Total Synthesis of (+)-Papulacandin D

Scott E. Denmark* Tetsuya Kobayashi and Christopher S. Regens

Department of Chemistry, University of Illinois Urbana-Champaign, Urbana, Illinois 61801

SUPPORTING INFORMATION

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General Experimental

All reactions were performed in oven (120 °C) and/or flame dried glassware under an atmosphere of dry nitrogen or argon, unless otherwise 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 $Mg(OMe)_2$ 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) isopropyl acetate (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 ($Pd_2(dba)_3 \bullet CHCl_3$) 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. Hexamethylphosphoramide (Aldrich, HMPA) was distilled and

then stored over 3Å molecular sieves prior to use. 2,4,6-Trichlorobenzoyl chloride (Aldrich), acrolein (Fluka) was 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%+), 2-(trimethylsilyl)ethoxymethyl chloride (SEM-Cl) (Aldrich, >95%), citric acid monohydrate (Fisher), lithium hydroxide monohydrate (Fisher), sodium thiosulfate pentahydrate (Aldrich, ACS Grade), pyridinium-*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 ($KOSiMe_3$) (Gelest, 95%), sodium *tert*-butoxide (NaO*t*-Bu) (Strem, 97%), hydrofluoric acid (HF) (Fisher, 49%), thionyl chloride ($SOCl_2$) (Aldrich, 97%), methyl iodide (MeI) (Aldrich, 98%), H_2O_2 (30% aq, Fisher), I_2 (Aldrich), 3,4-dihydro-2H-pyran (DHP) (Aldrich), trimethylsilyl chloride (TMS-Cl) (Aldrich, 98%), imidazole (Aldrich), tetrabutylammonium iodide (TBAI) (Aldrich, 97%), tetrabutylammonium trifluoromethanesulfonate (TBAOTf) (Aldrich, >99%), triisopropylsilyl chloride (TIPS-Cl) (Gelest), triisopropyl trifluoromethanesulfonate (TIPS-OTf) (Fluka), silver trifluoromethanesulfonate (AgOTf) (Aldrich), tert-butyldimethylsilyl chloride (TBS-Cl) (Aldrich), *p*-toluenesulfonic acid (TsOH) (Aldrich), *n*-butyronitrile (Aldrich), benzonitrile (PhCN) (Aldrich), ethyl sorbate (Fisher), sorbic acid (Fisher), triethyl phosphite (Aldrich) 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,[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

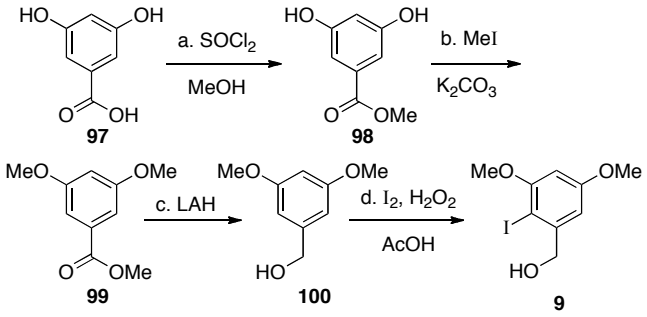
by s (singlet), d (doublet), t (triplet), q (quartet), sep (septet), m (multiplet), dd (doublet of doublets), ddd (doublet of doublet of doublets) dddd (doublet of doublet of doublet of doublets), tq (triplet of quartet), dt (doublet of triplet), td (triplet of doublets), nofoddd (non first order doublet 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

The following compounds were prepared by the procedures cited: allylpalladium(II) dimer,[8] ethyl 4-(diethoxyphosphinyl) tiglate,[9] (*S*)-(–)-citronellol,[10] allyltrichlorosilane,[11] *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*-**65**),[12] (*S*,*S*)-*N*,*N*'-bis[4,5-dihydro-3,5-dimethyl-4-(3 H-dinaphtho[2,1-d:1',2'-f][1,3,2]-2-oxo-diazaphosphepino)]-*N*,*N*'-dimethyl-1,5-pentadiamine ((*S*,*S*)-**104b**), ((*S*,*S*)-**104a-d** ((*S*,*S*)-**118**,[13] silyl enol ethers **60** and **110**,[14] di(*tert*-butyl)silyl ditriflate,[15] methyl (triphenylphosphoranylidene)acetate,[16] and trimethylsilylethoxy chlorocarbonate (TEOC-Cl),[17] tri-*O*-acetyl-D-glucal.[18]

Additional Optimization Experiments.

Preparation of Model Aromatic Iodide. The synthesis of the model protected aromatic iodide was accomplished in short order from 3,5-dihydroxybenzoic acid. Esterification of **97**, in the presence of thionyl chloride in MeOH, afforded methyl ester **98**. This was followed by protection of the resorcinol hydroxyl groups with methyl iodide, and reduction with lithium aluminum hydride affording benzyl alcohol **100** in excellent 75% yield over the three steps. Finally, electrophilic iodination of **100** provided the aromatic iodide **9** in good 76% yield.

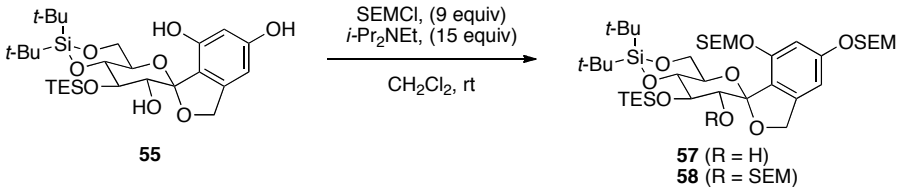


[a]Conditions: (a) $SOCl_2$, MeOH, reflux, 2 h, >99%; (b) K_2CO_3, MeI, acetone, reflux 0 h, >99%; (c) $LiAlH_4$, THF, 0 °C to rt, 75%; (d) I_2, H_2O_2, AcOH, 10 °C to 25°C, 3 h, 76%.

Scheme S1[a]

2-(Trimethylsilyl)-ethoxymethyl (SEM) Protection Optimization of the Spirocyclic Arylglycoside 55. A less sterically-demanding protecting group such as 2-(trimethylsilyl)-ethoxymethyl (SEM) ether was considered for the protection of the all three hydroxyl groups of triol **55**.[19] Unfortunately only two SEM groups were introduced to afford **57** as the major product, presumably due to a slow alkylation of the C(2)-hydroxyl group (Table S1, entries 1-4). To access the C(2) protected hydroxyl group, additives such as tetrabutylammonium iodide (TBAI) and AgOTf[20] were tested but with only moderate success (Table S1, entries 2-4). Resubjecting **58** to SEMCl in DMF, and in the presence of TBAI, again did not afford any of the tris-SEM ether 5**8** (Table S1, entry 5). Ultimately, **58** could be obtained in good yield using a combination of 3 equiv of TBAI and 9 equiv of AgOTf in DMF (Table S1, entry 6).

Table S1. SEM Protection of Triol **55**.



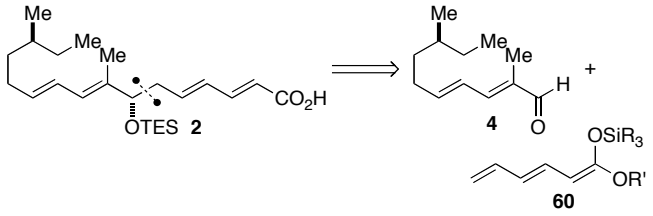
55

57 (R = H)
58 (R = SEM)

				yield, %[a]	
entry	additive, equiv.	conc. (**55**)	time, h	**57**	**58**
1	none	0.06 M	3	52	-
2	TBAI (4)	0.06 M	10	66	8
3	TBAI (4)	0.16 M	10	36	31
4	AgOTf (9)	0.016 M	3	53	19
5[b]	TABI (3)	0.6 M	10	82	-
6[c]	TABI (3) AgOTf (9)	0.6 M	3.5	-	74

[a.] Yield of isolated **57** and **58**. [b.] SEM-Cl (3.0 equiv), *i*-Pr_2NEt (5.0 equiv), TBAI (3.0 equiv), DMF, rt, 10 h. [c.] SEM-Cl (12.0 equiv), *i*-Pr_2NEt (20.0 equiv), TBAI (3.0 equiv), AgOTf (9.0 equiv), DMF, rt, 1 h.

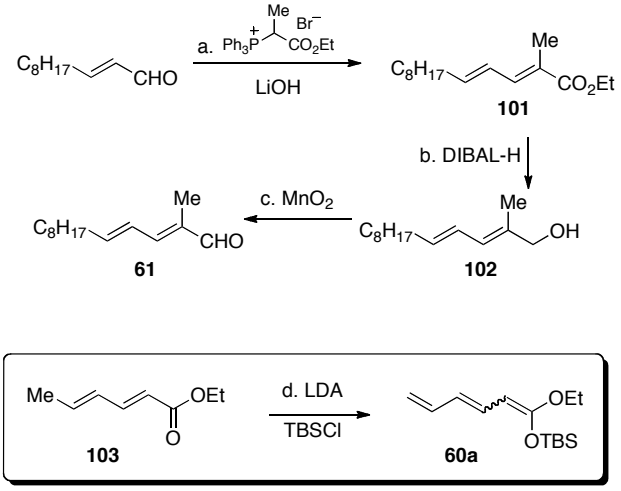
Model Study of Lewis-Base Catalyzed Asymmetric Aldol Addition Reactions. To set the C(7") stereogenic center of acid **2**, one of the most convergent routes would employ an asymmetric aldol addition reaction of a doubly vinylogous enolate **60** to aldehyde **4** (Scheme S3).



Scheme S2

To test this hypothesis, model aldehyde **61** was prepared (Scheme S3). Olefination of undecanal afforded dienoate **101** in 89% yield as a mixture (*E*/*Z,* 93:7) of geometrical isomers.

Dienoate **101** was then reduced to alcohol **102** with DIBAL-H, which was oxidized (MnO_2) to aldehyde **61** in 93% yield over the two steps.

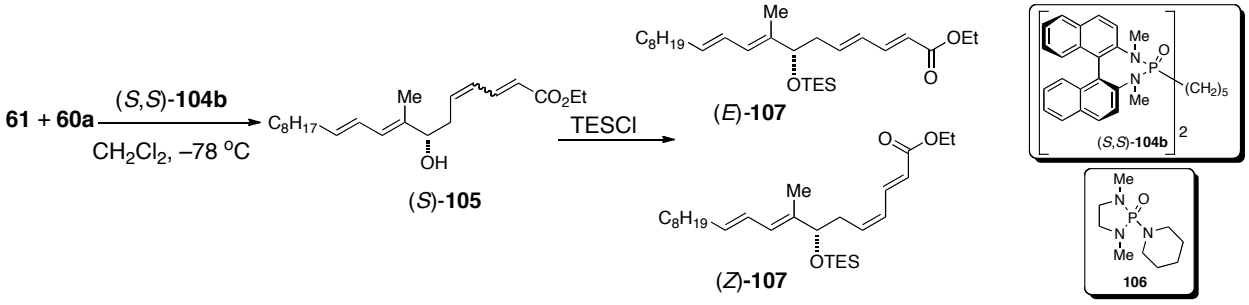


[a]Conditions: (a) $Ph_3CH(CH_3)CO_2EtBr$, LiOH, 3 Å MS, THF, reflux, (*E*/*Z* = 93:7), 97%.; (b) DIBAL-H, CH_2Cl_2, 0 °C, 89%.; (c) MnO_2, $CHCl_3$, 96%; (d) LDA, THF/HMPA, –78 °C, TBS-Cl, –78 to 0 °C, 81%.

Scheme S3.[a]

Next, the addition of trienyl silyl ketene acetal **60a** (easily prepared from ethyl sorbate, Scheme S3) to model aldehyde **61**, was tested under Lewis-base activation.[21] In the presence of silicon tetrachloride (1.0 equiv) and 0.01 equiv of bisphosphoramide catalyst (*S*,*S*)-**104b**,[22] the reaction provided only a 27% yield of product **105** after 3 h with exclusive ε-selectivity (Table S2, entry 1). To test if an increase in catalyst loading could effect a higher conversion, 0.4 equiv of monomeric, achiral catalyst **106** was used (Table S2, entry 2). After 3 h, the reaction was quenched and a 44% yield of the desired product was isolated as a mixture of geometrical isomers (*E*:*Z*, 75:25) which suffered elimination of the C(7") hydroxyl group. To circumvent this problem, it was found that immediate silyl protection of **105** provided a stable mixture of geometrical isomers, which were separable by preparative HPLC (Scheme S4). Once again the asymmetric doubly vinylogous aldol addition was attempted with 0.1 equiv of bisphosphoramide

(*S*,*S*)-**104b** (Table S2, entry 3). The tetraenoate was isolated in 53% yield as a 62:38 (*E*:*Z*) mixture of isomers. The mixture was immediately subjected to the TES protection conditions to afford a mixture of silyl ethers **107** in 93% yield, with little change to the isomeric ratio. The isomeric mixture was separated by HPLC and the enantiomeric purity of both isomers was determined by SFC analysis to be (61:39 er) for the *E*-isomer and (79:21 er) for the *Z*-isomer. To increase the yield of the aldol addition the reaction was run for 25 h, however little change in the yield and enantiomeric purity of either isomer was observed (Table S2, entry 4).



Scheme S4

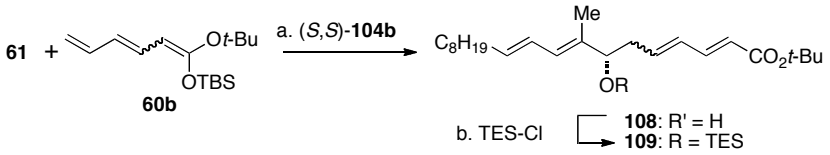
Table S2. Lewis-Base Catalyzed Doubly Vinylogous Aldol Reaction.

entry[a]	catalyst, (equiv)	time, h	*E*/Z, ratio[b]	er (*E*)/(Z)[c]	yield, %[d]
1	(*S*,*S*)-**104b** (0.01)	3	-	-	27
2	**106** (0.4)	3	75:25		44
3	(*S*,*S*)-**104b** (0.1)	3	62:38	(61:39) / (79:21)	53
4	(*S*,*S*)-**104b** (0.01)	25	60:40	(57:43) / (76:24)	55

[a.] Conditions: **60a** (1.2 equiv), $SiCl_4$ (1.1 equiv), *i*-Pr_2NEt (0.4 equiv), –78 °C, CH_2Cl_2. [b.] The isomer ratio was determined by coupling constants and nOe analysis. The isomers were separated by preparative HPLC. [c.] er determination from TES ether **107** using CSP-SFC analysis. [d.] Yield of isolated, isomeric mixture.

Previous studies in these laboratories with ester-derived dienolates demonstrated the site- and enantioselectivity of the addition is largely influenced by the size of the alkoxy substituents.[23] Therefore, the *tert*-butyl hexenoate-derived *tert*-dimethyl silyl ketene acetal **60b** was synthesized and subjected to the asymmetric aldol reaction.[24] The aldolate **108** was isolated as a mixture of geometrical isomers in 70% yield (Scheme S5). Subsequent, TES protection

proceeded quantitatively and the mixture of isomeric silyl ethers were separated by HPLC. Unfortunately, the enantiomeric ratio was not significantly improved (*E*-isomer, 60:40 er; *Z*-isomer, 78:22). Because of the low enantioselectivity, tedious separation and poor geometric selectivity,[25] of the doubly vinylogous aldol reaction, this approach was abandoned.

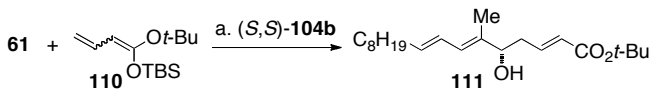


[a]Conditions: (a) (*S*,*S*)-**104b** (0.1 equiv), $SiCl_4$ (1.1 equiv), *i*-Pr_2NEt (0.4 equiv), CH_2Cl_2, –78 °C, 3 h, (*E*/*Z*; 64:34), (er (*E*/*Z*) (60:40/78:22)); 63%; (b) TES-Cl, Et_3N, rt, CH_2Cl_2, >99%.

Scheme S5[a]

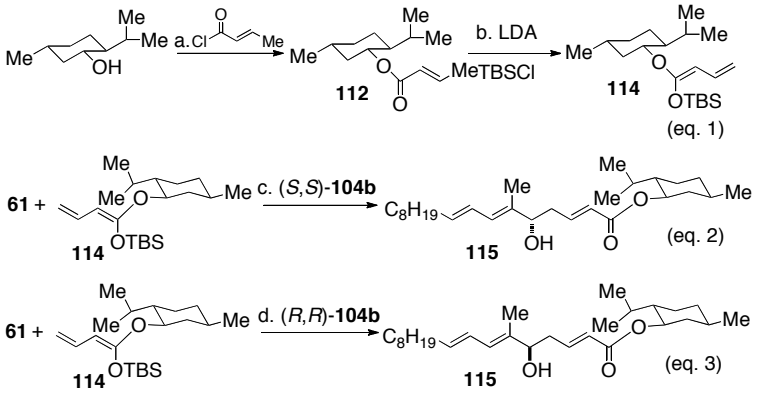
Vinylogous Aldol Addition. On the basis of extensive studies on these Lewis-based catalyzed, vinylogous aldol reaction of silyl dienol ethers,[21c-d] higher enantioselectivity and exclusive γ-site selectivity was anticipated. However, now a two-carbon homologation would be required to complete the synthesis of the fatty acid **2**. Thus, the *tert*-butyl propanoate-derived silyl ketene acetal **110**[23] was employed in the aldol reaction of **61**, under the action of (*S*,*S*)-**104b** at –78 °C for 3 h (Scheme S6). The aldol product **111** was isolated as a single geometrical isomer with high γ-selectivity, but unfortunately with poor enantioselectivity (60:40 er).

Potentially, catalyst control alone is not sufficient to obtain high enantiomeric ratios of α-methyl substituted unsaturated aldehydes such as **61**.[23] Therefore, to increase the enantio-selectivity, a diastereoselective aldol reaction was considered. Chiral silyl ketene acetal **114**, prepared from L-menthyl 2-propenoate **112** (Scheme S7), was employed in the aldol reaction catalyzed by (*S*,*S*)-**104b** to afford the product **115** in 31% yield and with an diastereomeric ratio of 66:34 (Scheme S7, eq. 2). However, when the aldol reaction was catalyzed by (*R*,*R*)-**104b**, **115** was isolated in 73% yield, but with lower diastereoselectivity (42:58) (Scheme S7, eq. 3).



[a]Conditions: (a) (*S*,*S*)-**104b** (0.1 equiv), $SiCl_4$ (1.1 equiv), *i*-Pr_2NEt (0.4 equiv), CH_2Cl_2, –78 °C, 3 h, (60:40 er), 80%.

Scheme S6[a]



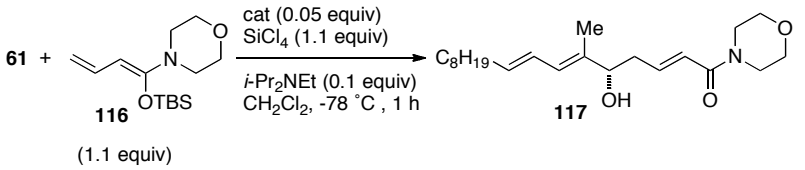
[a]Conditions: (a) crotyl chloride, Et_3N, 71%; (b) LDA, HMPA, –78 °C, TBSCl, –78 to rt, 79%; (c) (*S*,*S*)-**104b** (0.1 equiv), $SiCl_4$ (1.1 equiv), *i*-Pr_2NEt (0.4 equiv), CH_2Cl_2, –78 °C, 20 h, (66:34 dr), 31%. (d) (*R*,*R*)-**104b** (0.1 equiv), $SiCl_4$ (1.1 equiv), *i*-Pr_2NEt (0.4 equiv), CH_2Cl_2, –78 °C,8 h, (42:58 dr), 73%.

Scheme S7[a]

Given these disappointing results one final attempt was made to increase the yield and selectivity using the recently developed, asymmetric, vinylogous ketene aminal aldol reaction.[26] Dienolate **116** was employed in the aldol addition reaction of aldehyde **61** using 0.05 equiv of (*S*,*S*)-**104b** at –78 °C (Table S3, entry 1). After 1 h the reaction was quenched at –78 °C, and the γ-1,2 addition product **117** was isolated 81% yield, unfortunately with low enantioselectivity (55:45 er). Next, a number of other Lewis-base catalysts were surveyed to increase the enantioselectivity and an interesting trend was observed (Table S3, entries 2-5). In all previous studies, the five-methylene linked catalyst was optimal for the aldol addition.[26] However, in this

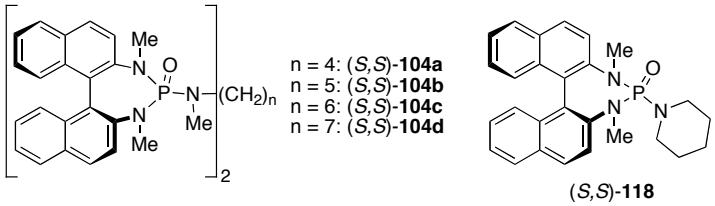
case, as the linker length increased the enantioselectivity increased. The highest selectivity was observed using the six and seven-carbon linker catalysts (~78:22 er) (Table S3, entries 3-4).

Table S3: Lewis-Base Ketene Aminal Dienolate Aldol Addition.



entry	cat.	n	additive (equiv)	yield, %[a]	er [b]
1	(*S*,*S*)-**104b**	5	-	81	55.1:44.9
2	(*S*,*S*)-**104a**	4	-	78	67.0:33.0
3	(*S*,*S*)-**104c**	6	-	87	77.8:22.2
4	(*S*,*S*)-**104d**	7	-	81	77.5 : 22.5
5	(*S*,*S*)-**118**	0	-	91	61.4:38.6
6[c]	(*S*,*S*)-**104d**	7	-	68	71.3:28.7
7	(*S*,*S*)-**104d**	7	Bu_4NOTf (0.05)	76	75.4:24.6

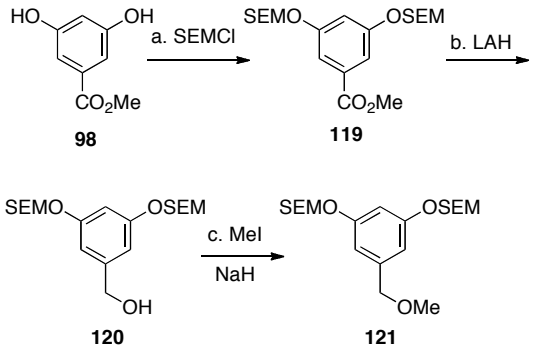
[a]Yield corresponds to isolated product. [b] The enantiomeric ratio was determined by CSP-SFC. [c] The reaction was run at –90 °C for 3 h.



Further modifications of the reaction conditions were examined to improve the enantioselectivity. At –90 °C, using 0.05 equiv of (*S*,*S*)-**104d** the reaction was a thick slurry and did not go to completion after 3 h. The yield and enantioselectivity was slightly lower compared to Table S3, entry 6. Finally, ammonium salts such as tetrabutylammonium triflate (Bu_4NOTf),[26] which has been demonstrated to increase the enantioselectivity, unfortunately, did not provide any advantage (Table S3, entry 7).

Although many attempts were made to set the C(7") stereogenic center through Lewis-base catalyzed aldol reactions, a suitable method providing a high yield and enantiomeric ratio were not found.

Model Study of SEM Deprotection. The last step in the synthesis is the global deprotection of all the silicon-protecting groups in the natural product. Standard fluoride sources such as TASF, TBAF, HF•Et_3N, etc. were expected cleave the protecting groups in one step, thus revealing the natural product. To find optimal conditions for the cleavage of the SEM protecting groups, it was decided to work with a simple model compound **121**. The model compound was prepared from methyl 3,5-dihydroxybenzoate as illustrated in scheme S8.



[a]Conditions: (a) SEM-Cl, *i*-Pr_2NEt, CH_2Cl_2, rt, 6 h, 97%-98%; (b) LAH, THF, 0 °C to rt, 30 min, 91%; (c) NaH, MeI, 0 °C to rt, 30 min, 97%.

Scheme S8[a]

A variety of conditions were surveyed that are known for silicon- and SEM ether deprotection (Table S4).[27] A solution of TBAF in HMPA in the presence of 4Å molecular sieves provided the mono-deprotected product **122** in 72% yield (Table S4, entry 1). Extending the reaction time and temperature led to decomposition of the starting material (Table S4, entries 2-3). The deprotection with tetramethylammonium fluoride[27c] (TMAF) in HMPA was extremely slow and provided only a 15% yield of **122** (Table S4, entry 4). Tris(dimethylamino)sulfonium difluorotrimethyl silicate[27c] (TASF) also gave **122** preferentially (Table S4, entries 5-6).

Surprisingly, the SEM-ethers were stable to buffered hydrofluoric acid (Table S4, entry 7). Mild Lewis acids such as ZnBr[27h] and ZnF[27h] were not effective (Table S4, entries 8-9).

Finally, the combination of $MgBr_2$ and *n*-BuSH[27e] gave the desired deprotected product quantitatively; however, a significant solvent effect was observed for the deprotection (Table S4, entries 10-11).

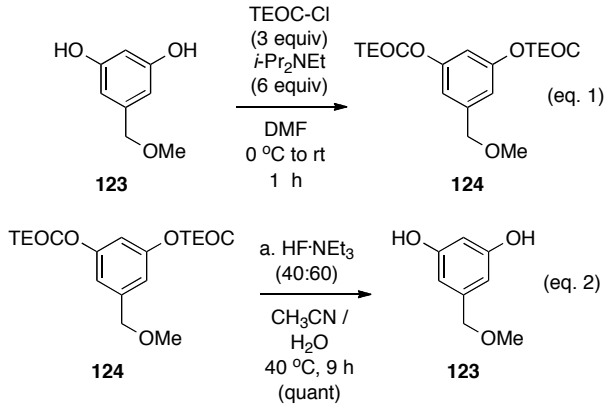
Table S4. Survey of SEM-ether Deprotection Conditions.

		yield, %[c]	
entry	conditions	**122**	**123**
1	TBAF•3H_2O (10 equiv), MS 4Å, HMPA, 1 h	72	-
2	TBAF•3H_2O (10 equiv), MS 4Å, HMPA, 12 h	12	21
3[a]	TBAF•3H_2O (10 equiv), MS 4Å, HMPA, 2 h	-	-
4[b]	TMAF•H_2O (10 equiv), HMPA, 40 h	15	-
5[d]	TASF (15 equiv), THF, 48 h	38	-
6	TASF (15 equiv) HMPA, 48 h	68	32
7	HF•NEt_3 (70:30) (12 equiv) H_2O/CH_3CN, rt , 48 h	-	-
8	$ZnBr_2$ (20 equiv) MeOH (40 equiv) CH_2Cl_2, 1 h	-	-
9	ZnF_2 (20 equiv) CH_2Cl_2, 12 h $MgBr_2$ (20 equiv) CH_3NO_2	-	-
10	(40 equiv) Et_2O, 3 h $MgBr_2$ (20 equiv), *n*-BuSH	-	-
11	(40 equiv) Et_2O, h	-	99

[a.] 50 °C.; [b.] **121** was recovered in 76%.; [c.] yields of isolated products.
[d.] Product was isolated as a 62:38 mixture of **121**:**122**.

2-(Trimethylethylsilylethoxycarbonyl) (TEOC) Protecting Group Strategy. The model resorcinol **123** was then protected as the bis TEOC carbonate quantitatively using 3 equiv TEOC-Cl, in the presence of 6 equiv *i*-Pr_2NEt (Scheme S9, eq. 1). To our delight, the TEOC groups in **124** could be quantitatively removed using a mixture of HF•NEt_3 (40:60) in CH_3CN at

40 ºC for 9 h (Scheme S9, eq. 2).[28]

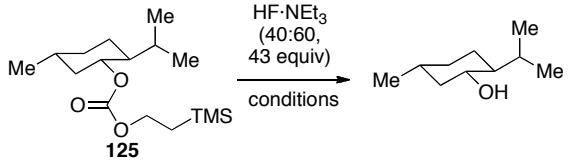


[a]Conditions: 42.9 equiv of fluoride was at 1.67 M.

Scheme S9[a]

Finally, to evaluate if the sterically congested C(2)-TEOC protecting group could be removed using HF•NEt_3 solution, TEOC protected menthol **125** was used as a test substrate. A variety of reaction variables were systematically surveyed (time, concentration of fluoride, HF•NEt_3 ratio, temperature and solvent) and some representative examples are presented in Table 5. These studies concluded that the rate of TEOC cleavage in DMSO was significantly faster than the other solvents (Table S5, entries 7 and 8).

Table S5. Model Study for the TEOC Deprotection of **125**.



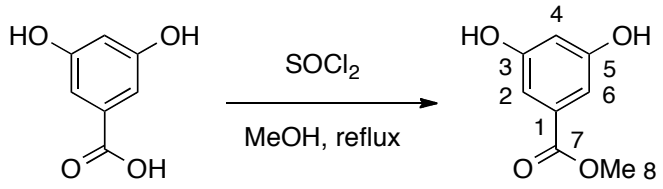
		Conditions			
entry[a,b]	solvent	conc. (fluoride, M)	temp, ºC	time, h	ratio (**125**:menthol)
1	CH_3CN/H_2O	1.67	40	9	90:10
2	CH_3CN/H_2O	1.67	40	42	76:24
3	CH_3CN/H_2O	2.51	40	9	87:13
4[c]	CH_3CN/H_2O	2.88	40	9	86:14
5	CH_3CN/H_2O	1.67	60	9	74:26
6	THF/H_2O	1.67	60	9	decomp.
7	$DMSO/H_2O$	1.67	60	9	22:78
8	$DMSO/H_2O$	1.67	40	9	72:28

[a.] The each reaction was carried out in a poly-styrene test tube using 5 mg of TEOC protected L-menthol. [b.] Time (entries 1, 2), concentration (entries 1, 3); HF:Et_3N-ratio (entries 3,4), reaction temp. (entries 1, 5) and solvent (entries 5, 6, 7 and entries 1, 8) were systematically surveyed. [c.] The HF:Et_3N-ratio was 46:54.

Experimental Procedures.

Preparation of Aromatic Iodides.

Preparation of Methyl 3,5-Dihydroxybenzoate (98)[29] [CSR-IV-89]



97 **98**

A 500-mL, three-necked, round-bottomed 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 (**97**, 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 rt. 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-bottomed 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 **98** as a powdery, beige solid.

Data for **98**:

mp: 168 - 169 ^{o}C (MeOH)

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

9.64 (br, 1 H, (OH)), 6.80 (d, J = 2.2, 2 H, HC(2)), 6.43 (t, J = 2.2, 1 H, HC(4)), 3.77 (s, 3 H, 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)

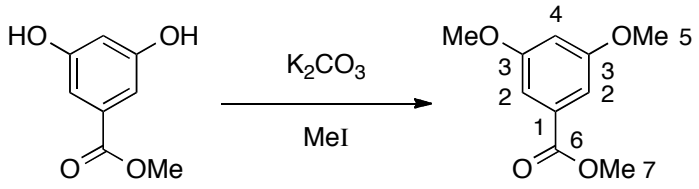
3560 (s), 3050 (s), 2910 (s), 1710 (s), 1590 (s), 1320 (m), 1280 (m)

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 3,5-Dimethyloxy-1-hydroxymethylbenzene (99)[30] [TK-VIII-49]



98 **99**

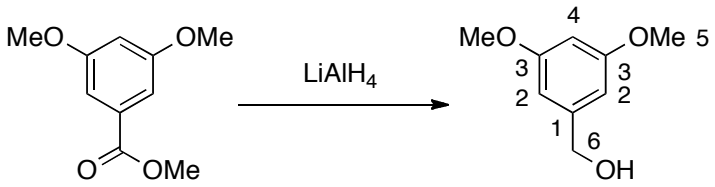
A 500-mL, three-necked, round-bottomed flask equipped with a large magnetic stir-bar, septum, water condenser, and nitrogen inlet was purged with nitrogen and charged with **98** (10.91 g, 64.88 mmol) and acetone (60 mL). Potassium carbonate (26.90 g, 194.64 mmol, 3.0 equiv) was added and a brown mixture was observed. Then, methyl iodide (12.12 mL, 194.64 mmol, 3.0 equiv) was added by syringe to the mixture. The mixture was heated at reflux for 10 h. After heating the contents were cooled to rt and the off-white precipitate was filtered using a medium 120 mL glass filter. The solvent was removed using rotary evaporation and the resultant residue was dissolved in CH_2Cl_2 (100 mL) and transferred to a 500-mL separatory funnel and washed with H_2O (100 mL). The aqueous layer was then extracted with CH_2Cl_2 (2 x 100 mL). The combined organic layers were washed with brine (100 mL), dried with Na_2SO_4 and then the solvent was removed using rotary evaporation to afford **99** (12.75 g, quant.) as light-yellow crystals. The physical and spectroscopic properties matched those described in the literature.[30]

Data for **99**:

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

7.19 (d, J = 2.0, 2 H, 1 H, HC(2)), 6.65 (t, J = 2.0, 1 H, HC(4)), 3.91 (s, 3 H, H_3C(6)), 3.83 (s, 6 H, H_3C(5))

Preparation of 3,5-Bis(methoxy)benzenemethanol (100)[30] [TK-VIII-50]



99 **100**

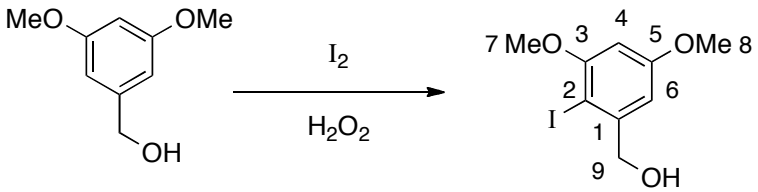
A 250-mL, two-necked, round-bottomed flask equipped with a magnetic stir-bar, argon inlet and a rubber septum was purged with argon and charged with **99** (12.73 g, 64.88 mmol) followed by THF (20 mL). The solution was then cooled to 0 °C using an ice bath. Lithium aluminum hydride (2.46 g, 64.88 mmol, 1.0 equiv)[7] was added cautiously over 15 min (maintaining the internal temperature between 10 to 15 °C). After the addition was complete the resulting solution was stirred at 0 °C for an additional 15 min and then warmed to rt and stirred for 30 min, whereupon the solution was once again cooled to 0 °C and Celite (10 g), EtOAc (~120 mL), MeOH (10 mL) and H_2O (5 mL) were sequentially added into the mixture. Upon warming to rt, the white suspension was filtered through Celite (100 g) and the Celite pad was washed with THF (40 mL). The filtrate was concentrated under reduced pressure by rotary evaporation. The resulting crude product (11.69 g) was purified by silica gel chromatography (SiO_2, 400 g, hexanes/EtOAc, 3:1 to EtOAc/hexanes, 2:1), to afford **100** (8.16 g, 75%) as white needles. The physical and spectroscopic properties matched those described in the literature.[30]

Data for **100**:

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

6.53 (d, J = 2.0, 2 H, HC(2)), 6.39 (t, J = 2.0, 1 H, HC(4)), 4.64 (s, 2 H, H_2C(6)), 3.80 (s, 6 H, H_3C(5)), 1.67 (s, 1 H, OH))

Preparation of 2-Iodo-3,5-bis(methoxy)benzenemethanol (9)[30] [TK-VIII-51]



100 **9**

To a 250-mL, single-necked, round-bottomed flask equipped with a magnetic stir-bar, argon inlet, was purged with argon and charged with **100** (8.16 g, 48.52 mmol) followed by

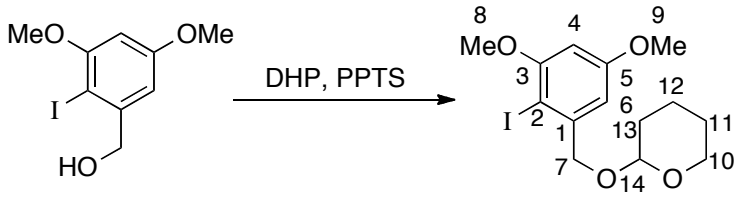
acetic acid (80 mL). To this solution, iodine (12.31 g, 48.52 mmol, 1.0 equiv) was added. The reddish-brown contents were maintained at 10 °C using an ice bath. Then 30% H_2O_2 aq. (6.17 g, 53.37 mmol, 1.1 equiv) was added to the slurry over 0.5 h. maintaining the temperature at 10 °C. The resultant suspension was stirred for an additional 30 min. at 0 °C and then warmed to rt and stirred at this temperature for 2 h. The reaction was not complete (as judged by TLC analysis); therefore, more 30% H_2O_2 (0.62 g, 5.34 mmol, 0.1 equiv) was added at to the mixture at rt. After 1 h the suspension was poured over sat. aq. $Na_2S_2O_5$ solution and was extracted with EtOAc (4 x 50 mL). The combined organic layers were washed with brine (200 mL), and sat. aq. $NaHCO_3$ (200 mL) (until the pH of the aqueous layer was >7). The organic layer was once again washed with brine (2 x 100 mL), dried with Na_2SO_4 and concentrated to give (13.96 g) colorless crystals. The solid was dissolved in EtOAc (40 mL) and hexane (~200 mL) was slowly added until the solution became turbid. Upon standing at rt crystallization occurred and after filtration and drying under vacuum **9** (10.8 g, 76%) was isolated as white needles. Note: for extended storage **9** must be kept at –20 °C. The physical and spectroscopic properties matched those described in the literature.[30]

Data for **9**:

^{1}H NMR: (400 MHz, $CDCl_3$)

6.73 (d, J = 3.2, 1 H, HC(6)), 6.39 (d, J = 3.2, 1 H, HC(4)), 4.68 (s, 2 H, H_2C(9)), 3.87 (s, 3 H, H_3C(7 or 8)), 3.83 (s, 3 H, H_3C(7 or 8)), 2.10 (s, 1 H, (OH))

Preparation of 2-Iodo-3,5-dimethoxy-1-(tetrahydropyran-2-yl)oxymethylbenzene (26) [TK-VIII-54]



9 **26**

To a 100-mL, single-necked, round-bottomed flask equipped with a magnetic stir-bar, argon inlet with septum, was charged with dihydropyran (0.97 mL, 10.59 mmol, 1.5 equiv), followed by CH_2Cl_2 (15 mL) and PPTS (177.4 mg, 0.706 mmol, 0.1 equiv). The contents were cooled to 0 °C in an ice-bath. Then a suspension of iodobenzyl alcohol **9** (2.08 g, 7.06 mmol) in

CH_2Cl_2 (10 mL) was added at 0 °C over 10 min. After addition, the contents were warmed to rt. Dihydropyran (0.97 mL, 10.59 mmol, 1.5 equiv) was added again to the mixture after 30 min, because the starting material was still observed by TLC analysis. After another 30 min of stirring, H_2O (50 mL) was added and the mixture was extracted with CH_2Cl_2 (3 x 50 mL). The organic layers were combined and washed with brine (2 x 50 mL), dried with Na_2SO_4, filtered and the solvent was removed under reduced pressure by rotary evaporation. The crude material was further purified using column chromatography (SiO_2, 70 g; hexanes/EtOAc, 3:1) to afford (2.67 g, >99%) THP ether **26** as a colorless wax.

Data for **26**:

mp: 55 - 57 ^oC (hexane/EtOAc, 3:1)

^{1}H NMR: (400 MHz, $CDCl_3$)

6.76 (d, J = 2.4, 1 H, HC(6)), 6.38 (d, J = 2.4, 1 H, HC(4)), 4.78 (t, J = 3.4, 1 H, HC(13)), 4.75 (d, J = 13.6, 1 H, H_2C(7a or 7b), 4.52 (d, J = 13.6, 1 H, H_2C(7a or 7b)), 3.94 (ddd, J = 11.8, 8.6, 3.3, 1 H, HaC(10)), 3.86 (s, 3 H, H_3C(8 or 9)), 3.83 (s, 3 H, H_3C(8 or 9)), 3.54-3.62 (m, 1 H, HeC(10)), 1.50-1.98 (m, 6 H, H_2C(11, 12, 13))

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

161.1 (C(3)), 158.5 (C(5)), 142.8 (C(1)), 105.6 (C(6)), 98.4 (C(14)), 97.6 (C(4)), 78.2 (C(2)), 73.2 (C(7)), 62.2 (C(10)), 56.4 (C(8 or 9)), 55.4 (C(8 or 9)), 30.5 (11 or 12 or 13)), 25.3 (11 or 12 or 13)), 19.4 (11 or 12 or 13))

IR: (neat)

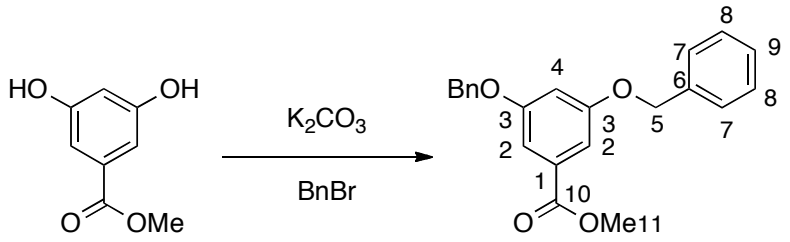
2939 (s), 1582 (s), 1452 (s), 1430 (s), 1387 (w), 1347 (m), 1323 (s), 1221 (w), 1200 (s), 1160 (s), 1128 (m), 1068 (m), 1034 (s), 975 (w)

MS: (EI, 70 eV)

378 (M^+, 5), 278 (100), 277 (75), 151 (78), 135 (14), 85 (28)

TLC: R_f 0.26 (hexanes/EtOAc, 10:1) [SiO_2, UV]

Preparation of Methyl 3,5-Bis(phenylmethoxy)benzoate (126)[29] [CSR-V-2]



98 **126**

A 500-mL, single-necked, round-bottomed flask equipped with a large magnetic stir-bar and nitrogen inlet was purged with nitrogen and charged with **98** (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 rt, the resulting mixture was stirred continuously at rt 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 **126** as a white crystalline powder.

Data for **126**:

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

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

7.45 (d, J = 7.1, 2 H, HC(7)), 7.41 (t, J = 7.1, 2 H, HC(8)), 7.37 (d, J = 7.1, 2 H, HC(9)), 7.34 (d, J = 2.2, 2 H, HC(2)), 6.83 (t, J = 2.4, 1 H, HC(4)), 5.09 (s, 4 H, HC(5)), 3.92 (s, 3 H, 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)

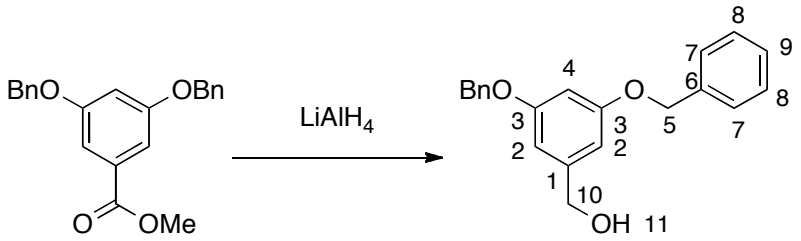
1714 (s), 1724 (s), 1597 (s), 1439 (s), 1378 (s), 1252 (s), 1083 (s), 966 (w), 868 (w), 763 (s)

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 (128)[29] [CSR-IV-95]



126 **127**

To a 250-mL, two-necked, round-bottomed flask equipped with a magnetic stir-bar, argon inlet and a rubber septum was purged with argon and charged with **126** (10.0 g, 28.7 mmol, 1.0 equiv) followed by THF (20 mL). The solution was then cooled to 0 ^oC 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 0.5 h (maintaining the internal temperature between 10 to 15 ^oC). After the addition was complete the resulting solution was stirred at rt for 3 h, whereupon the solution was once again cooled to 0 ^oC and H_2O (2.5 mL), 15% NaOH (2.5 mL), H_2O (7.5 mL) were added sequentially. Upon warming to rt, 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 **127** as white needles.

Data for **127**:

mp: 79 - 80 ^oC (EtOH)

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

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

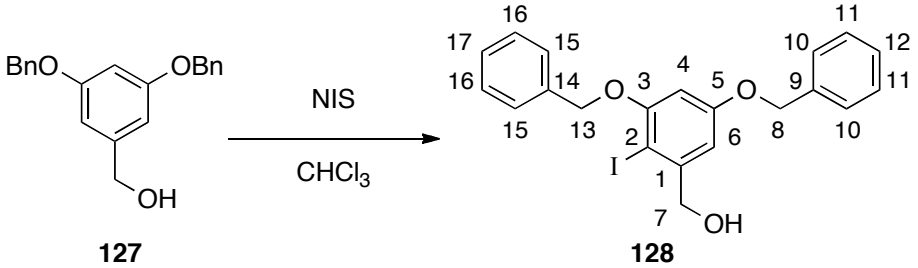
3303 (br), 3325 (m), 2923 (s), 1593 (m), 1497 (m), 1352 (m), 1285 (m), 1159 (s), 833 (m)

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 (128) [CSR-V-1]



A 250-mL, single-necked, round-bottomed flask equipped with a magnetic stir-bar, argon inlet, was purged with argon and charged with **127** (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 rt 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 **128**, as a white crystalline powder.

Data for **128**:

mp: 113-114 ^{o}C (4:1 heptane/isopropyl acetate)

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

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

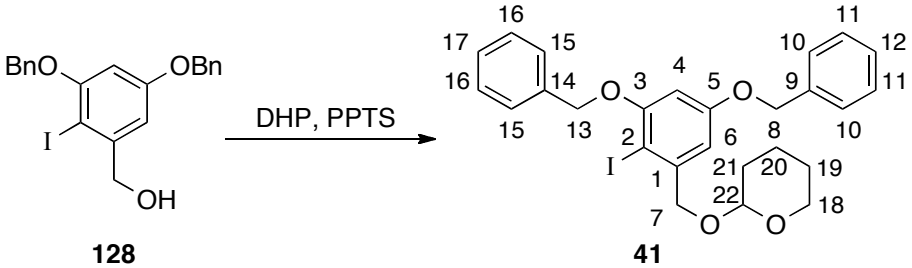
TLC: R_f 0.24 (hexanes/EtOAc, 10:1) [SiO_2, UV]

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 3,5-Bis(benzyloxy)-2-iodo-1-(tetrahydropyran-2-yloxymethyl)benzene (41) [TK-IX-95]



128 **41**

To a 100-mL, single-necked, round-bottomed flask equipped with a magnetic stir-bar and argon-inlet with septum, was added **128** (960.0 mg, 2.15 mmol) in CH_2Cl_2 (3 mL). The suspension was cooled to 0 ^{o}C and a solution of dihydropyran (0.29 mL, 3.23 mmol, 1.5 equiv) and PPTS (54.0 mg, 0.215 mmol, 0.1 equiv) in CH_2Cl_2 (2 mL) was added. After the addition, the

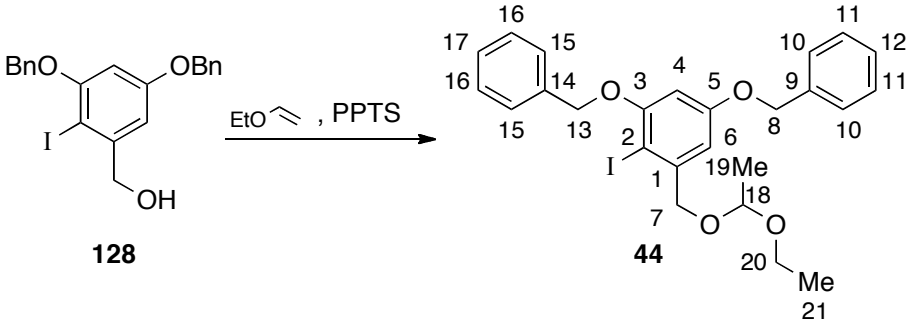
contents were warmed to rt. Then dihydropyran (0.29 mL, 3.23 mmol, 1.5 equiv) was again added to the mixture after 2 h, because starting material was still observed by TLC (hexane/EtOAc, 10:1). After another 1 h stirring, H_2O (30 mL) was added to the reaction and the mixture was extracted with EtOAc (3 x 30 mL). The combined organic layers were washed with brine (30 mL) and dried over Na_2SO_4, and then the solvent was removed under reduced pressure by rotary evaporation. The crude material was further purified by column chromatography (SiO_2, 70 g; hexanes/EtOAc, 7:1) to give (1.12 g, 98%) THP ether **41** as a colorless oil.

Data for **41**:

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

7.29-7.52 (m, 10H, HC(10, 11, 12, 15, 16, 17)), 6.85 (d, *J* = 2.9, 1 H, HC(4 or 6)), 6.49 (d, *J* = 2.9, 1 H, HC(4 or 6)), 5.11 (s, 2 H, H_2C(8 or 13), 5.06 (s, 2 H, H_2C(8 or 13)), 4.77 (t, *J* = 3.6, 1 H, HC(22)), 4.75 (d, *J* = 13.6, 1 H, HC(7a or 7b)), 4.53 (d, *J* = 13.6, 1 H, HC(7a or 7b)), 3.90 (ddd, *J* = 11.4, 8.9, 2.9, 1 H, HC(18a)), 3.53-3.60 (m, 1 H, HC(18b)), 1.48-1.94 (m, 6 H, H_2C(19, 20, 21))

Preparation of 3,5-Bis(benzyloxy)-2-iodo-1-(1-ethoxyethoxymethyl)benzene (44) [TK-X-24]



To a 100-mL, single-necked, round-bottomed flask equipped with a magnetic stir-bar and an argon inlet with a septum was charged with **128** (0.909 mg, 2.04 mmol, 1.0 equiv), followed by CH_2Cl_2 (4 mL). Then, ethyl vinyl ether (0.29 mL, 3.06 mmol, 1.5 equiv) and PPTS (51.3 mg, 0.204 mmol, 0.1 equiv) were added and the contents were stirred for 1 h at rt. The contents were quenched with H_2O (30 mL) and the aqueous layer was extracted with CH_2Cl_2 (3 x 30 mL). The combined organic layers were washed with brine (1 x 30 mL), dried with Na_2SO_4, and filtered. The contents were concentrated under reduced pressure by rotary evaporation. The crude product was purified using column chromatography (SiO_2, 70 g; hexane/EtOAc, 3:1) to provide (1.05 g, >99%) ethoxyethyl ether **44** as a light-yellow oil.

Data for **44**:

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

7.52-7.29 (m, 10H, HC(10, 11, 12, 15, 16, 17)), 6.85 (d, J = 3.1, 1 H, HC(4 or 6)), 6.49 (d, J = 3.1, 1 H, HC(4 or 6)), 5.11 (s, 2 H, H_2C(8 or 13)), 5.05 (s, 2 H, H_2C(8 or 13)), 4.87 (q, J = 5.0, 1 H, HC(18)), 4.64 (d, J = 12.5, 1 H, H_2C(7a)), 4.54 (d, J = 12.5, 1 H, HC(7b)), 3.60 (dq, J = 9.0, 7.0, 2 H, H_2C(20)), 1.40 (d, J = 5.0, 3 H, H_3C(19)), 1.22 (t, J = 7.0, 2 H, H_3C(21))

MS: (EI, 70 eV)

518 (M^+, 4), 446 (32), 152 (13), 91 (100), 77(10)

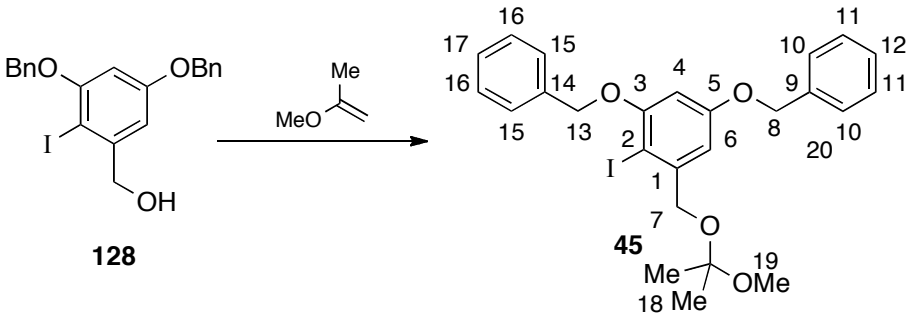
TLC: R_f 0.30 (hexanes/EtOAc, 10:1) [SiO_2, UV]

HRMS: $C_{25}H_{27}IO_4$ (518.38)

Calcd: 518.0956

Found: 518.0954

Preparation of 2-Iodo-3,5-bis(phenylmethoxy-1'-methoxy-1'-methylethoxymethyl)-benzenemethanol (45) [TK-X-26]



128 **45**

To a 25-mL, single-necked, round-bottomed flask equipped with a magnetic stir-bar, argon inlet with rubber septum, was charged with 2-methoxypropene (3.2 mL, 33.6 mmol, 15 equiv). Then a solution of **128** (1.0 g, 2.24 mmol, 1.0 equiv) in CH_2Cl_2 (4 mL) was added drop-wise over 5 min at rt. The contents were stirred at rt for an addition 20 min and the solvent was removed under reduced pressure by first rotary evaporation and then high vacuum. The desired product, **45** (1.05 g, 99%) was obtained as a colorless oil.

Data for **45**:

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

7.53-7.40 (m, 10H, HC(10, 11, 12, 15, 16, 17)), 6.87 (d, J = 2.7, 1 H, HC(4 or 6)),

6.49 (d, J = 2.7, 1 H, HC(4 or 6)), 5.12 (s, 2 H, H_2C(8 or 13)), 5.07 (s, 2 H, H_2C(8 or 13)), 4.47 (s, 2 H, H_2C(7)), 3.20 (s, 3 H, H_3C(19)), 1.42 (s, 6 H, $C(CH_3)$(18))

MS: (EI, 70 eV)

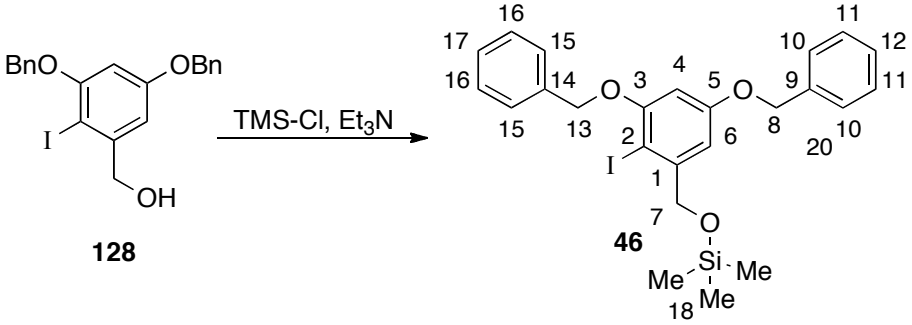
518 (M^+, 15), 447 (16), 446 (50), 149(33), 129(14), 125 (21), 111 (40), 109 (28), 97 (59), 91 (69), 84 (98), 57 (100)

HRMS: $C_{25}H_{27}IO_4$ (518.38)

Calcd: 518.09561

Found: 518.09544

2-Iodo-3,5-bis(phenylmethoxy-trimethylsilyl)benzenemethanol (46) [TK-IX-74]



To a 100-mL, single-necked, round-bottomed flask equipped with a magnetic stir-bar, argon inlet with a rubber septum, was charged with **128** (1.32 g, 2.96 mmol, 1.0 equiv), followed by THF (5 mL). Then Et_3N (0.83 mL, 5.92 mmol, 2.0 equiv) and TMS-Cl (0.56 mL, 4.44 mmol, 1.5 equiv) were added at rt. The contents were allowed to stir for 1 h at rt, then H_2O (30 mL) was added and the mixture was extracted with Et_2O (3 x 30 mL). The combined organic layers were washed with brine (30 mL) and dried with Na_2SO_4, filtered and concentrated under reduced pressure to give 1.63 g. The crude product was purified by column (SiO_2, 70 g; hexane/EtOAc, 7:1) to afford 1.36 g of **46** (89%) as a white solid.

Data for **46**:

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

7.52-7.28 (m, 10H, HC(10, 11, 12, 15, 16, 17)), 6.87 (d, J = 2.8, 1 H, HC(4 or 6)), 6.48 (d, J = 2.8, 1 H, HC(4 or 6)), 5.10 (s, 2 H, H_2C(8 or 13)), 5.06 (s, 2 H, H_2C(8 or 13)), 4.62 (s, 2 H, H_2C(7)), 0.19 (s, 9 H, $Si(CH_3)_3$(18))

IR: (KBr)

3088 (w), 3063 (m), 3031 (m), 2953 (M), 2871 (m), 1949 (w), 1869 (w), 1810 (w), 1582 (s), 1497 (s), 1438 (s), 1426 (s), 1375 (s), 1321 (s), 1278 (s), 1251 (s), 1215 (m), 1161 (s), 1063 (s) 874 (s), 842 (s)

MS: (EI, 70 eV)

518 (M^+, 23), 181 (15), 149 (51), 147 (14), 111 (11), 91 (100), 86 (17), 85 (25), 71 (33)

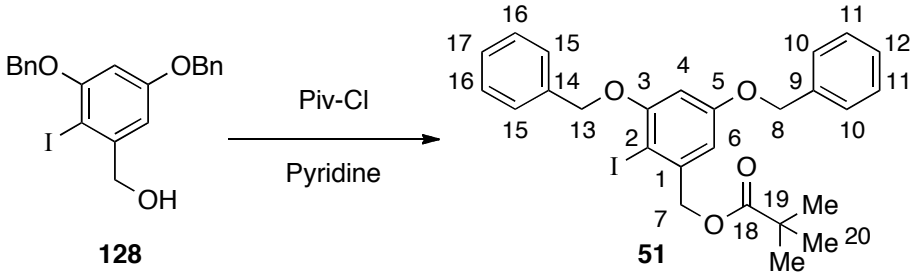
TLC: R_f 0.49 (hexanes/EtOAc, 10:1) [SiO_2, UV]

HRMS: $C_{24}H_{27}IO_3Si$ (518.46)

Calcd: 518.0778

Found: 518.0775

Preparation of 2-Iodo-3,5-bis(phenylmethoxy-2',2'-dimethylpropanoate)benzenemethanol (51) [CSR-V-27]



128 **51**

A 100-mL, two-necked, round-bottomed flask equipped with a magnetic stir-bar, argon inlet, and a rubber septum, was purged with argon and charged with **128** (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 rt 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, $NaHCO_{3(aq)}$ (30 mL) and brine (40 mL), dried $MgSO_4$, filtered, and concentrated. 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 **51** as white crystalline rhombuses.

Data for **51**:

mp: 50-51 ^oC (hexane)

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

7.49 (d, J = 7.6, 2 H, HC(16, 11)), 7.41-7.28 (m, 8H, HC(15, 17, 12, 10)), 6.69 (d, J = 2.7, 1 H, HC(6)), 6.52 (d, J = 2.4, 1 H, HC(4)), 5.13 (s, 2 H, H_2C(13)), 5.12 (s, 2 H, H_2C(8)), 5.04 (s, 2 H, H_2C(7)), 1.25 (s, 9 H, $C(H_3C)_3$(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, $KMnO_4$]

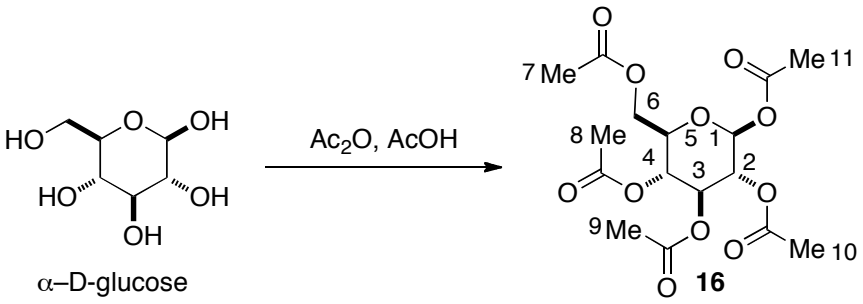
Analysis: $C_{26}H_{27}IO_4$ (530.39)

Calcd: C, 58.88 %; H, 5.13 %; I, 23.93 %

Found: C, 58.96 %; H, 5.15 %; I, 23.79 %

Preparation of Glucal Silanols.

Preparation of Pentaacetyl-β-D-glucose (16)[31] [TK-VIII-8]



To a 1000-mL, two-necked, round-bottomed flask equipped with a magnetic stir-bar, glass-stopper in one neck and a reflux-condenser with argon inlet in the other, was charged with NaOAc (7.50 g, 91.43 mmol, 1.1 equiv) in Ac_2O (105 mL, 1112.8 mmol, 13.37 equiv). The contents were heated to reflux using an oil bath to give a colorless suspension. Once at reflux

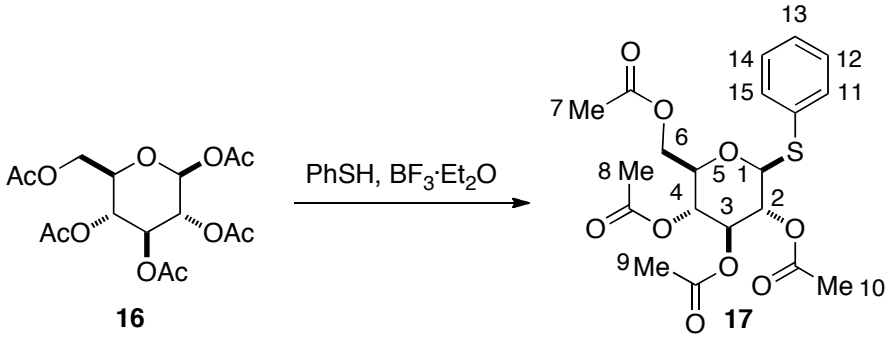
glucose (15.0 g, 83.26 mmol, 1.0 equiv) was added portion wise over 30 min. The contents were refluxed for another 30 min, at this point a light-yellow solution was observed. The contents were cooled to ambient temperature and H_2O (315 mL) was added (Note: the addition of water was slightly exothermic (~50 ^oC). This mixture was allowed to stand overnight (11 h). A colorless suspension formed overnight and was isolated using suction filtration. The solid was further dried by heating in a 80 ^oC water bath for 1 h to afford 34.75 g crude **16**. The crude product was recrystallized from hot EtOH (150 mL). The solution was cooled in an ice bath with stirring for 30 min; which gave 20.0 g (62%) of **16** as colorless needles. The physical and spectroscopic properties matched those described in the literature.[31]

Data for **16**:

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

5.71 (d, *J* = 8.7, 1 H, HC(1)), 5.25 (t, *J* = 9.2, 1 H, HC(3 or 4)), 5.14 (dd, *J* = 9.2, 8.7, 1 H, HC(2)), 5.13 (t, *J* = 9.2, 1 H, HC(3 or 4)), 4.29 (dd, *J* = 12.9, 4.6, 1 H, HC(6)), 4.11 (dd, *J* = 12.9, 2.3, 1 H, HC(6)), 3.84 (ddd, *J* = 9.2, 4.6, 2.3, 1 H, HC(5)), 2.11 (s, 3 H, H_3C(7 or 8 or 9 or 10 or 11)), 2.09 (s, 3 H, H_3C(7 or 8 or 9 or 10 or 11)), 2.04 (s, 3 H, H_3C(7 or 8 or 9 or 10 or 11)), 2.03 (s, 3 H, H_3C(7 or 8 or 9 or 10 or 11)), 2.01 (s, 3 H, H_3C(7 or 8 or 9 or 10 or 11))

Preparation of Phenyl 1-Thio-β-d-2,3,4,6-tetra-*O*-acetyl Glucoside (17)[32] [TK-VIII-9]



To a 250-mL, single-necked, round-bottomed flask equipped with a magnetic stir-bar and an argon inlet, was charged with **16** (20.0 g, 51.24 mmol, 1.0 equiv) followed by $CHCl_3$ (60 mL). Then thiophenol (10.52 mL, 102.48 mmol, 2.0 equiv) and BF_3•OEt (32.46 mL, 256.2 mmol, 5.0 equiv) was added. The contents were stirred at rt for 5 h. The reaction mixture was quenched with H_2O (100 mL) and extracted with CH_2Cl_2 (3 x 50 mL). The combined organic layers were washed with brine, dried with Na_2SO_4, filtered and concentrated to give 30.91 g crude **17**. The

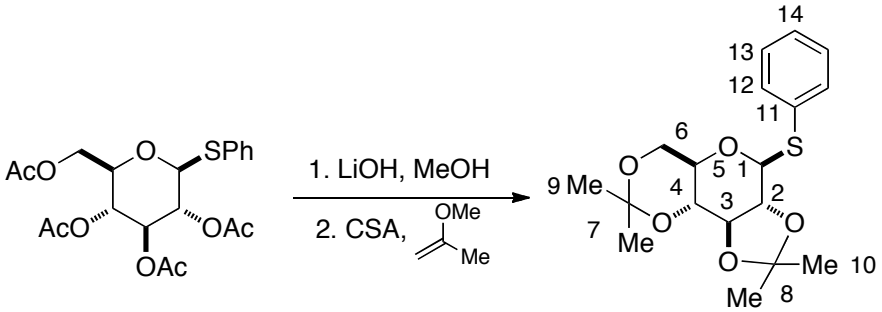
crude product was recrystallized from Et_2O/hexane (400 mL/2 L) affording 16.15 g, of **17** (72%) as white needles. The physical and spectroscopic properties matched those described in the literature.[32]

Data for **17**:

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

7.52-7.46 (m, 2 H, HC(11 or 12 or 13 or 14 or 15)), 7.36-7.28 (m, 3 H, HC(11 or 12 or 13 or 14 or 15)), 5.22 (t, *J* = 9.9, 1 H, HC(2 or 3 or 4)), 5.04 (t, *J* = 9.9, 1 H, HC(2 or 3 or 4)), 4.98 (t, *J* = 9.9, 1 H, HC(2 or 3 or 4)), 4.70 (d, *J* = 9.9, 1 H, HC(1)), 4.23 (dd, *J* = 16.0, 4.6, 1 H, HC(6a or 6b)), 4.18 (dd, *J* = 16.0, 2.9, 1 H, HC(6a or 6b)), 3.72 (ddd, *J* = 10.6, 4.6, 2.3, 1 H, HC(5)), 2.09 (s, 3 H, H_3C(7 or 8 or 9 or 10)), 2.08 (s, 3 H, H_3C(7 or 8 or 9 or 10)), 2.02 (s, 3 H, H_3C(7 or 8 or 9 or 10)), 1.99 (s, 3 H, H_3C(7 or 8 or 9 or 10))

Preparation of Phenyl 2,3,4,6-Di-*O*-isopropylidene-1-thio-β-d-gulcopyranoside (18)[38] **[TK VIII-10]**



17 **18**

To a 500-mL, two-necked, round-bottomed flask fitted with a nitrogen inlet, a septum, and a magnetic stir-bar was added **17** (16.15 g, 36.67 mmol) followed by dry MeOH (200 mL). Then LiOH (0.0768 g, 1.83 mmol, 0.05 equiv) was added. The solution was stirred rt for 1 h. Then $NH_4^+Cl^-$ (0.0979 g, 1.83 mmol, 0.05 equiv) was added to the mixture and MeOH was removed under reduced pressure using rotary evaporation. The resulting viscous oil was dissolved in toluene (100 mL) and once again concentrated under reduced pressure by rotary evaporation. This procedure was repeated three more times and the remaining volatiles were removed under high vacuum. Then dry DMF (150 mL) was added to the crude syrup, followed by camphorsulfonic acid (0.681 g, 2.93 mmol, 0.08 equiv) and 2-methoxypropene (14.05 mL,

146.68 mmol, 4.0 equiv). The mixture was stirred at rt for 3 h and quenched with saturated $NaHCO_{3(aq)}$ (150 mL) and extracted with Et_2O (3 x 100 mL). The combined organic layers were washed with brine (2 x 100 mL), dried with Na_2SO_4, filtered and concentrated. The crude product was purified by column chromatography (SiO_2, 300 g; hexane/EtOAc, 2:1 with 5% Et_3N) to give 10.6 g of bisacetonide **18** (82%) as a white solid. The physical and spectroscopic properties matched those described in the literature.[33]

Data for **18**:

mp: 120-124 °C (hexane)

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

7.58-7.53 (m, 2 H, HC(11 or 12 or 13 or 14)), 7.35-7.30 (m, 3 H, HC(11 or 12 or 13 or 14)), 4.89 (d, *J* = 10.0, 1 H, HC(2)), 4.00 (dd, *J* = 10.0, 5.4, 1 H, HC(6)), 3.88 (t, *J* = 10.0, 1 H, HC(2 or 3 or 4)), 3.86 (t, *J* = 10.0, 1 H, HC(2 or 3 or 4)), 3.68 (t, *J* = 10.0, 1 H, HC(2 or 3 or 4)), 3.34 (ddd, *J* = 10.0, 8.3, 5.4, 1 H, HC(5)), 3.32 (dd, *J* = 10.0, 8.3, 1 H, HC(6)), 1.53 (s, 3 H, H_3C(9a or 9b or 10a or 10b)), 1.50 (s, 3 H, H_3C(9a or 9b or 10a or 10b)), 1.45 (s, 3 H, H_3C(9a or 9b or 10a or 10b)), 1.43 (s, 3 H, H_3C(9a or 9b or 10a or 10b))

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

133.3, 131.7, 129.2, 128.6, 112.1, 100.0, 85.82, 79.5, 76.53, 73.3, 62.4, 29.2, 26.9, 26.7, 19.4

MS: (EI, 70 eV)

352 (M^+ (1)), 243 (24), 127 (29), 123 (13), 85 (14), 69 (100)

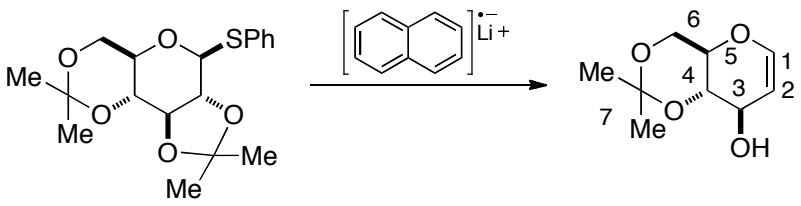
Opt. Rot.: $[\alpha]_D^{24}$ –67.4 (c = 1.00, MeOH)

HRMS: $C_{18}H_{25}O_5S$ (353.14)

Calcd: 353.1427

Found: 353.1423

Preparation of 1,5-Anhydro-4,6-*O*-isopropylidene-2-deoxy-D-arabino-hex-1-enitol (12)[33a] [TK-VIII-22]



18 **12**

The lithium naphthalenide solution was prepared as follows: to a flame dried 100-mL, single-necked, round-bottomed flask equipped with a magnetic stir-bar and an argon inlet with septum was added naphthalene (2.1 g, 16.38 mmol, 5.65 equiv), followed by THF (40 mL). Then, lithium metal (166 mg, 23.9 mmol, 8.24 equiv) was added at rt and the contents were stirred for 6 h at this temperature to give a dark green solution.

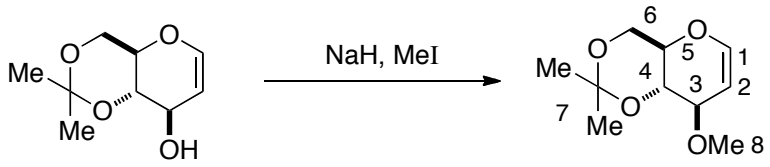
To a separate 250-mL, single-necked, round-bottomed flask equipped was a magnetic stir-bar and an argon inlet with septum, was added **18** (1.023 g, 2.90 mmol, 1.0 equiv), followed by THF (10 mL). The contents were cooled to –72 ^{o}C using a dry ice/2-propanol bath. Then, lithium naphthalenide solution (20 mL, 2.8 equiv) was added at –72 °C over the course of 30 min. The contents turned dark brown when the lithium naphthalenide solution was added. The contents were stirred for an additional 10 min and then quenched with H_2O (30 mL) at –72°C and upon warming was extracted with EtOAc (3x30 mL). The combined organic layers were washed with brine (30 mL), dried with Na_2SO_4, filtered and concentrated under reduced pressure by rotary evaporation. The crude product was purified three times by column chromatography (SiO_2, 70 g; hexane/EtOAc, 1/2 with 5% Et_3N, then SiO_2, 35 g; hexane/Et_2O, 1:1, then SiO_2, 80 g; hexane/ Et_2O, 1:1) to afford **12** (0.541 g, 100%) as a colorless oil.

Data for **12**:

^{1}H NMR: (400 MHz, $CDCl_3$)

6.30 (dd, *J* = 6.0, 1.7, 1 H, HC(1)), 4.74 (dd, *J* = 6.0, 1.9, 1 H, HC(2)), 4.35 (dt, *J* = 7.2, 1.9, 1 H, HC(3)), 3.96 (dd, *J* = 10.8, 5.0, 2 H, H_2C(6)), 3.87 – 3.67 (m, 2 H, HC(4 and 5)), 2.17 (br s, 1 H, (OH)), 1.44 (s, 3 H, H_3C(7a or 7b)), 1.54 (s, 3 H, H_3C(7a or 7b))

Preparation of 1,5-Anhydro-4,6-*O*-isopropylidene-3-*O*-methyl-2-deoxy-D-arabino-hex-1-enitol (19) [TK-VIII-58]



12 **19**

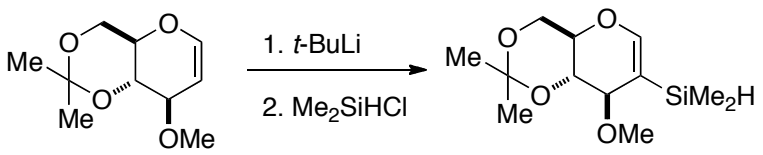
To a 50-mL, single-necked, round-bottomed flask equipped with a magnetic stir-bar and an argon inlet with septum, was charged with NaH (60% suspension in mineral oil, 438 mg, 10.95 mmol, 4.0 equiv). This was washed with hexane (2 x 2 mL) and suspended in THF (1 mL). To the suspension was added a solution of **12** (509.8 mg, 10.95 mmol, 1.0 equiv) in THF (4 mL) at rt. The mixture was stirred for an additional 20 min or until hydrogen evolution ceased. Then, MeI (0.68 mL, 10.95 mmol, 4.0 equiv) was added to the suspension. The contents were allowed to stir for 2 h at rt. This mixture was cooled to 0 ^{o}C in an ice bath, then H_2O (30 mL) was added. The aqueous layer was extracted with EtOAc (3 x 30 mL) and the combined organic layers were washed with brine (30 mL) and dried with Na_2SO_4, filtered and concentrated. The crude mixture was purified by column chromatography (SiO_2, 35 g; hexane/EtOAc, 3:1) to provide **19** (0.443 g, 81%) as a white oil.

Data for **19**:

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

6.32 (d, *J* = 2.0, 1 H, HC(1)), 4.80 (dd, *J* = 6.0, 2.0, 1 H, HC(2)), 3.91 (m, 3 H, HeC(C6), HC(3 or 4)), 3.84 (t, *J* = 10.0, 1 H, Ha(C6)), 3.73 (td, *J* = 10.0, 6.0, 1 H, HC(5)), 3.44 (s, 3 H, H_3C(8)), 1.55 (s, 3 H, H_3C(7a or 7b)), 1.44 (s, 3 H, H_3C(7a or 7b))

Preparation of 1,5-anhydro-2-dimethylsilyl-4,6-*O*-isopropylidene-3-*O*-methyl-2-deoxy-D-arabino-hex-1-enitol (20) [TK-VIII-60]



19 **20**

A 25-mL, flame-dried, single-necked, round-bottomed flask equipped with a magnetic stir-bar and an argon inlet with septum, was added **19** (53.9 mg, 0.269 mmol, 1.0 equiv), followed by THF (1.5 mL). The contents were cooled to –78 °C using a dry ice/2-propanol bath. Once at that temperature *t*-BuLi (1.7 M in pentane, 0.71 mL, 1.08 mmol, 4.0 equiv) was added over 1 min. The contents became bright yellow and were stirred at –78 °C for 30 min. Then dimethylchlorosilane (0.12 mL, 1.08 mmol, 4.0 equiv) was added to the yellow mixture over 1 min. The yellow color dissipated and a white precipitate formed. The reaction was stirred at –78 °C for 30 min, before quenching with H_2O (10 mL) and saturated $NaHCO_{3(aq)}$ (10 mL) at –78 °C. After warming to ambient temperature the organic layer was extracted with EtOAc (3 x 30 mL). The combined organic layers were washed with brine (30 mL) and dried with Na_2SO_4, filtered and concentrated to give the crude product (60.0 mg) as a light-yellow oil. The crude product was purified by column chromatography (SiO_2, 35 g; hexane/EtOAc, 7:1) to afford **20** (30.4 mg, 44%) as a colorless oil.

Data for **20**:

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

6.27 (d, *J* = 1.6, 1 H), 4.08-3.09 (m, 4 H), 3.82 (t, *J* = 10.3, 1 H), 3.72 (td, *J* = 10.3, 7.3), 3.50 (s, 3 H), 1.54 (s, 3 H), 1.42 (s, 3 H), 0.16 (d, *J* = 3.6, 6 H)

^{13}C NMR: (125.7 MHz, $CDCl_3$)

148.1, 108.4, 99.2, 72.9, 68.9, 61.7, 58.5, 28.9, 18.9, –3.3, –4.6

MS: (ESI)

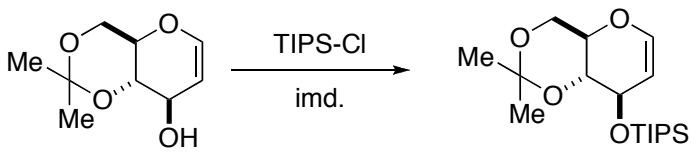
281 (M^+ + Na (100)), 277 (70), 265 (30), 195 (15)

HRMS: $C_{12}H_{22}O_4NaSi$ (281.38)

Calcd: 281.1185

Found: 281.1191

Preparation of 1,5-anhydro-4,6-*O*-isopropylidene-3-*O*-triisopropyl-silyl-2-deoxy-D-arabino-hex-1-enitol (15) [34] **[TK-VIII-70)]**



12 **15**

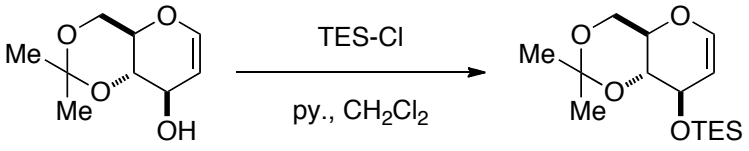
To a 25-mL, single-necked, round-bottomed flask equipped with a magnetic stir-bar and a reflux condenser containing an argon inlet with a septum on top of the reflux condenser, was added **12** (523 mg, 2.81 mmol, 1.0 equiv), followed by DMF (1.1 mL). Then, imidazole (73.1 mg, 1.07 mmol, 2.0 equiv) and chlorotriisopropylsilane (1.8 mL, 8.43 mmol, 1.5 equiv) was added. The contents were heated to 90 ^{o}C and stirred for 10 h. After cooling to ambient temperature, H_2O (30 mL) was added to the reaction mixture and the aqueous layer was extracted with EtOAc (3 x 30 mL). The combined organic layers were washed with brine (30 mL) and dried with Na_2SO_4, filtered and concentrated. The crude material was purified by column chromatography (SiO_2, 35 g; hexane/EtOAc, 10:1) to provide 164 mg of **15** (89%) as a colorless oil.

Data for **15**:

^{1}H NMR: (400 MHz, $CDCl_3$)

6.25 (dd, *J* = 6.5, 2.2, 1 H), 4.68 (dd, *J* = 6.5, 2.2, 1 H), 4.42 (dt, *J* = 7.2, 2.2, 1 H), 3.93 (dd, *J* = 10.1, 5.3, 1 H), 3.83 (dd, *J* = 10.1, 7.2, 1 H), 3.81 (t, *J* =10.1, 1 H), 3.70 (td, *J* = 10.1, 5.3, 1 H), 1.50 (s, 3 H), 1.40 (s, 3 H), 0.98 - 1.15 (m, 21H)

Preparation of 1,5-Anhydro-4,6-*O*-isopropylidene-3-*O*-triethylsilyl-2-deoxy-D-arabino-hex-1-enitol (29) [TK-IX-61]



12 **29**

To a 100-mL, single-necked, round-bottomed flask equipped with a magnetic stir-bar and argon inlet, was added **12** (754 mg, 4.05 mmol) along with CH_2Cl_2 (10 mL). Then pyridine (0.49 mL, 6.07 mmol, 1.5 equiv) was added, followed by triethylsilyl chloride (0.82 mL, 4.86 mmol,

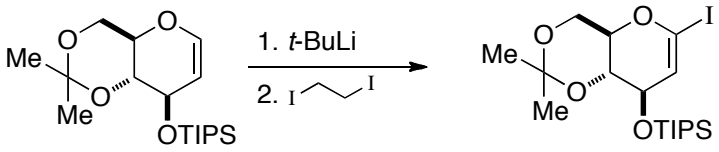
1.2 equiv). The contents were stirred for 10 h at rt. When the reaction was judged to be complete by TLC analysis (hexane/EtOAc, 7:1), H_2O(30 mL) was added. The aqueous layer was removed and extracted with CH_2Cl_2 (3 x 30 mL), washed with brine (30 mL), dried with Na_2SO_4, filtered and concentrated *in vacuo* to give a colorless oil. This oil was purified using column chromatography (SiO_2, 35 g; hexane/EtOAc, 10:1) to afford **29** (1.02 g, 84%) as a colorless oil.

Data for **29**:

^{1}H NMR: (400 MHz, $CDCl_3$)

6.25 (dd, *J* = 6.4, 2.0, 1 H), 4.62 (dd, *J* = 6.4, 2.0, 1 H), 4.30 (dt, *J* = 7.0, 2.0, 1 H), 3.93 (dd, *J* = 10.1, 5.5, 1 H), 3.81 (t, *J* = 7.0, 2.0, 1 H), 3.80 (dd, *J* = 10.1 7.0, 1 H), 3.70 (td, *J* = 10.1, 5.5, 1 H), 1.50 (s, 1 H), 1.40 (s, 3 H), 0.96 (t, *J* = 8.0, 9 H), 0.64 (dq, *J* = 17.4, 8.0, 3 H), 0.60 (dq, *J* = 17.4, 8.0, 3 H)

Preparation of 1,5-Anhydro-1-iodo-4,6-*O*-isopropylidene-3-*O*-triisopropylsilyl-2- deoxy-D-arabino-hex-1-enitol (21) [TK-VIII-89]



15 **21**

To a 250-mL, single-necked, round-bottomed flask equipped with a magnetic stir-bar and an argon inlet with a septum, was added TIPS ether (**15**, 1.69 g, 4.93 mmol, 1.0 equiv), followed by THF (10 mL). The contents were cooled to –78 ^{o}C using a dry ice/2-propanol bath. Once the internal temperature reached –78 ^{o}C *t*-BuLi (1.7 M in pentane, 11.6 mL, 19.74 mmol, 4.0 equiv) was added dropwise. The reaction mixture was warmed to 0 °C using an ice bath and stirred for 0.5 h at that temperature. The contents were once again cooled to –78 ^{o}C. To another 25-mL, single-necked, round-bottomed flask equipped with a magnetic stir-bar and an argon inlet with a septum, was added 1,2-diiodoethane (5.56 g, 19.74 mmol, 4.0 equiv), followed by THF (10 mL). This yellow suspension was cannula transferred into the above 250-mL round-bottomed flask containing lithio-**15**. After the addition the contents were warmed to rt giving a dark brown solution. After stirring for 0.5 h, at rt, saturated $NaHCO_{3(aq)}$ (50 mL) was added, and the aqueous layer was extracted with EtOAc (3 x 30 mL). The combined organic layers were washed with brine (30 mL) and dried with Na_2SO_4, filtered and concentrated under reduced pressure by rotary

evaporation, to give 3.18 g of a crude orange oil. The crude mixture was purified by column chromatography (SiO_2, 70 g; hexane/EtOAc, 10:1) afford **21** (2.3 g, 99%) as a light-yellow oil. Note: The product was contaminated with 3,3-dimethyl-1-iodobutane right after removal of the eluent from chromatography. This impurity was removed by adding EtOAc (30 mL) and removing EtOAc using rotary evaporation, this was repeated 3x to provide the pure product **21** (2.14 g, 93%) as a colorless oil that turned yellow over time.

Data for **21**:

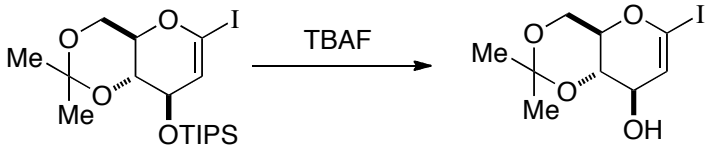
^{1}H NMR: (400 MHz, $CDCl_3$)

5.22 (d, *J* = 2.4, 1 H), 4.39 (dd, *J* = 7.0, 2.4, 1 H), 3.98 - 3.77 (m, 4 H), 1.50 (s, 3 H), 1.38 (s, 3 H), 0.98 - 1.14 (m, 21H)

^{13}C NMR: (125.7 MHz, $CDCl_3$)

116.6, 104.3, 99.6, 72.9, 72.5, 70.1, 61.2, 28.8, 18.8, 17.9, 12.2

Preparation of 1,5-Anhydro-1-iodo-4,6-*O*-isopropylidene-2-deoxy- D-arabino-hex-1-enitol (22) [TK-VIII-90]



21 **22**

To a 100-mL, single-necked, round-bottomed flask equipped with a magnetic stir-bar, argon inlet with septum, was charged with TIPS ether (**21**, 2.27 g, 4.85 mmol, 1.0 equiv), followed THF (24 mL). Then, TBAF•3H_2O (1.84 g, 5.83 mmol, 1.2 equiv) was added and the contents were stirred at rt for 0.5 h. Then H_2O (50 mL) was added and the aqueous layer was extracted with EtOAc (3 x 30 mL). The combined organic layers were washed with brine (30 mL) and dried with Na_2SO_4, filtered and concentrated. The crude material was purified by column chromatography (SiO_2, 70 g; gradient hexane/EtOAc, 3:1 (200 mL) then hexane/EtOAc 1:1) to afford **22** (1.5 g, 96%) as a colorless oil.

Data for **22**:

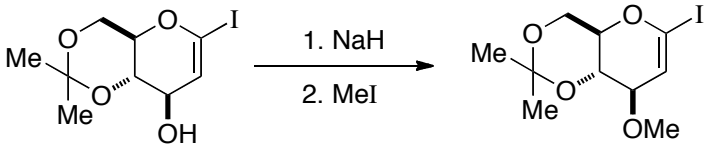
^{1}H NMR: (400 MHz, $CDCl_3$)

4.35 - 4.29 (m, 1 H), 3.93 - 4.01 (m, 3 H), 3.89 - 3.80 (m, 2 H), 2.11 (d, *J* = 6.0, 1 H), 1.54 (s, 3 H), 1.43 (s, 3 H)

^{13}C NMR: (125.7 MHz, $CDCl_3$)

114.8, 105.3, 99.9, 72.6, 72.5, 69.4, 60.9, 28.8, 18.9

Preparation of 1,5-Anhydro-1-iodo-4,6-*O*-isopropylidene-3-*O*-methyl-2-deoxy-D-arabino-hex-1-enitol (23) [TK-VIII-91]



22 **23**

To a 50-mL, single-necked, round-bottomed flask equipped with a magnetic stir-bar and an argon inlet was charged with NaH (60% suspension in mineral oil, 370.3 mg, 9.26 mmol, 2.0 equiv). This was washed with hexane (2 x 2 mL) and suspended in THF (3 mL). To the suspension was added a solution of **22** (1.45 g, 4.63 mmol) in THF (4 mL) at 0 °C. The reaction mixture was allowed to warm to rt. After stirring for 20 min, or when hydrogen evolution ceased, MeI (0.58 mL, 9.26 mmol, 2.0 equiv) was added to the suspension. The reaction mixture was stirred for 1 h at rt, then the mixture was cooled down with an ice-water bath and quenched with H_2O (30 mL). The organic layer was extracted with EtOAc (3 x 30 mL). Combined organic layers were washed with brine (30 mL) and dried with Na_2SO_4. The solvent was removed under reduced pressure to give a crude mixture. The crude mixture was purified by silica gel column chromatography (SiO_2, 70 g; hexane/EtOAc, 7:1) to give **23** (1.39 g, 92%) as a colorless oil.

Data for **23**:

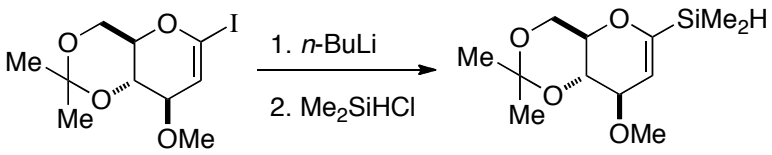
^{1}H NMR: (500 MHz, $CDCl_3$)

5.36 (d, J = 1.9, 1 H), 3.80 - 4.00 (m, 5 H), 3.42 (s, 3 H), 1.54 (s, 3 H), 1.43 (s, 3 H)

^{13}C NMR: (125.7 MHz, $CDCl_3$)

112.5, 105.6, 99.7, 77.6, 72.8, 70.8, 61.0, 56.9, 28.7, 18.9

Preparation of 1,5-Anhydro-1-dimethylsilyl-4,6-*O*-isopropylidene-3-*O*-methyl-2-deoxy-D-arabino-hex-1-enitol (24) [TK-VIII-92]



23 **24**

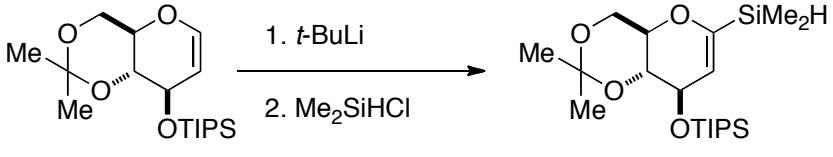
To a 100-mL single-necked, round-bottomed flask equipped with a magnetic stir-bar and an argon inlet with septum, was charged with iodide (**23**, 0.847 g, 2.60 mmol, 1.0 equiv) followed by THF (13 mL). The contents were cooled to –78 ^{o}C using a dry ice/2-propanol bath. Once at this temperature *n*-BuLi (1.6 M in hexane, 1.79 mL, 2.857 mmol, 1.1 equiv) was added slowly, and stirred for 20 min at –78°C. Then, chlorodimethylsilane (0.34 mL, 3.116 mmol, 1.2 equiv) was added to the mixture at –78°C. The reaction mixture was allowed to warm to rt. After stirring for 20 min, saturated $NaHCO_{3(aq)}$ (50 mL) was added to the mixture. The aqueous layer was extracted with EtOAc (3 x 30 mL). Combined organic layers were washed with brine (30 mL) and dried with Na_2SO_4. The solvent was removed under reduced pressure to give crude mixture (782 mg) as a light-yellow oil. The crude mixture was purified by silica gel column chromatography (SiO_2, 70 g; hexane/EtOAc, 7:1) to give **24** (479 mg, 71%) as colorless oil along with glucal **19** (73 mg, 14%) as a colorless oil.

Data for **24**:

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

5.07 (d, *J* = 2.0, 1 H), 4.00 (sept, *J* = 3.9, 1 H), 3.98 - 3.94 (m, 2 H), 3.92 (t, *J* = 10.7, 7.6, 1 H), 3.84 (t, *J* = 10.7, 1 H), 3.66 (td, *J* = 10.7, 5.9, 1 H), 3.46 (s, 3 H), 1.55 (s, 3 H), 1.44 (s, 3 H), 0.18 (d, *J* = 3.9, 6 H)

Preparation of 1,5-Anhydro-1-dimethylsilyl-4,6-*O*-isopropylidene-3-*O*-triisopropylsilyl-2-deoxy-D-arbino-hex-1-enitol (31) [TK-VIII-39]



15 **31**

To a 50-mL, two-necked, round-bottomed flask equipped with a magnetic stir-bar,

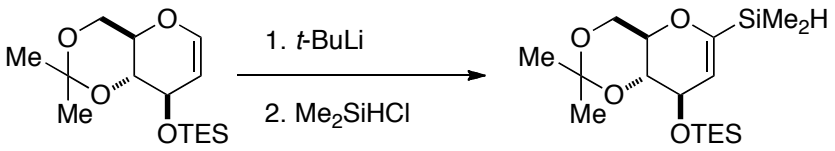
septum and argon inlet, glucal **15** (99 mg, 0.292 mmol) was added along with THF (2 mL). The contents were cooled to –78 °C using a dryice/2-propanol bath. Once at this temperature *t*-BuLi (1.7 M in pentane, 0.69 mL, 1.17 mol, 4.0 equiv) was added slowly to provide a bright yellow solution. The contents were warmed to 0 °C using an ice bath and stirred for 40 min. After stirring the dark yellow solution was once again cooled to –78 °C and chlorodimethylsilane (0.13 mL, 1.17 mmol, 4.0 equiv) was added to the mixture at –78 °C. The reaction mixture was allowed to warm to rt. After stirring for 30 min, H_2O (30 mL) was added and the aqueous layer was extracted with EtOAc (3 x 30 mL). The combined organic layers were washed with brine (30 mL), dried with Na_2SO_4 and concentrated to a crude colorless oil (168 mg). The crude material was then subjected to column chromatography (SiO_2, 35 g; hexane/EtOAc, 25:1) to afford **31** (123 mg, 0.308 mmol, >99%) as a colorless oil.

Data for **31**:

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

4.95 (d, *J* = 2.0, 1 H), 4.38 (dd, *J* = 7.2, 2.0, 1 H), 3.99 (sept, *J* = 4.0, 1 H), 3.93 (dd, *J* = 10.4, 5.2, 1 H), 3.81 (dd, *J* = 10.4, 7.2, 1 H), 3.80 (t, *J* = 10.4, 1 H), 3.64 (td, *J* = 10.4, 5.2, 1 H), 1.50 (s, 3 H), 1.39 (s, 3 H), 1.17-0.98 (m, 21H), 0.17 (d, *J* = 4.0, 6 H)

Preparation of 1,5-Anhydro-4,6-*O*-isopropylidene-1-dimethylsilyl-3-*O*-triethylsilyl-2-deoxy-D-arabino-hex-1-enitol (30) [TK-IX-63]



29 **30**

To a 100-mL, 3-necked, round-bottomed flask equipped with a magnetic stir-bar, septa and an argon inlet, glucal **29** (503 mg, 1.67 mmol) was added along with THF (6 mL). The contents were cooled to –78 °C using a dry ice/acetone bath. Once at this temperature *t*-BuLi (1.7 M in pentane, 3.9 mL, 6.69 mmol, 4.0 equiv) and the bright yellow contents were warmed to 0 °C using an ice bath. The contents were stirred at 0 °C for 0.5 h to give dark brown solution. Then the contents were once again cooled to –78 °C and chlorodimethylsilane (0.73 mL, 6.69 mmol, 4.0 equiv) was added to give a light-yellow suspension. After the addition to contents

were warmed to rt and stirred for 20 min, then saturated $NaHCO_3$ (30 mL) was added and the aqueous layer was extracted with EtOAc (3 x 30 mL). The combined organic layers were washed with brine (30 mL), dried with Na_2SO_4, filtered and concentrated. The crude yellow oil (678 mg) was purified using column chromatography (SiO_2, 35 g; hexane/EtOAc, 7:1) to give **30** (570 mg, 95%) as a colorless oil.

Data for **30**:

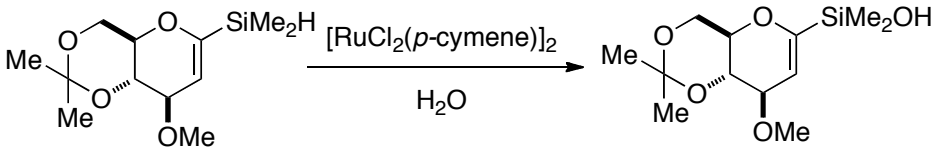
^{1}H NMR: (500 MHz, $CDCl_3$)

4.90 (d, *J* = 2.0, 1 H), 4.27 (dd, *J* = 7.1, 2.0, 1 H), 3.98 (sept, *J* = 3.6, 1 H), 3.93 (dd, *J* = 10.7, 5.7, 1 H), 3.80 (t, *J* = 10.7, 1 H), 3.78 (dd, *J* = 10.7, 7.1, 1 H), 3.64 (td, *J* = 10.7, 5.7, 1 H), 1.50 (s, 3 H), 1.40 (s, 3 H), 0.96 (t, *J* = 7.9, 9 H), 0.64 (dq, *J* = 22.0, 7.9, 9 H), 0.61 (dq, *J* = 22.0, 7.9, 3 H), 0.17 d, *J* = 3.6, 6 H)

MS: (ESI)

357 (M^+-1(100)), 317 (12), 299 (21), 265 (91), 149 (40)

Preparation of 1,5-Anhydro-1-dimethyl(hydroxyl)silyl-4,6-*O*-isopropylidene-3- *O*-methyl-2-deoxy-D-arabino-hex-1-enitol (25) [TK-IX-14]



24 **25**

To a 25-mL, single-necked, round-bottomed flask equipped with a magnetic stir-bar, open to the atmosphere, **24** (332.0 mg, 1.29 mmol) was added along with CH_3CN (3.0 mL). Then di-μ-chlorobis[(*p*-cymene)chlororuthenium(II)] (15.7 mg, 0.0257 mmol, 0.02 equiv) and H_2O (46.3 μL, 2.60 mol, 2.0 equiv) were successively added to the solution at rt. Gas evolution was observed from the orange solution. After 1 h the gas evolution ceased and the reaction was judged complete by TLC analysis (3:1 hexane/EtOAc). The solvent was removed under reduced pressure and the residue was purified by column chromatography (SiO_2, 35 g; hexane/EtOAc, 3:1-1:1) to give dimethylsilanol **25** (285.0 mg, 81%) as a colorless oil.

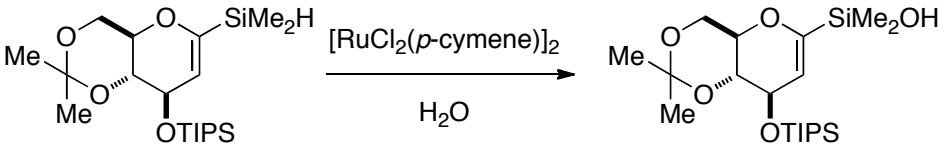
Data for **25**:

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

5.12 (d, *J* = 2.0, 1 H), 3.99 - 3.89 (m, 3 H), 3.84 (t, *J* = 10.4, 1 H), 3.66 (td, *J* =

10.4, 2.8, 1 H), 3.46 (s, 3 H), 1.82 (br s, 1 H), 1.55 (s, 3 H), 1.44 (s, 3 H), 0.25 (s, 6 H)

Preparation of 1,5-Anhydro-1-dimethyl(hydroxyl)silyl-4,6-*O*-isopropylidene3-*O*-triisopropylsilyl-2-deoxy-D-arabino-hex-1-enitol (11) [TK-VIII-40]



31 **11**

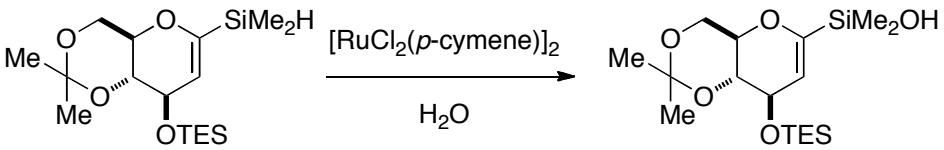
To a 25-mL, single-necked, round-bottomed flask equipped with a magnetic stir-bar, open to the atmosphere, **31** (56 mg, 0.139 mmol) was added along with CH_3CN (0.4 mL). Then Di-μ-chlorobis[(*p*-cymene)chlororuthenium(II)] (1.7 mg, 0.00278 mmol, 0.02 equiv) and H_2O (5 μL, 0.278 mmol, 2.0 equiv) were successively added to the solution at rt. Gas evolution was observed from the orange solution. After 0.5 h the gas evolution ceased and the reaction was judged complete by TLC analysis (10:1 hexane/EtOAc). The solvent was removed under reduced pressure and the residue was purified by silica gel column chromatography (SiO_2, 35 g, hexane/EtOAc, 7:1-3:1) to give dimethylsilanol **11** (35 mg, 61%) as a colorless oil.

Data for **11**:

^{1}H NMR: (400 MHz, $CDCl_3$)

5.00 (d, *J* = 1.9, 1 H), 4.39 (dd, *J* = 6.9, 1.9, 1 H), 3.94 (dd, *J* = 10.1, 6.0, 1 H), 3.80 (dt, *J* = 10.1, 6.9, 1 H), 3.80 (t, *J* = 10.1, 1 H), 3.64 (td, *J* = 10.1, 6.0, 1 H), 1.50 (s, 3 H), 1.39 (s, 3 H), 1.16-1.00 (m, 21H), 0.24 (s, 6 H)

Preparation of 1,5-Anhydro-4,6-*O*-isopropylidene-1-dimethyl(hydroxyl)silyl-3-*O*-triethylsilyl-2-deoxy-D-arabino-hex-1-enitol (32) [TK-IX-64]



30 **32**

To a 100-mL, single-necked, round-bottomed flask equipped with a magnetic stir-bar, open to the atmosphere, **30** (564 mg, 1.57 mmol) was added along with CH_3CN (5.0 mL). Then

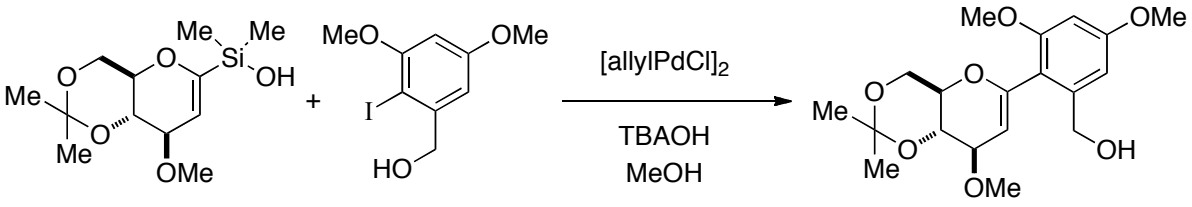
di-μ-chlorobis[(*p*-cymene)chlororuthenium(II)] (19.3 mg, 0.0315 mmol, 0.02 equiv) and H_2O (57 μL, 3.20 mmol, 2.0 equiv) were successively added to the solution at rt. Gas evolution was immediately observed from the orange solution. After 1 h the gas evolution ceased and the reaction was judged incomplete by TLC analysis (7:1 hexane/EtOAc). Then another equivalent of Di-μ-chlorobis[(*p*-cymene)chlororuthenium(II)] (19.3 mg, 0.0315 mmol, 0.02 equiv) was added to the flask. After an additional hour the gas evolution ceased and the reaction was judged complete by TLC analysis (7:1 hexane/EtOAc). The solvent was removed under reduced pressure and the residue was purified by column chromatography (SiO_2, 35 g; hexane/EtOAc, 7:1-3:1) to give dimethylsilanol **32** (414 mg, 70%) as a colorless oil.

Data for **32**:

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

4.95 (d, *J* = 2.0, 1 H), 4.28 (dd, *J* = 7.2, 2.0, 1 H), 3.94 (dd, *J* = 11.1, 4.8, 1 H), 3.80 (t, *J* = 11.1, 1 H), 3.77 (dd, *J* = 11.1, 7.2, 1 H), 3.64 (td, *J* = 11.1, 4.8, 1 H), 1.50 (s, 3 H), 1.40 (s, 3 H), 0.96 (t, *J* = 8.0, 9 H), 0.69 (dq, *J* = 21.9, 8.0, 3 H), 0.60 (dq, *J* = 21.9, 8.0, 3 H), 0.24 (s, 6 H)

Preparation of 1,5-Anhydro-4,6-*O*-isopropylidene-3-*O*-methyl-2-deoxy-1-(4,6-dimethoxy-2-hydroxymethyl)-D-arabino-hex-1-enitol (27a) [TK-IX-15] (Table 1, entry 1)

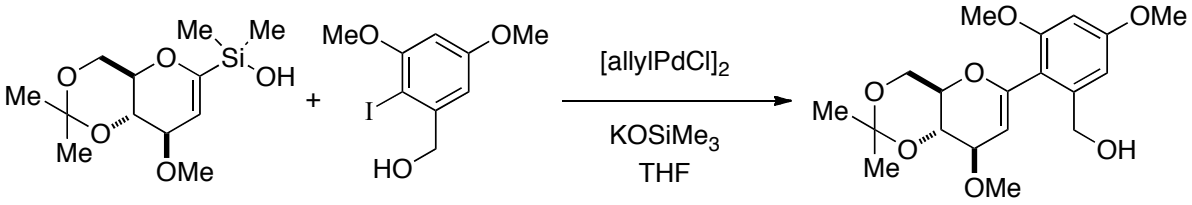


25 **9** **27a**

To a 25-mL, two-necked round-bottomed flask equipped with a magnetic stir-bar, septum and argon inlet, silanol **25** (51.7 mg, 0.188 mmol) was added, followed by a solution of tetrabutylammonium hydroxide (TBAOH) (1.0 M in methanol, 0.376 mL, 0.376 mmol, 2.0 equiv) was added. Then aromatic iodide **9** (55.3 mg, 0.188 mmol) was added along with $[allylPdCl]_2$ (3.4 mg, 0.0094 mmol, 0.05 equiv). The contents were stirred under an argon atmosphere for 5 h at rt. After this amount of time the mixture was filtered through SiO_2 (3 g), washing with EtOAc (100 mL). The filtrate was transferred to a 125-mL separatory funnel and

H_2O (30 mL) was added. The aqueous layer was washed with EtOAc (2 x 30 mL). The combined organic layers were washed with brine (30 mL) and dried with Na_2SO_4. The solvent was removed using rotary evaporation and the crude residue was purified by silica gel chromatography (SiO_2, 35 g; hexane/EtOAc gradient (7:1-3:1-1:1-EtOAc)). After chromatography aromatic iodide **9** (34 mg, 62%) was recovered along with glucal **19** (14 mg, 38%).

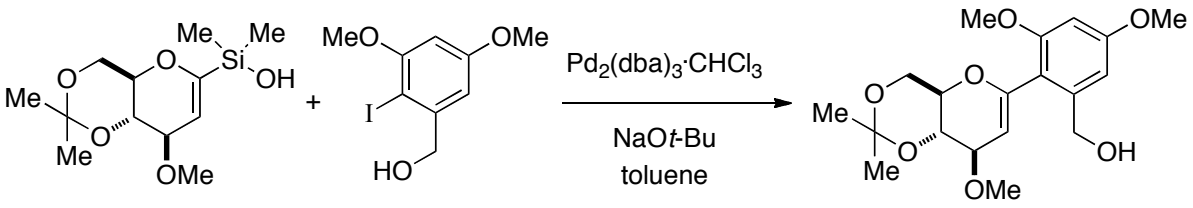
Preparation of 1,5-Anhydro-4,6-*O*-isopropylidene-3-*O*-methyl-2-deoxy-1-(4,6-dimethoxy-2-hydroxymethyl)-D-arabino-hex-1-enitol (27a) [TK-IX-56] (Table 1, entry 2)



25 **9** **27a**

To a 25-mL, two-necked round-bottomed flask equipped with a magnetic stir-bar, septum and argon inlet, silanol **25** (33.7 mg, 0.123 mmol) was added along with aromatic iodide **9** (36.2 mg, 0.123 mmol), $[allylPdCl]_2$ (2.4 mg, 0.0065 mmol, 0.05 equiv), and $KOSiMe_3$ (31.6 mg, 0.246 mmol, 2.0 equiv). The contents were flushed with argon 3x and THF (1.0 mL) was added. The contents were stirred under an argon atmosphere for 5 h at rt. After this amount of time the reaction was quenched by the addition of H_2O (30 mL). The aqueous layer was extracted with EtOAc (3 x 30 mL). The combined organic layers were washed with brine (30 mL) and dried with Na_2SO_4. The crude product was purified by column chromatography (SiO_2, 35 g; hexane/EtOAc gradient (7:1-3:1-1:1-EtOAc)). After chromatography aromatic iodide **9** (16 mg, 44%) was recovered along with glucal **19** (3 mg, 12%).

Preparation of 1,5-anhydro-4,6-*O*-isopropylidene-3-*O*-methyl-2-deoxy-1-(4,6-dimethoxy-2-hydroxymethyl)-D-arabino-hex-1-enitol (27a) (TK-IX-32) (Table 1, entry 3)



25 **9** **27a**

To a 25-mL, two-necked round-bottomed flask equipped with a magnetic stir-bar, septum and argon inlet, aromatic iodide **9** (68.2 mg, 0.186 mmol), NaO*t*-Bu (35.8 mg, 0.372 mmol, 2.0 equiv) and $Pd_2(dba)_3$•$CHCl_3$ (9.6 mg, 0.0093 mmol, 0.05 equiv) were added. The contents were flushed with argon 3x and toluene (0.2 mL) was added. Finally, a solution of silanol **25** (51.1 mg, 0.186 mmol) was added in toluene (0.6 mL). The contents were stirred under an argon atmosphere for 4 h at rt. After 4 h the mixture was filtered through SiO_2 (3 g), washing with EtOAc (100 mL). The filtrated was transferred to a 125-mL separatory funnel containing H_2O (30 mL). The aqueous layer was washed with EtOAc (2 x 30 mL). The combined organic layers were washed with brine (30 mL) and dried with Na_2SO_4. The solvent was removed using rotary evaporation. This crude residue was purified by silica gel chromatography (SiO_2, 35 g; hexane/EtOAc gradient (7:1-3:1-1:1-EtOAc)). After chromatography aromatic iodide **9** (12 mg, 17%) was recovered along with homodimerized silanol **28** (15 mg, 40%).

Data for **28**:

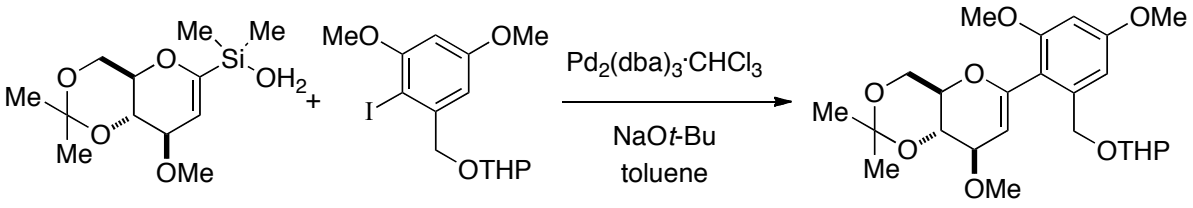
^{1}H NMR: (400 MHz, $CDCl_3$)

5.29 (d, *J* = 2.0, 2 H), 4.04 (dd, *J* = 7.5, 2.0, 2 H), 3.99 (dd, *J* = 10.2, 5.5, 2 H), 3.93 – 3.87 (m, 4 H), 3.74 (dt, *J* = 10.2, 5.5, 2 H), 3.45 (s, 6 H), 1.54 (s, 6 H), 1.44 (s, 6 H)

MS: (CI)

398 (M^+, 16), 368 (25), 367 (100), 342 (14), 335 (31), 323 (21), 285 (22), 279 (61), 101 (58), 83 (37), 59 (63)

Preparation of 1,5-Anhydro-4,6-*O*-isopropylidene-3-*O*-methyl-2-deoxy-1-(4,6-dimethoxy-2-(tetrahydropyran-2-yl)oxymethyl)-D-arabino-hex-1-enitol (27b) (TK-IX-36) (Table 1, entry 4) and (Table 2, entry 1)



25 **26** **27b**

To a 25-mL, two-necked, round-bottomed flask equipped with a magnetic stir-bar, septum and argon inlet, silanol **25** (49.3 mg, 0.18 mmol), aromatic iodide **26** (68.1 mg, 0.18 mmol, 1.0 equiv) and $Pd_2(dba)_3$•$CHCl_3$ (8.6 mg, 0.0094 mmol, 0.05 equiv) were added. The contents were flushed with argon 3x and toluene (0.8 mL) was added. Then NaO*t*-Bu (35 mg, 0.36 mmol, 2.0 equiv) was added and the contents were stirred under an argon atmosphere for 12 h at rt. After this amount of time the mixture was concentrated. The crude residue was purified by silica gel chromatography (SiO_2, 35 g; hexane/EtOAc gradient (7:1-3:1-1:1-1:1-EtOAc)). After chromatography aromatic iodide **26** (18.6 mg, 27%) was recovered along with homocoupled silanol **28** (7.0 mg, 20%) and the desired product **27b** (56.0 mg, 69%) as a colorless oil.

Data for **27b**:

^{1}H NMR: (400 MHz, $CDCl_3$)

6.65 (d, *J* = 2.4, 1/2 H), 6.64 (d, *J* = 2.4, 1/2 H), 6.39 (d, *J* = 2.4, 1/2 H), 6.38 (d, *J* = 2.4, 1/2 H), 4.88 (d, *J* = 2.0, 1/2 H), 4.86 (d, *J* = 2.0, 1/2 H), 4.72 (d, *J* = 11.6, 1 H), 4.71 - 4.66 (m, 1 H), 4.51 (d, *J* = 11.6, 1/2 H), 4.48 (d, *J* = 11.6, 1/2 H), 4.18 - 4.14 (m, 1 H), 4.11 - 4.05 (m, 1 H), 4.01 – 3.84 (m, 4 H), 3.81 (s, 3 H), 3.78 (s, 3 H), 3.58 - 3.51 (m, 1 H), 3.44 (s, 3 H), 1.92 - 1.40 (m, 6 H), 1.58 (s, 3 H), 1.47 (s, 3 H)

MS: (EI)

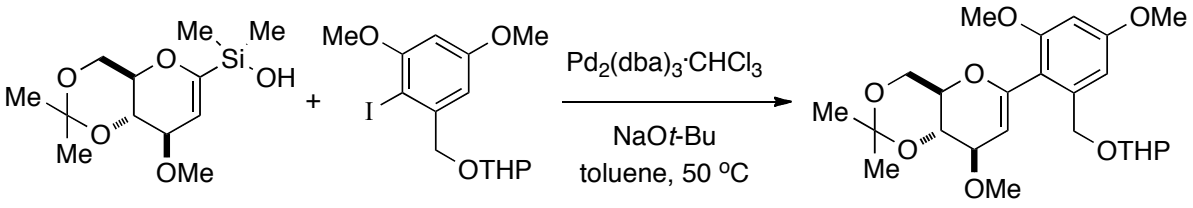
450 (M^+, 4), 366 (19), 350 (54), 334 (21), 333 (100), 308 (9), 275 (12), 259 (9), 235 (18), 233 (17), 205 (56), 195 (11), 193 (64), 101 (96), 85 (43)

HRMS: $C_{24}H_{34}O_8$ (450.52)

Calcd: 450.2254

Found: 450.2255

Preparation of 1,5-anhydro-4,6-*O*-isopropylidene-3-*O*-methyl-2-deoxy-1-(4,6-dimethoxy-2-(tetrahydropyran-2-yl)oxymethyl)-D-arabino-hex-1-enitol (27b) (TK-IX-28) (Table 2, entry 4)



25 **26** **27b**

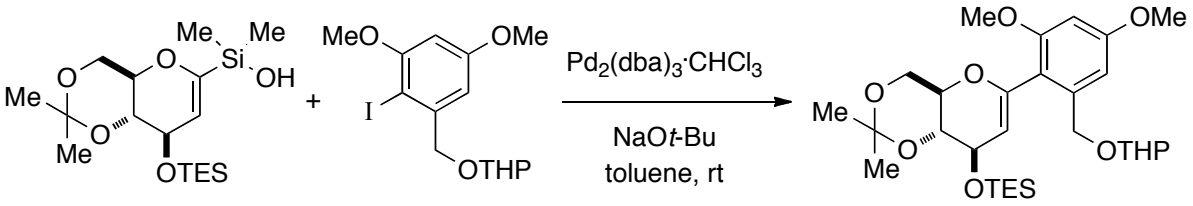
To a 25-mL, two-necked, round-bottomed flask equipped with a magnetic stir-bar, septum, water condenser and argon inlet, aromatic iodide **26** (68.1 mg, 0.182 mmol, 1.0 equiv), $Pd_2(dba)_3$•$CHCl_3$ (8.6 mg, 0.0094 mmol, 0.05 equiv) and NaO*t*-Bu (35 mg, 0.36 mmol, 2.0 equiv) were added. The contents were flushed with argon 3x and toluene (0.2 mL) was added. Finally, a solution of silanol **25** (50 mg, 0.18 mmol) was added in toluene (0.8 mL) and the reaction contents were added to a preheated (52 ^{o}C) oil bath and this mixture was stirred for 4 h. After 4 h the contents were concentrated. The crude product was purified by column chromatography (SiO_2, 35 g; hexane/EtOAc, 7:1). After chromatography aromatic iodide **26** (24 mg, 29%) was recovered along with homocoupled silanol **28** (6.0 mg, 17%) and the desired product **27b** (58.0 mg, 71%) as a colorless oil.

Data for **27b**:

^{1}H NMR: (400 MHz, $CDCl_3$)

6.65 (d, *J* = 2.4, 1/2 H), 6.64 (d, *J* = 2.4, 1/2 H), 6.39 (d, *J* = 2.4, 1/2 H), 6.38 (d, *J* = 2.4, 1/2 H), 4.88 (d, *J* = 2.0, 1/2 H), 4.86 (d, *J* = 2.0, 1/2 H), 4.72 (d, *J* = 11.6, 1 H), 4.71 - 4.66 (m, 1 H), 4.51 (d, *J* = 11.6, 1/2 H), 4.48 (d, *J* = 11.6, 1/2 H), 4.18 - 4.14 (m, 1 H), 4.11 - 4.05 (m, 1 H), 4.01 – 3.84 (m, 4 H), 3.81 (s, 3 H), 3.78 (s, 3 H), 3.58 - 3.51 (m, 1 H), 3.44 (s, 3 H), 1.92 - 1.40 (m, 6 H), 1.58 (s, 3 H), 1.47 (s, 3 H)

Preparation of 1,5-Anhydro-4,6-*O*-isopropylidene-3-*O*-triethylsilyl-2-deoxy-1-(4,6-dimethoxy-2-(tetrahydropyran-2-yl)oxymethyl)-D-arabino-hex-1-enitol (33) (TK-IX-28) (Table 2, entry 2)



32 **26** **33**

To a 25-mL, two-necked, round-bottomed flask equipped with a magnetic stir-bar, septum, and argon inlet, silanol **32** (65.9 mg, 0.176 mmol) was added along with aromatic iodide **26** (66.6 mg, 0.176 mmol) and the contents were flushed with argon 3x. Then toluene (0.8 mL) was added along with $Pd_2(dba)_3$•$CHCl_3$ (9.1 mg, 0.0088 mmol, 0.05 equiv) and NaO*t*-Bu (33. 8 mg, 0.352 mmol, 2.0 equiv). The mixture was stirred at rt for 12 h. After 12 h the mixture was concentrated using rotary evaporation. The crude mixture was purified by silica gel chromatography (SiO_2, 35 g; hexane/EtOAc, 7:1). After chromatography the desired product **33** (48.0 mg, 50%) was isolated as a colorless oil.

Data for **33**:

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

6.64 (d, *J* = 2.4, 1/2 H), 6.63 (d, *J* = 2.4, 1/2 H), 6.39 (d, *J* = 2.4, 1/2 H), 6.38 (d, *J* = 2.4, 1/2 H), 4.76-4.66 (m, 3 H), 4.56-4.42 (m, 2 H), 3.98-3.80 (m, 5 H), 3.81 (s, 1.5 H), 3.80 (s, 1.5 H), 3.78 (s, 3 H), 3.58-3.52 (m, 1 H), 1.92-1.48 (s, 1.5 H), 1.54 (s, 3 H), 1.42 (s, 3 H), 0.95 (t, *J* = 8.1, 9 H), 0.64 (dq, *J* = 22.7, 8.1, 3 H), 0.60 (dq, *J* = 22.7, 8.1, 3 H)

MS: (EI)

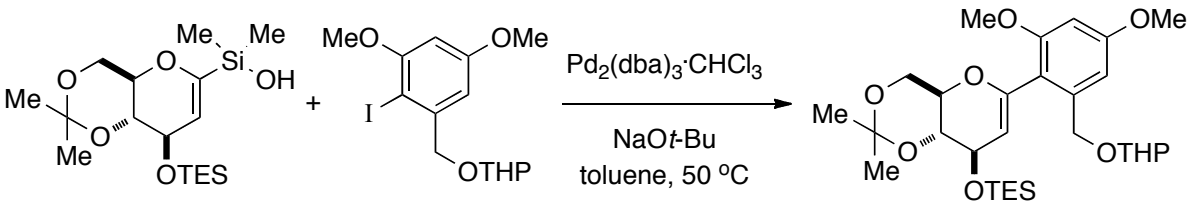
550 (M^+, 3), 466 (14), 450 (38), 351 (12), 377 (10), 351 (12), 336 (20), 333 (100), 307 (19), 305 (16), 293 (16), 275 (13), 259 (12), 233 (18), 231 (13), 205 (21), 204 (15), 195 (17), 193 (94), 191 (20), 189 (11), 187 (9), 179 (27), 175 (15), 115 (21), 103 (20), 101 (89), 91 (14), 85 (88), 75 (26), 67 (19), 29 (59), 57 (23)

HRMS: $C_{29\,H46}O_8Si$ (550.76)

Calcd: 550.2962

Found: 550.2963

Preparation of 1,5-Anhydro-4,6-*O*-isopropylidene-3-*O*-triethylsilyl-2-deoxy-1-(4,6-dimethoxy-2-(tetrahydropyran-2-yl)oxymethyl)-D-arabino-hex-1-enitol (33) (TK-IX-28) (Table 2, entry 5)



32 **26** **33**

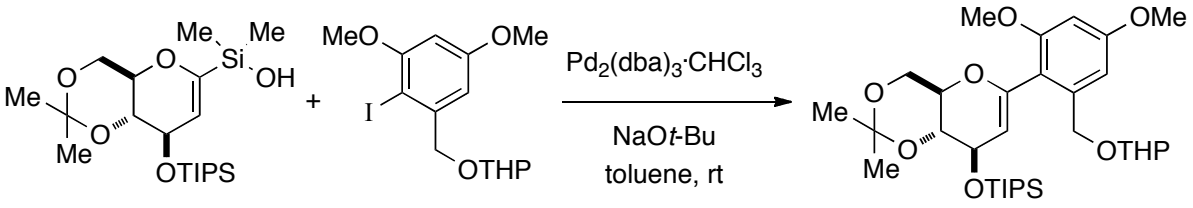
To a 25-mL, two-necked, round-bottomed flask equipped with a magnetic stir-bar, septum, and argon inlet, silanol **32** (68.7 mg, 0.183 mmol) and aromatic iodide **26** (69.2 mg, 0.183 mmol) were added. Then the contents were flushed with argon 3x and toluene (0.8 mL) was added along with $Pd_2(dba)_3$•$CHCl_3$ (9.5 mg, 0.0092 mmol, 0.05 equiv) and NaO*t*-Bu (35.2 mg, 0.366 mmol, 2.0 equiv). The mixture was added to a preheated (52 °C) oil bath and stirred at this temperature for 4 h. After 4 h the mixture was concentrated. The crude residue was purified by column chromatography (SiO_2, 35 g; hexane/EtOAc, 7:1-3:1). After chromatography the desired product **33** (68 mg, 67%) was isolated as a colorless oil.

Data for **33**:

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

6.64 (d, *J* = 2.4, 1/2 H), 6.63 (d, *J* = 2.4, 1/2 H), 6.39 (d, *J* = 2.4, 1/2 H), 6.38 (d, *J* = 2.4, 1/2 H), 4.76-4.66 (m, 3 H), 4.56-4.42 (m, 2 H), 3.98-3.80 (m, 5 H), 3.81 (s, 1.5 H), 3.80 (s, 1.5 H), 3.78 (s, 3 H), 3.58-3.52 (m, 1 H), 1.92-1.48 (s, 1.5 H), 1.54 (s, 3 H), 1.42 (s, 3 H), 0.95 (t, *J* = 8.1, 9 H), 0.64 (dq, *J* = 22.7, 8.1, 3 H), 0.60 (dq, *J* = 22.7, 8.1, 3 H)

Preparation of 1,5-Anhydro-4,6-*O*-isopropylidene-3-*O*-triisopropylsilyl-2-deoxy-1-(4,6-dimethoxy-2-(tetrahydropyran-2-yl)oxymethyl)-D-arabino-hex-1-enitol (34) (TK-IX-38) (Table 2, entry 3)



11 **26** **34**

To a 25-mL, two-necked, round-bottomed flask equipped with a magnetic stir-bar, septum, and argon inlet, silanol **11** (73.7 mg, 0.177 mmol) was added along with aromatic iodide **26** (66.9 mg, 0.177 mmol) and the contents were flushed with argon 3x. Then toluene (0.8 mL) was added, followed by the addition of $Pd_2(dba)_3$•$CHCl_3$ (9.3 mg, 0.009 mmol, 0.05 equiv) and NaO*t*-Bu (34 mg, 0.354 mmol, 2.0 equiv). The mixture was then stirred at rt for 12 h. After this amount of time the mixture was concentrated using rotary evaporation and the crude product was purified by column chromatography (SiO_2, 35 g; hexane/EtOAc, 7:1). After chromatography the desired product **34** was isolated as an inseparable mixture (94 mg) of silanol **11** (51%), aromatic iodide **26** (71%) and product **34** (<20% of product by ^{1}H-NMR integration).

Data for **34s**:

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

6.65 (d, *J* = 2.3, 1 H), 6.38 (d, *J* = 2.3, 1 H), 4.77-4.67 (m, 3 H), 4.59-4.51 (m, 2 H), 3.97-3.89 (m, 5 H), 3.81 (s, 3 H), 3.81 (s, 3 H), 3.77 (s, 3 H), 3.57-3.51 (m, 1 H), 1.91-1.48 (m, 6 H), 1.53 (s, 3 H), 1.41 (s, 3 H), 1.21-0.91 (m, 21H)

MS: (EI)

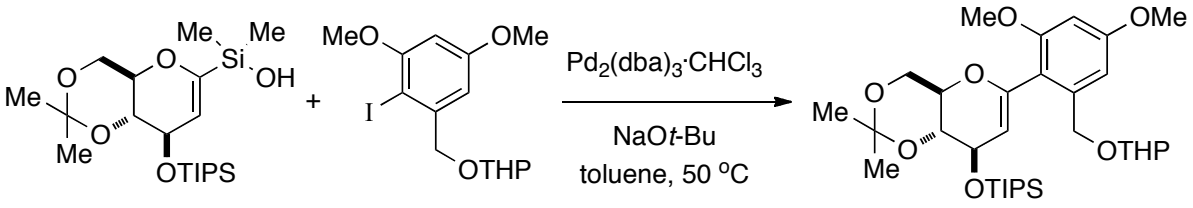
592 (M^+, 3), 549 (14), 508 (12), 492 (19), 491 (13), 465 (17), 450 (17), 449 (32), 407 (16), 391 (19), 389 (20), 377 (35), 335 (21), 334 (18), 333 (77), 259 (20), 215 (21), 205 (24), 195 (37), 193 (53), 191 (14), 179 (30), 173 (21), 101 (77), 85 (100), 59 (27)

HRMS: $C_{32}H_{52}O_8Si$ (592.84)

Calcd: 592.34313

Found: 592.34276

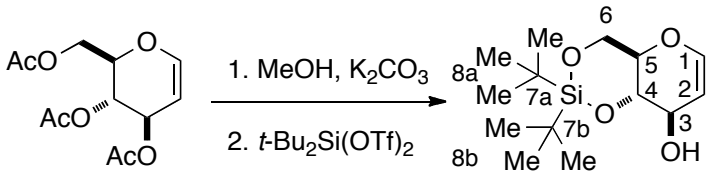
Preparation of 1,5-Anhydro-4,6-*O*-isopropylidene-3-*O*-triisopropylsilyl-2-deoxy-1-(4,6-dimethoxy-2-(tetrahydropyran-2-yl)oxymethyl)-D-arabino-hex-1-enitol (34) (TK-IX-37) (Table 2, entry 6)



11 **26** **34**

To a 25-mL, two-necked, round-bottomed flask equipped with a magnetic stir-bar, septum, and argon inlet, silanol **11** (76 mg, 0.182 mmol) was added along with aromatic iodide **26** (68.8 mg, 0.182 mmol) and the contents were flushed with argon 3x. Then toluene (0.8 mL) was added along with $Pd_2(dba)_3$•$CHCl_3$ (9.4 mg, 0.0091 mmol, 0.05 equiv) and NaO*t*-Bu (35.2 mg, 0.366 mmol, 2.0 equiv). The mixture was added to a preheated oil bath at 52 °C and stirred at this temperature for 4 h. After this amount of time the mixture was concentrated using rotary evaporation. The crude product was purified by silica gel chromatography (SiO_2, 35 g; hexane/EtOAc, 7:1-3:1). After chromatography the desired product **34** was isolated as an impure mixture (76 mg, 70% of product by ^{1}H-NMR integration).

Preparation of 1,5-Anhydro-4,6-O-[bis(1,1-dimethylethyl)silylene]-2-deoxy-*D*-arabino-1-hexenitol (129) [CSR-V-95][35]



35 **129**

To a 500-mL, two-necked, round-bottomed flask fitted with a nitrogen inlet, a septum, and magnetic stir-bar was added triacetoxyglucal **35** (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 rt 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 DMF (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[15] (14.8 mL, 40.6 mmol, 1.1 equiv) was added. The contents were warmed to rt 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 **129** as a white powder.

Data for **129**:

mp: 67-69 ºC (hexanes/EtOAc, 15:1)

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

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

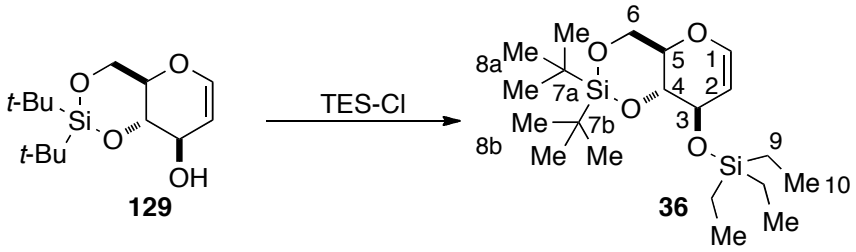
TLC: R_f 0.16 (hexanes/EtOAc, 20:1) [SiO_2, UV, $KMnO_4$]

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 (36) [CSR-V-96]



To a 500-mL, two-necked, round-bottomed flask fitted with a nitrogen inlet, septum, and magnetic stir-bar was added alcohol **129** (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 rt for 4 h. To this solution was added saturated $NaHCO_{3(aq)}$ (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. 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 **36** as a colorless oil.

Data for **36**:

bp: 145 ºC ($6.5x10^{-5}$ mmHg, ABT)

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

6.23 (dd, *J* = 6.0, 2.0, 1 H, HC(1)), 4.61 (dd, *J* = 6.0, 2.0, 1 H, HC(2)), 4.28 (dd, *J* = 7.0, 2.0, 1 H, HC(3)), 4.15 (dd, *J* = 10.5, 5.0, 1 H, HC(6e)), 3.96 (dd, *J* = 10.4, 7.0, 1 H, HC(4)), 3.95 (t, *J* =10.5, 1 H, HC(6a)), 3.80 (dt, *J* = 10.4, 5.0, 1 H, HC(5)), 1.07 (s, 9 H, $(CH_3)_3C$(8a or 8b)), 1.00 (s, 9 H, $(CH_3)_3C$(8a or 8b)), 0.99 (t, *J* = 8.0, 9 H, H_3C(10)), 0.66 (dq, *J* = 15.0, 8.0, 6 H, H_2C(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, $CHCl_3$)

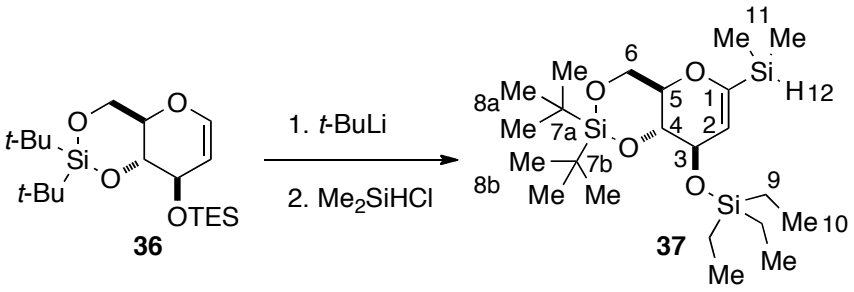
TLC: R_f 0.60 (hexanes/EtOAc, 10:1) [SiO_2, CAM]

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 (37) [CSR-V-66]



To a 25-mL, single-necked, round-bottomed flask fitted with an argon inlet adaptor with septum, and magnetic stir-bar was charged with **36** (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-bottomed 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 ^oC. The solution of metalated **36** added into the solution of dimethylchlorosilane via cannula. The white mixture was warmed to rt 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 **37** as a colorless. Further purification by diffusion pump distillation (140 ^oC, at 7.0 x 10^{-5} mmHg) afforded 1.90 g (4.23 mmol, 89%) of analytically pure **37** as a colorless oil.

Data for **37**:

bp: 140 ºC ($7.0x10^{-5}$ mmHg, ABT)

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

4.88 (d, *J* = 2.0, 1 H, HC(2)), 4.25 (dd, *J* = 7.3, 2.0, 1 H, HC(3)), 4.15 (dd, *J* = 10.3, 5.1, 1 H, (HeC(6)), 3.97 (sept, *J* = 3.7, 1 H, (SiH(12)), 3.94 (t, *J* = 10.3, 1 H, (HaC(6)), 3.93 (dd, *J* = 10.1, 7.0, 1 H, HC(4)), 3.74 (dt, *J* = 10.3, 5.1, 1 H, HC(5)), 1.06 (s, 9 H, $(CH_3)_3C$ (8a or 8b)), 1.00 (s, 9 H, $(CH_3)_3C$ (8a or 8b)), 0.99 (t, *J* = 8.0, 9 H, H_3C(10)), 0.69 (dq, *J* = 8.0, 2.0, 6 H, H_2C(9)), 0.158 (d, *J* = 3.7, 6 H, $Si(CH_3)_2$ (11))

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

157.6 (C(1)), 115.5 (C(2)), 77.2 (C(4)), 73.1 (C(5)), 71.1 (C(3)), 66.1 (C(6)), 27.4 (C(8a or 8b)), 26.9 (C(8a or 8b)), 22.7 (C(7a or 7b)), 19.8 (C(7a or 7b)), 6.8 (C(9)), 4.8 (C(10)), –5.5 (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)

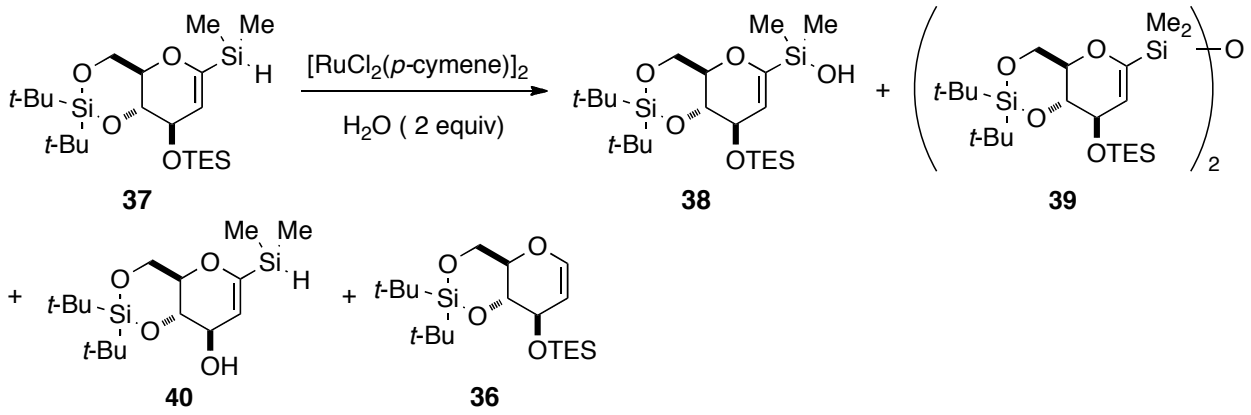
TLC: R_f 0.61 (hexanes/EtOAc, 20:1) [SiO_2, CAM]

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

Calcd: C, 57.59%; H, 10.10%

Found: C, 57.76%; H, 10.29%

Screening Conditions for Oxidative Hydrolysis (Table 3). Preparation 1,5-Anhydro-4,6-*O*-[bis(1,1-dimethylethyl)silylene]-2-deoxy-1-*C*-(hydroxydimethylsilyl))-3-*O*-(triethylsilyl)-*D*-arabino-1-hexenitol (38) survey of oxidative hydrolysis conditions (Table 3, entry 1)



To a 10-mL, single-necked, round-bottomed flask equipped with a magnetic stir-bar was charged with silane **37** (0.110 g, 0.238 mmol, 1.0 equiv) and CH_3CN (2.0 mL). Then H_2O (9.0 μL, 0.476 mmol, 2.0 equiv) was added followed by di-μ-chlorobis[(*p*-cymene)chlororuthenium(II)] (0.006 g, 0.0095 mmol, 0.04 equiv). After the addition, the orange solution was stirred open to air for 4 h at rt. 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 (10 mL). The aqueous layer was extracted with EtOAc (3 x 30 mL) and the combined organic extracts were washed with brine (10 mL). The contents were concentrated and immediately subjected to column chromatography ((SiO_2, 20 x 200 mm), hexanes/EtOAc, 15:1), which afforded 0.082 g (73%) of **38** as colorless viscous oil.

Data for **38**:

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

4.94 (d, *J* = 2.1, 1 H, HC(2)), 4.26 (dd, *J* = 7.3, 2.0, 1 H, HC(3)), 4.16 (dd, *J* = 10.1, 4.8, 1 H, HeC(6)), 3.94 (t, *J* = 10.1, 1 H, HaC(6)), 3.93 (dd, *J* = 10.1, 7.0, 1 H, HC(4)), 3.75 (dt, *J* = 10.1, 5.4, 1 H, HC(5)), 1.76 (s, 1 H, SiOH(12)), 1.06 (s, 9 H, $(CH_3)_3$C(8a or 8b)), 1.00 (s, 9 H, $(CH_3)_3$C(8a or 8b)), 0.99 (t, *J* = 7.7, 9 H,

$H_3C(10)$), 0.69 (dq, J = 7.7, 2.0, 6 H, $H_2C(9)$), 0.22 (s, 6 H, $Si(CH_3)_2(11)$)

Table 3, entry 2:

To a 20-mL, single-necked, round-bottomed flask equipped with a magnetic stir-bar was charged with silane **37** (0.564 g, 1.22 mmol, 1.0 equiv) and CH_3CN (12 mL). Then H_2O (44 μL, 2.45 mmol, 2.0 equiv) was added followed by di-μ-chlorobis[(*p*-cymene)chlororuthenium(II)] (0.029 g, 0.049 mmol, 0.04 equiv). After the addition, the orange solution was stirred open to air for 1 h at rt. 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 (20 mL). The aqueous layer was extracted with EtOAc (3 x 30 mL) and the combined organic extracts were washed with brine (20 mL). The contents were concentrated and immediately subjected to column chromatography ((SiO_2, 30 x 200 mm), hexanes/EtOAc, 15:1), which afforded 0.406 g (70%) of **38** as colorless viscous oil.

Table 3, entry 3:

To a 50-mL, single-necked, round-bottomed flask equipped with a magnetic stir-bar was charged with silane **37** (0.950 g, 2.07 mmol, 1.0 equiv) and CH_3CN (20 mL). Then H_2O (75 μL, 4.14 mmol, 2.0 equiv) was added followed by di-μ-chlorobis[(*p*-cymene)chlororuthenium(II)] (0.051 g, 0.083 mmol, 0.04 equiv). After the addition, the orange solution was stirred open to air for 1 h at rt. Over the course of the reaction the contents darkened from red to a final blood-red color. After 1 h the reaction was not complete by TLC analysis. A second portion of di-μ-chlorobis[(*p*-cymene)chlororuthenium(II)] (0.051 g, 0.083 mmol, 0.04 equiv) was added and the contents were stirred for another 1 h. The red solution was diluted with H_2O (50 mL). The aqueous layer was extracted with EtOAc (3 x 40 mL) and the combined organic extracts were washed with brine (40 mL). The contents were concentrated and immediately subjected to column chromatography ((SiO_2, 40 x 200 mm), hexanes/EtOAc, 15:1), which afforded 0.462 g (47%) of **38** as colorless viscous oil.

Table 3, entry 4:

To a 10-mL, single-necked, round-bottomed flask equipped with a magnetic stir-bar was charged with silane **37** (0.100 g, 0.218 mmol, 1.0 equiv) and CH_3CN (2.0 mL). Then H_2O (8 μL, 0.436 mmol, 2.0 equiv) was added followed by $[Ir(cod)Cl]_2$ (0.005 g, 0.007 mmol, 0.03 equiv).

After the addition, the orange solution was stirred open to air for 3 h at rt. Then the yellow solution was diluted with H_2O (10 mL). The aqueous layer was extracted with Et_2O (4 x 15 mL) and the combined organic extracts were washed with brine (10 mL). The contents were concentrated and immediately subjected to column chromatography ((SiO_2, 30 x 200 mm), hexanes/EtOAc, gradient 20 :1, 15:1, 10:1, 5 :1), which afforded 0.019 g (19%) of **37**, 0.054 g (52%) of **38**, 0.06 g (3%) **39** and 0.018 g, (23%) of **40**.

Data for **39**:

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

4.96 (d, *J* = 2.1, 1 H), 4.26 (dd, *J* = 7.3, 2.0, 1 H), 4.14 (dd, *J* = 10.1, 4.8, 1 H), 3.92 (t, *J* = 10.1, 1 H), 3.93 (dd, *J* = 10.1, 7.0, 1 H), 3.74 (dt, *J* = 10.1, 5.4, 1 H), 1.06 (s, 9 H), 1.00 (s, 9 H, 0.97 (t, *J* = 7.7, 9 H), 0.60 (dq, *J* = 7.7, 2.0, 6 H), 0.12 (s, 6 H)

Data for **40**:

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

4.71 (dd, *J* = 6.0, 2.0, 1 H), 4.27 (dd, *J* = 7.0, 2.0, 1 H), 4.15 (dd, *J* = 10.5, 5.0, 1 H), 3.96 (dd, *J* = 10.4, 7.0, 1 H), 3.95 (t, *J* =10.5, 1 H), 3.76 (dt, *J* = 10.4, 5.0, 1 H), 1.07 (s, 9 H), 1.00 (s, 9 H), 0.144 (d, *J* = 3.7, 6 H)

Table 3, entry 5:

To a 10-mL, single-necked, round-bottomed flask equipped with a magnetic stir-bar was charged with silane **37** (0.100 g, 0.218 mmol, 1.0 equiv) and *n*-butyronitrile (2.0 mL). Then H_2O (8 μL, 0.436 mmol, 2.0 equiv) was added followed by di-μ-chlorobis[(*p*-cymene)chlororuthenium(II)] (0.011 g, 0.0018 mmol, 0.08 equiv). After the addition, the orange solution was stirred open to air for 2 h at rt. Then the blood red solution was diluted with H_2O (10 mL). The aqueous layer was extracted with Et_2O (4 x 15 mL) and the combined organic extracts were washed with brine (10 mL). The contents were concentrated and immediately subjected to column chromatography ((SiO_2, 30 x 200 mm), hexanes/EtOAc, gradient 20:1, 15:1, 10:1, 5 :1), which afforded 0.090 g (87%) of **38**, and 0.05 g (2%) **39**.

Table 3, entry 6:

To a 10-mL, single-necked, round-bottomed flask equipped with a magnetic stir-bar was

charged with silane **37** (0.100 g, 0.218 mmol, 1.0 equiv) and *n*-butyronitrile (2.0 mL). Then H_2O (8 μL, 0.436 mmol, 2.0 equiv) was added followed by di-μ-chlorobis[(*p*-cymene)chlororuthenium(II)] (0.004 g, 0.007 mmol, 0.03 equiv). After the addition, the orange solution was stirred open to air for 4 h at rt. Then the blood red solution was diluted with H_2O (10 mL). The aqueous layer was extracted with Et_2O (4 x 15 mL) and the combined organic extracts were washed with brine (10 mL). The contents were concentrated and immediately subjected to column chromatography ((SiO_2, 30 x 200 mm), hexanes/EtOAc, 15:1), which afforded 0.079 g (84%) of **38**, and 0.07 g (4%) **39**.

Table 3, entry 7:

To a 10-mL, single-necked round-bottomed flask equipped with a magnetic stir-bar was charged with silane **37** (0.100 g, 0.218 mmol, 1.0 equiv) and THF (2.0 mL). Then H_2O (8 μL, 0.436 mmol, 2.0 equiv) was added followed by di-μ-chlorobis[(*p*-cymene)chlororuthenium(II)] (0.004 g, 0.007 mmol, 0.03 equiv). After the addition, the orange solution was stirred open to air for 4 h at rt. Then the blood red solution was diluted with H_2O (10 mL). The aqueous layer was extracted with Et_2O (4 x 15 mL) and the combined organic extracts were washed with brine (10 mL). The contents were concentrated and immediately subjected to column chromatography ((SiO_2, 30 x 200 mm), hexanes/EtOAc, 15:1), which afforded 0.051 g (54%) of **38**, 0.07 g (5%) **39**, and 0.024 g (27%) **36**.

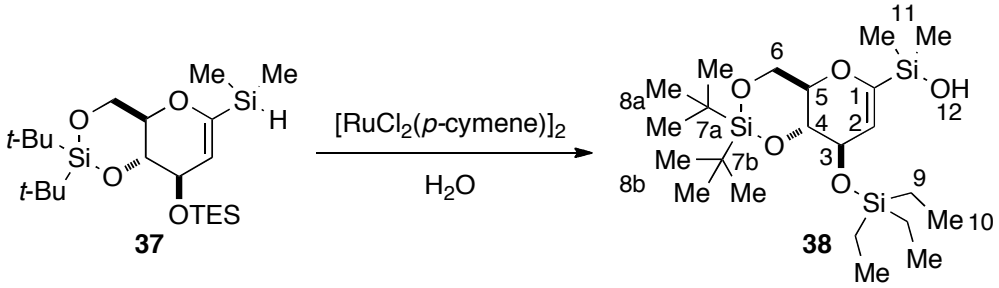
Table 3, entry 8:

To a 10-mL, single-necked, round-bottomed flask equipped with a magnetic stir-bar was charged with silane **37** (0.100 g, 0.218 mmol, 1.0 equiv) and benzonitrile (2.0 mL). Then H_2O (8 μL, 0.436 mmol, 2.0 equiv) was added followed by di-μ-chlorobis[(*p*-cymene)chlororuthenium(II)] (0.005 g, 0.009 mmol, 0.04 equiv). After the addition, the orange solution was stirred open to air for 4 h at rt. Then the blood red solution was diluted with H_2O (10 mL). The aqueous layer was extracted with Et_2O (4 x 15 mL) and the combined organic extracts were washed with brine (10 mL). The contents were concentrated and immediately subjected to column chromatography ((SiO_2, 30 x 200 mm), hexanes/EtOAc, 15:1), which afforded 0.085 g (90%) of **38**, and 0.06 g (4%) **39**.

Table 3, entry 9:

To a 10-mL, single-necked round-bottomed flask equipped with a magnetic stir-bar was charged with silane **37** (0.100 g, 0.218 mmol, 1.0 equiv) and benzene (1.0 mL). Then H_2O (8 μL, 0.436 mmol, 2.0 equiv) was added followed by a solution of di-μ-chlorobis[(*p*-cymene)chlororuthenium(II)] (0.004 g, 0.007 mmol, 0.03 equiv) in CH_3CN (1.0 mL). After the addition, the orange solution was stirred open to air for 1 h at rt. Then the blood red solution was diluted with H_2O (10 mL). The aqueous layer was extracted with Et_2O (4 x 15 mL) and the combined organic extracts were washed with brine (10 mL). The contents were concentrated and immediately subjected to column chromatography ((SiO_2, 30 x 200 mm), hexanes/EtOAc, 15:1), which afforded 0.081 g (86%) of **38**, and 0.08 g (7%) **39**.

Preparation of 1,5-Anhydro-4,6-*O*-[bis(1,1-dimethylethyl)silylene]-2-deoxy-1-*C*-(hydroxydimethylsilyl))-3-*O*-(triethylsilyl)-*D*-arabino-1-hexenitol (Table 3, entry 10) (38) [CSR-V-60]



To a 10-mL, single-necked, round-bottomed flask equipped with a magnetic stir-bar was charged with silane **37** (0.715 g, 1.56 mmol, 1.0 equiv) and benzene (4.0 mL). To another 50-mL, round-bottomed 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 **37** 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 rt. 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

38 as colorless, viscous oil.

Data for **38**:

bp: 145 ºC (2.0×10^{-5} mmHg, ABT)

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

4.94 (d, *J* = 2.1, 1 H, HC(2)), 4.26 (dd, *J* = 7.3, 2.0, 1 H, HC(3)), 4.16 (dd, *J* = 10.1, 4.8, 1 H, HeC(6)), 3.94 (t, *J* = 10.1, 1 H, HaC(6)), 3.93 (dd, *J* = 10.1, 7.0, 1 H, HC(4)), 3.75 (dt, *J* = 10.1, 5.4, 1 H, HC(5)), 1.76 (s, 1 H, SiOH(12)), 1.06 (s, 9 H, $(CH_3)_3$C(8a or 8b)), 1.00 (s, 9 H, $(CH_3)_3$C(8a or 8b)), 0.99 (t, *J* = 7.7, 9 H, H_3C(10)), 0.69 (dq, *J* = 7.7, 2.0, 6 H, H_2C(9)), 0.22 (s, 6 H, $Si(CH_3)_2$(11))

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

158.3 (C(1)), 114.8 (C(2)), 77.0 (C(4)), 73.1 (C(5)), 71.0 (C(3)), 66.1 (C(6)), 27.4 (C(8a or 8b)), 26.9 (C(8a or 8b)), 22.7 (C(7a or 7b)), 6.8 (C(9)), 4.9 (C(10)), –1.3 (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)

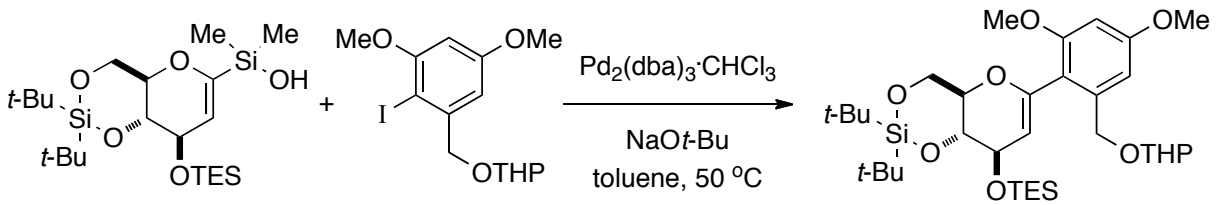
TLC: R_f 0.22 (hexanes/EtOAc, 10:1) [SiO_2, CAM]

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(methoxy)-6'-[(tetrahydropyran-2''-yl)methoxy]phenyl]-2-deoxy-3-O-triethylsilyl-*D*-arabino-1-hexenitol (42) [TK-IX-69]



38 **26** **42**

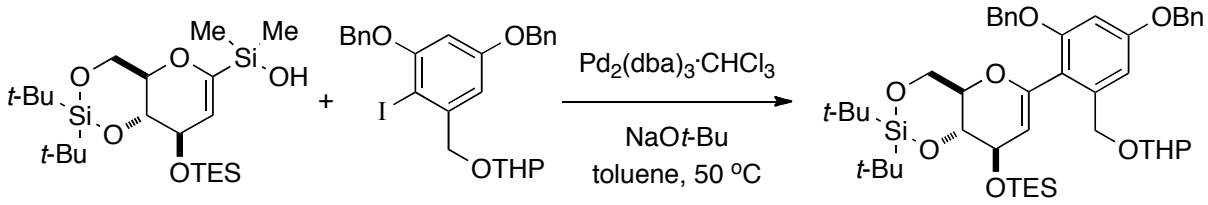
A 35-mL, single-necked, round-bottomed flask containing a magnetic stir-bar was charged with silanol **38** (0.0814 g, 0.171 mmol, 1.0 equiv), aromatic iodide **26** (0.0662 g, 0.171 mmol, 1.0 equiv) and $Pd_2(dba)_3$•$CHCl_3$ (0.0089 g, 0.0069 mmol, 0.05 equiv). A water condenser fitted with an argon inlet with a rubber septum was attached and the contents of the flask were placed under an atmosphere of argon. Toluene (0.8 mL) was added to give a purple-red mixture. Then the condenser was quickly removed and sodium *tert*-butoxide (0.0329 g, 0.342 mmol, 2.0 equiv) was added. Then the contents were stirred and heated under argon at 50 °C for 4 h. After 4 h the reaction solvent was removed under reduced pressure to give crude product. This material was subjected to column chromatography ((SiO_2, 35 g; hexanes/EtOAc, 7:1) to give 0.085 g (77%) of the desired product as a colorless oil.

Data for **42**:

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

6.63 (J = 2.3, 1/2 H), 6.62 (J = 2.3, 1/2 H), 6.39 (J = 2.3, 1/2 H), 6.38 (J = 2.3, 1/2 H), 4.75-4.65 (m, 3 H), 4.56-4.41 (m, 2 H), 4.17-3.90 (m, 5 H), 3.80 (s, 3 H), 3.78 (s, 3 H), 1.90-1.49 (m, 6 H), 1.08 (s, 9 H), 1.03 (s, 9 H), 0.98 (t, J = 8.1, 9 H), 0.70-0.59 (m, 6 H)

Preparation of 1,5-Anhydro-4,6-O-[bis(1,1-dimethylethyl)silylene]-1-C-[2',4'-bis(phenylmethoxy)-6'-[(tetrahydropyran-2''-yl)methoxy]phenyl]-2-deoxy-3-O-triethylsilyl-*D*-arabino-1-hexenitol (43) [TK-IX-96] (Scheme 8, eq. 2, Table 4, entry 1)



38 **41** **43**

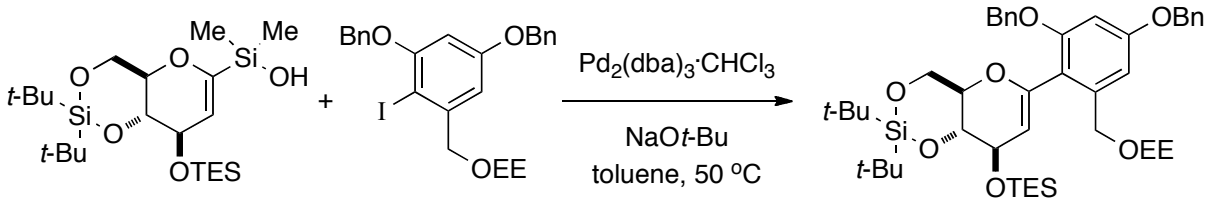
A 25-mL, single-necked, round-bottomed flask containing a magnetic stir-bar was charged with silanol **38** (0.0841 g, 0.183 mmol, 1.0 equiv), aromatic iodide **41** (0.0971 g, 0.183 mmol, 1.0 equiv) and $Pd_2(dba)_3$•$CHCl_3$ (0.0095 g, 0.0092 mmol, 0.05 equiv). A water condenser fitted with an argon inlet with a rubber septum was attached and the contents of the flask were placed under an atmosphere of argon. Toluene (0.8 mL) was added to give a purple-red mixture. Then the condenser was quickly removed and sodium *tert*-butoxide (0.0329 g, 0.342 mmol, 2.0 equiv) was added. Then the contents were stirred and heated under argon at 50 °C for 4 h. After 4 h the reaction solvent was removed under reduced pressure to give crude product. This material was subjected to column chromatography ((SiO_2, 35 g, hexanes/EtOAc, 7:1) to give 0.106 g (72%) of the desired product as a colorless oil. The desired product was further purified by a resubjecting the material to column chromatography (SiO_2, gradient (CH_2Cl_2-1% MeOH/ CH_2Cl_2-3%MeOH/ CH_2Cl_2-5%MeOH) to give pure **43** (0.095 g, 65%) as a colorless oil.

Data for **43**:

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

7.46-7.27 (m, 10H), 6.74 (d, *J* = 1.9, 1 H), 6.73 (d, *J* = 1.9, 1 H), 6.54 (d, *J* = 1.9, 1 H), 6.53 (d, *J* = 1.9, 1 H), 5.06 (s, 2 H), 5.02 (s, 2 H), 4.77-4.68 (m, 3 H), 4.57 (d, *J* = 11.7, 1/2 H), 4.51 (d, *J* = 11.7, 1/2 H), 4.40 (dd, *J* = 7.2, 2.4, 1/2 H), 4.38 (dd, *J* = 7.2, 2.4, 0.5), 4.19-3.87 (m, 5 H), 3.58-3.49 (m, 1 H), 1.92-1.48 (m, 6 H), 1.08 (s, 9 H), 1.01 (s, 9 H), 0.98 (t, *J* = 8.1, 9 H), 0.71-0.58 (m, 6 H)

Preparation of 1,5-Anhydro-4,6-O-[bis(1,1-dimethylethyl)silylene]-1-C-[2',4'-bis(phenylmethoxy)-6'-[(1''-ethoxyethoxy)methoxy]phenyl]-2-deoxy-3-O-triethylsilyl-*D*-arabino-1-hexenitol (48) [TK-X-27] (Table 4, entry 2)



38 **44** **48**

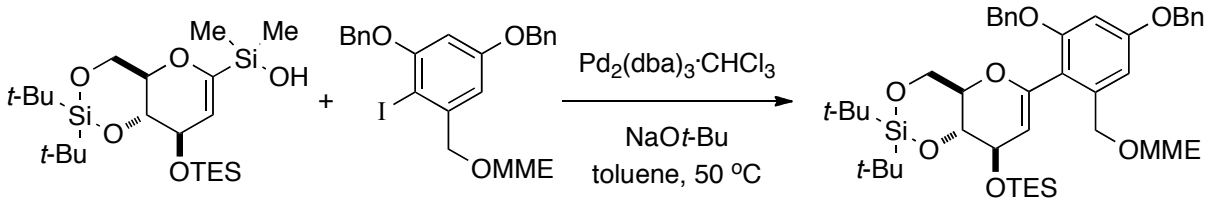
A 25-mL, single-necked, round-bottomed flask containing a magnetic stir-bar was charged with silanol **38** (0.0737 g, 0.155 mmol, 1.0 equiv), aromatic iodide **44** (0.0803 g, 0.183 mmol, 1.0 equiv) and $Pd_2(dba)_3$•$CHCl_3$ (0.0081 g, 0.0078 mmol, 0.05 equiv). A water condenser fitted with an argon inlet with a rubber septum was attached and the contents of the flask were placed under an atmosphere of argon. Toluene (0.8 mL) was added to give a purple-red mixture. Then the condenser was quickly removed and sodium *tert*-butoxide (0.0298 g, 0.310 mmol, 2.0 equiv) was added. Then the contents were stirred and heated under argon at 50 ˚C for 4 H. After 4 h the reaction solvent was removed under reduced pressure to give crude product. The crude material was loaded directly onto a silica column and purified twice by column chromatography ((SiO_2, 35 g, hexanes/EtOAc, 7:1), then ((SiO_2, 35 g), gradient (CH_2Cl_2-1% MeOH/ CH_2Cl_2-3%MeOH/ CH_2Cl_2-5%MeOH) to afford 0.0339 g (28%) of **48** as a colorless oil.

Data for **48**:

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

7.46-7.27 (m, 10H), 6.75 (d, *J* = 2.0, 1 H), 6.51 (d, *J* = 2.0, 1 H), 5.05 (s, 2 H), 5.02 (s, 2 H), 4.88 (q, *J* = 4.9, 1/2 H), 4.78 (q, *J* = 4.9, 1/2 H), 4.72 (d, *J* = 11.8, 1/2 H), 4.71 (d, *J* = 2.4, 1/2 H), 4.65 (d, *J* = 11.8, 1/2 H), 4.64 (d, *J* = 11.8, 1/2 H), 4.55 (d, *J* = 11.8, 1/2 H), 4.52 (d, *J* = 11.8, 1/2 H), 4.41-4.36 (m. 1 H), 4.19-4.12 (m, 1 H), 4.08-4.02 (m, 1 H), 4.00-3.89 (m, 2 H), 3.70-3.62 (m, 1 H), 3.56-3.48 (m, 1 H), 1.35 (d, *J* = 4.9, 1.5 H), 1.33 (d, *J* = 4.9, 1.5 H), 1.22 (t, *J* = 7.4, 1.5 H), 1.16 (t, *J* = 7.4, 1.5 H), 1.08 (s, 9 H), 1.00 (s, 9 H), 0.97 (t, *J* = 8.2, 9 H), 0.70-0.60 (m, 6 H)

Preparation of 1,5-Anhydro-4,6-O-[bis(1,1-dimethylethyl)silylene]-1-C-[2',4'-bis(phenylmethoxy)-6'-[(1''-methoxy-1''-methylethoxy)methoxy]phenyl]-2-deoxy-3-O-triethylsilyl-*D*-arabino-1-hexenitol (49) [TK-X-32] (Table 4, entry 3)



38 **45** **49**

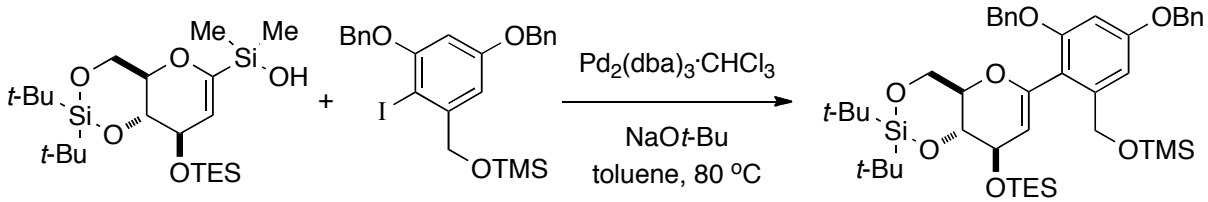
A 25-mL, single-necked, round-bottomed flask containing a magnetic stir-bar was charged with silanol **38** (0.074 g, 0.156 mmol, 1.0 equiv), aromatic iodide **45** (0.0809 g, 0.156 mmol, 1.0 equiv) and $Pd_2(dba)_3$•$CHCl_3$ (0.0081 g, 0.0078 mmol, 0.05 equiv). A water condenser fitted with an argon inlet with a rubber septum was attached and the contents of the flask were placed under an atmosphere of argon. Toluene (0.8 mL) was added to give a purple-red mixture. Then the condenser was quickly removed and sodium *tert*-butoxide (0.030 g, 0.312 mmol, 2.0 equiv) was added. Then the contents were stirred and heated under argon at 50 °C for 4 H. After 4 h the reaction solvent was removed under reduced pressure to give crude product. The crude material was loaded directly onto a silica column and purified twice by column chromatography ((SiO_2, 35 g, hexanes/EtOAc, 7:1), then ((SiO_2, 35 g), gradient (CH_2Cl_2-1% MeOH/ CH_2Cl_2-3%MeOH/ CH_2Cl_2-5%MeOH) to afford 0.032 g (26%) of **49** as a colorless oil.

Data for **49**:

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

7.46-7.26 (m, 10H), 6.73 (d, *J* = 2.0, 1 H), 6.52 (d, *J* = 2.0, 1 H), 5.08 (s, 2 H), 5.01 (s, 2 H), 4.72 (d, *J* = 2.0, 1 H), 4.47 (d, *J* = 11.5, 1 H), 4.43 (d, *J* = 11.5, 1 H), 4.38 (dd, *J* = 7.0, 2.0, 1 H), 4.20-4.13 (m, 1 H), 4.08-4.02 (m, 1 H), 4.00-3.88 (m, 3 H), 3.80-3.69 (m, 2 H), 3.22 (s, 3 H), 1.08 (s, 9 H), 1.00 (s, 9 H), 0.98 (t, *J* = 8.0, 9 H), 0.72-0.58 (m, 6 H)

Preparation of 1,5-Anhydro-4,6-O-[bis(1,1-dimethylethyl)silylene]-1-C-[2',4'-bis(phenylmethoxy)-6'-[(trimethylsilyl)methoxy]phenyl]-2-deoxy-3-O-triethylsilyl-*D*-arabino-1-hexenitol (50) [TK-X-12] (Table 4, entry 4)



38 **46** **50**

A 25-mL, single-necked, round-bottomed flask containing a magnetic stir-bar was charged with silanol **38** (0.0766 g, 0.167 mmol, 1.0 equiv), aromatic iodide **46** (0.0866 g, 0.167 mmol, 1.0 equiv) and $Pd_2(dba)_3$•$CHCl_3$ (0.0087 g, 0.0084 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 (0.8 mL) was added to give a purple-red mixture. Then the condenser was quickly removed and sodium *tert*-butoxide (0.0321 g, 0.334 mmol, 2.0 equiv) was added. Then the contents were stirred and heated under argon at 80 ^{o}C for 12h. After 12 h the reaction solvent was removed under reduced pressure to give crude product. The crude material was loaded directly onto a silica column and purified twice by column chromatography ((SiO_2, 35 g, hexanes/EtOAc, 7:1), then ((SiO_2, 35 g), gradient (CH_2Cl_2-1% MeOH/ CH_2Cl_2-3%MeOH) to afford 0.0470 g (36%) of **50** as a colorless oil.

Data for **50**:

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

7.45-7.27 (m, 10H), 6.78 (d, *J* = 2.5, 1 H), 6.50 (d, *J* = 2.5, 1 H), 5.07 (s, 2 H), 5.01 (s, 2 H), 4.74 (d, *J* = 13.5, 1 H), 4.69 (d, *J* = 13.5, 1 H), 4.69 (d, *J* = 2.2, 1 H), 4.39 (dd, *J* = 6.5, 2.2, 1 H), 4.14 (dd, *J* = 9.3, 4.2, 1 H), 4.06 (dd, *J* = 9.3, 6.5, 1 H), 3.97 (t, *J* = 9.3, 1 H), 3.92 (dt, *J* = 9.3, 4.2, 1 H), 1.18 (s, 9 H), 1.10 (s, 9 H), 0.98 (t, *J* = 8.0, 9 H), 0.67 (dq, *J* = 18.4, 8.0, 3 H), 0.64 (dq, *J* = 18.4, 8.0, 3 H), 0.14 (s, 9 H)

MS: (EI)

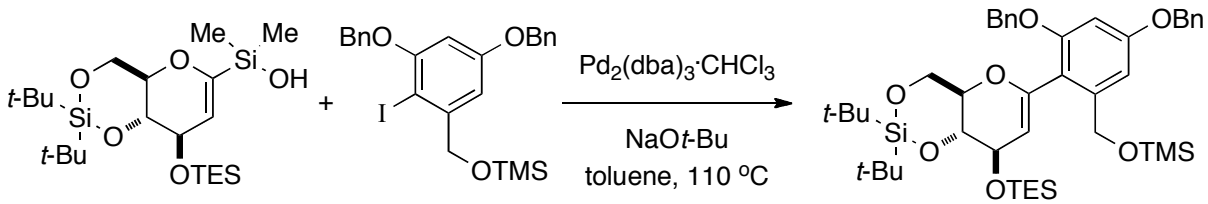
791 (M^+, 2), 447 (22), 446 (66), 223 (10), 205 (27), 181 (26), 129 (10), 91 (100), 77 (15), 73 (22), 59 (11)

HRMS: $C_{44}H_{66}O_7Si_3$ (791.25)

Calcd: 790.4116

Found: 790.4122

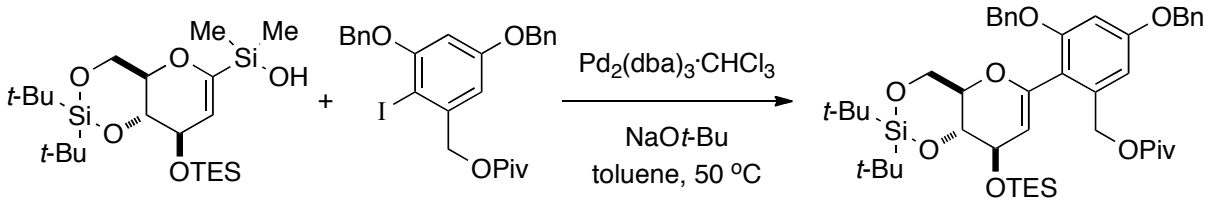
Preparation of 1,5-Anhydro-4,6-O-[bis(1,1-dimethylethyl)silylene]-1-C-[2',4'-bis(phenylmethoxy)-6'-[(trimethylsilyl)methoxy]phenyl]-2-deoxy-3-O-triethylsilyl-*D*-arabino-1-hexenitol (50) [TK-IX-91] (Table 4, entry 5)



38 **46** **50**

A 25-mL, single-necked, round-bottomed, flask containing a magnetic stir-bar was charged with silanol **38** (0.0846 g, 0.184 mmol, 1.0 equiv), aromatic iodide **46** (0.0954 g, 0.184 mmol, 1.0 equiv) and $Pd_2(dba)_3$•$CHCl_3$ (0.0092 g, 0.0092 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 (0.8 mL) was added to give a purple-red mixture. Then the condenser was quickly removed and sodium *tert*-butoxide (0.0354 g, 0.368 mmol, 2.0 equiv) was added. Then the contents were stirred and heated under argon at 110 ˚C for 2 H. After 2 h the reaction solvent was removed under reduced pressure to give crude product. The crude material was loaded directly onto a silica column and purified twice by column chromatography ((SiO_2, 35 g, hexanes/EtOAc, 7:1), then ((SiO_2, 35 g), gradient (CH_2Cl_2-1% MeOH/ CH_2Cl_2-3%MeOH) to afford 0.0760 g (52%) of **50** as a colorless oil.

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 (51) [TK-X-34] (Table 4, entry 6)



38 **47** **51**

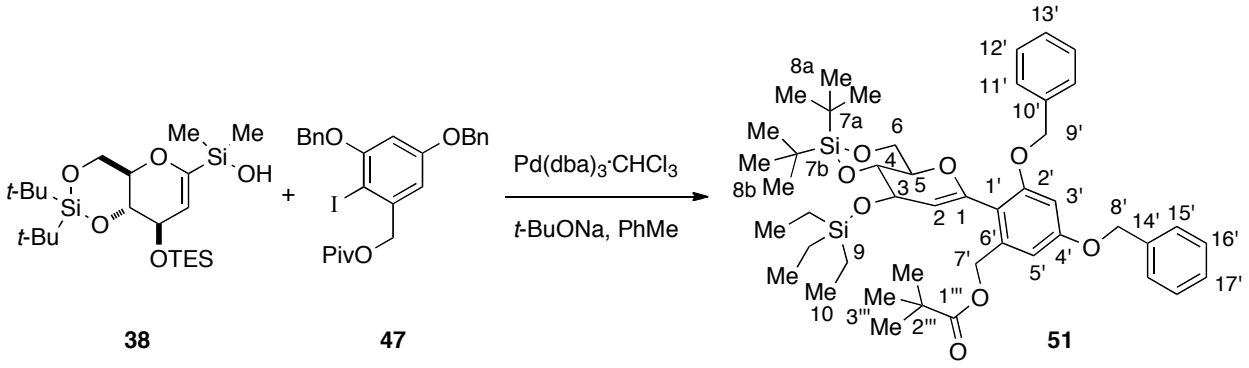
A 25-mL, single-necked, round-bottomed flask containing a magnetic stir-bar was charged with silanol **38** (0.0767 g, 0.162 mmol, 1.0 equiv), aromatic iodide **47** (0.0859 g, 0.162 mmol, 1.0 equiv) and $Pd_2(dba)_3$•$CHCl_3$ (0.0084 g, 0.0078 mmol, 0.05 equiv). A water condenser fitted with an argon inlet with a rubber septum was attached and the contents of the flask were placed under an atmosphere of argon. Toluene (0.8 mL) was added to give a purple-red mixture. Then the condenser was quickly removed and sodium *tert*-butoxide (0.0311g, 0.324 mmol, 2.0 equiv) was added. Then the contents were stirred and heated under argon at 50 ˚C for 4 h. After 4 h the reaction solvent was removed under reduced pressure to give crude product. The crude material was loaded directly onto a silica column and purified twice by column chromatography ((SiO_2, 35 g, hexanes/EtOAc, 7:1), then ((SiO_2, 35 g), gradient (CH_2Cl_2-1% MeOH/ CH_2Cl_2-3%MeOH) to afford 0.098 g (75%) of **51** as a colorless oil.

Data for **51**:

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

7.28-7.45 (m, 10 H, HC(15', 16', 17', 11', 12', 13')), 6.66 (d, *J* = 2.1, 1 H, HC(3' or 5')), 6.56 (d, *J* = 2.1, 1 H, HC(3' or 5')), 5.16 (d, *J* = 13.0, 1 H, HC(7'a)), 5.11 (d, *J* = 13.0, 1 H, HC(7'b)), 5.04 (s, 2 H, H_2C(8' or 9')), 5.02 (s, 2 H, H_2C(8' or 9')), 4.74 (d, *J* = 2.1, 1 H, HC(2)), 4.39 (dd, *J* = 7.0, 2.1, 1 H, HC(3)), 4.04 - 4.17 (m, 2 H, HC(4),HeC(6)), 3.97 (t, *J* = 10.5, 1 H, HaC(6)), 3.94 (dt, *J* = 10.5 4.4, 1 H, CC(5)), 1.21 (s, 9 H, HC(3''')), 1.18 (s, 9 H, $(CH_3)_3$C(8a or 8b)), 1.10 (s, 9 H, $(CH_3)_3$C(8a or 8b)), 0.98 (t, *J* = 8.0, 9 H, H_3C(10)), 0.67 (dq, *J* = 8.0 2.0 Hz, 6 H, H_2C(9))

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 (51) [CSR-VI-44]



A 25-mL, single-necked, round-bottomed flask containing a magnetic stir-bar was charged with aryl iodide **47** (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 **38** (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 5 H. 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 **51** as a colorless wax.

Data for **51**:

mp: 95-97 °C (CH_2Cl_2/hexanes, 2:1)

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

7.28-7.45 (m, 10 H, HC(15', 16', 17', 11', 12', 13')), 6.66 (d, *J* = 2.1, 1 H, HC(3' or 5')), 6.56 (d, *J* = 2.1, 1 H, HC(3' or 5')), 5.16 (d, *J* = 13.0, 1 H, HC(7'a)), 5.11 (d, *J*

= 13.0, 1 H, HC(7'b)), 5.04 (s, 2 H, H_2C(8' or 9')), 5.02 (s, 2 H, H_2C(8' or 9')), 4.74 (d, *J* = 2.1, 1 H, HC(2)), 4.39 (dd, *J* = 7.0, 2.1, 1 H, HC(3)), 4.04 - 4.17 (m, 2 H, HC(4),HeC(6)), 3.97 (t, *J* = 10.5, 1 H, HaC(6)), 3.94 (dt, *J* = 10.5 4.4, 1 H, HC(5)), 1.21 (s, 9 H, HC(3'")), 1.18 (s, 9 H, $(CH_3)_3C$(8a or 8b)), 1.10 (s, 9 H, $(CH_3)_3C$(8a or 8b)), 0.98 (t, *J* = 8.0, 9 H, H_3C(10)), 0.67 (dq, *J* = 8.0 2.0, 6 H, H_2C(9))

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

178.2 (C(1'")), 159.9 (C(2')), 157.9 (C(4')), 146.6 (C(1')), 137.6 (C(1)), 136.9 (C(10' or 14')), 136.6 (C(10' or 14')), 128.7 (C(6' or 11' or 12' or 13' or 15' or 16' or 17')), 128.4 (C(6' or 11' or 12' or 13' or 15' or 16' or 17')), 128.1 (C(6' or 11' or 12' or 13' or 15' or 16' or 17')), 127.8 (C(6' or 11' or 12' or 13' or 15' or 16' or 17')), 127.4 (C(6' or 11' or 12' or 13' or 15' or 16' or 17')), 126.9 (C(6' or 11' or 12' or 13' or 15' or 16' or 17')), 117.5 (C(2'")), 107.4 (C(2)), 105.5 (C(3' or 5')), 100.5 (C(3' or 5')), 73.2 (C(5)), 71.4 (C(3)), 70.3 (C(8' or 9')), 70.1 (C(8' or 9')), 66.0 (C(7')), 63.7 (C(6)), 38.8 (C(4)), 27.4 (C(8a or 8b)), 27.2 (C(3'")), 26.9 (C(8a or 8b)), 22.7 (C(7a or 7b)), 19.9 (C(7a or 7b)), 6.9 (C(9)), 4.8 (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)

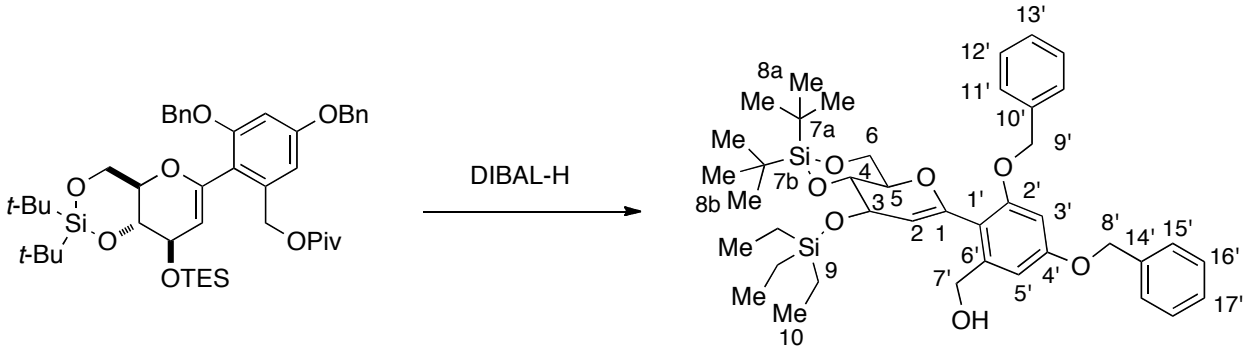
TLC: R_f 0.63 (3:1 hexanes/EtOAc) [SiO_2, CAM]

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 (52) [CSR-VI-59] (Scheme 9, eq. 1)



A 100-mL, single-necked, round-bottomed flask fitted with an argon inlet with a septum, and a magnetic stir-bar was charged with aryl glucal **51** (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 rt 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 **52** (98%) as a white solid.

Data for **52**:

mp: 50-51 °C (hexanes)

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

7.31-7.43 (m, 10H, HC(15', 16', 17', 11', 12', 13')), 6.74 (d, *J* = 2.2, 1 H, HC(3' or 5')), 6.55 (d, *J* = 2.2, 1 H, HC(3' or 5')), 5.07 (s, 2 H, H_2C(8' or 9')), 5.03 (s, 2 H, H_2C(8' or 9')), 4.76 (s, *J* = 2.2, 1 H, HC(7')), 4.65 (d, *J* = 6.6, 2 H, H_2C(2)), 4.40 (dd, *J* = 7.0, 2.2, 1 H, HC(3)), 4.15 (dd, *J* = 9.3, 3.7, 1 H, HeC(6)), 4.08 (dd, *J* = 7.0, 2.4, 1 H, HC(4)), 3.97 (t, *J* = 9.3, 1 H, HaC(6)), 3.97 (dt, *J* = 9.3, 3.7, 1 H, HC(5)), 1.90 (t, *J* = 6.6, 1 H, br(OH)), 1.08 (s, 9 H, $(CH_3)_3$C(8a or 8b)), 1.02 (s, 9

H, $(CH_3)_3C$(8a or 8b)), 0.98 (t, J = 8.0, 9 H, H_3C(10)), 0.66 (dq, J = 8.0, 2.0, 6 H, H_2C(9))

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

160.3 C(2')), 157.7 C(4')), 147.2 C(1')), 136.9 C(1)), 136.6 C(10' or 14')), 128.6 C(10' or 14')), 128.4 C(11' or 12' or 13' or 15' or 16' or 17')), 128.6 C(11' or 12' or 13' or 15' or 16' or 17')), 128.1 C(11' or 12' or 13' or 15' or 16' or 17')), 127.7 C(11' or 12' or 13' or 15' or 16' or 17')), 127.5 C(11' or 12' or 13' or 15' or 16' or 17')), 126.9 C(11' or 12' or 13' or 15' or 16' or 17')), 116.8 C(6')), 107.5 C(2)), 105.5 C(3' or 5')), 100.3 C(3' or 5')), 77.2 C(4)), 73.3 C(3)), 71.4 C(5)), 70.4 C(8' or 9')), 70.1 C(8' or 9')), 66.0 C(6)), 63.4 C(7')), 27.4 C(8a or 8b)), 26.9 C(8a or 8b)), 22.7 C(7a or 7b)), 26.9 C(7a or 7b)), 6.9 C(10)), 4.8 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)

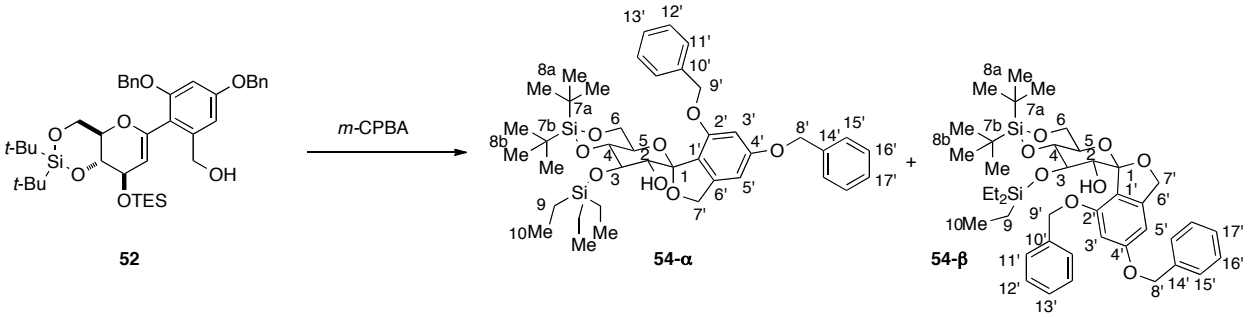
TLC: R_f0.15 (10:1 hexanes/EtOAc) [SiO_2, UV]

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(3 H),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 (54-α) and (1*R*,4'a*R*,7'*R*,8'*R*,8'a*R*)-Spiro[isobenzofuran-1(3 H),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 (54-β) [CSR-VIII-76]



A 250-mL, single-necked, round-bottomed flask fitted with an argon inlet with a septum, and a magnetic stir-bar was charged with **52** (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, single-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 **52**. The contents were stirred at 0 ºC for 5 min, and warmed to rt 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 (**54-α**:**54-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 **54-α**) of separated isomers. The separated isomers were recrystallized from hexanes (15 mL for **54-α**, 5 mL for **54-β**) to afford 0.733 g (77%) of **54-α** as a white, cubic solid and 0.142 g (15%) of **54-β** as a white powder.

Data for **54-α**:

mp: 130-131 °C (hexane)

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

7.29-7.39 (m, 10H, HC(15', 16', 17', 11', 12', 13')), 6.47 (d, *J* = 1.7, 1 H, HC(3')), 6.40 (d, *J* = 1.7, 1 H, HC(5')), 5.16 (d, *J* = 12.4, 1 H, HC(7'a)), 5.11 (s, 2 H, H_2C(8' or 9')), 5.07 (d, *J* = 12.4, 1 H, HC(7'b)), 5.00 (s, 2 H, H_2C(8' or 9')), 4.32 (dd, *J* =10.2, 7.3, 1 H, HC(2)), 4.13 (dd, *J* = 10.2, 4.4, 1 H, HC(6e)), 3.96 (dd, *J* = 10.2, 4.4, 1 H, HC(5)), 3.88 (t, *J* = 10.2, 1 H, HC(4)), 3.84 (t, *J* = 9.8, 1 H, HC(3)), 3.78 (t, *J* = 10.2, 1 H, HC(6a)), 1.84 (d, *J* = 7.3, 1 H, br(OH)), 1.08 (s, 9 H, $(CH_3)_3C$(8a or 8b)), 1.04 (s, 9 H, $(CH_3)_3C$(8a or 8b)), 0.99 (t, *J* = 8.0, 9 H, H_3C(10)), 0.70 (dq, *J* = 8.0, 2.0, 6 H, H_2C(9))

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

162.1 C(2')), 154.7 C(4')), 143.4 C(1')), 136.8 C(10' or14')), 136.6 C(10' or 14')), 128.7 C(11' or 12' or 13' or 15' or 16' or 17')), 128.5 C(11' or 12' or 13' or 15' or 16' or 17')), 128.1 C(11' or 12' or 13' or 15' or 16' or 17')), 127.8 C(11' or 12' or 13' or 15' or 16' or 17')), 127.4 C(11' or 12' or 13' or 15' or 16' or 17')), 126.7 C(11' or 12' or 13' or 15' or 16' or 17')), 118.2 C(6')), 110.85 C(1)), 100.5 C(3')), 98.4 C(5')), 77.8 C(4)), 76.6 C(2)), 73.2 C(5)), 73.2 C(3)), 70.4 C(8' or 9')), 69.7 C(8' or 9')), 68.9 C(7')), 67.1 C(6)), 27.6 C(8a or 8b)), 27.1 C(8a or 8b)), 22.8 C(7a or 7b)), 19.9 C(7a or 7b)), 7.0 C(10)), 5.2 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 **54-β**:

mp: 120-122 °C (hexane)

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

7.26-7.38 (m, 10H, HC(15', 16', 17', 11', 12', 13')), 6.42 (d, *J* = 2.0, 1 H, HC(3')), 6.32 (d, *J* = 2.0, 1 H, HC(5')), 5.31 (d, *J* = 14.2, 1 H, HC(8'a or 9'a)), 5.26 (d, *J* = 14.2, 1 H, HC(8'a or 9'a)), 5.14 (d, *J* = 12.8, 1 H, HC(7'a)), 4.92 (d, *J* = 12.8, 1 H, HC(7'b)), 4.90 (s, 2 H, H_2C(8' or 9')), 4.51 (t, *J* = 8.2, 1 H, HC(3)), 4.10 (dt, *J* = 9.4, 4.3, 1 H, HC(5)), 4.06 (dd, *J* = 9.4, 4.3, 1 H, HC(6e)), 3.97 (dd, *J* = 9.4, 8.2, 1 H, HC(4)), 3.92 (t, *J* = 8.2, 3.1, 1 H, HC(2)), 3.86 (t (br), *J* = 9.4, 1 H, HC(6a)), 2.56 (br d, 3.1, 1 H, OH)), 1.06 (s, 9 H, $(CH_3)_3C$(8a or 8b)), 0.98 (s, 9 H, $(CH_3)_3C$(8a or 8b)), 0.94 (t, *J* = 8.1, 9 H, H_3C(10)), 0.58-0.75 (m, 6 H, H_2C(9))

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

161.4 (C(2')), 153.8 (C(4')), 145.6 (C(1')), 136.4 (C(10' or14')), 136.2 (C(10' or 14')), 128.7 (C(11' or 12' or 13' or 15' or 16' or 17')), 128.6 (C(11' or 12' or 13' or 15' or 16' or 17')), 128.2 (C(11' or 12' or 13' or 15' or 16' or 17')), 127.7 (C(11' or 12' or 13' or 15' or 16' or 17')), 127.5 (C(11' or 12' or 13' or 15' or 16' or 17')), 125.9 (C(11' or 12' or 13' or 15' or 16' or 17')), 118.5 (C(6')), 113.0 (C(1)), 100.6 (C(3')), 99.3 (C(5')), 78.01 (C(4)), 77.8 (C(2)), 76.91 (C(5)), 71.3 (C(3)), 70.3 (C(8' or 9')), 69.6 (C(8' or 9')), 68.8 (C(7')), 67.22 (C(6)), 27.6 (C(8a or 8b)), 27.0 (C(8a or 8b)), 22.7 (C(7a or 7b)), 19.8 (C(7a or 7b)), 6.9 (C(10)), 5.1 (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]

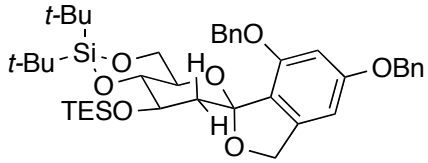
HRMS: $C_{41}H_{58}O_8Si_2$ (735.07)

Calcd: 735.3749

Found: 735.3782

Note: when acidic conditions were used for the cleavage of the benzylic protecting group non-oxidative cyclization was commonly observed.

(1*S*,4'a*R*,7'*R*,8'*R*,8'a*R*)-Spiro[isobenzofuran-1(3 H),6'(4'H)-pyrano[3-d][2-deoxy][1,3,]dioxasilin]-7'-ol, 2',2'-bis(1,1-dimethylethyl)-4'a,7',8',8'a-tetrahydro-5,7,-bis(phenylmethoxy)-8'- triethylsilyl (53) [TK-X-11] (Scheme 9, eq. 2)



53

Data for **53**:

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

7.20 – 7.43 (m, 10H), 6.45 (d, *J* = 1.9, 1 H), 6.39 (d, *J* = 1.9, 1 H), 5.12 (d, *J* = 12.4, 1 H), 5.09 (d, *J* = 12.4, 1 H), 5.07 (d, *J* = 12.7, 1 H), 5.00 (s, 2 H), 4.96 (d, *J* = 12.7, 1 H), 4.05 – 4.14 (m, 2 H), 3.95 (dt, *J* = 9.5, 4.1, 1 H), 3.88 (t, *J* = 9.5, 1 H), 3.77 (t, *J* = 9.5, 1 H), 2.79 (dd, *J* = 12.9, 9.5, 1 H), 2.08 (dd, *J* = 12.9, 4.8, 1 H), 1.08 (s, 9 H), 1.02 (s, 9 H), 0.97 (t, *J* = 8.1, 9 H), 0.95 (q, *J* = 8.1, 3 H), 0.92 (q, *J* = 8.1, 3 H)

MS: (EI)

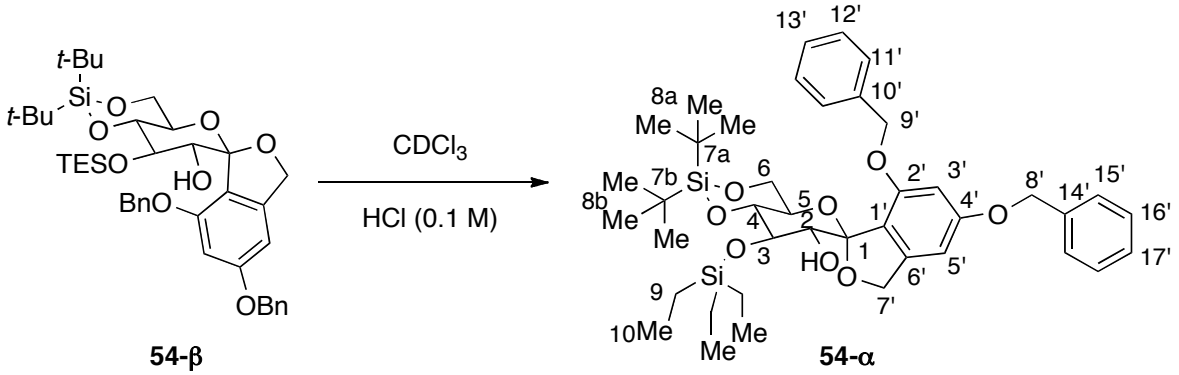
719 (M^+, 1), 662 (18), 661 (34), 446 (42), 374 (13), 344 (22), 201 (18), 158 (17), 156 (47), 149 (24), 141 (18), 139 (52), 115 (21), 111 (13), 111 (28), 105 (26), 103 (41), 97 (22), 91 (100), 87 (21), 85 (27), 83 (27), 79 (24), 77 (41), 75 (53), 71 (36), 69 (33), 57 (69), 55 (47)

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

Calcd: 718.37161

Found: 718.37211

Isomerization of 54-β to 54α [CSR-IX-13]



54-β **54-α**

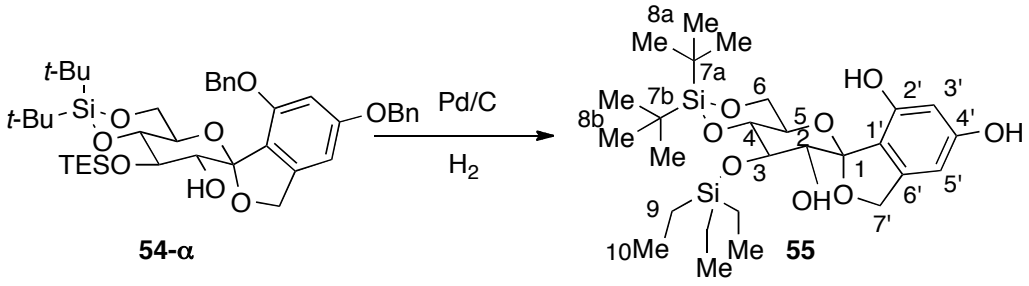
A solution of **54-β** (0.026 g, 0.035 mmol) in $CDCl_3$ (0.7 mL, containing HCl (0.1 M, titrated)) was analyzed by ^{1}H-NMR. Complete epimerization to **54-α** was observed after 12 h at 20 °C. After ^{1}H-NMR analysis the contents were diluted with CH_2Cl_2 (0.1 mL) and subjected to column chromatography ((SiO_2, 10 x 50 mm), hexanes/EtOAc, 7:1) to afford 0.025 g (96%) of **54-α**.

Data for **54-α**:

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

7.29-7.39 (m, 10H, HC(15', 16', 17', 11', 12', 13')), 6.47 (d, *J* = 1.7 Hz, 1 H, HC(3')), 6.40 (d, *J* = 1.7, 1 H, HC(5')), 5.16 (d, *J* = 12.4, 1 H, HC(7'a)), 5.11 (s, 2 H, H_2C(8' or 9')), 5.07 (d, *J* = 12.4, 1 H, HC(7'b)), 5.00 (s, 2 H, H_2C(8' or 9')), 4.32 (dd, *J* =10.2, 7.3, 1 H, HC(2)), 4.13 (dd, *J* = 10.2, 4.4, 1 H, HC(6e)), 3.96 (dd, *J* = 10.2, 4.4, 1 H, HC(5)), 3.88 (t, *J* = 10.2, 1 H, HC(4)), 3.84 (t, *J* = 9.8, 1 H, HC(3)), 3.78 (t, *J* = 10.2, 1 H, HC(6a)), 1.84 (d, *J* = 7.3, 1 H, br(OH)), 1.08 (s, 9 H, $(CH_3)_3$C(8a or 8b)), 1.04 (s, 9 H, $(CH_3)_3$C(8a or 8b)), 0.99 (t, *J* = 8.0, 9 H, H_3C(10)), 0.70 (dq, *J* = 8.0, 2.0, 6 H, H_2C(9))

Preparation of 1,1-anhydro-4,6-*O*-di-*tert*-butylsilylene-3-*O*-triethylsilyl-1-(2,4-dihydroxy-2-hydroxymethyl)-α-D-glucopyranose (55) [TK-X-54]



To a 25-mL, single-necked, round-bottomed flask equipped with a magnetic stir-bar was added **54-α** (0.103 g, 0.0553 mmol) followed by THF (5 mL). Then $NaHCO_3$ (0.030 g) was added along with 5% palladium on carbon (0.030 g). The flask was attached to hydrogen manifold and the flask was purged with hydrogen (3x) and stirred at rt under 1 atm of H_2 for 10 min and the apparatus was opened and another portion of 5% palladium on carbon (0.030 g) was added. The flask and manifold were flushed with H_2 one more time. The reaction was stirred at rt under 1 atm H_2 for 1 h. The reaction was still not complete after 1 h and another portion of 5% palladium on carbon (0.030 g) and $NaHCO_3$ (0.030 g) was added and the reaction was stirred under an H_2 atmosphere for another 10 h. The reaction contents and manifold were flushed with nitrogen and the contents were filtered through Celite (0.1 g) and the filter pad was washed with Et_2O (3 mL). The colorless filtrate was concentrated to a foamy solid using rotary evaporation. The contents were purified by column chromatography (SiO_2, 80 g; hexane/EtOAc gradient 3:1 to 1:1) to afford 0.0684 g (88%) **55** as a colorless oil.

Data for **55**:

Note: the chemical shifts of the ^{1}H-NMR spectrum were found to be dependant upon the concentration of the sample in $CDCl_3$

^{1}H NMR: (500 MHz, $CDCl_3$, 0.0386 M)

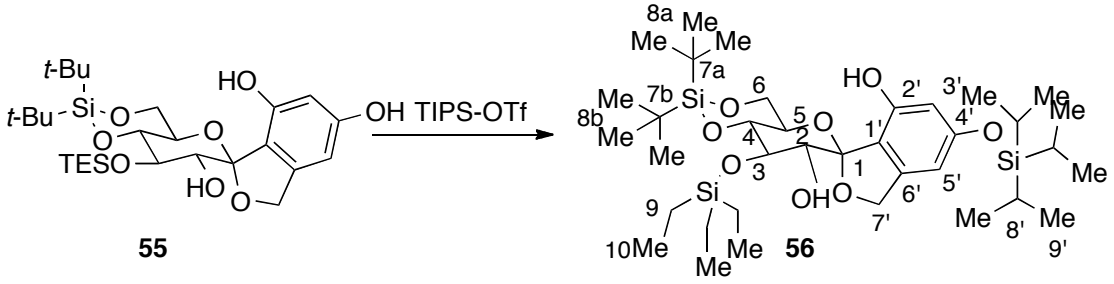
7.19 (s, 2 H, ArylOH)), 5.95 (s, 1 H, HC(3' or 5')), 5.91 (s, 1 H, HC(3' or 5')), 5.01 (t, J = 9.5, 1 H, H_2C(7a')), 4.91 (t, J = 9.5, 1 H, H_2C(7b')), 4.38 (t, J = 7.9, 1 H, HC(2)), 4.05 (dd, J = 9.5, 4.8, HeC(6)), 3.95 (dt, J = 9.5, 4.8, 1 H, HC(5)), 3.91 (t, J = 9.5, 1 H, HC(3)), 3.85 (t, J = 9.5, 1 H, HC(4)), 3.76 (t, J = 9.5, 1 H, HaC(6)), 2.80 (br, s, 1 H, HO(C2)), 1.07 (s, 9 H, $(H_3C)_3C$(8a or 8b)), 1.03 (s, 9 H, $(H_3C)_3C$(8a or 8b)), 1.00 (t, J = 8.0, 9 H, H_3C(10)), 0.76 (dq, J = 20.0, 8.0, 3 H,

$H_2C(9)$), 0.71 (dq, J = 20.0, 8.0, 3 H, $H_2C(9)$)

^{13}C NMR: (126 MHz, $CDCl_3$, 0.0386 M)

158.4, 151.9, 143.6, 115.6, 110.2, 103.1, 100.3, 77.5, 76.6, 73.2, 73.0, 69.0, 66.7, 27.5, 27.1, 22.7, 19.9, 7.0, 5.1

Preparation of 1,1-Anhydro-4,6-*O*-di-*tert*-butylsilylene-3-*O*-triethylsilyl-1-(6-hydroxy-2-hydroxymethyl-4-triisopropylsiloxyphenyl)-α-D-glucopyranose (56) [TK-X-54]



To a 50-mL, single-necked, round-bottomed flask containing a magnetic stir-bar and argon inlet was charged with triol **55** (0.0307 g, 0.0553 mmol, 1.0 equiv) and CH_2Cl_2 (2 mL). To the flask was added a solution of 2,6-lutidine (0.0178 g, 0.1659 mmol, 3.0 equiv) in CH_2Cl_2 (0.5 mL) and a solution of TIPS-OTf (0.037 g, 0.1217 mmol, 2.2 equiv) in CH_2Cl_2 (0.5 mL). The contents were stirred at rt for 1 h and the reaction mixture was quenched with H_2O (30 mL) and transferred to a separatory funnel. The organic layer was extracted and the aqueous was extracted with CH_2Cl_2 (3 x 30 mL). The combined organic phases were washed with brine (30 mL) and dried with Na_2SO_4. The contents were filtered and concentrated using rotary evaporation. The crude product was purified using column chromatography (Florisil, 35 g, hexane/EtOAc, 3:1) followed by a second column chromatography purification (SiO_2, 35 g, hexane/EtOAc, 10:1) to afford 0.0272 g (69%) of **56** as a colorless oil.

Data for **56**:

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

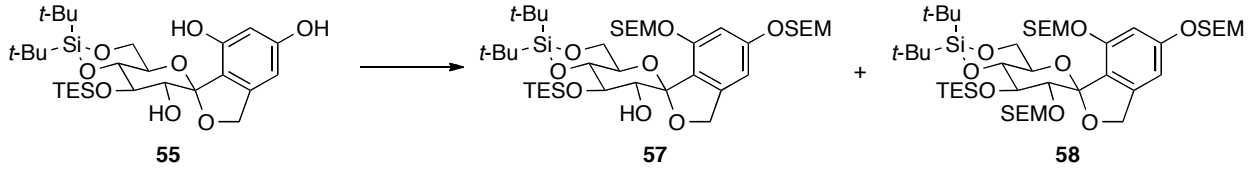
6.30 (d, J = 12.0, 1 H, HC(3' or 5')), 6.23 (d, J = 12.0, 1 H, HC(3' or 5')), 5.14 (s, 1 H, ArylOH)), 5.12 (d, J = 12.0, 1 H, $H_2C(7)$), 5.06 (d, J = 12.0, 1 H, $H_2C(7)$), 4.12 (dd, J = 9.0, 5.1, 1 H, HeC(6)), 4.10 (dd, J = 6.9, 6.0, 1 H, HC(2)), 3.98 (dt, J = 9.0, 5.1, 1 H, HC(5)), 3.86 (t, J = 9.0, 1 H, HaC(6)), 3.86 (dd, J = 9.0, 6.9, 1 H, HC(3)), 3.83 (t, J = 9.0, 1 H, HC(4)), 1.88 (d, J = 6.0, 1 H, OH)), 1.23 (sept., 3 H,

$(CH_3)_2CHSi(8')$), 1.08 (d, 9 H, $(CH_3)_2CHSi$ (9')), 1.07 (s, 9 H, $(H_3C)_3C$(8a or 8b)), 1.03 (s, 9 H, $(H_3C)_3C$(8a or 8b)), 1.00 (t, t = 8.4, 9 H, $H_3C(10)$), 0.71 (q, J = 8.4, $H_2C(9)$)

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

159.1, 151.5, 143.2, 116.1, 110.4, 107.1, 104.8, 77.7, 76.6, 73.9, 73.5, 68.9, 66.9, 27.5, 27.1, 22.7, 19.9, 17.9, 12.6, 6.9, 5.2

Preparation of 1,1-anhydro-4,6-*O*-di-*tert*-butylsilylene-3-*O*-trimethylsilyl-1-(4,6-bis(2-trimethylsilylethoxymethoxy)-2-hydroxymethylphenyl-α-D-glucopyranose (57) and 1,1-anhydro-4,6-*O*-di-*tert*-butylsilylene-3-*O*-trimethylsilyl-2-*O*-(2-trimethylsilylethoxy-methyl)-1-(4,6-bis(2-trimethylsilylethoxymethoxy)-2-hydroxymethylphenyl-α-D-glucopyranose (58) [TK-XI-35] (Table S1, entry 1)



To a 5-mL, round-bottomed flask equipped with a magnetic stir-bar, and an argon inlet **55** (0.018 g, 0.0324 mmol, 1.0 equiv) was added along with CH_2Cl_2 (0.2 mL). To this solution was added *i*-Pr_2NEt (0.03 mL, 0.162 mmol, 5.0 equiv), and a solution of 2-(trimethylsilyl)ethoxymethyl chloride (0.0095 g, 0.081 mmol, 2.5 equiv) in CH_2Cl_2 (0.3 mL). The contents were stirred at rt under an argon atmosphere for 3 h. After 3 h the reaction contents were transferred to a separatory funnel containing H_2O (15 mL). The organic layer was extracted and the aqueous was extracted with CH_2Cl_2 (3 x 20 mL). The organic layers were combined and washed with brine (30 mL), dried with Na_2SO_4, filtered and concentrated. The crude product was purified using column chromatography (SiO_2, 35 g; hexanes/EtOAc, 10:1) to give **57** (0.0138 g, 52%) as a colorless oil.

Data for **57**:

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

6.68 (d, J = 2.0, 1 H), 6.57 (d, J = 2.0, 1 H), 5.23 (s, 2 H), 5.17 (s, 2 H), 5.14 (d, J = 12.4, 1 H), 5.03 (d, J = 12.4, 1 H), 4.32 – 4.24 (m , 1 H), 4.08 (dd, J = 9.6, 4.8, 1 H), 3.86 – 3.67 (m, 7 H), 1.81 (d, J = 8.0, 1 H), 1.07 (s, 9 H), 1.04 (s, 9 H), 1.00

(t, J = 8.0, 9 H), 0.97 – 0.91 (m, 4 H), 0.72 (q, 6 H, J = 8.0), 0.01 (s, 9 H), –0.01 (s, 9 H)

MS: (EI, 70 eV)

815 (M^+, 0.5), 785 (5), 446 (10), 399 (16), 369 (35), 307 (39), 246 (10), 167 (13), 149 (100), 141 (16), 85 (25), 73 (32), 71 (28), 57 (34), 55 (20)

HRMS: $C_{39}H_{74}O_{10}Si_4$ (815.34)

Calcd: 814.4359

Found: 814.4360

Table S1, SI, entry 2:

To a 5-mL, round-bottomed flask equipped with a magnetic stir-bar, and an argon inlet **55** (0.0176 g, 0.0317 mmol, 1.0 equiv) was added along with CH_2Cl_2 (0.4 mL). To this solution was added *i*-Pr_2NEt (0.08 mL, 0.476 mmol, 15.0 equiv), a solution of 2-(trimethylsilyl)ethoxymethyl chloride (0.033 g, 0.285 mmol, 9.0 equiv) in CH_2Cl_2 (0.1 mL) and tetrabutylammonium iodide (0.046 g, 0.127 mmol, 4 equiv). The contents were stirred at rt under an argon atmosphere for 10 h. After 10 h the reaction contents were transferred to a separatory funnel containing H_2O (30 mL). The organic layer was extracted and the aqueous was extracted with CH_2Cl_2 (3 x 30 mL). The organic layers were combined and washed with brine (30 mL), dried with Na_2SO_4, filtered and concentrated. The crude product was purified using column chromatography (SiO_2, 35 g; hexanes/EtOAc, 3:1), followed by a second column (SiO_2, 35 g, hexanes/EtOAc, 10:1) gave **57** (0.017 g, 66%) as a colorless oil. Further purification, of the early fractions from the second column, using prep-TLC (SiO_2, 0.25 mm, hexanes/EtOAc, 10:1) gave **58** (0.002 g, 7%) as a colorless oil.

Data for **57**:

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

6.68 (d, J = 2.0, 1 H), 6.57 (d, J = 2.0, 1 H), 5.23 (s, 2 H), 5.17 (s, 2 H), 5.14 (d, J = 12.4, 1 H), 5.03 (d, J = 12.4, 1 H), 4.32 – 4.24 (m , 1 H), 4.08 (dd, J = 9.6, 4.8, 1 H), 3.86 – 3.67 (m, 7 H), 1.81 (d, J 8.0, 1 H), 1.07 (s, 9 H), 1.04 (s, 9 H), 1.00 (t, J = 8.0, 9 H), 0.97 – 0.91 (m, 4 H), 0.72 (q, 6 H, J = 8.0), 0.01 (s, 9 H), –0.01 (s, 9 H)

Data for **58**:

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

6.72 (d, *J* = 1.3, 1 H), 6.52 (d, *J* = 1.3, 1 H), 5.26 (d, *J* = 6.0, 1 H), 5.20 (d, *J* = 6.0, 1 H), 5.17 (d, *J* = 6.0, 1 H), 5.12 (d, *J* = 6.0, 1 H), 5.11 (d, *J* = 12.0, 1 H), 5.06 (d, *J* = 12.0, 1 H), 4.72 (d, *J* = 6.0, 1 H), 4.62 (d, *J* = 6.0, 1 H), 4.20 (d, *J* = 8.4, 1 H), 4.06 (dd, *J* = 8.4, 4.4, 1 H), 3.98 (t, *J* = 8.4, 1 H), 3.93 (dt, *J* = 8.4, 4.4, 1 H), 3.83 – 3.68 (m, 6 H), 2.87 (ddd, *J* = 12.2, 10.0, 5.0, 1 H), 2.74 (ddd, *J* = 12.2, 10.0, 5.0, 1 H), 1.08 (s, 9 H), 1.04 (s, 9 H), 1.00 (t, *J* = 8.0, 9 H), 0.98 – 0.92 (m 4 H), 0.72 (q, *J* = 8.0, 6 H), 0.61 (dt, *J* = 12.0, 5.2, 1 H), 0.41 (dt, *J* = 12.0, 5.2, 1 H), 0.01 (s, 18H), –0.14 (s, 9 H)

MS: (EI, 70 eV)

945 (M^+ (1)), 542 (15), 541 (32), 501 (18), 500 (33), 499 (74), 471 (12), 247 (16), 246 (61), 167 (10), 149 (50), 127 (11), 115 (16), 111 (15), 103 (19), 101 (15), 99 (12), 98 (11), 97 (24), 95 (13), 85 (32), 83 (29), 73 (100), 71 (44), 69 (40), 57 (64), 55 (42)

Table S1, SI, entry 3:

To a 5-mL, round-bottomed flask equipped with a magnetic stir-bar, and an argon inlet **55** (0.180 g, 0.326 mmol, 1.0 equiv) was added along with CH_2Cl_2 (1.0 mL). To this solution was added *i*-Pr_2NEt (0.85 mL, 4.89 mmol, 15.0 equiv), tetrabutylammonium iodide (0.482 g, 1.304 mmol, 4 equiv) and a solution of 2-(trimethylsilyl)ethoxymethyl chloride (0.343 g, 2.934 mmol, 9.0 equiv) in CH_2Cl_2 (1.0 mL). The contents were stirred at rt under an argon atmosphere for 10 h. After 10 h the reaction contents were transferred to a separatory funnel containing H_2O (30 mL). The organic layer was extracted and the aqueous was extracted with CH_2Cl_2 (3 x 30 mL). The organic layers were combined and washed with brine (30 mL), dried with Na_2SO_4, filtered and concentrated. The crude product was purified using column chromatography (SiO_2, 40 g; hexanes/EtOAc, 10:1), followed by a second column (SiO_2, 40 g, hexanes/EtOAc, 24:1) gave **57** (0.095 g, 36%) as a colorless oil and **58** (0.094 g, 31%) as a colorless oil. All data matched the above data reported for **57** and **58**.

Table S1, SI, entry 4:

To a 5-mL, round-bottomed flask equipped with a magnetic stir-bar, and an argon inlet **55** (0.018 g, 0.0324 mmol, 1.0 equiv) was added along with CH_2Cl_2 (1.0 mL). To this solution was added *i*-Pr_2NEt (0.06 mL, 0.324 mmol, 10.0 equiv), silver triflate (0.042 g, 0.162 mmol, 5.0 equiv) and a solution of 2-(trimethylsilyl)ethoxymethyl chloride (0.019 g, 0.162 mmol, 5.0 equiv) in CH_2Cl_2 (1.0 mL). The contents were stirred at rt under an argon atmosphere for 1 h, and an additional *i*-Pr_2NEt (0.03 mL, 0.162 mmol, 5.0 equiv), silver triflate (0.033 g, 0.130 mmol, 4.0 equiv) and 2-(trimethylsilyl)ethoxymethyl chloride (0.015 g, 0.130 mmol, 4.0 equiv) The reaction contents were allowed to stir for an additional 2 h. Then the reaction contents were transferred to a separatory funnel containing H_2O (30 mL). The organic layer was extracted and the aqueous was extracted with CH_2Cl_2 (3 x 30 mL). The organic layers were combined and washed with brine (30 mL), dried with Na_2SO_4, filtered and concentrated. The crude product was purified using column chromatography (SiO_2, 35 g; hexanes/EtOAc, 7:1), followed by a second column (SiO_2, 35 g, hexanes/EtOAc, 10:1) gave **57** (0.014 g, 53%) as a colorless oil. Fractions from the second column were submitted to a third chromatography (SiO_2, 35 g, hexane/EtOAc, 20:1) to afford **58** (0.006 g, 19%) as a colorless oil. All data matched the above data reported for **57** and **58**.

Table S1, SI, entry 5:

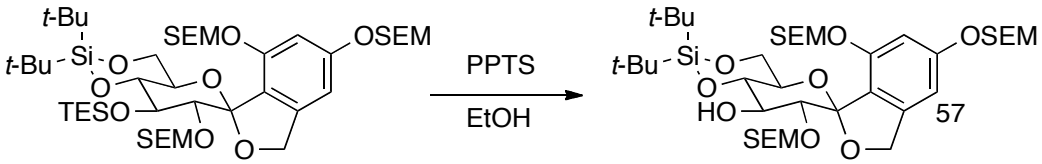
To a 5-mL, round-bottomed flask equipped with a magnetic stir-bar, and an argon inlet **57** (0.017 g, 0.0208 mmol, 1.0 equiv) was added along with DMF (0.2 mL). To this solution was added *i*-Pr_2NEt (0.02 mL, 0.104 mmol, 5.0 equiv), a solution of 2-(trimethylsilyl)ethoxymethyl chloride (0.0073 g, 0.0624 mmol, 3.0 equiv) in DMF (0.3 mL) and tetrabutylammonium iodide (0.023 g, 0.0624 mmol, 3.0 equiv). The contents were stirred at rt under an argon atmosphere for 10 h. After 10 h the reaction contents were transferred to a separatory funnel containing H_2O (30 mL). The organic layer was extracted and the aqueous was extracted with CH_2Cl_2 (3 x 30 mL). The organic layers were combined and washed with brine (30 mL), dried with Na_2SO_4, filtered and concentrated. The crude product was purified using column chromatography (SiO_2, 35 g; hexanes/EtOAc, 3:1) to give 0.014 g of recovered **57** (82%) as a colorless oil. All data matched the above data reported for **57**.

Table S1, SI, entry 6:

To a 5-mL, round-bottomed flask equipped with a magnetic stir-bar, and an argon inlet

55 (0.014 g, 0.017 mmol, 1.0 equiv) was added along with DMF (0.2 mL). To this solution was added *i*-Pr_2NEt (0.02 mL, 0.086 mmol, 5.0 equiv), a solution of 2-(trimethylsilyl)ethoxymethyl chloride (0.006 g, 0.052 mmol, 3.0 equiv) in DMF (0.3 mL), tetrabutylammonium iodide (0.019 g, 0.052, 3.0 equiv) and silver triflate (0.013 g, 0.052 mmol, 3.0 equiv). The contents were stirred at rt under an argon atmosphere for 2 h, and an additional *i*-Pr_2NEt (0.05 mL, 0.258 mmol, 15.0 equiv), silver triflate (0.040 g, 0.154 mmol, 9.0 equiv) and 2-(trimethylsilyl)ethoxymethyl chloride (0.012 g, 0.103 mmol, 6.0 equiv) The reaction contents were allowed to stir for an additional 1.5 h. Then the reaction contents were transferred to a separatory funnel containing H_2O (30 mL). The organic layer was extracted and the aqueous was extracted with CH_2Cl_2 (3 x 30 mL). The organic layers were combined and washed with brine (30 mL), dried with Na_2SO_4, filtered and concentrated. The crude product was purified using column chromatography (SiO_2, 35 g, hexanes/EtOAc, 10:1), followed by a second column (SiO_2, 35 g, hexanes/EtOAc, 20:1) gave **58** (0.012 g, 74%) as a colorless oil. All data matched the above data reported for **57** and **58**.

Preparation of 1,1-Anhydro-4,6-*O*-di-*tert*-butylsilylene-2-*O*-((2-trimethylsilylethoxy-methyl)-1-(4,6-bis(2-trimethylsilylethoxymethoxy)-2-hydroxymethylphenyl)-α-D-glucopyranose (59) [TK-XI-79]



To a 10-mL, round-bottomed flask equipped with a magnetic stir-bar and septum was added **58** (94.0 mg, 0.0994 mmol, 1.0 equiv). Then a solution of PPTS (2.5 mg, 0.01 mmol, 0.1 equiv) in EtOH (1.0 mL) was added to the flask and the solution was stirred at rt. After stirring for 2 h the reaction the contents were added to a solution of aqueous saturated $NaHCO_3$ (30 mL). The organic layer was removed and the aqueous was extracted with EtOAc (3 x 30 mL). The organic layers were combined and washed with brine (1 x 30 mL) and dried with Na_2SO_4. The solvent was removed by rotary evaporation and the crude product was purified using column chromatography (SiO_2, 40 g, hexanes/EtOAc gradient (10:1 to 7:1 to 3:1)) to give **58** (29 mg, 31%) and **59** (44 mg, 53%) as colorless oils.

Data for **59**:

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

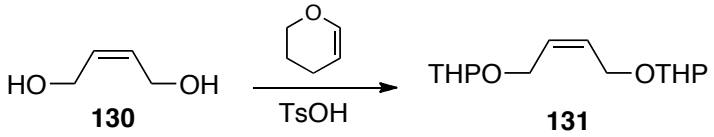
6.71 (d, *J* = 2.0, 1 H), 6.57 (d, *J* = 2.0, 1 H), 5.23 (d, *J* = 7.2, 1 H), 5.21 (d, *J* = 7.2, 1 H), 5.19 (d, *J* = 7.2, 1 H), 5.16 (d, *J* = 7.2, 1 H), 5.14 (d, *J* = 12.0, 1 H), 5.06 (d, *J* = 12.0, 1 H), 4.62 (d, *J* = 12.0, 1 H), 4.54 (d, *J* = 7.2, 1 H), 4.30 (d, *J* = 10.0, 1 H), 4.09 (dd, *J* = 10.0, 4.8, 1 H), 4.02 (dt, *J* = 10.0, 4.8, 1 H), 3.97 (t, *J* = 10.0, 1 H), 3.86 (t, *J* = 10.0, 1 H), 3.81 (t, *J* = 10.0, 1 H), 3.79-3.68 (m, 4 H), 3.61 (ddd, *J* = 11.6, 9.6, 5.2, 1 H), 3.30 (ddd, *J* = 11.6, 9.6, 5.2, 1 H), 2.00 (br s, 1 H, OH), 1.08 (s, 9 H), 1.03 (s, 9 H), 0.95 (t, *J* = 8.4, 4 H), 0.91-0.78 (m, 2 H), 0.00 (s, 9 H), 0.00 (s, 9 H), –0.05 (s, 9 H)

MS: (EI, 70 eV)

830 (M^+–1 (0.7)), 501 (12), 500 (54), 499 (54), 441 (11), 400 (10), 399 (32), 371 (11), 370 (24), 369 (72), 295 (18), 103 (20), 101 (13), 97 (11), 85 (12), 83 (12), 75 (16), 74 (10), 73 (100), 71 (15), 69 (13), 57 (26), 55 (15)

Preparation of Phosphonate (139)

Preparation of 1,4-Bis(tetrahydropyran-2-yloxy)-2-butene (131)[36] [TK-X-94]



To a 1000-L, single-necked, round-bottomed flask equipped with a magnetic stir-bar, and an argon inlet was added 3,4-dihydro-2 H-pyran (83.0 g, 987.2 mmol, 2.5 equiv) followed by CH_2Cl_2 (200 mL). To this solution was added *p*-TsOH (37.5 mg, 0.197 mmol, 0.0005 equiv). The contents were cooled to 0 ^oC using an ice bath and a precooled (0 ^oC) biphasic mixture of 2-butene-1,4-diol, **130**, (34.8 g, 394.88 mmol, 1.0 equiv) in CH_2Cl_2 (200 mL) was added over 20 min via cannula. After the addition the contents were allowed to warm to rt and stirred at this temperature for an additional 1 h. After this amount of time the mixture was filtered through SiO_2 (80 g), the SiO_2 pad was washed with hexane/EtOAc (3:1) (750 mL). The solvent was then removed using rotary evaporation. The residue was purified by short path distillation (bp 120-130 ^oC at 0.4 mmHg) to afford **131** (96.2 g, 95%) as a clear colorless oil. The data for **131** matched the data in the literature.[36]

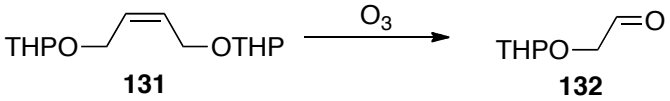
Data for **131**:

bp: 120-130 °C at 0.4 mmHg

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

4.63 (t, *J* = 3.5, 2 H), 4.29 (ddd, *J* = 11.1, 8.0, 2.8, 2 H), 4.11 (br quintet, *J* = 6.2, 2 H), 3.87 (ddd, *J* = 11.1, 8.0, 2.8, 2 H), 3.55-3.47 (m, 2 H), 1.90-1.46 (m, 12H)

Preparation of 2-(Tetrahydropyran-2-yloxy)ethanal (132)[36] [TK-X-96]



131 **132**

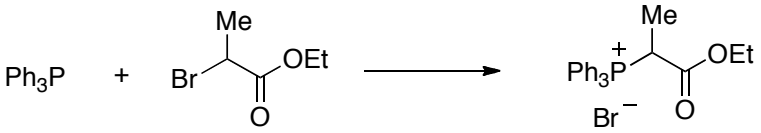
To a 1000-L, two-necked, round-bottomed flask equipped with a magnetic stir-bar, a stop-cock in one neck for an ozone outlet to a KI trap, a gas dispersion tube in a Teflon stopper was in the second neck, **131** (45.2 g, 176 mmol) was added. To this was added CH_2Cl_2 (600 mL) to give a colorless solution. The contents were cooled to –78 °C and ozone was bubbled through the solution for 2 h (or until the solution turned a light blue color). After the solution was blue N_2 was bubbled through the solution until the solution turned colorless again. While the solution was still at –78 °C a mixture of AcOH/H_2O (1:1, 110 mL) was added. After 5 min the cooling bath was removed and replaced with a 0 °C ice-bath. To this slurry was added zinc dust (33.9 g, 521 mmol, 2.9 equiv) slowly over 20 min with vigorous stirring. After another 10 min stirring at 0 °C, $NaHCO_3$ (50 g, 595 mmol, 3.4 equiv) was added to the suspension. The reaction mixture was filtered cold using a sintered glass filter. The gray metallic residue was washed with CH_2Cl_2 (600 mL). The filtrated was then transferred to a separatory funnel and washed saturated $NaHCO_{3(aq)}$ (1 x 1.5 L) and brine (1 x 0.5 L). The aqueous layer was separated and the organic layer was dried with Na_2SO_4, filtered and concentrated. The desired aldehyde **132** was obtained as a colorless oil (41.0 g, 81%) and was used immediately without purification in the next step.

Data for **132**:

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

9.76 (s, 1 H), 4.68 (t, *J* = 7.0, 1 H), 4.24 (d, *J* = 21.0, 1 H), 4.17 (d, *J* = 21.0, 1 H), 3.93-3.80 (m, 1 H), 3.65-3.45 (m, 1 H), 1.95-1.50 (m, 6 H)

Preparation of Triphenyl(1-ethoxycarbonylethyl)phosphonium bromide (134)[37] [TK-X-92]



133 **134**

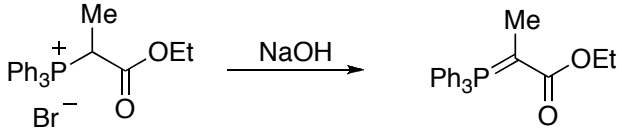
In a 1000-mL, round-bottomed flask equipped with a magnetic stir-bar and argon inlet was added triphenylphosphine (80.6 g, 307 mmol, 1.0 equiv) along with ethyl 2-bromopropionate (59.8 mL, 461 mmol, 1.5 equiv). Then the mixture was heated to 50 ^{o}C under an argon atmosphere for 10 h. After 10 h, hexane (250 mL) was added to the solid and the solid cake was broken up with a spatula. Once small pieces were formed the solid was collected by suction filtration. The solid was crushed into smaller pieces in the Büchner filter using a motor and washed with hexane (2 x 250 mL). Then the solid was transferred to a 500 mL round-bottomed flask and further dried under reduced pressure (0.08 mmHg) for 1 H. After drying phosphonium salt **134** was obtained as a white powder (132 g, 97%).

Data for **134**:

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

8.00-7.90 (m, 6 H), 7.80-7.60 (m, 9 H), 6.85 (dq, J = 14.0, 7.0, 1 H), 3.98 (dq, J = 18.6, 7.0, 2 H), 1.65 (dd, J = 21.0, 7.0, 3), 0.97 (t, J = 7.0, 3 H)

Preparation of Triphenyl(1-ethoxycarbonylethyl)phosphorane (135)[37] [TK-X-97]



134 **135**

To a 100-mL, round-bottomed flask equipped with a magnetic stir-bar, NaOH (20.0 g, 500 mmol, 2.05 equiv) was dissolved in H_2O (200 mL). This basic solution was then cooled to 0 ^{o}C using an ice bath. Once at this temperature, a solution of **134** (108 g, 244 mmol, 1.0 equiv) in CH_2Cl_2 (100 mL) was added slowly with vigorous stirring. After the addition the biphasic yellow solution was warmed to rt over 30 min. Then the contents were transferred to a separatory funnel and the organic layer was extracted. The aqueous layer was washed with CH_2Cl_2 (50 mL). The combined organic extracts were washed with brine (2 x 100 mL) or until the washing were neutral in pH. The organic layer was then dried with Na_2SO_4, filtered and concentrated using

rotary evaporation. The desired ylide **135** was obtained as a yellow crystalline solid (90 g, quant).

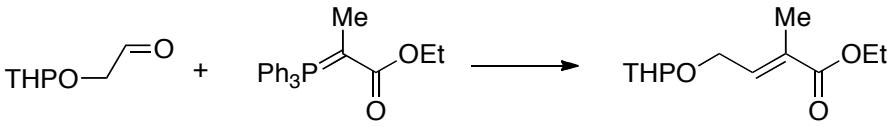
Data for **135**:

mp: 157-158 (hexane)

^{1}H NMR: (400 MHz, $CDCl_3$)

7.75-7.20 (m, 15 H), 4.06 (q, J = 7.0, 2H$_{minor}$), 3.72 (q, J = 7.0, 2H$_{major}$), 1.62 (d, J = 16.7, 3H$_{major}$), 1.60 (d, J = 16.7, 3H$_{minor}$), 1.25 (t, J = 7.0, 3H$_{minor}$), 0.45 (t, J = 7.0, 3H$_{major}$)

Preparation of Ethyl 2-*E*-2-methyl-4-(tetrahydropyran-2-yl)-2-butenoate (136)[38] [CSR-VII-095]



132 **135** **136**

To a 500-ml, single-necked, round-bottomed flask containing a magnetic stir-bar, and an argon inlet with septum aldehyde **132** (35.2 g, 243.6 mmol, 1.0 equiv) was added. Then a precooled (0 ^{o}C) solution of ylide **135** (88.3 g, 243.6 mmol, 1.0 equiv) in CH_2Cl_2 (200 mL) was added via cannula. The yellow mixture was stirred at 0 ^{o}C for 30 min and then warmed to rt. Once at rt the contents were stirred for an additional 1.5 h. After this amount of time the solvent was removed using rotary evaporation, to this viscous crude residue was added pentane (300 mL) and white precipitate formed. The precipitate was collected by suction filtration. The filtrate was concentrated once again by rotary evaporation to give an oily solid. Once again pentane (300 mL) was added and the precipitate was collected by suction filtration. The filtrate was concentrated to give a colorless oil (69.4 g). This was divided into two portions and each portion (~35 g) was filtered over an SiO_2 plug (100 g), washing with pentane/Et_2O (1/3, 500 mL). After concentration and drying, using high vacuum (0.09 mmHg), 51.5 g (93%) of **136** was obtained as a colorless oil.

Data for **136**:

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

6.83 (dt, J = 1.2, 6.3, 1 H), 4.66 (t, J = 3.4, 1 H), 4.41 (ddd, J = 14.3, 5.7, 1.2, 1 H), 4.22-4.15 (m, 1 H), 3.87 (ddd, J = 11.4, 8.6, 2.9, 1 H), 3.56-3.50 (m, 1 H),

1.85 (d, J = 0.9, 3 H), 1.90-1.80 (m, 1 H), 1.77-1.70 (m, 1 H), 1.60-1.49 (m, 4 H), 1.30 (t, J = 7.2, 3 H)

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

167.6, 137.8, 129.3, 98.3, 63.9, 62.1, 60.7, 30.5, 25.4, 19.2, 14.2, 12.8

IR: (film)

2943 (s), 2872 (m), 1714 (s), 1656 (w), 1454 (w), 1442 (w), 1367 (m), 1248 (s), 1201 (m), 1183 (m), 1137 (s), 1118 (s), 1075 (m), 1055 (m), 1031 (s), 977 (m), 907 (w), 870 (w), 815 (w)

MS: (EI, 70 eV)

229 (M^++1, 34), 144 (18), 128 (10), 127 (36), 99 (37), 85 (100)

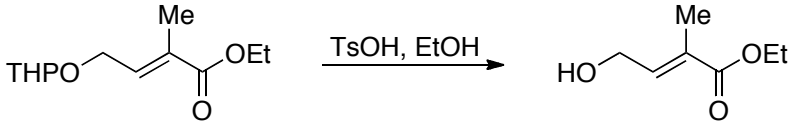
TLC: R_f 0.40 (10:1 hexanes/EtOAc) [SiO_2, UV]

HRMS: $C_{12}H_{20}O_4$ (228.28)

Calcd: 229.1440

Found: 229.1437

Preparation of Ethyl 2*E*-4-hydroxy-2-methyl-2-butenoate (137)[38] [CSR-VII-96]



136 **137**

To a 500-mL, single-necked, round-bottomed flask containing a magnetic stir-bar, argon inlet with a septum **136** (51.4 g, 225.2 mmol, 1.0 equiv) was added followed by absolute EtOH (225 mL). To this solution was added *p*-toluenesulfonic acid monohydrate (2.14 g, 11.3 mmol, 0.05 equiv) and the contents were stirred at rt for 3 h. After 3 h, pentane/Et_2O (1:1, 400 mL) was added. Then the contents were filtered through a SiO_2 plug (240 g), washing with pentane/Et_2O (1:1, 2 x 400 mL). The filtrate was concentrated to give a colorless crude oil (80 g). The crude material was purified using column chromatography (SiO_2, 300 g; pentane/E_2O, 3:1) this was repeated 2x to afford **137** (31.8 g, 98%) as a light-yellow oil.

Data for **137**:

bp: 92 ^oC (ABT, 1.0x10^{-3} mmHg)

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

6.82 (dt, J = 1.2, 6.1, 1 H), 4.35 (t, J = 6.1, 2 H), 4.20 (q, J = 7.0, 2 H), 1.84 (q, J

= 1.3, 3 H), 1.60 (br, s, 1 H), 1.30 (t, J = 7.0, 3 H)

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

167.7, 139.8, 128.8, 60.7, 59.7, 14.2, 12.7

IR: (film)

3432 (m), 2983 (w), 2934 (w), 2874 (w), 1713 (s), 1653 (w), 1447 (w), 1368 (m), 1262 (s), 1131 (s), 1031 (s)

MS: (EI, 70 eV)

144 (M^+, 10), 127 (13), 115 (81), 99 (100), 98 (75), 97 (38), 87 (68), 71 (57), 70 (19), 69 (89), 59 (16), 53 (29), 51 (10)

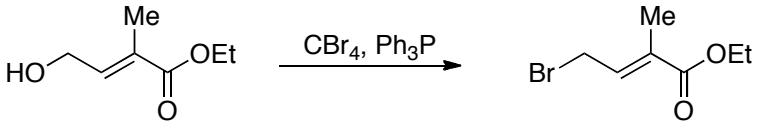
TLC: R_f0.13 (10:1 hexanes/EtOAc) [SiO_2, UV, CAM]

HRMS: $C_7H_{12}O_3$ (144.08)

Calcd: 144.07865

Found: 144.07888

Preparation of Ethyl (2*E*)-4-Bromo-2-methyl-2-butenoate (138)[39] [CSR-VII-100]



137 **138**

To a 1000-mL, three-necked, round-bottomed flask equipped with a dropping funnel, septa, and argon inlet alcohol **137** (27.7g, 191.9 mmol, 1.0 equiv) was added along with CH_2Cl_2 (20 mL). Then CBr_4 (95.5 g, 287.9 mmol, 1.5 equiv) was added. Finally a solution of triphenylphosphine (60.4 g, 230.3 mmol, 1.2 equiv) in CH_2Cl_2 (180 mL) was added to the dropping funnel and was added dropwise over 1 h. The internal temperature was maintained at 20-26 ^oC using an ice-bath. When the addition was complete the color of the reaction media changed from light-yellow to orange and a precipitate started to form. The color finally faded to a light-yellow mixture over 20 min. Then Et_2O (100 mL) and pentane (200 mL) was added slowly to the mixture. The precipitate was collected by suction filtration (2x), and washed with pentane (200 mL). Again a precipitate formed in the filtrate and was collected. Finally, the filtrate solution was concentrated to a light-yellow oil (101 g). This was purified by Kugelrohr distillation (90-100 ^oC(ABT), 0.4 mmHg) to afford bromide **138** (36.6 g, 92%) as a light-yellow oil.

Data for **138**:

bp: 90-100 °C (ABT, 0.4 mmHg)

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

6.92 (tdt, *J* = 8.5, 1.5, 1.5, 1 H), 4.22 (q, *J* = 7.0, 2 H), 4.04 (d, *J* = 8.5, 2 H), 1.91 (d, *J* = 1.5, 3 H), 1.30 (t, *J* = 7.0, 3 H)

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

167.2, 134.7, 132.2, 61.0, 26.1, 14.2, 12.2

IR: (film)

2982 (w), 1713 (s), 1647 (w), 1445 (w), 1367 (m), 1265 (s), 1174 (s), 1159 (s), 1103 (s), 1028 (w)

MS: (EI, 70 eV)

208 (M^++1, 11), 207 (M^+, 3), 206 (11), 163 (16), 161 (17), 127 (32), 113 (11), 99 (100), 82 (14), 81 (98), 81 (14), 71 (18), 52 (45)

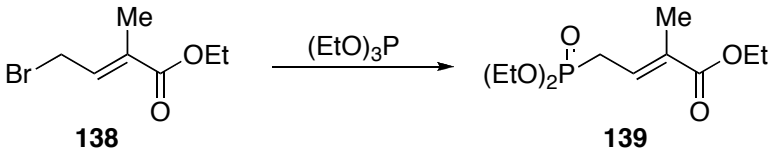
TLC: R_f 0.68 (10:1 hexanes/EtOAc) [SiO_2, UV]

HRMS: $C_7H_{11}BrO_2$ (207.07)

Calcd: 205.99424

Found: 205.99463

Preparation of Ethyl (2*E*)-4-Diethoxyphosphonyl-2-methyl-2-butenoate (139)[39] [CSR-VIII-3]



138 **139**

To a 250-mL, single-necked, round-bottomed flask equipped with a magnetic stir-bar, and a condenser, bromide **138** (36.2 g, 174.8 mmol) followed by triethyl phosphite (43.6 g, 262.3 mmol, 1.5 equiv) and the contents were flushed with argon. Next, the solution was heated to 60 °C for 5 h. Then benzene (50 mL) was added and the contents were concentrated using the rotary evaporation, heating the water bath to 50 °C at 22 mmHg. This procedure was repeated 5x to give the crude product (39.4 g) as a yellow oil. This was divided into 2 portions and each portion was purified by column chromatography (SiO_2, 300 g, hexanes/EtOAc, 1:1) to give **139** (26.3 g, 57%) as a colorless oil.

Data for **139**:

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

6.92 (tdt, *J* = 8.1, 1.5, 1.5, 1 H), 4.21 (q, *J* = 7.1, 2 H), 4.19-4.08 (m, 4 H), 2.75 (dd, *J* = 23.2, 8.1, 2 H), 1.90 (d, *J* = 3.6, 3 H), 1.40-1.28 (m, 9 H)

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

167.4, 131.9, 131.8, 130.1, 130.0, 62.2, 62.1, 60.7, 28.2, 26.9, 16.5, 16.4, 14.2, 12.6, 12.5

^{31}P NMR: (161 MHz, $CDCl_3$)

26.6

IR: (film)

3478 (m), 2983 (s), 2934 (m), 2909 (m), 1711 (s), 1650 (m), 1478 (w), 1445 (m), 1392 (m), 1367 (m), 1254 (s), 1174 (s), 1105 (s), 1026 (s), 967 (s), 834 (w), 748 (m)

MS: (EI, 70 eV)

264 (M^+, 55), 219 (40), 218 (66), 191 (19), 190 (54), 182 (14), 163 (40), 162 (59), 155 (100), 139 (11), 138 (51), 137 (18), 135 (19), 134 (58), 127 (58), 125 (21), 110 (27), 109 (77), 99 (92), 91 (18), 83 (30), 82 (65), 81 (79), 71 (26), 65 (28), 54 (31), 53 (40)

TLC: R_f0.40 (1:1 hexanes/EtOAc) [UV]

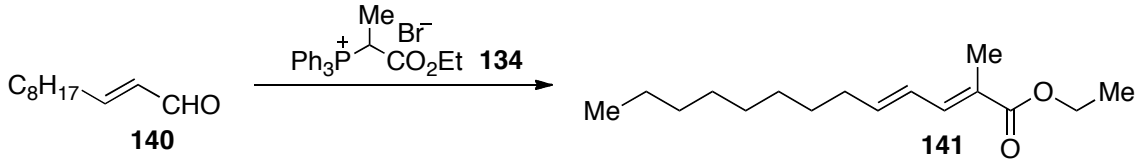
HRMS: $C_{11}H_{21}O_5P$ (264.26)

Calcd: 264.1127

Found: 264.1123

Preparation of Model Side-Chain Aldehyde 61

Preparation of Ethyl (2*E*,4*E*)-2-Methyl-2,4-tridecadienoate (141) [CSR-VI-90]



To a 100-mL, single-necked, round-bottomed flask containing a magnetic stir-bar, condenser, and argon inlet was added **140** (2.52 g, 15.0 mmol, 1.0 equiv), THF (30 mL) and LiOH•H_2O (0.692 g, 16.5 mmol, 1.1 equiv). Then phosphonium bromide **134** (7.31 g, 16.5 mmol, 1.1 equiv) and molecular sieves 4Å (7.5 g) were added to the mixture. The mixture was then heated to reflux and stirred at this temperature for 3 h. After this amount of time, the suspension was filtered through Celite (3 g) washing the filter pad with hexane/EtOAc (7:1) (100 mL). The solvent was removed using rotary evaporation to give the crude product (7.74 g, 93:7 *E*/*Z* ratio) as a yellow sludge. The crude product was purified using column chromatography ((SiO_2, 60 x 250 mm,), hexanes/EtOAc, 100:1, followed by another column chromatography ((SiO_2, 50 x 200 mm), hexane/EtOAc, 100:1)). After distillation 8.14 g (83%) of *E*,*E*-**141** was obtained as a colorless oil.

Data for **141**:

bp: 100 °C at $1x10^{-4}$ mmHg

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

7.16 (d, *J* = 12.2, 1 H), 6.33 (ddt, *J* = 15.4, 12.2, 1.4, 1 H), 6.08 (dt, *J* = 15.4, 7.4, 1 H), 4.20 (q, *J* = 7.0, 2 H), 2.18 (qd, *J* = 7.5, 1.0, 2 H), 1.92 (s, 3 H), 1.30 (t, *J* = 7.0, 3 H), 1.50 – 1.20 (m, 12H), 0.89 (t, *J* = 7.0, 3 H)

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

167.7, 142.1, 140.8, 127.5, 123.9, 60.1, 32.9, 31.9, 29.4, 29.2, 29.0, 22.7, 20.6, 14.3, 14.1

IR: (neat)

3033 (w), 2927 (s), 2956 (s), 2855 (s), 1704 (s), 1640 (s), 1610 m), 1465 (m), 1390 (m), 1367 (s), 1290 (s), 1173 (m), 1105 (s), 971 (s), 748 (m)

MS: (EI)

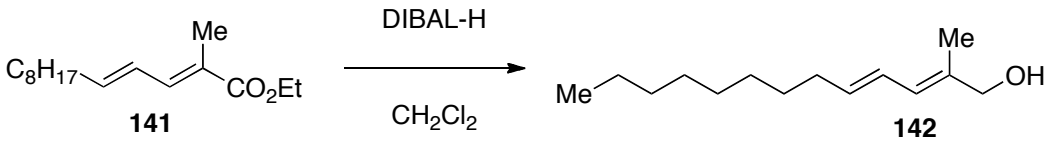
252 ((M^+) 44), 207 (19), 140 (28), 139 (100), 112 (35), 111 (32), 95 (17), 81 (27), 79 (22), 67 (16)

TLC: R_f 0.74 (7:1 hexanes/EtOAc) [SiO_2, CAM]

Analysis: $C_{16}H_{28}O_2$ (252.39)

Calcd:	C, 76.14%,	H, 11.18%
Found:	C, 75.99%,	H, 11.12%

Preparation of (2*E*,4*E*)-2-Methyl-2,4-tridecadienol (142) [CSR-VII-2]



To a 100-mL, single-necked, round-bottomed flask containing a magnetic stir-bar, and argon inlet with septum was added **141** (1.24 g, 4.91 mmol, 1.0 equiv) and the contents were flushed with argon. Then CH_2Cl_2 (12 mL) was added and the colorless solution was cooled to 0 ^oC. Next, DIBAL-H (10.8 mL, 1.0 M in hexane, 10.8 mmol, 2.2 equiv) was added drop-wise over 10 min. The solution became bright yellow and faded to a colorless solution after all the DIBAL-H was added. After the addition the contents were allowed to warm to rt over the course of 2 h. Then Celite (3 g) was added to the reaction flask along with CH_2Cl_2 (20 mL). Then H_2O (~4 mL) was added very slowly until the contents became gelatinous. To this slurry EtOAc (10 mL) was added and the contents were filtered using a glass fritted funnel. The filter cake was washed with additional EtOAc (30 mL). The filtrate was dried with Na_2SO_4, filtered and concentrated to give colorless oil. This oil was purified by diffusion pump distillation to afford 0.919 g, (89%) **142** as a colorless oil.

Data for **142**:

bp: 120 °C at $3.4x10^{-4}$ mmHg

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

6.27 (ddt, *J* = 14.4, 11.6, 7.0, 1 H), 6.02 (d, *J* = 11.6, 1 H), 5.70 (dt, *J* = 14.4, 7.0, 1 H), 4.08 (d, *J* = 6.0, 2 H), 2.10 (q, *J* = 7.0, 2 H), 1.79 (s, 3 H), 1.50 – 1.20 (m, 12H), 0.89 (t, *J* = 7.0, 3 H)

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

135.6, 134.8, 125.9, 125.7, 69.0, 33.2, 32.1, 29.7, 29.6, 29.5, 29.4, 22.9, 14.3, 14.3

IR: (neat)

3324 (s), 2956 (m), 2924 (s), 2854 (s), 1458 (w), 1378 (w), 1067 (w), 1006 (w), 967 (m)

MS: (EI)

210 ((M^+) 54), 141 (14), 112 (12), 111 (31), 109 (18), 98 (100), 95 (90), 93 (41), 84 (33), 83 (58), 82 (35), 81 (62), 79 (38), 77 (23), 71 (42), 70 (28), 69 (60), 67 (53), 57 (45)

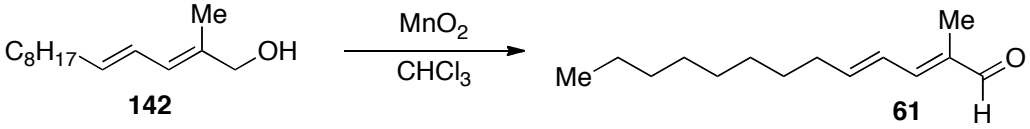
TLC: R_f 0.14 (7:1 hexanes/EtOAc) [SiO_2, UV]

Analysis: $C_{14}H_{26}O$ (210.36)

Calcd: C, 79.94%, H, 12.46%

Found: C, 79.69%, H, 12.71%

Preparation of (2*E*,4*E*)-2-Methyl-2,4-tridecadienal (61) [CSR-VII-11]



To a 250-mL, single-necked, round-bottomed flask containing a magnetic stir-bar, equipped with a condenser and argon inlet with septum was added **142** (2.20 g, 10.46 mmol, 1.0 equiv) followed by $CHCl_3$ (25 mL). Then MnO_2 (7.28 g, 83.68 mmol, 8.0 equiv) was added and the black mixture was heated under reflux for 1 h. The black mixture was filtered over Celite (3 g) washing with CH_2Cl_2 (30 mL). The yellow filtrate was concentrated using rotary evaporation. The yellow crude oil was purified by column chromatography (60 x 220 mm, hexane/EtOAc gradient, 20:1 to 10:1). The material was further purified by diffusion pump distillation to give 2.03 g (93%) of **61** as a light-yellow oil.

Data for **61**:

bp: 98 °C at 8.0×10^{-4} mmHg

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

9.41 (s, 1 H), 6.82 (d, J = 11.2, 1 H), 6.52 (ddt, J = 15.2, 11.2, 1.2, 1 H), 6.24 (dt, J = 15.2, 7.6, 1 H), 2.24 (q, J = 7.6, 2 H), 1.83 (s, 3 H), 1.50 – 1.20 (m, 12H), 0.88 (t, J = 7.0, 3 H)

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

195.2, 176.9, 149.4, 146.0, 135.9, 125.8, 33.4, 31.8, 29.4, 29.2, 28.8, 22.6, 14.1,

9.4

IR: (neat)

2955 (s), 2926 (s), 2855 (s), 1684 (s), 1636 (s), 1465 (w), 1378 (w), 1361 (w), 1208 (m), 1009 (m), 966 (m), 836 (w)

MS: (EI)

208 ((M^+) 9), 96 (14), 95 (100), 67 (8)

TLC: R_f0.44 (7:1 hexanes/EtOAc) [SiO_2, UV]

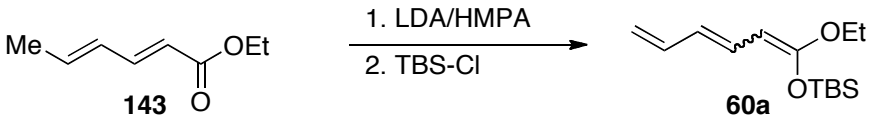
Analysis: $C_{14}H_{24}O$ (208.34)

Calcd: C, 80.71%, H, 11.61%

Found: C, 80.74%, H, 11.60%

Model Lewis-Base Aldol Reactions

Preparation of (1*E*,3*E*,5*E*)-1-Ethoxy-1-*tert*-butyldimethylsiloxy-1,3,5-hexatriene (60a) [TK-XI-47]



To a 100-mL, three-necked, round-bottomed flask equipped with a magnetic stir-bar, argon inlet, and two septa in the remaining necks, *i*-Pr_2NH (1.54 mL, 11.0 mmol, 1.1 equiv) was added followed by THF (10 mL) and the contents were cooled to 0 ^oC using an ice bath. To this solution was added *n*-BuLi (6.9 mL, 11.0 mmol, 1.1 equiv, 1.6 M in hexanes) drop-wise over 5 min. The bright yellow solution was stirred for an additional 30 min at 0 ^oC. After this amount of time the solution was cooled to –78 ^oC using a dry ice/2-propanol bath. Then, HMPA (2.1 mL, 12 mmol, 1.2 equiv) was added and stirred for 30 min at –78 ^oC. Finally, ethyl sorbate **143** (1.47 mL, 10 mmol, 1.0 equiv) was added dropwise over 5 min. The contents were again stirred for 30 min at –78 ^oC. Next, a solution of TBS-Cl (1.66 g, 11 mmol, 1.1 equiv) in THF (6 mL) was added to the reaction and the contents were allowed to warm slowly to ambient temperature (ca 40-50 min). Then pentane (50 mL) was added and the contents were transferred to a separatory funnel. The organic layer was washed with H_2O (3 x 50 mL) and dried with Na_2SO_4. The solvent was removed under reduced pressure, and the crude material was purified using Kugelrohr distillation (160 ^oC at 0.35 mmHg) providing **60a** (2.1 g, 81%, 90:10 mixture of isomers) as a

very light-yellow oil.

Data for **60a**:

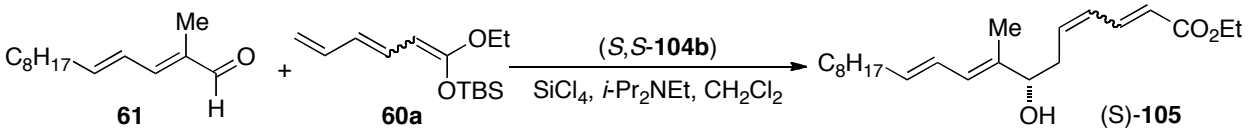
bp: 160 °C (ABT, at 0.35 mmHg)

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

6.43 (dd, *J* = 16.0, 10.2, 1 H), 6.37 (dt, *J* = 17.0, 10.2, 1 H), 5.94 (dd, *J* = 16.0, 10.2, 1 H), 4.99 (d, *J* = 17.0, 1H$_{minor}$), 4.97 (d, *J* = 17.0, 1H$_{major}$), 4.83 (d, *J* = 10.2, 1H$_{minor}$), 4.81 (d, *J* = 10.2, 1H$_{major}$), 4.52 (d, *J* = 10.2, 1H$_{minor}$), 4.44 (d, *J* = 10.2, 1H$_{major}$), 3.96 (q, *J* = 7.0, 2H$_{minor}$), 3.81 (q, *J* = 7.0, 2H$_{minor}$), 1.30 (t, *J* = 7.0, 3H$_{major}$), 1.26 (t, *J* = 7.0, 3H$_{minor}$), 0.96 (s, 9 H$_{major}$), 0.91 (s, 9 H$_{minor}$), 0.23 (s, 6H$_{minor}$), 0.19 (s, 6H$_{major}$)

Preparation of Ethyl (*S*)-(2*E*,4*E*,8*E*,10*E*)-7-Hydroxy-8-methyl-2,4,8,10-nonadeca-tetraenoate (105), Ethyl (*S*)-(2*E*,4*E*,8*E*,10*E*)-7-Triethylsiloxy-8-methyl-2,4,8,10-nonadeca-tetraenoate ((*E*)-107) and Ethyl (*S*)-(2*E*,4*Z*,8*E*,10*E*)-7-Triethylsiloxy-8-methyl-2,4,8,10-nonadeca-tetraenoate ((*Z*)-107), Table 2, SI.

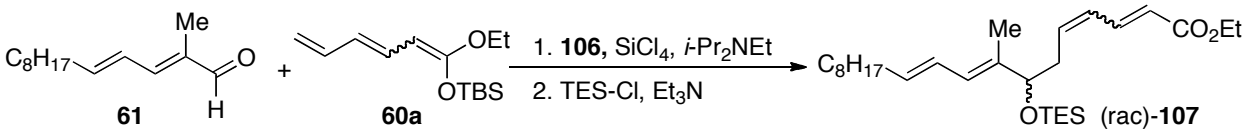
Table S2, SI, entry 1 [TK-XI-50]



To a 25-mL, two-necked, round-bottomed flask equipped with a magnetic stir-bar, argon inlet, and septum aldehyde **61** (50.8 mg, 0.244 mmol, 1.0 equiv) was added, followed by (*S,S*-**104b**) (2.1 mg, 0.00244 mmol, 0.01 equiv) was added. The contents were flushed with argon and CH_2Cl_2 (1.0 mL) was added and the contents were cooled to –78 ^oC using a dry ice/2-propanol bath. Then $SiCl_4$ (0.03 mL, 0.2684 mmol, 1.1 equiv) was added and the contents were stirred for 10 min at this temperature. Next, a solution of trienolate **60a** (74.6 mg, 0.293 mmol, 1.2 equiv) in CH_2Cl_2 (1.0 mL) was added and the contents were stirred for 3 h at –78 ^oC. The reaction was quenched by pouring the cold contents directly into a vigorously stirring solution of sat. KF:1.0 M KH_2PO_4 (1:1(v/v), 20 mL) in an Erlenmeyer. The reaction flask was rinsed with CH_2Cl_2 (3 x 2 mL). The contents were stirred for 1 h at rt and the emulsion was transferred to a separatory funnel. The aqueous was extracted with CH_2Cl_2 (3 x 30 mL). The combined organic extracts

were washed with brine (1 x 30 mL) and dried with Na_2SO_4 and concentrated to give a light-yellow oil that was immediately subjected to column chromatography (SiO_2, 35 g; 7:1-3:1, hexane/EtOAc). This material was subjected to once again to column chromatography (SiO_2, 35 g, 3:1, hexanes/EtOAc) to give (*S*)-**105** (23 mg, 27%) as a colorless oil. The material was unstable and was characterized as the corresponding silyl ether (*E*, *Z*-**107**) see data below.

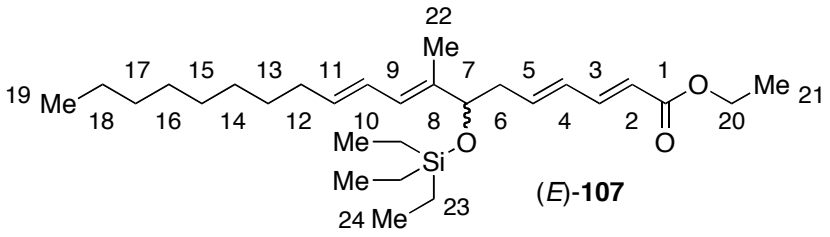
Table 2, SI, entry 2 [TK-XI-65]



To a 25-mL, two-necked, round-bottomed flask equipped with a magnetic stir-bar, argon inlet, and septum aldehyde **61** (78.0 mg, 0.374 mmol, 1.0 equiv) was added, followed by **71** (32.6 mg, 0.15 mmol, 0.4 equiv) was added. The contents were flushed with argon and CH_2Cl_2 (1.0 mL) was added and the contents were cooled to –78 ^oC using a dry ice/2-propanol bath. Then, *i*-Pr_2NEt (0.01 mL, 0.075 mmol, 0.2 equiv) and $SiCl_4$ (0.05 mL, 0.411 mmol, 1.1 equiv) were added and the contents were stirred for 10 min at this temperature. Next, a solution of trienolate **60a** (114.2 mg, 0.449 mmol, 1.2 equiv) in CH_2Cl_2 (1.0 mL) was added and the contents were stirred for 3 h at –78 ^oC. The reaction was quenched by pouring the cold contents directly into a vigorously stirring solution of sat. KF:1.0 M KH_2PO_4 (1:1 (v/v), 30 mL) in an Erlenmeyer. The reaction flask was rinsed with CH_2Cl_2 (3 x 2 mL). The contents were stirred for 15 min at rt and the emulsion was filtered through a pad of Celite (3 g) eluting with CH_2Cl_2 (50 mL). The filtrate was washed with brine (1 x 30 mL), dried with Na_2SO_4 and concentrated to give a light-yellow oil that was immediately subjected to column chromatography (SiO_2, 40 g, 7:1, hexane/EtOAc) to give (*rac*-**105**) (58.0 mg, 44%) as a light-yellow oil. This material was immediately used in the subsequent step.

To a 25-mL, two-necked, round-bottomed flask equipped with a magnetic stir-bar, argon inlet, and septum, (*rac*-**105**) (58.0 mg, 0.166 mmol, 1.0 equiv) was added, followed by CH_2Cl_2 (2.0 mL). Then Et_3N (50.4 mg, 0.498 mmol, 3.0 equiv) and TES-Cl (50.0 mg, 0.332 mmol, 2.0 equiv) was added and the contents were stirred at rt, under argon, for 2 h. The reaction mixture was quenched with H_2O (30 mL) and transferred to a separatory funnel. The aqueous layer was extracted with CH_2Cl_2 (3 x 30 mL). The organic layers were combined, washed with brine (30

mL), dried with Na_2SO_4, filtered and concentrated to a yellow oil. The crude material was purified using column chromatography (SiO_2, 40 g; 10:1, hexanes/EtOAc). This gave a mixture of geometrical isomers (39.0 mg, 51%, *E*/*Z* = 75:25) as a pale yellow oil. The isomers (8 mg (*E*),(*Z*)-**107**) were separated using preparative HPLC (Waters μ Porasil (SiO_2, 10 μm), 1% EtOAc/hexanes, 5 mL/min). This provided (*E*)-**107** (1.7 mg) and (*Z*)-**107** (2.2 mg).



(*E*)-**107**

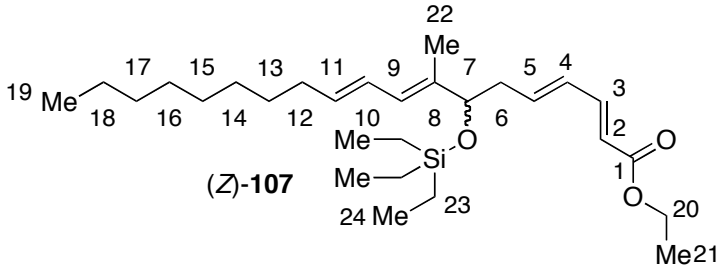
Data for (*E*)-**107**:

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

7.24 (dd, *J* = 15.6, 11.2, 1 H, HC(3)), 6.19 (ddt, *J* = 14.2, 11.2, 1.0, 1 H, HC(10)), 6.17 (dd, *J* = 15.6, 11.2, 1 H, HC(4)), 6.05 (dt, *J* = 15.6, 7.8, 1 H, HC(5)), 5.91 (d, *J* = 11.2, 1 H, HC(9)), 5.78 (d, *J* = 15.6, 1 H, HC(2)), 5.65 (dt, *J* = 14.2, 7.1, 1 H, HC(11)), 4.20 (q, *J* = 7.0, 2 H, H_2C(20)), 4.05 (t, *J* = 6.0, 1 H, HC(7)), 2.44-2.28 (m, 2 H, H_2C(6)), 2.09 (q, *J* = 7.3, 2 H, H_2C(12)), 1.69 (s, 3 H, H_3C(22)), 1.43-1.18 (m, 12H, H_2C(13-18)), 1.29 (t, *J* = 7.0, 3 H, H_3C(21)), 0.91 (t, *J* = 8.0, 9 H, H_3C(24)), 0.88 (t, *J* = 7.0, 3 H, H_3C(19)), 0.55 (q, *J* = 8.0, 6 H, H_2C(24))

SFC: (OD, 1.5% MeOH, 40 °C, 3.0 mL/min, 125 bar)

t_R = (7*R*)-(*E*)-**107**, 5.239 min (50%), t_R = (7*S*)-(*E*)-**107**, 5.808 min (50%)



(*Z*)-**107**

Data for (*Z*)-**107**:

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

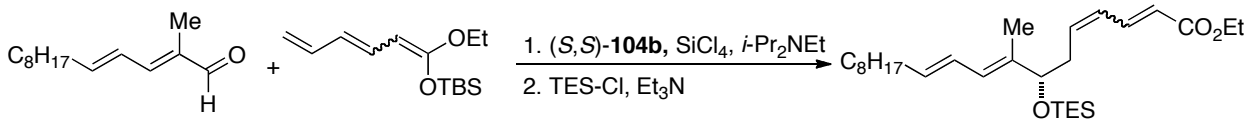
7.56 (dd, *J* = 15.6, 11.0, 1 H, HC(3)), 6.20 (dd, *J* = 15.6, 11.6, 1 H, HC(10)), 6.16

(t, J = 11.0, 1 H, HC(4)), 5.92 (d, J = 11.6, 1 H, HC(9)), 5.86 (d, J = 15.6, 1 H, HC(2)), 5.82 (dt, J = 11.0, 7.5, 1 H, HC(5)), 5.65 (dt, J = 14.4, 7.2, 1 H, HC(11)), 4.20 (q, J = 7.0, 2 H, H_2C(20)), 4.06 (t, J = 6.0, 1 H, HC(7)), 2.58-2.44 (m, 2 H, H_2C(6)), 2.09 (q, J = 7.3, 2 H, H_2C(12)), 1.55 (s, 3 H, H_3C(22)), 1.30 (t, J = 7.0, 3 H, H_3C(21)), 1.43-1.18 (m, 12 H, H_2C(12-18)), 0.92 (t, J = 8.0, 9 H, H_3C(24)), 0.88 (t, J = 7.0, 3 H, H_3C(19)), 0.55 (q, J = 8.0, 6 H, H_2C(24))

SFC: (OD, 5.0% MeOH, 40 °C, 3.0 mL/min, 125 bar)

t_R = (7*R*)-(*Z*)-**107**, 2.33 min (50%), t_R = (7*S*)-(*Z*)-**107**, 2.95 min (50%)

Table S2, SI, entry 3 [TK-XI-73]

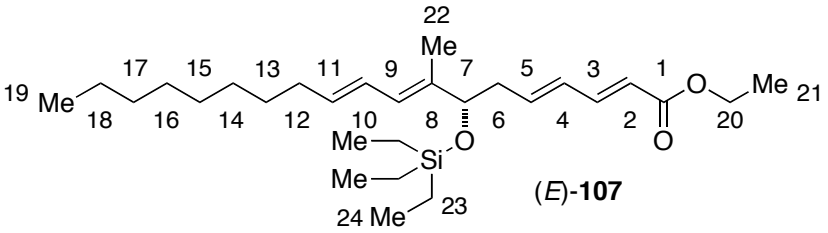


61 **60a** (*S*)-**107**

To a 25-mL, two-necked, round-bottomed flask equipped with a magnetic stir-bar, argon inlet, and septum aldehyde **61** (70.1 mg, 0.346 mmol, 1.0 equiv) was added, followed by (*S*,*S*)-**104b** (29.7 mg, 0.035 mmol, 0.1 equiv) was added. The contents were flushed with argon and CH_2Cl_2 (1.0 mL) was added and the contents were cooled to –78 °C using a dry ice/2-propanol bath. Then, *i*-Pr_2NEt (0.02 mL, 0.138 mmol, 0.4 equiv) and $SiCl_4$ (0.04 mL, 0.381 mmol, 1.1 equiv) were added and the contents were stirred for 10 min at this temperature. Next, a solution of trienolate **60a** (106 mg, 0.415 mmol, 1.2 equiv) in CH_2Cl_2 (1.0 mL) was added and the contents were stirred for 3 h at –78 °C. The reaction was quenched by pouring the cold contents directly into a vigorously stirring solution of sat. KF:1.0 M KH_2PO_4 (1:1 (v/v), 30 mL) in an Erlenmeyer. The reaction flask was rinsed with CH_2Cl_2 (3 x 2 mL). The contents were stirred for 15 min at rt and the emulsion was filtered through a pad of Celite (3 g) eluting with CH_2Cl_2 (50 mL). The filtrate was washed with brine (1 x 30 mL), dried with Na_2SO_4 and concentrated to give a light-yellow oil that was immediately subjected to column chromatography (SiO_2, 40 g; 7:1, hexane/EtOAc) to give (*S*)-**105** (63.7 mg, 53%) as a light-yellow oil. This material was immediately used in the subsequent step.

To a 25-mL, two-necked, round-bottomed flask equipped with a magnetic stir-bar, argon inlet, and septum, (*S*)-**105** (63.7 mg, 0.183 mmol, 1.0 equiv) was added, followed by CH_2Cl_2 (1.0

mL). Then Et_3N (55.6 mg, 0.549 mmol, 3.0 equiv) and TES-Cl (55.2 mg, 0.366 mmol, 2.0 equiv) was added and the contents were stirred at rt, under argon, for 2 h. The reaction mixture was quenched with sat. $NaHCO_{3(aq)}$ (30 mL) and transferred to a separatory funnel. The aqueous layer was extracted with CH_2Cl_2 (3 x 30 mL). The organic layers were combined, washed with brine (30 mL), dried with Na_2SO_4, filtered and concentrated to a yellow oil. The crude material was purified using column chromatography (SiO_2, 40 g, 10:1, hexanes/EtOAc). This gave a mixture of geometrical isomers (78.0 mg, 92%, *E*/*Z* = 62:38) as a pale yellow oil. The isomers (10.1 mg (*E*),(*Z*)-**107**) were separated using preparative HPLC (Waters μ Porasil (SiO_2, 10 μm), 1% EtOAc/hexanes, 5 mL/min). This provided (*E*)-**107** (3.5 mg) and (*Z*)-**107** (3.2 mg).

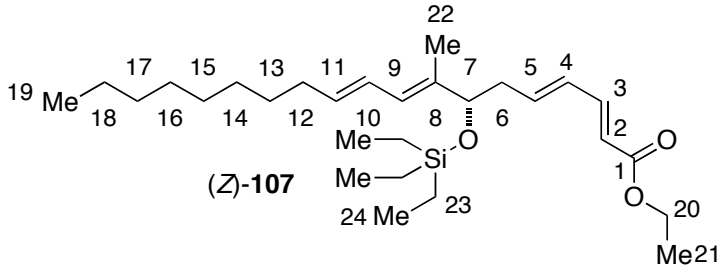


(*E*)-**107**

Data for (*E*)-**107**:

SFC: (OD, 1.5% MeOH, 40 °C, 3.0 mL/min, 125 bar)

t_R = (7*R*)-(*E*)-**107**, 5.29 min (39%), t_R = (7*S*)-(*E*)-**107**, 5.82 min (61%)



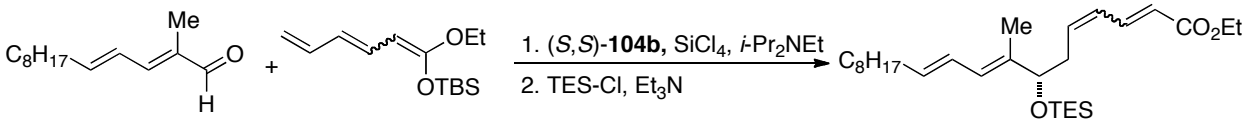
(*Z*)-**107**

Data for (*Z*)-**107**:

SFC: (OD, 5.0% MeOH, 40 °C, 3.0 mL/min, 125 bar)

t_R = (7*R*)-(*Z*)-**107**, 2.30 min (21%), t_R = (7*S*)-(*Z*)-**107**, 2.91 min (79%)

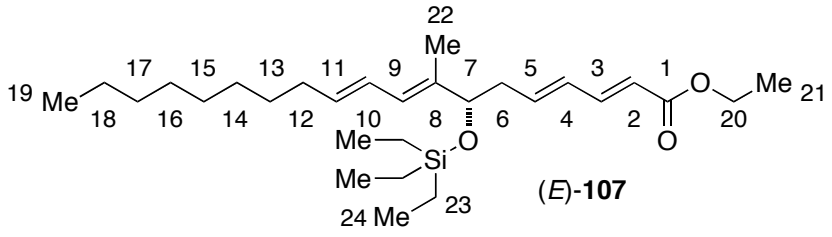
Table S2, SI, entry 4 [TK-XI-73]



61 **60a** (*S*)-**107**

To a 25-mL, two-necked, round-bottomed flask equipped with a magnetic stir-bar, argon inlet, and septum aldehyde **61** (71.2 mg, 0.342 mmol, 1.0 equiv) was added, followed by (*S*,*S*)-**104b** (2.9 mg, 0.0034 mmol, 0.01 equiv) was added. The contents were flushed with argon and CH_2Cl_2 (1.0 mL) was added and the contents were cooled to –78 °C using a dry ice/2-propanol bath. Then, *i*-Pr_2NEt (0.02 mL, 0.138 mmol, 0.4 equiv) and $SiCl_4$ (0.04 mL, 0.376 mmol, 1.1 equiv) were added and the contents were stirred for 10 min at this temperature. Next, a solution of trienolate **60a** (104 mg, 0.410 mmol, 1.2 equiv) in CH_2Cl_2 (1.0 mL) was added and the contents were stirred for 25 h at –78 °C. The reaction was quenched by pouring the cold contents directly into a vigorously stirring solution of sat. KF:1.0 M KH_2PO_4 (1:1 (v/v), 30 mL) in an Erlenmeyer. The reaction flask was rinsed with CH_2Cl_2 (3 x 2 mL). The contents were stirred for 15 min at rt and the emulsion was filtered through a pad of Celite (3 g) eluting with CH_2Cl_2 (50 mL). The filtrate was washed with brine (1 x 30 mL), dried with Na_2SO_4 and concentrated to give a light-yellow oil that was immediately subjected to column chromatography (SiO_2, 40 g; 7:1, hexane/EtOAc) to give (*S*)-**105** (65.0 mg, 55%) as a light-yellow oil. This material was immediately used in the subsequent step.

To a 25-mL, two-necked, round-bottomed flask equipped with a magnetic stir-bar, argon inlet, and septum, (*S*)-**105** (32.1 mg, 0.092 mmol, 1.0 equiv) was added, followed by CH_2Cl_2 (1.0 mL). Then Et_3N (29.9 mg, 0.276 mmol, 3.0 equiv) and TES-Cl (27.7 mg, 0.184 mmol, 2.0 equiv) was added and the contents were stirred at rt, under argon, for 2 h. The reaction mixture was quenched with sat. $NaHCO_{3(aq)}$ (30 mL) and transferred to a separatory funnel. The aqueous layer was extracted with CH_2Cl_2 (3 x 30 mL). The organic layers were combined, washed with brine (30 mL), dried with Na_2SO_4, filtered and concentrated to a yellow oil. The crude material was purified using column chromatography (SiO_2, 40 g; 10:1, hexanes/EtOAc). This gave a mixture of geometrical isomers (29.8 mg, 70%, *E*/*Z* = 60:40) as a pale yellow oil. The isomers (7.0 mg (*E*),(*Z*)-**107**) were separated using preparative HPLC (Waters μPorasil (SiO_2, 10 μm), 1% EtOAc/hexanes, 5 mL/min). This provided (*E*)-**107** (2.0 mg) and (*Z*)-**107** (2.0 mg).

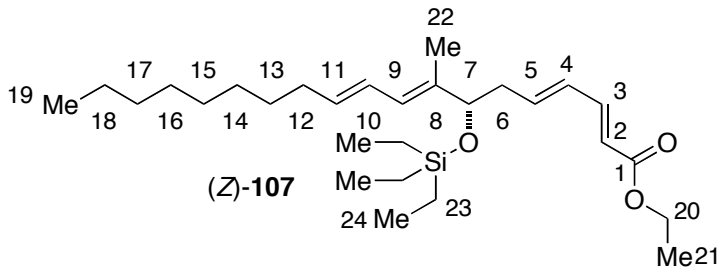


(*E*)-**107**

Data for (*E*)-**107**:

SFC: (OD, 1.5% MeOH, 40 °C, 3.0 mL/min, 125 bar)

t_R = (7*R*)-(*E*)-**107**, 5.29 min (43%), t_R = (7*S*)-(*E*)-**107**, 5.82 min (57%)



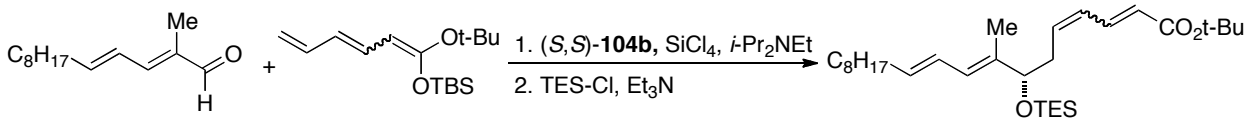
(*Z*)-**107**

Data for (*Z*)-**107**:

SFC: (OD, 5.0% MeOH, 40 °C, 3.0 mL/min, 125 bar)

t_R = (7*R*)-(*Z*)-**107**, 2.30 min (24%), t_R = (7*S*)-(*Z*)-**107**, 2.91 min (76%)

Preparation of *tert*-Butyl (*S*)-(2*E*,4*E*,8*E*,10*E*)-7-Hydroxy-8-methyl-2,4,8,10-nonadeca-tetraenoate (108), *tert*-Butyl (*S*)-(2*E*,4*E*,8*E*,10*E*)-7-Triethylsiloxy-8-methyl-2,4,8,10-nonadeca-tetraenoate ((*E*)-109) and *tert*-Butyl (*S*)-2*E*,4*Z*,8*E*,10*E*)-7-Triethylsiloxy-8-methyl-2,4,8,10-nonadecatetraenoate ((*Z*)-109) [TK-XI-85], [TK-XI-86]

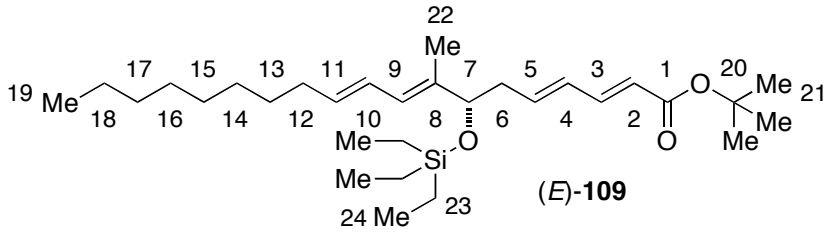


61 **60b** (*S*)-**109**

To a 25-mL, two-necked, round-bottomed flask equipped with a magnetic stir-bar, argon inlet, and septum aldehyde **61** (76.0 mg, 0.365 mmol, 1.0 equiv) was added, followed by (*S*,*S*)-**104b** (30.8 mg, 0.0365 mmol, 0.1 equiv) was added. The contents were flushed with argon and CH_2Cl_2 (1.0 mL) was added and the contents were cooled to –78 °C using a dry ice/2-propanol

bath. Then, *i*-Pr_2NEt (0.03 mL, 0.146 mmol, 0.4 equiv) and $SiCl_4$ (0.05 mL, 0.402 mmol, 1.1 equiv) were added and the contents were stirred for 10 min at this temperature. Next, a solution of trienolate **60b** (111 mg, 0.438 mmol, 1.2 equiv) in CH_2Cl_2 (1.0 mL) was added and the contents were stirred for 3 h at –78 °C. The reaction was quenched by pouring the cold contents directly into a vigorously stirring solution of sat. KF:1.0 M KH_2PO_4 (1:1 (v/v), 30 mL) in an Erlenmeyer. The reaction flask was rinsed with CH_2Cl_2 (3 x 2 mL). The contents were stirred for 15 min at rt and the emulsion was filtered through a pad of Celite (5 g) eluting with CH_2Cl_2 (50 mL). The filtrate was washed with brine (1 x 30 mL), dried with Na_2SO_4 and concentrated to give a light-yellow oil that was immediately subjected to column chromatography (SiO_2, 40 g; 7:1, hexane/EtOAc) to give (*S*)-**108** (74.0 mg, 63%) as a colorless oil. This material was immediately used in the subsequent step.

To a 25-mL, two-necked, round-bottomed flask equipped with a magnetic stir-bar, argon inlet, and septum, (*S*)-**108** (74.0 mg, 0.197 mmol, 1.0 equiv) was added, followed by CH_2Cl_2 (1.0 mL). Then Et_3N (0.08 mL, 0.591 mmol, 3.0 equiv) and a solution of TES-Cl (59.4 mg, 0.394 mmol, 2.0 equiv) in CH_2Cl_2 (1.0 mL) was added and the contents were stirred at rt, under argon, for 2 h. The reaction mixture was quenched with sat. H_2O (30 mL) and transferred to a separatory funnel. The aqueous layer was extracted with CH_2Cl_2 (3 x 30 mL). The organic layers were combined, washed with brine (30 mL), dried with Na_2SO_4, filtered and concentrated to a yellow oil. The crude material was purified using column chromatography (SiO_2, 40 g; 10:1, hexanes/EtOAc). This gave a mixture of geometrical isomers (97 mg, 99%, *E*/*Z* = 64:34) as a pale yellow oil. The isomers (7.5 mg (*E*),(*Z*)-**109**) were separated using preparative HPLC (Waters µPorasil (SiO_2, 10 µm), 1% EtOAc/hexanes, 5 mL/min). This provided (*E*)-**109** (3.9 mg) and (*Z*)-**109** (2.2 mg).

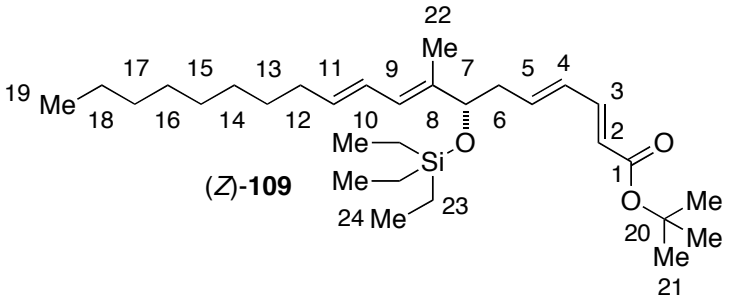


(*E*)-**109**

Data for (*E*)-**109**:

SFC: (OD, 0.1% MeOH, 40 °C, 3.0 mL/min, 125 bar)

t_R = (7*R*)-(*E*)-**109**, 16.26 min (40%), t_R = (7*S*)-(*E*)-**109**, 17.40 min (60%)



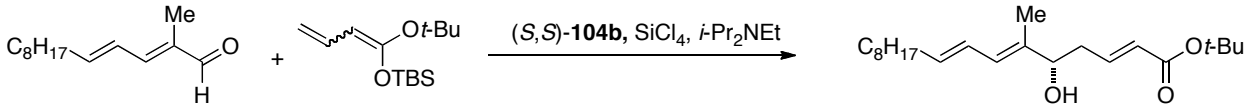
(*Z*)-**109**

Data for (*Z*)-**109**:

SFC: (OD, 1.5% MeOH, 40 °C, 3.0 mL/min, 150 bar)

t_R = (7*R*)-(*Z*)-**109**, 4.26 min (22%), t_R = (7*S*)-(*Z*)-**109**, 4.83 min (78%)

Preparation of *tert*-Butyl (*S*)-((2*E*,6*E*,8*E*)-5-Hydroxy-6-methyl-2,6,8-heptadeca-trienoate (111) [TK-XI-098]



61 **110** **111**

To a 25-mL, two-necked, round-bottomed flask equipped with a magnetic stir-bar, argon inlet, and septum aldehyde **61** (52.7 mg, 0.253 mmol, 1.0 equiv) was added, followed by (*S*,*S*)-**104b** (21.3 mg, 0.0253 mmol, 0.1 equiv) was added. The contents were flushed with argon and CH_2Cl_2 (1.0 mL) was added and the contents were cooled to –78 °C using a dry ice/2-propanol bath. Then, *i*-Pr_2NEt (0.02 mL, 0.101 mmol, 0.4 equiv) and $SiCl_4$ (0.03 mL, 0.278 mmol, 1.1 equiv) were added and the contents were stirred for 10 min at this temperature. Next, a solution of dienolate **110** (85.9 mg, 0.304 mmol, 1.2 equiv) in CH_2Cl_2 (1.0 mL) was added and the contents were stirred for 3 h at –78 °C. The reaction was quenched by pouring the cold contents directly into a vigorously stirring solution of sat. KF:1.0 M KH_2PO_4 (1:1 (v/v), 30 mL) in an Erlenmeyer. The reaction flask was rinsed with CH_2Cl_2 (3 x 2 mL). The contents were stirred for 15 min at rt and the emulsion was filtered through a pad of Celite (5 g) eluting with CH_2Cl_2 (50 mL). The filtrate was washed with brine (1 x 30 mL), dried with Na_2SO_4 and concentrated to give a colorless oil that was immediately subjected to column chromatography (SiO_2, 40 g; 7:1, hexane/EtOAc) to give **111** (71 mg, 80%) as a colorless oil.

Data for **111**:

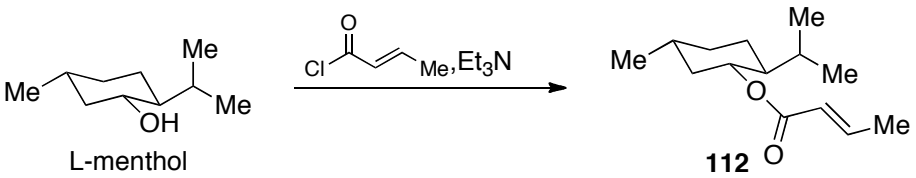
^{1}H NMR: (500 MHz, $CDCl_3$)

6.82 (dt, *J* = 14.8, 7.3, 1 H), 6.22 (dd, *J* = 15.1, 10.8, 1 H), 6.03 (d, *J* = 10.8, 1 H), 5.82 (d, *J* = 15.5, 1 H), 5.71 (dt, *J* = 14.8, 7.3, 1 H), 4.17-4.14 (m, 1 H), 2.44-2.41 (m, 2 H), 2.10 (q, *J* = 7.1, 2 H), 1.74 (s, 3 H), 1.47 (s, 9 H), 1.41-1.20 (m, 12H), 0.88 (t, *J* = 6.7, 3 H)

SFC: (AD, 5.0% MeOH, 40 °C, 3.0 mL/min, 125 bar)

t_R = (5*S*)-**111**, 5.39 min (60%), t_R = (5*R*)-**111**, 6.91 min (40%)

Preparation of 1-(1'*R*,2'*S*,5'*S*)-5-Methyl-2'-(1-methylethyl)cyclohexyl 2-Butenoate (112)[40] [TK-XI-96]



To a single-necked, round-bottomed flask equipped with a magnetic stir-bar and an argon inlet was added *L*-menthol (2.14 g, 13.67 mmol, 1.0 equiv), followed by CH_2Cl_2 (15 mL). To this solution was added Et_3N (2.86 mL, 20.51 mmol, 1.5 equiv) and the contents were cooled to 0 °C using an ice bath. Once at this temperature crotonyl chloride (1.59 mL, 20.51, 1.5 equiv) was added drop-wise over 5 min. After the addition the contents were allowed to warm to ambient temperature (ca. 1 h). The reaction mixture was quenched with H_2O (30 mL) and extracted with CH_2Cl_2 (3 x 30 mL). The organic layers were combined and washed with brine (1 x 30 mL), dried with Na_2SO_4, filtered and concentrated to a brown oil. The crude product was purified using column chromatography (SiO_2, 80 g; hexanes/EtOAc, 96/4), followed by a second column chromatography (SiO_2, 80 g; hexanes/EtOAc, 96/4) to afford **112** (2.19 g, 71%) as a colorless oil.

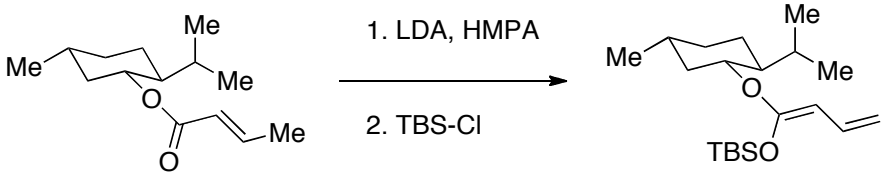
Data for **112**:

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

5.97-5.98 (m, 1 H), 5.19-5.16 (m, 1 H), 5.15 (t, *J* = 1.4, 1 H), 4.68 (dt, *J* = 4.4, 10.9, 1 H), 3.07 (dt, *J* = 6.9, 1.3, 2 H), 2.02-1.96 (m, 1 H), 1.90-1.81 (m, 1 H), 1.71-1.63 (m, 2 H), 1.53-1.43 (m, 1 H), 1.42-1.34 (m, 1 H), 1.10-0.80 (m, 9 H),

0.75 (d, *J* = 6.9, 3 H)

Preparation of 1-(1'*R*,2'*S*,5'*S*)-5-Methyl-2'-(1-methylethyl)cyclohexoxy-1-*tert*-butyldimethylsiloxy-1,3-butadiene (114) [TK-XII-10]



112 **114**

To a 100-mL, three-necked, round-bottomed flask equipped with a magnetic stir-bar, argon inlet, and two septa in the remaining necks, diisopropylamine (0.27 mL, 1.96 mmol, 1.1 equiv) was added followed by THF (1 mL) and the contents were cooled to 0 °C using an ice bath. To this solution was added *n*-BuLi (1.23 mL, 1.96 mmol, 1.1 equiv, 1.6 M in hexanes) dropwise over 5 min. The bright yellow solution became orange and was stirred for an additional 30 min at 0 °C. After this amount of time the solution was cooled to –78 °C using a dry ice/2-propanol bath. Then, HMPA (0.37 mL, 2.14 mmol, 1.2 equiv) was added and stirred for 30 min at –78 °C. Finally, a solution **112** (400 mg, 1.78 mmol, 1.0 equiv) in THF (1 mL) was added dropwise over 5 min. The contents were again stirred for 30 min at –78 °C. Next, a solution of TBS-Cl (296 g, 1.96 mmol, 1.1 equiv) in THF (1 mL) was added to the reaction and the contents were allowed to warm slowly to ambient temperature (ca 30 min). Then pentane (50 mL) was added and the contents were transferred to a separatory funnel. The organic layer was washed with H_2O (3 x 50 mL) and dried with Na_2SO_4. The solvent was removed under reduced pressure, and the crude material was purified using Kugelrohr distillation (175-180 °C at 0.50 mmHg) providing **114** (475 g, 79% as a 10:1 mixture of isomers) as a colorless oil.

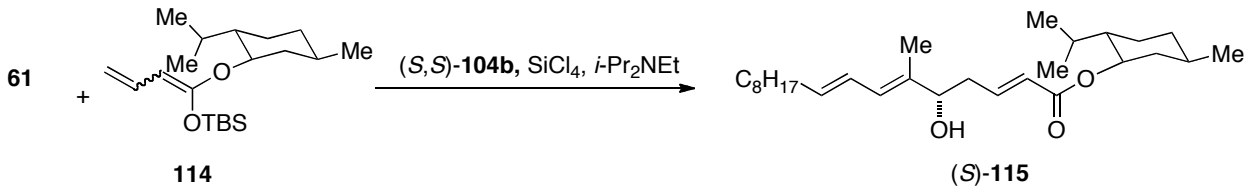
Data for **114**:

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

6.63-6.48 (m, 1 H), 4.79 (dd, *J* = 17.2, 2.2, 1 H), 4.55 (dd, *J* = 10.4, 2.1, 1 H), 4.47 (d, *J* = 10.4, 1 H), 3.77 (dt, *J* = 4.1, 10.5, 1 H), 2.28-2.20 (m, 1 H), 2.15-2.07 (m, 1 H), 2.02-1.93 (m, 1 H), 1.73-1.62 (m, 2 H), 1.56 (s, 9 H), 0.96-0.85 (m, 9 H), 0.17 (s, 6 H)

Note: ^{1}H-NMR data is described only for the major isomer (*E*,*E*-**114**)

Preparation of 1-Menthyl (*S*)-(2*E*,6*E*,8*E*)-5-Hydroxy-6-methyl-2,6,8-heptadeca-trienoate (*S*-115) [TK-XII-16]



114 (*S*)-**115**

To a 25-mL, two-necked, round-bottomed flask equipped with a magnetic stir-bar, argon inlet, and septum aldehyde **61** (55.2 mg, 0.265 mmol, 1.0 equiv) was added, followed by (*S*,*S*)-**104b** (22.3 mg, 0.0265 mmol, 0.1 equiv) was added. The contents were flushed with argon and CH_2Cl_2 (1.0 mL) was added and the contents were cooled to –78 °C using a dry ice/2-propanol bath. Then, *i*-Pr_2NEt (0.02 mL, 0.106 mmol, 0.4 equiv) and $SiCl_4$ (0.035 mL, 0.292 mmol, 1.1 equiv) were added and the contents were stirred for 10 min at this temperature. Next, a solution of dienolate **114** (107.7 mg, 0.318 mmol, 1.2 equiv) in CH_2Cl_2 (0.5 mL) was added and the contents were stirred for 20 h at –78 °C. The reaction was quenched by pouring the cold contents directly into a vigorously stirring solution of sat. KF:1.0 M KH_2PO_4 (1:1 (v/v), 30 mL) in an Erlenmeyer. The reaction flask was rinsed with CH_2Cl_2 (3 x 2 mL). The contents were stirred for 15 min at rt and the emulsion was filtered through a pad of Celite (3 g) eluting with CH_2Cl_2 (50 mL). The filtrate was washed with brine (1 x 30 mL), dried with Na_2SO_4 and concentrated to give a colorless oil that was immediately subjected to column chromatography (SiO_2, 40 g; gradient 7:1-3:1-1:1, hexane/EtOAc) to give (*S*)-**115** (35 mg, 31%) as a colorless oil.

Data for (*S*)-**115**:

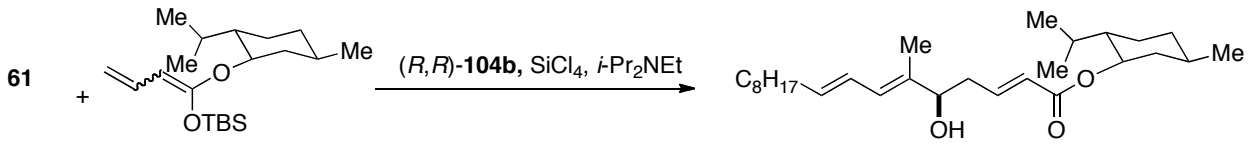
^{1}H NMR: (400 MHz, $CDCl_3$)

6.90 (dt, *J* = 15.6, 7.4, 1 H), 6.22 (dd, *J* = 15.0, 10.8, 1 H), 6.03 (d, *J* = 10.8, 1 H), 5.90 (d, *J* = 15.6, 1 H), 5.71 (dt, *J* = 15.0, 7.0, 1 H), 4.73 (dt, *J* = 4.4, 10.9, 1 H), 4.22-4.15 (m, 1 H), 2.50-2.42 (m, 2 H), 2.10 (q, *J* = 7.2, 2 H), 2.04-1.97 (m, 1 H), 1.91-1.81 (m, 1 H), 1.75 (s, 3 H), 1.72-1.64 (m, 2 H), 1.44-1.19 (m, 12H), 1.10-0.8 (m, 9 H), 0.88 (t, *J* = 7.0, 3 H), 0.75 (d, *J* = 7.0, 3 H)

SFC: (AD, 6.0% MeOH, 40 °C, 3.0 mL/min, 125 bar)

t_R = (5*S*)-**115**, 11.5 min (66%), t_R = (5*R*)-**115**, 12.2 min (34%)

Preparation of 1-Menthyl (*R*)-(2*E*,6*E*,8*E*)-5-Hydroxy-6-methyl-2,6,8-heptadeca-trienoate (*R*-115) [TK-XII-19]



114 (*R*)-**115**

To a 25-mL, two-necked, round-bottomed flask equipped with a magnetic stir-bar, argon inlet, and septum aldehyde **61** (63.0 mg, 0.302 mmol, 1.0 equiv) was added, followed by (*R*,*R*)-**104b** (22.3 mg, 0.0265 mmol, 0.1 equiv) was added. The contents were flushed with argon and CH_2Cl_2 (1.0 mL) was added and the contents were cooled to –78 °C using a dry ice/2-propanol bath. Then, *i*-Pr_2NEt (0.02 mL, 0.121 mmol, 0.4 equiv) and $SiCl_4$ (0.04 mL, 0.332 mmol, 1.1 equiv) were added and the contents were stirred for 10 min at this temperature. Next, a solution of silyl dienolate **114** (122.6 mg, 0.362 mmol, 1.2 equiv) in CH_2Cl_2 (0.5 mL) was added and the contents were stirred for 8 h at –78 °C. The reaction was quenched by pouring the cold contents directly into a vigorously stirring solution of sat. KF:1.0 M KH_2PO_4 (1:1 (v/v), 30 mL) in an Erlenmeyer. The reaction flask was rinsed with CH_2Cl_2 (3 x 2 mL). The contents were stirred for 15 min at rt and the emulsion was filtered through a pad of Celite (3 g) eluting with CH_2Cl_2 (50 mL). The filtrate was washed with brine (1 x 30 mL), dried with Na_2SO_4 and concentrated to give a colorless oil that was immediately subjected to column chromatography (SiO_2, 40 g; gradient 7:1-3:1, hexane/EtOAc) to give (*R*)-**115** (95 mg, 73%) as a colorless oil.

Data for (*R*)-**115**:

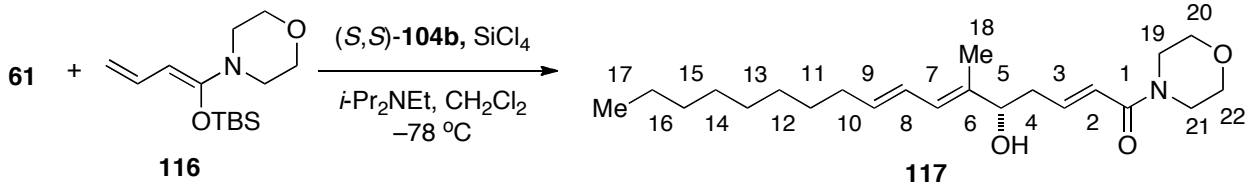
^{1}H NMR: (400 MHz, $CDCl_3$)

6.90 (dt, *J* = 15.6, 7.7, 1 H), 6.22 (dd, *J* = 15.0, 10.8, 1 H), 6.03 (d, *J* = 10.8, 1 H), 5.90 (d, *J* = 15.6, 1 H), 5.71 (dt, *J* = 15.0, 7.0, 1 H), 4.73 (dt, *J* = 4.4, 10.9, 1 H), 4.22-4.15 (m, 1 H), 2.50-2.42 (m, 2 H), 2.10 (q, *J* = 7.2, 2 H), 2.04-1.97 (m, 1 H), 1.91-1.81 (m, 1 H), 1.75 (s, 3 H), 1.72-1.64 (m, 2 H), 1.44-1.19 (m, 12H), 1.10-0.8 (m, 9 H), 0.88 (t, *J* = 7.0, 3 H), 0.75 (d, *J* = 7.0, 3 H)

SFC: (AD, 5.0% MeOH, 40 °C, 3.0 mL/min, 125 bar)

t_R = (5*R*)-**115**, 2.21 min (58%), t_R = (5*S*)-**115**, 2.49 min (42%)

Screening Lewis-Base Catalysts for the Preparation of Morpholinyl (*S*)-(2*E*,8*E*,10*E*)-5-Hydroxy-6-methyl-2,8,10-hexadecatrienamide (117) (Table S3, SI, entry 1) [CSR-VI-29]



To a 5-mL Schlenk flask equipped with a magnetic stir-bar, (*S,S*)-**104b** (10.5 mg, 0.0125mmol, 0.05 equiv) was added, followed by CH_2Cl_2 (1.25 mL). Then aldehyde **61** (52 mg, 0.25 mmol, 1.0 equiv) and *i*-Pr_2NEt (4.5 μL, 0.025 mmol, 0.1) were added. The solution was cooled to –78 °C. Once at this temperature $SiCl_4$ (43 μL, 0.275 mmol, 1.1 equiv) was added. Next, ketene aminal **116** (81 mg, 0.275 mmol, 1.1 equiv) was added as a solution in CH_2Cl_2 (1.25 mL) dropwise over 5 min. This light-yellow solution was stirred at –78 °C for 2 h. After this amount of time 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 (10 mL), at rt. 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 rt. 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), EtOAc/MeOH, 19:1) to afford 72 mg (81%) of **117** as light-yellow oil.

Data for **117**:

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

6.81 (dt, *J* = 15.4, 7.2, 1 H), 6.24 (ddt, *J* = 14.4, 10.6, 1.4, 1 H), 6.20 (ddt, *J* = 15.4, 8.0, 1.4, 1 H), 6.02 (d, *J* = 10.6, 1 H), 5.73 (dt, *J* = 14.4, 7.2, 1 H), 4.21–4.19 (m, 1 H), 3.76 – 3.34 (m, 8H), 2.52 – 2.41 (m, 2 H), 2.10 (q, *J* = 7.2, 2 H), 1.76 (s, 3 H), 1.65 (br, OH), 1.45 – 1.16 (m, 12H), 0.88 (t, *J* = 7.0, 3 H)

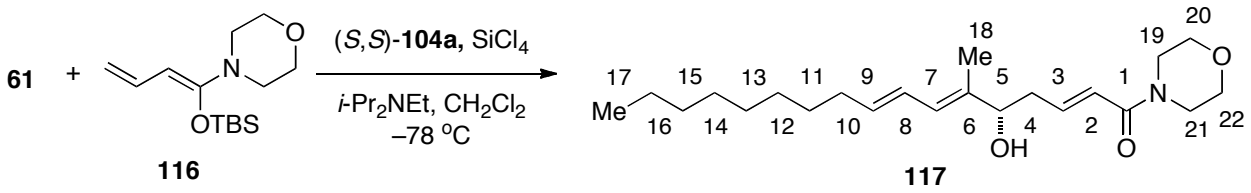
MS: (EI, 70 eV)

363 ((M^+) 4), 209 (21), 164 (20), 155 (100), 140 (27), 132 (13), 114 (28), 105 (82), 97 (24), 96 (15), 95 (84), 77 (44), 70 (20)

SFC: (Chiapas-OB, oven 40 °C, 3.0 mL/min, 2.0% MeOH, 125 bar),

(5*S*)-**117**: 12.57 min (44.9%), (5*R*)-**117**: 14.88 min (55.1%)

(Table S3, SI, entry 2) [CSR-VI-39]



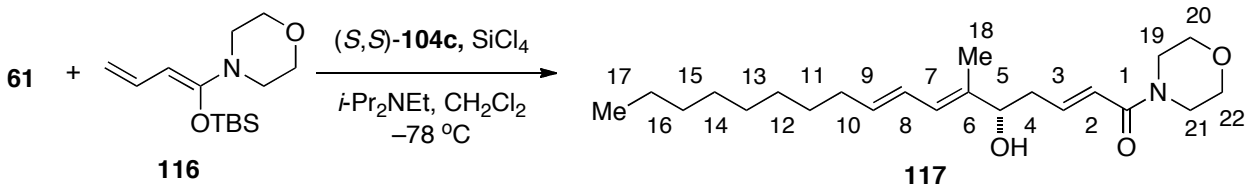
To a 5-mL, Schlenk-flask equipped with a magnetic stir-bar, (*S,S*)-**104a** (10.0 mg, 0.0125 mmol, 0.05 equiv) was added, followed by CH_2Cl_2 (1.25 mL). Then aldehyde **61** (52 mg, 0.25 mmol, 1.0 equiv) and *i*-Pr_2NEt (4.5 μL, 0.025 mmol, 0.1) were added. The solution was cooled to –78 °C. Once at this temperature $SiCl_4$ (43 μL, 0.275 mmol, 1.1 equiv) was added. Next, ketene ammonal **116** (81 mg, 0.275 mmol, 1.1 equiv) was added as a solution in CH_2Cl_2 (1.25 mL) dropwise over 5 min. This light-yellow solution was stirred at –78 °C for 2 h. After this amount of time 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 (10 mL), at rt. 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 rt. 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), EtOAc/MeOH, 19:1) to afford 69 mg (78%) of **117** as light-yellow oil.

Data for **117**:

SFC: (Chiapas-OB, oven 40 °C, 3.0 mL/min, 2.0% MeOH, 125 bar),

(5*S*)-**117**: 12.57 min (67.0%), (5*R*)-**117**: 14.88 min (33.0%)

(Table S3, SI, entry 3) [CSR-VI-41]

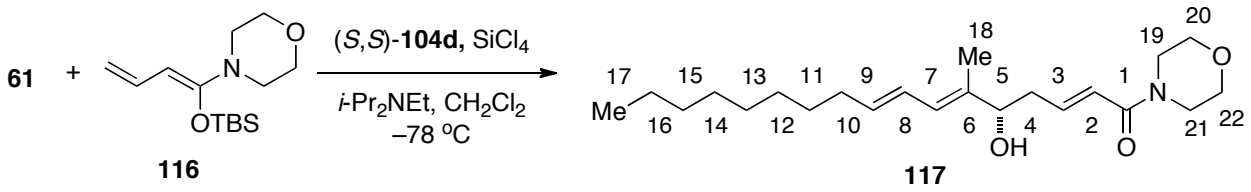


To a 5-mL Schlenk-flask equipped with a magnetic stir-bar, (*S,S*)-**104c** (10.7 mg, 0.0125 mmol, 0.05 equiv) was added, followed by CH_2Cl_2 (1.25 mL). Then aldehyde **61** (52 mg, 0.25 mmol, 1.0 equiv) and *i*-Pr_2NEt (4.5 μL, 0.025 mmol, 0.1) were added. The solution was cooled to –78 °C. Once at this temperature $SiCl_4$ (43 μL, 0.275 mmol, 1.1 equiv) was added. Next, ketene ammonal **116** (81 mg, 0.275 mmol, 1.1 equiv) was added as a solution in CH_2Cl_2 (1.25 mL) dropwise over 5 min. This light-yellow solution was stirred at –78 °C for 2 h. After this amount of time 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 (10 mL), at rt. 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 rt. 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), EtOAc/MeOH, 19:1) to afford 77 mg (87%) of **117** as light-yellow oil.

Data for **117**:

SFC: (Chiapas-OB, oven 40 °C, 3.0 mL/min, 2.0% MeOH, 125 bar),
(5*S*)-**117**: 12.57 min (77.8%), (5*R*)-**117**: 14.88 min (22.2%)

(Table S3, SI, entry 4) [CSR-VII-23]

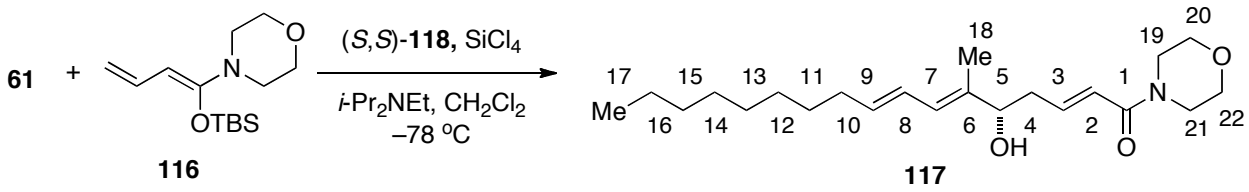


To a 5-mL Schlenk-flask equipped with a magnetic stir-bar, (*S,S*)-**104d** (11.0 mg, 0.0125 mmol, 0.05 equiv) was added, followed by CH_2Cl_2 (1.25 mL). Then aldehyde **61** (52 mg, 0.25 mmol, 1.0 equiv) and *i*-Pr_2NEt (4.5 μL, 0.025 mmol, 0.1) were added. The solution was cooled to –78 °C. Once at this temperature $SiCl_4$ (43 μL, 0.275 mmol, 1.1 equiv) was added. Next, ketene ammonal **116** (81 mg, 0.275 mmol, 1.1 equiv) was added as a solution in CH_2Cl_2 (1.25 mL) dropwise over 5 min. This light-yellow solution was stirred at –78 °C for 2 h. After this amount of time 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 (10 mL), at rt. 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 rt. 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), EtOAc/MeOH, 19:1) to afford 75 mg (84%) of **117** as light-yellow oil.

Data for **117**:

SFC: (Chiapas-OB, oven 40 °C, 3.0 mL/min, 2.0% MeOH, 125 bar),
(5*S*)-**117**: 12.57 min (77.5%), (5*R*)-**117**: 14.88 min (22.5%)

(Table S3, SI, entry 5) [CSR-VI-47]

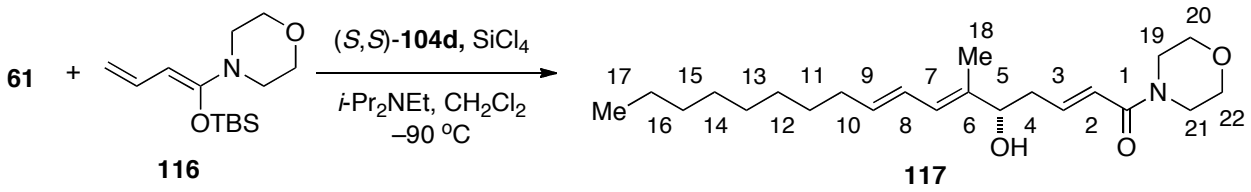


To a 5-mL Schlenk-flask equipped with a magnetic stir-bar, (*S,S*)-**118** (5.5 mg, 0.0125 mmol, 0.05 equiv) was added, followed by CH_2Cl_2 (1.25 mL). Then aldehyde **61** (52 mg, 0.25 mmol, 1.0 equiv) and *i*-Pr_2NEt (4.5 μL, 0.025 mmol, 0.1) were added. The solution was cooled to –78 °C. Once at this temperature $SiCl_4$ (43 μL, 0.275 mmol, 1.1 equiv) was added. Next, ketene ammonal **116** (81 mg, 0.275 mmol, 1.1 equiv) was added as a solution in CH_2Cl_2 (1.25 mL) dropwise over 5 min. This light-yellow solution was stirred at –78 °C for 2 h. After this amount of time 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 (10 mL), at rt. 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 rt. 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), EtOAc/MeOH, 19:1) to afford 5.5 mg (91%) of **117** as light-yellow oil.

Data for **117**:

SFC: (Chiapas-OB, oven 40 °C, 3.0 mL/min, 2.0% MeOH, 125 bar),
(5*S*)-**117**: 12.57 min (61.4%), (5*R*)-**117**: 14.88 min (38.6%)

(Table S3, SI, entry 6) [CSR-VII-27]

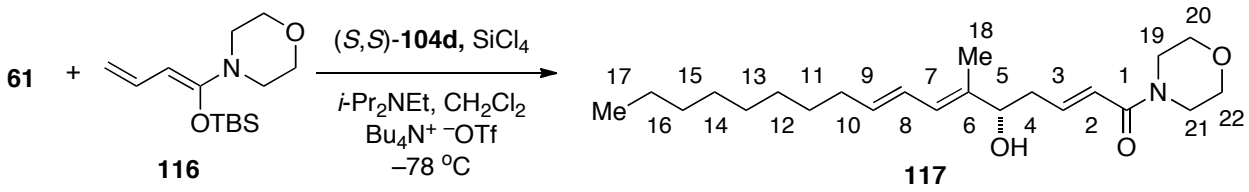


To a 5-mL Schlenk-flask equipped with a magnetic stir-bar, (*S,S*)-**104d** (11.0 mg, 0.0125 mmol, 0.05 equiv) was added, followed by CH_2Cl_2 (1.25 mL). Then aldehyde **61** (52 mg, 0.25 mmol, 1.0 equiv) and *i*-Pr_2NEt (4.5 μL, 0.025 mmol, 0.1) were added. The solution was cooled to –90 °C. Once at this temperature $SiCl_4$ (43 μL, 0.275 mmol, 1.1 equiv) was added. Next, ketene ammonal **116** (81 mg, 0.275 mmol, 1.1 equiv) was added as a solution in CH_2Cl_2 (1.25 mL) dropwise over 5 min. This light-yellow solution was stirred at –90 °C for 3 h. After this amount of time 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 (10 mL), at rt. 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 rt. 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), EtOAc/MeOH, 19:1) to afford 61 mg (68%) of **117** as light-yellow oil.

Data for **117**:

SFC: (Chiapas-OB, oven 40 °C, 3.0 mL/min, 2.0% MeOH, 125 bar),
(5*S*)-**117**: 12.57 min (71.3%), (5*R*)-**117**: 14.88 min (28.7%)

(Table S3, SI, entry 7) [CSR-VII-25]

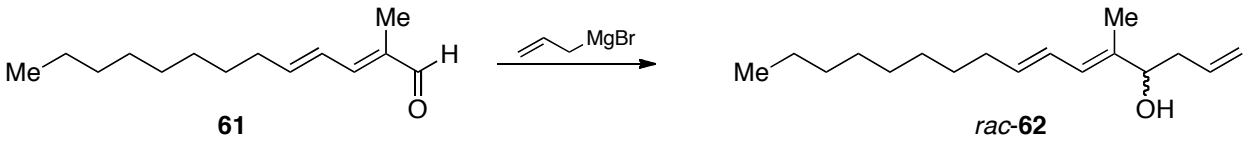


To a 5-mL, Schlenk-flask equipped with a magnetic stir-bar, (*S,S*)-**104d** (11.0 mg, 0.0125 mmol, 0.05 equiv) and nBu$_4$N^{+-}OTf (5.0 mg, 0.0125 mmol, 0.05 equiv) were added, followed by CH_2Cl_2 (1.25 mL). Then aldehyde **61** (52 mg, 0.25 mmol, 1.0 equiv) and i-Pr$_2$NEt (4.5 μL, 0.025 mmol, 0.1) were added. The solution was cooled to –78 °C. Once at this temperature $SiCl_4$ (43 μL, 0.275 mmol, 1.1 equiv) was added. Next, ketene ammonal **116** (81 mg, 0.275 mmol, 1.1 equiv) was added as a solution in CH_2Cl_2 (1.25 mL) dropwise over 5 min. This light-yellow solution was stirred at –78 °C for 2 h. After this amount of time 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 (10 mL), at rt. 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 rt. 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), EtOAc/MeOH, 19:1) to afford 68 mg (76%) of **117** as light-yellow oil.

Data for **117**:

SFC: (Chiapas-OB, oven 40 °C, 3.0 mL/min, 2.0% MeOH, 125 bar),
(5*S*)-**117**: 12.57 min (75.4%), (5*R*)-**117**: 14.88 min (24.6%)

Preparation of 5-Methyl-1,5,7-hexadecatrien-4-ol (*rac*-62) [TK-XII-32]



61 *rac*-**62**

To a 100-mL, three-necked, round-bottomed flask equipped with a magnetic stir-bar, argon inlet and septa in two of the necks **61** (209 mg, 1.00 mmol, 1.0 equiv) was added and the contents were flushed with argon. Then Et_2O (3.0 mL) was added and the light-yellow solution was cooled to 0 ^oC using an ice-bath. Once at 0 ^oC, allyl magnesium bromide (3.0 mL, 1.5 mmol, 1.5 equiv, 0.5 M in Et_2O) was added and the contents were stirred for 1 h. Then Celite (1 g) and Et_2O (3 mL) were added at 0 ^oC and the reaction was quenched with H_2O (0.1 mL). This mixture was filtered through a pad of Celite (3 g), washing with Et_2O (30 mL). The solvent was removed using rotary evaporation to give a light-yellow oil. The crude material was purified using column chromatography (SiO_2, 40 g) hexanes/EtOAc, 7:1) to give *rac*-**62** (240 mg, 90%) as a colorless oil.

Data for *rac*-**62**:

^{1}H NMR: (500 MHz, $CDCl_3$)
6.24 (ddt, *J* = 14.3, 10.5, 1.4, 1 H), 6.03 (d, *J* = 10.5, 1 H), 5.78 (ddt, *J* = 16.7, 9.5, 6.2, 1 H), 5.70 (dt, *J* = 14.3, 7.1, 1 H), 5.14 (dq, *J* = 16.7, 1.0, 1 H), 5.11 (dq, *J* = 9.5, 1.0, 1 H), 4.08 (t, *J* = 6.3, 1 H), 2.40-2.27 (m, 2 H), 2.10 (q, *J* = 7.1, 2 H), 1.75 (s, 3 H), 1.62 (br, s, 1 H), 1.43-1.20 (m, 12H), 0.88 (t, *J* = 7.0, 3 H)

MS: (ESI)
249 ((M^+-1) 100), 231 (27), 188 (35), 186 (41), 178 (50), 141 (38), 101 (22)

HRMS: for $C_{17}H_{30}O$ (250.42) found $C_{17}H_{29}O$ (249.41)
Calcd: 249.2218
Found: 249.2218

Preparation of Methyl (2*E*,6*E*,8*E*)-5-Hydroxy-6-methyl-2,6,8-heptadecatrienoate (*rac*-63) [TK-XII-29]

rac-**62** *rac*-**63**

To a 25-mL, single-necked, round-bottomed flask equipped with a magnetic stir-bar and an argon inlet was added *rac*-**62** (51.3 mg, 0.205 mmol, 1.0 equiv), followed by methyl acrylate (0.24 mL, 2.67 mmol, 13 equiv). To this solution was added Grubb's 2nd generation catalyst (G2) (8.5 mg, 0.01 mmol, 0.05 equiv). The red/brown contents were stirred for 1 h at rt. After this amount of time the reaction contents were directly subjected to column chromatography (SiO_2, 40 g; hexanes/EtOAc, 3:1) to give *rac*-**63** (55.0 mg, 87%) as a colorless oil.

Data for *rac*-**63**:

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

6.94 (dt, *J* = 16.0, 8.0, 1 H), 6.22 (dd, *J* = 14.4, 11.2, 1 H), 6.04 (d, *J* = 11.2, 1 H), 5.91 (d, *J* = 16.0, 1 H), 5.72 (dt, *J* = 14.4, 7.2, 1 H), 4.20-4.15 (m, 1 H), 3.72 (s, 3 H), 2.52-2.42 (m, 2 H), 2.10 (q, *J* = 7.2, 2 H), 1.77 (s, 3 H), 1.42-1.20 (m, 12H), 0.88 (t, *J* = 7.0, 3 H)

Preparation of (2*E*,6*E*,8*E*)-5-Hydroxy-6-methyl-2,6,8-heptatrienal (*rac*-64) [TK-XII-30]

rac-**62** *rac*-**64**

To a 25-mL, single-necked, round-bottomed flask equipped with a magnetic stir-bar and an argon inlet was added *rac*-**62** (54.6 mg, 0.218 mmol, 1.0 equiv), followed by acrolein (0.19 mL, 2.83 mmol, 13 equiv). To this solution was added Grubb's 2nd generation catalyst (G2) (9.3 mg, 0.011 mmol, 0.05 equiv). The red/brown contents were stirred for 1 h at rt. After this amount of time the reaction contents were directly subjected to column chromatography ((SiO_2, 40 g) hexanes/EtOAc gradient, 7:1-3:1) to give *rac*-**64** (49.0 mg, 81%) as a colorless oil.

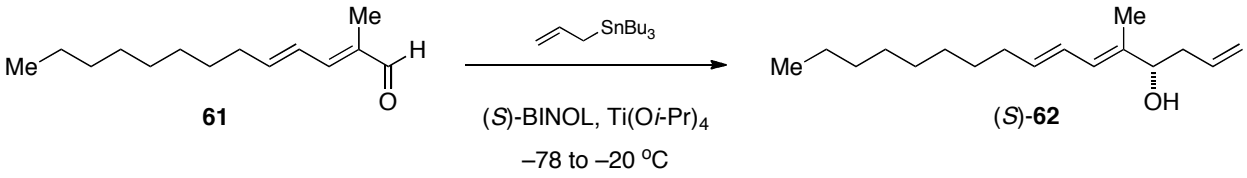
Data for *rac*-**64**:

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

9.50 (d, *J* = 8.0, 1 H), 6.84 (dt, *J* = 15.4, 7.2, 1), 6.22 (ddt, *J* = 14.4, 10.6, 1.4, 1 H), 6.04 (d, *J* = 10.6, 1 H), 5.73 (dt, *J* =14.4, 7.2, 1 H), 4.27-4.19 (m, 1 H), 2.68-2.52 (m, 2 H), 2.10 (q, *J* = 7.2, 2 H), 1.76 (s, 3 H), 1.65 (br d, *J* = 3.2, 1 H), 1.45-1.16 (m, 12H), 0.88 (t, *J* = 7.0, 3 H)

Model Allylation Reactions

Preparation of (*S*)-5-Methyl-1,5,7,-hexadecatrien-4-ol (*S*-62)[41] (Table 5, entry 1) [TK-XII-52]



In a 25-mL, Schlenk-flask equipped with a magnetic stir-bar, reflux condenser and argon inlet were placed (*S*)-(–)-BINOL (34.4 mg, 0.12 mmol, 0.24 equiv) and molecular sieves 4Å (350 mg) were added and the contents were flushed with argon. Then CH_2Cl_2 (0.5 mL) was added followed by Ti(O*i*-Pr)$_4$ (0.03 mL, 0.1 mmol, 0.2 equiv). The suspension was heated to reflux and stirred for 1 h. The reaction mixture was allowed to cool down to rt and then a solution of aldehyde **61** (103 mg, 0.494 mmol, 1.0 equiv) in CH_2Cl_2 (0.5 mL) was added. The contents were cooled to –78 ^{o}C and allyltributyltin (0.2 mL, 0.644 mmol, 1.3 equiv) was added to the suspension. The reaction mixture was sealed and kept in the freezer (–20 ^{o}C) for 24 h without stirring. After this amount of time the reaction mixture was quenched with aqueous saturated $NaHCO_3$ (1 mL) and stirred for 15 min. The suspension was filtered through Celite (1 g) and the solvent was removed under reduced pressure. The crude mixture was purified by column chromatography ((SiO_2, 30 x 120 mm), hexane/EtOAc, 10:1) to give 37 mg (30%) of (*S*)-**62** as a colorless oil.

Data for (*S*)-**62**:

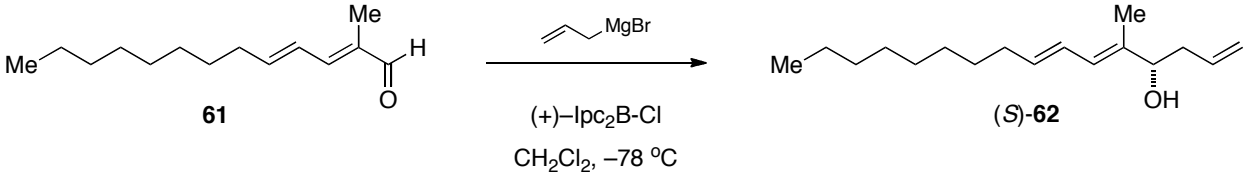
^{1}H NMR: (500 MHz, $CDCl_3$)

6.24 (ddt, *J* = 14.3, 10.5, 1.4, 1 H), 6.03 (d, *J* = 10.5, 1 H), 5.78 (ddt, *J* = 16.7, 9.5, 6.2, 1 H), 5.70 (dt, *J* = 14.3, 7.1, 1 H), 5.14 (dq, *J* = 16.7, 1.0), 5.11 (dq, *J* = 9.5,

1.0, 1 H), 4.08 (t, *J* = 6.3, 1 H), 2.40 – 2.27 (m, 2 H), 2.10 (q, *J* = 7.1, 2 H), 1.75 (s, 3 H), 1.62 (br, s, 1 H), 1.43 – 1.20 (m, 12 H), 0.88 (t, *J* = 7.0, 3 H)

SFC: (Chiralpak-OJ, oven 40 °C, 3.0 mL/min, 0.5% MeOH, 125 bar),
(3*S*)-**62**: 3.69 min (99.4%), (3*R*)-**62**: 4.03 min (0.6%)

(Table 5, entry 2)[42] **[TK-XII-39]**

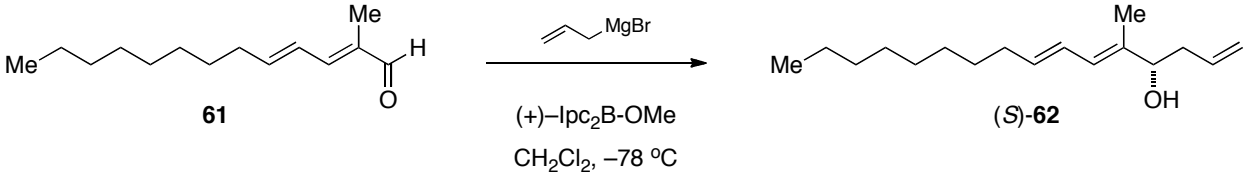


To a 25-mL, two-necked round-bottomed flask equipped with a magnetic stir-bar, argon inlet and septum was added (+)–Ipc-Cl (160.3 mg, 0.50 mmol, 1.0 equiv) followed by Et_2O (0.5 mL) and the contents were cooled to –78 °C using an 2-propanol/dry-ice bath. Then allyl magnesium bromide (0.4 mL, 0.50 mmol, 1.0 equiv, 1.25 M) was added and the contents were stirred at –78 °C for 30 min. After this amount of time the contents were allowed to warm to rt and stirred for an additional 30 min at this temperature. Then the contents were cooled back to –78 °C and a solution of **61 (**105 mg, 0.054 mmol, 1.04 equiv) in Et_2O (1.0 mL) was added and the contents were stirred at –78 °C for 1 h. The mixture was then warmed to rt and stirred for an additional 30 min. To this mixture was added NaOH (3N, 0.16 mL) and H_2O_2 (30% aq, 0.16 mL). Then the contents were transferred to a separatory funnel containing H_2O (30 mL). The aqueous layer was extracted with EtOAc (3x30 mL). The organic layers were combined and washed with brine (1x30 mL), dried with Na_2SO_4 and concentrated to a yellow oil. The crude material was purified using column chromatography ((SiO_2, 40 g) hexanes/EtOAc, 7:1) to afford (*S*)-**62** (88.2 mg, 70%) as a colorless oil.

Data for (*S*)-**62**:

SFC: (Chiralpak-OJ, oven 40 °C, 3.0 mL/min, 0.5% MeOH, 125 bar),
(3*S*)-**62**: 3.69 min (89.5%), (3*R*)-**62**: 4.03 min (10.5%)

(Table 5, entry 3)[42a] **[TK-XII-68]**

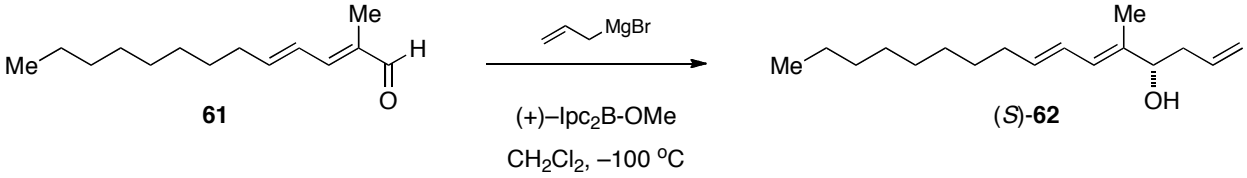


To a 25-mL, two-necked round-bottomed flask equipped with a magnetic stir-bar, argon inlet and septum was added (+)–Ipc-OMe (239.1 mg, 0.756 mmol, 1.0 equiv) followed by Et_2O (1.0 mL). Then the contents were cooled to –78 °C using a 2-propanol/dry-ice bath. Once at –78 °C allylmagnesium bromide (0.34 mL, 0.756 mmol, 1.5 equiv, 2.2 M) was added and the contents were allowed to warm to rt and stirred for 1 h at this temperature. Then the contents were cooled back to –78 °C and a solution of **61** (105 mg, 0.054 mmol, 1.04 equiv) in Et_2O (1.0 mL) was added and the contents were stirred at –78 °C for 3 h. The mixture was quenched with ethanolamine (0.1 mL) and the contents were warmed to rt and stirred at this temperature for 3 h. To this mixture was added H_2O (30 mL) and EtOAc (30 mL). The resulting suspension was filtered through Celite (3 g). The organic layer was separated and the aqueous was extracted with EtOAc (2x30 mL). The combined organic layers were washed with brine (1x30 mL), dried with Na_2SO_4 and concentrated to a yellow oil. The crude material was purified using column chromatography ((SiO_2, 40 g; hexanes/EtOAc, 10:1) to afford (*S*)-**62** (92.6 mg, 73%) as a colorless oil.

Data for (*S*)-**62**:

SFC: (Chiralpak-OJ, oven 40 °C, 3.0 mL/min, 0.5% MeOH, 125 bar),
(3*S*)-**62**: 3.69 min (95.7%), (3*R*)-**62**: 4.03 min (4.3%)

(Table 5, entry 4)[42a] **[TK-XII-70]**



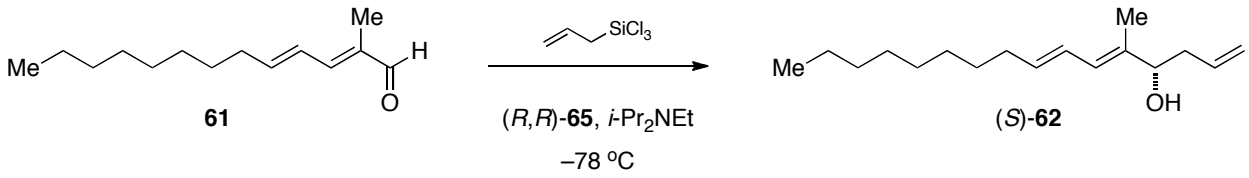
To a 25-mL, two-necked, round-bottomed flask equipped with a magnetic stir-bar, argon inlet and septum was added (+)–Ipc-OMe (239.1 mg, 0.756 mmol, 1.0 equiv) followed by Et_2O (1.0 mL). Then the contents were cooled to –78 °C using a 2-propanol/dry-ice bath. Once at –78 °C allylmagnesium bromide (0.34 mL, 0.756 mmol, 1.5 equiv, 2.2 M) was added and the

contents were allowed to warm to rt and stirred for 1 h at this temperature. Then Et_2O was removed *in vacuo*. The resulting residue was diluted with pentane (2x2 mL) and filtered *via* cannula to another 25-mL, two-necked round-bottomed flask. The pentane was removed *in vacuo* and Et_2O (1.0 mL) was added. Then the contents were cooled to –100 °C and a solution of **61 (**105 mg, 0.054 mmol, 1.04 equiv) in Et_2O (1.0 mL) was added and the contents were stirred at –100 °C for 10 h. The mixture was quenched with ethanolamine (0.1 mL) and the contents were warmed to rt and stirred at this temperature for 3 h. To this mixture was added H_2O (30 mL) and EtOAc (30 mL). The resulting suspension was filtered through Celite (3 g). The organic layer was separated and the aqueous was extracted with EtOAc (2x30 mL). The combined organic layers were washed with brine (1x30 mL), dried with Na_2SO_4 and concentrated to a yellow oil. The crude material was purified using column chromatography (SiO_2, 40 g; hexanes/EtOAc, 10:1) to afford (*S*)-**62** (89.0 mg, 71%) as a colorless oil.

Data for (*S*)-**62**:

SFC: (Chiralpak-OJ, oven 40 °C, 3.0 mL/min, 0.5% MeOH, 125 bar),
(3*S*)-**62**: 3.69 min (95.4%), (3*R*)-**62**: 4.03 min (4.6%)

(Table 5, entry 5) [CSR-VII-50]



To a 5-mL Schlenk-flask equipped with a magnetic stir-bar bar, (*R,R*)-**65** (8.0 mg, 0.125 mmol, 0.05 equiv), CH_2Cl_2 (0.25 mL), and *i*-Pr_2NEt (0.25 mL) were added. This solution was cooled to –78 °C using a 2-propanol/dry ice bath. Once at this temperature, allyltrichlorosilane (86 mg, 0.5 mmol, 2.0 equiv) was added, followed by aldehyde **61** (56 mg, 1.0 mmol, 1.0 equiv) drop-wise over 5 min. The resulting yellow solution was stirred at –78 °C for 8 h. Then the reaction mixture was transferred via cannula into 25-mL Erlenmeyer flask containing a vigorously stirring solution of a 1:1 mixture of saturated, aqueous $NaHCO_3$ and saturated, aqueous KF solution (10 mL), at rt. 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 rt. 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

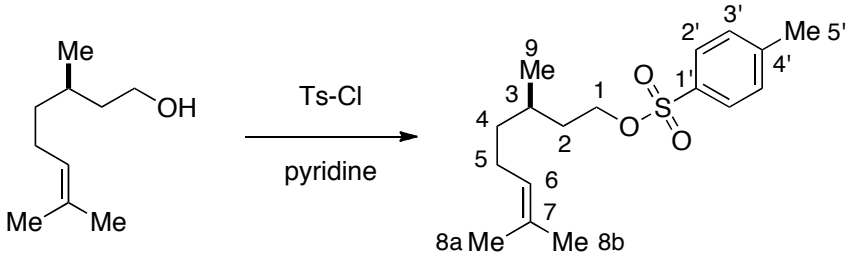
with EtOAc (3 x 20 mL), and the combined organic layers were washed with brine (20 mL). The organic solution was dried over Na_2SO_4 and concentrated under reduced pressure to afford a yellow oil. The crude product was purified using column chromatography ((SiO_2, 30 x 200 mm), hexanes/EtOAc, 20:1 to 10:1) to afford 48 mg (76%) of (*S*)-**62** as a clear, colorless oil.

Data for (*S*-**62**):

SFC: (Chiralpak-OJ, oven 40 °C, 3.0 mL/min, 0.5% MeOH, 125 bar),
(3*S*)-**62**: 3.69 min (94.6%), (3*R*)-**62**: 4.03 min (5.3%)

Preparation of Side-Chain 2

Preparation of (*S*)- 2,6-Dimethyl-6-octenyl 4'-Methylbenzenesulfonate (66)[43] [CSR-VII-63]



(*S*)-citronellol **66**

A 50-mL, two-necked, round-bottomed flask containing a magnetic stir-bar, glass stopcock, and nitrogen inlet was charged with (*S*)-citronellol (6.0 g, 38.9 mmol, 1.0 equiv) and 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 rt. The thick, white suspension was stirred at rt 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 **66** as a colorless oil.

Data for **66**:

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

7.79 (d, *J* = 8.3, 2 H, HC(2')), 7.34 (d, *J* = 8.3, 2 H, HC(3')), 5.02 (t, *J* = 7.3, 1 H, CH(6)), 4.02-4.10 (m, 2 H, CH_2(1)), 2.45 (s, 3 H, H_3C(5')), 1.83-1.98 (m, 2 H, H_2C(5)), 1.71-1.64 (m, 2 H, H_2C(3)), 1.67 (s, 3 H, H_3C(8a or 8b)), 1.57 (s, 3 H, H_3C (8a or 8b)), 1.56-1.49 (m, 1 H, HC(2a)), 1.39-1.46 (m, 1 H, HC(2b)), 1.21-1.27 (m, 1 H, HC(4a)), 1.06-1.13 (m, 1 H, CH(4b)), 0.82 (d, *J* = 6.6, 3 H, H_3C(9))

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

144.9 (C(4')), 133.5 (C(7)), 131.7 (C(1')), 130.0 (C(2')), 128.1 (C(3')), 124.6 (C(6)), 69.3 (C(1)), 36.9 (C(4)), 35.9 (C(2)), 29.1 (C(3)), 25.9 (C(8a or 8b)), 25.5 (C(5)), 21.9 (C(5')), 19.3 (C(9)), 17.9 (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)

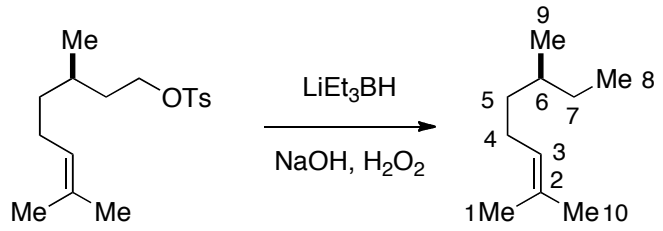
TLC: R_f0.30 (10:1 hexanes/EtOAc) [SiO_2, UV]

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

Calcd: 310.1603

Found: 310.1605

Preparation of (*S*)- 2,6-Dimethyl-2-octene (67)[44] [CSR-VII-88]



66 **67**

A 250-mL, two-necked, round-bottomed flask containing a magnetic stir-bar, septum, and argon inlet was charged with **66** (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 **67** as a colorless liquid.

Data for **67**:

bp: 76-80 °C at 30 mmHg

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

5.11 (tq, *J* = 7.3, 1.5, 1 H, HC(3)), 1.87-2.06 (m, 2 H, H_2C(4)), 1.69 (s, 3 H, H_3C(1 or 10)), 1.61 (s, 3 H, H_3C(1 or 10)), 1.28-1.38 (m, 3 H, H_2C(5), HC(6)), 1.08-1.18 (m, 2 H, H_2C(7)), 0.86 (t, *J* = 7.2, 3 H, H_3C(8)), 0.86 (d, *J* = 6.4, 3 H, H_3C(9))

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

131.0 (C(2)), 125.1 (C(3)), 36.7 (7)), 34.0 (4)), 29.4 (6)), 25.7 (5)), 25.6 (1 or 10)), 19.1 (9)), 17.6 (1 or 10)), 11.4 (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)

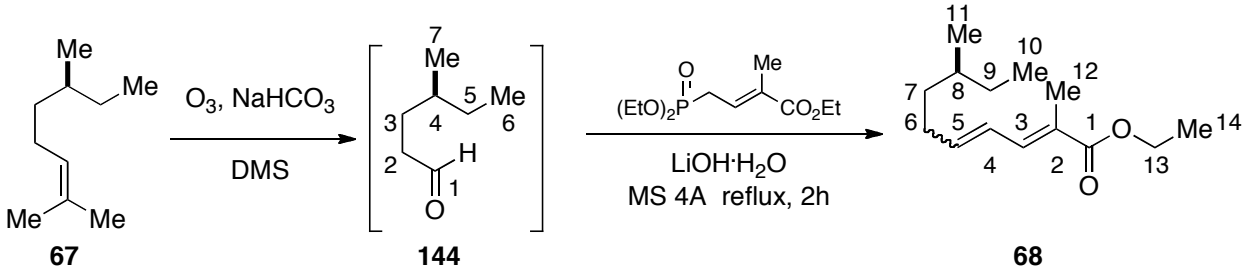
Opt. rot. : $[\alpha]_D^{24}$ 10.8 ($CHCl_3$, c = 2.00)

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 (68) [CSR-VIII-5]



67 **144** **68**

A 25-mL, single-necked, round-bottomed flask containing a stir-bar, Teflon thermometer adaptor and gas dispersion tube through the Teflon adaptor was charged with **67** (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 rt 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, single-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, single-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 **144** rinsing the flask with THF (0.5 mL). The contents were heated to reflux (oil bath temperature 75 ^{o}C) and stirred for 2.5 h. The contents became yellow and turbid as the reaction progressed. Upon cooling to rt 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*)-**68** and (*E*,*Z*)-**68** 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 **68** as a colorless oil.

Data for **144**:

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

9.77 (d, J = 1.7, 1 H, HC(1)), 2.48-2.36 (m, 2 H, H_2C(2)), 1.70-1.63 (m, 1 H, H_2C(3a or 3b)), 1.47-1.40 (m, 1 H, H_2C(3a or 3b)), 1.40-1.31(m, 2 H, H_2C(5a or 5b, 4)), 1.20-1.12 (m, 1 H, CH_2(5a or 5b)), 0.87 (t, J = 7.4, 3 H, H_3C(6)), 0.86 (d, J = 6.5, 3 H, CH_3(7))

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

203.3 (C(1)), 41.7 (C(2)), 34.0 (C(4)), 29.1 (C(5)), 28.5 (C(3)), 18.8 (C(7)),11.3 (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 **68**:

bp: 100 °C at $1x10^{-5}$ mmHg (ABT)

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

7.50 (dt, *J* = 11.9, 1.2, 1 H, HC(3), (*Z*-isomer)), 7.16 (d, *J* = 11.5, 1 H, HC(3), (*E*-isomer)), 6.34 (ddt, *J* = 14.4, 11.6, and 1.4, 1 H, HC(4), (*E*-isomer)), 6.27 (ddt, *J* = 11.6, 11.2, and 1.4, 1 H, HC(4), (*Z*-isomer)), 6.08 (dt, *J* = 14.4, 7.2, 2 H, H_2C(5), (*E*-isomer)), 5.83 (dt, *J* = 11.2, 7.2, 1 H, HC(5), (*Z*-isomer)), 4.22 (q, *J* = 7.2, 2 H, H_2C(13), (*Z*-isomer)), 4.20 (q, *J* = 7.2, 2 H, H_2C(13), (*E*-isomer)), 2.34-2.10 (m, 2 H, H_2C(6), (*Z* and *E*- isomer)), 1.93 (d, *J* = 0.8, 3 H, H_3C(12), (*Z*-isomer)), 1.92 (d, *J* = 0.8, 3 H, H_3C(12), (*E*-isomer)), 1.30 (t, *J* = 7.0, 3 H, H_3C(14), (*E*-isomer)), 1.49-1.10 (m, 5 H, H_2C(7,9) and HC(8), (*Z* and *E*-isomer)), 0.88 (d, *J* = 6.0, 3 H, HC(11), (*E*-isomer)), 0.87 (t, *J* = 8.0, 3 H, HC(10), (*E*-isomer))

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

168.7 (C(1), (*E*-isomer)), 143.4 (C(5), (*E*-isomer)), 140.2 (C(3), (*Z*-isomer)), 138.6 (C(3), (*E*-isomer)) ,132.8 (C(5), (*Z*-isomer)), 125.8 (C(4), (*E*-isomer)), 125.0 (C(2), (*E*-isomer)), 123.6 (C(4), (*Z*-isomer)), 60.5 (C(13), (*Z*-isomer)), 60.4 (C(13), (*E*-isomer)), 36.2 (C(7), (*Z*-isomer)), 35.7 (C(7), (*E*-isomer)), 33.9 (C(8), (*E*-isomer)), 30.9 (C(6), (*E*-isomer)), 29.3 (C(9), (*E*-isomer)), 19.0 (C(11), (*E*-isomer)), 14.3 (C(12), (*E*-isomer)), 12.5 (C(14), (*E*-isomer)), 11.3 (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)

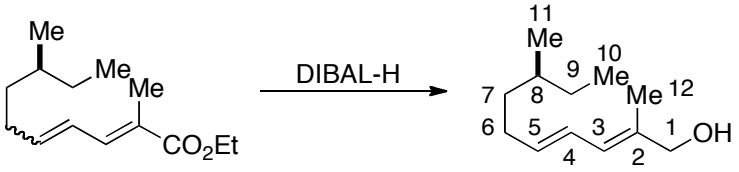
TLC: R_f0.39 (10:1 hexanes/EtOAc) [SiO_2, UV]

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*E*,4*E*)-2,8-Dimethyldecadienol (69)[35] [CSR-VIII-8]



68 **69**

A 100-mL, single-necked, recovery-flask containing a magnetic stir-bar and an argon inlet with a septum, was charged with ester **68** (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, 15.1 mmol, 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*)-**69**) and 0.013 g (11%, (*E*,*Z*)-**69**) as colorless oils.

Data for (*E*,*E*)-**69**:

bp: 95 °C (8.5×10^{-5} mmHg, ABT)

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

6.25 (ddt, *J* = 10.7, 15.1, and 1.5, 1 H, HC(4)), 6.02 (d, *J* = 11.0, 1 H, HC(3)), 5.70 (dt, *J* = 15.0, 7.1, 1 H, HC(5)), 4.01 (s, 2 H, $H_2C(1)$), 2.18-2.05 (nfoddd, *J* = 15, 9.0, and 7.3, 2 H, $H_2C(6)$), 1.78 (s, 3 H, $H_3C(12)$), 1.61(s, 1 H, br (OH), 1.29-1.45 (m, 3 H, CH(8), $CH_2(9)$), 1.11-1.24 (m, 2 H, $CH_2(7)$), 0.86 (t, *J* = 7.3, 3 H, $H_3C(10)$), 0.86 (d, *J* = 6.8, 3 H, $H_3C(11)$)

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

135.6 (C(5)), 134.6 (C(2)), 125.6 (C(4)), 125.4 (C(3)), 68.8 (C(1)), 36.2 (C(7)), 33.9 (C(8)), 30.5 (C(6)), 29.4 (C(9)), 19.0 (C(11)), 14.1 (C(12)), 11.3 (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*,*Z*)-**69**:

bp: 95 °C (8.5 x 10^{-5} mmHg, ABT)

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

6.33 (dt, *J* = 11.2, 1.5, 1 H, HC(3)), 6.02 (d, *J* = 11.0, 1.5, 1 H, HC(4)), 5.48 (dt, *J* = 10.7, 7.3, 1 H, HC(5)), 4.10 (d, *J* = 5.6, 2 H, H_2C(1)), 2.16-2.23 (m, 2 H, H_2C(6)), 1.79 (s, 3 H, H_3C(12)), 1.32-1.43 (m, 3 H, HC(8), H_2C(9)), 1.25 (s, 1 H, (br(OH)), 1.13-1.22 (m, 2 H, H_2C(7)), 0.87 (t, *J* = 7.3, 3 H, H_3C(10)), 0.87 (d, *J* = 6.1, 3 H, H_3C(11))

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

137.0 (C(2)), 133.2 (C(5)), 123.8 (C(4)), 120.4 (C(3)), 69.1 (C(1)), 36.7 (C(7)), 34.3 (C(8)), 29.6 (C(9)), 25.5 (C(6)), 19.3 (C(11)), 14.2 (C(12)), 11.6 (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)

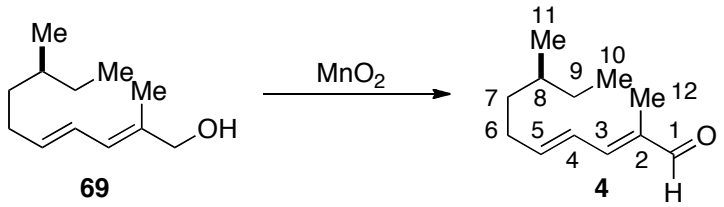
TLC: R_f0.18 (CH_2Cl_2) [SiO_2, UV]

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

Calcd: 182.1667

Found: 182.1671

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



69 **4**

A 100-mL, single-necked, recovery-flask containing a magnetic stir-bar, water condenser, and an argon inlet with a septum was charged with alcohol **69** (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 rt 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 that was purified by column chromatography ((SiO_2, 50 x 180 mm), hexane/EtOAc, 20:1) to afford 0.943 g (89%) of aldehyde **4** as a light-yellow oil.

Data for **4**:

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

9.41(s, 1 H, HC(1)), 6.83 (d, J = 11.2, 1 H, HC(3)), 6.52 (ddt, J = 15.0, 11.1, and 1.5, 1 H, HC(4)), 6.24 (dt, J = 15.0, 7.1, 1 H, HC(5)), 2.10-2.33 (m, 2 H, H_2C(6)), 1.83 (s, 3 H, H_3C(12)), 1.43-1.50 (m, 1 H, HC(9a or 9b)), 1.32-1.39 (m, 2 H, HC(9a or 9b), HC(8)), 1.24-1.30 (m, 1 H, HC(7a or 7b)), 1.13-1.21 (m, 1 H, HC(7a or 7b)), 0.89 (d, J = 6.4, 3 H, H_3C(11)), 0.88 (t, J = 7.3, 3 H, CH_3(10))

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

195.2 (C(1)), 149.5 (C(3)), 146.3 (C(5)), 135.8 (C(2)), 125.7 (C(4)), 35.5 (C(7)), 34.0 (C(8)), 31.1 (C(6)), 29.3 (C(9)), 19.0 (C(11)), 11.3 (C(10)), 9.4 (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)

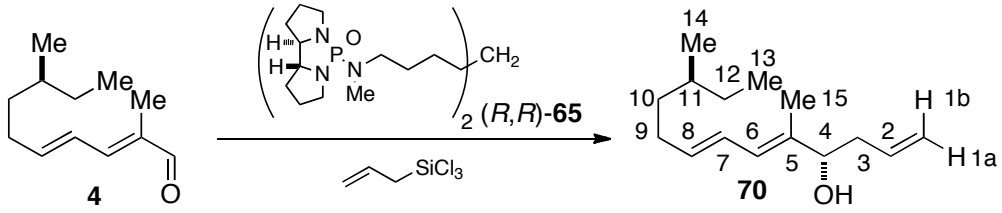
TLC: R_f 0.36 (10:1 hexanes/EtOAc) [SiO_2, UV]

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

Calcd: 180.1515

Found: 180.1514

Preparation of (4*S*,11*S*)(5*E*,7*E*)-4-Hydroxy-5,11-Dimethyltridecatriene (70) [CSR-VIII-43]



In a 5-mL Schlenk-flask were placed a magnetic stir-bar, phosphoramide (*R,R*)-**65** (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 ^oC 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 **4** (180 mg, 1.0 mmol, 1.0 equiv) drop-wise. The reaction mixture was stirred at –70 ^oC 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 rt. 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 rt. 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 **70** as a clear, colorless oil.

Data for **70**:

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

6.24 (ddt, *J* = 15.0, 10.9, and 1.5, 1 H, HC(7)), 6.02 (d, *J* = 10.9, 1 H, HC(6)), 5.78 (ddt, *J* = 17.1, 10.3, and 7.3, 1 H, HC(2)), 5.68 (dt, *J* = 16.8, 7.3, 1 H, HC(8)), 5.14 (dd, *J* = 10.3, 1.7, 1 H, HC(1a)), 5.10 (dq, *J* = 16.8, 1.5, 1 H, HC(1b)), 4.08 (t, *J* = 6.8, 1 H, HC(4)), 2.27-2.40 (m, 2 H, $H_2C(3)$), 2.02-2.20 (m, 2 H, $H_2C(9)$), 1.75 (s, 3 H, $H_3C(15)$), 1.62 (d, *J* = 6.8, 1 H, (br(OH)), 1.30-1.44 (m, 3 H, HC(11), $H_2C(12)$), 1.12-1.23 (m, 2 H, $H_2C(10)$), 0.86 (d, *J* = 6.8, 3 H, $H_3C(14)$), 0.86 (t, *J* = 7.1, 3 H, $H_3C(13)$)

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

136.3 (C(5)), 135.7 (C(8)), 134.7 (C(2)), 125.6 (C(7)), 125.5 (C(6)), 117.8 (C(1)), 76.2 (C(4)), 39.9 (C(3)), 36.1 (C(10)), 33.2 (C(11)), 30.5 (C(9)), 29.3 (C(12)), 19.0 (C(14)), 12.3 (C(15)), 11.3 (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)

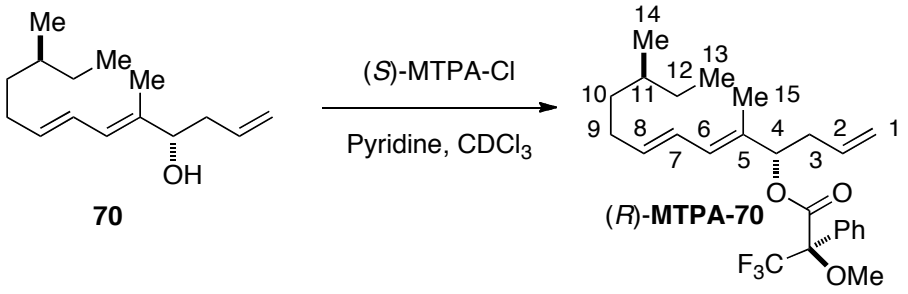
TLC: R_f 0.22 (hexanes/EtOAc, 10:1) [SiO_2, CAM]

SFC: (4*R*)-**70**: 3.22 min (4.1%), (4*S*)-**70**: 3.50 min (95.9%) (Chiralpak-AD, 3.0 mL/min, 3.0% MeOH, 150 bar),

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

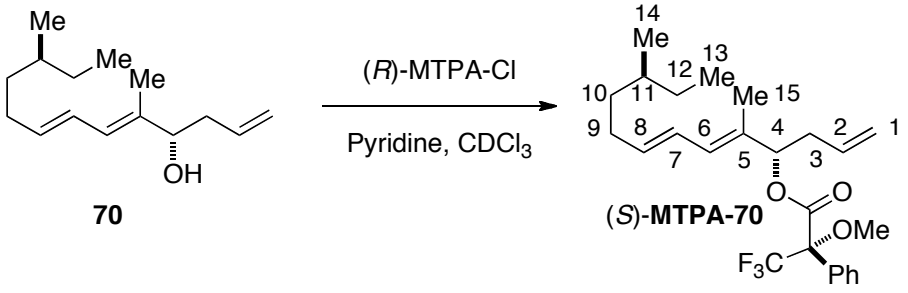
Calcd:	C, 81.02%,	H, 11.79%
Found:	C, 80.94%,	H, 11.81%

Determination of the C(4) Configuration of (4*S*,11*S*) (5*E*,7*E*)-4-Hydroxy-5,11-Dimethyltridecatriene (R-MTPA-70, 96) [CSR-VIII-29]



In a 5-mm NMR tube was placed a solution of allyl alcohol **70** (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-methoxy-α-trifluoromethylphenylacetyl chloride (8.4 μL, 0.045 mmol, 2.5 equiv). The reaction mixture was thoroughly mixed and stood for 2 h at rt. The crude Mosher ester (*R*)-**MTPA-70** was analyzed by ^{1}H-NMR (Table 6).

Determination of the C(4) Configuration of (4*S*,11*S*) (5*E*,7*E*)-4-Hydroxy-5,11-Dimethyltridecatriene (S-MTPA-70, 95) [CSR-VIII-30]

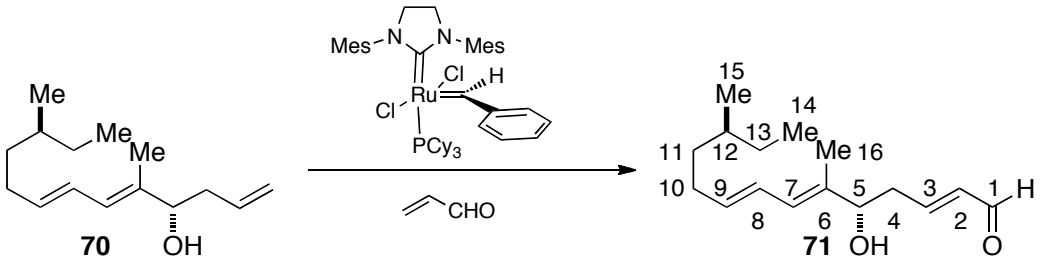


In a 5-mm NMR tube was placed a solution of allyl alcohol **70** (4.0 mg, 0.0180 mmol) in $CDCl_3$ (0.5 mL). To the solution was added sequentially pyridine (0.2 mL, 0.196 mmol, 11 equiv) and (*R*)-α-methoxy-α-trifluoromethylphenylacetyl chloride (8.4 μL, 0.045 mmol, 2.5 equiv). The reaction mixture was thoroughly mixed and was stood for 2 h at rt. The crude Mosher ester (*S*)-**MTPA-70** was analyzed by ^{1}H-NMR (Table 6).

Table 6: Mosher Ester Analysis. Assignment of C(4) Stereocenter of **70**

Assignment	δ-**70**	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*)(2*E*,6*E*,8*E*)-5-Hydroxy-6,12-Dimethyltetradecatrienal (71) [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 **70** (222.3 mg, 1.0 mmol, 1.0 equiv) along with CH_2Cl_2 (1 mL). The solution of **70** was transferred via cannula into the flask. Bubbling was observed and the contents were stirred at rt 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 **71** as a clear, yellow oil.

Data for **71**:

bp: 120 ºC (3.0×10^{-5} mmHg, ABT)

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

9.49 (d, *J* = 8.1, 1 H, HC(1)), 6.83 (dt, *J* = 15.6, 7.2, 1 H, HC(3)), 6.22 (dd, *J* = 15.0, 10.7, 1 H, HC(8)), 6.17 (dd, *J* = 15.6, 7.3, 1 H, HC(2)), 6.04 (d, *J* = 10.7, 1 H, HC(7)), 5.72 (dt, *J* = 15.0, 7.3, 1 H, HC(9)), 4.22 (t, *J* = 6.4, 1 H, HC(5)), 2.54-2.65 (m, 2 H, $H_2C(4)$), 2.05-2.20 (m, 2 H, $H_2C(10)$), 1.78 (s, 1 H, (br(OH)), 1.75 (s, 3 H, $H_3C(16)$), 1.29-1.43 (m, 3 H, HC(12), $H_2C(13)$), 1.11-1.23 (m, 2 H, $H_2C(11)$), 0.86 (d, *J* = 6.4, 3 H, $H_3C(15)$), 0.86 (t, *J* = 7.6, 3 H, $H_3C(14)$)

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

194.3 (C(1)), 155.0 (C(3)), 137.0 (C(9)), 135.7 (C(6)), 134.8 (C(2)), 126.7 (C(7)), 125.4 (C(8)), 76.2 (C(5)), 38.4 (C(4)), 36.3 (C(13)), 34.1 (C(12)), 30.8 (C(10)), 29.5 (C(11)), 19.2 (C(15)), 12.3 (C(16)), 11.5 (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)

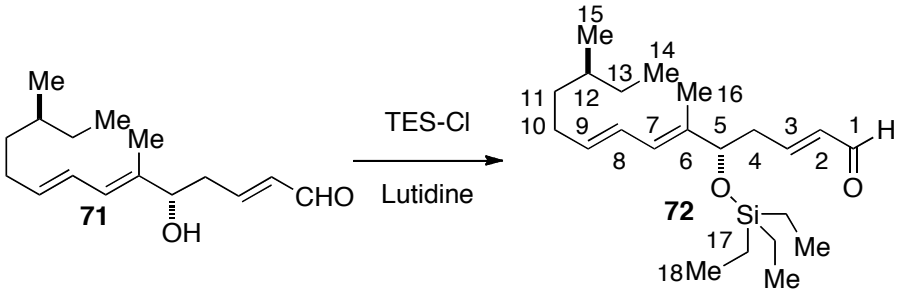
TLC: R_f 0.20 (hexanes/EtOAc, 10:1) [SiO_2, CAM]

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*)(2*E*,6*E*,8*E*)-6,12-Dimethyl-5-(triethylsilyloxy)tetradecatrienal (72) [CSR-VIII-68]



To a 35-mL, one-neck, round-bottomed flask equipped with an argon inlet with a septum, were placed aldehyde **71** (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 **72** as a clear, yellow oil.

Data for **72**:

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

9.48 (d, *J* = 7.8, 1 H, HC(1)), 6.80 (dt, *J* = 15.6, 8.1, 1 H, HC(3)), 6.20 (dd, *J* = 15.0, 10.7, 1 H, HC(8)), 6.13 (dd, *J* = 15.6, 8.0, 1 H, HC(2)), 5.96 (d, *J* = 10.8, 1 H, HC(7)), 5.67 (dt, *J* = 15.0, 7.3, 1 H, HC(9)), 4.16 (t, *J* = 5.4, 1 H, HC(5)), 2.46-2.61 (m, 2 H, H_2C(4)), 2.04-2.18 (m, 2 H, H_2C(10)), 1.71 (s, 3 H, H_3C(16)), 1.29-1.45 (m, 3 H, HC(12), H_2C(13)), 1.12-1.25 (m, 3 H, H_3C(11)), 0.93 (t, *J* = 8.0, 3 H H_3C(18)), 0.86 (d, *J* = 6.0, 3 H H_3C(15)), 0.86 (t, *J* = 7.3, 3 H, H_3C(14)), 0.57 (q, *J* = 8.0, 2 H, H_2C(17))

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

194.3 (C(1)), 155.8 (C(3)), 136.2 (C(6)), 136.0 (C(7)), 135.0 (C(9)), 126.1 (C(2)), 126.0 (C(8)), 76.9 (C(5)), 40.3 (C(4)), 36.4 (C(13)), 34.3 (C(12)), 30.8 (C(10)), 29.6 (C(11)), 19.3 (C(15)), 12.2 (C(16)), 11.6 (C(14)), 7.1 (C(18)), 5.0 (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)

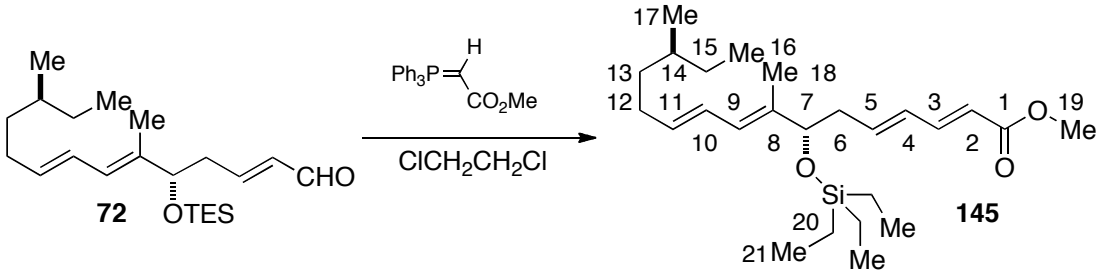
TLC: R_f 0.44 (hexanes/EtOAc, 10:1) [SiO_2, CAM]

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*)(2*E*,4*E*,8*E*,10*E*)-8,14-Dimethyl-7-(triethylsilyloxy)hexadecatetraenoate (145) [CSR-VIII-77]



To a 50-mL, single-necked, round-bottomed flask equipped with a magnetic stir-bar, argon inlet with a septum, and water condenser, were placed aldehyde **72** (365 mg, 1.00 mmol, 1.0 equiv), 1,2-dichloroethane (5 mL). To a 5-mL single-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 rt 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*)-**145** to

(*E,E,E,Z*)-**145** 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*)-**145** and 0.029 g (7%) of 2-(*Z*)-**145** as a clear, yellow oils.

Data for (*E,E,E,E*)-**145**:

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

7.25 (dd, *J* = 15.4, 10.7, 1 H, HC(3)), 6.20 (dd, *J* = 14.9, 10.7, 1 H, HC(10)), 6.18 (dd, *J* = 15.3, 11.0, 1 H, HC(4)), 6.06 (dt, *J* = 15.3, 7.6, 1 H, HC(5)), 5.91 (d, *J* = 15.4, 1 H, HC(9)), 5.79 (d, *J* = 15.4, 1 H, HC(2)), 5.65 (dt, *J* = 14.9, 7.0, 1 H, HC(11)), 4.05 (t, *J* = 5.9, 1 H, HC(7)), 3.76 (s, 3 H, H_3C(19)), 2.30-2.43 (m, 2 H, H_2C(6)), 2.20-2.02 (m, 2 H, H_2C(12)), 1.69 (s, 3 H, H_3C(18)), 1.45-1.30 (m, 3 H, HC(14), H_2C(15)), 1.25-1.12 (m, 2 H, H_2C(13)), 0.90 (t, *J* = 8.1, 9 H, H_3C(21)), 0.86 (d, *J* = 7.0, 3 H, H_3C(17)), 0.86 (t, *J* = 6.8, 3 H, H_3C(16)), 0.55 (q, *J* = 8.1, 6 H, H_2C(20))

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

168.0 (C(1)), 145.4 (C(3)), 141.5 (C(5)), 136.9 (C(8)), 135.5 (C(11)), 130.2 (C(4)), 125.8 (C(10)), 125.7 (C(9)), 119.3 (C(2)), 77.7 (C(7)), 51.7 (C(19)), 40.7 (C(6)), 36.5 (C(13)), 34.3 (C(14)), 30.8 (C(12)), 29.6 (C(15)), 19.3 (C(17)), 12.1 (C(18)), 11.6 (C(16)), 7.1 (C(21)), 4.8 (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, $CHCl_3$)

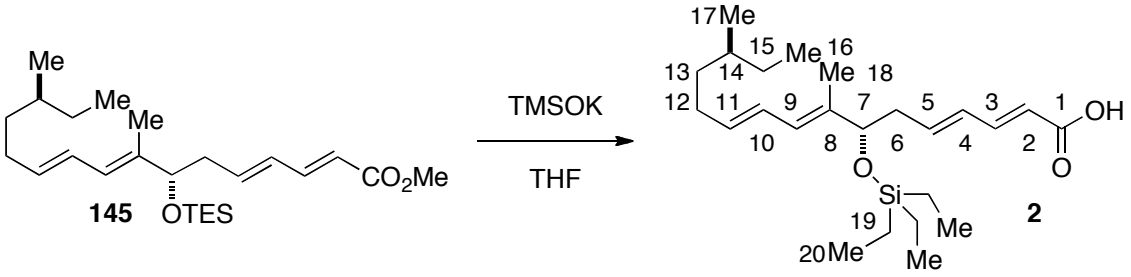
TLC: R_f 0.47 (hexanes/EtOAc, 10:1) [SiO_2, UV]

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



To a 25-mL, single-necked, round-bottomed flask equipped with a magnetic stir-bar, and an argon inlet with a septum were placed ester **145** (57.9 mg, 0.138 mmol, 1.0 equiv) and THF (1 mL). To a 5-mL, single-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 **145** 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 rt, 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, 1 H, HC(3)), 6.25-6.18 (m, 2 H, HC(10) and HC(4)), 6.12 (dt, *J* = 15.3, 7.5, 1 H, HC(5)), 5.92 (d, *J* = 10.5, 1 H, HC(9)), 5.78 (d, *J* = 15.8, 1 H, HC(2)), 5.66 (dt, *J* = 14.5, 7.2, 1 H, HC(11)), 4.06 (t, *J* = 6.4 Hz, 1 H, HC(7)), 2.46-2.30 (m, 2 H, HC(6)), 2.24-2.00 (m, 2 H, HC(12)), 1.88 (s, 3 H, HC(18)), 1.48-1.08 (m, 5 H, H_2C(13) and H_2C(15) and HC(14)), 0.92 (t, *J* = 7.9, 9 H, HC(20)), 0.86 (d, *J* = 6.8, 3 H, HC(17)), 0.86 (t, *J* = 7.2, 3 H, H_3C(16)), 0.55 (q, *J* = 7.9, 6 H, HC(19))

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

172.2 (C(1)), 147.3 (C(3)), 142.5 (C(5)), 136.6 (C(8)), 135.3 (C(11)), 129.9

(C(4)), 125.6 (C(10)), 125.6 (C(9)), 118.5 (C(2)), 77.4 (C(7)), 40.5 (C(6)), 36.2 (C(13)), 34.0 (C(14)), 30.6 (C(12)), 29.4 (C(15)), 19.1 (C(17)), 11.9 (C(18)), 11.3 (C(16)), 6.8 (C(19)), 4.8 (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]

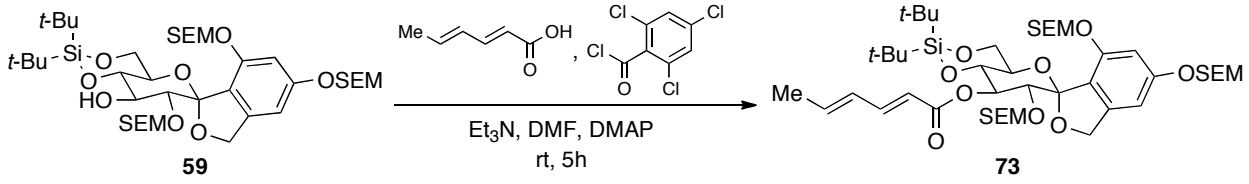
HRMS: $C_{24}H_{42}O_3SiNa$

Calcd: 429.2825

Found: 429.2821

Model Acylation of Arylglycoside 59

Preparation of 1,1-Anhydro-4,6-*O*-di*tert*-butylsilylene-2-*O*-(2-trimethylsilylethoxy-methyl)-1-(4,6-bis(2-trimethylsilylethoxymethoxy)-2-hydroxymethylphenyl)-3-*O*-(2,4-hexadienoyl)-α-D-glucopyranose (73) [TK-XI-80]



To a 25-mL, single-necked, round-bottomed flask equipped with a magnetic stir-bar and argon inlet was added 2,4-hexadienoic acid (5.0 mg, 0.0458 mmol, 2.0 equiv), followed by DMF (0.3 mL) and Et_3N (0.01 mL, 0.0687 mmol, 3.0 equiv). Then a solution of 2,4,6-trichlorobenzoyl chloride (11.1 mg, 0.0458 mmol, 2.0 equiv) in DMF (0.2 mL) was added and the contents were stirred at rt for 1 h. To this mixture was added a solution of **59** (19.0 mg, 0.0229 mmol, 1.0 equiv) in DMF (0.5 mL), followed by DMAP (5.6 mg, 0.0458 mmol, 2.0 equiv) and the contents were stirred at room temperature for 36 h. The reaction mixture was quenched with H_2O (30 mL) and extracted with EtOAc (3x30 mL). The combined organic extracts were washed with brine

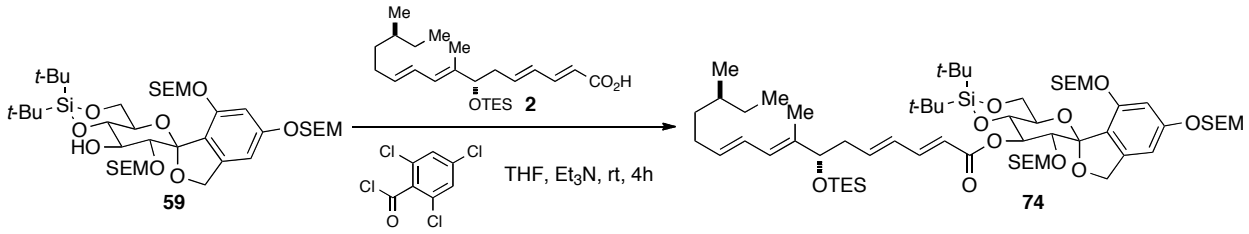
(1x30 mL) and dried with Na_2SO_4, filtered and concentrated to a brown oil (50.0 mg). The crude product was purified using column chromatography ((SiO_2, 70 g; hexanes/EtOAc, 10:1) to afford **73** (6.6 mg, 31%) and recovered **59** (9.6 mg, 51%) both as colorless oils.

Data for **73**:

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

7.32 (d, *J* = 14.3, 9.5, 1 H), 6.70 (d, *J* = 1.0, 1 H), 6.55 (d, *J* = 1.0, 1 H), 6.20 (dd, *J* = 14.3, 9.5, 1 H), 6.14 (dt, *J* = 14.3, 7.1, 1 H), 5.85 (d, *J* = 14.3, 1 H), 5.54 (t, *J* = 9.5, 1 H), 5.27 (d, *J* = 6.7, 1 H), 5.23 (d, *J* = 6.7, 1 H), 5.18 (d, *J* = 6.7, 1 H), 5.15 (d, *J* = 6.7, 1 H), 5.15 (d, *J* = 13.3, 1 H), 5.10 (d, *J* = 13.3, 1 H), 4.44 (d, *J* = 9.5, 1 H), 4.43 (d, *J* = 7.1, 1 H), 4.18 (d, *J* = 7.1, 1 H), 4.34-4.04 (m, 2 H), 3.92 (t, *J* = 4.8, 1 H), 3.85-3.66 (m, 5 H), 1.85 (d, *J* = 5.8, 3 H), 1.01 (s, 9 H), 0.99 (s, 9 H), 1.05-0.92 (m, 4 H), 0.72-0.55 (m, 2 H), 0.20 (s, 9 H), 0.00 (s, 9 H), –0.13 (s, 9 H)

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-triethylsiloxy-2,4,8,10-hexadecatetraenoyl)-2-*O*-(2-trimethylsilyl-ethoxycarbonyl)-1-(4,6-dihydroxy-2-hydroxymethylphenyl)-α-D-glucopyranose (74) [TK-XII-97]



To a 25-mL, two-necked, round-bottomed flask equipped with a magnetic stir-bar, argon inlet and septum, acid **2** (10.0 mg, 0.0253 mmol, 4.2 equiv) was added. The contents were flushed with argon. Then a solution of Et_3N (5.1 mg, 0.0506 mmol, 2.0 equiv) in THF (0.1 mL), followed by a solution of 2,4,6-trichlorobenzoyl chloride (6.8 mg, 0.0278 mmol, 1.1 equiv) in THF (0.1 mL) and the contents were stirred at rt for 1 h. After 1 h the reaction was still not complete, therefore, a solution of Et_3N (5.1 mg, 0.0506 mmol, 2.0 equiv) in THF (0.1 mL) and a solution of 2,4,6-trichlorobenzoyl chloride (6.8 mg, 0.0278 mmol, 1.1 equiv) in THF (0.1 mL) were added and the contents were stirred at rt for 2 h. After this amount of time a solution of **59**

(5.0 mg, 0.0060 mmol, 1.0 equiv) in THF (0.5 mL) was added and the contents were stirred at rt for 4 h. Then the contents were quenched with H_2O (30 mL). The organic layer was extracted and the aqueous layer was extracted with EtOAc (3x30 mL). The combined organic layers were washed with brine (1x30 mL), dried with Na_2SO_4, filtered and concentrated to a yellow film. The crude product was purified by column chromatography (SiO_2, 40 g; hexanes/EtOAc, 7:1), then 2x ((SiO_2, 40 g), hexanes/THF, 10:1) to afford **74** (6.4 mg, 88%) as a yellow oil.

Data for **74**:

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

7.31 (dd, *J* = 15.0, 10.0, 1 H), 6.71 (d, *J* = 1.0, 1 H), 6.56 (d, *J* = 1.0, 1 H), 6.20 (dd, *J* = 15.0, 10.0 Hz, 1 H), 6.19 (dd, *J* = 15.0, 10.0, 1 H), 6.06 (dt, *J* = 15.0, 7.5, 1 H), 5.92 (d, *J* = 10.0, 1 H), 5.87 (d, *J* = 15.0, 1 H), 5.65 (dt, *J* = 15.0, 7.5, 1 H), 5.54 (t, *J* = 10.0, 1 H), 5.28 (d, *J* = 6.0, 1 H), 5.23 (d, *J* = 6.0, 1 H), 5.18 (d, *J* = 10.0, 1 H), 5.15 (d, *J* = 14.0, 1 H), 5.14 (d, *J* = 6.0, 1 H), 5.11 (d, *J* = 14.0, 1 H), 4.45 (d, *J* = 10.0, 1 H), 4.44 (d, *J* = 6.5, 1 H), 4.40 (d, *J* = 6.5, 1 H), 4.17-4.06 (m, 2 H), 4.04 (dd, *J* = 7.5, 5.5, 1 H), 3.92 (t, *J* = 10.0, 1 H), 3.86-3.60 (m, 5 H), 3.21 (ddd, *J* = 11.5, 10.0, 5.0, 1 H), 3.00 (ddd, *J* = 11.5, 10.0, 5.0, 1 H), 2.42-2.23 (m, 2 H), 2.20-2.00 (m, 2 H), 1.70 (s, 3 H), 1.48-1.10 (m, 5 H), 1.06-0.82 (m, 4 H), 1.01 (s, 9 H), 0.99 (s, 9 H), 0.91 (t, *J* = 7.5, 9 H), 0.87 (d, *J* = 6.0, 3 H), 0.87 (t, *J* = 6.0, 3 H), 0.67 (ddd, *J* = 13.5, 11.5, 5.0, 1 H), 0.59 (ddd, *J* = 13.5, 11.5, 5.0, 1 H), 0.54 (q, *J* = 7.5, 6 H), 0.02 (s, 9 H), 0.00 (s, 9 H), –0.13 (s, 9 H)

MS: (ESI)

1220 (M^+, 95), 1219 (100), 1069 (15), 1003 (10)

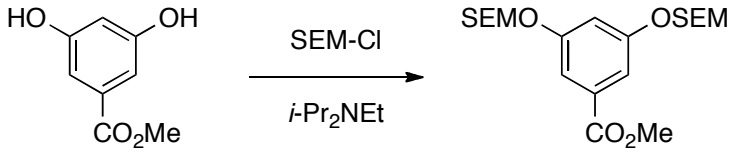
HRMS: $C_{63}H_{114}O_{13}Si_5$ (1220.00)

Calcd: 1219.7184

Found: 1219.7184

Model Protection and Deprotection Studies

Preparation of Methyl 3,5-bis(2-trimethylsilylethoxy)benzoate (119) [TK-XIII-65]



98 **119**

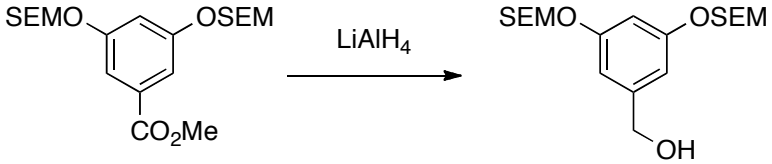
To a 25-mL, single-necked, round-bottomed flask equipped with a magnetic stir-bar and an argon inlet was added **98** (168.2 mg, 1.00 mmol, 1.0 equiv) followed by THF (1.0 mL). Then *i*-Pr_2Net (0.52 mL, 3.0 mmol, 3.0 equiv) and the solution was cooled to 0 ^oC. Once at this temperature, 2-(trimethylsilylethoxy) chloride (SEM-Cl) (366.8 mg, 2.20 mmol, 2.2 equiv) was added and the contents were slowly warmed to rt. After stirring for 4 h at rt the reaction was still not complete, therefore, a second portion of *i*-Pr_2NEt (0.52 mL, 3.0 mmol, 3.0 equiv) and SEM-Cl (366.8 mg, 2.20 mmol, 2.2 equiv) was added at rt. The contents were allowed to stir for 1 h at rt. The reaction was finally quenched with H_2O (30 mL) and extracted with CH_2Cl_2 (3x30 mL). The combined organic extracts were washed with brine (30 mL), dried with Na_2SO_4, filtered and concentrated using rotary evaporation. The crude material was purified using column chromatography ((SiO_2, 40 g, hexanes/EtOAc, 7:1) to afford **119** (419 mg, 98%) as a colorless oil.

Data for **119**:

^{1}H NMR: (400 MHz, $CDCl_3$)

7.36 (d, J = 2.3, 2 H), 6.92 (t, J = 2.3, 1 H), 5.23 (s, 4 H), 3.90 (s, 3 H), 3.75 (t, J = 8.1, 4 H), 0.95 (t, J = 8.1, 4 H), 0.00 (s, 18H)

Preparation of 1-Hydroxymethyl-3,5-bis(2-trimethylsilethoxymethoxy) benzoate (120) [TK-XIII-66]



119 **120**

To a 100-mL, single-necked, round-bottomed flask equipped with a magnetic stir-bar and argon inlet **119** (410.0 mg, 0.956 mmol, 1.0 equiv) was added, followed by THF (2 mL). the

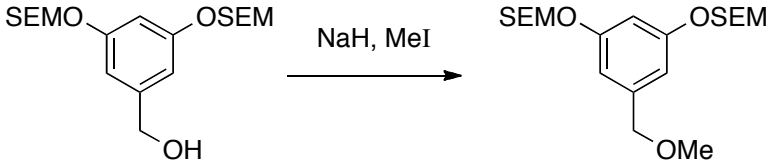
contents were cooled to 0 °C using an ice bath and $LiAlH_4$ (72.6 mg, 1.912 mmol, 2.0 equiv) was added in one portion. The mixture was then slowly warmed to rt. After stirring at rt for 30 min the contents were once again cooled to 0 °C and Celite (3 g) was added. The reaction was carefully quenched with H_2O (0.5 mL) or until a colorless suspension is observed. Then the mixture was stirred for an additional 30 min at 0 °C to break up the solids formed during the quench. The suspension was filtered through Celite (1 g) washing with Et_2O (10 mL). The filtrated was concentrated and the resulting colorless oil was subjected to column chromatography (SiO_2, 40 g; hexanes/EtOAc, 7:1) to afford **120** (350 mg, 91%) as a colorless oil.

Data for **120**:

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

6.77-6.63 (m, 3 H), 5.20 (s, 2 H), 4.64 (br s, 1 H), 3.75 (t, *J* = 8.0, 4 H), 0.97 (t, *J* = 8.0, 4 H), 0.00 (s, 18H)

Preparation of 1-Methoxymethyl-3,5-bis(2-trimethylsilylethoxymethoxy)benzene (121) [TK-XII-67]



120 **121**

To a 100-mL, two-necked, round-bottomed flask equipped with a magnetic stir-bar, argon inlet and septum a suspension of NaH (68.8 mg, 1.72 mmol, 2.0 equiv, 60% suspension in mineral oil) was added. Then THF (1.0 mL) was added and the contents were cooled to 0 °C. Once at 0 °C, a solution of **120** (345.0 mg, 0.861 mmol, 1.0 equiv) in THF (1.0 mL) was added drop-wise. After the addition the contents were warmed to rt and stirred for 30 min at this temperature. Then a solution of MeI (365.2 mg, 2.853 mmol, 3.0 equiv) in THF (0.5 mL) was added. The reaction contents were stirred for an additional 1 h at rt and were cooled to 0 °C. The contents were quenched at this temperature with H_2O (30 mL) and the aqueous layer was extracted with EtOAc (3x30 mL). The combined organic layers were washed with brine (30 mL), dried with Na_2SO_4, filtered and concentrated. The crude material was purified using column chromatography ((SiO_2, 40 g), hexanes/EtOAc, 7:1) to give **121** (346 mg, 97%) as a colorless oil.

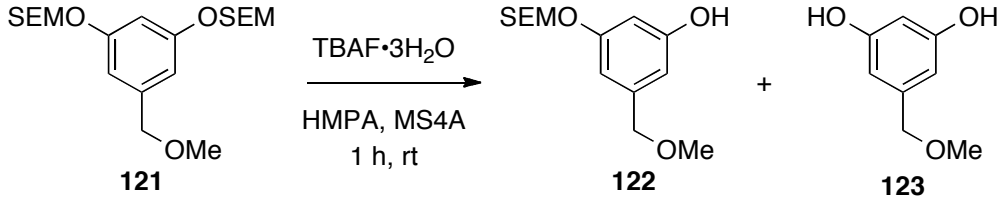
Data for **121**:

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

6.70-6.63 (m, 3 H), 5.20 (s, 4 H), 4.39 (s, 2 H), 3.74 (t, J = 8.0, 4 H), 3.38 (s, 3 H), 0.96 (t, J = 8.0, 4 H), 0.00 (s, 18H)

Model Deprotection of SEM Ethers, Table S4, SI.

Preparation of 3,5-Dihydroxy-1-methoxymethylbenzene (123) (Table S4, SI, entry 1) [TK-XIII-16]



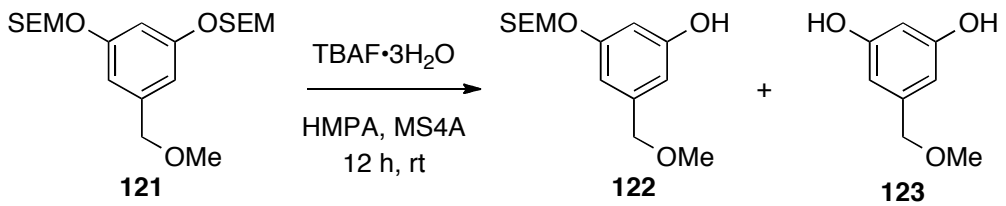
To a 25-mL, single-necked, round-bottomed flask equipped with a magnetic stir-bar and an argon inlet, **121** (40.4 mg, 0.0974 mmol, 1.0 equiv) was added. Next, molecular sieves 4Å (100 mg) were added. Then a solution of TBAF•$3H_2O$ (307.3 mg, 0.974 mmol, 10 equiv) in HMPA (0.35 mL) was added and the contents were stirred at rt for 1 h. The suspension was filtered and diluted with H_2O (30 mL) and the aqueous layer was extracted with EtOAc (3x30 mL). The combined organic extracts were washed with brine (30 mL), dried with Na_2SO_4, filtered and concentrated. The residue was purified by column chromatography (SiO_2, 40 g; hexanes/EtOAc, 10:1) to give mono-SEM ether **122** (20.0 mg, 72%) as a colorless oil.

Data for **122**:

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

6.58 (t, J = 2.5, 1 H), 6.48 (d, J = 2.5, 2 H), 5.19 (s, 2 H), 5.05 (br s, 1 H), 4.38 (s, 2 H), 3.74 (t, J = 8.0, 2 H), 3.39 (s, 3 H), 0.97 (t, J = 8.0, 2 H), 0.00 (s, 9 H)

(Table S4, SI, entry 2) [TK-XIII-17]



To a 25-mL, single-necked, round-bottomed flask equipped with a magnetic stir-bar and

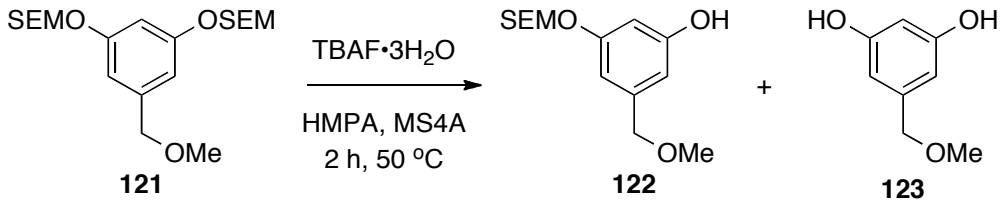
an argon inlet, **121** (20.0 mg, 0.0703 mmol, 1.0 equiv) was added. Next, molecular sieves 4Å (70 mg) were added. Then a solution of TBAF•3H_2O (221.8 mg, 0.703 mmol, 10 equiv) in HMPA (0.35 mL) was added and the contents were stirred at rt for 12 h. The suspension was filtered and diluted with 2N HCl (30 mL) and the aqueous layer was extracted with EtOAc (3x30 mL). The combined organic extracts were washed with brine (30 mL), dried with Na_2SO_4, filtered and concentrated. The residue was purified by column chromatography (SiO_2, 40 g; hexanes/EtOAc, 3:1-1:1) to give mono-SEM ether **122** (2.3 mg, 12%) and **123** (2.3 mg, 21%) both as a colorless oils.

Data for **123**:

^{1}H NMR: (400 MHz, $CDCl_3$)

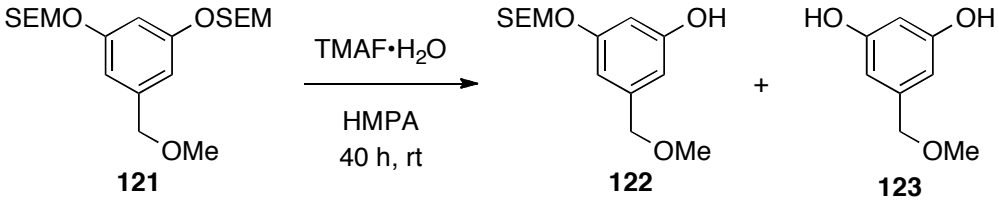
6.40 (d, J = 2.5, 2 H), 6.27 (t, J = 2.5, 1 H), 4.82 (br s, 2 H), 4.36 (s, 2 H), 3.38 (s, 3 H)

(Table S4, SI, entry 3) [TK-XIII-20]



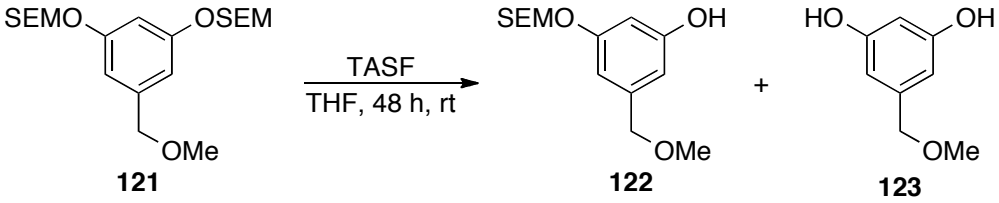
To a 25-mL, single-necked, round-bottomed flask equipped with a magnetic stir-bar and an argon inlet, **121** (33.3 mg, 0.0803 mmol, 1.0 equiv) was added. Next, molecular sieves 4Å (80 mg) were added. Then a solution of TBAF•3H_2O (253.4 mg, 0.803 mmol, 10 equiv) in HMPA (0.40 mL) was added and the contents were added to a preheated 50 ^oC oil bath and stirred at this temperature for 2 h. The suspension was filtered and diluted with 2N HCl (30 mL) and the aqueous layer was extracted with EtOAc (3x30 mL). The combined organic extracts were washed with brine (30 mL), dried with Na_2SO_4, filtered and concentrated. ^{1}H-NMR analysis identified decomposition of starting material.

(Table S4, SI, entry 4) [TK-XIII-18]



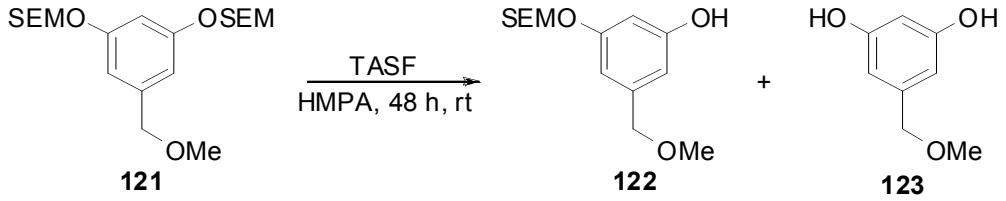
To a 25-mL, single-necked, round-bottomed flask equipped with a magnetic stir-bar and an argon inlet, TMAF (67.3 mg, 0.723 mmol, 10 equiv) was added, followed by HMPA (0.2 mL). Then, H_2O (26μL, 0.723 mmol, 10 equiv) and a solution of **121** (30.0 mg, 0.0723 mmol, 1.0 equiv) in HMPA (0.15 mL) were added. The contents were stirred at rt for 40 h. The suspension was directly subjected to column chromatography ((SiO_2, 40 g), hexanes/EtOAc, 7:1, 3:1, 1:1) to afford **122** (3.1 mg, 15%) and recovered **123** (22.8 mg, 76%) both as colorless oils.

(Table S4, SI, entry 5) [TK-XIII-47]



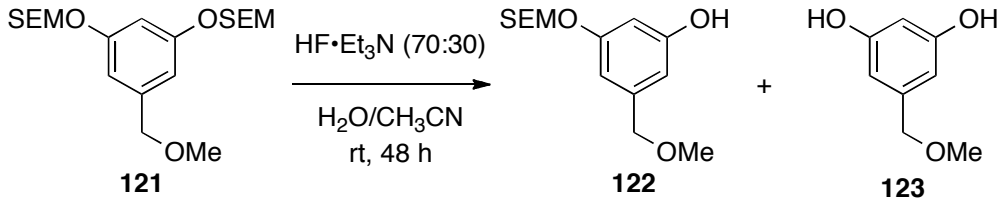
To a 25-mL, single-necked, round-bottomed flask equipped with a magnetic stir-bar and an argon inlet, **121** (5.0 mg, 0.012 mmol, 1.0 equiv) was added, followed by THF (0.3 mL). Then TASF (49.6 mg, 0.18 mmol, 15 equiv) was added and the contents were stirred at rt for 48 h. The suspension was quenched with H_2O (30 mL) and the aqueous layer was extracted with EtOAc (3x30 mL). The organic layers were combined and washed with brine (1x30 mL), dried with Na_2SO_4, filtered and concentrated. The residue was purified by column chromatography ((SiO_2, 5 g), hexanes/EtOAc, 7:1, 1:1) to afford a mixture of **122** and **123** (4.7 mg, 100%, 62:38 mixture) as a colorless oil.

(Table S4, SI, entry 6) [TK-XIII-55]



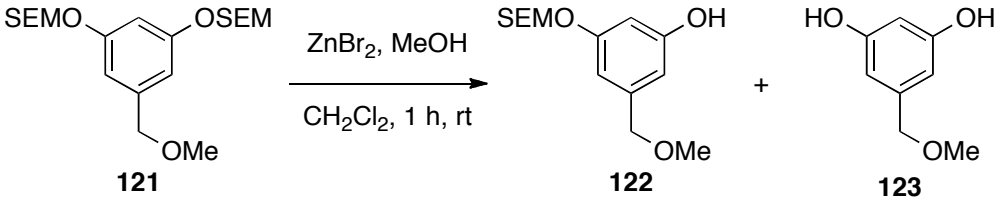
To a 25-mL, single-necked, round-bottomed flask equipped with a magnetic stir-bar and an argon inlet, **121** (5.0 mg, 0.012 mmol, 1.0 equiv) was added, followed by HMPA (0.3 mL). Then TASF (49.6 mg, 0.18 mmol, 15 equiv) was added and the contents were stirred at rt for 48 h. The suspension was quenched with H_2O (30 mL) and the aqueous layer was extracted with EtOAc (3x30 mL). The organic layers were combined and washed with brine (1x30 mL), dried with Na_2SO_4, filtered and concentrated. The residue was purified by column chromatography (SiO_2, 5 g; hexanes/EtOAc, 7:1, 3:1, 1:1) to afford **122** (2.3 mg, 68%) and **123** (0.6 mg, 32%) both as colorless oils.

(Table S4, SI, entry 7) [TK-XIII-68]



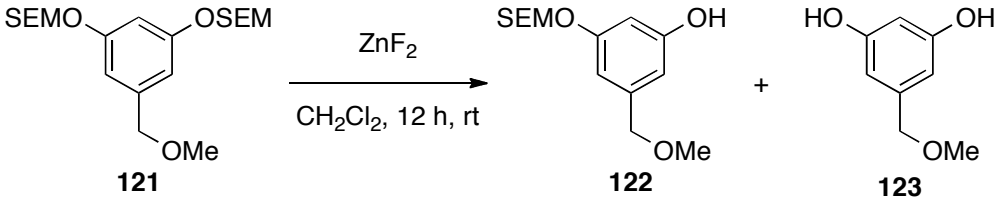
To a 20-mL Teflon vial, equipped with a magnetic stir-bar and an argon inlet, **121** (5.0 mg, 0.012 mmol, 1.0 equiv) was added, followed by CH_3CN (0.2 mL). To a separate 15-mL plastic screw-caped vial, equipped with a magnetic stir-bar was added 49% HF (2.5 mL, 72.21 mmol), Et_3N (4.7 mL, 30.95 mmol) and CH_3CN (10 mL). Note: This solution provided a 70:30 mixture of HF•Et_3N (4.20 M). To the solution of **121** in CH_3CN was added HF•Et_3N (0.1 mL, 0.420 mmol, 35 equiv, 70:30 mixture) and the contents were stirred at rt for 48 h. After this amount of time, only **121** was observed by either TLC or ^{1}H-NMR analysis of the crude reaction mixture.

(Table S4, SI, entry 8) [TK-XIII-48]



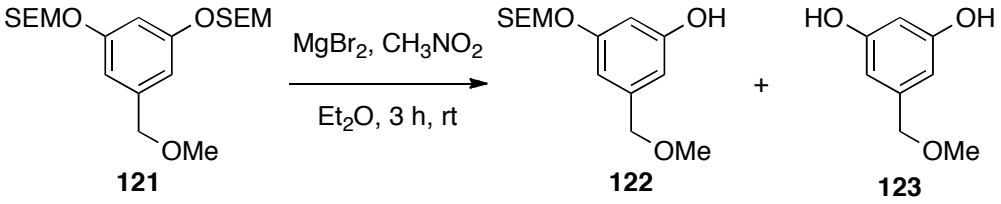
To a 25-mL, single-necked, round-bottomed flask equipped with a magnetic stir-bar and an argon inlet, **121** (5.0 mg, 0.012 mmol, 1.0 equiv) was added, followed by CH_2Cl_2 (0.3 mL). Then $ZnBr_2$ (61.2 mg, 0.25 mmol, 20 equiv) was added, followed by MeOH (0.02 mL, 0.48 mmol, 40 equiv) and the contents were stirred at rt for 1 h. The suspension was quenched with H_2O (30 mL) and the aqueous layer was extracted with EtOAc (3x30 mL). The organic layers were combined and washed with brine (1x30 mL), dried with Na_2SO_4, filtered and concentrated. Analysis of the crude material by TLC and ^{1}H-NMR suggested that **121** had decomposed under these deprotection conditions.

(Table S4, SI, entry 9) [TK-XIII-48]



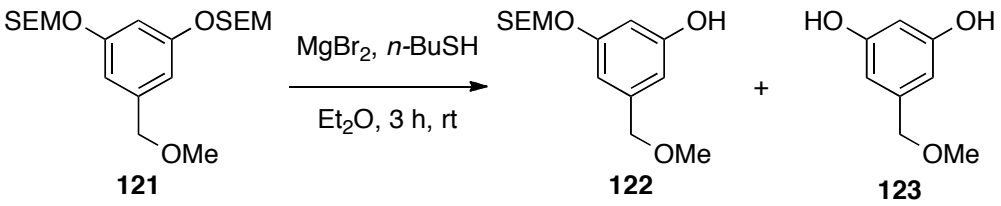
To a 10-mL, single-necked, round-bottomed flask equipped with a magnetic stir-bar and an argon inlet, **121** (5.0 mg, 0.012 mmol, 1.0 equiv) was added, followed by CH_2Cl_2 (0.3 mL). Then ZnF_2 (24.8 mg, 0.24 mmol, 20 equiv) was added and the contents were stirred at rt for 12 h. The suspension was quenched with H_2O (30 mL) and the aqueous layer was extracted with EtOAc (3x30 mL). The organic layers were combined and washed with brine (1x30 mL), dried with Na_2SO_4, filtered and concentrated. Analysis of the crude material by TLC and ^{1}H-NMR suggested that **121** had decomposed under these deprotection conditions.

(Table S4, SI, entry 10) [TK-XIII-19]



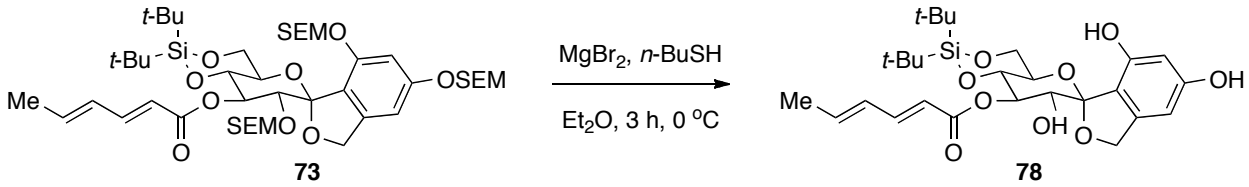
To a 25-mL, single-necked, round-bottomed flask equipped with a magnetic stir-bar and an argon inlet, $MgBr_2$ (226.3 mg, 1.45 mmol, 20 equiv) was added. Then Et_2O (1.0 mL) and CH_3NO_2 (157 μL, 2.89 mmol, 40 equiv) were added. Finally, **121** (30.0 mg, 0.072 mmol, 1.0 equiv) was added as a solution in Et_2O (1.0 mL) and the contents were stirred at rt for 3 h. The suspension was quenched with H_2O (30 mL) and the aqueous layer was extracted with EtOAc (3x30 mL). The organic layers were combined and washed with brine (1x30 mL), dried with Na_2SO_4, filtered and concentrated. Analysis of the crude material by TLC and ^{1}H-NMR suggested that **121** had decomposed under these deprotection conditions.

(Table S4, SI, entry 11) [TK-XIII-26]



To a 25-mL, single-necked, round-bottomed flask equipped with a magnetic stir-bar and an argon inlet, **121** (11.3 mg, 0.027 mmol, 1.0 equiv) was added, followed by Et_2O (0.5 mL). Then *n*-BuSH (0.06 mL, 0.544 mmol, 20 equiv) and $MgBr_2$ (100.2 mg, 0.544 mmol, 20 equiv) were added. The contents were stirred at rt for 1 h and the resultant suspension was directly subjected to column chromatography (SiO_2, 40 g; hexanes/EtOAc, 1:1) providing **123** (4.2 mg, 100%) as a colorless oil.

Preparation of 4,6-*O*-di-*tert*-Butylsilylene-3-*O*-hexadienoyl-1-(4,6-dihydroxy-1-hydroxy-1-hydroxy-methylphenyl)gluconopyranose (78) [TK-XIII-31]



73 **78**

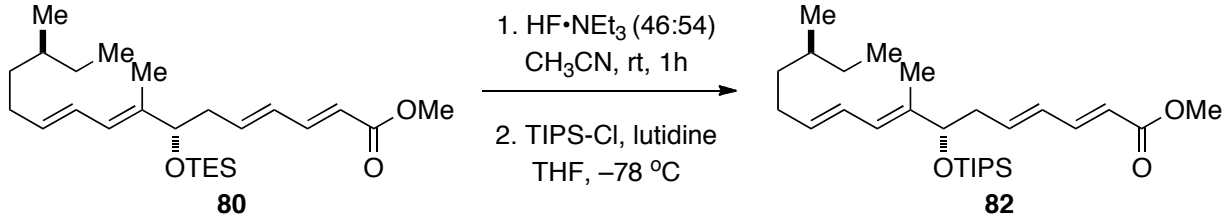
To a 10-mL, single-necked, round-bottomed flask equipped with a magnetic stir-bar and an argon inlet was added $MgBr_2$ (22.6 mg, 0.123 mmol, 60 equiv), followed by Et_2O (0.5 mL). To this suspension was added *n*-BuSH (0.01 mL, 0.123 mmol, 60 equiv) and CH_3NO_2 (0.01 mL, 0.123 mmol, 60 equiv). The contents were cooled to 0 °C using an ice bath. Once at this temperature a solution of **73** (1.9 mg, 0.0021 mmol, 1.0 equiv) in Et_2O (0.5 mL) was added and stirred at 0 °C for 30 min. Then the contents were allowed to warm to rt and stirred at this temperature for 2.5 h. The contents were cooled back to 0 °C and quenched with H_2O (30 mL) and the aqueous was extracted with EtOAc (3x30 mL). The combined organic layers were washed with brine (30 mL) and dried with Na_2SO_4, filtered and concentrated. The crude material was purified by column chromatography ((SiO_2, 40 g, hexanes/EtOAc, 1:1) to afford **78** (1.1 mg, 100%) as a yellow oil.

Data for **78**:

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

7.33 (dd, *J* = 15.4, 9.7, 1 H), 6.22 (s, 1 H), 6.28-6.11 (m, 2 H), 6.60 (s, 1 H), 5.78 (d, *J* = 15.4, 1 H), 5.67 (br s, 1 H), 5.31 (t, *J* = 9.9, 1 H), 5.24 (br s, 1 H), 5.15 (d, *J* = 13.2, 1 H), 5.05 (d, *J* = 13.2, 1 H), 4.33 (t, *J* = 9.9, 1 H), 4.19-4.05 (m, 2 H), 4.01 (t, *J* = 9.9, 1 H), 3.90 (t, *J* = 9.9, 1 H), 1.87 (d, *J* = 6.6, 3 H), 1.04 (s, 9 H), 1.00 (s, 9 H)

Preparation of (7*S*,14*S*)-(2*E*,4*E*,8*E*,10*E*)-8,14-Dimethyl-7-hydroxy-2,4,8,10-hexadecatetraenoate (80) [TK-XIII-61] and (7*S*,14*S*)-(2*E*,4*E*,8*E*,10*E*)-8,14-Dimethyl-7-triisopropylsiloxy-2,4,8,10-hexadecatetraenoate (82) [TK-XIII-62]



To a 10-mL polyethylene test tube, equipped with a magnetic stir-bar and argon inlet, **80** (2.1 mg, 0.0049 mmol, 1.0 equiv) was added. Then, HF•NEt_3 (0.1 mL, 0.143 mmol, 29 equiv, HF•NEt_3 = 46:54, 1.434 M in H_2O/CH_3CN) was added and the contents were stirred at rt for 1 H.

Note: the HF•NEt_3 solution was prepared as follows: HF (2.5 mL, 2.95 g, 72.21 mmol, 49%), NEt_3 (12.6 mL, 30.95 mmol), and CH_3CN (10 mL) were added to a polyethylene bottle with a stir-bar. After stirring for 10 min (0.5 mL, 1.506 mmol) of the above solution was added to another polyethylene bottle containing CH_3CN (0.5 mL) to give HF•NEt_3 (46:54, 1.434 M).

After 1 H, the contents were diluted with H_2O (20 mL) and the organic layer was extracted with EtOAc (3x30 mL). The combined organic layers were dried with Na_2SO_4, filtered, and concentrated. The crude material was purified by column chromatography ((SiO_2, 5 g), hexanes/EtOAc, 1:1) to give **82** (1.5 mg, 100%) as a colorless oil. This material was directly added to another 10-mL polyethylene test tube, equipped with a magnetic stir-bar and argon inlet, **82** (1.5 mg, 0.00489 mmol, 1.0 equiv) was added, followed by 2,6-lutidine (10.5 mg, 0.0978 mmol, 20 equiv). Then the contents were cooled to –78 ^oC and a solution of TIPS-Cl (15.0 mg, 0.0489 mmol, 10 equiv) in THF (0.2 mL) was added and the contents were added to a 0 ^oC ice-bath. After stirring at 0 ^oC for 2 H, the contents were contents were quenched with H_2O (20 mL). The aqueous layer was extracted with EtOAc (3x30 mL) and the combined organic extracted were washed with brine (20 mL). The organic layer was then dried using Na_2SO_4, filtered and concentrated to a light-yellow oil. The crude contents were purified using column chromatography ((SiO_2, 5 g), hexanes/EtOAc, 10:1) to afford **82** (2.2 mg, 100%) as a colorless oil.

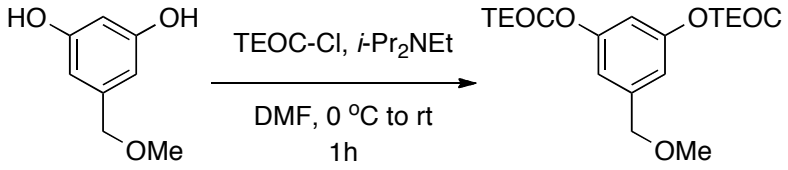
Data for **82**:

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

7.24 (dd, *J* = 15.0, 11.0, 1 H), 6.22-6.12 (m, 2 H), 6.04 (dt, *J* = 15.0, 7.5, 1 H),

5.90
(d, *J* = 15.0, 1 H), 5.78 (d, *J* = 15.0, 1 H), 5.67-5.60 (m, 1 H), 4.19 (t, *J* = 7.0, 1 H), 3.73 (s, 3 H), 2.43 (t, *J* = 7.0, 2 H), 2.20-2.00 (m, 2 H), 1.48-0.80 (m, 32H)

Preparation of 3,5-Bis(2-trimethylsilylethoxycarbonyloxy)-1-methoxymethylbenzene (124) [TK-XIV-12]



123 **124**

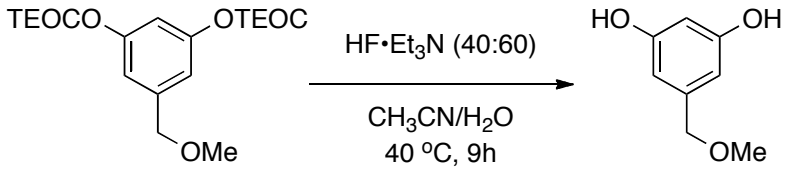
To a 10-mL, single-necked, round-bottomed flask equipped with a magnetic stir-bar and an argon inlet was added **123** (17.7 mg, 0.115 mmol, 1.0 equiv), DMF (0.3 mL) and *i*-Pr_2NEt (0.09 mL, 0.69 mmol, 6.0 equiv). The contents were then cooled 0 °C and TEOC-Cl (62.3 mg, 0.345 mmol, 3.0 equiv) was added and the contents were allowed to warm to rt and stirred at this temperature for 1 H. Then the contents were quenched with H_2O (30 mL) and the aqueous was extracted with EtOAc (3x30 mL). The combined organic extracts were washed with brine (30 mL), dried with Na_2SO_4, filtered and concentrated. The crude material was purified using column chromatography ((SiO_2, 40 g), hexanes/EtOAc, 7:1-3:1) to give **124** (50.2 mg, 99%) as a colorless oil.

Data for **124**:

^{1}H NMR: (400 MHz, $CDCl_3$)
7.06 (d, *J* = 2.0, 2 H), 7.00 (t, *J* = 2.0, 1 H), 4.46 (s, 2 H), 4.39-4.30 (m, 4 H), 3.39 (s, 3 H), 1.18-1.09 (m, 4 H), 0.08 (s, 18H)

Model TEOC Deprotection of 124

Preparation of 3,5-Dihydroxy-1-methoxymethylbenzene (123)[TK-XIII-99]



124 **123**

To a 10-mL polystyrene test tube, equipped with a magnetic stir-bar, air condenser and argon inlet, **124** (5.0 mg, 0.0177 mmol, 1.0 equiv) was added, followed by CH_3CN (0.1 mL). Then HF•NEt_3 (0.2 mL, 0.502 mmol, 42.9 equiv, HF•NEt_3 (40:60, 1.67 M in H_2O/CH_3CN)) was added and the contents were added to preheated (40 ^oC) oil bath.

Note: the buffered HF solution was prepared as follows: HF (2.5 mL, 72.21 mmol, 49% in H_2O) was added to a polyethylene bottle containing CH_3CN (10 mL). Then Et_3N (16.29 mL, 108.32 mmol) was added to give HF•NEt_3 (40:60, 2.51 M in H_2O/CH_3CN).

The mixture was stirred for 9 h at 40 ^oC and quenched with H_2O (20 mL). The aqueous layer was extracted with EtOAc (3x20 mL) and the combined organic extracts were washed with brine (1x30 mL), dried with Na_2SO_4, filtered and concentrated. The crude material was purified using column chromatography ((SiO_2, 5 g), hexanes/EtOAc, 1:1) to afford **123** (2.0 mg, 100%) as a colorless oil.

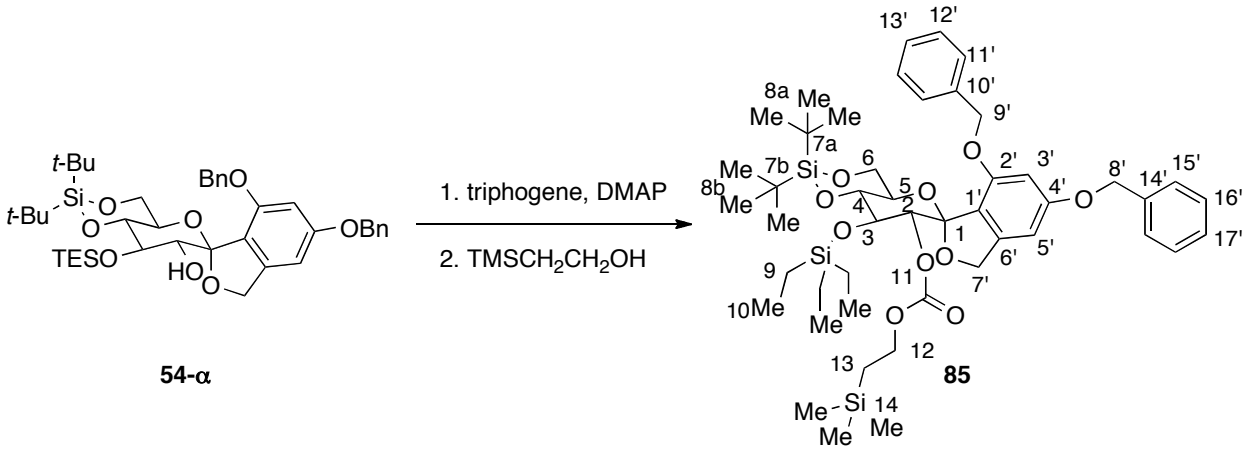
Data for **123**:

^{1}H NMR: (400 MHz, $CDCl_3$)

6.40 (d, J = 2.5, 2 H), 6.27 (t, J = 2.5, 1 H), 4.82 (br s, 2 H), 4.36 (s, 2 H), 3.38 (s, 3 H)

Preparation of Arylglycoside 90

Preparation of (1*R*,4'a*R*,7'*R*,8'*R*,8'a*R*)-Spiro[isobenzofuran-1(3 H),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) (85) [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 rt 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 **54-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 **54-α** was added drop wise via cannula into the Schlenk flask. The flask containing **54-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 rt. Upon warming the contents became a yellow solution, which eventually became a yellow mixture. The mixture was stirred at rt 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 rt. 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 **85** as a white foam.

Data for **85**:

mp: 53-55 °C (10:1 hexanes/EtOAc)

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

7.29-7.47 (m, 10H, HC(15', 16', 17', 11', 12', 13')), 6.43 (d, *J* = 1.7, 1 H, HC(3')), 6.35 (d, *J* = 1.7, 1 H, HC(5')), 5.47 (d, *J* = 10.0, 1 H, HC(2)), 5.13 (d, *J* = 12.0, 2 H, H_2C(7a')), 5.12 (d, *J* = 12.0, 1 H, HC(8a' or 9a')), 5.09 (d, *J* = 12.0, 1 H, HC(8b' or 9b')), 5.08 (d, *J* = 12.0, 1 H, HC(7b')), 4.98 (s, 2 H, H_2C(8b' or 9b')), 4.32 (dd, *J* =10.2, 7.3, 1 H, HC(5)), 4.14 (dd, *J* = 10.0, 5.0, 1 H, HC(6e)), 4.04 (t, *J* = 9.0, 1 H, HC(4)), 3.98 (dt, *J* = 7.8, 1.2, 2 H, H_2C(12)), 3.85 (t, *J* = 10.0, 1 H, HC(6a)), 3.82 (t, *J* = 9.5, 1 H, HC(3)), 1.07 (s, 9 H, $(CH_3)_3C$(8a or 8b)), 1.03 (s, 9 H, $(CH_3)_3C$(8a or 8b)), 0.96 (t, *J* = 8.0, 9 H, H_3C(10)), 0.82 (dt, *J* = 8.0, 2.6 Hz, 2 H, H_2C(13)), 0.66 (dq, *J* = 8.0, 2.0, 6 H, H_2C(9)), –0.04 (s, 9 H, H_3C(14))

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

162.5 (C(2')), 155.8 (C(11)), 154.6 (C(4')), 143.7 (C(1')), 137.3 (C(10' or 14')), 136.8 (C(10' or 14')), 128.9 (C(15', 16', 7', 11', 12', 13')), 128.6 (C(15', 16', 17', 11', 12', 13')), 128.3 (C(15', 16', 17', 11', 12', 13')), 127.8 (C(15', 16', 17', 11', 12', 13')), 127.7 (C(15', 16', 17', 11', 12', 13')), 127.0 (C(15', 16', 17', 11', 12', 13')), 117.2 (C(6')), 109.7 (C(1)), 100.4 (C(3')), 98.2 (C(5')), 78.1 (C(4)), 77.5 (C(2)), 74.2 (C(5)), 73.8 (C(3)), 70.6 (C(8' or 9')), 70.3 (C(8' or 9')), 69.0 (C(6)), 67.3 (C(7')), 66.2 (C(12)), 27.8 (C(8a or 8b)), 27.3 (C(8a or 8b)), 23.1 (C(7a or 7b)), 20.2 (C(7a or 7b)), 17.5 (C(13)), 7.2 (C(10)), 5.3 (C(9)), –1.4 (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)

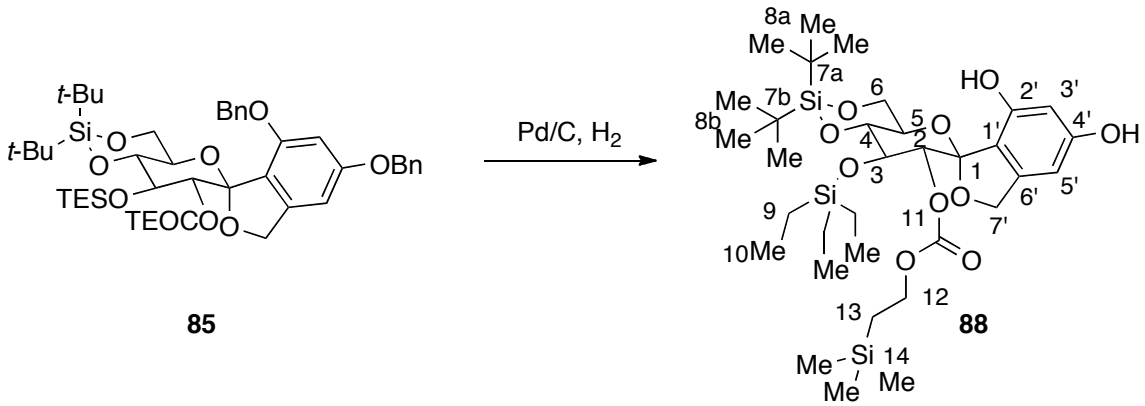
TLC: R_f 0.22 (10:1 hexanes/EtOAc) [SiO_2, CAM]

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(3 H),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) (88) [CSR-VIII-79]



To a 100-mL, single-necked, round-bottomed flask equipped with a magnetic stir-bar was added **85** (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 rt 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 **88** as a powdery, white solid.

Data for **88**:

mp: 106-108 °C (THF)

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

6.35 (d, J = 2.0, 1 H, HC(3')), 6.22 (d, J = 2.0, 1 H, HC(5')), 6.20 (s, 1 H, br(OH)), 6.09 (s, 1 H, br(OH)), 5.26 (d, J = 9.0, 1 H, HC(2)), 5.08 (d, J = 11.8, 1 H,

HC(7a')), 5.05 (d, J = 11.8, 1 H, HC(7b')), 4.15 (dd, J = 10.0, 4.6, 1 H, HC(6e)), 4.11 (t, J = 8.8, 1 H, HC(3)), 4.01 (t, J = 8.5, 2 H, H_2C(12)), 4.07-4.00 (m, 1 H, HC(5)), 3.95 (t, J = 8.8, 1 H, HC(4)), 3.90 (t, J = 10.0, 1 H, HC(6a)), 1.08 (s, 9 H, $(CH_3)_3C$(8a or 8b)), 1.04 (s, 9 H, $(CH_3)_3C$(8a or 8b)), 0.97 (t, J = 8.1, 9 H, H_3C(10)), 0.84 (dt, J = 8.5, 2.0, 2 H, H_2C(13)), 0.68 (dq, J = 8.1, 2.0, 2 H, H_2C(9)), –0.04 (s, 9 H, $(CH_3)_3Si$(14))

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

159.5 (C(2')), 155.4 (C(11)), 151.9 (C(4')), 143.6 (C(1')), 115.0 (C(6')), 108.8 (C(1)), 103.6 (C(3')), 100.5 (C(5')), 78.3 (C(4)), 77.8 (C(2)), 74.0 (C(5)), 73.6 (C(3)), 68.9 (C(6)), 67.0 (C(7')), 66.6 (C(12)), 27.6 (C(8a or 8b)), 27.1 (C(8a or 8b)), 22.7 (C(7a or 7b)), 20.0 (C(7a or 7b)), 17.8 (C(13)), 6.9 (C(10)), 5.1 (C(9)), –1.7 (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)

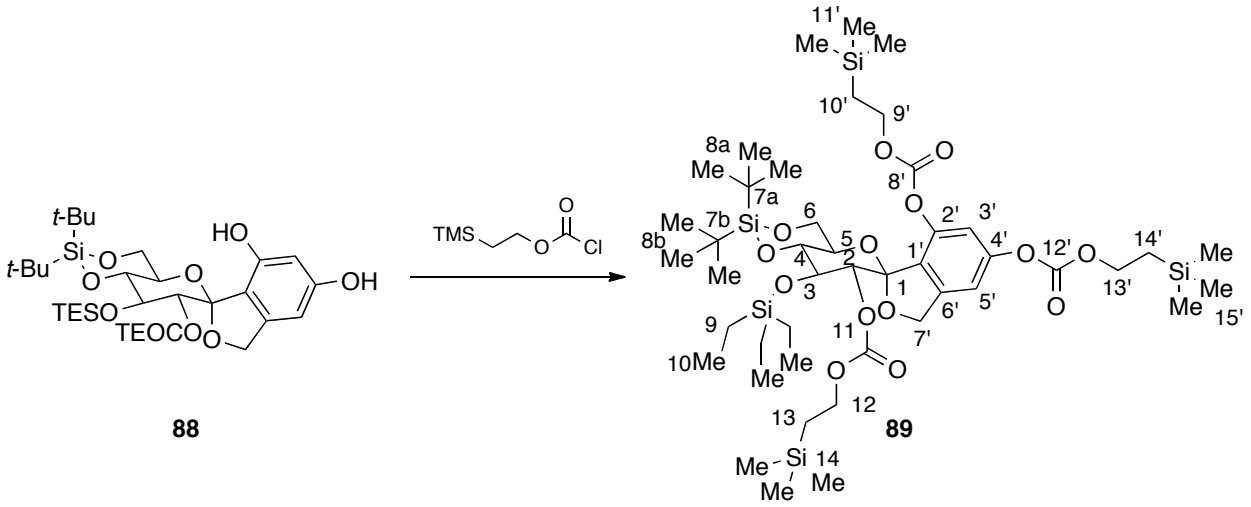
TLC: R_f 0.20 (10:1 hexanes/EtOAc) [SiO_2, CAM]

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(3 H),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) (89) [CSR-VII-62]



To a 25-mL Schlenk flask equipped with a magnetic stir-bar and an argon inlet with a septum was added **88** (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 rt 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 **89** as a colorless glassy solid.

Data for **89**:

mp: 40-42 °C (10:1 hexanes/EtOAc)

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

7.10 (d, *J* = 2.0, 1 H, HC(3' or 5')), 6.95 (d, *J* = 2.0, 1 H, HC(3' or 5')), 5.35 (d, *J* = 9.5, 1 H, HC(2)), 5.16 (s, 2 H, H_2C(7')), 4.27 4.38 (m, 4 H, CH_2(9') and 13')), 4.09

(dd, J = 9.8, 4.8, 1 H, HC(6e)), 4.07 (t, J = 9.2, 1 H, HC(3)), 3.94-4.03 (m, 3 H, H_2C(12) and HC(5)), 3.88 (t, J = 9.2, 1 H, HC(4)), 3.77 (t, J = 9.8, 1 H, HC(6a)), 1.09-1.15 (m, 4 H, H_2C(10' and 14')), 1.08 (s, 9 H, $(CH_3)_3C$(8a or 8b)), 1.03 (s, 9 H, $(CH_3)_3C$(8a or 8b)), 0.97 (t, J = 8.1, 9 H, H_3C(10)), 0.81-0.86 (m, 2 H, H_2C(13)), 0.66 (q, J = 8.1, 6 H, H_2C(9)), 0.08 (s, 9 H, HC(11' or 15')), 0.07 (s, 9 H, HC(11' or 15')), –0.05 (s, 9 H, HC(14))

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

154.2 (C(11)), 153.1 (C(2')), 152.8 (C(8' or 12')), 152.6 (C(8' or 12')), 146.8 (C(4')), 143.2 (C(1')), 124.9 (C(6')), 115.3 (C(3')), 111.4 (C(5')), 108.8 (C(1)), 77.7 (C(4)), 76.7 (C(2)), 73.7 (C(5)), 73.2 (C(3)), 68.9 (C(6)), 67.6 (C(9' or 13')), 67.6 (C(9' or 13')), 66.7 (C(7')), 66.4 (C(12)), 27.6 (C(8a or 8b)), 27.0 (C(8a or 8b)), 22.8 (C(7a or 7b)), 20.0 (C(7a or 7b)), 17.5 (C(10' or 14')), 17.5 (C(10' or 14')), 17.2 (C(13)), 6.9 (C(10)), 5.0 (C(9)), –1.5 (C(11' or 15')), –1.6 (C(11' or 15')), –1.7 (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

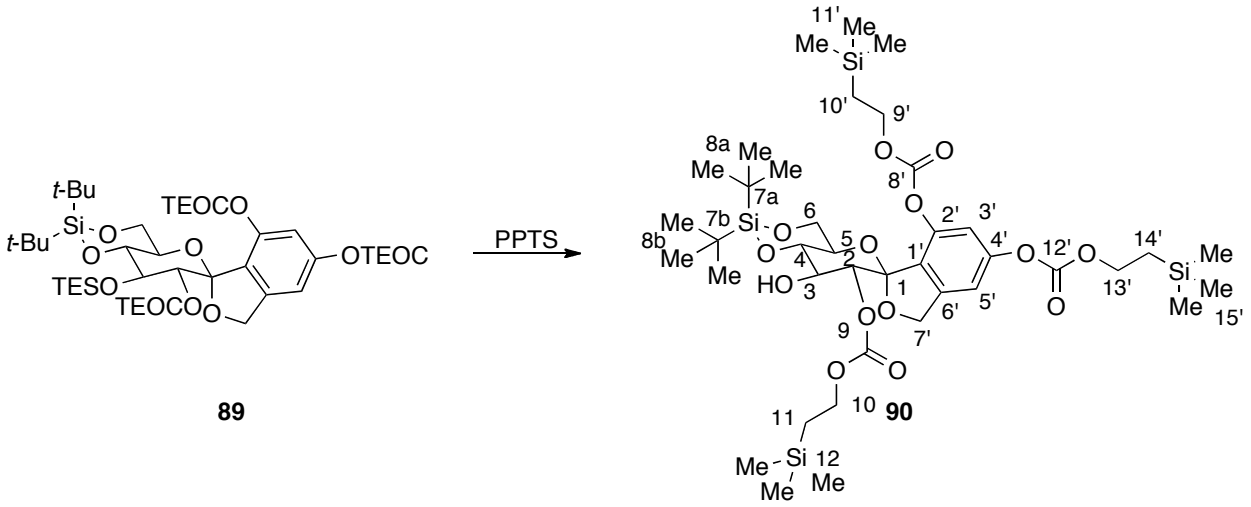
Found: 1009.4443

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(3 H),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)
(90) [CSR-IX-1]



To a 35-mL, single-necked, round-bottomed flask equipped with a magnetic stir-bar and an argon inlet with a septum was added **89** (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 rt 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 **90** as a colorless, glassy solid.

Data for **90**:

mp: 51-54 °C (7:1 hexanes/EtOAc)

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

7.11 (d, *J* = 1.7, 1 H, HC(3' or 5')),4 6.97 (d, *J* = 1.7, 1 H, HC(3' or 5')), 5.48 (d, *J* = 10.0, 1 H, HC(2)), 5.20 (d, *J* = 5.2, 1 H, HC(7'a)), 5.17 (d, *J* = 5.2, 1 H, HC(7'b)), 4.28-4.38 (m, 4 H, H_2C(9' and 13')), 4.07-4.13 (m, 2 H, HC(6e and 3)), 3.99-4.08 (m, 4 H, H_2C(10) and HC(6a) and HC(4)), 2.63 (d, *J* = 2.4, 1 H, (OH)),

1.12-1.15 (m, 4 H, H_2C(10' and 14')), 1.10 (s, 9 H, $C(CH_3)_3$(8a or 8b)), 1.02 (s, 9 H, $C(CH_3)_3$(8a or 8b)), 0.97 (t, J = 8.8, 2 H, CH_2(11)), 0.07 (s, 9 H, H_3C(11' or 15')), 0.07 (s, 9 H, H_3C(11' or 15')), –0.05 (s, 9 H, H_3C(12))

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

154.5 (C(9)), 153.2 (C (2')), 152.9 (C(8' or 12')), 152.5 (C(8' or 12')), 146.7 (C(4')), 143.3 (C(1')), 124.8 (C(6')), 115.3 (C(3')), 111.5 (C(5')), 108.6 (C(1)), 77.4 (C(4)), 75.9 (C(2)), 73.0 (C(5)), 68.4 (C(3)), 67.6 (C(9' or 13')), 67.7 (C(9' or 13')), 66.9 (C(6)), 66.8 (C(7')), 66.5 (C(10)), 27.4 (C(8a or 8b)), 27.0 (C(8a or 8b)), 22.7 (C(7a or 7b)), 20.0 (C(7a or 7b)), 17.5 (C(10' or 14')), 17.5 (C(10' or 14')), 17.1 (C(11)), –1.5 (C(11' or 15')), –1.6 (C(11' or 15')), 1.6 (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)

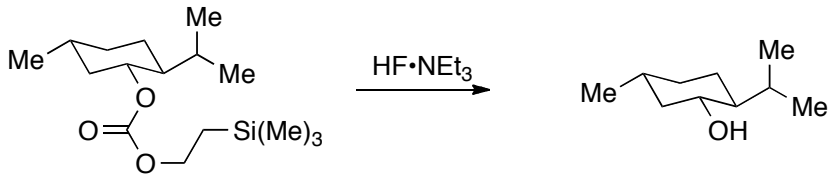
TLC: R_f 0.20 (15:1 hexanes/EtOAc) [SiO_2, CAM]

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%

Model Deprotection of TEOC (Table S5, SI)

Preparation of Menthol (Table S5, SI, entry 1) [TK-XVI-67]



125 menthol

To a 10-mL polystyrene test tube equipped with a magnetic stir-bar, argon inlet and air condenser, **125** (5.0 mg, 0.0661 mmol, 1.0 equiv) was added, followed by CH_3CN (0.14 mL). Then HF•NEt_3 (0.28 mL, 0.714 mmol, 43 equiv, 1.67 M, 40:60 ratio in H_2O/CH_3CN) was added and the contents were added to an oil bath preheated to 40 ^oC. The mixture was stirred at this

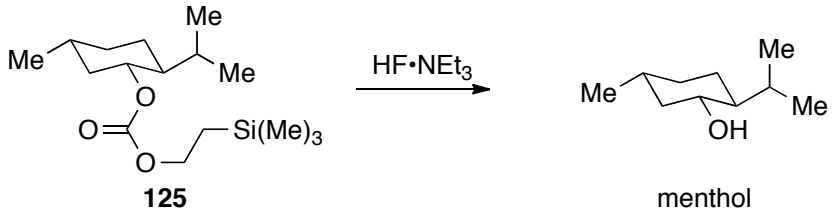
temperature for 9 h. After this amount of time the reaction mixture was diluted with H_2O (30 mL) and extracted with EtOAc (3x30 mL). The combined organic layers were washed with brine (30 mL), dried with Na_2SO_4 and concentrated. The crude product was analyzed by ^{1}H-NMR to give a 90:10 ratio of **125** and menthol. The data for menthol matched that of commercial material.

Data for **125**:

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

4.50 (dt, *J* = 11.0, 4.0, 1 H), 4.25-4.15 (m, 2 H), 2.10-1.92 (m, 2 H), 1.70-1.64 (m, 2 H), 1.54-1.35 (m, 2 H), 1.09-0.99 (m, 4 H), 0.91 (d, *J* = 6.3, 3 H), 0.89 (d, *J* = 6.3, 3 H), 0.90-0.82 (m, 1 H), 0.78 (d, *J* = 6.3, 3 H), 0.04 (s, 9 H)

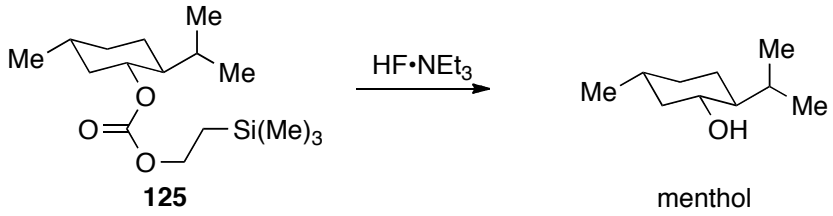
(Table S5, SI, entry 2) [TK-XVI-60]



125 menthol

To a 10-mL polystyrene test tube equipped with a magnetic stir-bar, argon inlet and air condenser, **125** (5.0 mg, 0.0661 mmol, 1.0 equiv) was added, followed by CH_3CN (0.14 mL). Then HF•NEt_3 (0.28 mL, 0.714 mmol, 43 equiv, 1.67 M, 40:60 ratio in H_2O/CH_3CN) was added and the contents were added to an oil bath preheated to 40 ^oC. The mixture was stirred at this temperature for 42 h. After this amount of time the reaction mixture was diluted with H_2O (30 mL) and extracted with EtOAc (3x30 mL). The combined organic layers were washed with brine (30 mL), dried with Na_2SO_4 and concentrated. The crude product was analyzed by ^{1}H-NMR to give a 76:24 ratio of **125** and menthol. The data for menthol matched that of commercial material.

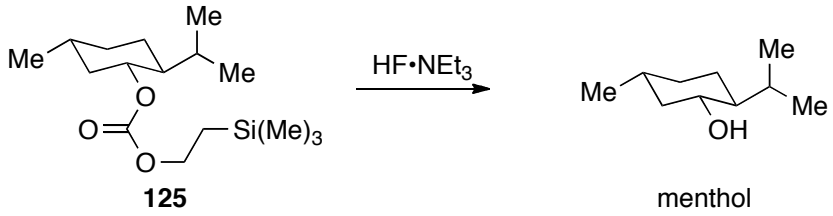
(Table S5, SI, entry 3) [TK-XVI-67]



125 menthol

To a 10-mL polystyrene test tube equipped with a magnetic stir-bar, argon inlet and air condenser, **125** (5.0 mg, 0.0661 mmol, 1.0 equiv) was added. Then HF•NEt_3 (0.28 mL, 0.714 mmol, 43 equiv, 2.51 M, 40:60 ratio in H_2O/CH_3CN) was added and the contents were added to an oil bath preheated to 40 ^oC. The mixture was stirred at this temperature for 9 h. After this amount of time the reaction mixture was diluted with H_2O (30 mL) and extracted with EtOAc (3x30 mL). The combined organic layers were washed with brine (30 mL), dried with Na_2SO_4 and concentrated. The crude product was analyzed by ^{1}H-NMR to give an 87:13 ratio of **125** and menthol. The data for menthol matched that of commercial material.

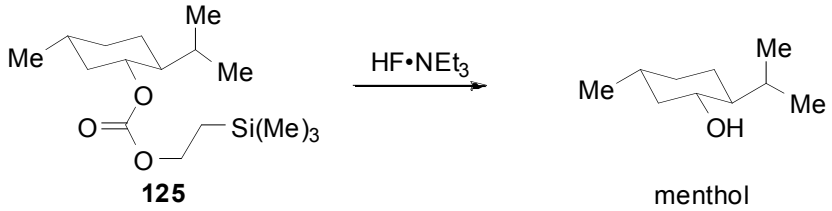
(Table S5, SI, entry 4) [TK-XVI-67]



125 menthol

To a 10-mL polystyrene test tube equipped with a magnetic stir-bar, argon inlet and air condenser, **125** (5.0 mg, 0.0661 mmol, 1.0 equiv) was added. Then HF•NEt_3 (0.25 mL, 0.714 mmol, 43 equiv, 2.88 M, 46:54 ratio in H_2O/CH_3CN) was added and the contents were added to an oil bath preheated to 40 ^oC. The mixture was stirred at this temperature for 9 h. After this amount of time the reaction mixture was diluted with H_2O (30 mL) and extracted with EtOAc (3x30 mL). The combined organic layers were washed with brine (30 mL), dried with Na_2SO_4 and concentrated. The crude product was analyzed by ^{1}H-NMR to give an 86:14 ratio of **125** and menthol. The data for menthol matched that of commercial material.

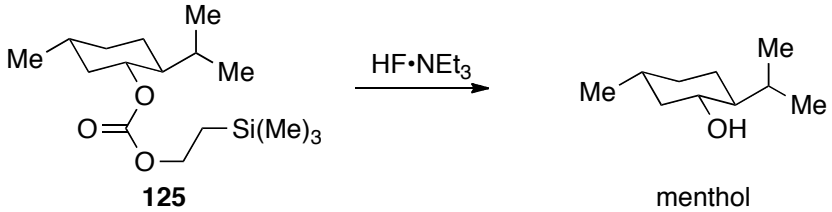
(Table S5, SI, entry 5) [TK-XVI-67]



125 menthol

To a 10-mL polystyrene test tube equipped with a magnetic stir-bar, argon inlet and air condenser, **125** (5.0 mg, 0.0661 mmol, 1.0 equiv) was added, followed by CH_3CN (0.14 mL). Then HF•NEt_3 (0.28 mL, 0.714 mmol, 43 equiv, 1.67 M, 40:60 ratio in H_2O/CH_3CN) was added and the contents were added to an oil bath preheated to 60 ^oC. The mixture was stirred at this temperature for 9 h. After this amount of time the reaction mixture was diluted with H_2O (30 mL) and extracted with EtOAc (3x30 mL). The combined organic layers were washed with brine (30 mL), dried with Na_2SO_4 and concentrated. The crude product was analyzed by ^{1}H-NMR to give a 74:26 ratio of **125** and menthol. The data for menthol matched that of commercial material.

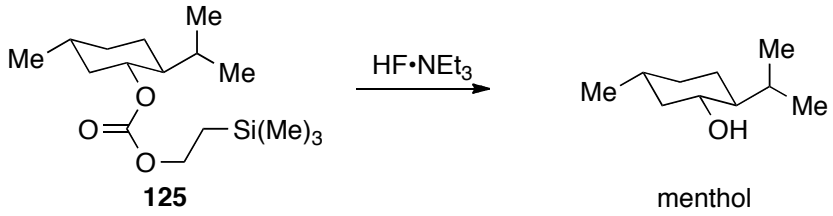
(Table S5, SI, entry 6) [TK-XVI-68]



125 menthol

To a 10-mL polystyrene test tube equipped with a magnetic stir-bar, argon inlet and air condenser, **125** (5.0 mg, 0.0661 mmol, 1.0 equiv) was added, followed by THF (0.14 mL). Then HF•NEt_3 (0.28 mL, 0.714 mmol, 43 equiv, 1.67 M, 40:60 ratio in H_2O/THF) was added and the contents were added to an oil bath preheated to 60 ^oC. The mixture was stirred at this temperature for 9 h. After this amount of time the reaction mixture was diluted with H_2O (30 mL) and extracted with EtOAc (3x30 mL). The combined organic layers were washed with brine (30 mL), dried with Na_2SO_4 and concentrated. By ^{1}H-NMR analysis it was determined that both decomposition of the **125** or menthol had occurred. Further analysis or experimentation was not pursued.

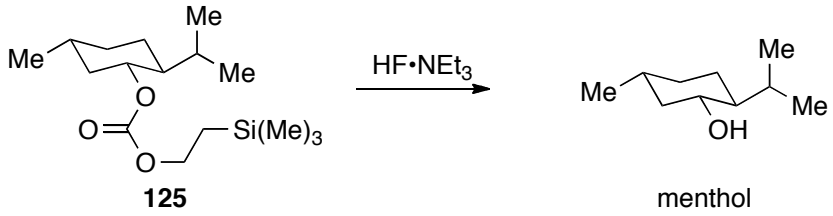
(Table S5, SI, entry 7) [TK-XVI-68]



125 menthol

To a 10-mL polystyrene test tube equipped with a magnetic stir-bar, argon inlet and air condenser, **125** (5.0 mg, 0.0661 mmol, 1.0 equiv) was added, followed by DMSO (0.14 mL). Then HF•NEt_3 (0.28 mL, 0.714 mmol, 43 equiv, 1.67 M, 40:60 ratio in H_2O/DMSO) was added and the contents were added to an oil bath preheated to 60 ^oC. The mixture was stirred at this temperature for 9 H. After this amount of time the reaction mixture was diluted with H_2O (30 mL) and extracted with EtOAc (3x30 mL). The combined organic layers were washed with brine (30 mL), dried with Na_2SO_4 and concentrated. The crude product was analyzed by ^{1}H-NMR to give a 22:78 ratio of **125** and menthol. The data for menthol matched that of commercial material.

(Table S5, SI, entry 8) [TK-XVI-68]

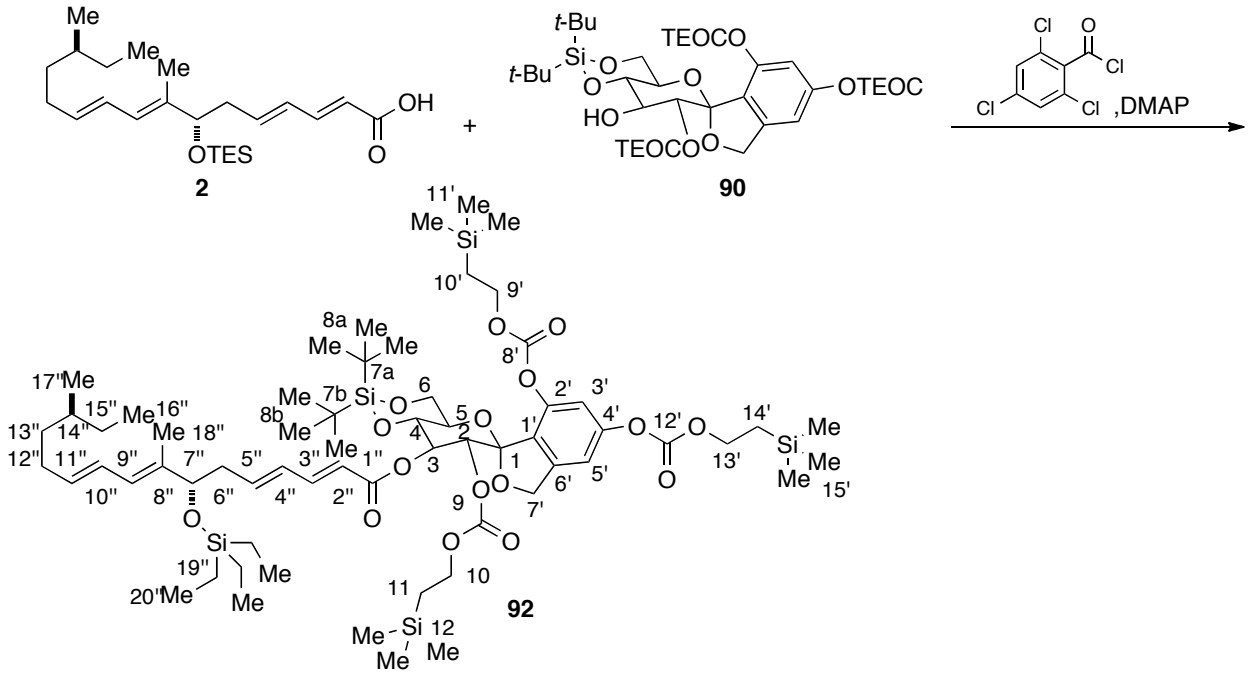


125 menthol

To a 10-mL polystyrene test tube equipped with a magnetic stir-bar, argon inlet and air condenser, **125** (5.0 mg, 0.0661 mmol, 1.0 equiv) was added, followed by DMSO (0.14 mL). Then HF•NEt_3 (0.28 mL, 0.714 mmol, 43 equiv, 1.67 M, 40:60 ratio in H_2O/DMSO) was added and the contents were added to an oil bath preheated to 40 ^oC. The mixture was stirred at this temperature for 9 H. After this amount of time the reaction mixture was diluted with H_2O (30 mL) and extracted with EtOAc (3x30 mL). The combined organic layers were washed with brine (30 mL), dried with Na_2SO_4 and concentrated. The crude product was analyzed by ^{1}H-NMR to give a 72:28 ratio of **125** and menthol. The data for menthol matched that of commercial material.

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 (92) [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 rt for 1 h. To a 5-mL, conical-flask equipped with a magnetic stir-bar and an argon inlet with septum was added **90** (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 **90** 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 **90**. This mixture was stirred at rt 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 **92**, as a colorless glass.

Data for **92**:

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

7.28 (dd, *J* = 14.9, 11.3, 1 H, HC(3")), 7.11 (d, *J* = 1.8, 1 H, HC(3' or 5')), 6.97 (d, *J* = 1.8, 1 H, HC(3' or 5')), 6.24-6.14 (m, 2 H, HC(4") and HC(10")), 6.07 (dt, *J* = 15.7, 7.8, 1 H, HC(5")), 5.92 (d, *J* = 11.3, 1 H, HC(9")), 5.82 (d, *J* = 14.9, 1 H, HC(2")), 5.65 (dt, *J* = 14.4, 7.2, 1 H, HC(11")), 5.61 (t, *J* = 9.9, 1 H, HC(3)), 5.52 (d, *J* = 9.9, 1 H, HC(2)), 5.20 (s, 2 H, H_2C(7')), 4.42-4.29 (m, 4 H, H_2C(9') and H_2C(13')), 4.16-4.09 (m, 3 H, HC(6e) and HC(10)), 4.07-3.90 (m, 4 H, H_2C(10) and HC(6a) and HC(4)), 3.84-3.76 (m, 2 H, HC(7") and HC(5)), 2.44-2.27 (m, 2 H, H_2C(12")), 2.22-2.00 (m, 2 H, H_2C(6")), 1.69 (s, 3 H, H_3C(18")), 1.46-1.30 (m, 3 H, HC(14") and H_2C(15")), 1.24-1.17 (m, 2 H, H_2C(13")), 1.18-1.09 (m, 4 H, CH_2(10') and H_2C(14')), 1.02 (s, 9 H, $(CH_3)_3C$(8a or 8b)), 0.99 (s, 9 H, $(CH_3)_3C$(8a or 8b)), 0.91 (t, *J* = 7.8, 9 H, H_3C(20")), 0.87 (d, *J* = 6.1, 3 H, H_3C(17")), 0.87 (t, *J* = 7.3, 3 H, H_3C(16")), 0.81-0.76 (m, 2 H, H_2C(11)), 0.54 (q, *J* = 7.8, 6 H, H_2C(19")), 0.09 (s, 9 H, H_3C(11') or (15')), 0.07 (s, 9 H, H_3C(11') or (15')), –0.04 (s, 9 H, H_3C(12))

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

166.0 (C(1")), 154.1 (9)), 153.2 (2')), 152.9 (C(8' or 12')), 152.5 (C(8' or 12')), 146.7 (C(4')), 145.2 (C(3")), 143.4 (C(1')), 141.0 (C(5")), 136.7 (C(8")), 135.2 (C(11")), 130.2 (4")), 125.6 (C(10")), 125.5 (C(9")), 124.5 (C(6')), 119.2 (C(2")), 115.3 (C(3')), 111.6 (C(5')), 108.7 (C(1)), 77.5 (C(7")), 77.2 (C(4)), 75.5 (C(2)), 74.5 (C(3)), 73.4 (C(5)), 72.6 (C(9' or 13')), 68.9 (C(9' or 13')), 67.7 (C(7')), 66.9 (C(6)), 66.6 (C(10)), 40.5 (C(6")), 36.2 (C(13")), 34.0 (C(14")), 30.6 (C(12")), 29.3 (C(15")), 27.3 (C(8a or 8b)), 26.9 (C(8a or 8b)), 22.6 (C(7a or 7b)), 20.0 (C(7a or 7b)), 17.6 (10' or 14')), 17.5 (10' or 14')), 17.1 (C(13")), 11.2 (C(18")), 11.3 (C(16")), 6.8 (C(19")), 4.8 (C(20")), –1.5 (C(11' or 15')), –1.6 (C(11' or 15')),

–1.7 (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, $CHCl_3$)

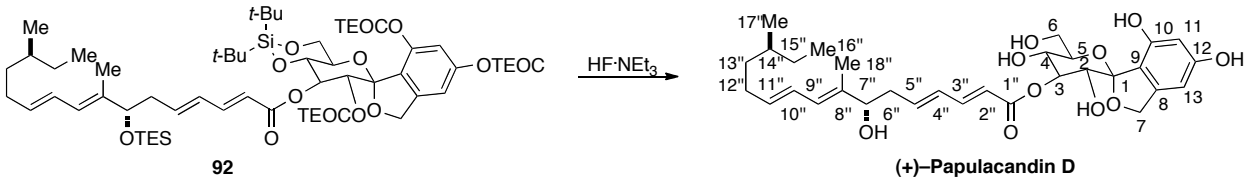
TLC: R_f 0.12 (hexanes/EtOAc, 10:1) [SiO_2, CAM]

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]



92 **(+)–Papulacandin D**

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 (**92**) (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 rt for 5 min, then at 60 ^oC (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 ^oC 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, 1 H, HC(3")), 6.25 (ddt, *J* = 15.7, 10.8, and 1.6, 1 H, HC(4")), 6.23 (dd, *J* = 14.9, 10.7, 1 H, HC(10")), 6.20 (m, 1 H, HC(11)), 6.19 (m, 1 H, HC(13)), 6.12 (dt, *J* = 15,4, 14.9, 1 H, HC(5")), 5.98 (dd, *J* = 10.7, 0.6, 1 H, HC(9")), 5.92 (d, *J* = 15.3, 1 H, HC(2")), 5.66 (dt, *J* = 14.9, 7.3, 1 H, HC(11")), 5.34 (t, *J* = 9.7, 1 H, HC(3)), 5.02 (AB q, *J* = 12.9 Hz, 2 H, $H_2C(7)$), 4.34 (d, *J* = 10.1, 1 H, HC(2)), 4.07 (t, *J* = 6.6, 1 H, HC(7")), 3.88 (ddd, *J* = 10.3, 4.8, and 2.4, 1 H, HC(5)), 3.79-3.66 (m, 2 H, $H_2C(6)$), 3.68 (t, *J* = 9.8, 1 H, HC(4)), 2.42 (t, *J* = 7.2, 2 H, $H_2C(6")$), 2.18-2.04 (m, 2 H, $H_2C(12")$), 1.71 (s, 3 H, $H_3C(18")$), 1.50-1.30 (m, 2 H, $H_2C(13")$), 1.30-1.11 (m, 2 H, $H_2C(15")$), 1.28-1.11 (m, 1 H, HC(14")), 0.87 (t, *J* = 7.3, 3 H, $H_3C(16")$), 0.87 (d, *J* = 6.5, 3 H, $H_3C(17")$)

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

169.2 (C(1")), 161.7 (C(12)), 154.9 (C(10)), 146.6 (C(3")), 145.7 (C(8)), 142.1 (C(5")), 137.7 (C(8")), 136.4 (C(11")), 131.7 (C(10")), 127.3 (4")), 127.2 (C(9")), 121.1 (C(2")), 116.8 (C(9)), 112.2 (C(1)), 103.0 (C(11)), 100.0 (13)), 78.5 (C(3)), 77.7 (C(7")), 75.9 (C(5)), 72.0 (C(2)), 69.9 (C(4)), 62.6 (C(6)), 40.1 (C(6")), 37.7 (C(13")), 35.4 (C(14")), 31.7 (C(12")), 30.6 (C(15")), 19.6 (C(18")), 12.3 (C(17")), 11.6 (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 S6: ^{13}C NMR Spectroscopic Properties

carbon No.	natural (ppm)[45]	CSR-IX-95 (ppm)	Synthetic (ppm)[35]	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	0.20
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 S7: ^{1}H NMR Spectroscopic Properties

hydrogen No.	natural (ppm)[45]	CSR-IX-95 (ppm)	synthetic (ppm)[35]
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 (AB q, *J* = 12 Hz)	5.02 (AB q, *J* = 12.9 Hz)	5.03 (AB q, *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 S8: Physiochemical Properties

property	natural[45]	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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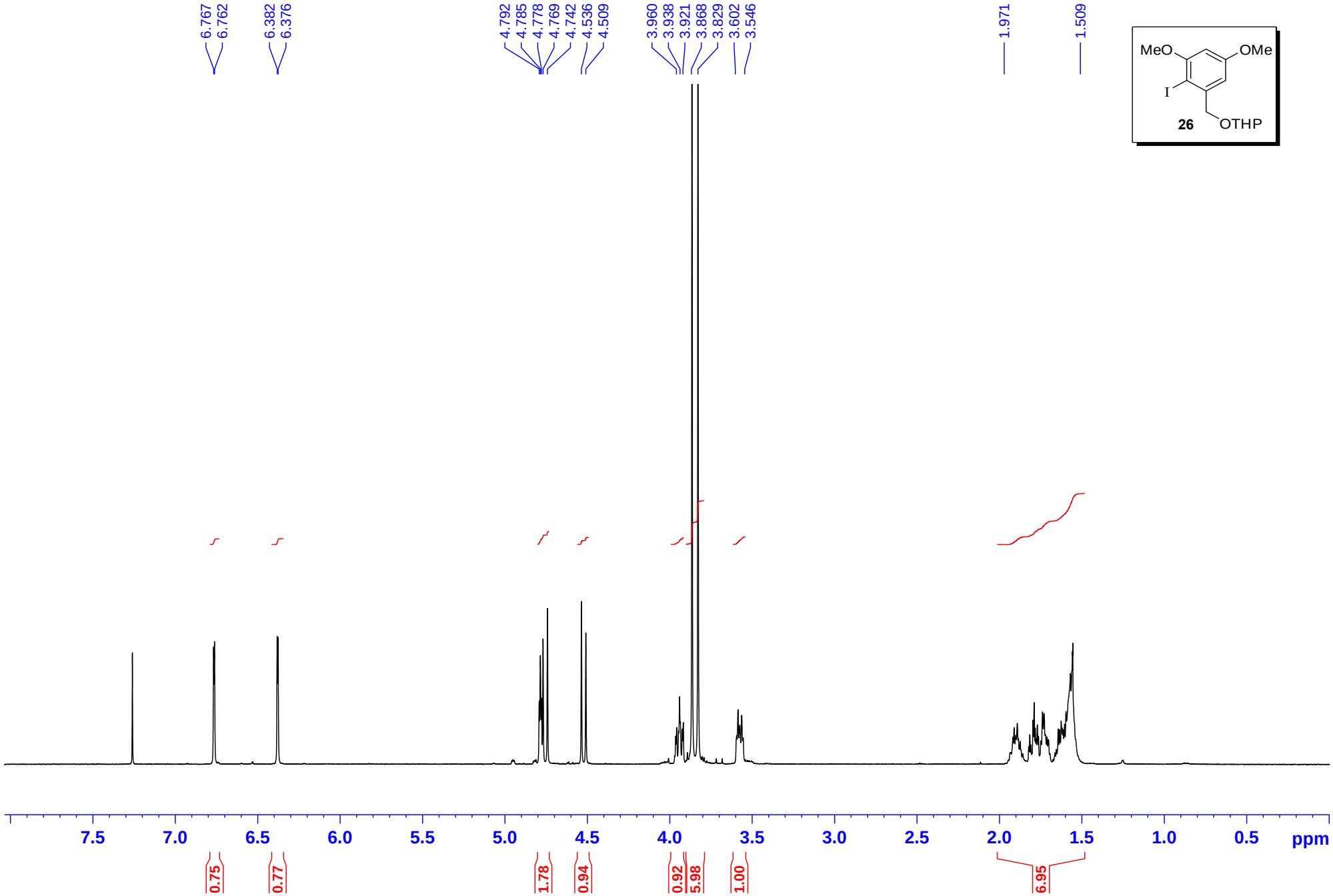
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3.829
3.602
3.546
1.971
1.509
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OMe
I
OTHP
26
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6.5
6.0
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5.0
4.5
4.0
3.5
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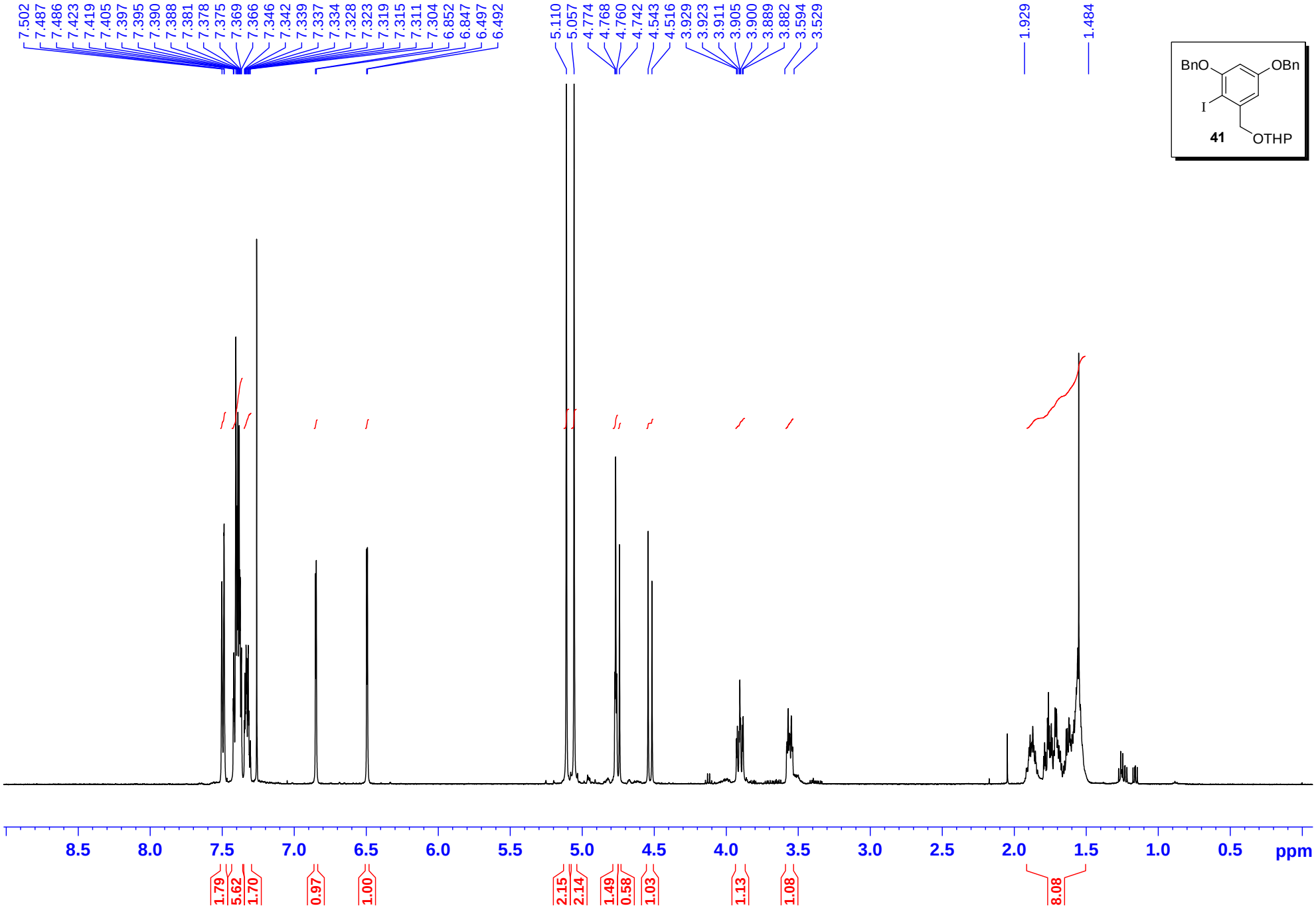
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7.369
7.366
7.346
7.342
7.339
7.337
7.334
7.328
7.323
7.319
7.315
7.311
7.304
6.852
6.847
6.497
6.492
5.110
5.057
4.774
4.768
4.760
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4.543
4.516
3.929
3.923
3.911
3.905
3.900
3.889
3.882
3.594
3.529
1.929
1.484
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OBn
I
41
OTHP
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7.5
7.0
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5.5
5.0
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3.5
3.0
2.5
2.0
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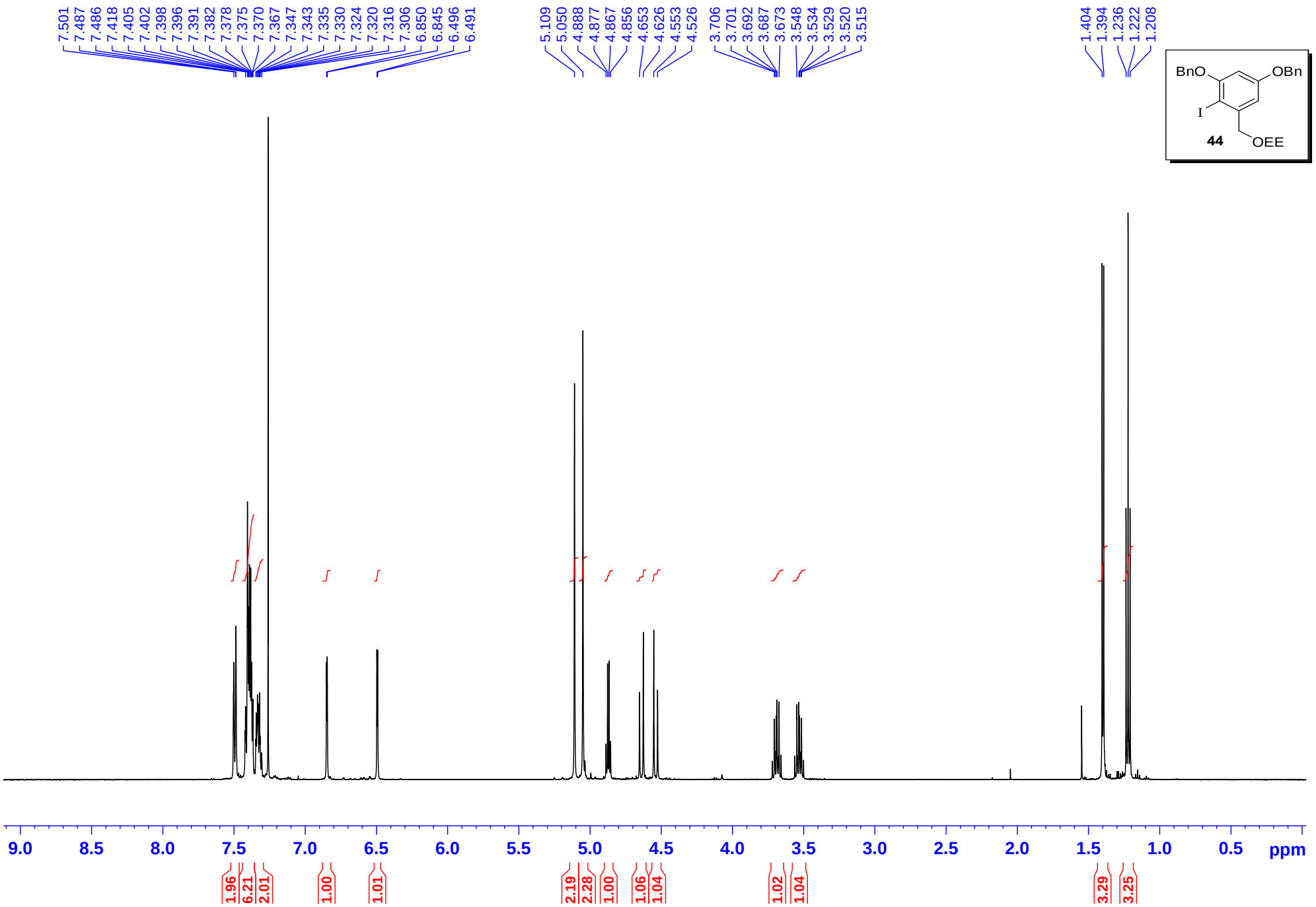
8.08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7.343
7.335
7.330
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7.320
7.316
7.306
6.850
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6.491
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5.050
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OBn
I
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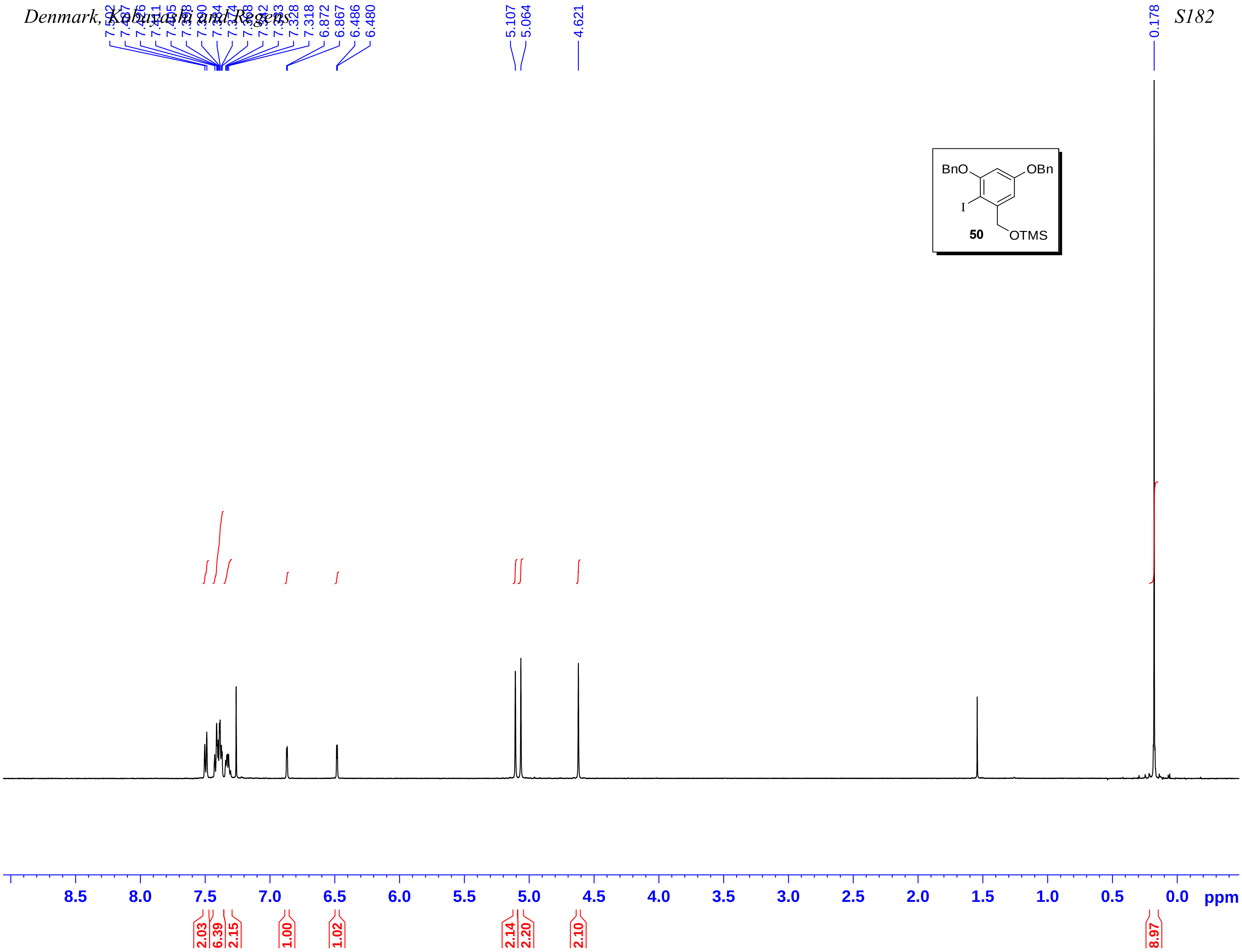
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2.15
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1.02
2.14
2.20
2.10
8.97
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7.0
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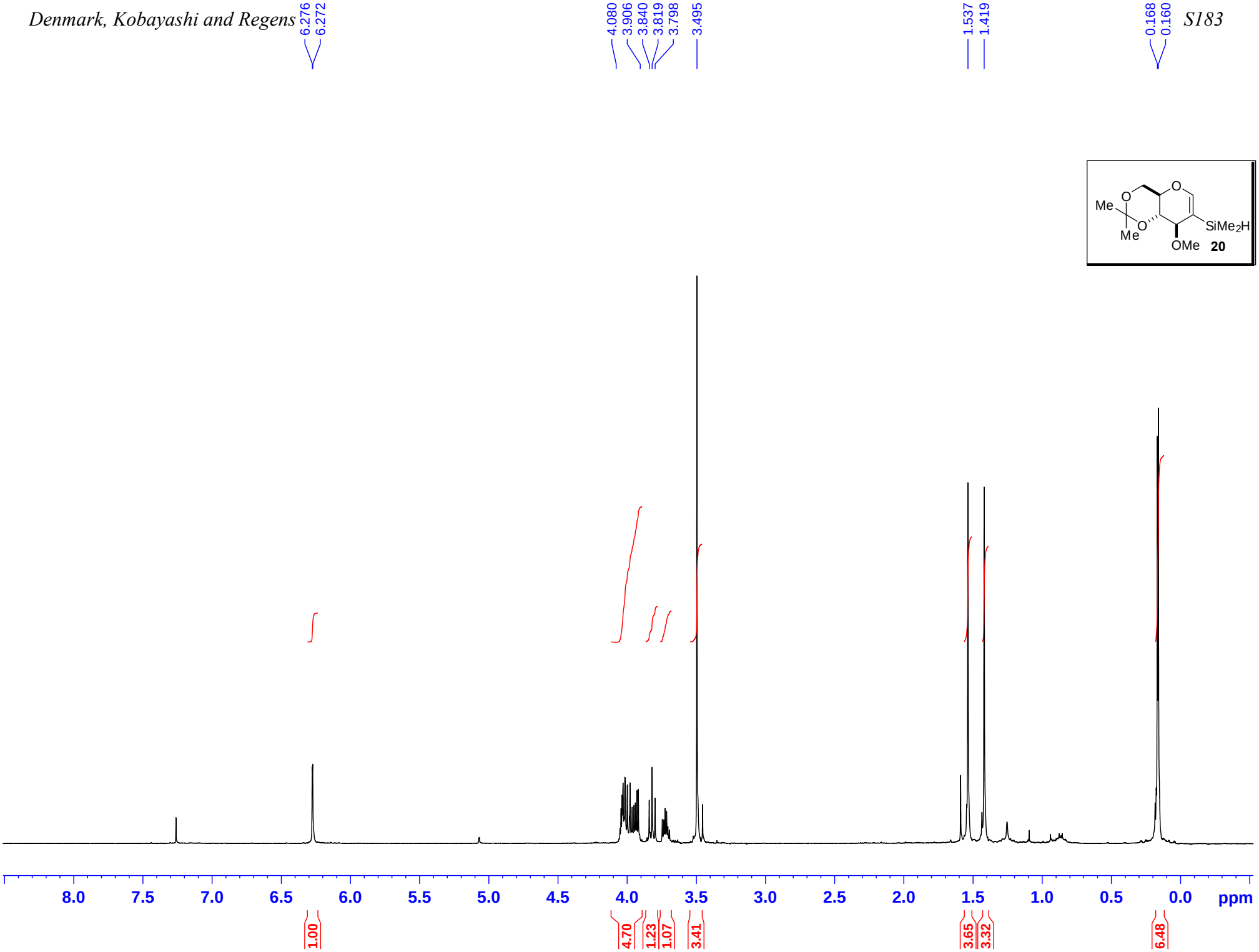
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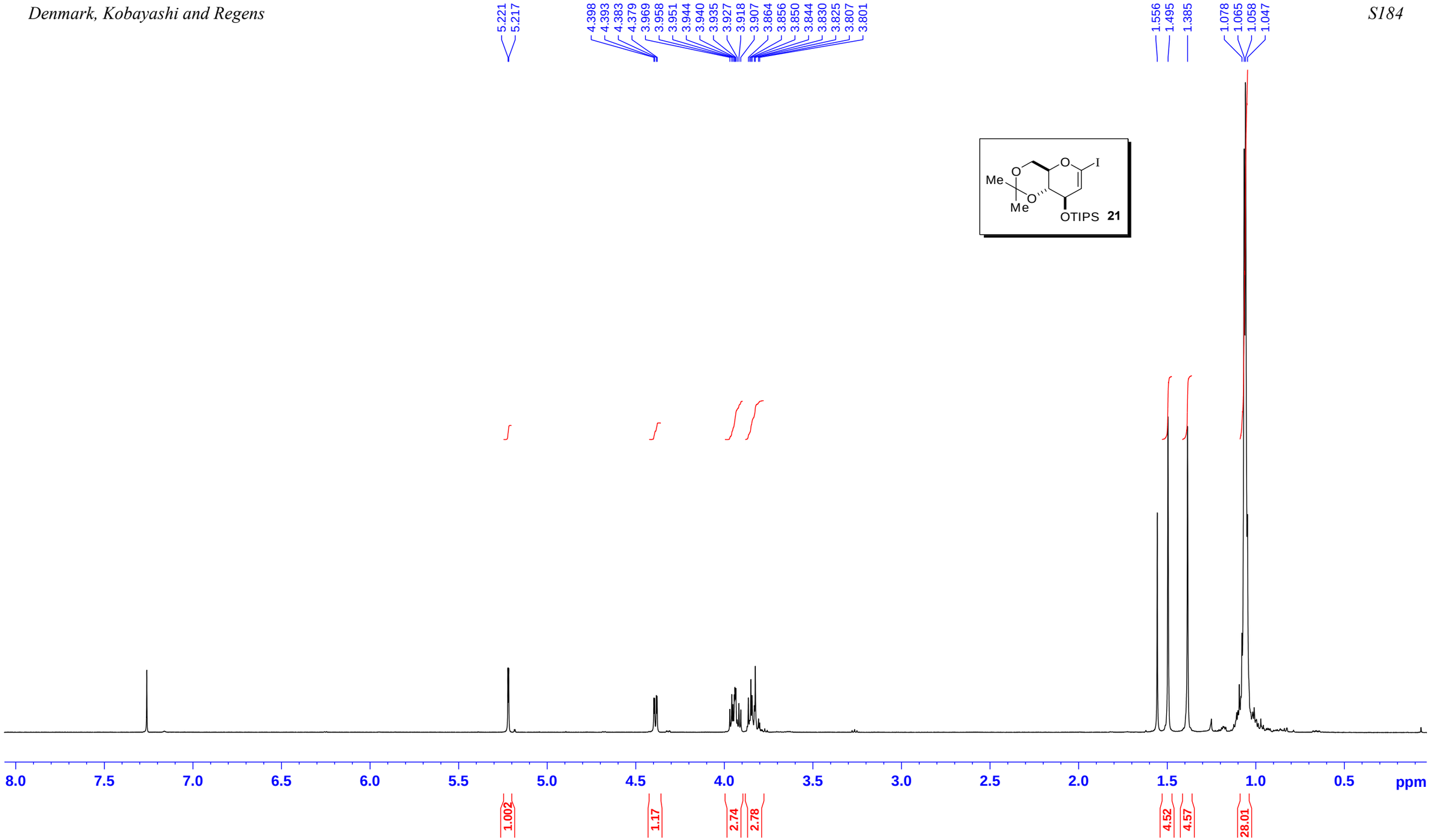
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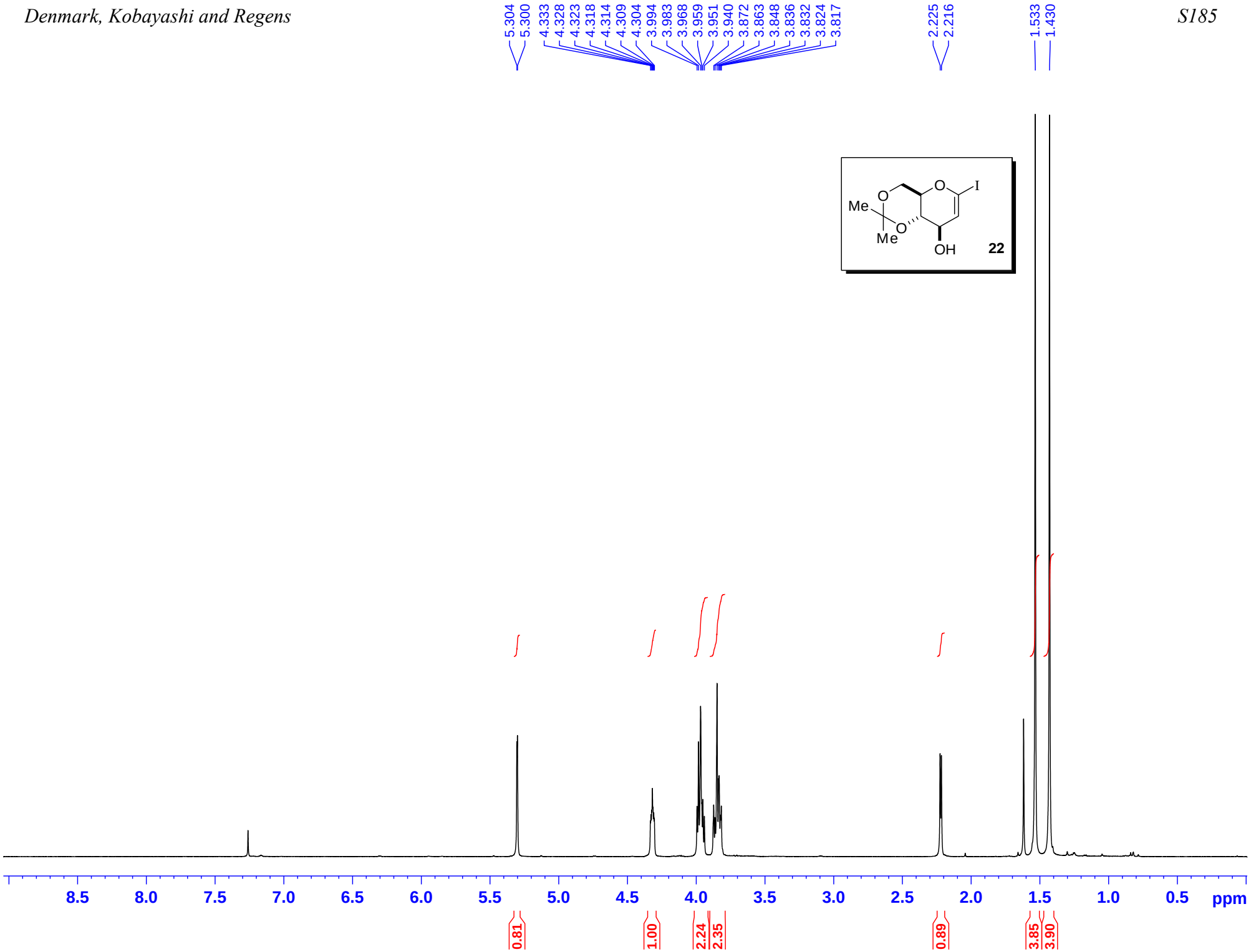
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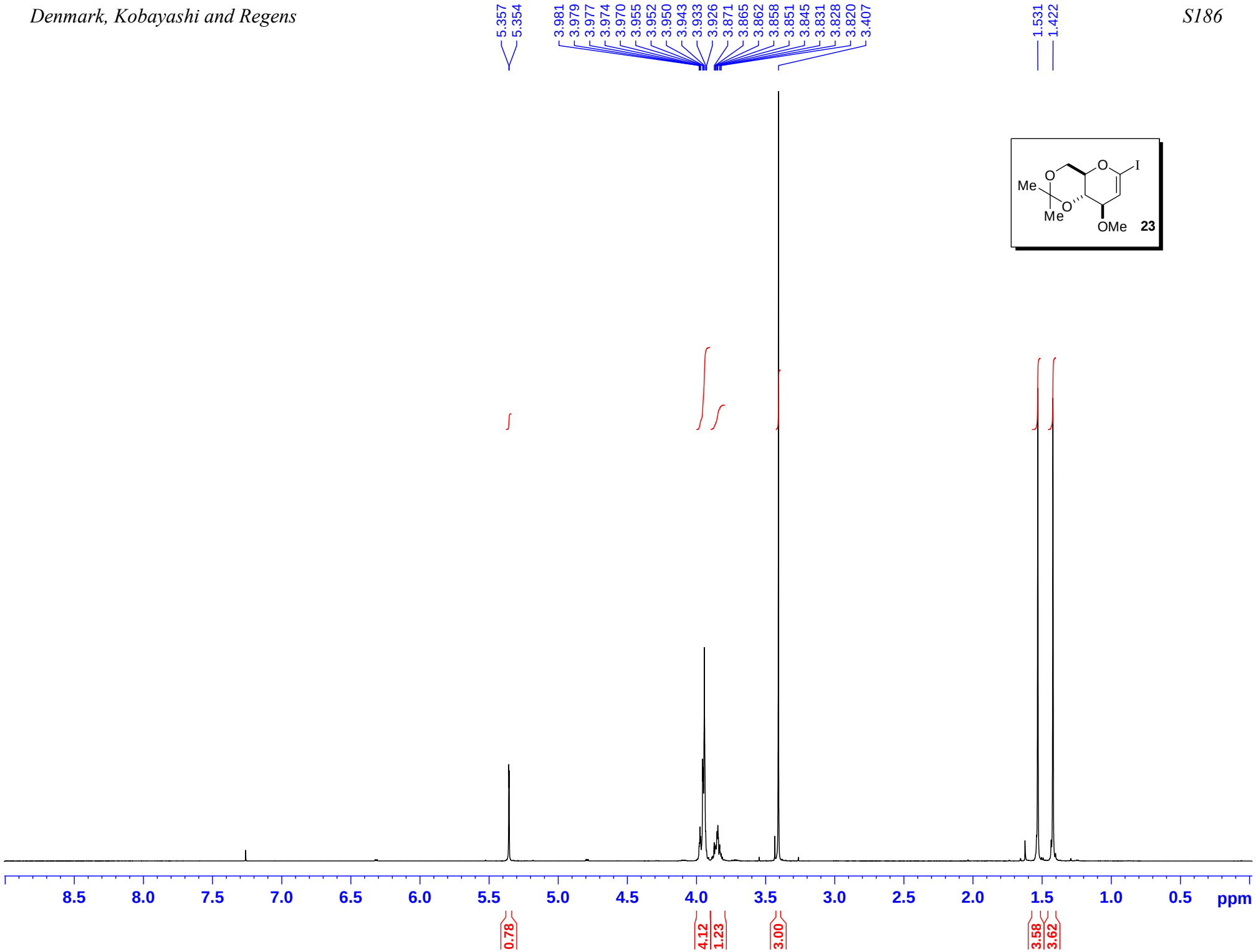
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3.845
3.831
3.828
3.820
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1.422
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Me
O
I
OMe
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7.5
7.0
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5.5
5.0
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3.5
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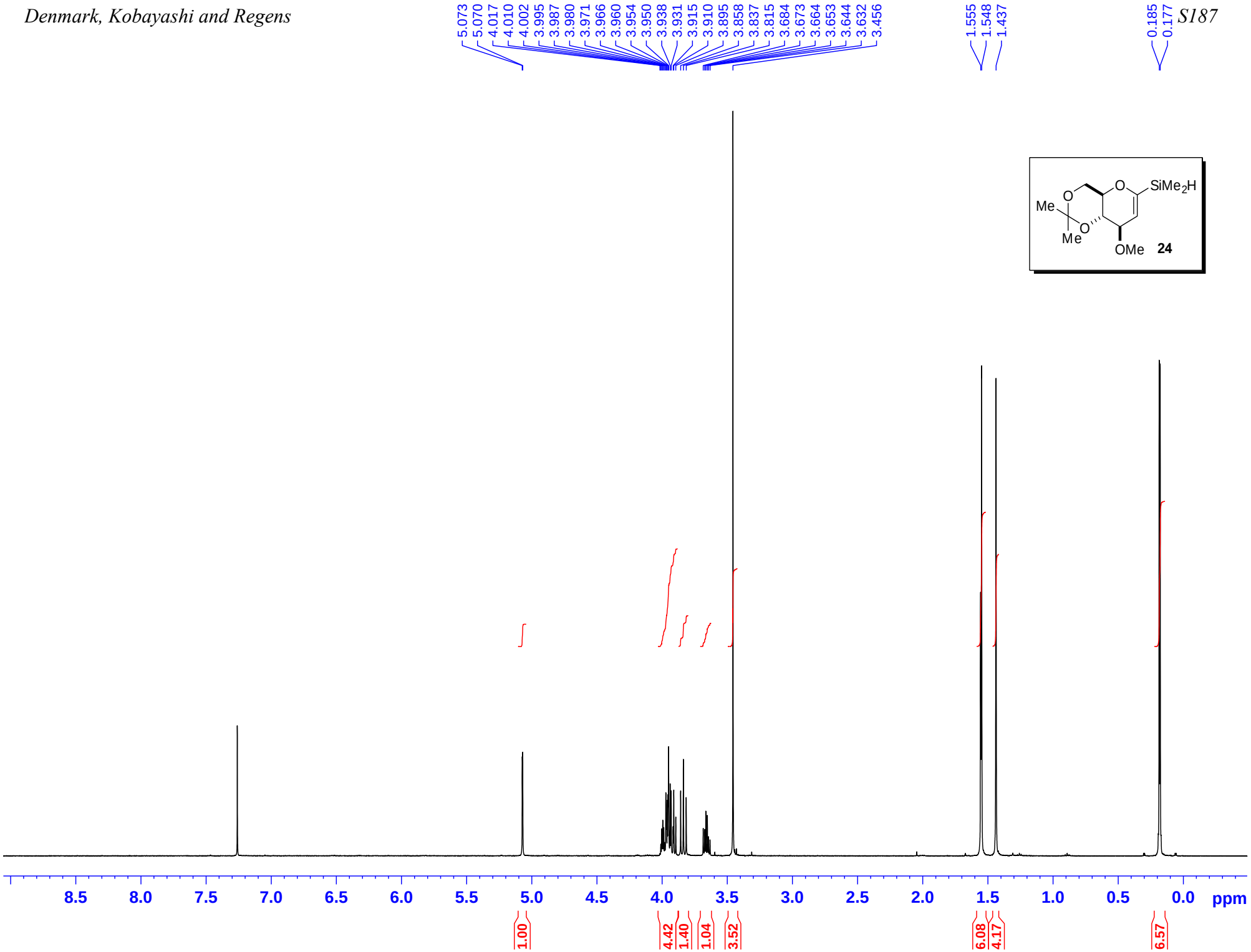
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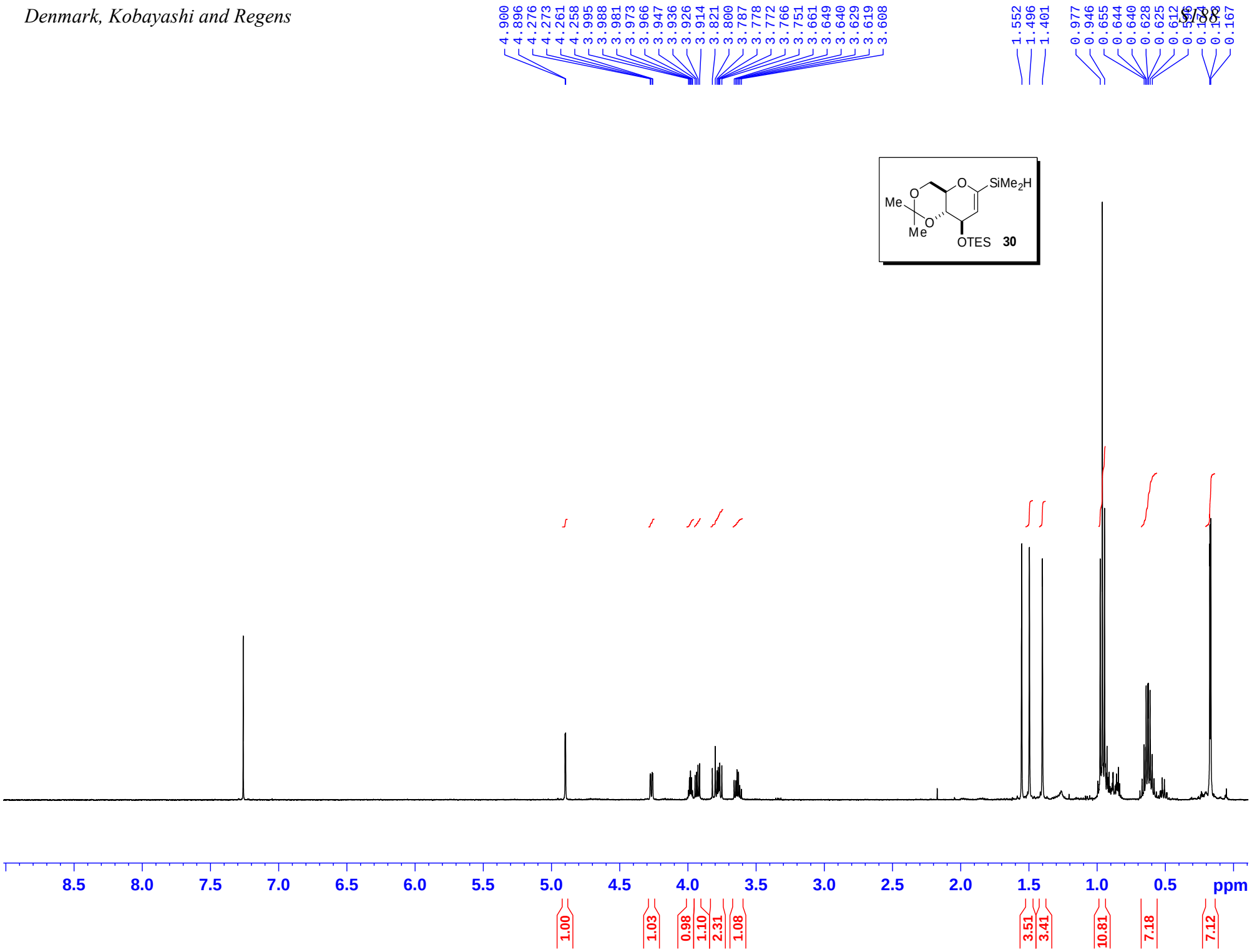
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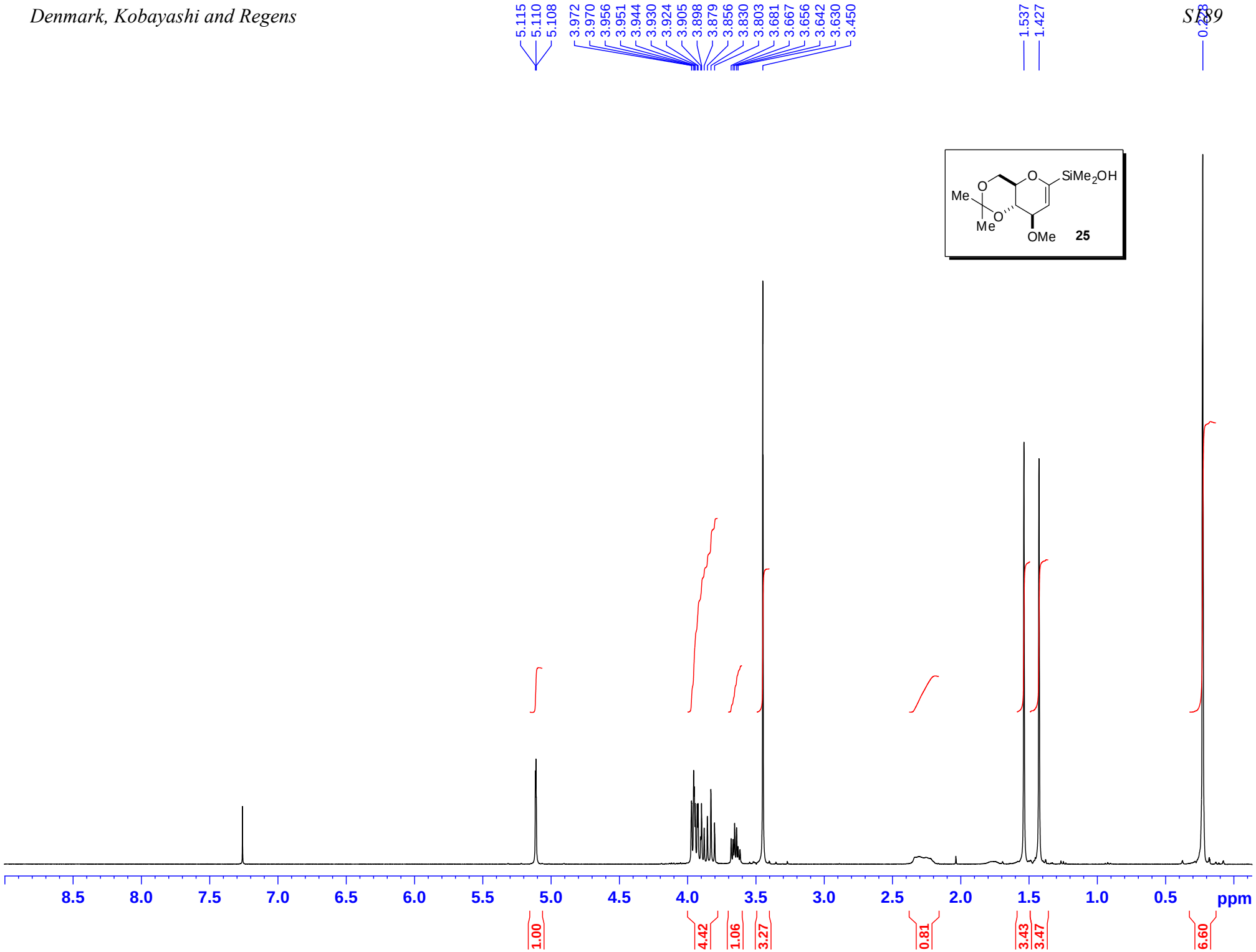
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Me
O
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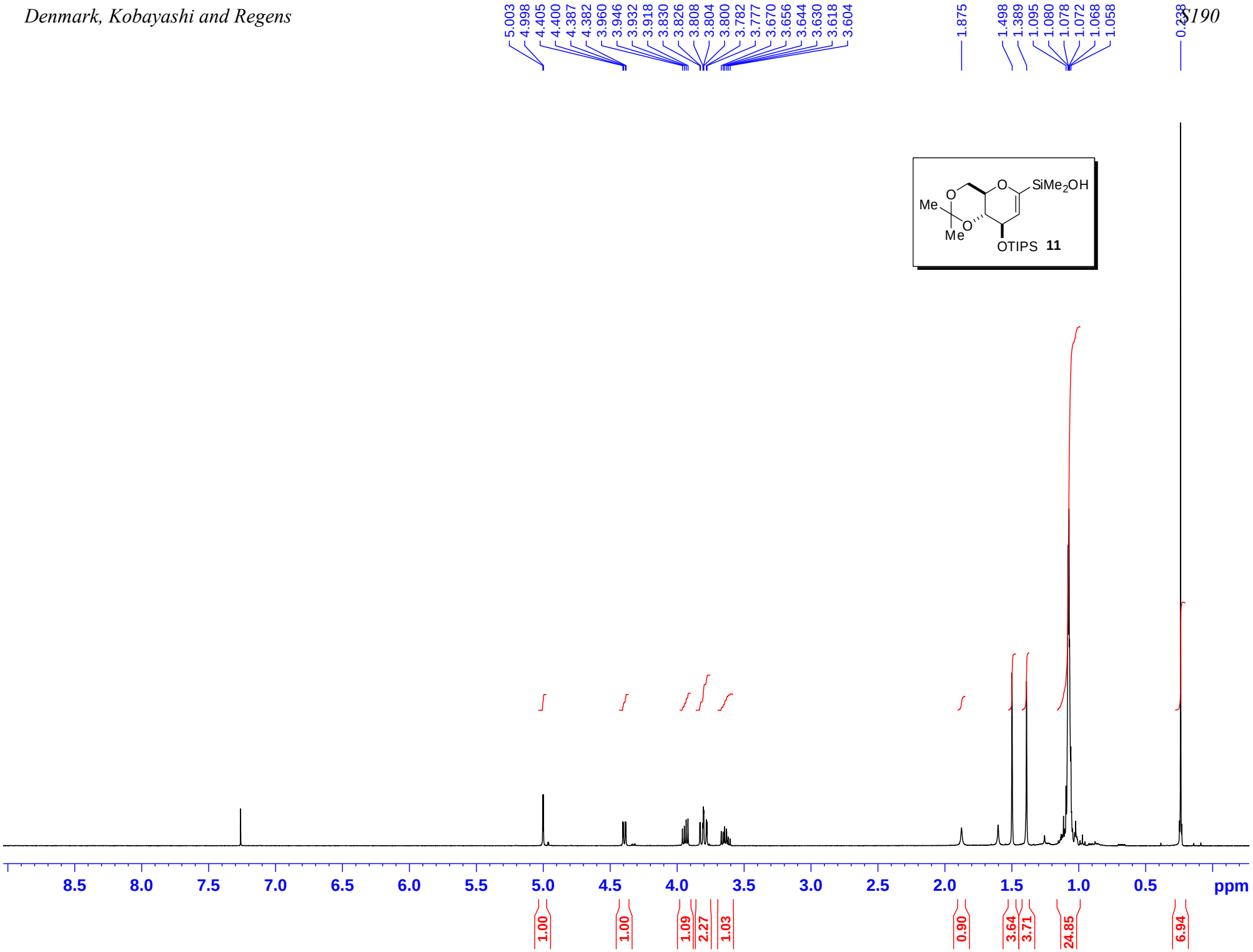
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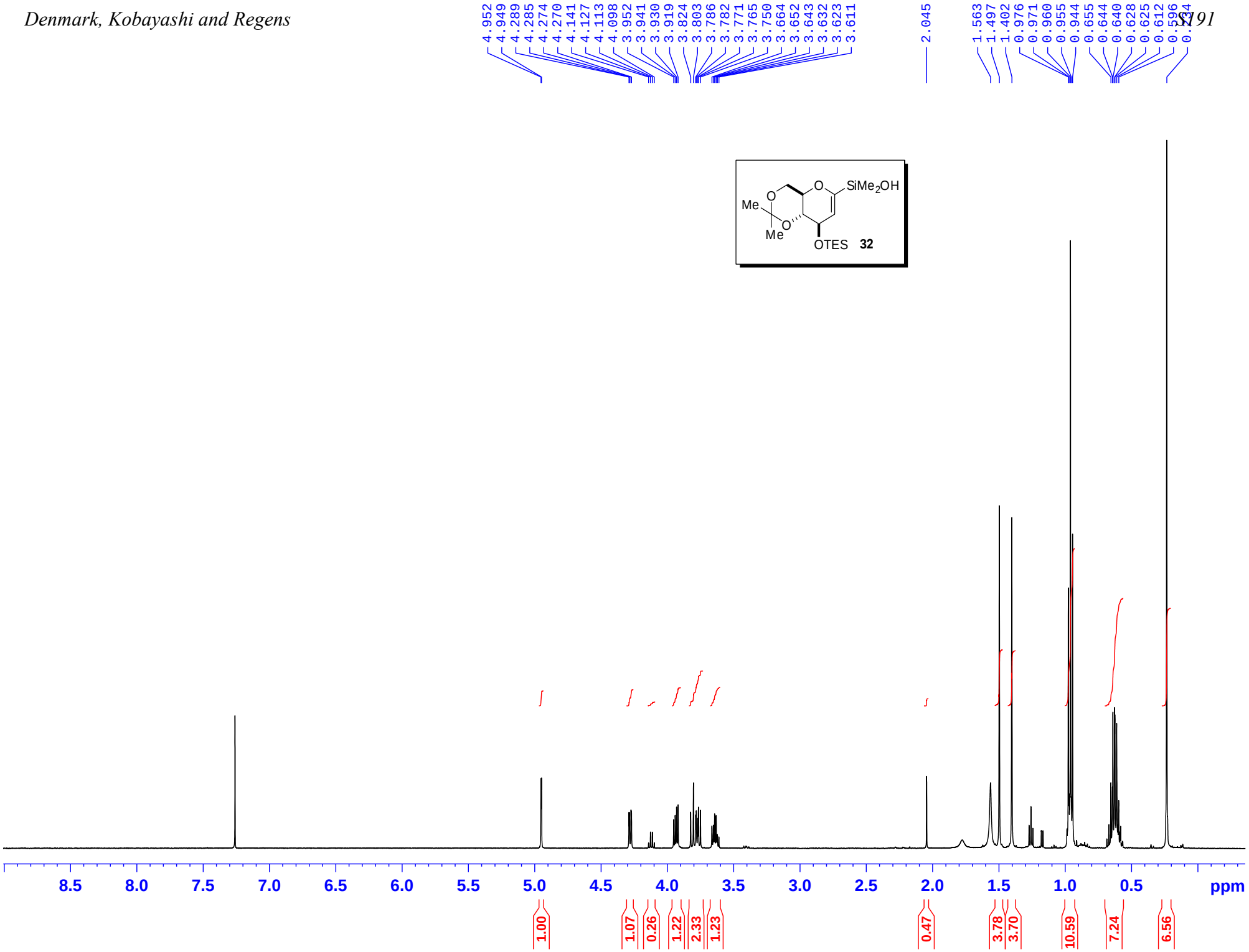
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3.643
3.632
3.623
3.611
2.045
1.563
1.497
1.402
0.976
0.971
0.960
0.955
0.944
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0.644
0.640
0.628
0.625
0.612
0.596
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Me
Me
OTES
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7.5
7.0
6.5
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5.5
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4.0
3.5
3.0
2.5
2.0
1.5
1.0
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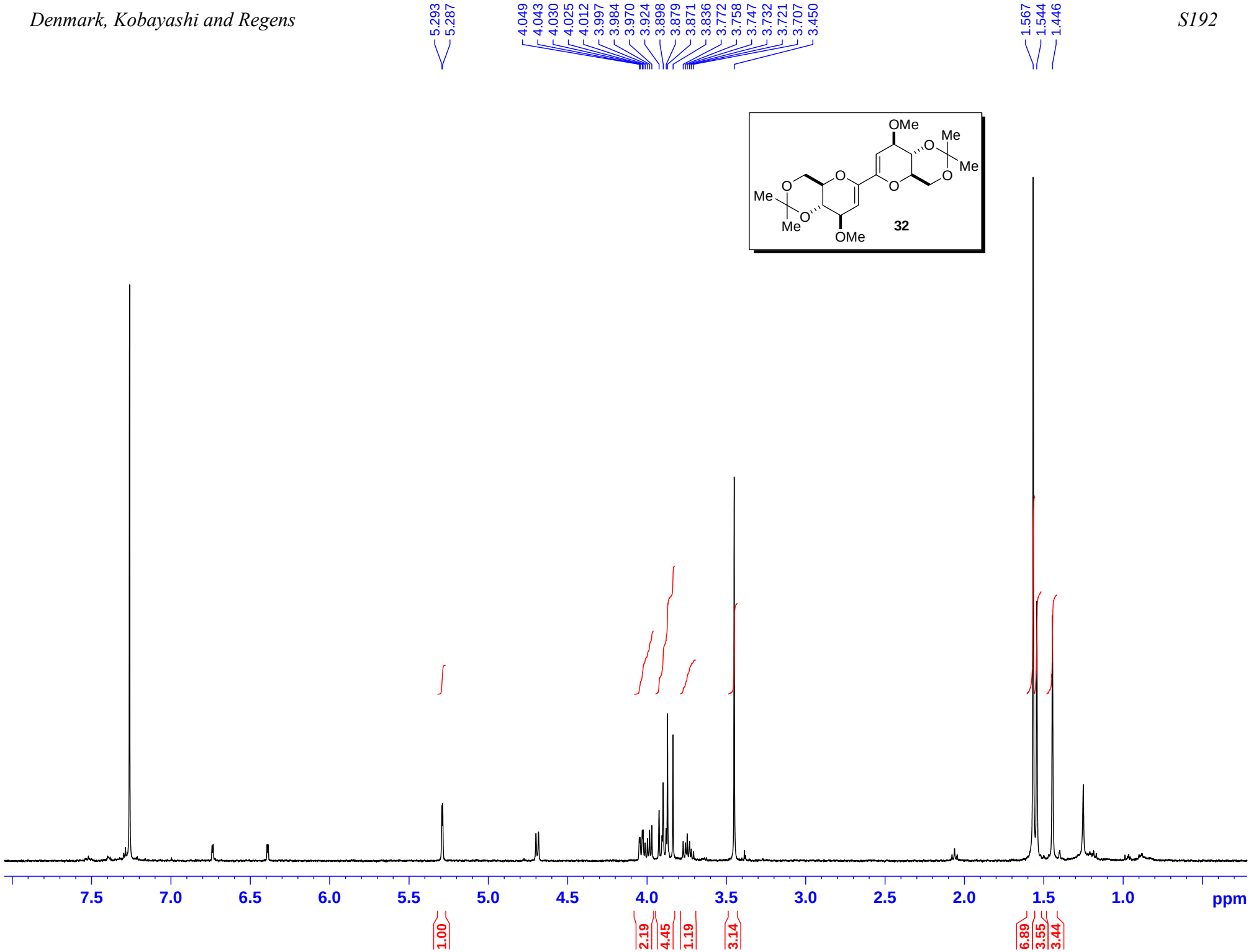
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3.732
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1.567
1.544
1.446
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Me
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O
O
Me
O
Me
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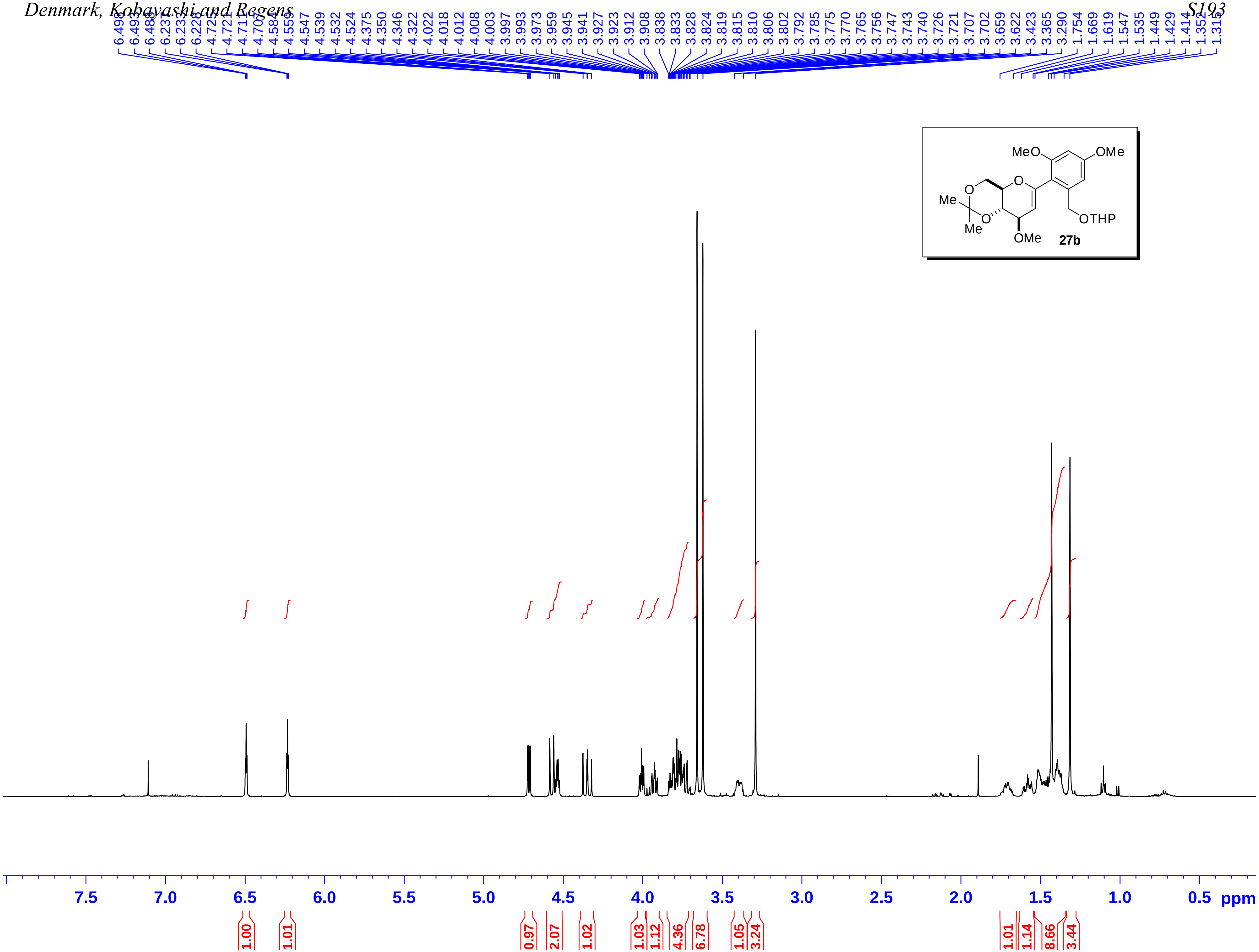
3.55
3.44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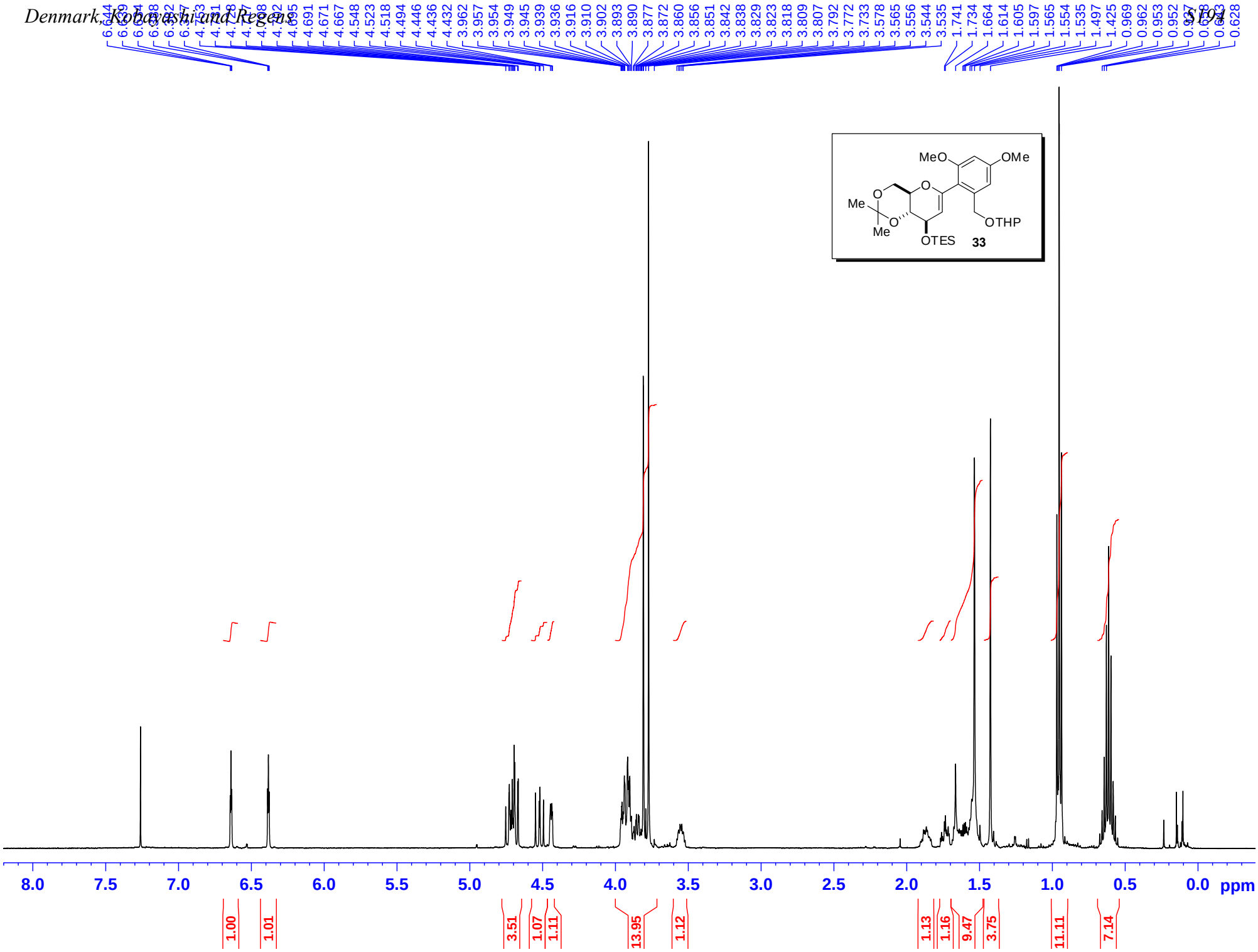
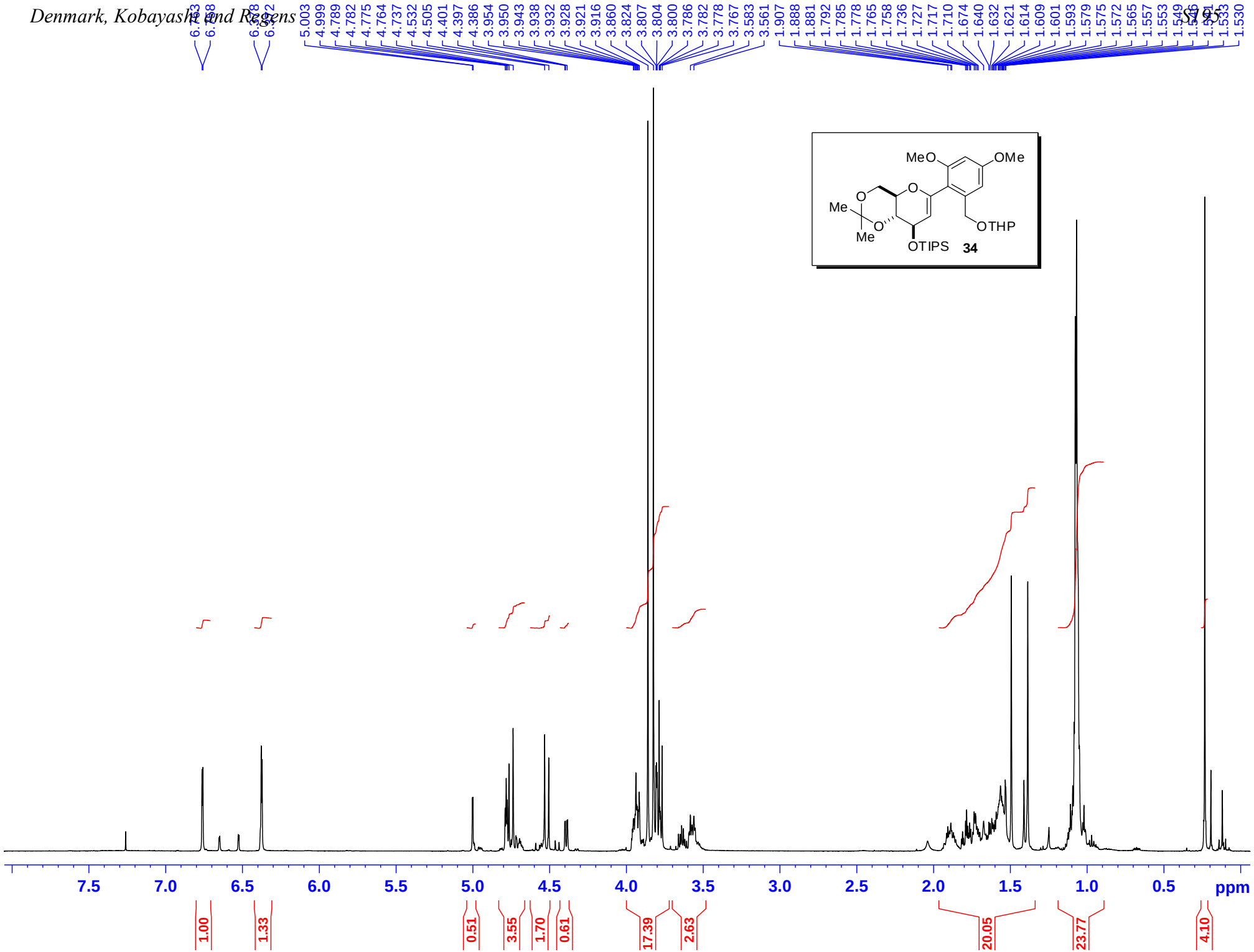
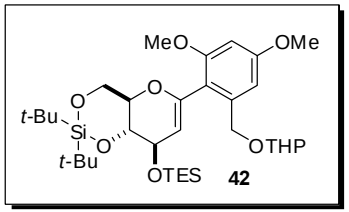
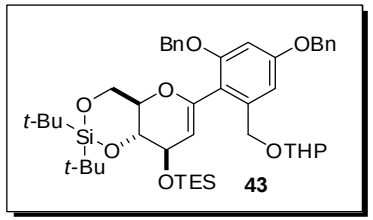
6.493
6.488
6.237
6.233
6.228
4.725
4.721
4.711
4.706
4.584
4.555
4.547
4.539
4.532
4.524
4.375
4.350
4.346
4.322
4.022
4.018
4.012
4.008
4.003
3.997
3.993
3.973
3.959
3.945
3.941
3.927
3.923
3.912
3.908
3.838
3.833
3.828
3.824
3.819
3.815
3.810
3.806
3.802
3.792
3.785
3.775
3.770
3.765
3.756
3.747
3.743
3.740
3.726
3.721
3.707
3.702
3.659
3.622
3.423
3.365
3.290
1.754
1.669
1.619
1.547
1.535
1.449
1.429
1.414
1.352
1.315
MeO
OMe
O
Me
Me
OMe
OTHP
27b
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
1.00
1.01
0.97
2.07
1.02
1.03
1.12
4.36
6.78
1.05
3.24
1.01
1.14
8.66
3.44


MeO
OMe
O
O
Me
O
Me
OTHP
OTES
33
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
1.00
1.01
3.51
1.07
1.11
13.95
1.12
1.13
1.16
9.47
3.75
11.11
7.14

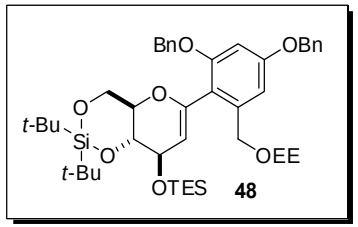

MeO
OMe
O
O
Me
O
Me
OTHP
OTIPS
34
ppm


MeO
OMe
O
O
t-Bu
Si
O
t-Bu
OTHP
OTES
42

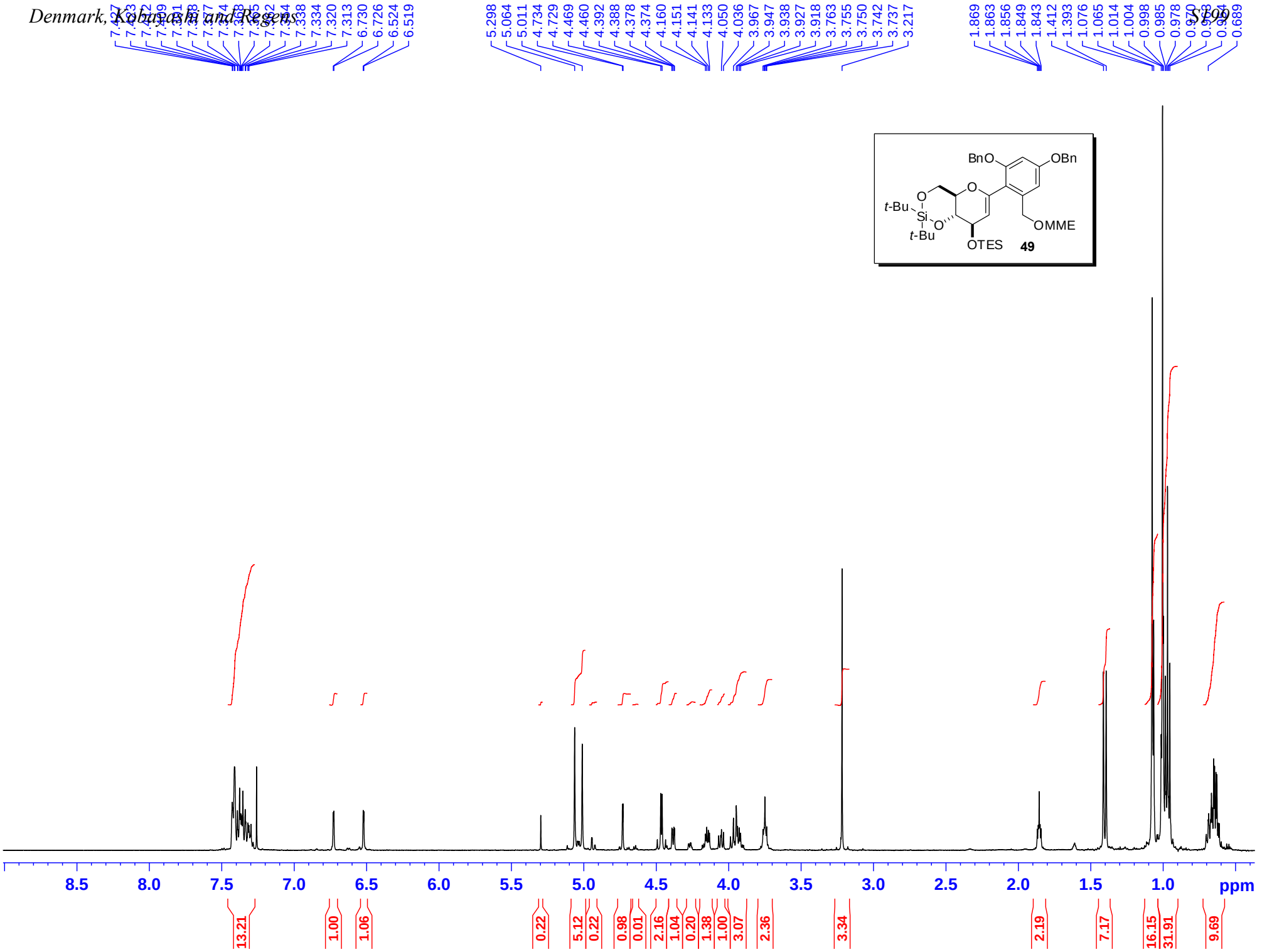
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
ppm
0.79
0.97
2.86
1.70
0.75
0.77
2.87
6.58
1.02
0.99
6.39
0.68
16.82
8.75
5.31

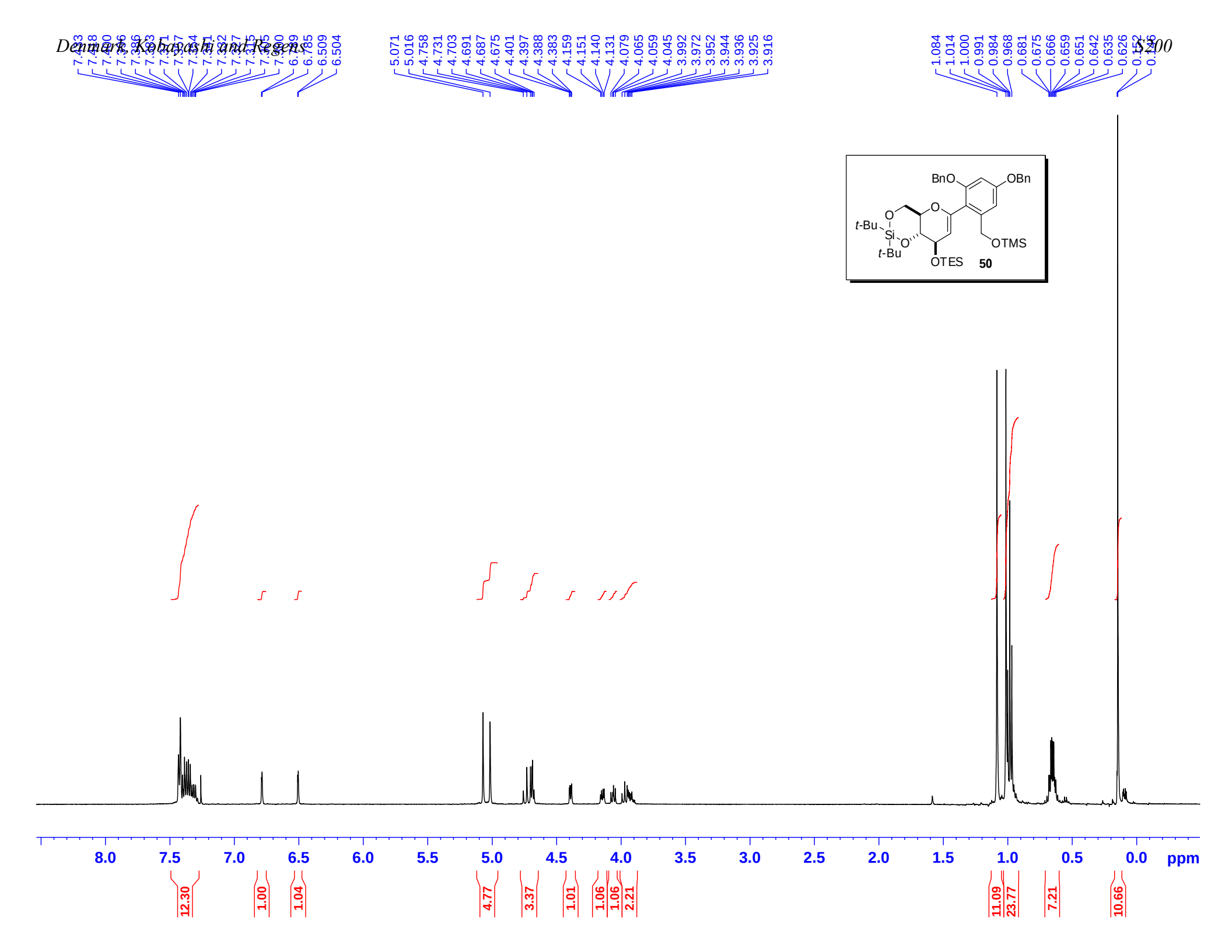

BnO
OBn
O
O
t-Bu
Si
O
t-Bu
OTHP
OTES
43

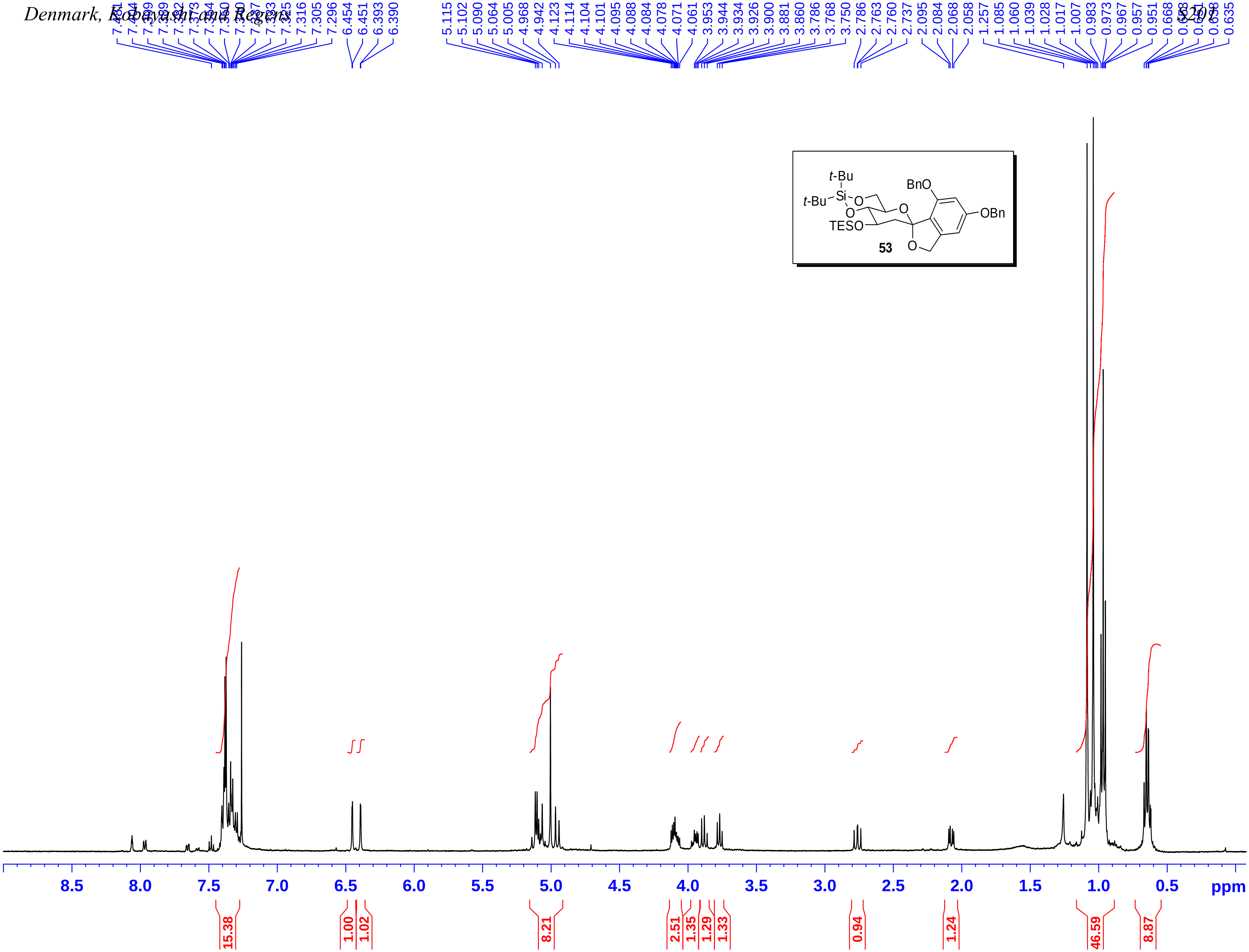
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
12.28
1.00
0.94
4.76
3.52
0.97
1.07
1.01
1.09
3.52
0.97
7.01
34.64
7.34


BnO
OBn
O
O
t-Bu
Si
O
t-Bu
OEE
OTES
48

8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
ppm
11.35
1.00
1.00
4.42
0.93
1.02
0.98
0.92
0.97
0.22
1.24
0.96
2.80
0.92
0.91
3.24
3.36
13.62
28.50
8.71


7.427
7.423
7.422
7.419
7.401
7.388
7.377
7.374
7.368
7.355
7.352
7.344
7.338
7.334
7.320
7.313
6.730
6.726
6.524
6.519
5.298
5.064
5.011
4.734
4.729
4.469
4.460
4.392
4.388
4.378
4.374
4.160
4.151
4.141
4.133
4.050
4.036
3.967
3.947
3.938
3.927
3.918
3.763
3.755
3.750
3.742
3.737
3.217
1.869
1.863
1.856
1.849
1.843
1.412
1.393
1.076
1.065
1.014
1.004
0.998
0.985
0.978
0.970
0.938
0.924
0.689
BnO
OBn
O
O
t-Bu
Si
O
t-Bu
OMME
OTES
49
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
ppm
13.21
1.00
1.06
0.22
5.12
0.22
0.98
0.01
2.16
1.04
0.20
1.38
1.00
3.07
2.36
3.34
2.19
7.17
16.15
31.91
9.69


BnO
OBn
O
O
t-Bu
Si
O
t-Bu
OTMS
OTES
50
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
12.30
1.00
1.04
4.77
3.37
1.01
1.06
1.06
2.21
11.09
23.77
7.21
10.66



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7.296
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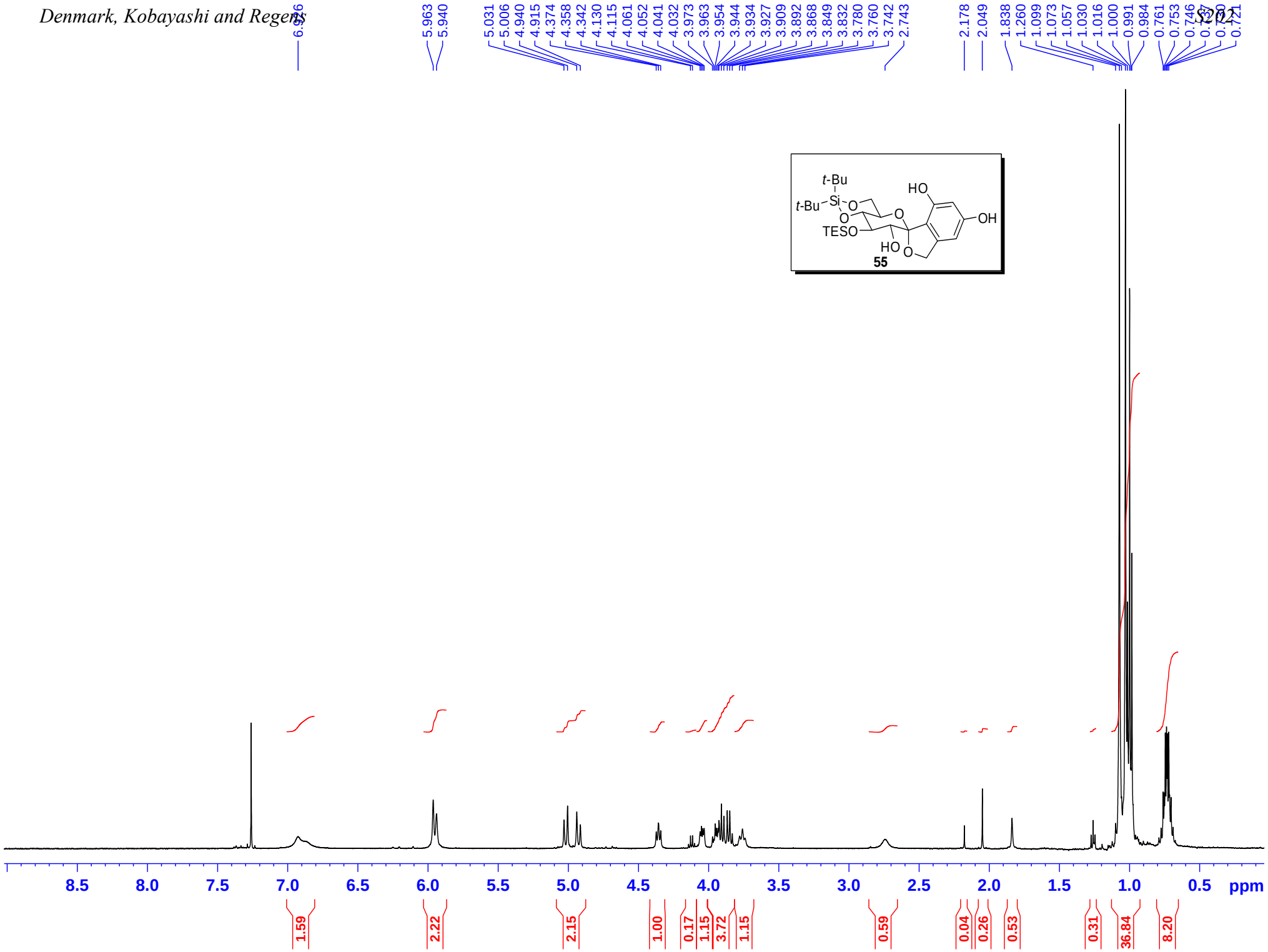
6.451
6.393
6.390
5.115
5.102
5.090
5.064
5.005
4.968
4.942
4.123
4.114
4.104
4.101
4.095
4.088
4.084
4.078
4.071
4.061
3.953
3.944
3.934
3.926
3.900
3.881
3.860
3.786
3.768
3.750
2.786
2.763
2.760
2.737
2.095
2.084
2.068
2.058
1.257
1.085
1.060
1.039
1.028
1.017
1.007
0.983
0.973
0.967
0.957
0.951
0.668
0.635
t-Bu
t-Bu
Si
O
O
O
TESO
BnO
OBn
O
53
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
15.38
1.00
1.02
8.21
2.51
1.35
1.29
1.33
0.94
1.24
46.59
8.87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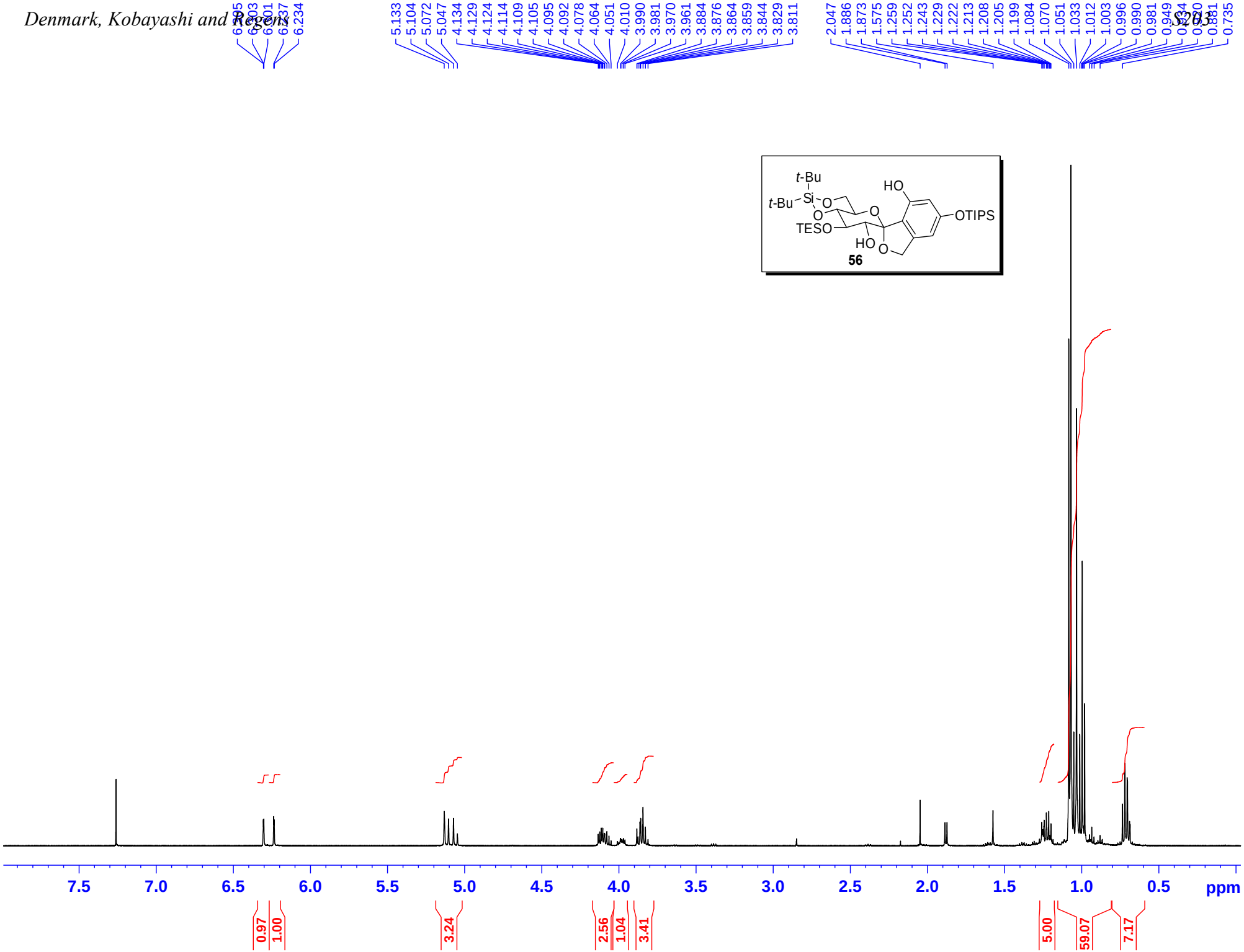
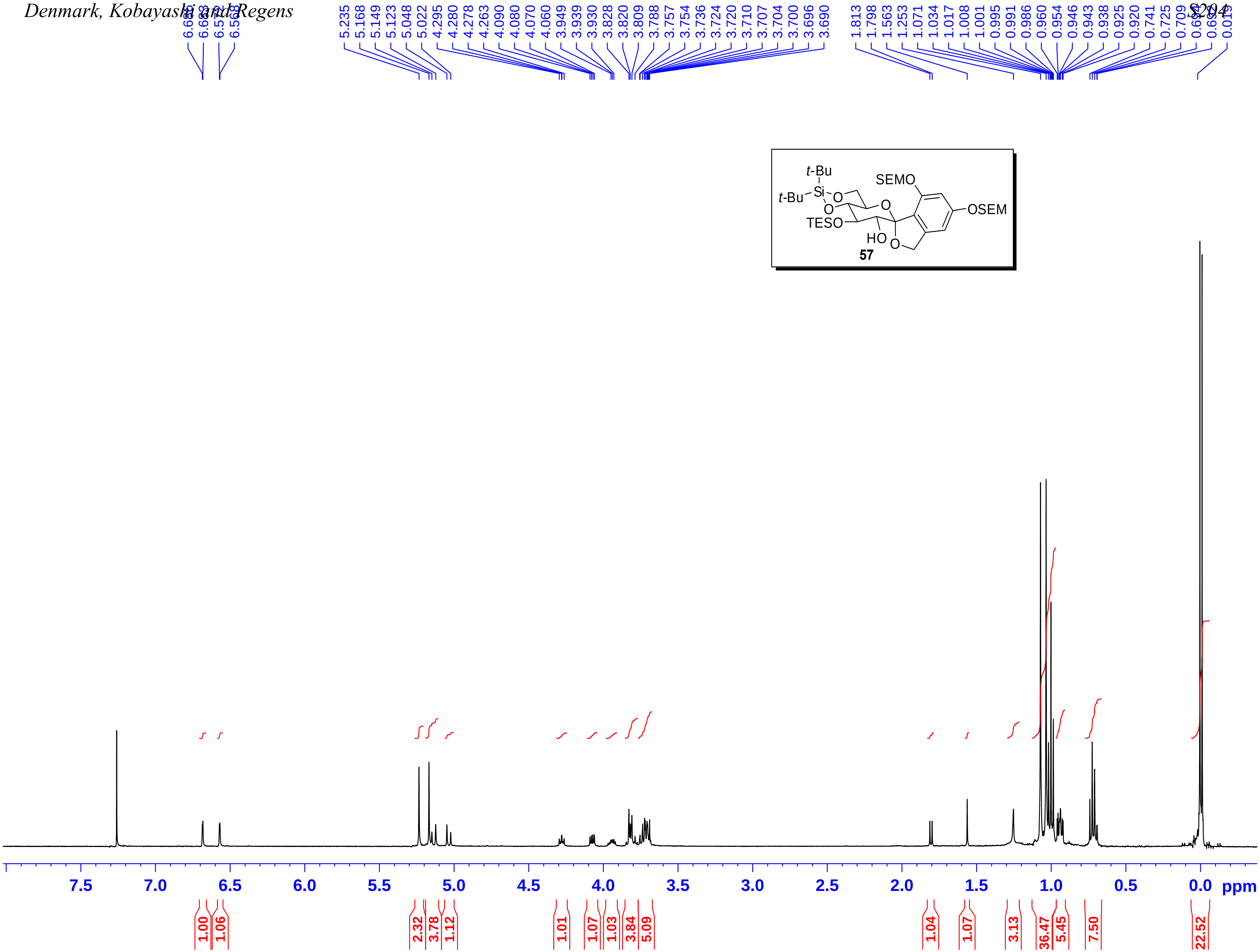
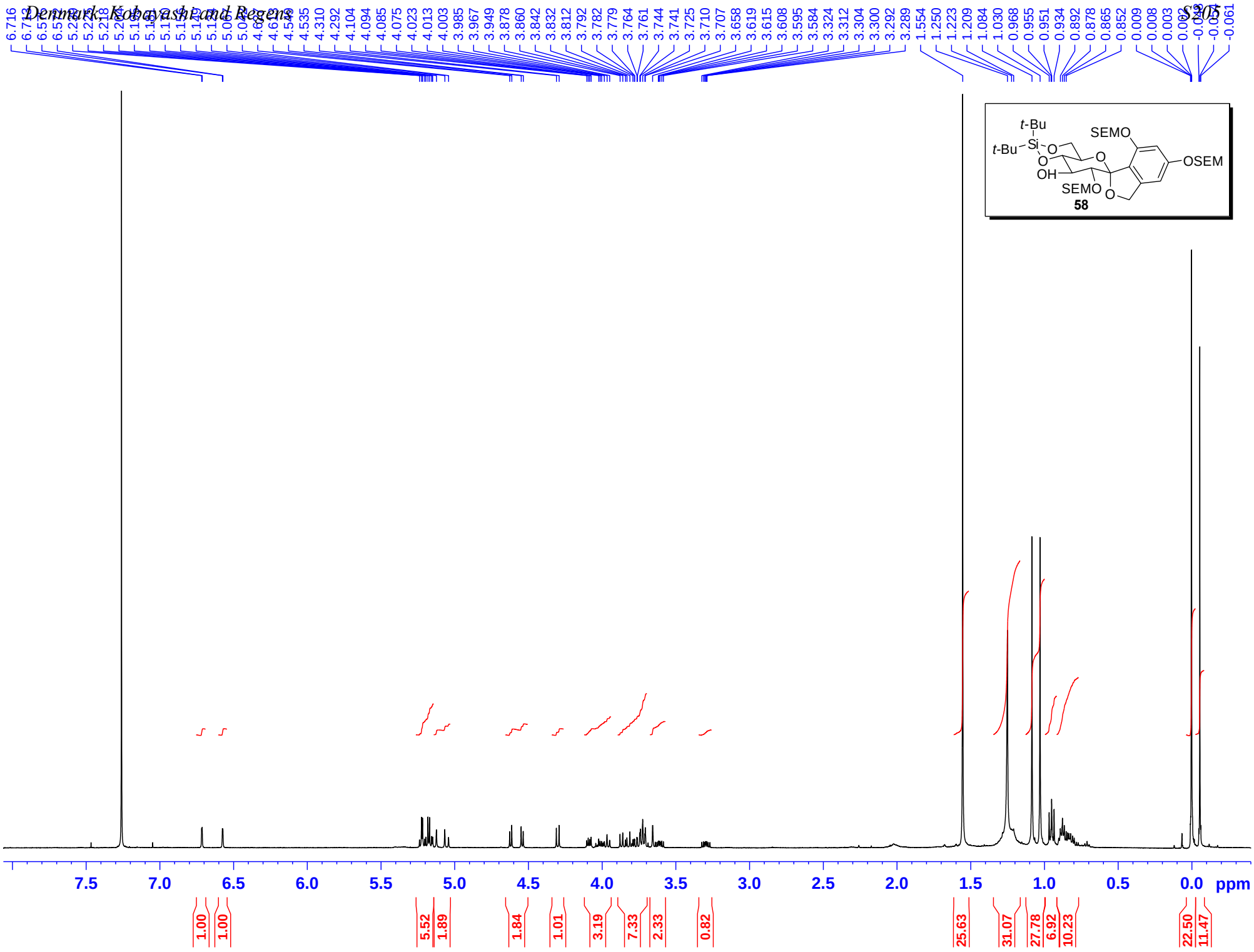
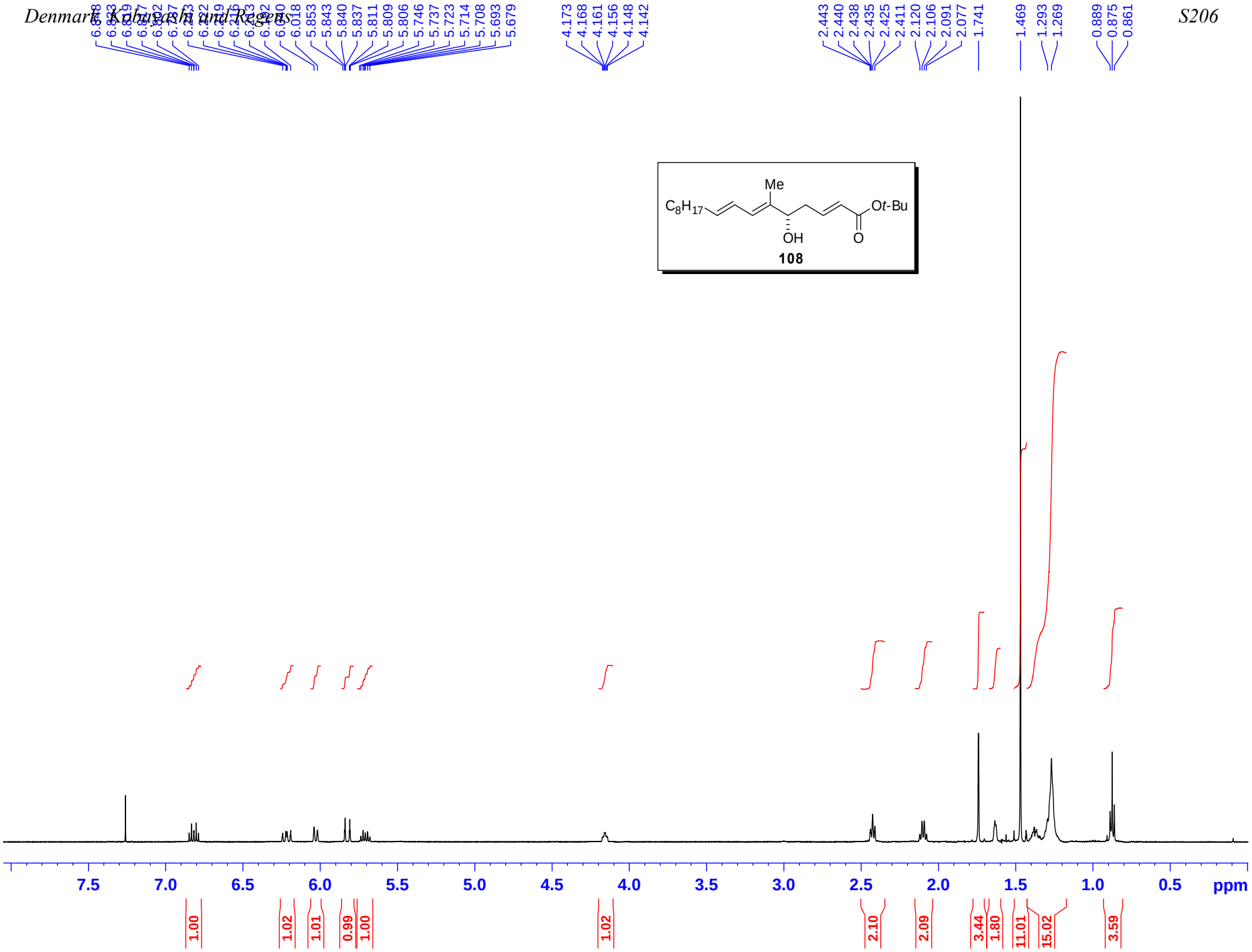
5.963
5.940
5.031
5.006
4.940
4.915
4.374
4.358
4.342
4.130
4.115
4.061
4.052
4.041
4.032
3.973
3.963
3.954
3.944
3.934
3.927
3.909
3.892
3.868
3.849
3.832
3.780
3.760
3.742
2.743
2.178
2.049
1.838
1.260
1.099
1.073
1.057
1.030
1.016
1.000
0.991
0.984
0.761
0.753
0.746
0.730
0.721
t-Bu
t-Bu
Si
O
O
TESO
O
HO
HO
O
OH
55
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
1.59
2.22
2.15
1.00
0.17
1.15
3.72
1.15
0.59
0.04
0.26
0.53
0.31
36.84
8.20


6.235
6.203
6.201
6.137
6.234
5.133
5.104
5.072
5.047
4.134
4.129
4.124
4.114
4.109
4.105
4.095
4.092
4.078
4.064
4.051
4.010
3.990
3.981
3.970
3.961
3.884
3.876
3.864
3.859
3.844
3.829
3.811
2.047
1.886
1.873
1.575
1.259
1.252
1.243
1.229
1.222
1.213
1.208
1.205
1.199
1.084
1.070
1.051
1.033
1.012
1.003
0.996
0.990
0.981
0.949
0.934
0.920
0.881
0.735
t-Bu
t-Bu
Si
O
O
O
TESO
HO
HO
O
OTIPS
56
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
0.97
1.00
3.24
2.56
1.04
3.41
5.00
59.07
7.17


t-Bu
t-Bu
Si
O
O
TESO
SEMO
OSEM
HO
O
O
57
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
1.00
1.06
2.32
3.78
1.12
1.01
1.07
1.03
3.84
5.09
1.04
1.07
3.13
36.47
5.45
7.50
22.52


t-Bu
t-Bu
Si
O
O
O
OH
SEMO
SEMO
O
OSEM
58
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
1.00
1.00
5.52
1.89
1.84
1.01
3.19
7.33
2.33
0.82
25.63
31.07
27.78
6.92
10.23
22.50
11.47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6.823
6.819
6.817
6.812
6.807
6.803
6.792
6.789
6.779
6.773
6.762
6.760
6.018
5.853
5.843
5.840
5.837
5.811
5.809
5.806
5.746
5.737
5.723
5.714
5.708
5.693
5.679
4.173
4.168
4.161
4.156
4.148
4.142
2.443
2.440
2.438
2.435
2.425
2.411
2.120
2.106
2.091
2.077
1.741
1.469
1.293
1.269
0.889
0.875
0.861
Me
C8H17
Ot-Bu
OH
O
108
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
1.00
1.02
1.01
0.99
1.00
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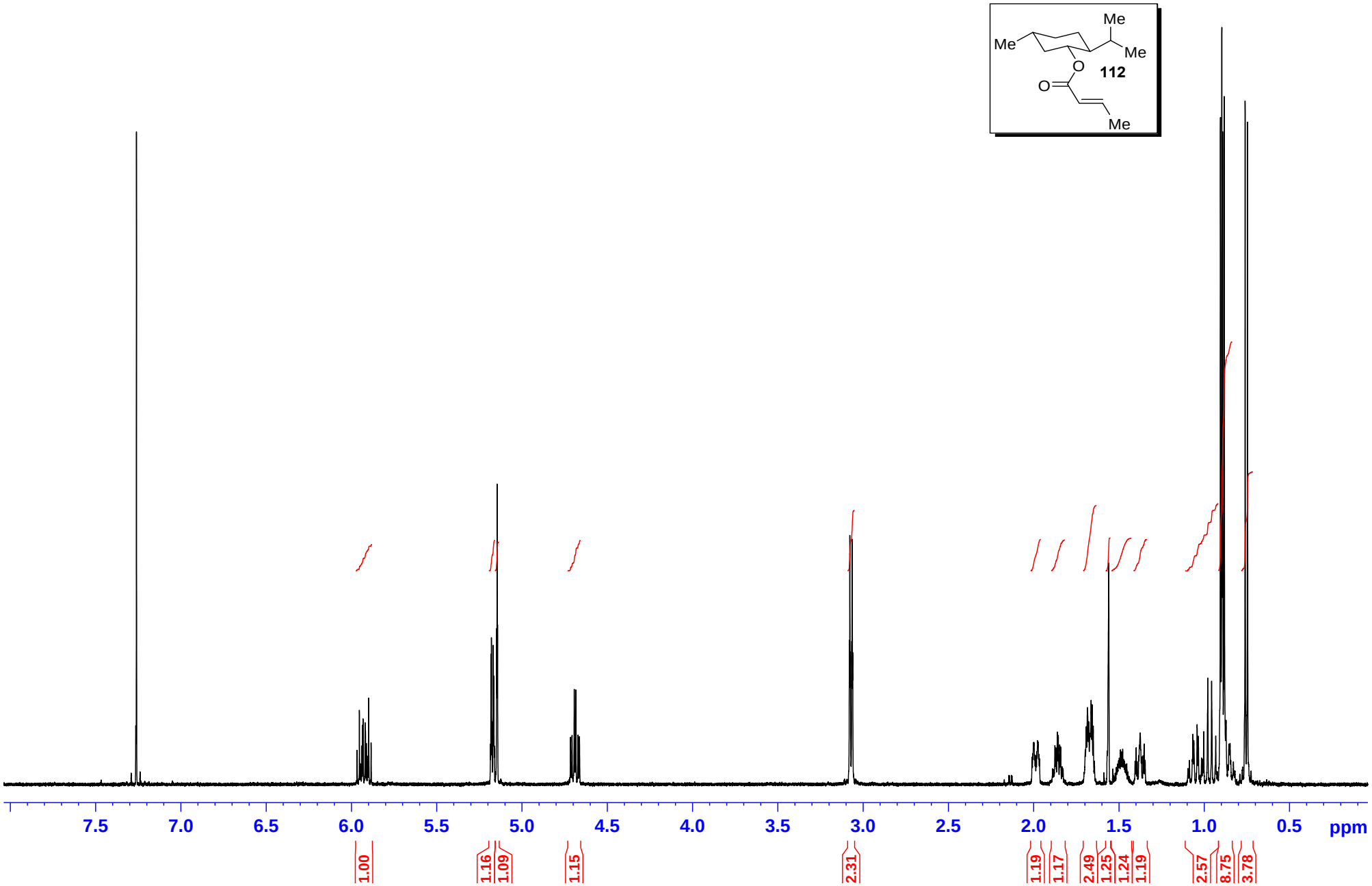
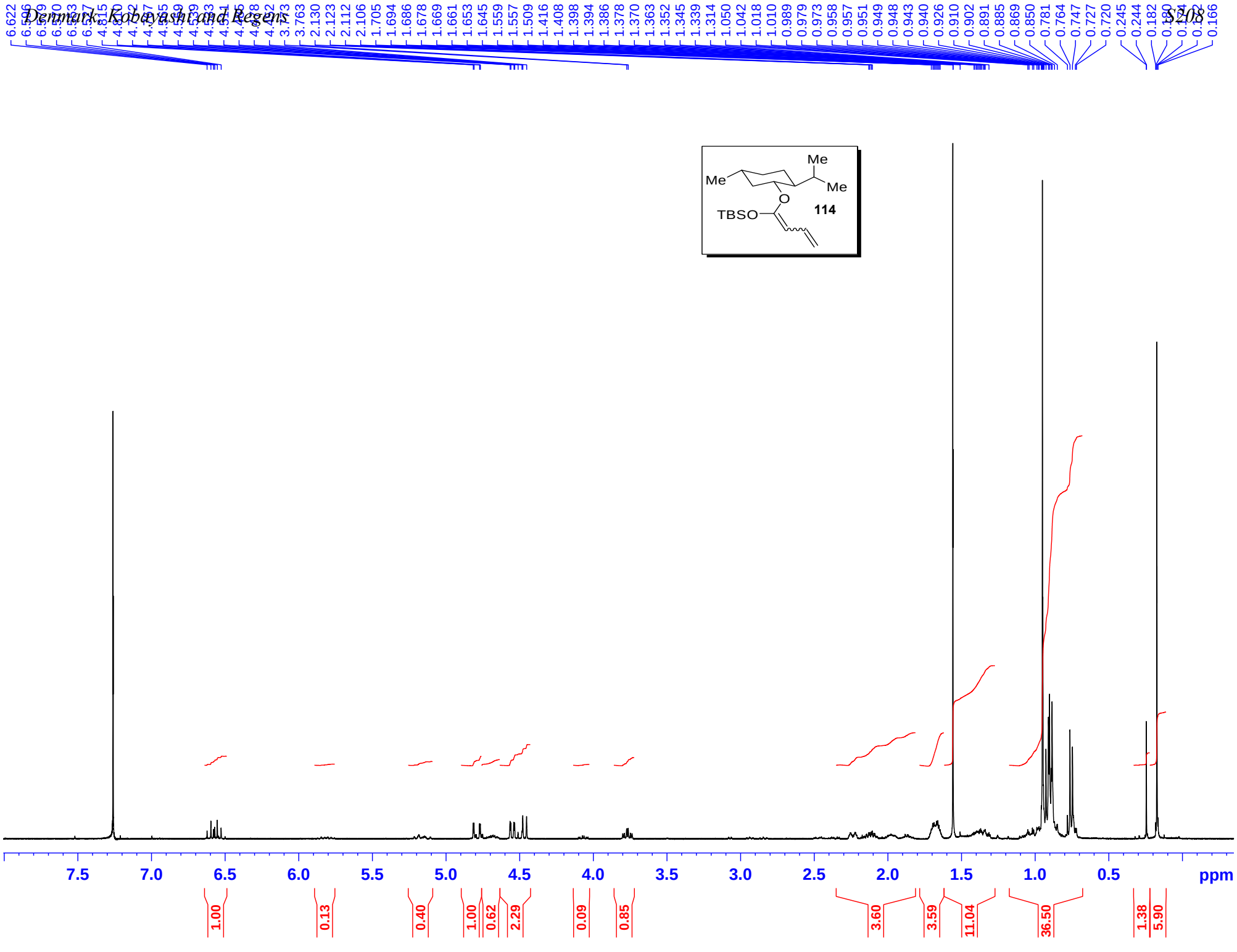
2.10
2.09
3.44
1.80
11.01
15.02
3.59


Me
Me
Me
O
O
112
Me
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
1.00
1.16
1.09
1.15
2.31
1.19
1.17
2.49
1.25
1.24
1.19
2.57
8.75
3.78


Me
Me
Me
O
TBSO
114
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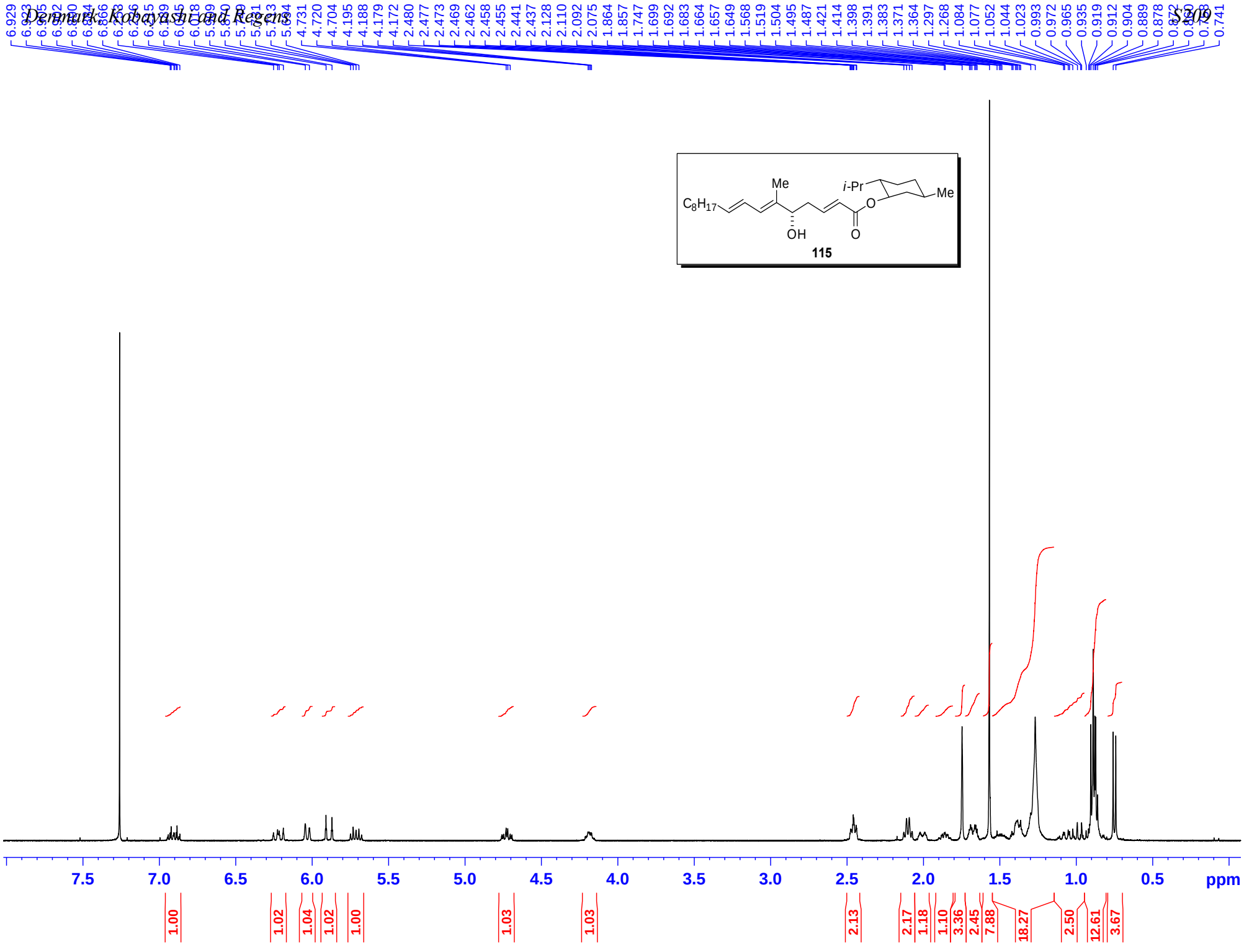
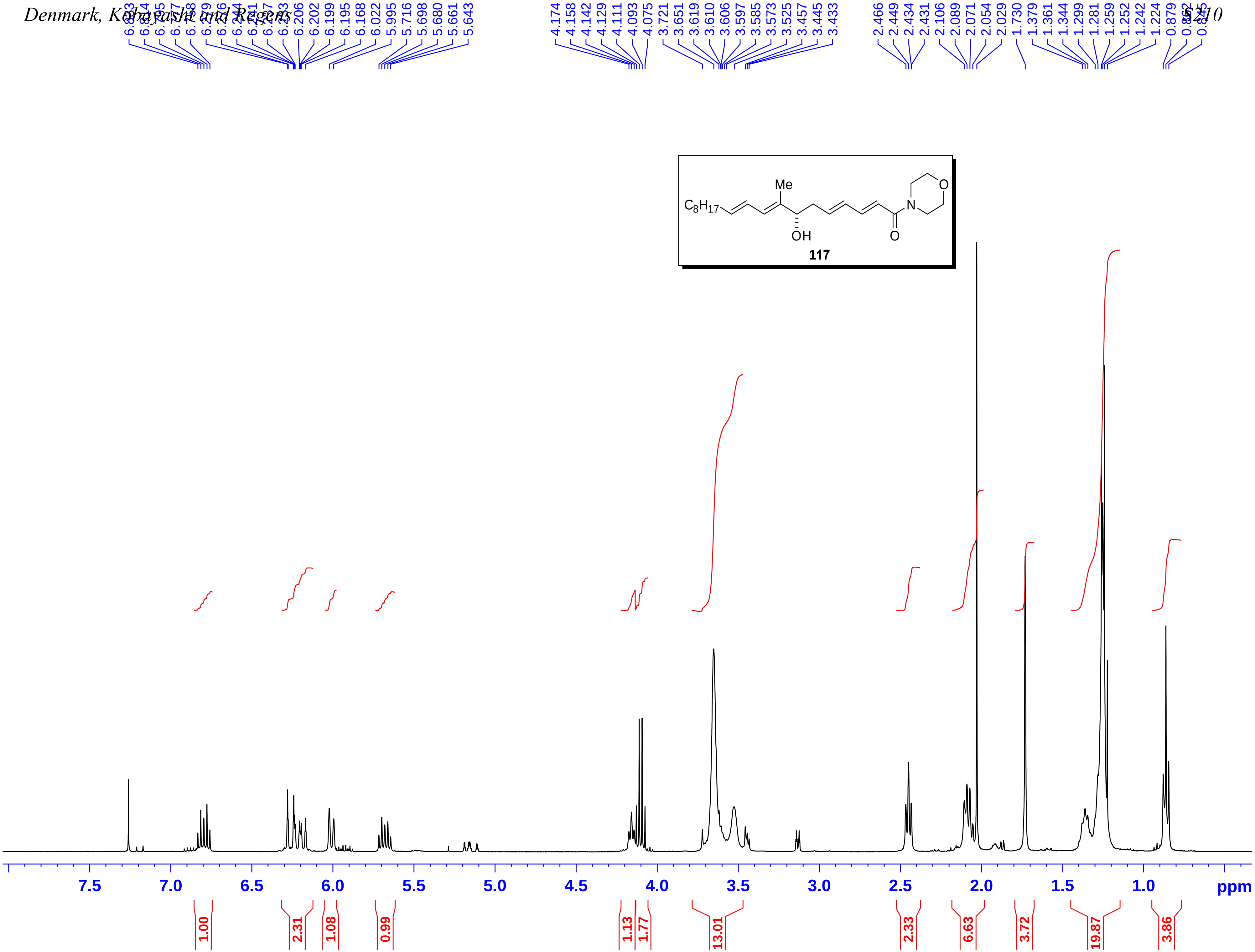
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
1.00
0.13
0.40
1.00
0.62
2.29
0.09
0.85
3.60
3.59
11.04
36.50
1.38
5.90


Me
i-Pr
C8H17
O
Me
OH
O
115
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
1.00
1.02
1.04
1.02
1.00
1.03
1.03
2.13
2.17
1.18
1.10
3.36
2.45
7.88
18.27
2.50
12.61
3.67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6.168
6.022
5.995
5.716
5.698
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5.661
5.643
4.174
4.158
4.142
4.129
4.111
4.093
4.075
3.721
3.651
3.619
3.610
3.606
3.597
3.585
3.573
3.525
3.457
3.445
3.433
2.466
2.449
2.434
2.431
2.106
2.089
2.071
2.054
2.029
1.730
1.379
1.361
1.344
1.299
1.281
1.259
1.252
1.242
1.224
0.879
Me
C_8H_{17}
OH
O
N
117
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
ppm
1.00
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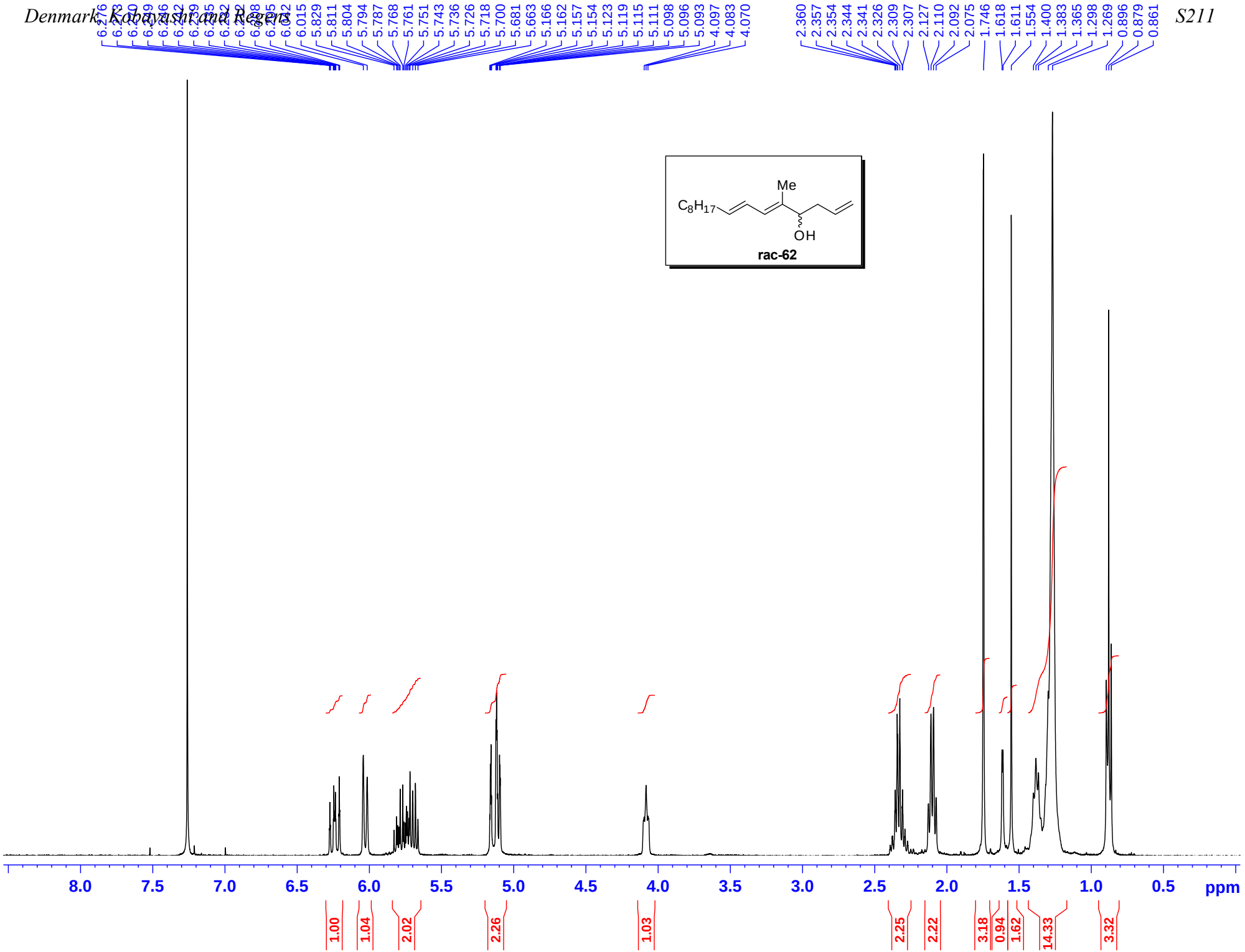
1.08
0.99
1.13
1.77
13.01
2.33
6.63
3.72
19.87
3.86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6.269
6.266
6.262
6.259
6.255
6.252
6.248
6.245
6.242
6.015
5.829
5.811
5.804
5.794
5.787
5.768
5.761
5.751
5.743
5.736
5.726
5.718
5.700
5.681
5.663
5.166
5.162
5.157
5.154
5.123
5.119
5.115
5.111
5.098
5.096
5.093
4.097
4.083
4.070
2.360
2.357
2.354
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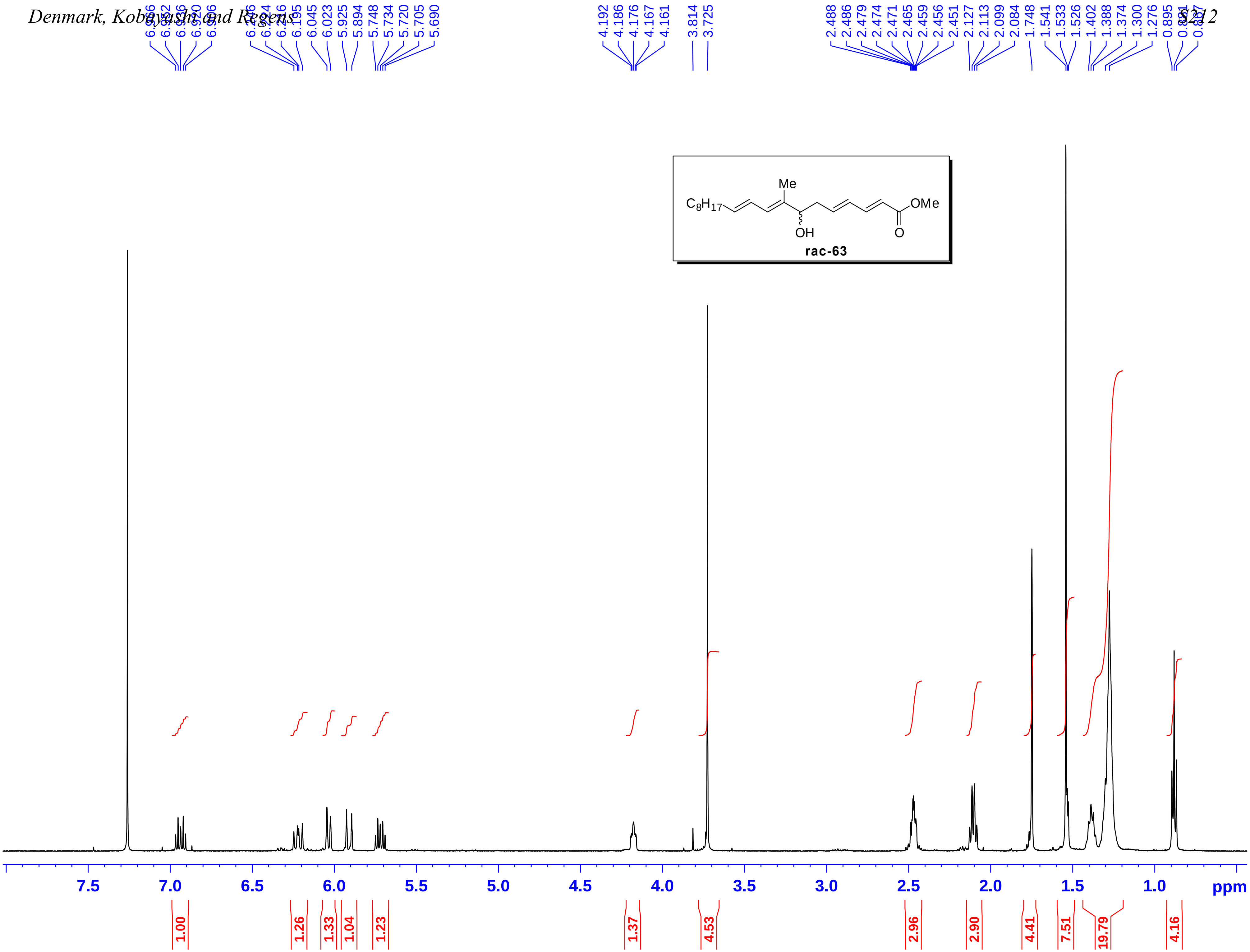
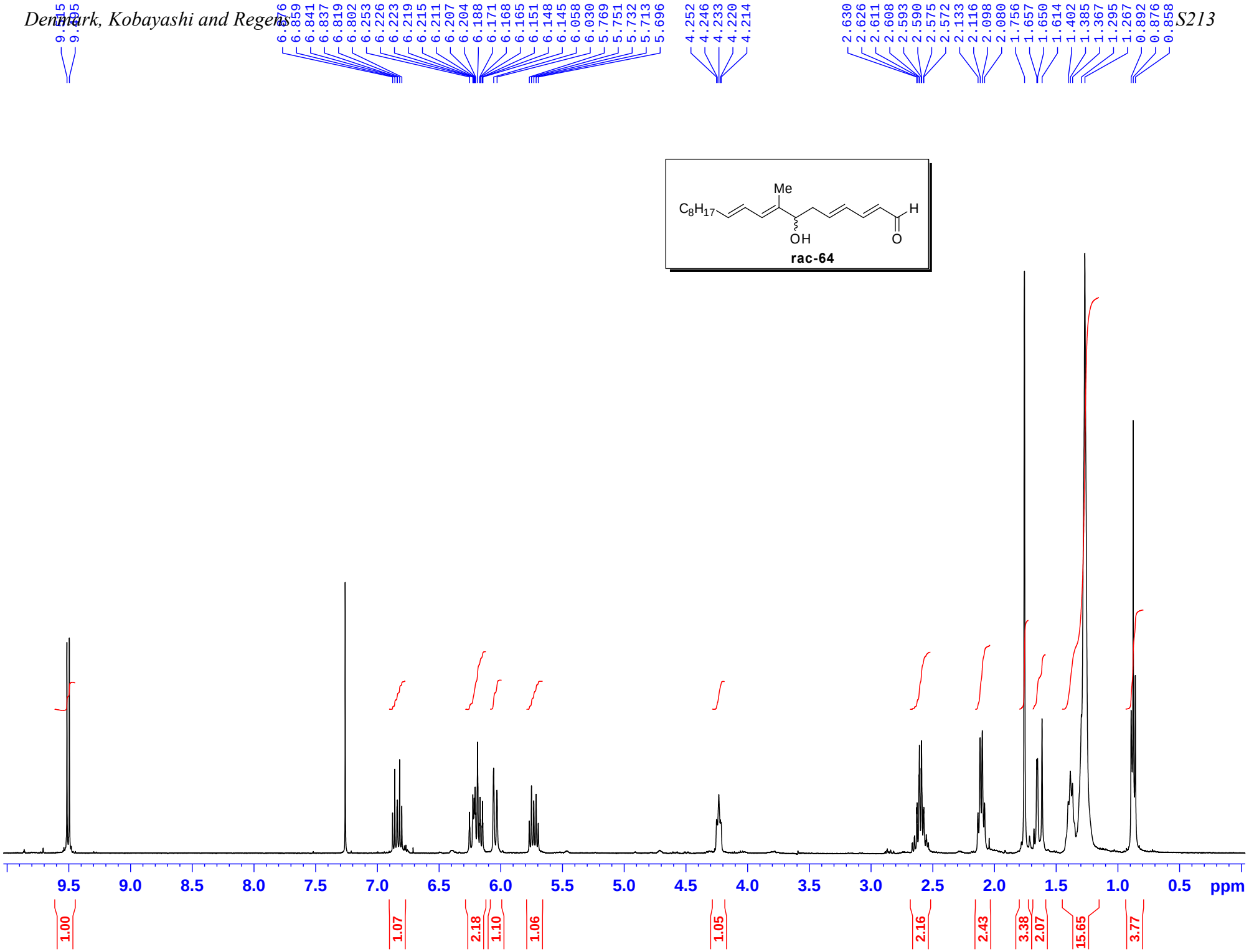
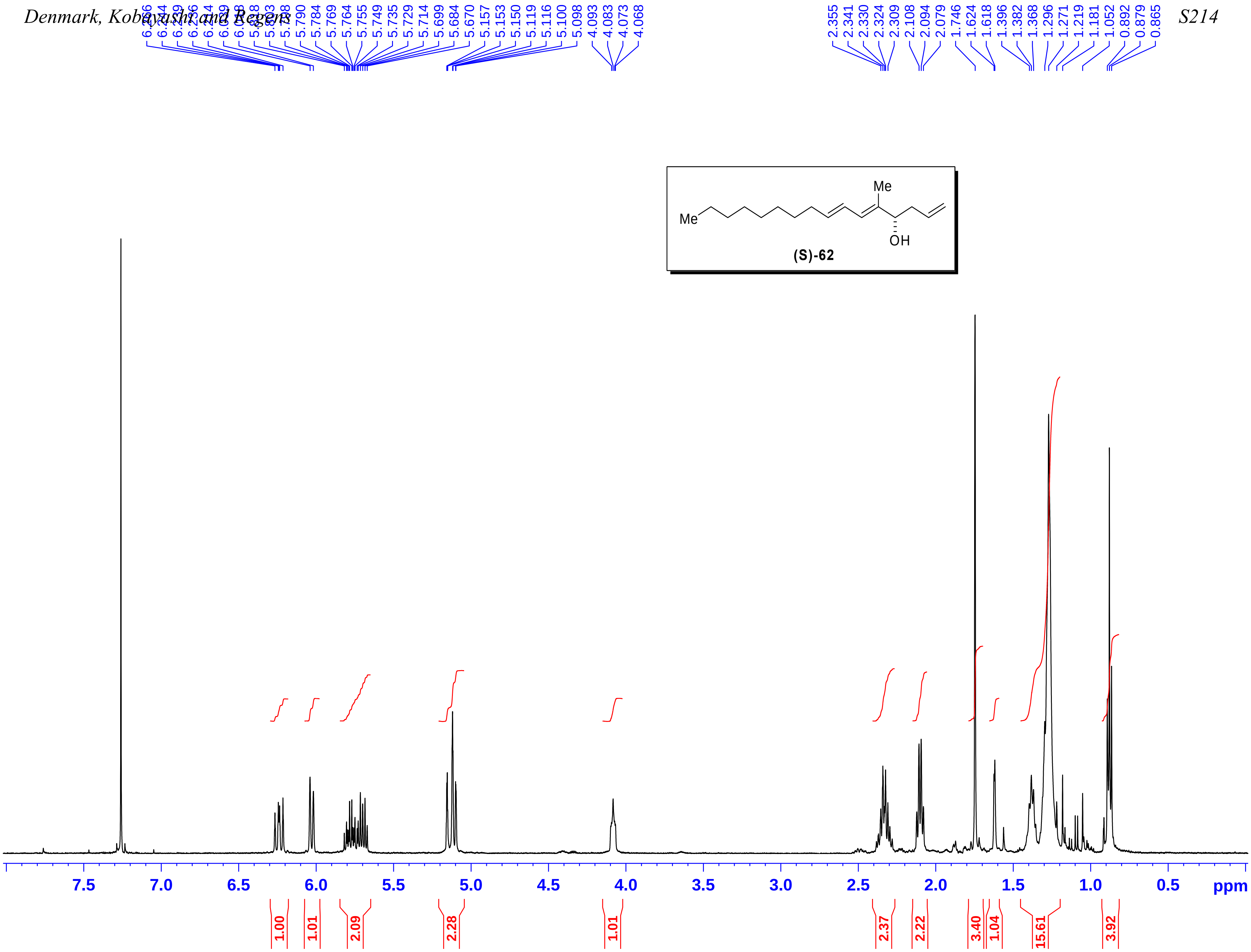
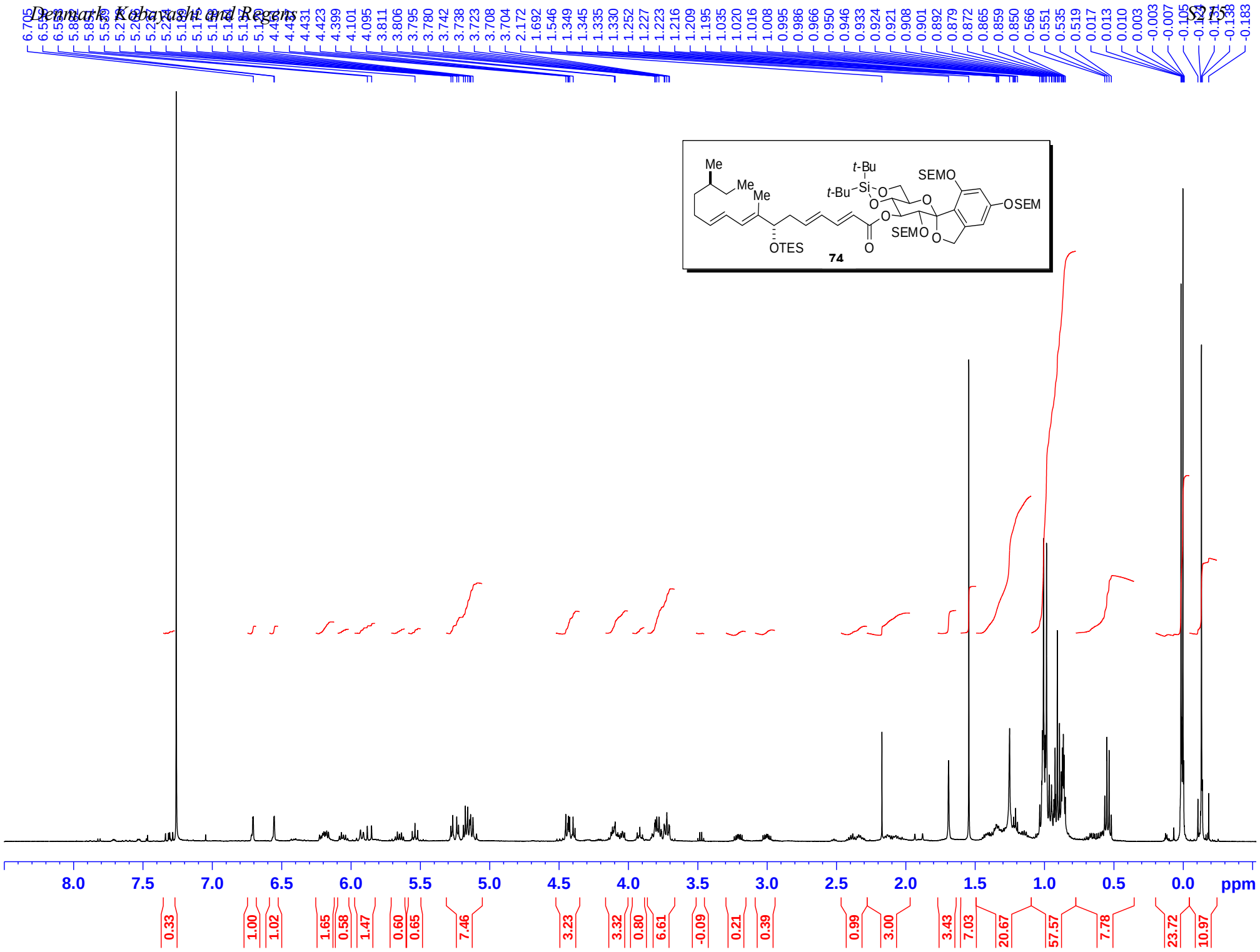
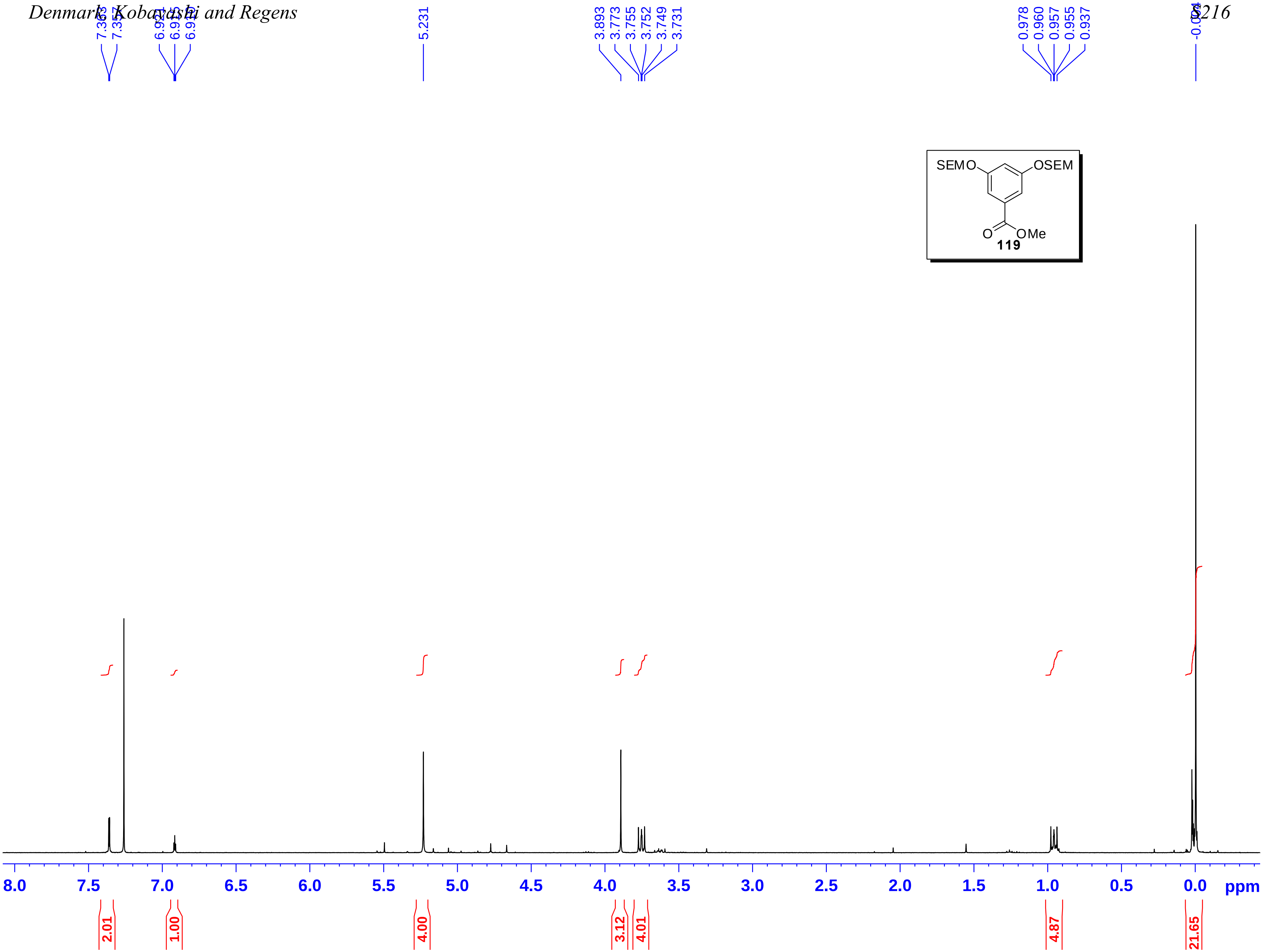
2.341
2.326
2.309
2.307
2.127
2.110
2.092
2.075
1.746
1.618
1.611
1.554
1.400
1.383
1.365
1.298
1.269
0.896
0.879
0.861
Me
C8H17
OH
rac-62
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
1.00
1.04
2.02
2.26
1.03
2.25
2.22
3.18
0.94
1.62
14.33
3.32

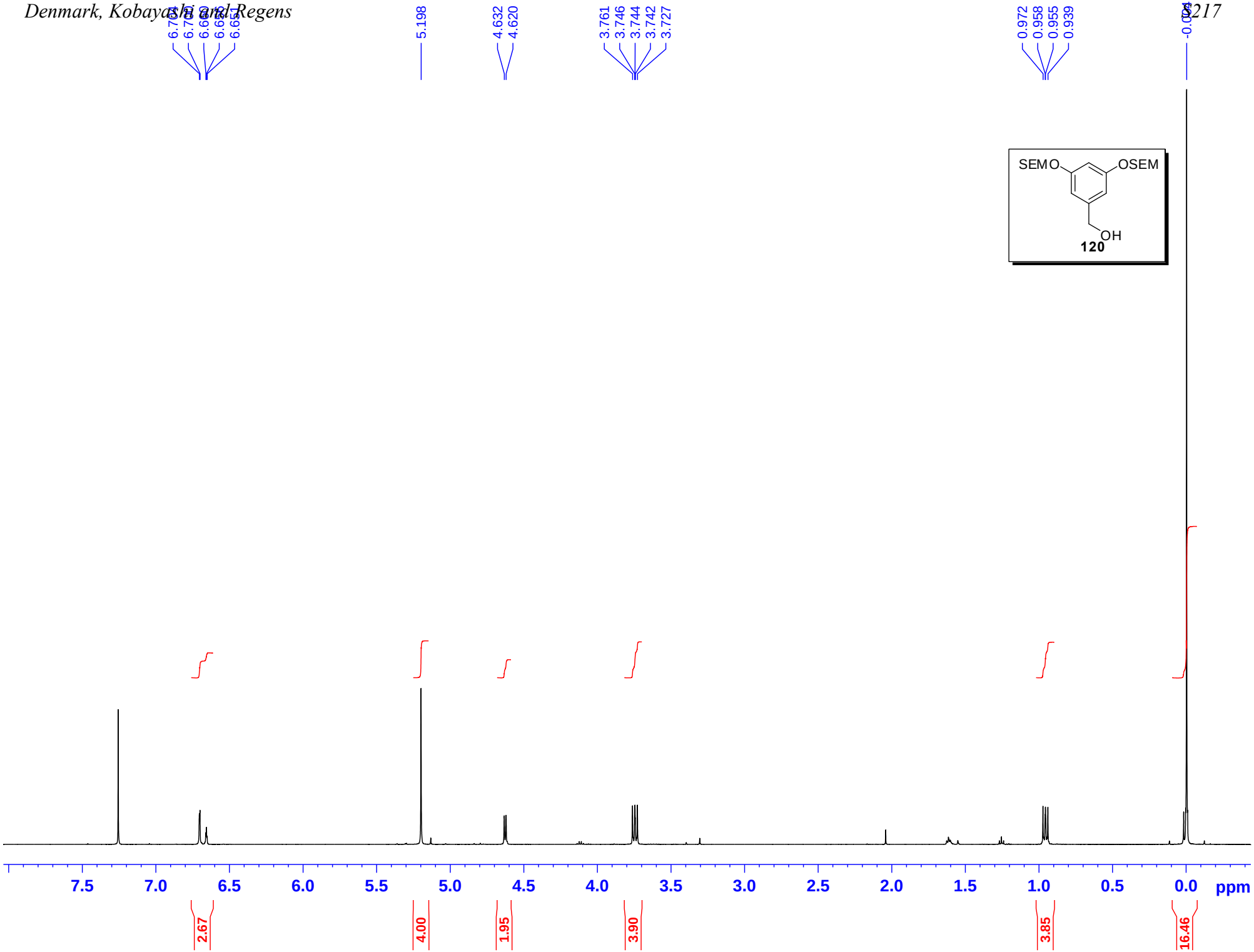

6.246
6.224
6.216
6.195
6.045
6.023
5.925
5.894
5.748
5.734
5.720
5.705
5.690
4.192
4.186
4.176
4.167
4.161
3.814
3.725
2.488
2.486
2.479
2.474
2.471
2.465
2.459
2.456
2.451
2.127
2.113
2.099
2.084
1.748
1.541
1.533
1.526
1.402
1.388
1.374
1.300
1.276
0.895
Me
C_8H_{17}
OMe
OH
O
rac-63
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
ppm
1.00
1.26
1.33
1.04
1.23
1.37
4.53
2.96
2.90
4.41
7.51
19.79
4.16

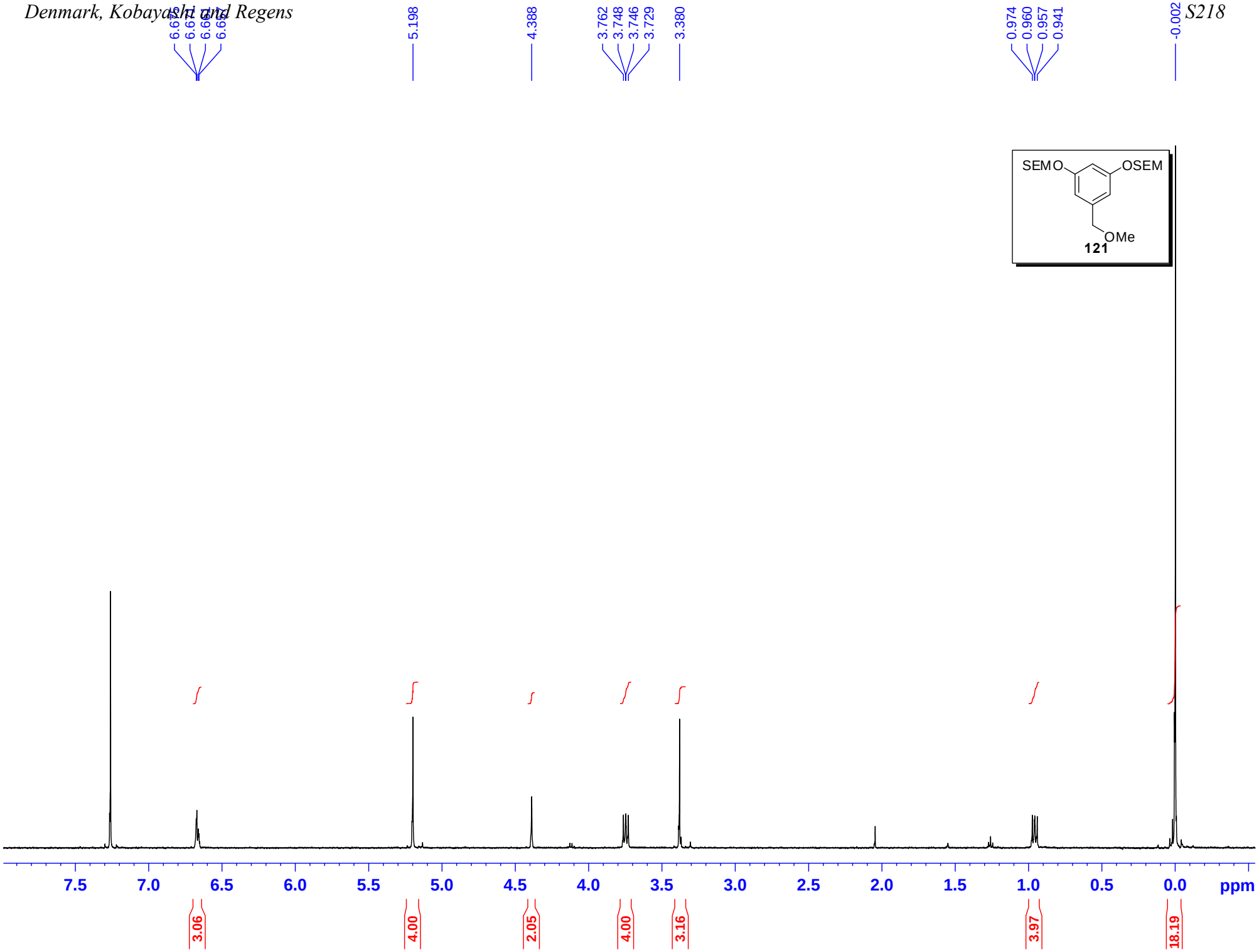

9.495
9.475
6.876
6.859
6.841
6.837
6.819
6.802
6.253
6.226
6.223
6.219
6.215
6.211
6.207
6.204
6.188
6.171
6.168
6.165
6.151
6.148
6.145
6.058
6.030
5.769
5.751
5.732
5.713
5.696
4.252
4.246
4.233
4.220
4.214
2.630
2.626
2.611
2.608
2.593
2.590
2.575
2.572
2.133
2.116
2.098
2.080
1.756
1.657
1.650
1.614
1.402
1.385
1.367
1.295
1.267
0.892
0.876
0.858
Me
C8H17
H
OH
O
rac-64
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
1.00
1.07
2.18
1.10
1.06
1.05
2.16
2.43
3.38
2.07
15.65
3.77

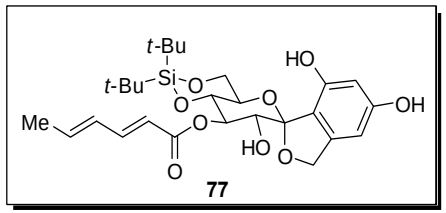

5.790
5.784
5.769
5.764
5.755
5.749
5.735
5.729
5.714
5.699
5.684
5.670
5.157
5.153
5.150
5.119
5.116
5.100
5.098
4.093
4.083
4.073
4.068
2.355
2.341
2.330
2.324
2.309
2.108
2.094
2.079
1.746
1.624
1.618
1.396
1.382
1.368
1.296
1.271
1.219
1.181
1.052
0.892
0.879
0.865
Me
Me
OH
(S)-62
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
1.00
1.01
2.09
2.28
1.01
2.37
2.22
3.40
1.04
15.61
3.92

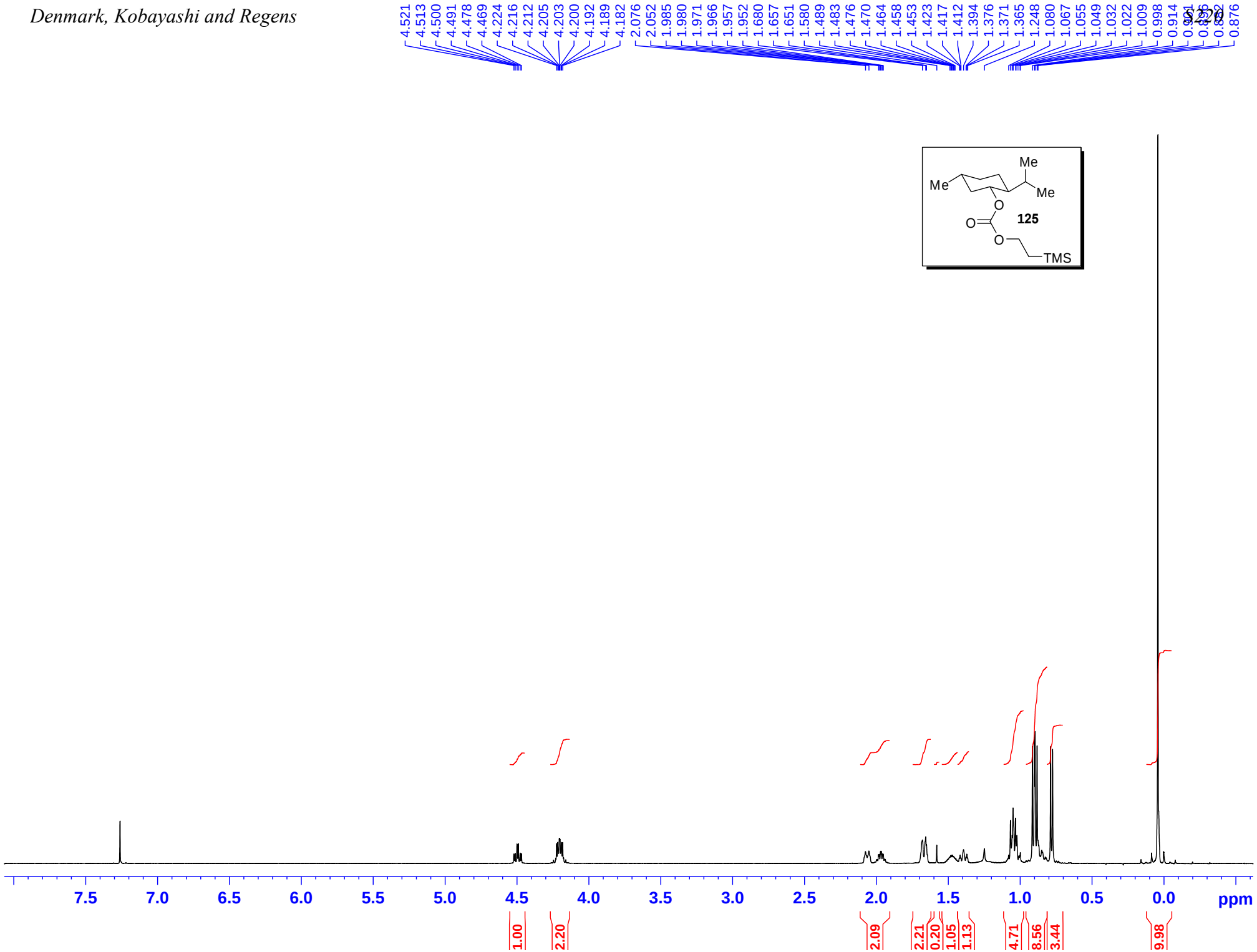

Me
Me
Me
OTES
t-Bu
t-Bu
Si
O
O
O
O
O
SEMO
SEMO
O
OSEM
O
74

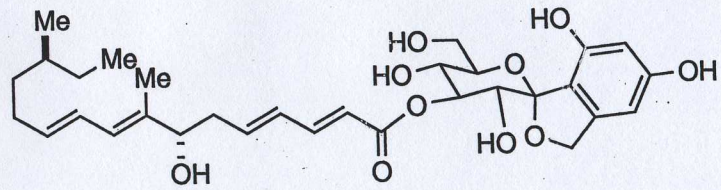

7.363
5.231
3.893
3.773
3.755
3.752
3.749
3.731
0.978
0.960
0.957
0.955
0.937
SEMO
OSEM
O
OMe
119
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
2.01
1.00
4.00
3.12
4.01
4.87
21.65


6.674
6.664
6.655
5.198
4.632
4.620
3.761
3.746
3.744
3.742
3.727
0.972
0.958
0.955
0.939
0.000
SEMO
OSEM
OH
120
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
2.67
4.00
1.95
3.90
3.85
16.46

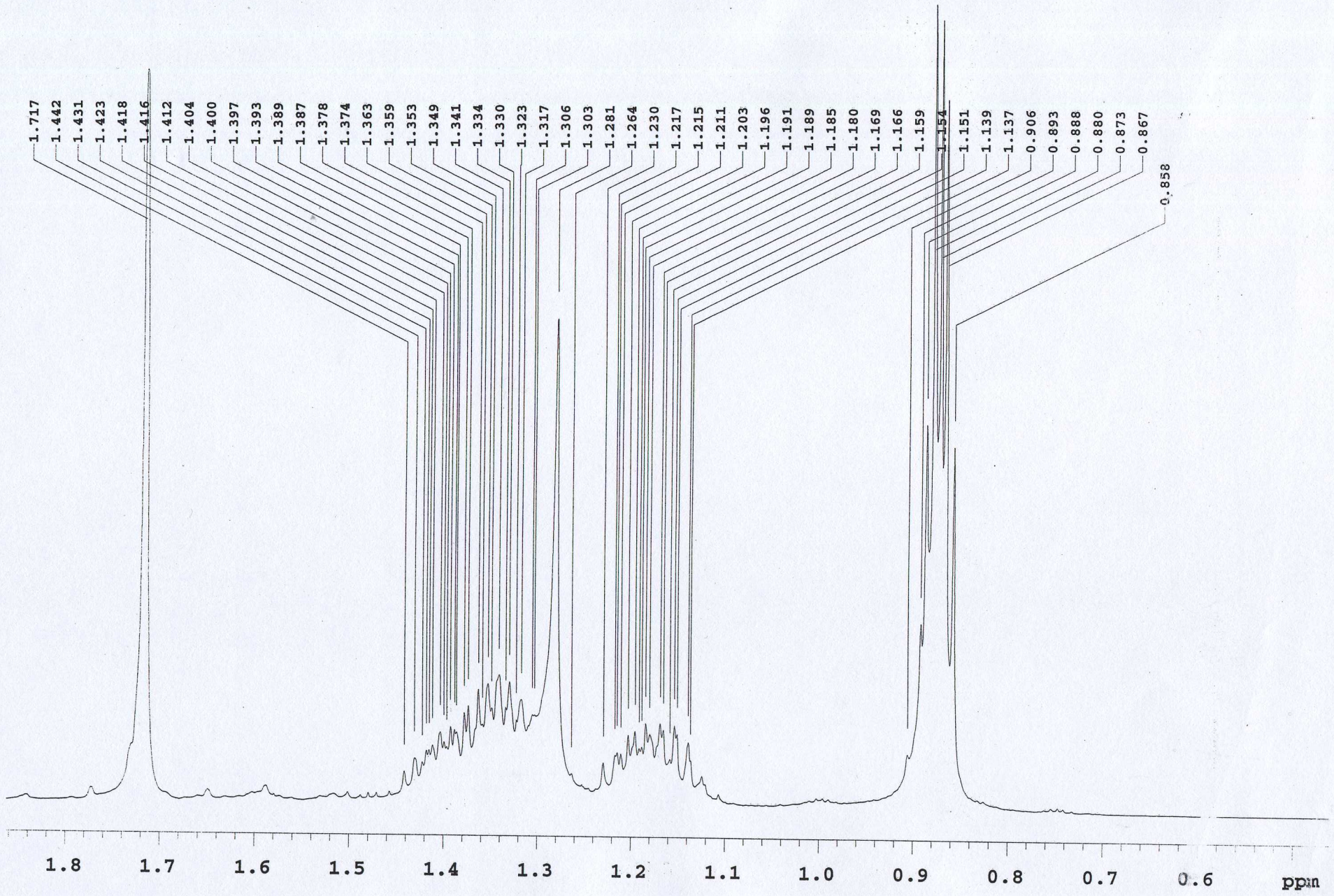

6.674
6.671
6.666
6.663
5.198
4.388
3.762
3.748
3.746
3.729
3.380
0.974
0.960
0.957
0.941
-0.002
SEMO
OSEM
OMe
121
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
3.06
4.00
2.05
4.00
3.16
3.97
18.19

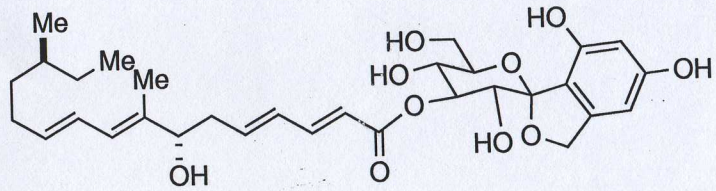

t-Bu
t-Bu
Si
O
O
O
O
O
HO
OH
HO
O
Me
O
77


4.521 4.513 4.500 4.491 4.478 4.469 4.224 4.216 4.212 4.205 4.203 4.200 4.192 4.189 4.182 2.076 2.052 1.985 1.980 1.971 1.966 1.957 1.952 1.680 1.657 1.651 1.580 1.489 1.483 1.476 1.470 1.464 1.458 1.453 1.423 1.417 1.412 1.394 1.376 1.371 1.365 1.248 1.080 1.067 1.055 1.049 1.032 1.022 1.009 0.998 0.914 0.876
Me
Me
Me
O
O
O
125
TMS
7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm
1.00 2.20 2.09 2.21 0.20 1.05 1.13 4.71 8.56 3.44 9.98

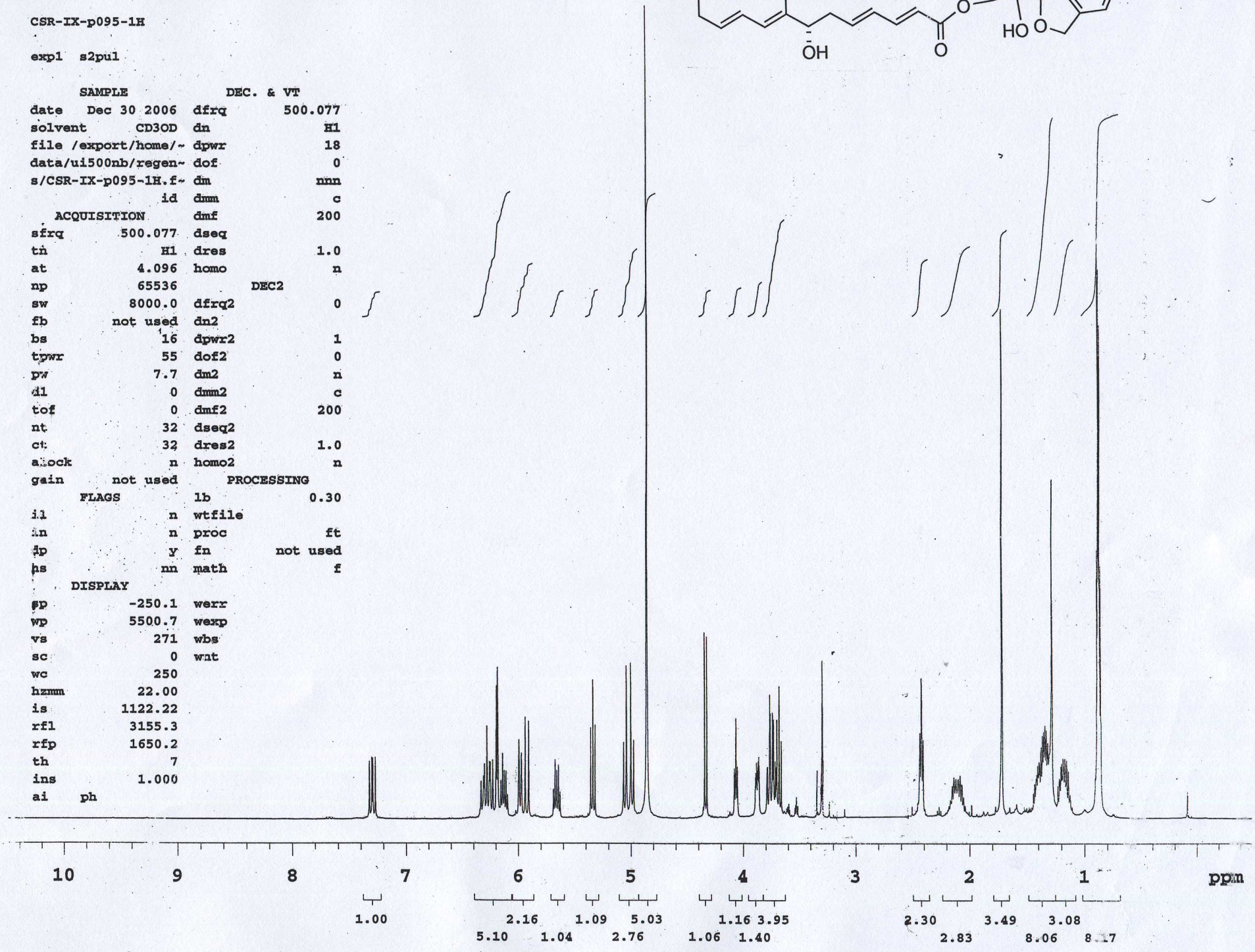


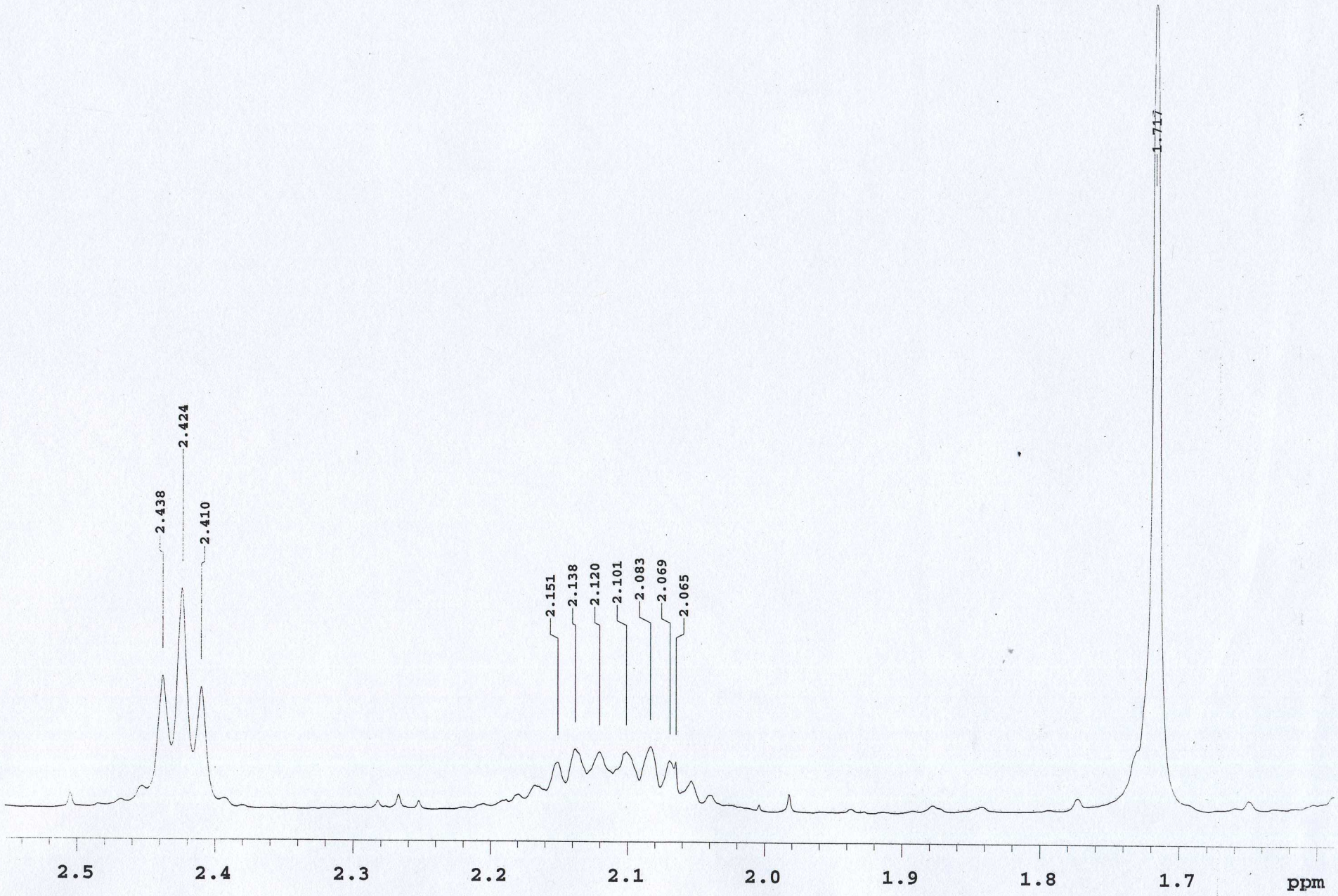

```
CSR-IX-p095-1H

exp1  s2pul

      SAMPLE              DEC. & VT
date    Dec 30 2006  dfrq        500.077
solvent       CD3OD  dn             H1
file /export/home/~  dpwr           18
data/ui500nb/regen~  dof             0
s/CSR-IX-p095-1H.f~  dm            nnn
                 id  dmm             c
   ACQUISITION       dmf           200
sfrq        500.077  dseq
tn               H1  dres          1.0
at             4.096  homo            n
np             65536        DEC2
sw            8000.0  dfrq2           0
fb         not used   dn2
bs               16   dpwr2           1
tpwr             55   dof2            0
pw              7.7   dm2             n
d1               0    dmm2            c
tof              0    dmf2          200
nt              32    dseq2
ct              32    dres2         1.0
alock            n    homo2           n
gain       not used       PROCESSING
      FLAGS            lb          0.30
il                n   wtfile
in                n   proc            ft
dp                y   fn         not used
hs               nn   math            f
    DISPLAY
sp           -250.1   werr
wp           5500.7   wexp
vs              271   wbs
sc                0   wnt
wc              250
hzmm          22.00
is          1122.22
rfl         3155.3
rfp         1650.2
th                7
ins           1.000
ai    ph
```

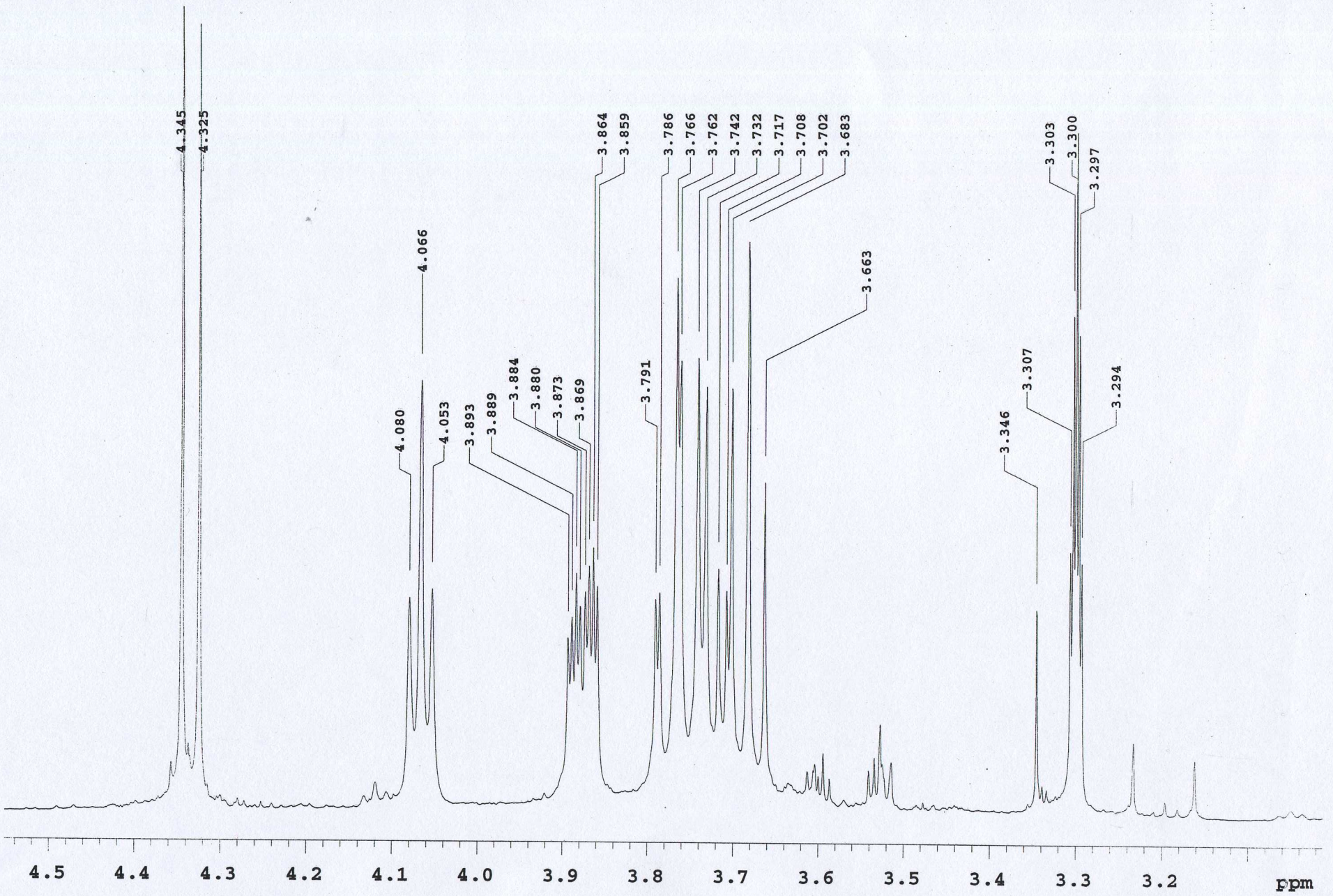

1.717
1.442
1.431
1.423
1.418
1.416
1.412
1.404
1.400
1.397
1.393
1.389
1.387
1.378
1.374
1.363
1.359
1.353
1.349
1.341
1.334
1.330
1.323
1.317
1.306
1.303
1.281
1.264
1.230
1.217
1.215
1.211
1.203
1.196
1.191
1.189
1.185
1.180
1.169
1.166
1.159
1.154
1.151
1.139
1.137
0.906
0.893
0.888
0.880
0.873
0.867
0.858
1.8
1.7
1.6
1.5
1.4
1.3
1.2
1.1
1.0
0.9
0.8
0.7
0.6
ppm

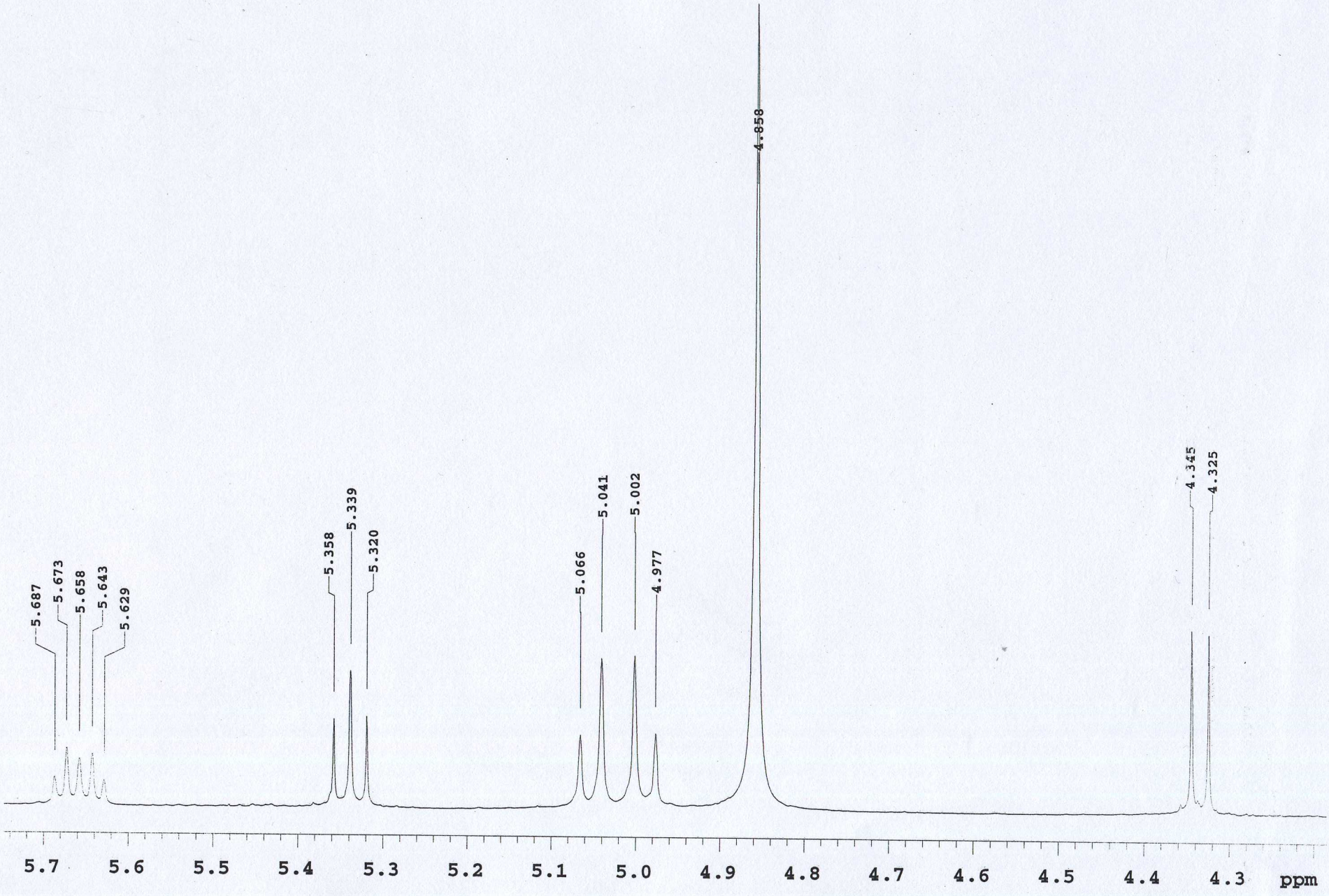


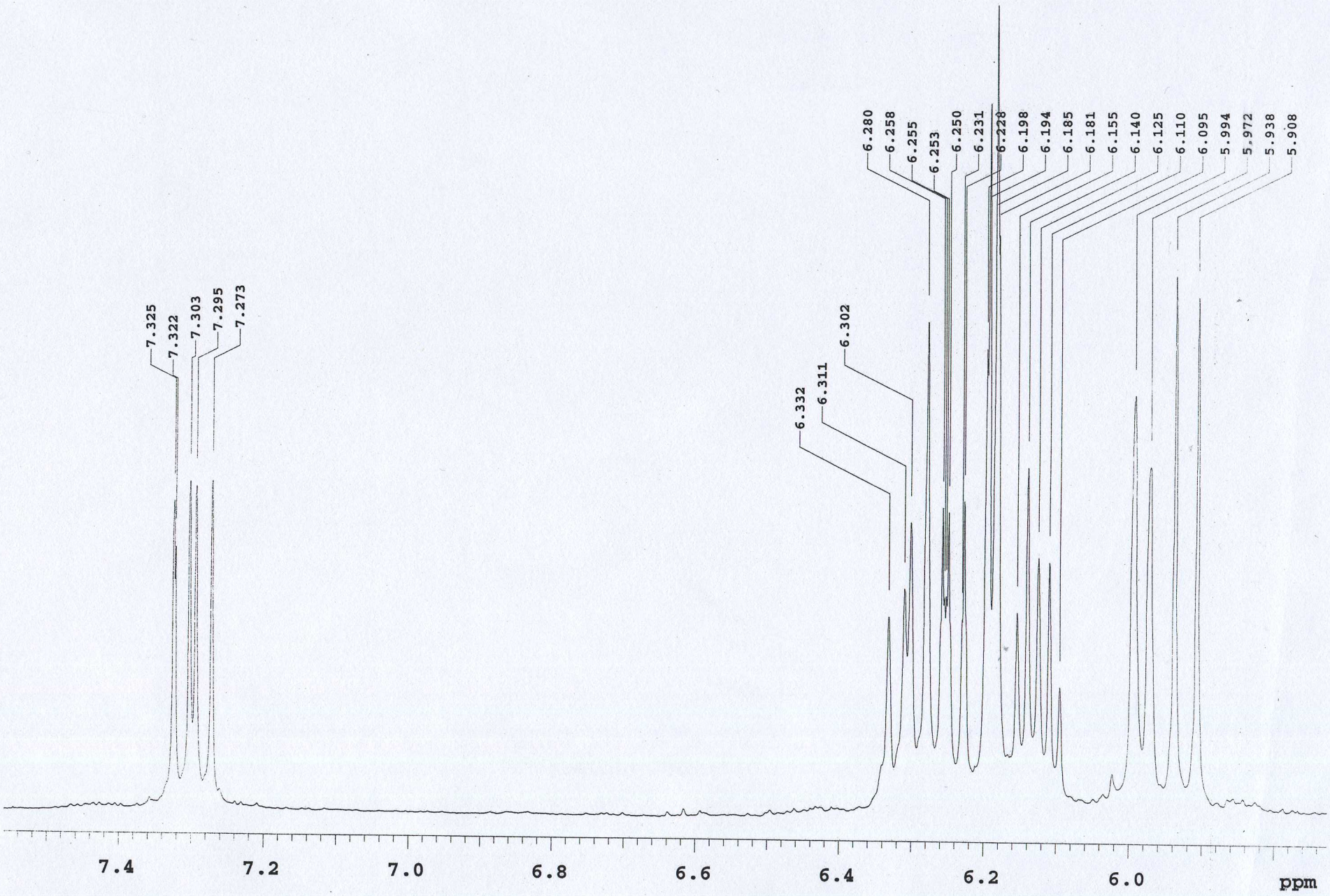

```
CSR-IX-p095-1H

exp1  s2pul

      SAMPLE              DEC. & VT
date    Dec 30 2006  dfrq        500.077
solvent       CD3OD  dn                H1
file /export/home/~  dpwr              18
data/ui500nb/regen~  dof                0
s/CSR-IX-p095-1H.f~  dm               nnn
                 id  dmm                c
   ACQUISITION       dmf              200
sfrq        500.077  dseq
tn               H1  dres             1.0
at            4.096  homo               n
np            65536        DEC2
sw           8000.0  dfrq2              0
fb         not used  dn2
bs               16  dpwr2              1
tpwr             55  dof2               0
pw              7.7  dm2                n
d1                0  dmm2               c
tof               0  dmf2             200
nt               32  dseq2
ct               32  dres2            1.0
alock             n  homo2              n
gain       not used      PROCESSING
      FLAGS          lb              0.30
il                n  wtfile
in                n  proc              ft
dp                y  fn          not used
hs               nn  math               f
    DISPLAY
sp           -250.1  werr
wp           5500.7  wexp
vs              271  wbs
sc                0  wnt
wc              250
hzmm          22.00
is          1122.22
rfl         3155.3
rfp         1650.2
th                7
ins           1.000
ai    ph
```

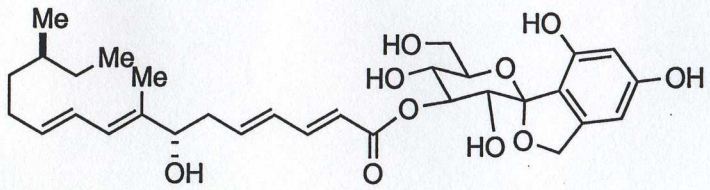



2.438
2.424
2.410
2.151
2.138
2.120
2.101
2.083
2.069
2.065
1.717
2.5
2.4
2.3
2.2
2.1
2.0
1.9
1.8
1.7
ppm


4.345
4.325
4.080
4.066
4.053
3.893
3.889
3.884
3.880
3.873
3.869
3.864
3.859
3.791
3.786
3.766
3.762
3.742
3.732
3.717
3.708
3.702
3.683
3.663
3.346
3.307
3.303
3.300
3.297
3.294
4.5
4.4
4.3
4.2
4.1
4.0
3.9
3.8
3.7
3.6
3.5
3.4
3.3
3.2
ppm


5.687
5.673
5.658
5.643
5.629
5.358
5.339
5.320
5.066
5.041
5.002
4.977
4.858
4.345
4.325
5.7
5.6
5.5
5.4
5.3
5.2
5.1
5.0
4.9
4.8
4.7
4.6
4.5
4.4
4.3
ppm


7.325
7.322
7.303
7.295
7.273
6.332
6.311
6.302
6.280
6.258
6.255
6.253
6.250
6.231
6.228
6.198
6.194
6.185
6.181
6.155
6.140
6.125
6.110
6.095
5.994
5.972
5.938
5.908
7.4
7.2
7.0
6.8
6.6
6.4
6.2
6.0
ppm



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

exp1 s2pul

SAMPLE		DEC. & VT	
date	Dec 30 2006	dfrq	499.700
solvent	CD3OD	dn	H1
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