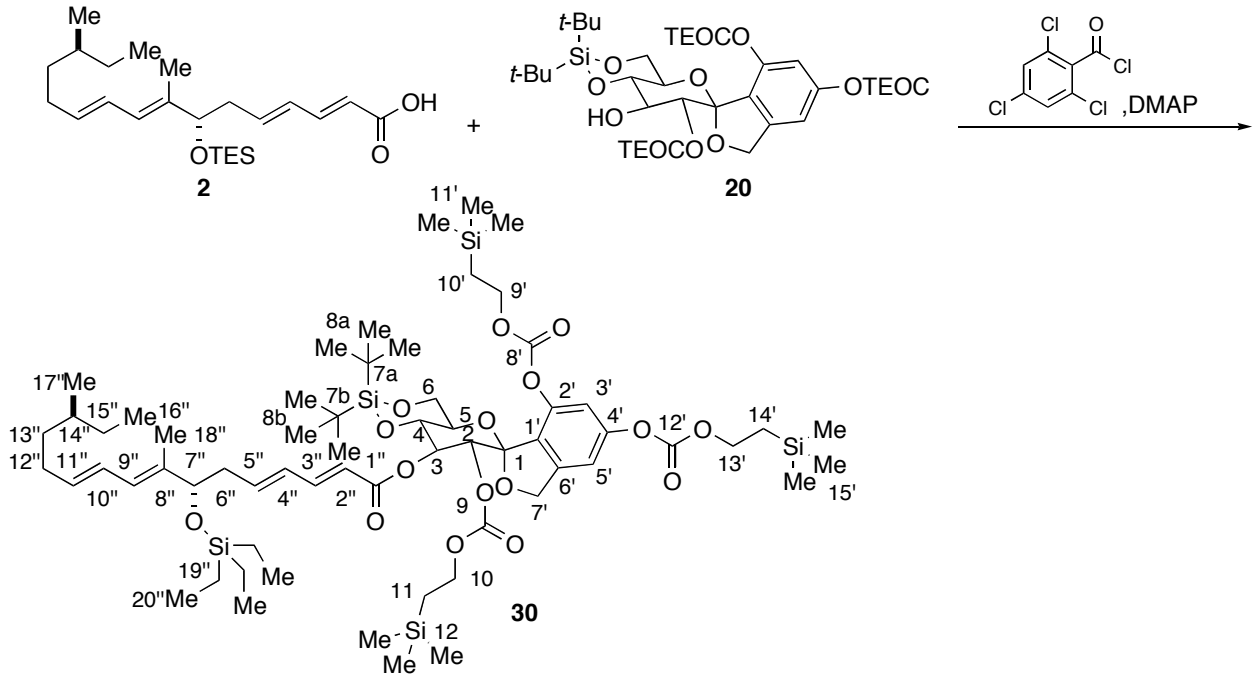
HRMS: $C_{24}H_{42}O_3SiNa$

Calcd: 429.2825

Found: 429.2821

Acylation and Global Deprotection

Preparation of 1,1-Anhydro-4,6-*O*-di-*tert*-butylsilylene-3-*O*-(7''*S*,14''*S*)-2''*E*,4''*E*,8''*E*,10''*E*-8'',14''-dimethyl-7''-triethylsilioxy-2'',4'',8'',10''-hexadecatetraenoyl)-2-*O*-(2-trimethylsilyl-ethoxycarbonyl)-1-(2',5'-dihydroxy-6'-hydroxymethylphenyl)-α-*D*-glucopyranose (30) [CSR-IX-58]



To a 10-mL Schlenk flask, flushed with argon, equipped with a magnetic stir-bar and a rubber septum was added acid **2** (0.048 g, 0.119 mmol, 1.3 equiv) followed by toluene (1.7 mL) and triethylamine (141 μL, 1.01 mmol, 11 equiv). To this yellow solution was added 2,4,6-trichlorobenzoyl chloride (40 μL, 0.258 mol, 2.8 equiv) and the contents were stirred at room temperature for 1 h. To a 5-mL, conical-flask, equipped with a magnetic stir-bar and an argon inlet with septum was added **20** (0.080 g, 0.092 mmol, 1.0 equiv) along with DMAP (0.029 g, 0.239 mmol, 2.6 equiv). Then toluene (1.3 mL) was added and the contents were stirred until all

the DMAP had dissolved (~5 min). The solution of **20** and DMAP was cannula transferred into the Schlenk flask, washing the conical-flask with toluene (0.2 mL). The contents became heterogeneous upon the addition of DMAP and **20**. This mixture was stirred at room temperature for 3 h, then toluene (7 mL) was added, followed by saturated, aqueous $NaHCO_3$ solution (5 mL). The contents of the flask were transferred to a 60-mL separatory funnel and the aqueous layer was extracted. The aqueous extract was diluted with H_2O (10 mL) and extracted with toluene (3 x 17 mL). The combined organic extracts were washed with H_2O (1 x 20 mL), brine (1 x 20 mL) and then were dried (Na_2SO_4), filtered, and concentrated to a yellow oil. The crude product was purified using column chromatography ((SiO_2, 40 x 180), hexanes/EtOAc, 15:1 to 7:1)) to afford a viscous, colorless oil. The oil was dried under reduced pressure (0.08 mmHg) at 40 ^oC for 8 h to afford 0.101 g (87%) of **30**, as a colorless glass.

Data for **30**:

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

7.28 (dd, *J* = 14.9, 11.3 Hz, 1H, CH(3")); 7.11 (d, *J* = 1.8 Hz, 1H, CH(3' or 5')); 6.97 (d, *J* = 1.8 Hz, 1H, CH(3' or 5')); 6.24-6.14 (m, 2H, CH(4") and CH(10")); 6.07 (dt, *J* = 15.7, 7.8 Hz, 1H, CH(5")); 5.92 (d, *J* = 11.3 Hz, 1H, CH(9")); 5.82 (d, *J* = 14.9 Hz, 1H, CH(2")); 5.65 (dt, *J* = 14.4, 7.2 Hz, 1H, CH(11")); 5.61 (t, *J* = 9.9 Hz, 1H, HC(3)); 5.52 (d, *J* = 9.9 Hz, 1H, HC(2)); 5.20 (s, 2H, CH_2(7')); 4.42-4.29 (m, 4H, CH_2(9') and CH_2(13')); 4.16-4.09 (m, 3H, CH(6e) and CH(10)); 4.07-3.90 (m, 4H, CH_2(10) and CH(6a) and CH(4)); 3.84-3.76 (m, 2H, CH(7") and CH(5)); 2.44-2.27 (m, 2H, CH_2(12")); 2.22-2.00 (m, 2H, CH_2(6")); 1.69 (s, 3H, CH_3(18")); 1.46-1.30 (m, 3H, CH(14") and CH_2(15")); 1.24-1.17 (m, 2H, CH_2(13")); 1.18-1.09 (m, 4H, CH_2(10') and CH_2(14')); 1.02 (s, 9H, $C(CH_3)_3$(8a or 8b)); 0.99 (s, 9H, $C(CH_3)_3$(8a or 8b)); 0.91 (t, *J* = 7.8 Hz, 9H, CH_3(20")); 0.87 (d, *J* = 6.1 Hz, 3H, CH_3(17")); 0.87 (t, *J* = 7.3 Hz, 3H, CH_3(16")); 0.81-0.76 (m, 2H, CH_2(11)); 0.54 (q, *J* = 7.8 Hz, 6H, CH_2(19")); 0.09 (s, 9H, CH_3(11') or (15')); 0.07 (s, 9H, CH_3(11') or (15')); -0.04 (s, 9H, CH_3(12))

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

166.04 (C(1")); 154.13 (9)); 153.23 (2')); 152.88 (C(8' or 12')); 152.46 (C(8' or 12')); 146.72 (C(4')); 145.24 (C(3")); 143.40 (C(1')); 140.99 (C(5")); 136.74 (C(8")); 135.21 (C(11")); 130.17 (4")); 125.59 (C(10")); 125.47 (C(9")); 124.51

(C(6')); 119.15 (C(2")); 115.27 (C(3')); 111.59 (C(5')); 108.73 (C(1)); 77.45 (C(7")); 77.20 (C(4)); 75.53 (C(2)); 74.53 (C(3)); 73.39 (C(5)); 72.62 (C(9' or 13')); 68.92 (C(9' or 13')); 67.72 (C(7')); 66.89 (C(6)); 66.61 (C(10)); 40.51 (C(6")); 36.19 (C(13")); 34.04 (C(14")); 30.58 (C(12")); 29.33 (C(15")); 27.34 (C(8a or 8b)); 26.87 (C(8a or 8b)); 22.63 (C(7a or 7b)); 19.97 (C(7a or 7b)); 17.55 (10' or 14')); 17.49 (10' or 14')); 17.06 (C(13")); 11.18 (C(18")); 11.32 (C(16")); 6.80 (C(19")); 4.75 (C(20")); -1.50 (C(11' or 15')); -1.57 (C(11' or 15')); -1.66 (C(12))

IR: (film)

2957 (s); 2933 (s); 2876 (s); 1764 (s); 1641 (w); 1459 (w); 1382 (w); 1250 (s); 1176 (m); 1096 (m); 1065 (m); 1012 (m); 973 (m); 859 (m); 873 (s)

MS: (ESI)

1283((M^+ + Na (100)); 1019 (13); 782 (5); 489 (18)

Opt. Rot.: $[\alpha]_D^{24}$ -21.6 (c = 0.51, $CHCl_3$)

TLC: R_f 0.12 (hexanes/EtOAc, 10/1) [SiO_2, CAM]

HRMS: $C_{63}H_{108}O_{16}Si_5Na$

Calcd: 1283.6382

Found: 1283.6431

Preparation of 1,1-Anhydro-1,C[-6-hydroxymethyl)-2,4-phenyl]-3-*O*-[(7''*S*, 14''*S*)-8''-14---dimethyl-7''-(hydroxy)hexadecane-2''*E*,4''*E*,8''*E*,10''*E*-tetraenoyl]-α-*D*-glucopyranose or Papulacandin D [CSR-IX-95]

30 **Papulacandin D (37)**

To a 25-mL, Teflon-flask, equipped with a magnetic stir-bar, an air condenser, and an argon inlet with a rubber septum) was added protected papulacandin D (**30**) (0.045 g, 0.037 mmol, 1.0 equiv and the apparatus was flushed with argon. To a separate plastic container equipped with a magnetic stir bar was added DMSO (10 mL), triethylamine (16.29 mL), and HF

(49%, 2.5 mL) and the contents were stirred vigorously. Then 6 mL of this buffered HF solution (14.26 mmol, 400 equiv, fluoride) was added to the Teflon flask *via* syringe. The contents were stirred at room temperature for 5 min, then at 60 ^{o}C (oil bath temperature) for 18 h. The biphasic yellow reaction mixture was directly subjected to column chromatography ((SiO_2, 50 x 100 mm), EtOAc to EtOAc/MeOH, 9 /1)). DMSO was removed form the isolated product under reduced pressure (8.5 x 10^{-5} mmHg) at 30 ^{o}C for 8 h. Then the resulting, yellow film was once again purified using column chromatography ((SiO_2, 20 x 10 mm), chloroform/MeOH, 9/1)). After concentration the contents were dissolved in EtOAc (10 mL), filtered and concentrated *in vacuo* to afford 22 mg (89%) of papulacandin D as a light-yellow foam.

Data for Papulacandin D:

^{1}H NMR: (500 MHz, CD_3OD)

7.30 (dd, *J* = 15.8, 11.5 Hz, 1H, CH(3")); 6.25 (ddt, *J* = 15.7, 10.8, and 1.6 Hz, 1H, CH(4")); 6.23 (dd, *J* = 14.9, 10.7 Hz, 1H, CH(10")); 6.20 (m, 1H, CH(11)); 6.19 (m, 1H, CH(13)); 6.12 (dt, *J* = 15,4, 14.9 Hz, 1H, CH(5")); 5.98 (dd, *J* = 10.7, 0.6 Hz, 1H, CH(9")); 5.92 (d, *J* = 15.3 Hz, 1H, CH(2")); 5.66 (dt, *J* = 14.9, 7.3 Hz, 1H, CH(11")); 5.34 (t, *J* = 9.7 Hz, 1H, CH(3)); 5.02 (ABq, *J* = 12.9 Hz, 2H, CH_2(7)); 4.34 (d, *J* = 10.1 Hz, 1H, CH(2)); 4.07 (t, *J* = 6.6 Hz, 1H, CH(7")); 3.88 (ddd, *J* = 10.3, 4.8, and 2.4 Hz, 1H, CH(5)); 3.79-3.66 (m, 2H, CH_2(6)), 3.68 (t, *J* = 9.8 Hz, 1H, CH(4)); 2.42 (t, *J* = 7.2 Hz, 2H, CH_2(6")); 2.18-2.04 (m, 2H, CH_2(12")); 1.71 (s, 3H, CH_3(18")); 1.50-1.30 (m, 2H, CH_2(13")); 1.30-1.11 (m, 2H, CH_2(15")); 1.28-1.11 (m, 1H, CH(14")); 0.87 (t, *J* = 7.3 Hz, 3H, CH_3(16")); 0.87 (d, *J* = 6.5 Hz, 3H, CH_3(17"))

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

169.15 (C(1")); 161.74 (C(12)); 154.86 (C(10)); 146.63 (C(3")); 145.73 (C(8)); 142.06 (C(5")); 137.70 (C(8")); 136.36 (C(11")); 131.67 (C(10")); 127.27 (4")); 127.22 (C(9")); 121.14 (C(2")); 116.76 (C(9)); 112.22 (C(1)); 103.01 (C(11)); 100.01 (13)); 78.46 (C(3)); 77.71 (C(7")); 75.94 (C(5)); 71.99 (C(2)); 69.87 (C(4)); 62.62 (C(6)); 40.09 (C(6")); 37.68 (C(13")); 35.36 (C(14")); 31.74 (C(12")); 30.59 (C(15")); 19.59 (C(18")); 12.29 (C(17")); 11.56 (C(16"))

IR: (film)

3351 (br, s); 2960 (s); 2855 (s); 1698 (s); 1640 (s); 1613 (s); 1463 (s); 1377 (s);

1260 (s); 1006 (s); 978 (s); 885 (w)

MS: (ESI)

575((M^+ + 1 (75)); 359 (100); 782 (5); 283 (13)

Opt. Rot.: $[\alpha]_D^{24}$ 8.78 (c = 0.21, MeOH)

TLC: R_f 0.46 (chloroform/MeOH, 4/1) [SiO_2, UV, I_2]

UV-Vis: λ_{max} (232); (238); (260)

HRMS: $C_{31}H_{43}O_{10}$

Calcd: 575.2856

Found: 575.2874

Table 2: ^{13}C NMR Spectroscopic Properties

Carbon No.	Natural (ppm)[19]	CSR-IX-95 (ppm)	Synthetic (ppm)[18]	Difference (ppm)
1	111.9	112.22	112.1	0.12
2	78.2	71.99	71.9	0.09
3	75.5	78.46	78.4	0.06
4	73.7	69.87	69.8	0.07
5	71.7	75.94	75.8	0.14
6	62.2	62.62	62.5	0.12
7	69.5	73.95	73.8	0.15
8	145.3	145.73	145.5	0.23
9	116.4	116.76	116.7	0.06
10	161.4	154.86	154.7	0.16
11	100.0	103.01	103.0	0.01
12	154.4	161.74	161.5	0.24
13	103.0	100.10	99.9	0.2
1"	169.0	169.15	169.0	0.15
2"	120.7	121.14	120.9	0.24
3"	146.4	146.63	146.4	0.23
4"	127.1	127.27	127.1	0.17
5"	137.4	142.06	141.8	0.26
6"	39.8	40.09	40.0	0.09
7"	77.3	77.71	77.5	0.21
8"	136.0	137.7	137.5	0.2
9"	131.3	127.22	127.0	0.22
10"	126.9	131.67	131.5	0.17
11"	141.8	136.36	136.2	0.16
12"	31.4	31.74	31.6	0.14
13"	37.3	37.68	37.5	0.18
14"	35.0	35.36	35.2	0.16
15"	30.3	30.59	30.4	0.19
16"	11.6	11.86	11.7	0.16
17"	19.4	12.29	12.2	0.09
18"	12.2	19.59	19.4	0.19

Table 3: ^{1}H NMR Spectroscopic Properties

Hydrogen No.	Natural (ppm)[19]	CSR-IX-95 (ppm)	Synthetic (ppm)[18]
2	4.34 (d, *J* = 10Hz)	4.34 (d, *J* = 10.1 Hz)	4.33 (d, *J* = 10.0 Hz)
3	5.34 (t, *J* = 10Hz)	5.34 (t, *J* = 9.7 Hz)	5.34 (t, *J* = 9.7 Hz)
4	-	3.68 (t, *J* = 9.8 Hz)	3.68 (t, 9.7 Hz)
5	-	3.88 (ddd, *J* = 10.3, 4.8 and 2.4 Hz)	3.87 (ddd, *J* = 10.1, 4.8, and 2.3 Hz)
6	-	3.79-3.66 (m)	3.70-3.66 (m)
7	5.03 (ABq, *J* = 12 Hz)	5.02 (ABq, *J* = 12.9 Hz)	5.03 (ABq, *J* = 12.6 Hz)
11	6.19 (s)	6.20 (m)	6.20 (m)
13	6.20 (s)	6.19 (m)	6.19 (m)
2"	-	5.92 (d, *J* = 15.3 Hz)	5.92 (d, *J* = 15.3 Hz)
3"	-	7.30 (dd, *J* = 15.8 Hz, 11.5 Hz)	7.30 (dd, *J* = 15.2, 10.1 Hz)
4"	-	6.25 (ddt, *J* = 15.7, 10.8, and 1.6 Hz)	6.25 (ddt, *J* = 15.0, 10.8, and 1.3 Hz)
5"	-	6.12 (dt, *J* = 15.4 and 14.9 Hz)	6.12 (dt, *J* = 15.2, 14.7 Hz)
6"	-	2.42 (t, *J* = 7.2 Hz)	2.42 (t, *J* = 7.0 Hz)
7"	-	4.07 (t, *J* = 6.6 Hz)	4.07 (t, *J* = 6.6 Hz)
9"	-	5.98 (dd, *J* = 10.7, 0.6 Hz)	6.00 (dd, *J* = 10.8, 0.7 Hz)
10"	-	6.23 (dd, *J* = 14.9, 10.7 Hz)	6.23 (dd, *J* = 14.7, 10.7 Hz)
11"	-	5.66 (dt, *J* = 7.3 Hz, 14.9 Hz)	5.66 (dt, *J* = 7.0 Hz, 15.0 Hz)
12"	-	2.18-2.04 (m)	2.18-2.04 (m)
13"	-	1.50-1.30 (m)	1.49-1.29 (m)
14"	-	1.28-1.11 (m)	1.28-1.11 (m)
15"	-	1.30-1.10 (m)	1.30-1.10 (m)
16"	-	0.87 (t, *J* = 7.3 Hz)	0.87 (t, *J* = 7.3 Hz)
17"	-	0.87 (d, *J* = 6.5 Hz)	0.87 (d, *J* = 6.6 Hz)
18"	-	1.71 (s)	1.71 (d, *J* = 0.5 Hz)

Table 4: Physiochemical Properties

Property	Natural[19]	CSR-IX-p95
Appearance	white foam	light yellow foam
m.p.	127~130 ^{o}C	126-128 ^{o}C
Spec. Opt. Rot.	+7 ± 1 ^{o} (MeOH)	8.78 (c = 0.21, MeOH)
UV $\lambda_{max\ (nm)}$	230, 235, 261 (EtOH)	232, 238, 260 (EtOH)
TLC	0.58 (silica gel, $CHCl_3$/MeOH, 4/1)	0.46 (silica gel, $CHCl_3$/MeOH, 4/1)

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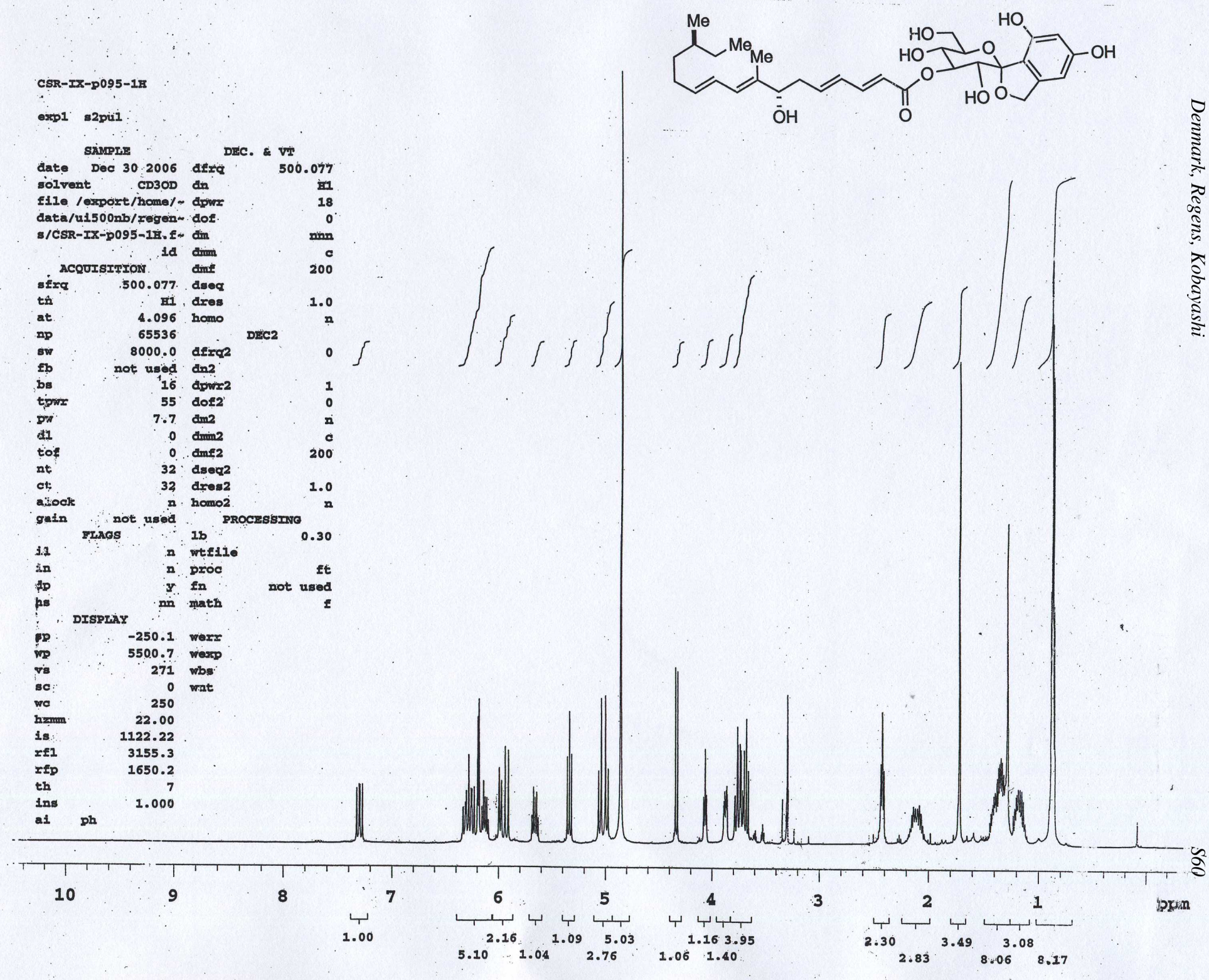
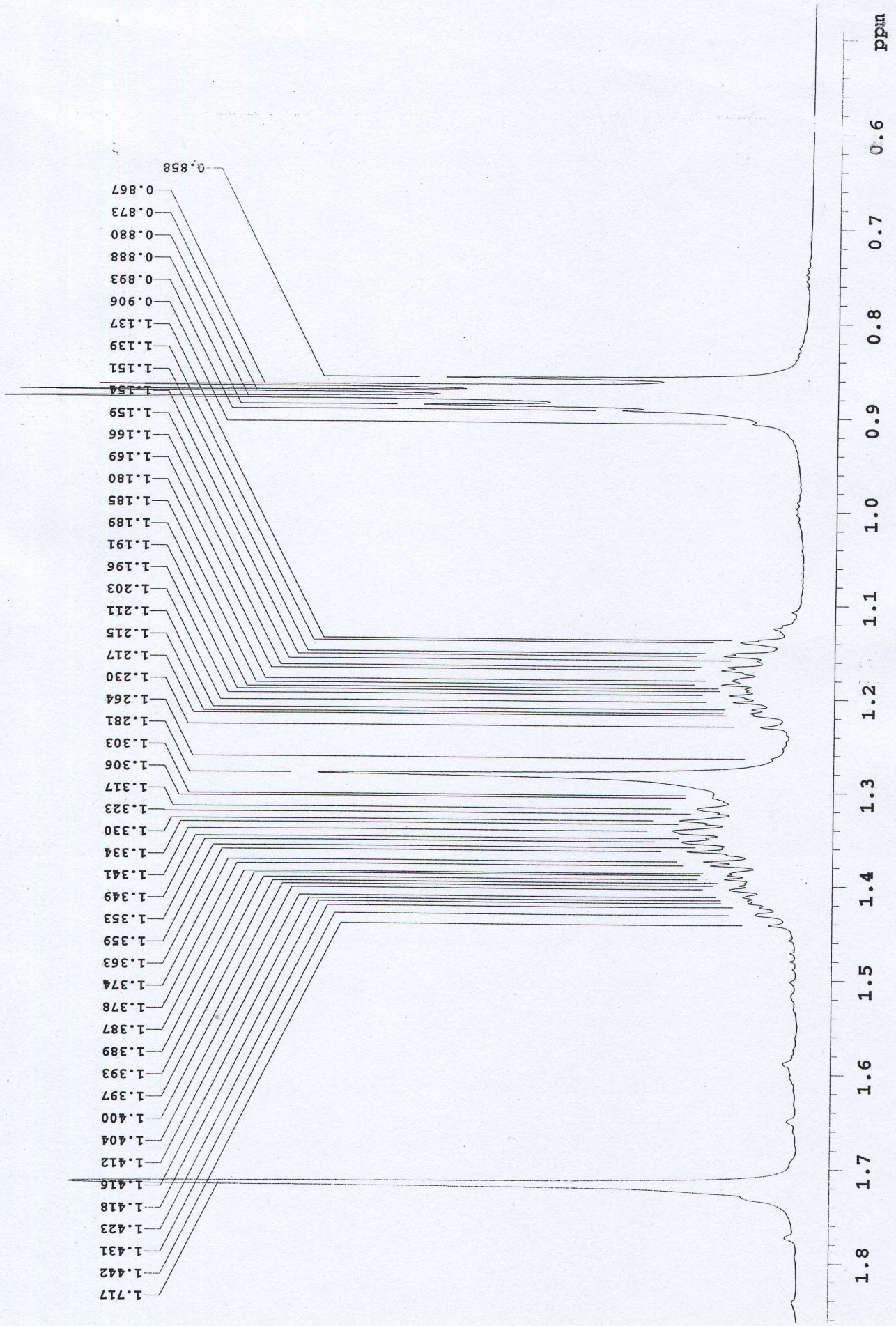


Denmark, Regens, Kobayashi

S60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1.159
1.166
1.169
1.180
1.185
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1.196
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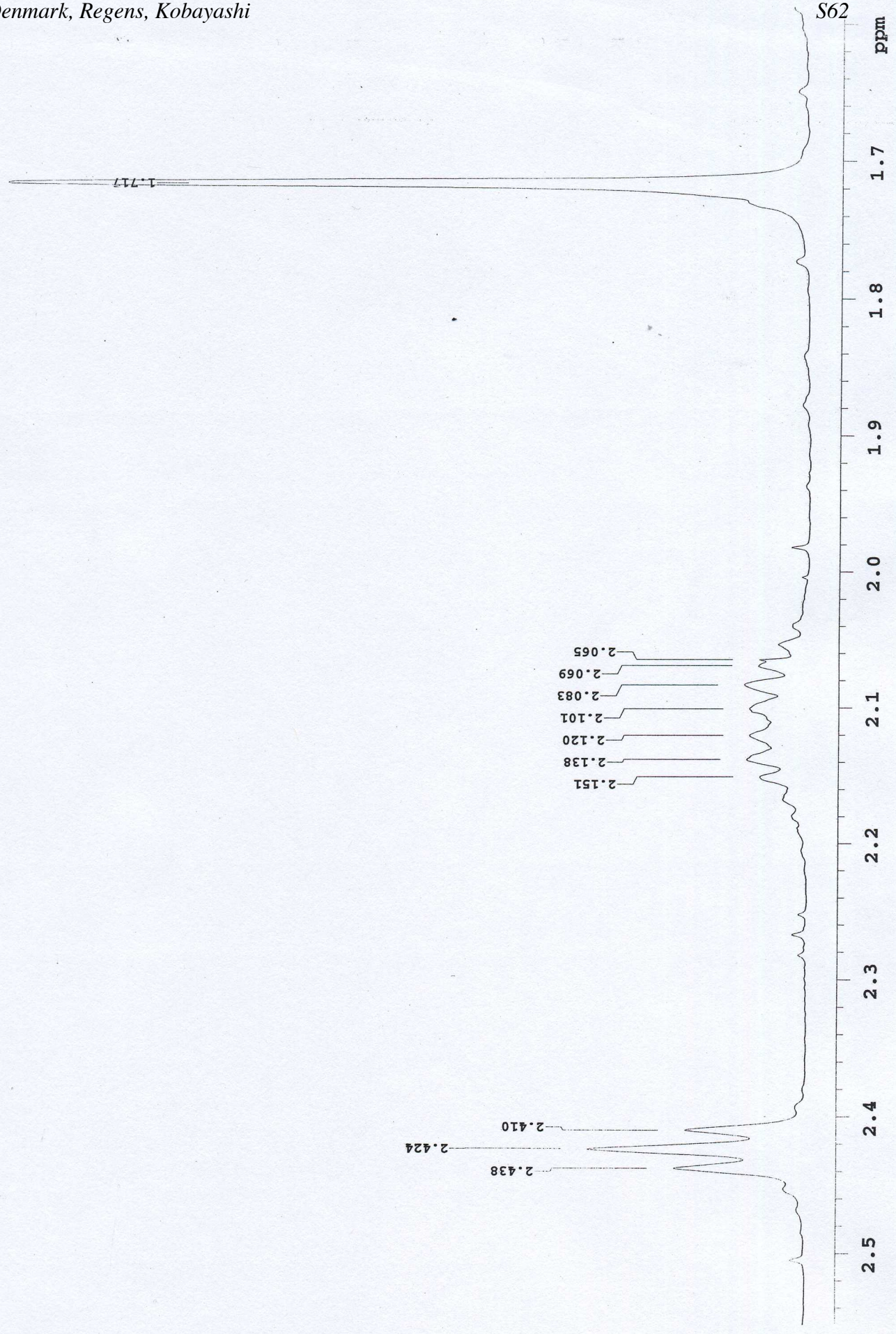
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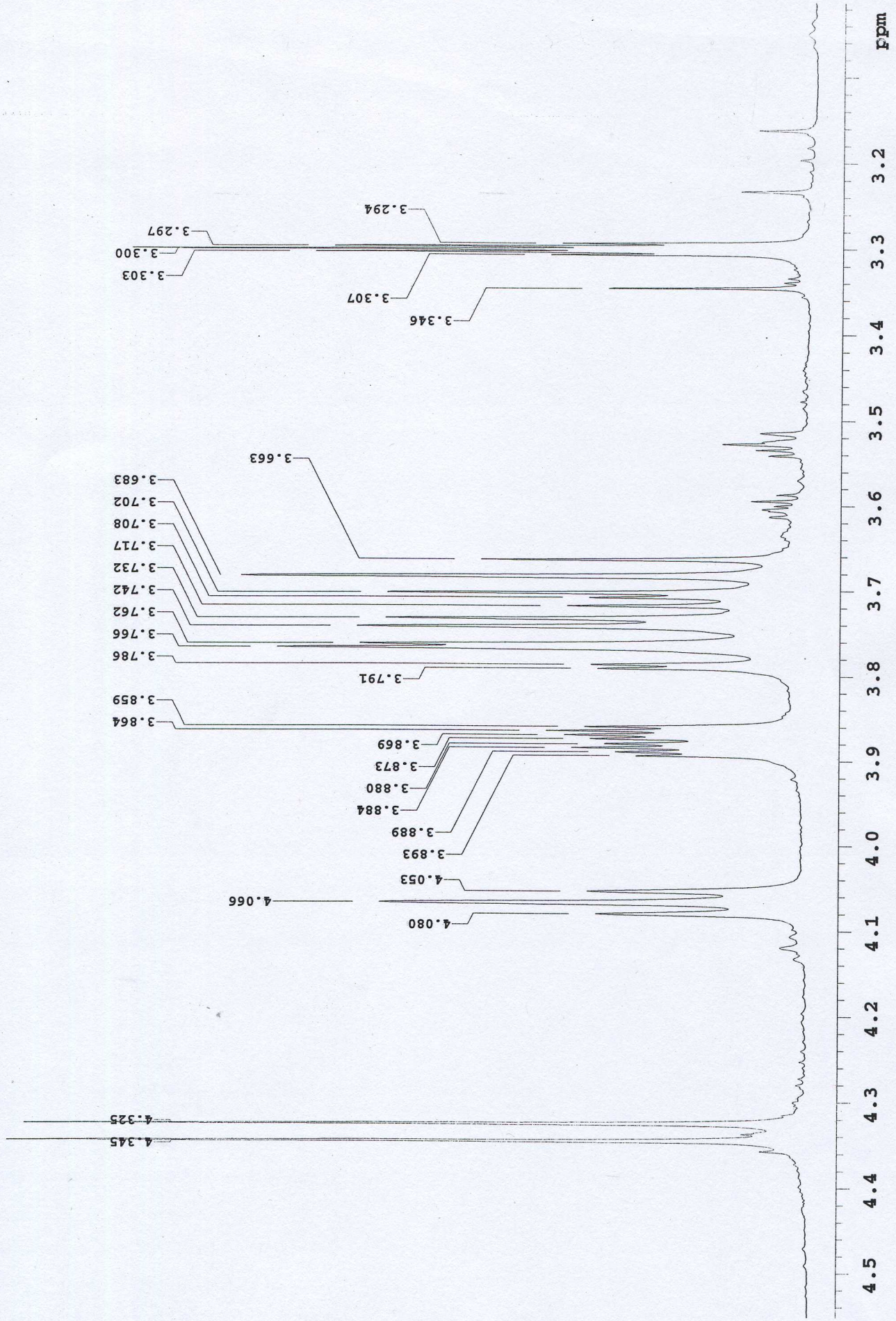
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3.859
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3.786
3.766
3.762
3.742
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3.708
3.702
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3.346
3.307
3.303
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3.297
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4.5
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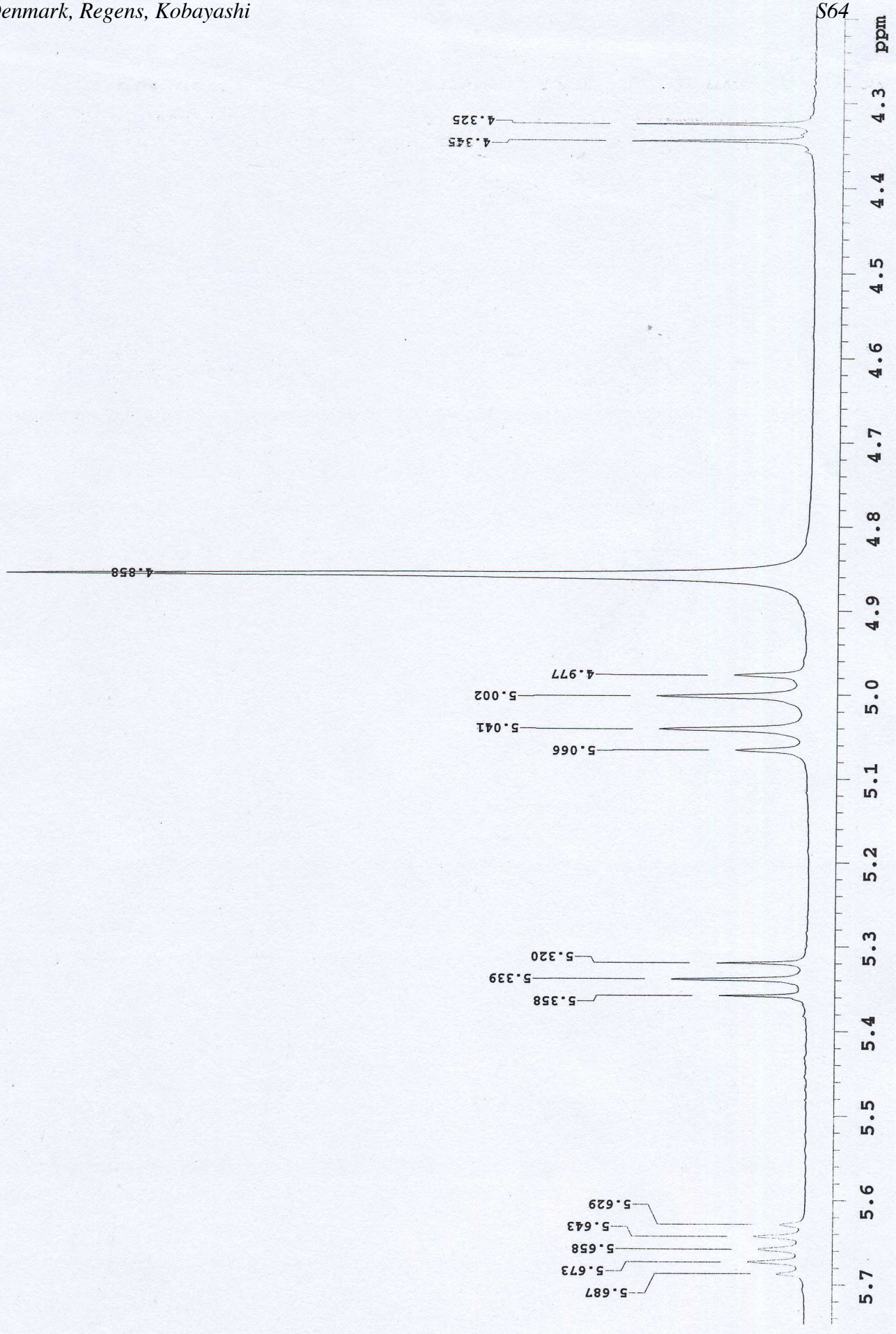
4.0
3.9
3.8
3.7
3.6
3.5
3.4
3.3
3.2
ppm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5.673
5.687
ppm
4.3
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4.5
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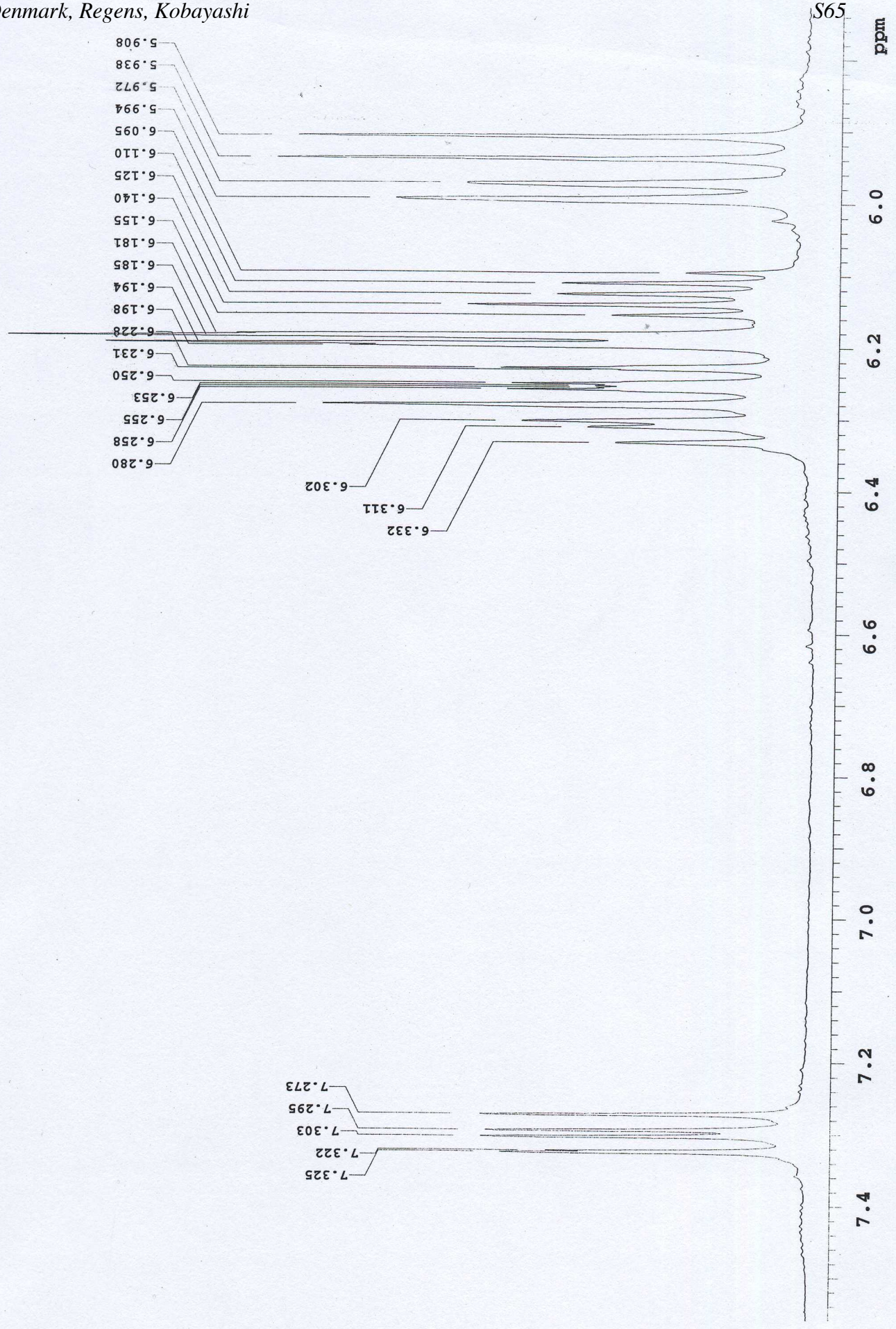
5.7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6.198
6.228
6.231
6.250
6.253
6.255
6.258
6.280
6.302
6.311
6.332
7.273
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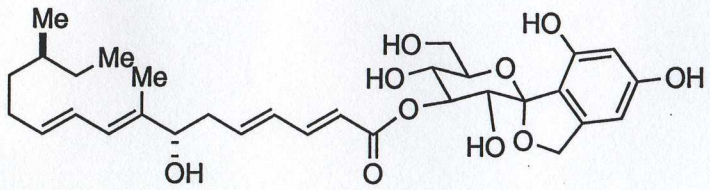
7.4



C R-IX-p095-papulacandin-D-13C

exp1 s2pul

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file	/export/home/~	dpwr	42
data/u500/regens/C~		dof	-827.6
SR-IX-p095-papulac~		dm	yyy
andin-D-13C.fid		dmm	w
ACQUISITION		dmf	13369
sfrq	125.663	dseq	
tn	C13	dres	90.0
at	1.086	homo	n
np	65536	DEC2	
sw	30165.9	dfrq2	0
fb	16600	dn2	
bs	16	dpwr2	1
ss	1	dof2	0
tpwr	57	dm2	n
pw	3.3	dmm2	c
d1	1.000	dmf2	10000
tof	1884.7	dseq2	
nt	1e+07	dres2	1.0
ct	7140	homo2	n
alock	n	PROCESSING	
gain	not used	lb	1.00
FLAGS		wtfile	
il	n	proc	ft
in	n	fn	not used
dp	y	math	f
hs	nn		
DISPLAY		werr	
sp	-1090.8	wexp	
wp	30165.0	wbs	
vs	620	wnt	
sc	0		
wc	250		
hzmm	4.10		
is	500.00		
rfl	7267.4		
rfp	6175.7		
th	9		
ins	100.000		
nn	ph		