Supporting Information

for

Total synthesis of peloruside A via kinetic lactonization and relay RCM cyclization reactions (and identification of iso-peloruside A)

Thomas R. Hoye,*[1] Junha Jeon,[1] Lucas C. Kopel,[1] Troy D. Ryba,[1] Manomi A. Tennakoon,[1] & Yini Wang[1]

[1] *Department of Chemistry, University of Minnesota*

207 Pleasant St SE, Minneapolis, MN 55455

*hoye@umn.edu

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General Experimental

^{1}H and ^{13}C NMR spectra were recorded on Varian Inova 8001 (800 MHz), Varian Inova 500 (500 MHz), Varian Inova 300 (300 MHz), Varian VXR 300 (300 MHz), and Varian Unity-plus 400 (400 MHz) spectrometers. ^{1}H NMR chemical shifts in $CDCl_3$ are referenced to TMS (0.00 ppm) and in PhH-d_6 to 7.16. Non-first order multiplets are identified as "nfom". ^{13}C NMR chemical shifts in $CDCl_3$ are referenced to chloroform (77.23 ppm). A spurious peak at *ca.* 5 ppm is sometimes present in the copies of the ^{1}H NMR spectra that were processed using iNMR software. The following format was used to report peaks: chemical shift in ppm [multiplicity, coupling constant(s) in Hz, integral, and assignment]. ^{1}H NMR assignments are indicated by structure environment, e.g., CH_aH$_b$. Some complex structures are numbered in order to simplify proton assignment numbering and naming. Peloruside skeleton numbering was consistently used, even in cases where the systematic name of the compound results in a different atom numbering scheme. Coupling constant analysis was guided by methods we have described elsewhere.[1]

Infrared (IR) spectra were recorded on a Prospect MIDAC FT-IR spectrometer using a NaCl plate (thin film). Absorptions are reported in cm^{-1}.

Electron impact (EI) mass spectrometry was performed on a Finnigan MAT 95 mass spectrometer at 70 eV. Samples were introduced using a direct insertion probe heated from 25-320 °C at 50 ºC/min. Electrospray ionization (ESI) mass spectrometry was performed on a Bruker BioTOF II. All HRMS data were recorded in the ESI mode. Samples were introduced as solutions in methanol.

GCMS data were recorded either on a Hewlett Packard 5971 MSD (Mass Selective Detector) or Agilent 5975 insert XL MSD at 70 eV. The methods used are noted parenthetically: 5025015 refers to 2 min @ 50 °C – 20 °C/min – 3 min @ 250 °C (a 50 °C initial temperature that was held for 2 minutes followed by a 20 °C/min ramp to a final temperature of 250 °C that was held for 3 minutes for a total run time of 15 minutes). 5029019 refers to: 2 min @ 50 °C – 20 °C/min – 3 min @ 290 °C. 5032021 refers to: 2 min @ 50 °C – 20 °C/min – 5 min @ 320 °C. A letter H following the method number (e.g., 5029019H) notes that the detector was scanning masses from 50 to 600 *m/z* rather than 50 to 400 *m/z*.

Tandem liquid chromatography/low resolution mass spectroscopy (LCMS) using multimode ESI-APCI ionization was performed on an Agilent Technologies 1100 series liquid

chromatography equipped with an Agilent Technologies G1956B LC/MSD SL mass selective detector. A C8-column (150 mm, 5 μm), methanol/water solvent mixtures, and flow rate of 0.5 mL/min was used.

Optical rotation data were recorded on a JASCO DIP-370 digital polarimeter using a 500-100 mm length 3.5 mm diameter cell.

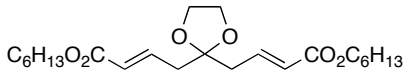
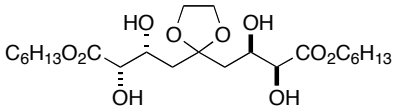
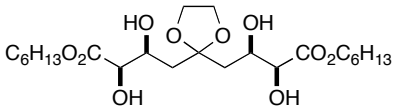
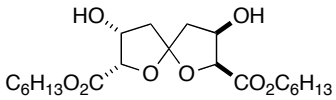
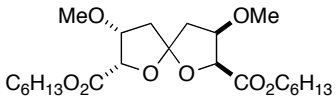
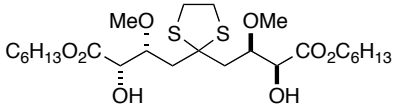
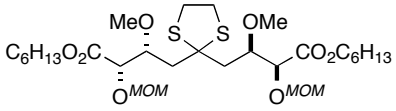
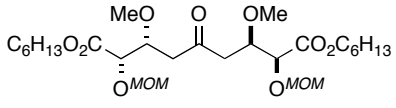
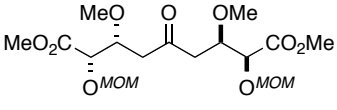
G2 is the second generation Grubbs initiator [Ru=CHPh(Cl)$_2$(PCy$_3$)(H$_2$IMes)].

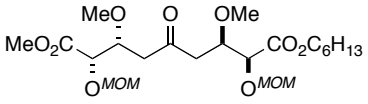
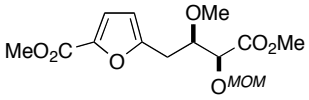
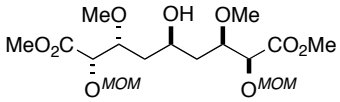
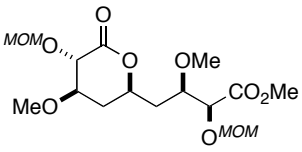
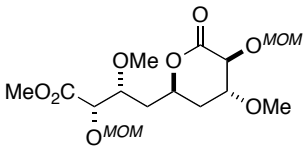
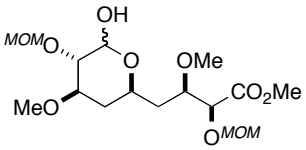
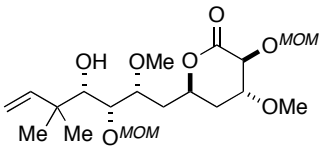
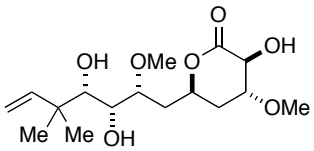
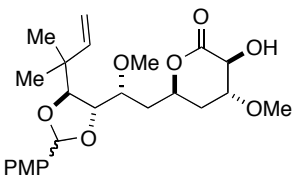
Reactions requiring anhydrous conditions were performed under an atmosphere of nitrogen or argon in flame or oven dried glassware. Anhydrous benzene and BF_3•OEt_2 were distilled from CaH_2. Anhydrous THF, diethyl ether, toluene, and methylene chloride were tapped immediately prior to use after being passed through a column of activated alumina. Triethylamine and pyridine were distilled from KOH. DMF and DMSO were stored over 4Å molecular sieves. The concentration of anionic solutions (e.g., *n*-BuLi, Grignards, Red-Al®) was titered by spectroscopic (No-D NMR) methods.[2]

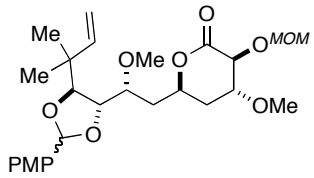
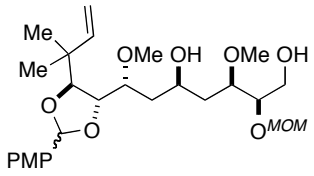
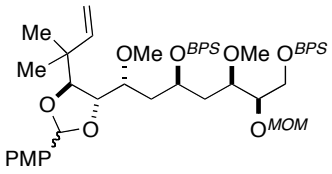
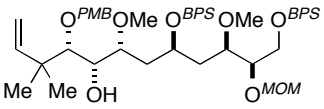
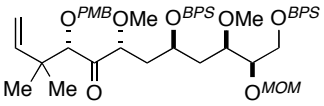
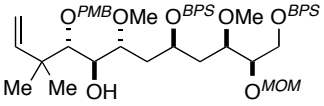
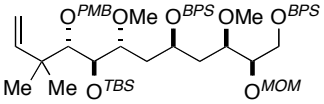
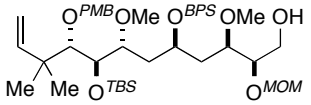
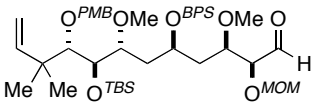
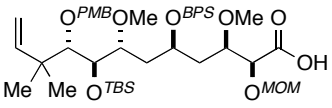
MPLC refers to medium pressure liquid chromatography (25-200 psi) using hand-packed columns of Silasorb silica gel (18-32 μm, 60 Å pore size), a Waters HPLC pump, a Waters R401 differential refractive index detector, and a Gilson 116 UV detector. Flash chromatography was performed using E. Merck silica gel (230-400 mesh).

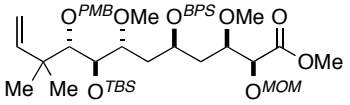
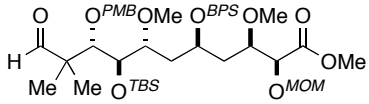
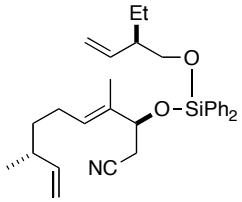
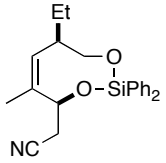
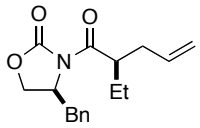
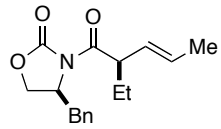
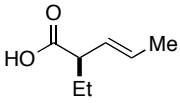
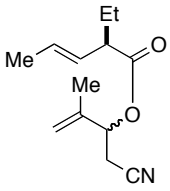
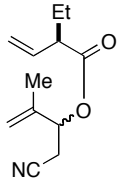
Table of Isolated Compounds

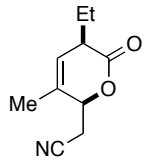
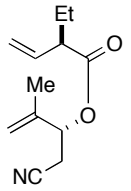
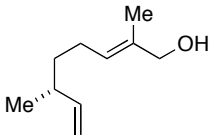
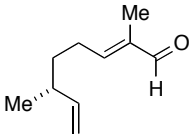
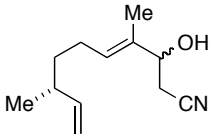
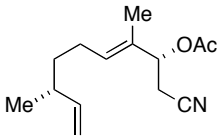
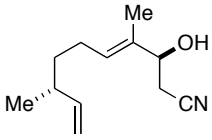
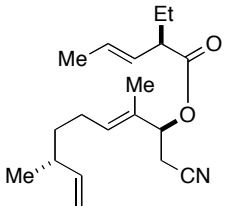
Structures not shown in the main manuscript but described here in the Supplementary Information (Master) and (NMR Spectra) documents are numbered with the form "***SI-##***".

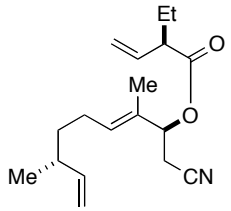
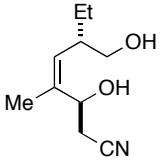
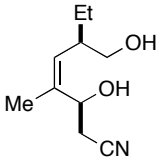
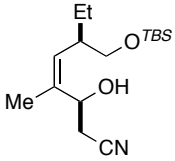
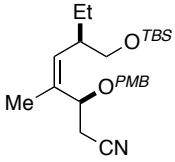
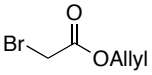
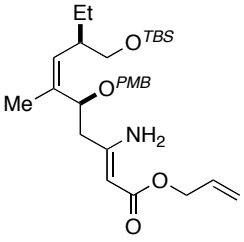
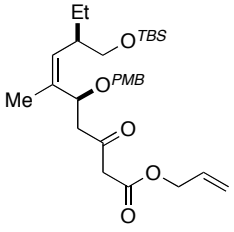
Structure	***Compound #***	***Procedure begins on page:***	***NMR spectra on page:***
	***SI-1***	12	77-78
	***7***	13	79-80
	***SI-2***	13	*na*
	***SI-3***	14	81-82
	***8***	15	83-84
	***SI-4***	16	85-86
	***SI-5***	17	87-88
	***SI-6***	17	89-90
	***4***	18	91-92

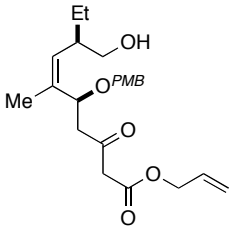
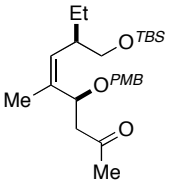
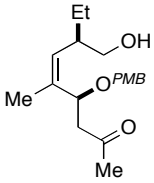
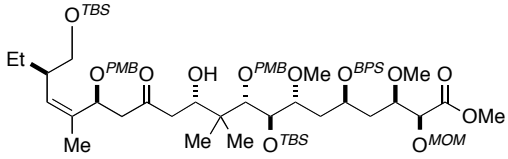
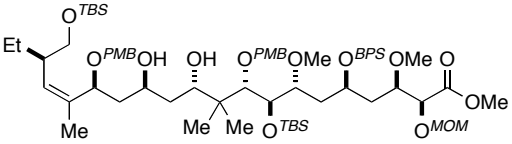
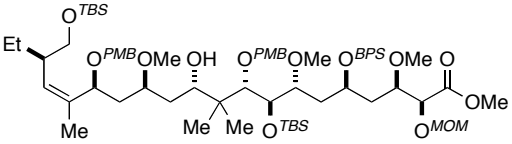
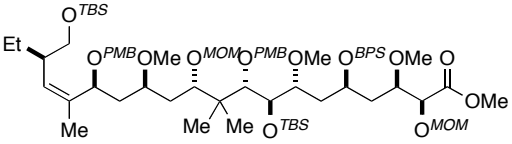
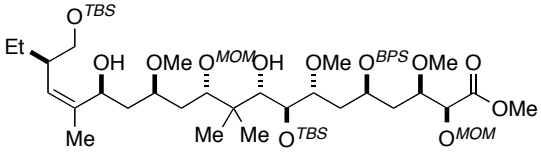
	***SI-7***	18	93
	***SI-8***	18	*na*
	***9***	19	94-95
	***11***	20	96-97
	***SI-9***	20	98-99
	***SI-10***	22	100-101
	***SI-11***	23	102-103
	***SI-12***	24	104-105
	***SI-13***	25	106-107

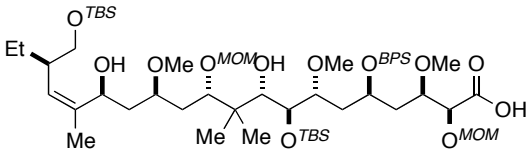
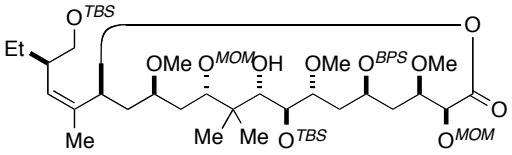
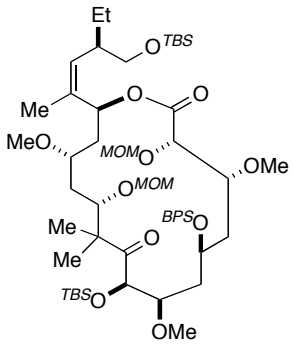
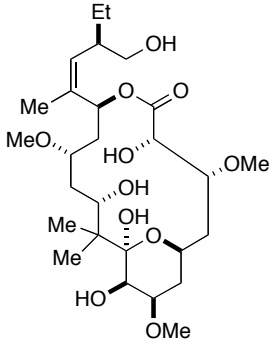
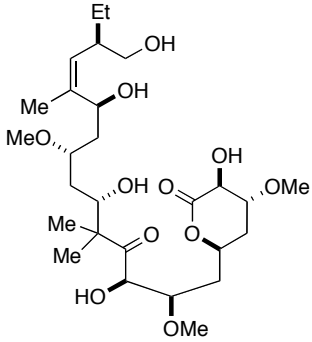
	***12***	26	108-109
	***SI-14***	28	110-111
	***SI-15***	29	112-113
	***SI-16***	31	114-115
	***SI-17***	32	116-117
	***SI-18***	33	118-119
	***13***	34	120-121
	***SI-19***	36	122-123
	***SI-20***	37	124-125
	***SI-21***	38	126-127

	***SI-22***	39	128-129
	***2***	41	130-131
	***5a***	42	*na*
	***16***	43	*na*
	***18***	44	132-133
	***SI-24***	45	134-135
	***19***	46	136-137
	***SI-25a***	47	138-139
	***SI-25b***	48	140-141

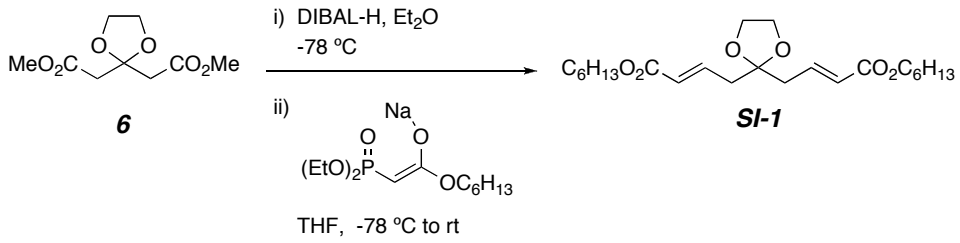
	***20***	49, 54, 54	142-143
	***SI-27***	49	*na*
	***SI-28***	50	*na*
	***SI-29***	50	144-145
	***SI-30***	51	146-147
	***SI-31***	52	*na*
	***15***	52	148-149
	***5b***	53	150-151

	***24***	54	*na*
	***SI-32***	55	152
	***SI-33***	55	153-154
	***SI-34***	56	155-156
	***17***	57	157-158
	***SI-35***	61	159
	***SI-36***	58	160
	***21***	59	161

	***SI-37***	59	*na*
	***3***	60	162-163
	***SI-38***	60	*na*
	***25***	62	164-165
	***26***	63	166-167
	***SI-40***	65	168-169
	***SI-41***	66	170-171
	***27***	67	172-173

	***28***	69	174-175
	***29***	70	176-177
	***30***	71	178-179
	***1 (Peloruside A)***	73	180-184
	***iso-1 (Isopeloruside A)***	73	185-186

Dihexyl 1,3-Dioxolane-2,2-di[(*E*)-2-butenoate] (SI-1)



Ketal **6** (10.0 g, 45.9 mmol)[3] was added to a 1L, 3-neck flask, dissolved in Et_2O (182 mL, 0.25M) and cooled to -78 ºC (careful temperature control is important; the use of an internal temperature probe is recommended). Recently titrated DIBAL-H (82 mL, 101 mmol, 1.23 M in toluene) was cannulated into a dry graduated addition funnel. This colorless DIBAL-H solution was added dropwise to the colorless ethereal solution with constant stirring and under a N_2 atmosphere at -78 ºC. During the dropwise DIBAL-H addition, the THF solution of sodium hexyl phosphonoacetate was prepared according to the following protocol. NaH (3.07 g, 128 mmol), a stir bar, and THF (240 mL, 0.5M) were combined in an oven dried round bottom flask under N_2, and the mixture was cooled to 0 ºC. With vigorous stirring, hexyl phosphonoacetate (38.5 g, 137 mmol) was added dropwise. Gas was evolved and the solution eventually became a homogeneous red color as a result of a minor impurity in the hexyl phosphonoacetate. This solution was transferred by cannula dropwise to the DIBAL-H solution, taking care that the rate of addition did not warm the temperature beyond -70 ºC. Once all of the phosphonoacetate anion was added, the reaction flask was removed from the dry-ice bath and the mixture was allowed to stir while warming to room temperature for 1-2 h. At room temperature the red orange solution was transferred to a 2L Erlenmeyer flask equipped with a stir bar. Small portions of saturated aqueous Rochelle's salt (Na,K-tartrate) were added and the reaction was monitored very closely for exotherm and intermittently cooled with an ice bath if necessary. The mixture turned from homogeneous to a gelatinous suspension and, upon addition of more sat. aq. Rochelle's salt, back to homogeneous. Portions of Et_2O were added to replace some that was lost to evaporation if the mixture became excessively warm. The mixture was allowed to stir for an additional 18 h, at which time the aqueous and organic layers were homogeneous and clear. The layers were separated and the aqueous layer was extracted with EtOAc (3 x 300 mL). The organic layers were combined, washed with brine (100 mL), dried over Na_2SO_4, and concentrated *in vacuo* to

provide a redish-orange oil. This oil, which contains the excess phosphonoacetate and the desired product, was purified by flash chromatography (6:1 hexanes:ethyl acetate) to provide the bis enone ketal **SI-1** (80%) as a light yellow colored oil.

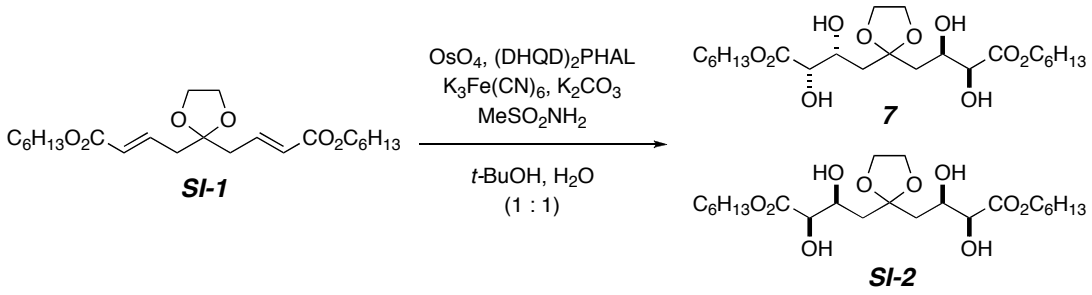
^{1}H NMR (500 MHz, $CDCl_3$): δ 6.91 (dt, *J* = 15.3 and 7.4 Hz, 2H, HC=C*H*CH_2), 5.90 (dt, *J* = 15.6 and 1.6 Hz, 2H, *H*C=$CHCH_2$), 4.12 (t, *J* = 6.8 Hz, 4H, CO_2CH_2), 3.97 (s, 4H, OCH_2CH_2O), 2.53 (dd, *J* = 7.4 and 1.2 Hz, 4H, HC=$CHCH_2$), 1.64 (m, 4H, OCH_2CH_2), 1.32 (m, 12H, $(CH_2)_3Me$), and 0.89 (t, *J* = 7.1 Hz, 6H, CH_3).

^{13}C NMR (125 MHz, $CDCl_3$): δ 166.3, 142.5, 125.1, 109.5, 65.6, 64.7, 40.9, 31.5, 28.7, 25.7, 22.7, and 14.3.

HR ESI-MS: Calcd for $C_{23}H_{38}O_6Na$ $(M+Na)^+$: 433.2566 Found: 433.2597.

TLC: R_f = 0.59; 3:1 hexanes:ethyl acetate.

Dihexyl 1,3-Dioxolane-2,2-bis[(*2R,3S*)-2,3-dihydroxybutanoate] (7)



$K_3Fe(CN)_6$ (31.2 g, 94.8 mmol) and K_2CO_3 (13.1 g, 94.8 mmol) were added to a dry round bottom flask equipped with a stir bar. $(DHQD)_2PHAL$ (246 mg, 0.316 mmol) and OsO_4 (40 mg, 0.16 mmol) were added to the dry mixture, and this mixture was stirred until it appeared well mixed. A 1:1 mixture of a *t*-BuOH:H_2O (158 mL total volume) was next added, and the heterogeneous, biphasic solution was stirred for 10 minutes and then cooled to 0 ºC (internal temperature probe). *bis*-Enone **SI-1** (6.5 g, 15.8 mmol) was added to this cooled heterogeneous solution using a minimal amount of *t*-BuOH, followed by the addition of $MeSO_2NH_2$ (3.76 g, 39.5 mmol). The resulting orange mixture was allowed to stir at 0 ºC until all the starting material had been consumed by TLC analysis (approximately 72 h). Solid Na_2SO_3 was added at 0 ºC until the yellow solution turned brown. The mixture was diluted with water (200 mL) and extracted with EtOAc (3 x 200 mL). The organic layer was then washed with 0.1N KOH and brine, dried over Na_2SO_4, and concentrated in vacuo to provide **7** (88%) as white foam [minor

amounts of **SI-2** (**7-*meso***) were detectable by ^{1}H NMR analysis and could be removed after the following reaction by recrystallization].

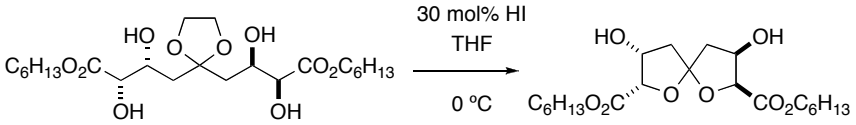
^{1}H NMR (500 MHz, $CDCl_3$): δ 4.23 (m, 2H, H_aCOH), 4.23 (m, 4H, CO_2CH_2), 4.07 (s, 4H, OCH_2CH_2O), 4.03 (m, 2H, H_bCOH), 3.14 (br s, 2H, O*H*), 3.08 (d, *J* = 7.0 Hz, 1H, O*H*), 2.23 (dd, *J* = 15.0 and 9.9 Hz, 2H, CH_aH_b), 1.96 (dd, *J* = 15.2 and 2.8 Hz, 2H, CH_aH_b), 1.69 (pent, *J* = 6.9 Hz, 4H, $CO_2CH_2CH_2$), 1.33 (m, 12H, $(CH_2)_3Me$), and 0.89 (t, *J* = 6.9 Hz, 6H, CH_3).

^{13}C NMR (125 MHz, $CDCl_3$): δ 173.0, 111.1, 74.2, 69.0, 66.2, 64.9, 39.7, 31.5, 28.6, 25.5, 22.6, and 14.1.

HR ESI-MS: Calcd for $C_{23}H_{42}O_{10}Na$ $(M+Na)^+$: 501.2676 Found: 501.2747.

TLC: R_f = 0.40; 1:3 hexanes:ethyl acetate.

Dihexyl (2*S*,3*R*,7*S*,8*R*)-3,8-Dihydroxy-1,6-dioxaspiro[4.4]nonane-2,7-dicarboxylate (SI-3)



7 ***SI-3***

To tetrol **7** (1.24 g, 2.9 mmol) was added THF (5.8 mL, 0.5M) and this solution was cooled to 0 ºC. A brown colored sample of aqueous HI (65 µL, 870 µmol;) was added dropwise, and the solution was stirred at 0 ºC until the reaction was deemed complete by careful TLC analysis (approximately 3 h). Saturated aqueous $NaHCO_3$ (5 mL) was added dropwise followed by saturated aqueous Na_2SO_3 until the yellow color disappeared. This solution was then diluted with water (5 mL). The aqueous layer was extracted with EtOAc (3 x 50 mL), and the combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated *in vacuo* to provide spirocycle **SI-3** (83%). The spirocycle **SI-3** was recrystalized using either Et_2O/hexanes or EtOAc/hexanes to produce white needles.

^{1}H NMR (500 MHz, $CDCl_3$): δ 4.78 (dddd, *J* = 6.7, 5.1, 5.1, and 3.7 Hz, 2H, *H*COH), 4.63 (d, *J* = 5.9 Hz, 2H, $HCCO_2$), 4.22 (dt, *J* = 10 and 6.6 Hz, 2H, $CO_2CH_aH_b$), 4.20 (dt, *J* = 10 and 6.6 Hz, 2H, $CO_2CH_aH_b$), 2.76 (dd, *J* = 14.4 and 6.7 Hz, 2H, CH_aH_b), 2.27 (dd, *J* = 14.0 and 3.4 Hz, 2H, CH_aH_b), 2.20 (d, *J* = 5.6 Hz, 2H, O*H*), 1.67 (pent, *J* = 6.8 Hz, 4H, $CO_2CH_2CH_2$), 1.31 (m, 12H, $(CH_2)_3Me$), and 0.89 (t, *J* = 6.2 Hz, 6H, CH_3).

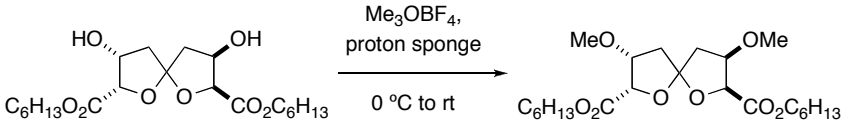
^{13}C NMR (125 MHz, $CDCl_3$): δ 169.5, 114.7, 81.1, 72.6, 65.7, 44.6, 31.5, 28.6, 25.6, 22.7, and 14.2.

HR ESI-MS: Calcd for $C_{21}H_{36}O_8Na$ $(M+Na)^+$: 439.2308 Found: 439.2334.

TLC: R_f = 0.50; 1:3 hexanes:ethyl acetate.

mp = 101–105 ºC.

Dihexyl (2*S*,3*R*,7*S*,8*R*)-3,8-Dimethoxy-1,6-dioxaspiro[4.4]nonane-2,7-dicarboxylate (8)



SI-3 ***8***

Spirocycle **SI-3** (9.30 g, 22.3 mmol) was dissolved in CH_2Cl_2 (223 mL, 0.1M) and the solution was cooled to 0 ºC. 1,8-Bis(dimethylamino)naphthalene (Proton Sponge,™ 21.5 g, 89.3 mmol) was added followed by trimethyloxonium tetrafluoroborate (Meerwein's salt, 13.2 g, 89.3 mmol), and the resulting mixture was stirred for 18 h at room temperature, at which time no more starting material was present (TLC analysis). Water(75 mL) ansaturated aqueous NH_4Cl (100 mL) were added sequentially. The aqueous layer was extracted with EtOAc (3 x 250 mL), and the combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated *in vacuo*. To prevent decomposition, immediate flash chromatography (2:1 hexanes/ethyl acetate) was required to remove the residual Proton Sponge. The bis-methyl ether **8** was obtained (8.33 g, 84%) as a colorless oil.

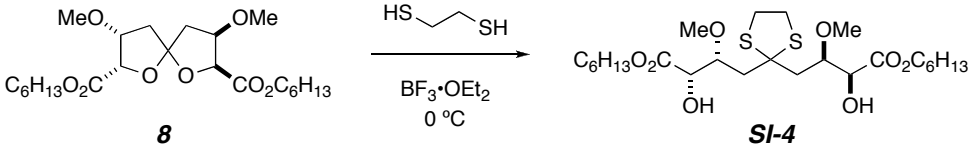
^{1}H NMR (500 MHz, $CDCl_3$): δ 4.68 (d, J = 6.0 Hz, 2H, $HCCO_2$), 4.35 (ddd, J = 6, 5, and 5 Hz, 2H, C*H*OMe), 4.20 (dt, J = 10 and 6.6 Hz, 2H, $CO_2CH_aH_b$), 4.15 (dt, J = 10 and 6.6 Hz, 2H, $CO_2CH_aH_b$), 3.31 (s, 6H, OCH_3), 2.64 (dd, J = 13.7 and 6.2 Hz, 2H, CH_aH_b), 2.29 (dd, J = 13.7 and 5.2 Hz, 2H, CH_aH_b), 1.64 (pent, J = 6.9 Hz, 4H, $CO_2CH_2CH_2$), 1.32 (m, 12H, $(CH_2)_3Me$), and 0.89 (t, J = 6.2 Hz, 6H, CH_3).

^{13}C NMR (75 MHz, $CDCl_3$): δ 163.3, 115.1, 81.3, 79.8, 65.3, 57.9, 41.2, 31.6, 28.7, 25.7, 22.7, and 14.2.

HR ESI-MS: Calcd for $C_{23}H_{40}O_8Na$ $(M+Na)^+$: 467.2621 Found: 467.2618.

TLC: R_f = 0.52; 2:1 hexanes:ethyl acetate.

Dihexyl 1,3-Ditholane-2,2-bis[(*2R,3S*)-3-hydroxy-2-methoxybutanoate] (SI-4)



8 ***SI-4***

Spiroketal **8** (14.7 g, 33.1 mmol) was dissolved in 1,2-ethanedithiol (285 mL, 0.116M) and the solution was cooled to 0 ºC. BF_3•OEt_2 (42.0 mL, 331 mmol) was added against the side of the round bottom in order to pre-cool it. The reaction mixture was stirred for 3.5 h at 0 ºC and quenched by the dropwise addition of saturated aqueous $NaHCO_3$ (150 mL). Water (50 mL) was added and the mixture was extracted with Et_2O (3 x 400 mL). The combined organic layers were washed with 15% aq. NaOH (1 x 100 mL) to remove some of the excess thiol. The organic layer was dried over Na_2SO_4 and concentrated *in vacuo* to provide crude diol **SI-4**, which was still contaminated with a signifigant amount of 1,2-ethanedithiol. This thiol was removed using a high vacuum rotory evaporator to give crude **SI-4** as a colorless oil, which was used in the next reaction without further purification. Bleach solution was used to treat all glassware that had contacted these reaction liquids to prevent the odor of 1,2-ethanedithiol from diffusing into the lab.

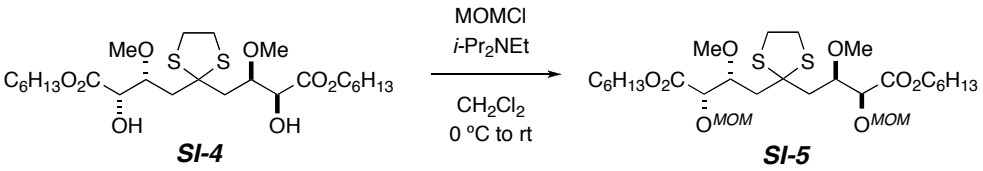
^{1}H NMR (500 MHz, $CDCl_3$): δ 4.44 (dd, *J* = 8.1 and 1.9 Hz, 2H, *H*COH), 4.24 (dt, *J* = 10 and 6.6 Hz, 2H, $CO_2CH_aH_b$), 4.20 (dt, *J* = 10 and 6.6 Hz, 2H, $CO_2CH_aH_b$), 3.93 (ddd, *J* = 6.3, 4.5, and 2.1 Hz, 2H, *H*COMe), 3.34 (s, 10H, OCH_3 and SCH_2CH_2S), 2.90 (d, *J* = 8.9 Hz, 1H, O*H*), 2.53 (dd, *J* = 15.3 and 6.0 Hz, 2H, CH_aH_b), 2.20 (dd, J = 15.4 and 4.5 Hz, 2H, CH_aH_b), 1.73-1.63 (m, 4H, $CO_2CH_2CH_2$), 1.35 (m, 12H, $(CH_2)_3Me$), and 0.89 (t, *J* = 7.4 Hz, 6H, CH_3).

^{13}C NMR (125 MHz, $CDCl_3$): δ 173.5, 80.4, 73.4, 67.9, 65.9, 57.7, 43.7, 40.2, 31.5, 28.7, 25.7, 22.7, and 14.1.

HR ESI-MS: Calcd for $C_{25}H_{46}O_8S_2Na$ $(M+Na)^+$: 561.2532 Found: 561.2567.

TLC: R_f = 0.31; 2:1 hexanes:ethyl acetate.

Dihexyl 1,3-Ditholane-2,2-bis[(*2R,3S*)-3-(methoxymethoxy)-2-methoxybutanoate] (SI-5)



SI-4 ***SI-5***

To 500 mL round bottom equipped with a stir bar, under N_2, containing crude diol **SI-4** (33.1 mmol) was added CH_2Cl_2 (110 mL, 0.3M) and *i*Pr_2NEt (95.9 mL, 497 mmol). Upon cooling the solution to 0 ºC, MOMCl (56.0 mL, 331 mmol; from $MeOCH_2OMe$ + MeCOCl[4]) was added dropwise and the reaction mixture warmed to room temperature and stirred until no additional diol was observed by TLC. After recooling to 0 ºC, saturated aqueous $NaHCO_3$ (100 mL) and H_2O (100 mL) were added sequentially. This mixture was warmed to room temperature and stirred for 15 minutes. The aqueous layer was extracted with EtOAc (3 x 400 mL) and the combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated *in vacuo*. Flash chromatography (3:1 hexanes / ethyl acetate) provided **SI-5** as a colorless oil (18.7 g, 90%, 2 steps from **8**).

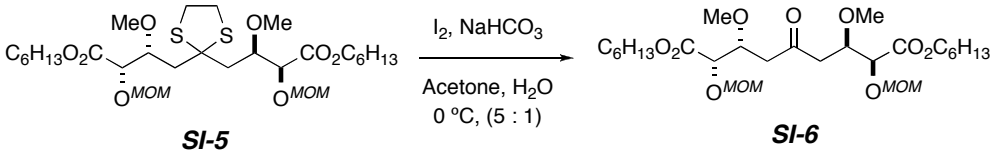
^{1}H NMR (500 MHz, $CDCl_3$): δ 4.76 (d, *J* = 7.0 Hz, 2H, OC*H*$_a$H$_b$OMe), 4.74 (d, *J* = 7.0 Hz, 2H, OCH$_a$*H*$_b$OMe), 4.45 (d, *J* = 3.7 Hz, 2H, *H*COMOM), 4.17 (dd, *J* = 6.9 and 1.5 Hz, 2H, *H*COMe), 3.43 (s, 6H, OC*H*$_3$), 3.39 (s, 6H, OC*H*$_3$), 3.32 (s, 4H, SC*H*$_2$C*H*$_2$S), 2.47 (dd, *J* = 15.6 and 4.5 Hz, 2H, C*H*$_a$H$_b$), 2.17 (dd, *J* = 15.4 and 5.5 Hz, 2H, CH$_a$*H*$_b$), 1.66 (pent, J = 7.4 Hz, 4H, $CO_2CH_2CH_2$), 1.33 (m, 12H, (C*H*$_2$)$_3$Me), 0.89 (t, *J* = 7.1 Hz, 6H, C*H*$_3$).

^{13}C NMR (125 MHz, $CDCl_3$): δ 171.1, 96.9, 80.1, 77.9, 68.6, 65.4, 57.9, 56.6, 44.0, 40.0, 31.6, 28.8, 25.8, 22.7, and 14.2.

HR ESI-MS: Calcd for $C_{29}H_{54}O_{10}S_2Na$ $(M+Na)^+$: 649.3056 Found: 649.3056.

TLC: R_f = 0.50; 2:1 hexanes:ethyl acetate.

Dihexyl (2*S*,3*R*,7*R*,8*S*)-3,7-Dimethoxy-2,8-di(methoxymethoxy)-5-oxononanedioate (SI-6)



SI-5 ***SI-6***

To dithiane **SI-5** (12.0 g, 19.1 mmol) was added a 5:1 mixture of acetone:water (159 mL total volume, 0.12M). $NaHCO_3$ powder (12.8 g, 153 mmol) was added, and the heterogeneous solution was cooled to 0 ºC. Crystalline I_2 (16.5 g, 64.9 mmol) was added and the solution turned a deep purple/black color. This mixture was stirred at 0 ºC for 3 h. Additional portions of $NaHCO_3$ powder (6.42 g, 77.0 mmol) and I_2 (8.2 g, 32.5 mmol) were added. Stirring continued until TLC analysis indicated that all starting material had been consumed. Saturated aqueous $NaHCO_3$ (50 mL) was then added followed by saturated aqueous Na_2SO_3 until the orange/yellow color disappeared. Water (50 mL) was added and the aqueous layer was extracted with EtOAc (3 x 250 mL. The combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated *in vacuo*. Flash chromatography (2:1 hexanes / ethyl acetate) provided ketone **SI-6** (9.57 g, 91%) as a colorless oil.

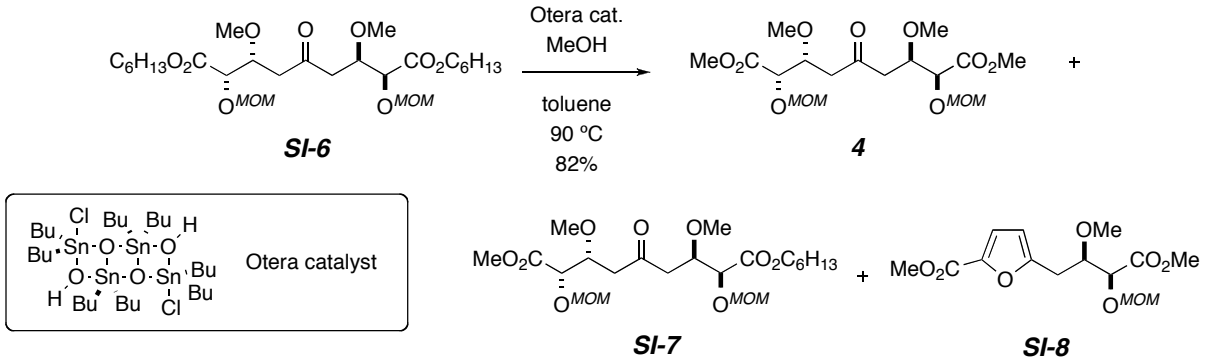
^{1}H NMR (500 MHz, $CDCl_3$): δ 4.71 (d, J = 7.0 Hz, 2H, OCH_aH$_b$OMe), 4.68 (d, J = 6.9 Hz, 2H, OCH$_a$$H_b$OMe), 4.28 (d, J = 4.2 Hz, 2H, HCOMOM), 4.17 (m, 6H, HCOMe and CO_2CH_2), 3.39 (s, 6H, OCH_3), 3.37 (s, 6H, OCH_3), 2.82 (dd, J = 18.0 and 8.1 Hz, 2H, CH_aH$_b$), 2.78 (dd, J = 17.6 and 5.6 Hz, 2H, CH$_a$$H_b$), 1.66 (pent, J = 7.0 Hz, 4H, $CO_2CH_2CH_2$), 1.34 (m, 12H, $(CH_2)_3$Me), 0.89 (t, J = 6.8 Hz, 6H, CH_3).

^{13}C NMR (75 MHz, $CDCl_3$): δ 206.5, 170.6, 96.8, 76.3, 65.5, 58.9, 56.5, 44.2, 31.6, 28.7, 25.7, 22.7, and 14.2.

HR ESI-MS: Calcd for $C_{27}H_{50}O_{11}Na$ $(M+Na)^+$: 573.3251 Found: 573.3259.

TLC: R_f = 0.28; 2:1 hexanes:ethyl acetate.

Dimethyl (2*S*,3*R*,7*R*,8*S*)-3,7-Dimethoxy-2,8-di(methoxymethoxy)-5-oxononanedioate (4)



To a large nitrogen-flushed culture tube containing hexyl ester ketone **SI-6** (1.50 g, 2.72 mmol) was added toluene (9.1 mL, 0.3 M), MeOH (6.6 mL, 163 mmol; shaken with solid K_2CO_3 immediately before use), and Otera catalyst (1.45 g, 1.36 mmol). The septum on the culture tube was replaced by a screw cap with a Teflon liner and the mixture was stirred at 90 ºC for 3 days. The solution was transferred to a round bottom flask using $CHCl_3$ and concentrated *in vacuo*. Gradient flash chromatography (2:1 -> 1:1 -> 1:2 hexanes/ethyl acetate) provided the methyl ester ketone **4** (860 mg, 77%) as a colorless oil.

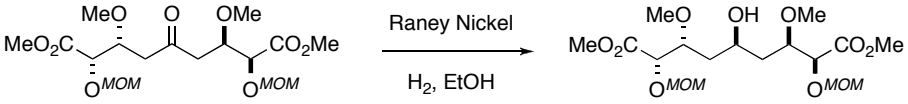
^{1}H NMR (500 MHz, $CDCl_3$): δ 4.71 (d, *J* = 7.0 Hz, 2H, OCH_aH$_b$OMe), 4.68 (d, *J* = 6.9 Hz, 2H, OCH$_a$$H_b$OMe), 4.29 (d, *J* = 4.0 Hz, 2H, *H*COMOM), 4.19 (ddd, *J* = 7.2, 5.1, and 4.0 Hz, 2H, *H*COMe), 3.78 (s, 6H, CO_2CH_3), 3.39 (s, 6H, OCH_3), 3.38 (s, 6H, OCH_3), 2.85 (dd, *J* = 17.5 and 7.4 Hz, 2H, CH_aH$_b$), and 2.78 (dd, *J* = 17.5 and 5.1 Hz, 2H, CH$_a$$H_b$).

^{13}C NMR (125 MHz, $CDCl_3$): δ 206.2, 170.9, 96.8, 76.9, 76.3, 58.9, 56.4, 52.2, and 44.1.

HR ESI-MS: Calcd for $C_{17}H_{30}O_{11}Na$ $(M+Na)^+$: 433.1680 Found: 433.1685.

TLC: R_f = 0.26; 1:1 hexanes:ethyl acetate.

Dimethyl (2*S*,3*R*,7*R*,8*S*)-5-Hydroxy-3,7-Dimethoxy-2,8-di(methoxymethoxy)nonanedioate (9)



4 ***9***

To ketone **4** (1.02 g, 2.49 mmol) was added EtOH (25.0 mL, 0.1 M) and black Raney nickel (4 mL of an aqueous heterogeneous solution; commercially available reagent, used as received) in a Fischer-Porter pressure tube equipped with the largest possible stir bar. The tube was flushed 3 times with H_2 and then filled with 50 psi of H_2. The heterogeneous solution was vigorously stirred until it was determined by TLC analysis of aliquots that the ketone had been fully consumed. The reaction residue was filtered through a pad of Celite® using ethyl acetate, and the filtrate was concentrated *in vacuo* to give the carbinol **9** as a colorless oil (935 mg, 91%).

^{1}H NMR (500 MHz, $CDCl_3$): δ 4.73 (d, *J* = 7.0 Hz, 1H, OCH_{a1}H$_{b1}$OMe), 4.72 (d, *J* = 7.0 Hz, 1H, OCH_{a2}H$_{b2}$OMe), 4.71 (d, *J* = 7.0 Hz, 1H, OCH$_{a1}$$H_{b1}$OMe), 4.70 (d, *J* = 7.0 Hz, 1H, OCH$_{a2}$$H_{b2}$OMe), 4.27 (d, *J* = 4.2 Hz, 1H, *H*COMOM), 4.24 (d, *J* = 4.0 Hz, 1H, *H*COMOM),

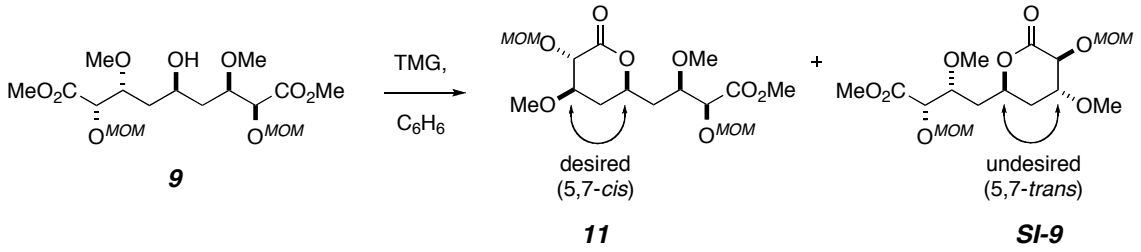
4.03-3.97 (m, 1H, *H*COH), 3.93 (ddd, *J* = 9.2, 3.7, and 3.7 Hz, 1H, *H*COMe), 3.86 (ddd, *J* = 7.4, 7.3, and 4.3 Hz, 1H, *H*COMe), 3.78 (s, 3H, CO_2CH_3), 3.77 (s, 3H, CO_2CH_3), 3.48 (s, 3H, OCH_3), 3.46 (s, 3H, OCH_3), 3.41 (s, 3H, OCH_3), 3.40 (s, 3H, OCH_3), and 1.75-1.61 (m, 4H, $CH_{a1}H_{b1}$ and $CH_{a2}H_{b2}$).

^{13}C NMR (125 MHz, C_6D_6): δ 171.5, 171.2, 97.2, 97.1, 82.0, 79.1, 78.7, 77.6, 67.5, 59.2, 58.2, 56.3, 56.2, 51.7, 51.6, 39.7, and 38.9.

HR ESI-MS: Calcd for $C_{17}H_{32}O_{11}Na$ $(M+Na)^+$: 435.1837 Found: 435.1829.

TLC: R_f = 0.33; 1:3 hexanes:ethyl acetate.

(8*S*,7*R*,5*S*)-5-[(2*S*,3*R*)-1,3-Dimethoxy-2-(methoxymethoxy)-1-oxobutyl]-7-methoxy-8-(methoxymethoxy)tetrahydropyran-1-one (*CAS*: D-Glycero-L-galacto-nonaric acid, 4,6-dideoxy-2,8-bis-O-(methoxymethyl)-3,7-di-O-methyl-, 9,5-lactone, 1-methyl ester, 11) and (2*S*,3*R*,5*R*)-5-[(7*S*,8*R*)-7,9-Dimethoxy-8-(methoxymethoxy)-9-oxobutyl]-3-methoxy-2-(methoxymethoxy)tetrahydropyran-1-one (SI-9) (*CAS:* D-Glycero-L-galacto-nonaric acid, 4,6-dideoxy-2,8-bis-O-(methoxymethyl)-3,7-di-O-methyl-, 1,5-lactone, 9-methyl ester, SI-9)



Benzene (150 mL, 0.015 M) was added to a 500 mL round bottom flask containing alcohol **9** (930 mg, 2.26 mmol). 1,1,3,3-Tetramethylguanidine (0.57 mL, 4.51 mmol) was added dropwise and the solution was stirred for 24 h at ambient temperature. Trifluoroacetic acid (0.174 mL, 2.25 mmol) was added dropwise and the reaction mixture was stirred for 3-5 minutes and then partitioned into CH_2Cl_2 and saturated aqueous $NaHCO_3$ (50 mL). The aqueous layer was extracted with CH_2Cl_2. The organic layers were combined, dried over Na_2SO_4, and concentrated *in vacuo* to afford **11** and **SI-9** (842 mg, 98%) as a colorless oil. (**11**:**SI-9** 12:1) The crude mixture of lactones **11** and **SI-9** was used in the next reaction without purification.

Characterization Data for 11

^{1}H NMR (500 MHz, $CDCl_3$): δ 5.02 (d, *J* = 6.8 Hz, 1H, OC$H_{a1}$$H_{b1}$OMe), 4.80 (d, *J* = 6.8 Hz, 1H, OC$H_{a2}$$H_{b2}$OMe), 4.73 (d, *J* = 8.0 Hz, 1H, $OCH_{a1}H_{b1}$OMe), 4.72 (d, *J* = 7.0 Hz, 1H, $OCH_{a2}H_{b2}$OMe), 4.54-4.46 (m, 1H, *H*COC=O), 4.28 (d, *J* = 3.6 Hz, 1H, *H*COMOM), 4.16 (d, *J* = 8.0 Hz, 1H, *H*COMOM), 3.91 (ddd, *J* = 6.6, 6.6, and 3.3 Hz, 1H, *H*COMe), 3.78 (s, 3H, CO_2CH_3), 3.65 (ddd, *J* = 10.2, 8.0, and 5.0 Hz, 1H, *H*COMe), 3.47 (s, 3H, OCH_3), 3.46 (s, 3H, OCH_3), 3.40 (s, 3H, OCH_3), 3.38 (s, 3H, OCH_3), 2.38 (ddd, *J* = 13.9, 5.0, and 2.9 Hz, 1H, C$H_{a1}$$H_{b1}$), 2.09 (ddd, *J* = 14.4, 7.7, and 6.8 Hz, 1H, C$H_{a2}$$H_{b2}$), 1.98 (ddd, *J* = 14.4, 6.7, and 5.0 Hz, 1H, $CH_{a2}H_{b2}$), and 1.72 (ddd, *J* = 13.9, 11.5, and 10.1 Hz, 1H, $CH_{a2}H_{b2}$).

^{13}C NMR (75 MHz, $CDCl_3$): δ 171.0, 170.7, 97.1, 96.9, 77.8, 76.3, 75.2, 73.7, 66.1, 58.3, 57.6, 56.6, 56.4, 52.4, 35.9, and 34.3.

HR ESI-MS: Calcd for $C_{16}H_{28}O_{10}Na$ $(M+Na)^+$: 403.1580 Found: 403.1585.

TLC: R_f = 0.25; 1:1 hexanes:ethyl acetate.

Characterization Data for SI-9 [sample obtained following the experiment that follows in which the L-selectride reduction proceeds much faster for **11** (to give **SI-10**) than for **SI-9**]

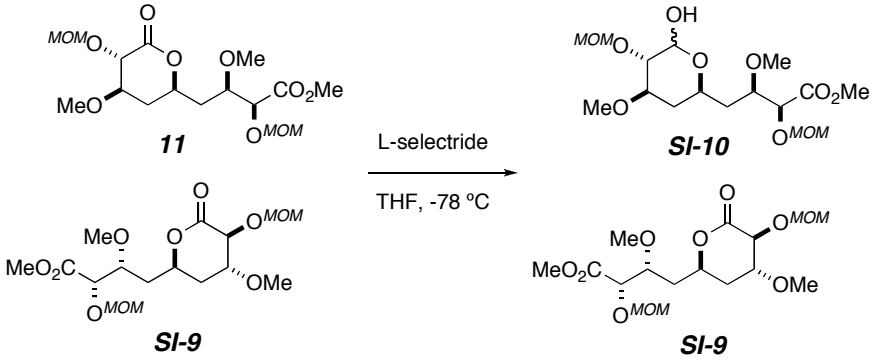
^{1}H NMR (500 MHz, $CDCl_3$): δ 4.94 (d, *J* = 6.8 Hz, 1H, OC$H_{a1}$$H_{b1}$OMe), 4.77 (d, *J* = 6.8 Hz, 1H, $OCH_{a1}H_{b1}$OMe), 4.76-4.66 (m, 1H, *H*COC=O), 4.72 (d, *J* = 7.0 Hz, 1H, OC$H_{a2}$$H_{b2}$OMe), 4.69 (d, *J* = 7.0 Hz, 1H, $OCH_{a2}H_{b2}$OMe), 4.38 (d, *J* = 6.4 Hz, 1H, *H*COMOM), 4.23 (d, *J* = 4.0 Hz, 1H, *H*COMOM), 3.95 (ddd, *J* = 9.3, 8.0, and 4.0 Hz, 1H, *H*COMe), 3.78 (s, 3H, CO_2CH_3), 3.65 (ddd, *J* = 6.4, 6.4, and 1.9 Hz, 1H, *H*COMe), 3.46 (s, 3H, OCH_3), 3.45 (s, 3H, OCH_3), 3.42 (s, 3H, OCH_3), 3.40 (s, 3H, OCH_3), and 2.03 (ddd, *J* = 15.1, 2.4, and 2.4 Hz, 1H, C$H_{a1}$$H_{b1}$), 1.94 (ddd, *J* = 15.1, 11.2, and 6.4 Hz, 1H, $CH_{a1}H_{b1}$), and 1.87-1.82 (m, 2H, C$H_{a2}$$H_{b2}$).

^{13}C NMR (125 MHz, $CDCl_3$): δ 170.8, 170.3, 96.5, 95.9, 77.3, 77.1, 76.0, 73.7, 71.7, 59.2, 57.1, 56.2, 55.9, 52.0, 37.0, and 34.5.

HR ESI-MS: Calcd for $C_{16}H_{28}O_{10}Na$ $(M+Na)^+$: 403.1580 Found: 403.1598.

TLC: R_f = 0.30; 1:1 hexanes:ethyl acetate.

(2*R*,3S,4*R*,6*R*)- and (2*S*,3S,4*R*,6*R*)-Methyl 2-Hydroxy-4-methoxy-3-(methoxymethoxy)tetrahydro-2*H*-pyran-6-[(2*R*,3*S*)-2-methoxy-3-(methoxymethoxy)]butanoate (SI-10)



To a 100 mL round bottom flask containing the mixture of lactones **11** and **SI-9** (0.845 g, 2.22 mmol) was added THF (22.3 mL, 0.1M). This solution was cooled to -78 ºC, L-selectride (2.44 mL, 2.44 mmol, 1.0M in THF) was added dropwise, and the resulting mixture was stirred for 1 h at -78 ºC. Saturated aqueous $NaHCO_3$ (30 mL) was added at -78 ºC and the resulting mixture was warmed to room temperature. Water (15 mL) was added and the mixture was extracted with ethyl acetate (3 x 150 mL). The combined organic layers were dried over Na_2SO_4 and concentrated *in vacuo* to afford a residue that was purified via MPLC (100% ethyl acetate) to provide **SI-10** as an *ca.* 2:1 mixture of major (*ax*-C2-OH) and minor (*eq*-C2-OH) anomers (722 mg, 87%) as a colorless oil.

^{1}H NMR (500 MHz, $CDCl_3$): δ 5.34 (dd, *J* = 3.2 and 3.2 Hz 1H, *H*COH$_{(maj)}$), 4.87 (d, *J* = 6.2 Hz, 1H, OC*H*HOMe), 4.85 (d, 6.4 Hz, 1H, OC*H*HOMe), 4.80 (d, *J* = 6.4 Hz, 1H, OC*H*HOMe), 4.76 (d, *J* = 7.1 Hz, 1H, OC*H*HOMe), 4.76 (d, *J* = 6.6 Hz, 1H, OC*H*HOMe), 4.75 (d, *J* = 7.2 Hz, 1H, OC*H*HOMe), 4.72 (d, *J* = 7.0 Hz, 1H, OC*H*HOMe), 4.72 (d, *J* = 7.1 Hz, 1H, OC*H*HOMe), 4.54 (dd, *J* = 7.6 and 4.3 Hz, 1H, *H*COH$_{(min)}$), 4.28 (d, *J* = 3.4 Hz, 1H, *H*COMOM$_{(maj)}$), 4.26 (d, *J* = 3.4 Hz, 1H, *H*COMOM$_{(min)}$), 4.16-4.09 (m, 1H, *H*COCOH$_{(maj)}$), 3.90 (ddd, *J* = 7.4, 6.2, and 3.5 Hz, 1H, *H*COMe$_{(min)}$), 3.85 (ddd, *J* = 7.5, 5.8, and 3.3 Hz, 1H, *H*COMe$_{(maj)}$), 3.782 (s, 3H, $CO_2CH_{3\ (maj)}$), 3.780 (s, 3H, $CO_2CH_{3\ (min)}$), 3.63 (ddd, *J* = 11.3, 9.6, and 5.0 Hz, 1H, *H*COMe$_{(maj)}$), 3.61-3.53 (m, 1H, *H*COCOH$_{(min)}$), 3.52 (dd, *J* = 9.3, and 3.6 Hz, 1H, *H*COMOM$_{(maj)}$), 3.47 (s 3H, OCH_3), 3.43 (s 3H, OCH_3), 3.42 (s 3H, OCH_3), 3.41 (s 3H, OCH_3), 3.37 (s 3H, OCH_3), 3.36 (s 3H, OCH_3), 3.35-3.28 (m, 1H, *H*COMe$_{(min)}$), 3.19 (dd, *J* = 9.0 and

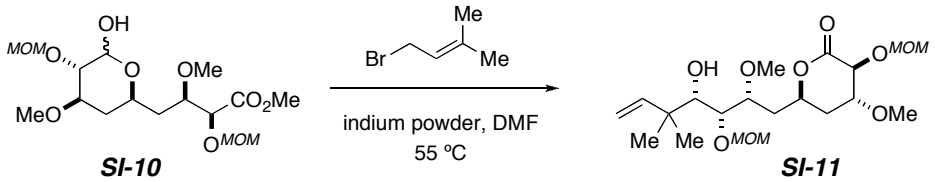
7.6 Hz, 1H, *H*COMOM$_{(min)}$), 2.16-2.08 (m, 1H, C*H*$_{a1}$H$_{b1(maj)}$), 2.14-2.07 (m, 1H, C*H*$_{a1}$H$_{b1(min)}$), 2.07-1.97 (m, 1H, C*H*$_{a2}$H$_{b2(min)}$), 1.94-1.80 (m, 2H, C*H*$_{a2}$*H*$_{b2(maj)}$), 1.90-1.81 (m, 1H, CH$_{a2}$*H*$_{b2(min)}$), and 1.44-1.31 (m, 1H, CH$_{a1}$*H*$_{b1(min)}$).

^{13}C NMR (125 MHz, $CDCl_3$): δ 171.6, 171.4, 98.1, 97.3, 96.81, 96.77, 96.73, 92.7, 82.9, 79.6, 79.1, 78.4, 78.1, 76.54, 76.49, 76.0, 68.5, 64.1, 58.11, 58.07, 57.4, 56.51, 56.48, 55.9, 55.7, 52.2, 36.6, 36.1, 35.1, and 34.9.

HR ESI-MS: Calcd for $C_{16}H_{30}O_{10}Na$ $(M+Na)^+$: 405.1731 Found: 405.1751.

TLC: R_f = 0.29; 1:3 hexanes:ethyl acetate.

(3*S*,4*R*,6*R*)-6-[(2*R*,3*R*,4*S*)-4-Hydroxy-2-methoxy-3-(methoxymethoxy)-5,5-dimethyl-6-heptenyl]-4-methoxy-3-(methoxymethoxy)tetrahydro-2*H*-pyran-2-one (SI-11)



To a threaded culture tube containing the epimeric lactols **SI-10** (1.46 g, 3.81 mmol) was added DMF (19.0 mL, 0.2M), 1-bromo-3-methyl-2-butene (1.76 mL, 15.2 mmol), and indium powder (1.75g, 15.2 mmol). The tube was capped and the reaction mixture was stirred at 55 ºC for 18 h. The mixture was cooled to room temperature and transferred to a 250 mL Erlenmeyer flask using ethyl acetate. Saturated aqueous $NaHCO_3$ (100 mL) was slowly added to quench the reaction, and additional water was added. The mixture was extracted with EtOAc (4 x 200 mL), and the combined organic layers were dried with Na_2SO_4 and concentrated *in vacuo* to provide **SI-11** (1.28 g, 80%) as a colorless oil. The crude product **SI-11** was used in the next reaction without purification.

^{1}H NMR (500 MHz, $CDCl_3$): δ 5.83 (dd, *J* = 17.4 and 10.9 Hz, 1H, CH_2=C*H*), 5.06 (d, *J* = 10.7 Hz, 1H, C*H*$_a$H$_b$=CH), 5.04 (d, *J* = 17.7 Hz, 1H, CH$_a$*H*$_b$=CH), 4.94 (d, *J* = 6.8 Hz, 1H, OC*H*$_{a1}$H$_{b1}$OMe), 4.77 (d, *J* = 6.8 Hz, 1H, OCH$_{a1}$*H*$_{b1}$OMe), 4.73 (d, *J* = 6.9 Hz, 1H, OC*H*$_{a2}$H$_{b2}$OMe), 4.72-4.63 (m, 1H, *H*COC=O), 4.65 (d, *J* = 6.8 Hz, 1H, OCH$_{a2}$*H*$_{b2}$OMe), 4.37 (d, *J* = 6.5 Hz, 1H, *H*COMOM), 3.76 (d, *J* = 4.3 Hz, 1H, *H*COMOM), 3.66 (ddd, *J* = 11.3, 4.3, and 1.8 Hz, 1H, *H*COMe), 3.63 (ddd, *J* = 6.5, 6.5, and 2.1 Hz, 1H, *H*COMe), 3.46 (s, 3H,

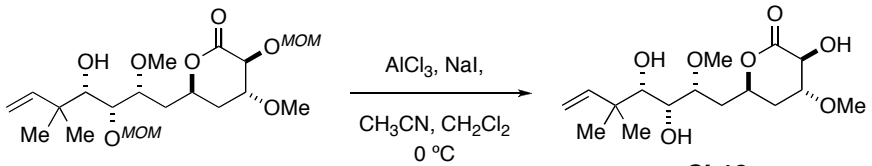
OCH_3), 3.43 (s, 3H, OCH_3), 3.41 (s, 3H, OCH_3), 3.38 (s, 3H, OCH_3), 2.61 (d, J = 9.9 Hz, 1H, OH), 2.02 (ddd, J = 15.1, 2.4, and 2.4 Hz, 1H, CH_{a1}H$_{b1}$), 1.94 (ddd, J = 15.0, 10.3, and 1.8 Hz, 1H, CH_{a2}H$_{b2}$), 1.92 (ddd, J = 15.1, 11.2, and 6.5 Hz, 1H, CH$_{a1}$$H_{b1}$), 1.74 (ddd, J = 14.9, 11.3, and 2.1 Hz, 1H, CH$_{a2}$$H_{b2}$), and 1.03 (s, 6H, C(C$H_3$)$_2$).

^{13}C NMR (125 MHz, $CDCl_3$): δ 170.6, 144.9, 112.9, 97.9, 96.2, 77.7, 77.3, 74.1 73.7, 73.2, 72.3, 58.4, 57.3, 56.9, 56.2, 42.1, 35.8, 34.9, 24.5, and 21.9.

HR ESI-MS: Calcd for $C_{20}H_{36}O_9Na$ $(M+Na)^+$: 443.2252 Found: 443.2259.

TLC: R_f = 0.67; 1:3 hexanes:ethyl acetate.

(3*S*,4*R*,6*R*)-6-[(2*R*,3*R*,4*S*)-3,4-Dihydroxy-2-methoxy-5,5-dimethyl-6-heptenyl]-3-hydroxy-4-methoxytetrahydro-2*H*-pyran-2-one (SI-12)



SI-11 ***SI-12***

To a 500 mL round bottom flask was added $AlCl_3$ (3.56 g, 26.7 mmol) and acetonitrile (84.8 mL, 0.021 M). The solution was cooled to 0 ºC, and NaI (4.00 g, 26.7 mmol) was added. After 5 minutes lactone **SI-11** (677 mg, 1.78 mmol) was added as a solution in CH_2Cl_2 (30 mL). The resulting mixture was stirred for 8 minutes at 0 ºC. Saturated aqueous $NaHCO_3$ (100 mL) was added, followed by saturated aqueous Na_2SO_3 until all yellow color disappeared. The solution was diluted with H_2O and the aqueous layer was extracted with EtOAc (3 x 250 mL). The combined organic layers were dried with Na_2SO_4 and concentrated *in vacuo* to provide triol **SI-12** (546 mg, 92%) as a colorless oil. The crude triol **SI-12** was used in the next reaction without purification.

^{1}H NMR (500 MHz, $CDCl_3$): δ 5.88 (dd, J = 17.4 and 10.9 Hz, 1H, CH_2=CH), 5.11 (dd, J = 10.9 and 1.3 Hz, 1H, CH_aH$_b$=CH), 5.09 (dd, J = 17.4 and 1.3 Hz, 1H, CH$_a$$H_b$=CH), 4.80-4.69 (m, 1H, HCOC=O), 4.35 (dd, J = 6.0 and 2.7 Hz, 1H, H_{lact}COH), 3.72 (dd, J = 6.6 and 4.7 Hz, 1H, H_{acyc}COH), 3.58 (ddd, J = 8.9, 6.3, and 2.3 Hz, 1H, HCOMe), 3.51 (ddd, J = 9.7, 4.5, and 2.9 Hz, 1H, HCOMe), 3.48 (s, 3H, OCH_3), 3.45 (s, 3H, OCH_3), 3.38-3.33 (m, 2H, HCOH, OH),

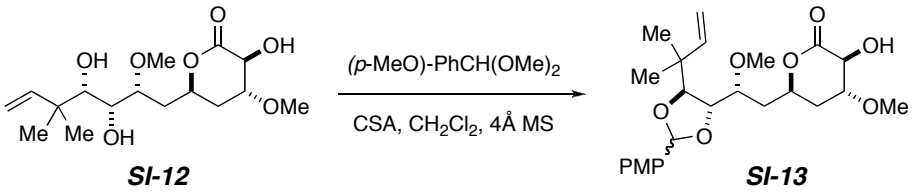
2.03-1.94 (m, *2*H, C$H_{a1}H_{b1}$), 1.88 (ddd, *J* = 14.7, 9.3, and 3.1 Hz, 1H, CH_{a2}H$_{b2}$), 1.77 (ddd, *J* = 14.8, 9.6, and 3.4 Hz, 1H, CH$_{a2}H_{b2}$), 1.08 (s, 3H, CCH_3), and 1.07 (s, 3H, CCH_3).

^{13}C NMR (125 MHz, $CDCl_3$): δ 174.2, 145.2, 113.7, 80.1, 78.8, 76.0, 73.0, 72.6, 69.1, 59.5, 57.5, 41.7, 36.8, 36.1, 23.8, and 22.7.

HR ESI-MS: Calcd for $C_{16}H_{28}O_7Na$ $(M+Na)^+$: 355.1727 Found: 355.1698.

TLC: R_f = 0.36; 1:3 hexanes:ethyl acetate.

(3*S*,4*R*,6*R*)-3-Hydroxy-4-methoxy-6-[(2*R*)-2-methoxy-2-((4*S*,5*S*)-2-(4-methoxyphenyl)-5-(2-methylbut-3-en-2-yl)-1,3-dioxolan-4-yl)ethyl]tetrahydro-2*H*-pyran-2-one (SI-13)



SI-12 ***SI-13***

To a 100 mL round bottom flask containing triol **SI-12** (520 mg, 1.56 mmol) was added CH_2Cl_2 (31.2 mL, 0.05 M) and 4 Å molecular sieves (100 mg). After 10 minutes *p*-anisaldehyde dimethylacetal (0.43 mL, 2.5 mmol) was added to the flask. Camphorsulfonic acid (CSA, 22 mg, 0.078 mmol) was added and the mixture was stirred at room temperature for 9 minutes, at which time TLC showed no sign of the starting triol **SI-12**. The reaction was quenched by the addition of saturated aqueous $NaHCO_3$ (30 mL). Water was added and the mixture was extracted with EtOAc (3 x 100 mL). The combined organic layers were dried over Na_2SO_4 and concentrated *in vacuo* to afford a residue that was purified via MPLC (1:1 hexanes/ethyl acetate) to provide alcohol **SI-13** (609 mg, 87%) as an epimeric mixture of PMP acetals.

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.42 (d, *J* = 8.6 Hz, 2H, MeOPhH_a), 7.41 (d, *J* = 8.6 Hz, 2H, MeOPhH_a), 6.90 (d, *J* = 8.7 Hz, 2H, MeOPhH_b), 6.89 (d, *J* = 8.7 Hz, 2H, MeOPhH_b), 5.95 (dd, *J* = 17.5 and 10.8 Hz, 1H, CH_2=C*H*), 5.92 (dd, *J* = 17.5 and 10.8 Hz, 1H, CH_2=C*H*), 5.92 (s, 1H, MeOPhC*H*), 5.85 (s, 1H, MeOPhC*H*), 5.15 (dd, *J* = 10.2 and 1.3 Hz, 1H, CH_{a1}H$_{b1}$=CH), 5.13 (dd, *J* = 10.2 and 1.2 Hz, 1H, CH_{a2}H$_{b2}$=CH), 5.11 (dd, *J* = 17.5 and 1.3 Hz, 1H, CH$_{a1}H_{b1}$=CH), 5.11 (dd, *J* = 17.5 and 1.3 Hz, 1H, CH$_{a2}H_{b2}$=CH), 4.83-4.73 (m, 1H, *H*COC=O), 4.83-4.73 (m, 1H, *H*COC=O), 4.36 (dd, *J* = 6.0 and 2.8 Hz, 1H, *H*CO(CH)PMP), 4.33 (dd, *J* = 6.0 and 2.7 Hz,

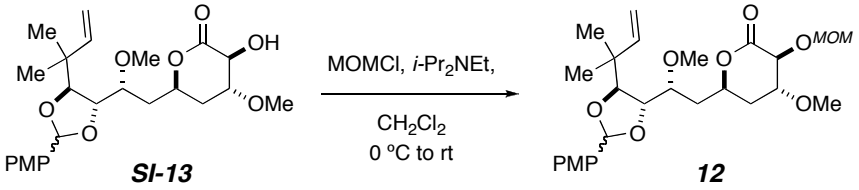
1H, *H*CO(CH)PMP), 4.06 (dd, *J* = 5.8 and 3.3 Hz, 1H, *H*COMe), 3.98 (d, *J* = 5.7 Hz, 1H, *H*COH), 3.98 (d, *J* = 5.8 Hz, 1H, *H*COH), 3.85 (dd, *J* = 5.7 and 2.8 Hz, 1H, *H*COMe), 3.81 (s, 3H, PhOCH_3), 3.80 (s, 3H, PhOOCH_3), 3.63-3.33 (m, 3H, *H*CO(CH)PMP, *H*COMe, and O*H*), 3.63-3.33 (m, 3H, *H*CO(CH)PMP, *H*COMe, and O*H*), 3.54 (s, 3H, OCH_3), 3.46 (s, 3H, OCH_3), 3.46 (s, 6H, OCH_3), 2.05-1.77 (m, 4H, C$H_{a1}H_{b1}$ and C$H_{a2}H_{b2}$), 2.05-1.77 (m, 4H, C$H_{a1}H_{b1}$ and C$H_{a2}H_{b2}$), 1.18 (s, 3H, CCH_3), 1.15 (s, 3H, CCH_3), 1.12 (s, 3H, CCH_3), and 1.10 (s, 3H, CCH_3).

^{13}C NMR (125 MHz, $CDCl_3$): δ 174.22, 174.17, 160.7, 160.6, 143.8, 130.3, 129.7, 128.6, 128.4, 114.1, 113.93, 113.90, 113.8, 104.7, 104.4, 84.4, 84.2, 80.7, 79.6, 78.7, 76.9, 73.0, 72.9, 72.6, 61.1, 57.4, 55.5, 41.1, 39.8, 38.6, 37.5, 35.9, 24.3, 24.1, 23.5, and 22.9.

HR ESI-MS: Calcd for $C_{20}H_{36}O_9Na$ $(M+Na)^+$: 473.2146 Found: 473.2146.

TLC: R_f = 0.30; 1:1 hexanes:ethyl acetate.

(3*S*,4*R*,6*R*)-4-Methoxy-6-((2*R*)-2-methoxy-2-((4*S*,5*S*)-2-(4-methoxyphenyl)-5-(2-methylbut-3-en-2-yl)-1,3-dioxolan-4-yl)ethyl)-3-(methoxymethoxy)tetrahydro-2*H*-pyran-2-one (12)



To a 50 mL round bottom flask containing the alcohol acetals **SI-13** (609 mg, 1.35 mmol) was added CH_2Cl_2 (4.5 mL, 0.3 M) and *i*Pr_2NEt (6.60 mL, 40.5 mmol). The solution was coled to 0 ºC, MOMCl (4.56 mL, 27.0 mmol; from $MeOCH_2OMe$ + MeCOCl[4]) was added dropwise, and the solution was warmed to room temperature and stirred until no starting alcohol **SI-13** was observed by TLC. The mixture was recooled to 0 ºC, and saturated aqueous $NaHCO_3$ (15 mL) and water (15 mL) were added sequentially. The mixture was warmed to room temperature and stirred for 15 minutes. The aqueous layer was extracted with EtOAc (3 x 100 mL) and the combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated *in vacuo*. Flash chromatography (1:1 hexanes / ethyl acetate) provided lactone **12** (661 mg, 99%), which was not further purified.

Characterization Data for 12 (*major*) (from the 2:1 mixture of acetal epimers)

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.43 (d, *J* = 8.7 Hz, 2H, MeOPhH_a), 6.90 (d, *J* = 8.7 Hz, 2H, MeOPhH_b), 5.95 (dd, *J* = 17.4 and 10.9 Hz, 1H, CH_2=C*H*), 5.92 (s, 1H, MeOPhC*H*), 5.17-5.07 (m, 2H, CH_2=CH), 4.95 (d, *J* = 6.8 Hz, 1H, OCH_aH$_b$OMe), 4.77 (d, *J* = 6.8 Hz, 1H, OCH$_a$$H_b$OMe), 4.76-4.72 (m, 1H, *H*COC=O), 4.38 (d, *J* = 6.2 Hz, 1H, *H*COMOM) 3.98 (d, *J* = 5.7 Hz, 1H, *H*CO(CH)PMP), 3.85 (dd, *J* = 5.7 and 2.7 Hz, 1H, *H*CO(CH)PMP), 3.81 (s, 3H, PhOCH_3), 3.65 (ddd, *J* = 6.3, 6.3, and 1.5 Hz, 1H, *H*COMe), 3.57 (s, 3H, OCH_3), 3.52 (ddd, *J* = 10.5, 2.7, and 2.7 Hz, 1H, *H*COMe), 3.47 (s, 3H, OCH_3), 3.40 (s, 3H, OCH_3), 2.08-1.75 (m, 4H, C$H_{a1}H_{b1}$ and C$H_{a2}H_{b2}$), 1.15 (s, 3H, CCH_3), and 1.12 (s, 3H, CCH_3).

Characterization Data for 12 (*minor*) (from the 2:1 mixture of acetal epimers)

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.42 (d, *J* = 8.7 Hz, 2H, MeOPhH_a), 6.89 (d, *J* = 8.7 Hz, 2H, MeOPhH_b), 5.92 (dd, *J* = 16.8 and 10.7 Hz, 1H, CH_2=C*H*), 5.85 (s, 1H, MeOPhC*H*), 5.17-5.07 (m, 2H, CH_2=CH), 4.94 (d, *J* = 6.8 Hz, 1H, OCH_aH$_b$OMe), 4.77 (d, *J* = 6.9 Hz, 1H, OCH$_a$$H_b$OMe), 4.72-4.70 (m, 1H, *H*COC=O), 4.37 (d, *J* = 6.2 Hz, 1H, *H*COMOM) 4.04 (dd, *J* = 5.8 and 3.2 Hz, 1H, *H*CO(CH)PMP), 3.98 (d, *J* = 5.8 Hz, 1H, *H*CO(CH)PMP), 3.80 (s, 3H, PhOCH_3), 3.65 (ddd, *J* = 6.3, 6.3, and 1.5 Hz, 1H, *H*COMe), 3.60 (ddd, *J* = 10.4, 3.1, and 3.1 Hz, 1H, *H*COMe), 3.49 (s, 3H, O*Me*), 3.46 (s, 3H, OCH_3), 3.40 (s, 3H, OCH_3), 2.08-1.75 (m, 4H, C$H_{a1}H_{b1}$ and C$H_{a2}H_{b2}$), 1.18 (s, 3H, CCH_3), and 1.10 (s, 3H, CCH_3).

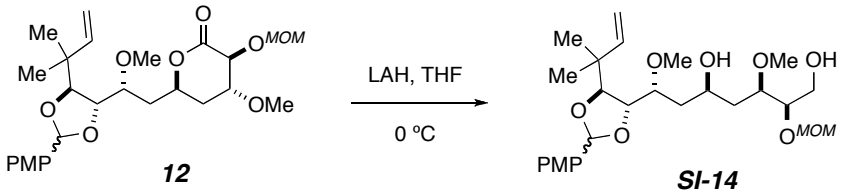
Characterization Data for the Mixture of 12 (*major*) and 12 (*minor*) (2:1)

^{13}C NMR (125 MHz, $CDCl_3$): δ 170.6, 170.5, 160.6, 143.7, 130.3, 129.7, 128.6, 128.4, 114.0, 113.9, 113.8, 104.6, 104.3, 96.1, 84.4, 84.1, 80.8, 79.8, 78.7, 77.62, 77.58, 76.9, 74.0, 73.9, 72.3, 72.2, 61.3, 60.3, 57.3, 56.2, 55.4, 41.1, 39.7, 38.9, and 37.8.

HR ESI-MS: Calcd for $C_{26}H_{38}O_9Na$ $(M+Na)^+$: 517.2408 Found: 517.2440.

TLC: R_f = 0.48; 1:1 hexanes:ethyl acetate.

(2*R*,3*R*,5*S*,7*R*)-3,7-Dimethoxy-2-(methoxymethoxy)-7-[(4*S*,5*S*)-2-(4-methoxyphenyl)-5-(2-methyl-3-buten-2-yl)-1,3-dioxolan-4-yl]heptane-1,5-diol (SI-14)



To a 100 mL round bottom flask was added $LiAlH_4$ powder (153 mg, 4.02 mmol). THF (20.1 mL, 0.2 M) was added and the solution was cooled to 0 ºC. Lactone **12** (660 mg, 1.34 mmol) was slowly added as a solution in THF (13.4 mL) and the resulting solution was stirred for 1 h, at which time no starting lactone **12** was visible by TLC. Water (0.157 mL), aqueous 15% NaOH (0.157 mL), and water (0.471 mL) were added sequentially to the well-stirred solution at 0 ºC, and the resulting suspension was stirred for 30 minutes while warming to room temperature. This mixture was filtered through a pad of Celite® with the aid of ethyl acetate, and the filtrate was concentrated *in vacuo* to give the crude diol **SI-14**. Purification by flash chromatography, although not necessary for the following reaction, provided **SI-14** (642 mg, 96%).

Characterization Data for SI-14 (*major*) (from the 2:1 mixture of acetal epimers)

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.43 (d, *J* = 8.8 Hz, 2H, MeOPhH_a), 6.89 (d, *J* = 8.7 Hz, 2H, MeOPhH_b), 5.97 (dd, *J* = 17.5 and 10.9 Hz, 1H, CH_2=C*H*), 5.94 (s, 1H, MeOPhC*H*), 5.10 (dd, *J* = 11.0 and 1.5 Hz, 1H, C$H_a$$H_b$=CH), 5.09 (dd, *J* = 17.5 and 1.4 Hz, 1H, $CH_a$$H_b$=CH), 4.74 (d, *J* = 6.9 Hz, 1H, OC$H_a$$H_b$OMe), 4.70 (d, *J* = 6.9 Hz, 1H, OC$H_a$$H_b$OMe), 4.08-3.96 (m, 1H, *H*COH), 3.99 (d, *J* = 5.7 Hz, 1H, *H*CO(CH)PMP), 3.90 (dd, *J* = 5.7 and 2.8 Hz, 1H, *H*CO(CH)PMP), 3.80 (s, 3H, PhOCH_3), 3.78-3.71 (m, 2H, *H*COMOM and C$H_a$$H_b$OH), 3.67-3.56 (m, 2H, *H*COMe and $CH_a$$H_b$OH), 3.59 (s, 3H, OC$H_3$), 3.53-3.44 (m, 1H, *H*OMe), 3.48 (s, 3H, OCH_3), 3.42 (s, 3H, OCH_3), 3.34 (d, *J* = 2.0 Hz, 1H, CHO*H*), 2.91 (dd, *J* = 7.9 and 3.4 Hz, 1H, CH_2O*H*), 1.84-1.71 (m, 2H, C$H_{a1}$$H_{b1}$ and C$H_{a2}$$H_{b2}$), 1.70-1.62 (m, 1H, $CH_{a1}$$H_{b1}$), 1.60-1.51 (m, 1H, $CH_{a2}$$H_{b2}$), 1.14 (s, 3H, CC$H_3$), and 1.12 (s, 3H, CC$H_3$).

Characterization Data for SI-14 (*minor*) (from the 2:1 mixture of acetal epimers)

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.43 (d, *J* = 8.7 Hz, 2H, MeOPhH_a), 6.88 (d, *J* = 8.7 Hz, 2H, MeOPhH_b), 5.93 (dd, *J* = 17.6 and 10.8 Hz, 1H, CH_2=C*H*), 5.84 (s, 1H, MeOPhC*H*), 5.13 (dd, *J* = 10.8 and 1.2 Hz, 1H, C$H_a$$H_b$=CH), 5.09 (dd, *J* = 17.5 and 1.3 Hz, 1H, $CH_a$$H_b$=CH), 4.74 (d, *J*

= 6.9 Hz, 1H, OCH_aH$_b$OMe), 4.69 (d, *J* = 6.9 Hz, 1H, OCH$_a$$H_b$OMe), 4.08-3.96 (m, 1H, *H*COH), 4.06 (dd, *J* = 6.1 and 3.0 Hz, 1H, *H*CO(CH)PMP), 3.99 (d, *J* = 6.1 Hz, 1H, *H*CO(CH)PMP), 3.80 (s, 3H, PhOCH_3), 3.78-3.71 (m, 2H, *H*COMOM and CH_aH$_b$OH), 3.67-3.56 (m, 2H, *H*COMe and CH$_a$$H_b$OH), 3.50 (s, 3H, OC$H_3$), 3.53-3.44 (m, 1H, *H*OMe), 3.46 (s, 3H, OCH_3), 3.42 (s, 3H, OCH_3), 3.34 (d, *J* = 1.7 Hz, 1H, CH$_2$O*H*), 2.92 (dd, *J* = 6.8, 3.5 Hz, CH$_2$O*H*), 1.84-1.71 (m, 2H, CH_{a1}H$_{b1}$ and CH_{a2}H$_{b2}$), 1.70-1.62 (m, 1H, CH$_{a1}$$H_{b1}$), 1.60-1.51 (m, 1H, CH$_{a2}$$H_{b2}$), 1.17 (s, 3H, CC$H_3$), and 1.10 (s, 3H, CC$H_3$).

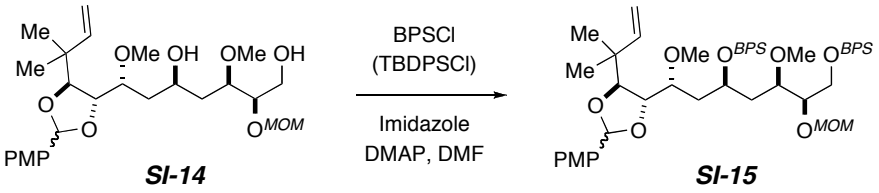
Characterization Data for mixture of SI-14 (*major*) and SI-14 (*minor*) (2:1)

^{13}C NMR (125 MHz, $CDCl_3$): δ 160.59, 160.55, 144.05, 144.00, 130.6, 130.0, 128.6, 128.5, 113.86, 113.82, 113.5, 112.4, 104.6, 104.2, 97.7, 84.7, 84.3, 82.4, 82.3, 81.1, 80.9, 80.4, 79.6, 77.8, 68.2, 68.1, 67.1, 62.4, 62.3, 60.5, 59.8, 58.34, 58.30, 56.1, 55.5, 41.1, 40.6, 39.8, 39.7, 37.19, 37.16, 24.2, 24.0, 23.6, and 23.0.

HR ESI-MS: Calcd for $C_{26}H_{42}O_9Na$ $(M+Na)^+$: 521.2721 Found: 521.2724.

TLC: R_f = 0.32; 100% ethyl acetate.

(5*S*,7*R*,8*R*)-7-Methoxy-5-[(*R*)-2-methoxy-2-((4*S*,5*S*)-2-(4-methoxyphenyl)-5-(2-methyl-3-buten-2-yl)-1,3-dioxolan-4-yl)ethyl]-8-(methoxymethoxy)-2,2,12,12-tetramethyl-3,3,11,11-tetraphenyl-4,10-dioxa-3,11-disilatridecane (SI-15)



SI-14 ***SI-15***

To a 100 mL round bottom flask containing crude diol **SI-14** (~6.27 mmol) was added DMF (20.9 mL, 0.3 M), imidazole (1.92 g, 28.2 mmol), DMAP (77 mg, 0.63 mmol), and BPSCl (6.5 mL, 25.1 mmol). The reaction mixture was stirred for 24 h, at which time TLC showed no remaining diol **SI-14**. After the reaction mixture was cooled to 0 ºC, saturated aqueous $NaHCO_3$ was added followed by dilution with H_2O and Et_2O. This mixture was warmed to room temperature and stirred for 15-30 minutes. The aqueous layer was extracted with Et_2O (3 x 200 mL), and the combined organic layers were dried over Na_2SO_4 and concentrated *in vacuo*. Residual DMF was removed by a high vacuum rotary evaporator. Flash chromatography (6:1 hexanes/ethyl acetate) provided bis-TBDPS ether **SI-15** in excellent yield (5.06 g, 92%, 3-steps).

Characterization Data for SI-15 (*major*) (from the 2:1 mixture of acetal epimers)

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.73-7.59 (m, 8H, Ph*H*), 7.46-7.20 (m, 14H, Ph*H* and MeOPhH_a), 6.88 (d, *J* = 8.7 Hz, 2H, MeOPhH_b), 5.86 (dd, *J* = 17.9 and 10.5 Hz, 1H, CH_2=C*H*), 5.77 (s, 1H, MeOPhC*H*), 5.00 (dd, *J* = 10.9 and 1.5 Hz, 1H, CH_aH$_b$=CH), 4.99 (dd, *J* = 17.0 and 1.5 Hz, 1H, CH$_a$$H_b$=CH), 4.68 (d, *J* = 6.8 Hz, 1H, OCH_aH$_b$OMe), 4.54 (d, *J* = 6.8 Hz, 1H, OCH$_a$$H_b$OMe), 4.15-4.08 (m, 1H, *H*COTBDPS), 3.84 (d, *J* = 5.3 Hz, 1H, *H*CO(CH)PMP), 3.80 (s, 3H, PhOCH_3), 3.74 (dd, *J* = 5.3 and 3.7 Hz, 1H, *H*CO(CH)PMP), 3.68-3.56 (m, 3H, *H*COMOM and CH_2OTBDPS), 3.45 (ddd, *J* = 9.4, 2.5, and 2.5 Hz, 1H, *H*COMe), 3.31 (ddd, *J* = 8.6, 3.7, and 3.7 Hz, 1H, *H*COMe), 3.24 (s, 3H, OCH_3), 3.18 (s, 3H, OCH_3), 3.11 (s, 3H, OCH_3), 1.92 (ddd, *J* = 14.7, 8.8, and 3.8 Hz, 1H, CH_{a1}H$_{b1}$), 1.75-1.66 (m, 2H, CH$_{a1}$$H_{b1}$ and CH_{a2}H$_{b2}$), 1.63 (ddd, *J* = 14.2, 8.9, and 2.8 Hz, 1H, CH$_{a2}$$H_{b2}$), 1.05 (s, 3H, CC$H_3$), 1.04 (s, 9H, SiC(C$H_3$)$_3$), 1.02 (s, 3H, CC$H_3$), and 1.01 (s, 9H, SiC(CH_3)$_3$).

Characterization Data for SI-15 (*minor*) (from the 2:1 mixture of acetal epimers)

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.73-7.59 (m, 8H, Ph*H*), 7.46-7.20 (m, 14H, Ph*H* and MeOPhH_a), 6.84 (d, *J* = 8.7 Hz, 2H, MeOPhH_b), 5.86 (dd, *J* = 17.9 and 10.5 Hz, 1H, CH_2=C*H*), 5.78 (s, 1H, MeOPhC*H*), 5.04 (dd, *J* = 10.9 and 1.7 Hz, 1H, CH_aH$_b$=CH), 5.01 (dd, *J* = 17.5 and 1.2 Hz, 1H, CH$_a$$H_b$=CH), 4.66 (d, *J* = 6.6 Hz, 1H, OCH_aH$_b$OMe), 4.52 (d, *J* = 6.5 Hz, 1H, OCH$_a$$H_b$OMe), 4.15-4.08 (m, 1H, *H*COTBDPS), 3.92-3.89 (m, *2*H, *H*CO(CH)PMP and *H*CO(CH)PMP), 3.80 (s, 3H, PhOCH_3), 3.68-3.56 (m, 3H, *H*COMOM and CH_2OTBDPS), 3.48-3.40 (m, 1H, *H*COMe), 3.42 (ddd, *J* = 9.1, 2.7, and 2.7 Hz, 1H, *H*COMe), 3.23 (s, 3H, OCH_3), 3.15 (s, 3H, OCH_3), 3.03 (s, 3H, OCH_3), 1.96-1.86 (m, 1H, CH_{a1}H$_{b1}$), 1.75-1.66 (m, 2H, CH$_{a1}$$H_{b1}$ and CH_{a2}H$_{b2}$), 1.66-1.58 (m, 1H, CH$_{a2}$$H_{b2}$), 1.04 (s, 3H, CC$H_3$), 1.03 (s, 9H, SiC(C$H_3$)$_3$), 1.02 (s, 3H, CC$H_3$), and 1.01 (s, 9H, SiC(CH_3)$_3$).

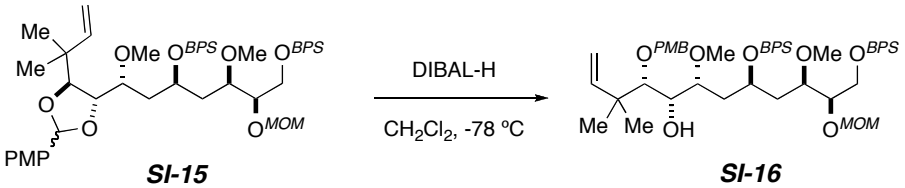
Characterization Data for mixture of SI-15 (*major*) and SI-15 (*minor*) (2:1)

^{13}C NMR (125 MHz, $CDCl_3$): δ 160.5, 160.4, 144.2, 144.1, 136.24, 136.18, 135.8, 135.7, 134.5, 134.1, 133.6, 130.2, 129.78, 129.75, 129.66, 128.6, 128.5, 127.88, 127.86, 127.79, 127.72, 127.63, 127.55, 113.77, 113.73, 113.3, 104.5, 103.7, 97.0, 84.4, 84.1, 80.9, 79.1, 77.3, 69.0, 68.9, 68.2, 63.6, 63.5, 59.3, 58.6, 58.2, 55.9, 55.5, 41.0, 39.81, 39.79, 39.4, 39.1, 38.9, 27.3, 27.0, 24.2, 24.0, 23.5, 22.8, 19.56, 19.53, 19.32, and 19.30.

HR ESI-MS: Calcd for $C_{58}H_{78}O_9Si_2Na$ $(M+Na)^+$: 997.5077 Found: 997.5110.

TLC: R_f = 0.47; 6:1 hexanes:ethyl acetate.

(4*S*,5*S*,6*R*,8*R*,10*R*,11*R*)-8,12-bis(*tert*-Butyldiphenylsilyloxy)-6,10-dimethoxy-4-(4-methoxybenzyloxy)-11-(methoxymethoxy)-3,3-dimethyl-1-dodecen-5-ol (SI-16)



SI-15 ***SI-16***

The following procedure was performed in duplicate parallel procedures and the contents of each reaction vessel were combined at the point of workup. To a screw capped culture tube fitted with a septum closure and containing bis-BPS ether **SI-15** (700 mg, 0.718 mmol) was added CH_2Cl_2 (6.5 mL, 0.11 M). The reaction mixture was cooled to -78 ºC and DIBAL-H (6.5 mL, 7.15 mmol, 1.1 M in toluene) was added and the septum was replaced quickly with a teflon-lined screw cap. The reaction solution was kept at -78 ºC for 48 h. The cap was replaced again with a septum and ethyl acetate (6.5 mL) was added dropwise down the side of the culture tube to quench the excess DIBAL-H. Both reaction mixtures were then transferred to the same 250 mL Erlenmeyer flask equipped with a stir bar using ethyl acetate and warmed to room temperature. Small portions of saturated aqueous Rochelle's salt (Na,K-Tartrate) were added were added with virorous stirring, carefully, and with cooling so as to avoid any large exotherm. Upon this addition, the mixture turned from homogeneous to a gelatinous suspension and, upon addition of more saturated aqueous Rochelle's salt, back to homogeneous. The two-phase solution in the Erlynmeyer flask was then allowed to stir for an additional 18 h. The layers were separated and the aqueous layer was extracted with EtOAc (3 x 250 mL). The combined organic layers were dried over Na_2SO_4 and concentrated *in vacuo*. Purification by flash chromatography (3:1 hexanes:ethyl acetate) provided the alcohol **SI-16** (1.33 g, 95%).

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.75-7.60 (m, 8H, Ph*H*), 7.46-7.20 (m, 14H, Ph*H* and MeOPhH_a), 6.86 (d, *J* = 8.5 Hz, 2H, MeOPhH_b), 5.77 (dd, *J* = 17.5 and 10.8 Hz, 1H, CH_2=C*H*), 4.96 (dd, *J* = 17.5 and 1.2 Hz, 1H, CH_aH$_b$=CH), 4.95 (dd, *J* = 10.8 and 1.3 Hz, 1H, CH$_a$$H_b$=CH), 4.69 (d, *J* = 6.7 Hz, 1H, OCH_aH$_b$OMe), 4.55 (d, *J* = 10.4 Hz, 1H, MeOPhCH_aH$_b$), 4.54 (d, *J* = 6.7 Hz, 1H, OCH$_a$$H_b$OMe), 4.43 (d, *J* = 10.4 Hz, 1H, MeOPhCH$_a$$H_b$), 4.17-4.08 (m, 1H, *H*COTBDPS), 3.81 (s, 3H, PhOCH_3), 3.69-3.56 (m, 3H, *H*COMOM, CH_2OTBDPS), 3.48 (ddd, *J* = 9.8, 2.9, and 2.9 Hz, 1H, *H*COMe), 3.46 (ddd, *J* = 6.7, 4.5, and 2.1 Hz, 1H, *H*COH), 3.25 (s,

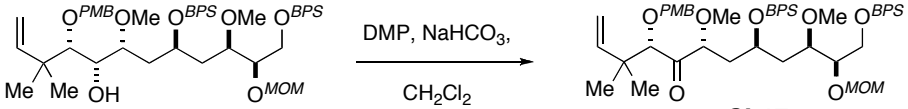
3H, OCH_3), 3.22 (ddd, J = 6.0, 6.0, and 4.3 Hz, 1H, *H*COMe), 3.17 (s, 3H, OCH_3), 3.15 (s, 3H, OCH_3), 3.12 (d, J = 1.9 Hz, *H*COPMB), 2.84 (d, J = 7.0 Hz, 1H, O*H*), 1.78 (app t, J = 5.9 Hz, 2H, C$H_{a1}H_{b1}$), 1.70 (ddd, J = 13.8, 9.3, and 3.7 Hz, 1H, CH_{a2}H$_{b2}$), 1.63 (ddd, J = 14.2, 8.5, and 3.2 Hz, 1H, CH$_{a2}$$H_{b2}$), 1.032 (s, 9H, SiC(C$H_3$)$_3$), 1.030 (s, 9H, SiC(C$H_3$)$_3$), 1.02 (s, 3H, CC$H_3$), and 0.99 (s, 3H, CC$H_3$).

^{13}C NMR (125 MHz, $CDCl_3$): δ 159.4, 145.3, 136.3, 136.1, 135.79, 135.74, 134.7, 134.1, 133.6, 133.58, 130.5, 129.9, 129.8, 129.70, 129.69, 129.4, 127.88, 127.87, 127.7, 127.6, 113.9, 112.9, 97.0, 83.5, 80.5, 79.0, 77.3, 74.5, 70.2, 69.2, 63.7, 58.4, 58.1, 55.8, 55.5, 42.7, 38.7, 37.9, 27.3, 27.0, 24.6, 21.5, 19.6, and 19.3.

HR ESI-MS: Calcd for $C_{58}H_{80}O_9Si_2Na$ $(M+Na)^+$: 999.5233 Found: 999.5252.

TLC: R_f = 0.52; 3:1 hexanes:ethyl acetate.

(4*S*,6*R*,8*S*,10*R*,11*R*)-8,12-bis(*tert*-Butyldiphenylsilyloxy)-6,10-dimethoxy-4-(4-methoxybenzyloxy)-11-(methoxymethoxy)-3,3-dimethyl-1-dodecen-5-one (SI-17)



SI-16 ***SI-17***

To a 100 mL round bottom flask containing alcohol **SI-16** (1.15 g, 1.18 mmol) was added CH_2Cl_2 (25.6 mL, 0.046 M). The solution was cooled to 0 ºC followed by the addition of powdered $NaHCO_3$ (445 mg, 5.30 mmol) and Dess-Martin periodinane (619 mg, 1.46 mmol) to the reaction mixture. The solution was warmed to room temperature and stirred for 18 h. The mixture was cooled to 0 ºC and saturated aqueous $NaHCO_3$ (10 mL) and saturated aqueous $Na_2S_2O_3$ (20 mL) were added. The two-phase mixture was warmed to room temperature and stirred till both layers were clear. The mixture was diluted with H_2O (20 mL) and Et_2O (50 mL), and the aqueous layer was extracted with Et_2O (3 x 75 mL). The combined organic layers were dried with Na_2SO_4 and concentrated *in vacuo* to provide the crude ketone **SI-17** in >90%, which was used in the next reaction without purification.

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.69-7.57 (m, 8H, Ph*H*), 7.45-7.18 (m, 14H, Ph*H* and MeOPhH_a), 6.83 (d, J = 8.7 Hz, 2H, MeOPhH_b), 5.99 (dd, J = 17.4 and 10.9 Hz, 1H, CH_2=C*H*),

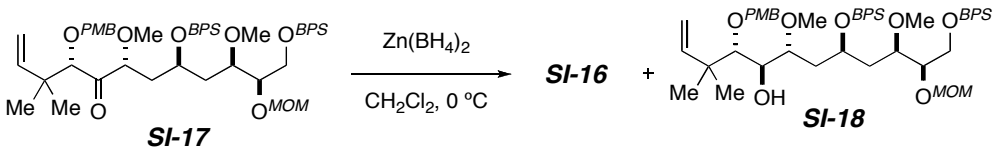
4.99 (dd, J = 10.9 and 1.3 Hz, 1H, CH_aH$_b$=CH), 4.97 (dd, J = 17.4 and 1.3 Hz, 1H, CH$_a$$H_b$=CH), 4.65 (d, J = 6.8 Hz, 1H, OCH_aH$_b$OMe), 4.51 (d, J = 11.0 Hz, 1H, MeOPhCH_aH$_b$), 4.49 (d, J = 6.8 Hz, 1H, OCH$_a$$H_b$OMe), 4.35 (dd, J = 10.1 and 2.4 Hz, 1H, *H*COMe), 4.29 (d, J = 11.0 Hz, 1H, MeOPhCH$_a$$H_b$), 4.24 (dddd, J = 9.6, 9.6, 2.7, and 2.7 Hz, 1H, *H*COTBDPS), 3.77 (s, 3H, PhOCH_3), 3.74 (s, 1H, *H*COPMB), 3.61-3.54 (m, 1H, CH_aH$_b$OTBDPS), 3.54-3.47 (m, 2H, CH$_a$$H_b$OTBDPS and *H*COMOM), 3.25 (ddd, J = 10.3, 2.7, and 2.7 Hz, 1H, *H*COMe), 3.22 (s, 3H, OCH_3), 3.05 (s, 3H, OCH_3), 3.02 (s, 3H, OCH_3), 1.88 (ddd, J = 14.1, 9.4, and 2.5 Hz, 1H, CH_{a1}H$_{b1}$), 1.71-1.60 (m, 2H, CH$_{a1}$$H_{b1}$ and CH_{a2}H$_{b2}$), 1.48 (ddd, J = 13.9, 9.8, and 2.4 Hz, 1H, CH$_{a2}$$H_{b2}$), 1.10 (s, 3H, CC$H_3$), 1.08 (s, 3H, CC$H_3$), 1.03 (s, 9H, SiCC$H_3$), and 1.02 (s, 9H, SiCC$H_3$).

^{13}C NMR (125 MHz, $CDCl_3$): δ 211.6, 159.4, 144.0, 136.2, 136.1, 135.8, 135.7, 134.7, 134.0, 133.6, 133.5, 129.9, 129.8, 129.7, 129.6, 127.9, 127.7, 127.5, 113.9, 113.1, 97.1, 89.3, 80.8, 79.3, 77.4, 74.1, 67.9, 63.7, 58.6, 57.4, 55.8, 55.4, 41.8, 39.7, 38.5, 27.3, 27.0, 23.84, 23.79, 19.6, and 19.3.

HR ESI-MS: Calcd for $C_{58}H_{78}O_9Si_2Na$ $(M+Na)^+$: 999.5077 Found: 997.5086.

TLC: R_f = 0.48; 6:1 hexanes:ethyl acetate (eluted 2 x).

(4*S*,5*R*,6*R*,8*R*,10*R*,11*R*)-8,12-bis(*tert*-Butyldiphenylsilyloxy)-6,10-dimethoxy-4-(4-methoxybenzyloxy)-11-(methoxymethoxy)-3,3-dimethyl-1-dodecen-5-ol (SI-18)



To a 250 mL round bottom flask containing crude ketone **SI-17** (~1.18 mmol) was added CH_2Cl_2 (58.8 mL, 0.02 M) and cyclohexene (1.17 mL, 11.6 mmol). The reaction was cooled to 0 ºC and $Zn(BH_4)_2$[5] (11.8 mL, 5.89 mmol, 0.5 M in Et_2O) was added. The solution was stirred for 50 minutes at 0 ºC until TLC showed complete consumption of the starting material. Saturated aqueous NH_4Cl (30 mL) was added at 0 ºC to quench the reaction. The mixture was diluted with CH_2Cl_2 and the aqueous layer was extracted with CH_2Cl_2 (3 x 100 mL). The combined organic layers were dried with Na_2SO_4 and concentrated *in vacuo* to leave a residue that was purified by

MPLC (3:1 hexanes:EtOAc) to provide **SI-18** (710 mg, 62%, 2-steps) [along with the more rapidly eluting epimer **SI-16** (242 mg, 21%)].

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.70-7.58 (m, 8H, Ph*H*), 7.46-7.16 (m, 14H, Ph*H* and MeOPhH_a), 6.81 (d, J = 8.7 Hz, 2H, MeOPhH_b), 6.05 (dd, J = 17.6 and 10.8 Hz, 1H, CH_2=C*H*), 5.03 (dd, J = 17.6 and 1.3 Hz, 1H, CH_aH$_b$=CH), 4.98 (dd, J = 10.8 and 1.3 Hz, 1H, CH$_a$$H_b$=CH), 4.64 (d, J = 6.8 Hz, 1H, OCH_aH$_b$OMe), 4.64 (d, J = 10.9 Hz, 1H, MeOPhCH_aH$_b$), 4.50 (d, J = 6.7 Hz, 1H, OCH$_a$$H_b$OMe), 4.40 (d, J = 11.1 Hz, 1H, MeOPhCH$_a$$H_b$), 4.28-4.21 (m, 1H, *H*COTBDPS), 3.98 (ddd, J = 7.1, 2.4, and 2.4 Hz, 1H, *H*COH), 3.77 (s, 3H, PhOCH_3), 3.70 (ddd, J = 10.6, 2.4, and 2.4 Hz, 1H, *H*COMe), 3.60 (dd, J = 12.9 and 7.5 Hz, 1H, CH_aH$_b$OTBDPS), 3.56-3.51 (m, 2H, CH$_a$$H_b$OTBDPS and *H*COMOM), 3.35 (ddd, J = 9.6, 3.1, and 3.1 Hz, 1H, *H*COMe), 3.22 (s, 3H, OCH_3), 3.15 (d, J = 7.2 Hz, 1H, *H*COPMB), 3.10 (s, 3H, OCH_3), 3.06 (s, 3H, OCH_3), 2.00 (d, J = 2.4 Hz, 1H, O*H*), 1.95 (ddd, J = 14.2, 10.6, and 3.0 Hz, 1H, CH_{a1}H$_{b1}$), 1.79 (ddd, J = 14.7, 9.0, and 2.4 Hz, 1H, CH$_{a1}$$H_{b1}$), 1.70 (ddd, J = 13.7, 9.5, and 3.6 Hz, 1H, CH_{a2}H$_{b2}$), 1.59 (ddd, J = 13.8, 9.4, and 3.2 Hz, 1H, CH$_{a2}$$H_{b2}$), 1.12 (s, 3H, CC$H_3$), 1.11 (s, 3H, CC$H_3$), 1.03 (s, 9H, SiCC$H_3$), and 0.97 (s, 9H, SiCOCH_3)$_3$).

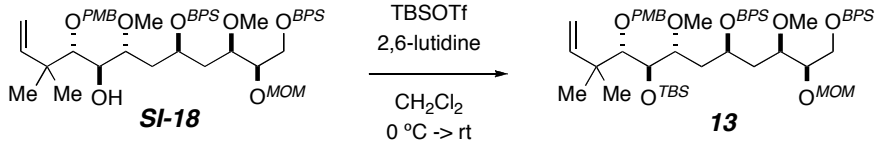
^{13}C NMR (125 MHz, $CDCl_3$): δ 159.0, 146.5, 136.2, 136.1, 135.8, 135.7, 134.9, 134.3, 133.63, 133.57, 131.0, 129.8, 129.60, 129.56, 128.7, 127.8, 127,6, 127.5, 113.7, 111.5, 97.1, 85.7, 79.6, 78.5, 77.5, 74.6, 71.6, 68.9, 63.7, 58.4, 56.5, 55.8, 55.4, 42.4, 39.9, 36.4, 27.3, 27.0, 25.5, 22.9, 19.5, and 19.3.

HR ESI-MS: Calcd for $C_{58}H_{80}O_9Si_2Na$ $(M+Na)^+$: 999.5233 Found: 999.5227.

TLC: R_f = 0.23; 6:1 hexanes:ethyl acetate (eluted 2 x).

$[\alpha]_D^{24}$ = +18.5 (c = 0.55, $CDCl_3$).

(5*R*,6*R*,8*S*,10*R*,11*R*)-8-(*tert*-Butyldiphenylsilyloxy)-6,10-dimethoxy-5-[(*S*)-1-(4-methoxybenzyloxy)-2,2-dimethylbut-3-enyl]-11-(methoxymethoxy)-2,2,3,3,15,15-hexamethyl-14,14-diphenyl-4,13-dioxa-3,14-disilahexadecane (13)



To a 50 mL round bottom flask containing alcohol **SI-18** (651 mg, 0.666 mmol) was added CH_2Cl_2 (13.3 mL, 0.05 M). The solution was cooled to 0 ºC and 2,6-lutidine (0.470 mL, 4.00 mmol) and TBSOTf (0.69 mL, 3.00 mmol) were added. The solution was warmed to room temperature and stirred for 2 h until TLC showed complete consumption of the starting material. The reaction mixture was cooled to 0 ºC and quenched by addition of saturated aqueous $NaHCO_3$ (20 mL). The mixture was diluted with CH_2Cl_2, and the aqueous layer was extracted with CH_2Cl_2 (3 x 75 mL). The combined organic layers were dried with Na_2SO_4 and concentrated *in vacuo* to provide a crude mixture that was purified by column chromatography (9:1 hexanes:EtOAc) to provide **13** (649 mg, 89%).

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.66-7.11 (m, 22H, Ph*H* and MeOPhH_a), 6.85 (d, *J* = 8.6 Hz, 2H, MeOPhH_b), 5.99 (dd, *J* = 17.6 and 10.8 Hz, 1H, CH_2=C*H*), 5.00 (dd, *J* = 17.7 and 1.4 Hz, 1H, CH_aH$_b$=CH), 4.97 (dd, *J* = 10.7 and 1.2 Hz, 1H, CH$_a$$H_b$=CH), 4.86 (d, *J* = 11.0 Hz, 1H, MeOPhCH_aH$_b$), 4.67 (d, *J* = 6.8 Hz, 1H, OCH_aH$_b$OMe), 4.46 (d, *J* = 6.7 Hz, 1H, OCH$_a$$H_b$OMe), 4.39 (d, *J* = 11.0 Hz, 1H, MeOPhCH$_a$$H_b$), 4.27-4.20 (m, 1H, *H*COTBDPS), 4.11 (s, 1H, *H*COTBS), 3.78 (s, 3H, PhOCH_3), 3.81-3.75 (m, 1H, *H*COMe), 3.54 (ddd, *J* = 7.3, 3.6, and 3.6 Hz, 1H, *H*COMOM), 3.48 (dd, *J* = 10.8 and 3.8 Hz, 1H, CH_aH$_b$OTBDPS), 3.39 (dd, *J* = 10.8 and 7.7 Hz, 1H, CH$_a$$H_b$OTBDPS), 3.29 (s, 1H, *H*COPMB), 3.18 (s, 3H, OCH_3), 3.11 (ddd, *J* = 10.5, 2.8, and 2.8 Hz, 1H, *H*COMe), 3.07 (s, 3H, OCH_3), 3.01 (s, 3H, OCH_3), 1.93-1.84 (m, 2H, C$H_{a1}H_{b1}$), 1.52 (ddd, *J* = 13.6, 10.4, and 3.2 Hz, 1H, CH_{a2}H$_{b2}$), 1.38 (ddd, *J* = 13.3, 10.4, and 2.3 Hz, 1H, CH$_{a2}$$H_{b2}$), 1.082 (s, 3H, CC$H_3$), 1.075 (s, 3H, CC$H_3$), 1.00 (s, 9H, SiC(C$H_3$)$_3$), 0.98 (s, 9H, SiC(C$H_3$)$_3$), 0.90 (s, 9H, SiC(C$H_3$)$_3$), 0.05 (s, 3H, SiOC$H_3$), and 0.02 (s, 3H, SiC$H_3$).

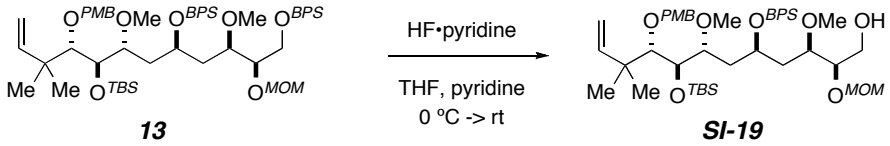
^{13}C NMR (125 MHz, $CDCl_3$): δ 158.9, 145.8, 136.2, 136.1, 135.9, 135.8, 135.6, 134.5, 133.55, 133.52, 131.3, 129.60, 129.55, 129.3, 129.2, 129.1, 127.6, 127.3, 127.1, 113.5, 111.7, 97.0, 91.7, 79.2, 78.8, 75.6, 73.6, 68.6, 64.0, 58.5, 56.4, 55.5, 55.2, 41.9, 40.1, 37.4, 27.2, 26.9, 26.1, 25.7, 23.9, 19.4, 19.1, 18.2, -4.0, and -4.9.

HR ESI-MS: Calcd for $C_{64}H_{94}O_9Si_3Na$ $(M+Na)^+$: 1113.6098 Found: 1113.615.

TLC: R_f = 0.38; 9:1 hexanes:ethyl acetate.

$[\alpha]_D^{24}$ = +23.4 (c = 0.35, $CDCl_3$).

(2*R*,3*R*,5*S*,7*R*,8*R*,9*S*)-8-(*tert*-Butyldimethylsilyloxy)-5-(*tert*-butyldiphenylsilyloxy)-3,7-dimethoxy-9-(4-methoxybenzyloxy)-2-(methoxymethoxy)-10,10-dimethyl-11-dodecen-1-ol (SI-19)



13 ***SI-19***

The following procedure was performed in duplicate parallel procedures and the contents of each reaction vessel were combined at the point of workup. To a plastic culture tube containing **13** (324 mg, 0.297 mmol) was added THF (9.2 mL, 0.032M) and pyridine (9.2 mL, 0.032M). The solution was cooled to 0 ºC and HF•pyridine (1.78 mL of a 70% HF/30% pyridine solution) was added dropwise. The reaction was stirred at room temperature for 6 h, at which time TLC showed no sign of **13**. The mixture was diluted with EtOAc (~150 mL total) and the content of both tubes were transferred to a single 500 mL Erlenmeyer flask. Saturated aqueous $NaHCO_3$ (~250 mL) was slowly added to the mixture until no further evolution of gas was observed. The aqueous layer was extracted with EtOAc (2 x 250 mL). The combined organic layers were washed with H_2O (1 x 100 mL), saturated $CuSO_4$ (2 x 100 mL), and saturated NaCl (1 x 100 mL). The organic layer was dried with Na_2SO_4 and concentrated *in vacuo* to leave a residue that was purified by column chromatography (3:1 hexanes:EtOAc) to provide the primary alcohol **SI-19** (459 mg, 91%).

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.70 (dd, *J* = 8.0 and 1.5 Hz, 2H, Ph*H*), 7.64 (dd, *J* = 8.0 and 1.4 Hz, 2H, Ph*H*), 7.41-7.27 (m, 8H, Ph*H* and MeOPhH_a), 6.85 (d, *J* = 8.6 Hz, 2H, MeOPhH_b), 6.00 (dd, *J* = 17.6 and 10.8 Hz, 1H, CH_2=C*H*), 5.00 (dd, *J* = 17.7 and 1.4 Hz, 1H, CH_aH$_b$=CH), 4.98 (dd, *J* = 10.8 and 1.4 Hz, 1H, CH$_a$$H_b$=CH), 4.79 (d, *J* = 11.1 Hz, 1H, MeOPhCH_aH$_b$), 4.51 (d, *J* = 6.8 Hz, 1H, OCH_aH$_b$OMe), 4.40 (d, *J* = 11.1 Hz, 1H, MeOPhCH$_a$$H_b$), 4.37 (d, *J* = 6.9 Hz, 1H, OCH$_a$$H_b$OMe), 4.20-4.13 (m, 1H, *H*COTBDPS), 4.12 (br s, 1H, *H*COTBS), 3.79 (s, 3H, PhOCH_3), 3.74 (dd, *J* = 10.4 and 2.4 Hz, 1H, *H*COMe), 3.37-3.29 (m, 2H, CH_2OH), 3.30 (s, 3H, OCH_3), 3.28 (d, *J* = 1.2 Hz, 1H, *H*COPMB), 3.20 (ddd, *J* = 7.8, 3.9, and 3.9 Hz, 1H, *H*COMOM), 3.12 (s, 3H, OCH_3), 3.10 (ddd, *J* = 8.0, 3.8, and 3.8 Hz, 1H, *H*COMe), 3.03 (s, 3H, OCH_3), 2.83 (dd, *J* = 8.2 and 4.1 Hz, 1H, O*H*), 1.94 (ddd, *J* = 14.5, 8.8, and 2.2 Hz, 1H, CH_{a1}H$_{b1}$), 1.87 (ddd, *J* = 14.2, 10.4, and 2.9 Hz, 1H, CH$_{a1}$$H_{b1}$), 1.62 (ddd, *J* = 13.4, 8.7, and 4.6

Hz, 1H, CH_{a2}H$_{b2}$), 1.43 (ddd, J = 13.6, 8.9, and 4.2 Hz, 1H, CH$_{a2}$$H_{b2}$), 1.10 (s, 3H, CC$H_3$), 1.08 (s, 3H, CC$H_3$), 1.01 (s, 9H, SiCC$H_3$)$_3$), 0.93 (s, 9H, SiCC$H_3$)$_3$), 0.07 (s, 3H, SiC$H_3$), and 0.04 (s, 3H, SiC$H_3$).

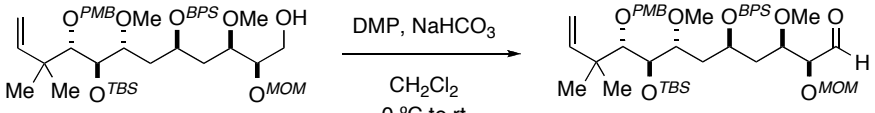
^{13}C NMR (125 MHz, $CDCl_3$): δ 159.0, 145.8, 136.2, 135.4, 134.5, 131.5, 129.6, 129.5, 129.3, 127.6, 127.5, 114.1, 113.69, 113.66, 111.9, 97.5, 91.8, 81.7, 79.3, 79.0, 75.7, 73.5, 68.8, 68.7, 63.1, 58.2, 56.5, 55.9, 55.4, 41.9, 39.6, 38.0, 27.3, 26.2, 25.8, 24.4, 19.5, 18.4, -4.0, and -4.6.

HR ESI-MS: Calcd for $C_{48}H_{76}O_9Si_2Na$ $(M+Na)^+$: 875.4920 Found: 875.4926.

TLC: R_f = 0.27; 3:1 hexanes:ethyl acetate.

$[\alpha]_D^{24}$ = +37.7 (c = 0.35, $CDCl_3$).

(2*S*,3*R*,5*S*,7*R*,8*R*,9*S*)-8-(*tert*-Butyldimethylsilyloxy)-5-(*tert*-butyldiphenylsilyloxy)-3,7-dimethoxy-9-(4-methoxybenzyloxy)-2-(methoxymethoxy)-10,10-dimethyl-11-dodecenal (SI-20)



SI-19 ***SI-20***

To a 50 mL round bottom flask containing alcohol **SI-19** (459 mg, 0.538 mmol) was added CH_2Cl_2 (11.6 mL, 0.046 M). The solution was cooled to 0 ºC and powdered $NaHCO_3$ (181 mg, 2.15 mmol) and Dess-Martin periodinane (285 mg, 0.672 mmol) were added. The solution was warmed to room temperature and stirred until monitoring by TLC showed complete consumption of the starting material. The reaction mixture was cooled to 0 ºC and saturated aqueous $NaHCO_3$ (5 mL) and saturated aqueous $Na_2S_2O_3$ (10 mL) were added. The two-phase mixture was warmed to room temperature and stirred till both layers were clear. The mixture was diluted with water (5 mL) and Et_2O (50 mL), and the aqueous layer was extracted with Et_2O (3 x 75 mL). The combined organic layers were dried with Na_2SO_4 and concentrated *in vacuo* to provide the desired aldehyde **SI-20**. The crude product was carried on to the next reaction without purification.

^{1}H NMR (500 MHz, $CDCl_3$): δ 9.40 (d, J = 1.0 Hz , 1H, HC=O), 7.70 (dd, J = 7.9 and 1.4 Hz, 2H, PhH), 7.66 (dd, J = 8.0 and 1.3 Hz, 2H, PhH), 7.41-7.25 (m, 8H, PhH and MeOPhH_a), 6.85

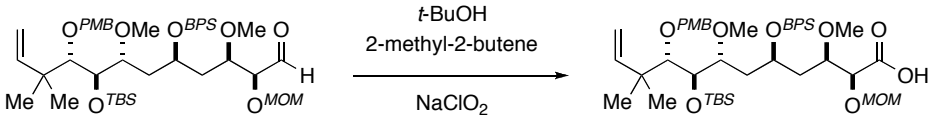
(d, J = 8.6 Hz, 2H, MeOPhH_b), 5.97 (dd, J = 17.7 and 10.8 Hz, 1H, CH_2=CH), 5.00 (dd, J = 17.4 and 1.3 Hz, 1H, CH_aH$_b$=CH), 4.97 (dd, J = 10.6 and 1.2 Hz, 1H, CH$_a$$H_b$=CH), 4.72 (d, J = 11.1 Hz, 1H, MeOPhCH_aH$_b$), 4.50 (d, J = 6.8 Hz, 1H, OCH_aH$_b$OMe), 4.40 (d, J = 11.4 Hz, 1H, MeOPhCH$_a$$H_b$), 4.32 (d, J = 6.9 Hz, 1H, OCH$_a$$H_b$OMe), 4.16-4.09 (m, 1H, HCOTBDPS), 4.11 (br s, 1H, HCOTBS), 3.79 (s, 3H, PhOCH_3), 3.69 (d, J = 9.9 Hz, 1H, HCOMe), 3.52-3.47 (m, 1H, HCOMe), 3.38 (d, J = 2.9 Hz, 1H, HCOMOM), 3.28-3.26 (m, 1H, HCOPMB), 3.26 (s, 3H, OCH_3), 3.11 (s, 3H, OCH_3), 2.98 (s, 3H, OCH_3), 1.99 (ddd, J = 15.0, 8.7, and 1.6 Hz, 1H, CH_{a1}H$_{b1}$), 1.86 (ddd, J = 14.4, 10.7, and 3.5 Hz, 1H, CH$_{a1}$$H_{b1}$), 1.79 (ddd, J = 13.5, 7.6, and 5.3 Hz, 1H, CH_{a2}H$_{b2}$), 1.50 (ddd, J = 13.3, 7.5, and 5.1 Hz, 1H, CH$_{a2}$$H_{b2}$), 1.08 (s, 3H, CC$H_3$), 1.06 (s, 3H, CC$H_3$), 1.02 (s, 9H, SiC(C$H_3$)$_3$), 0.93 (s, 9H, SiC(C$H_3$)$_3$), 0.07 (s, 3H, SiC$H_3$), and 0.05 (s, 3H, SiC$H_3$).

^{13}C NMR (125 MHz, $CDCl_3$): δ 202.7, 159.1, 145.8, 136.3, 134.4, 131.5, 129.7, 129.6, 129.3, 127.7, 127.6, 113.7, 111.9, 97.4, 91.7, 83.7, 79.0, 78.5, 75.7, 73.4, 68.8, 68.66, 68.65, 58.4, 56.4, 56.3, 55.4, 41.9, 39.9, 38.3, 27.3, 26.2, 25,8, 24.5, 19.6, 18.4, -4.0, and -4.6.

HR ESI-MS: Calcd for $C_{48}H_{74}O_9Si_2Na$ $(M+Na)^+$: 873.4764 Found: 873.4750.

TLC: R_f = 0.38; 6:1 hexanes:ethyl acetate.

(2*S*,3*R*,5*S*,7*R*,8*R*,9*S*)-8-(*tert*-Butyldimethylsilyloxy)-5-(*tert*-butyldiphenylsilyloxy)-3,7-dimethoxy-9-(4-methoxybenzyloxy)-2-(methoxymethoxy)-10,10-dimethyl-11-dodecenoic acid (SI-21)



SI-20 ***SI-21***

To a 250 mL round bottom flask containing the crude aldehyde **SI-20** (~0.538 mmol) was added *t*-BuOH (31.7 mL, 0.017 M) and 2-methyl-2-butene (10.4 mL, 0.052 M). To a vial equipped with a stir bar was added NaH_2PO_4 (487 mg, 5.38 mmol), $NaClO_2$ (371 mg, 2.69 mmol), and water (14.2 mL, 0.19 M in $NaClO_2$). Once the mixture in the vial became homogeneous, the aqueous solution was added to the reaction flask. The reaction mixture was stirred at room temperature for 1 h. The solution was then cooled to 0 ºC, and a newly prepared saturated solution of

$NaHSO_3$ (8 mL) was added. The mixture was diluted with water (75 mL), and the aqueous layer was extracted with ethyl acetate (3 x 100 mL). The combined organic layers were dried with Na_2SO_4 and concentrated *in vacuo* to provide the desired carboxylic acid **SI-21**. The crude product was immediately carried on to the next step without purification.

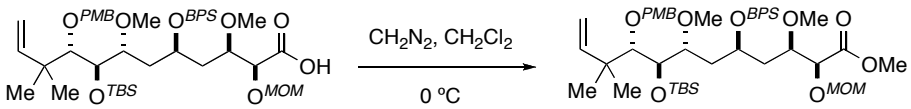
^{1}H NMR (500 MHz, $CDCl_3$): δ 7.69 (dd, *J* = 8.0 and 1.5 Hz, 2H, Ph*H*), 7.64 (dd, *J* = 8.0 and 1.5 Hz, 2H, Ph*H*), 7.41-7.28 (m, 8H, Ph*H* and MeOPhH_a), 6.86 (d, *J* = 8.6 Hz, 2H, MeOPhH_b), 5.97 (dd, *J* = 17.6 and 10.8 Hz, 1H, CH_2=C*H*), 5.00 (dd, *J* = 17.4 and 1.3 Hz, 1H, CH_aH$_b$=CH), 4.97 (dd, *J* = 10.5 and 1.3 Hz, 1H, CH$_a$$H_b$=CH), 4.72 (d, *J* = 11.1 Hz, 1H, MeOPhCH_aH$_b$), 4.56 (d, *J* = 6.8 Hz, 1H, OCH_aH$_b$OMe), 4.41 (d, *J* = 11.1 Hz, 1H, MeOPhCH$_a$$H_b$), 4.36 (d, *J* = 6.8 Hz, 1H, OCH$_a$$H_b$OMe), 4.19-4.09 (m, 1H, *H*COTBDPS), 4.10 (s, 1H, *H*COTBS), 3.79 (s, 3H, PhOCH_3), 3.78 (d, *J* = 2.8 Hz, 1H, *H*COMOM), 3.69 (dd, *J* = 10.4 and 2.1 Hz, 1H, *H*COMe), 3.50 (ddd, *J* = 9.0, 3.5, and 3.5 Hz, 1H, *H*COMe), 3.28 (d, *J* = 1.1 Hz, 1H, *H*COPMB), 3.25 (s, 3H, OCH_3), 3.10 (s, 3H, OCH_3), 3.08 (s, 3H, OCH_3), 1.97 (ddd, *J* = 13.8, 9.1, and 4.2 Hz, 1H, CH_{a1}H$_{b1}$), 1.88 (ddd, *J* = 14.6, 10.3, and 2.8 Hz, 1H, CH$_{a1}$$H_{b1}$), 1.76 (ddd, *J* = 13.8, 9.8, and 4.2 Hz, 1H, CH_{a2}H$_{b2}$), 1.48 (ddd, *J* = 13.8, 8.9, and 3.8 Hz, 1H, CH$_{a2}$$H_{b2}$), 1.08 (s, 3H, CC$H_3$), 1.07 (s, 3H, CC$H_3$), 1.02 (s, 9H, SiC(C$H_3$)$_3$), 0.92 (s, 9H, SiC(C$H_3$)$_3$), 0.06 (s, 3H, SiC$H_3$), and 0.03 (s, 3H, SiC$H_3$).

^{13}C NMR (125 MHz, $CDCl_3$): δ 173.8, 159.0, 145.8, 136.3, 136.2, 135.0, 134.3, 131.5, 129.6, 129.5, 129.3, 127.6, 127.5, 113.7, 111.9, 97.0, 91.8, 79.0, 78.8, 76.9, 75.7, 73.4, 68.6, 58.8, 56.5, 56.4, 55.4, 42.0, 40.5, 38.0, 27.3, 26.2, 25.8, 24.4, 19.5, 18.4, -4.0, and -4.6.

HR ESI-MS: Calcd for $C_{48}H_{74}O_{10}Si_2Na$ $(M+Na)^+$: 889.4713 Found: 889.4744.

TLC: R_f = 0.51; 100% ethyl acetate.

Methyl (2*S*,3*R*,5*S*,7*R*,8*R*,9*S*)-8-(*tert*-Butyldimethylsilyloxy)-5-(*tert*-butyldiphenylsilyloxy)-3,7-dimethoxy-9-(4-methoxybenzyloxy)-2-(methoxymethoxy)-10,10-dimethyl-11-dodecenoate (SI-22)



SI-21 ***SI-22***

To a 125 mL Erlenmeyer flask (flask A) equipped with a septum and a stir bar and containing the crude carboxylic acid **SI-21** (~0.538 mmol) was added CH_2Cl_2 (38 mL, 0.014 M), and the solution was cooled to 0 ºC. *N*-Methyl-*N*-nitroso-*p*-toluenesulfonamide (Diazald®, 1.10 g, 5.13 mmol) and ethanol (18 mL) were added to a 150 mL side-arm Erlenmeyer flask (flask B) equipped with a stir bar. The top of flask B was capped with a septum and fitted with a piece of teflon tubing having one end placed into the ethanol solution and the other connected to a N_2 line under positive pressure. The side-arm of flask B was also fitted with a septum and connected to flask A with a second piece of teflon tubing with ends placed in the headspace of flask B and into the solution of CH_2Cl_2 in flask A. The N_2 flow was then regulated so that constant gas sparging was observed in both flasks. An aqueous solution of sodium hydroxide (1 M) was added at a constant rate to flask B and the contents of both flasks were stirred until all the yellow color in flask B had disappeared. Complete esterification was judged from the yellow color of the solution in flask A. The teflon tubing was removed from flask A and a few drops of acetic acid were added until the CH_2Cl_2 solution turned colorless. Saturated aqueous $NaHCO_3$ (20 mL) was added to quench any excess acetic acid. The reaction mixture was diluted with CH_2Cl_2 (50 mL) and the aqueous layer was extracted with CH_2Cl_2 (3 x 75 mL). The combined organic layers were dried with Na_2SO_4 and concentrated *in vacuo* to provide a mixture of the desired product **SI-22**. (Partial cleavage of the MOM ether was observed; this was not observed in a subsequent experiment where Et_2O rather than CH_2Cl_2 was used as the solvent for workup and extraction. If necessary, the MOM ether could be re-installed by taking this crude reaction mixture and subjecting it to the previously described procedure for MOM ether formation.) Flash column chromatography (4:1 hexanes:EtOAc) gave the methyl ester **SI-22** (414 mg, 87%, 3-steps).

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.71 (dd, *J* = 8.0 and 1.5 Hz, 2H, Ph*H*), 7.62 (dd, *J* = 8.0 and 1.4 Hz, 2H, Ph*H*), 7.39-7.23 (m, 8H, Ph*H* and MeOPhH_a), 6.86 (d, *J* = 8.7 Hz, 2H, MeOPhH_b), 5.98 (dd, *J* = 17.6 and 10.8 Hz, 1H, CH_2=C*H*), 5.00 (dd, *J* = 17.2 and 1.5 Hz, 1H, CH_aH$_b$=CH), 4.97 (dd, *J* = 10.8 and 1.8 Hz, 1H, CH$_a$$H_b$=CH), 4.82 (d, *J* = 11.1 Hz, 1H, MeOPhCH_aH$_b$), 4.52 (d, *J* = 7.0 Hz, 1H, OCH_aH$_b$OMe), 4.42 (d, *J* = 7.0 Hz, 1H, OCH$_a$$H_b$OMe), 4.41 (d, *J* = 11.2 Hz, 1H, MeOPhCH$_a$$H_b$), 4.19 (dddd, *J* = 9.3, 7.8, 3.7, and 3.7 Hz, 1H, *H*COTBDPS), 4.10 (s, 1H, *H*COTBS), 3.79 (s, 3H, PhOCH_3), 3.79 (d, *J* = 3.0 Hz, 1H, *H*COMOM), 3.71 (dd, *J* = 9.3 and 3.3 Hz, 1H, *H*COMe), 3.62 (s, 3H, CO_2CH_3), 3.52 (ddd, *J* = 9.1, 3.1, and 3.1 Hz, 1H, *H*COMe),

3.28 (d, J = 1.1 Hz, 1H, *H*COPMB), 3.19 (s, 3H, OCH_3), 3.05 (s, 3H, OCH_3), 3.01 (s, 3H, OCH_3), 1.97-1.85 (m, 3H, C$H_{a1}H_{b1}$ and CH_{a2}H$_{b2}$), 1.40 (ddd, J = 14.6, 9.3, and 3.1 Hz, 1H, CH$_{a2}H_{b2}$), 1.08 (s, 3H, CCH_3), 1.07 (s, 3H, CCH_3), 1.02 (s, 9H, SiC(CH_3)$_3$), 0.93 (s, 9H, SiC(CH_3)$_3$), 0.06 (s, 3H, SiCH_3), and 0.04 (s, 3H, SiCH_3).

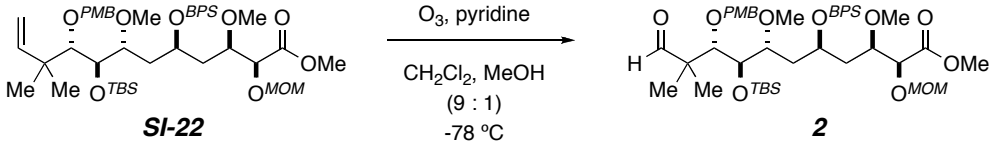
^{13}C NMR (125 MHz, $CDCl_3$): δ 171.1, 158.8, 145.7, 136.1, 136.0, 135.2, 134.1, 131.3, 129.3, 129.2, 129.1, 127.4, 127.2, 113.5, 111.7, 96.3, 91.7, 78.9, 78.8, 77.5, 75.5, 73.4, 68.6, 58.5, 56.3, 56.1, 55.2, 51.6, 41.8, 40.9, 37.8, 27.1, 26.1, 25.6, 24.1, 19.3, 18.2, -4.2, and -4.8.

HR ESI-MS: Calcd for $C_{49}H_{76}O_{10}Si_2Na$ $(M+Na)^+$: 903.4869 Found: 903.4868.

TLC: R_f = 0.52; 3:1 hexanes:ethyl acetate.

$[\alpha]_D^{24}$ = +13.1 (c = 0.45, $CDCl_3$).

Methyl (2*S*,3*R*,5*S*,7*R*,8*R*,9*S*)-8-(*tert*-Butyldimethylsilyloxy)-5-(*tert*-butyldiphenylsilyloxy)-3,7-dimethoxy-9-(4-methoxybenzyloxy)-2-(methoxymethoxy)-10,10-dimethyl-11-oxoundecanoate (2)



SI-22 ***2***

A 9:1 mixture of CH_2Cl_2:MeOH (13.7 mL, 0.02M) was added to a 50 mL round bottom flask containing alkene **SI-22** (241 mg, 0.273 mmol). This solution was cooled to -78 ºC and pyridine (0.22 mL, 2.73 mmol) was added. A stream of ozone in oxygen was bubbled through the solution until the first sign of a light blue color. At this point TLC analysis showed complete consumption of the starting material. Pure oxygen was then sparged through the system to remove residual ozone, during which time the solution became colorless. Dimethyl sulfide (6.0 mL) was added and the reaction mixture was warmed to room temperature and stirred for 6 h. The solution was concentrated under reduced pressure and the residue was purified by column chromatography (3:1 hexanes:EtOAc) to provide aldehyde **2** (181 mg, 75%) as a colorless oil.

^{1}H NMR (500 MHz, $CDCl_3$): δ 9.41 (s, 1H, *H*C=O), 7.73 (dd, J = 8.0 and 1.6 Hz, 2H, Ph*H*), 7.66 (dd, J = 8.0 and 1.4 Hz, 2H, Ph*H*), 7.43-7.28 (m, 6H, Ph*H*), 7.18 (d, J = 8.7 Hz, 2H, MeOPhH_a), 6.85 (d, J = 8.7 Hz, 2H, MeOPhH_b), 4.54 (d, J = 6.9 Hz, 1H, OCH_aH$_b$OMe), 4.53 (d,

J = 11.1 Hz, 1H, MeOPhCH_aH$_b$), 4.46 (d, J = 6.9 Hz, 1H, OCH$_a$$H_b$OMe), 4.28 (d, J = 11.1 Hz, 1H, MeOPhCH$_a$$H_b$), 4.15-4.09 (m, 1H, *H*COTBDPS), 3.91 (d, J = 3.2 Hz, 1H, *H*COMOM), 3.87 (dd, J = 4.8 and 1.9 Hz, 1H, *H*COTBS), 3.80 (s, 3H, PhOCH_3), 3.67 (s, 3H, $CO_2C$$H_3$), 3.72-3.62 (m, 1H, *H*COMe), 3.44 (d, J = 4.8 Hz, 1H, *H*COPMB), 3.40 (ddd, J = 6.7, 4.8, and 1.9 Hz, 1H, *H*COMe), 3.23 (s, 3H, OCH_3), 3.14 (s, 3H, OCH_3), 3.07 (s, 3H, OCH_3), 1.95 (ddd, J = 13.8, 8.4, and 4.9 Hz, 1H, CH_{a1}H$_{b1}$), 1.90-1.81 (m, 2H, C$H_{a2}$$H_{b2}$), 1.62 (ddd, J = 13.9, 8.0, and 4.4 Hz, 1H, CH$_{a1}$$H_{b1}$), 1.09 (s, 3H, CC$H_3$), 1.07 (s, 3H, CC$H_3$), 1.01 (s, 9H, SiC(C$H_3$)$_3$), 0.90 (s, 9H, SiC(C$H_3$)$_3$), 0.08 (s, 3H, SiC$H_3$), and 0.04 (s, 3H, SiC$H_3$).

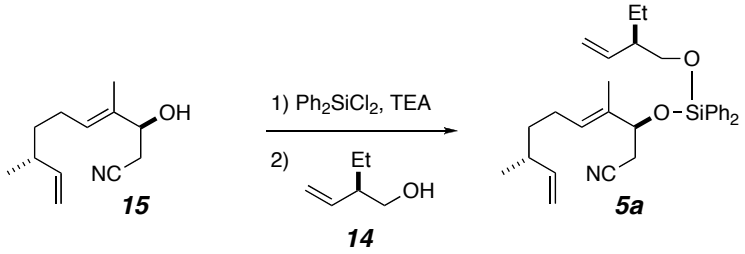
^{13}C NMR (125 MHz, $CDCl_3$): δ 204.2, 171.3, 159.2, 136.3, 136.2, 134.7, 134.1, 130.5, 129.72, 129.67, 129.0, 127.8, 127.6, 113.8, 96.7, 85.8, 79.6, 78.9, 77.5, 74.9, 74.1, 69.2, 58.5, 57.0, 56.3, 55.4, 51.9, 50.2, 40.0, 38.5, 27.2, 26.4, 20.8, 19.5, 19.0, 18.5, -3.4, and -4.3.

HR ESI-MS: Calcd for $C_{48}H_{74}O_{11}Si_2Na$ $(M+Na)^+$: 905.4662 Found: 905.4677.

TLC: R_f = 0.52; 3:1 hexanes:ethyl acetate.

$[\alpha]_D^{24}$ = -4.33 (c = 0.30, $CDCl_3$).

(-)- (3*S*,4*E*,8*R*)-3-[(((2*R*)-2-Ethyl-3-buten-1-yl)oxy)diphenylsilyloxy]-4,8-dimethyl-4,9-decadienenitrile (5a)



Dichlorodiphenylsilane (2.37 g, 9.4 mmol) then triethylamine (2.17 mL, 15.6 mmol) was dissolved in CH_2Cl_2 (90 mL) under an argon atmosphere and the solution was cooled to 0 ºC. Alcohol **15**[6] (2.0 g, 10.4 mmol) in CH_2Cl_2 (15 mL) was added by syringe pump over 4 h. The reaction mixture was allowed to warm to room temperature and was stirred overnight. Additional triethylamine (1.96 mL, 14.1 mmol, 1.5 equv) was added followed by alcohol **14**[7,8] (1.20 g, 9.4 mmol) in CH_2Cl_2 (15 mL) by syringe pump over 4 h. The reaction mixture was again stirred overnight. The resulting mixture was concentrated *in vacuo* and filtered through a pad of SiO_2 with 4:1 hexanes:EtOAc to give a crude product. Purification by flash

chromatography (60:1 hexanes:EtOAc, containing 0.5% Et_3N) afforded heterosilaketal **5a** (1.92 g, 41%) as a colorless oil.

"**^{1}H NMR** (500 MHz, $CDCl_3$): δ 7.63 (m, 4H, Ar*H*), 7.47-7.34 (m, 6H, Ar*H*), 5.65 (ddd, *J* = 17.5, 10.5, 8.0 Hz, 1H, *H*C=CH_2), 5.62 (ddd, *J* = 17.0, 10.5, 8.5 Hz, 1H, *H*C=CH_2), 5.38 [dd, *J* = 7.0, 7.0 Hz, 1H, CH_2*H*C=C(Me)], 5.06 (dd, *J* = 10.5, 1.0 Hz, 1H, HC=C*H*$_{cis}$$H_{trans}$), 5.04 (dd, *J* = 17.0, 1.0 Hz, 1H, HC=CH_{cis}*H*$_{trans}$), 4.94 (dd, *J* = 17.5, 1.0 Hz, 1H, HC=C*H*$_{trans}$$H_{cis}$), 4.92 (dd, *J* = 10.5, 1.0 Hz, 1H, HC=CH_{trans}*H*$_{cis}$), 4.48 [dd, *J* = 7.0, 7.0 Hz, 1H, C*H*(OSi)CH_2C≡N], 3.68 (dd, *J* = 10.0, 6.5 Hz, 1H, C*H*$_a$$H_b$OSi), 3.65 (dd, *J* = 10.0, 6.0 Hz, 1H, CH_a*H*$_b$OSi), 2.61 (dd, *J* = 16.0, 7.0 Hz, 1H, C*H*$_a$$H_b$CN), 2.55 (dd, *J* = 16.0, 7.0 Hz, 1H, CH_a*H*$_b$CN), 2.14 [m, 1H, H_2C=CHC*H*(Et)CH_2], 2.08 (m, 1H, C*H*(Me)CH=CH_2], 1.93 [m, 2H, C*H*$_2$HC=C(Me)CH], 1.60 [s, 3H, CH_2HC=C(*Me*)], 1.57 [m, 1H, =CHCH(C*H*$_a$$H_b$Me)], 1.32-1.22 [m, 3H, =CHCH(CH_a*H*$_b$Me) and C*H*$_2$CH(Me)HC=CH_2], 0.97 [d, *J* = 7.0 Hz, 3H, CH(*Me*)CH=CH_2], and 0.85 (t, *J* = 7.5 Hz, 3H, CH(CH_2*Me*)CH_2OSi].

^{13}C NMR (125 MHz, $CDCl_3$): δ 144.3, 139.7, 135.0, 134.9, 134.6, 133.1, 132.1, 130.4, 130.3, 129.4, 127.8, 127.7, 117.3, 115.9, 112.8, 73.8, 66.2, 47.9, 37.4, 35.8, 25.3, 25.2, 23.5, 20.2, 11.4, and 10.9.

IR (neat): 3070, 2961, 2923, 2872, 2247, 1639, 1592, 1457, 1429, 1117, 1063, 913, and 700 cm^{-1}.

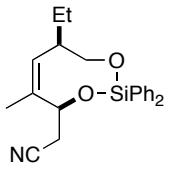
HR-FABMS: *m/z* Calcd for $C_{30}H_{39}NO_2Si$ $(M+H)^+$: 474.2828. Found: 474.2820.

$[\alpha]_D^{24}$ = -10.5 ° (*c* = 1.54, CH_2Cl_2).

GC-LRMS: t_R = 13.9 min; *m/z*: 473 (M+), 433 (M+ -CH_2CN), 404 (M+ - EtCHCH=CH_2), 374, 281, 253, 222, 199, 183, 139, 123, and 77.

TLC: R_f = 0.48 (Hex:EtOAc = 6:1)."[6]

(+)-(4*S*,7*R*)-7-Ethyl-5-methyl-2,2-diphenyl-1,3-dioxa-2-silacyclooct-5-ene-4-acetonitrile (16)



16

Heterosilaketal **5a** (30 mg, 0.06 mmol) was dissolved in toluene (40 mL) and added to a 100 mL

round-bottomed flask equipped with a reflux condenser fitted with inlet and outlet needles for constant nitrogen sparging through the solution. **G2** (2.7 mg, 0.003 mmol) was added and the reaction mixture was heated at 65 ºC (bath temperature). Additional **G2** was added in 3 portions (total of 13.0 mg, 0.014 mmol), while the reaction was continuously heated for 2 d. The reaction mixture was concentrated *in vacuo* and filtered through a pad of SiO_2 to give the crude product. MPLC (19:1 hexanes:EtOAc) afforded the cyclic silaketal **16** (20 mg, 92%) as a colorless oil that gradually turned to white flakey crystals.

"**^{1}H NMR** (500 MHz, $CDCl_3$): δ 7.69 (m, 2H, Ar*H*), 7.58 (m, 2H, Ar*H*), 7.43-7.33 (m, 6H, Ar*H*), 5.20 [dd, *J* = 8.0, 6.0 Hz, 1H, =C(Me)C*H*OSi], 5.17 [dd, *J* = 9.0, 1.0 Hz, 1H, *H*C=C(Me)], 4.13 (dd, *J* = 11.0, 3.0 Hz, 1H, CH(Et)C$H_a$$H_b$OSi), 3.62 [dd, *J* = 11.0, 11.0 Hz, 1H, CH(Et)C$H_a$$H_b$OSi], 2.85 (dd, *J* = 16.0, 8.0 Hz, 1H, C$H_a$$H_b$C≡N), 2.69 (dd, *J* = 16.0, 6.0 Hz, 1H, C$H_a$$H_b$C≡N), 2.63 [m, 1H, =CHC*H*(Et)], 1.76 [d, *J* = 1.0 Hz, 3H, HC=C(*Me*)], 1.33 [m, 1H, (C$H_a$$H_b$Me)], 1.21 (m, 1H, C$H_a$$H_b$Me), and 0.87 (t, *J* = 7.5 Hz, 3H, CH_2*Me*).

NOE: A NOE between HC=C(*Me*) and *H*C=C(Me) as well as between HC=C(*Me*) and C*H2*C≡N) was observed in a ^{1}D NOE experiment.

^{13}C NMR (75 MHz, $CDCl_3$): δ 136.7, 135.6, 134.7, 134.4, 130.3, 130.2, 128.0, 127.8, 117.6, 69.8, 66.8, 42.7, 24.6, 23.4, 18.3, and 11.8.

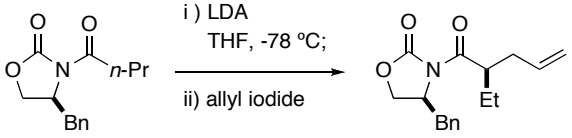
HR-CIMS: *m/z* Calcd for $C_{22}H_{25}NO_2Si$ $(M+NH_4)^+$: 381.1998. Found: 381.2000.

$[\alpha]_D^{24}$ = +58.50 (*c* = 1.00, CH_2Cl_2)

GC-LRMS: t_R = 12.80 min; *m/z*: 363 (M^+), 335, 323 (M^+ -CH_2CN), 292, 265, 252, 223, 199, 181, 105, and 77 (Ph^+).

TLC: R_f = 0.35 (Hex:EtOAc = 6 :1)."[6]

(4*S*)-4-Phenylmethyl-3-[(2*R*)-2-ethyl-4-pentenoyl]oxazolidin-2-one (18)



SI-23 ***18***

Diisopropylamine (6.55 mL, 46.4 mmol) was dissolved in THF (38 mL, 1 M) and cooled to 0 °C. *n*-BuLi (22.6 mL, 1.97 M, 44.4 mmol) was added and the mixture was stirred for 30 min.

The mixture was then cooled to -78 ºC and imide **SI-23** (9.56 mL, 38.6 mmol) was added. This solution was stirred for 30 min at -78 ºC and allyl iodide (7.07 mL, 77.3 mmol) was added. After 2 h the solution was warmed to room temperature. The reaction mixture was quenched with aqueous NH_4Cl and extracted with diethyl ether. The combined organic layers were washed with brine, dried over $MgSO_4$, and concentrated *in vacuo* to give the crude product. MPLC (7.5:1 hexanes:EtOAc) afforded the allylated imide **18** (7.4 g, 67 %) as a clear colorless oil.

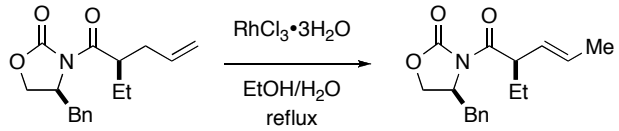
^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.36-7.26 (m, 3H, ArH_mH_p), 7.25-7.20 (m, 2H, ArH_o), 5.83 (dddd, J = 17.1, 10.1, 7.0, 7.0 Hz, 1H, CH_2CH=CH_2), 5.10 (dddd, *J* = 17.1, 1.9, 1.5, 1.5 Hz, 1H, CH=C$H_{trans}H_{cis}$), 5.05 (dddd, *J* = 10.1, 1.9, 1.0, 1.0 Hz, 1H, CH=C$H_{trans}H_{cis}$), 4.69 (dddd, *J* = 10.1, 6.6, 3.5, 3.5 Hz, 1H, C*H*N), 4.21-4.12 (m, 2H, OCH_2), 3.85 (dddd, *J* = 7.9, 7.9, 5.8, 5.8 Hz, 1H, EtC*H*CH_2), 3.30 (dd, *J* = 13.3, 3.3 Hz, 1H, PhCH_aH_b), 2.67 (dd, *J* = 13.3, 10.0 Hz, 1H, PhCH_aH_b), 2.48 (ddddd, *J* = 14.0, 7.5, 7.5, 1.2, 1.2 Hz, 1H, CH_aH_bCH=CH_2), 2.33 (ddddd, *J* = 14.0, 6.9, 5.7, 1.3, 1.3 Hz, 1H, CH_aH_bCH=CH_2), 1.75 (ddq, *J* = 13.6, 7.8, 7.5 Hz, C$H_aH_b$$CH_3$), 1.66 (dqd, *J* = 13.2, 7.5, 5.7 Hz, 1H, $CH_aH_b$$CH_3$), and 0.92 (t, *J* = 7.4 Hz, 3H, CH_2CH_3).

^{13}C NMR ($CDCl_3$, 75 MHz): δ 176.1, 153.4, 135.6, 135.5, 129.6, 129.1, 127.5, 117.3, 66.1, 55.7, 43.9, 38.3, 36.5, 24.8, and 11.8.

TLC: R_f = 0.45 in 4:1 hexanes:EtOAc.

GCMS (5029021): t_R= 12.53 min, *m/z* 287 (M^+, 37), 259 (50), 196 (10), 178 (35), 111 (100), 91 (40), 83 (80), and 55 (49).

(4*S*)-4-Phenylmethyl-3-[(2*R*,3*E*)-2-ethyl-3-pentenoyl]oxazolidin-2-one (SI-24)



18 ***SI-24***

Allylated imide **18** (8.32 g, 29.0 mmol) was dissolved in EtOH/water (41.5 mL/4.20 mL). $RhCl_3$•$3H_2O$ (151 mg, 0.725 mmol) was added and the mixture was heated to 80 ºC for 7.5 h (reaction progress was monitored by GCMS). Most of the organic volatiles were removed *in vacuo* and the remaining aqueous mixture was extracted with EtOAc. The extracts were washed with water, dried over $MgSO_4$, and concentrated *in vacuo* to give **SI-24** as a brown oil (8.16 g,

98%, *E*/*Z* isomers; *ca.* 15:1), which was sufficiently pure to use for the next reaction.

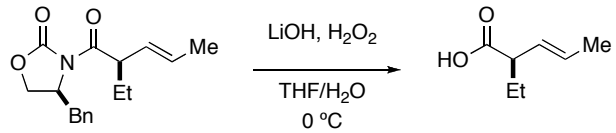
^{1}H NMR ($CDCl_3$, 300 MHz; *E* isomer): δ 7.35-7.26 (m, 3H, ArH_mH_p), 7.21-7.18 (m, 2H, ArH_o), 5.72 (dq, *J* = 15.3, 6.4 Hz, 1H, CH=C*H*CH_3), 5.51 (ddq, *J* = 15.3, 8.6, 1.5 Hz, 1H, C*H*=$CHCH_3$), 4.78-4.66 (m, 1H, CHN), 4.27 (app q, *J* = 7.5 Hz, 1H, EtC*H*CH_2), 4.22-4.08 (m, 2H, CH_2O), 3.22 (dd, *J* = 13.4, 3.3 Hz, 1H, PhC$H_a$$H_b$), 2.78 (dd, *J* = 13.4, 9.2 Hz, 1H , Ph$CH_a$$H_b$), 1.82 (ddq, *J* = 11.5, 7.4, 7.4 Hz, C$H_a$$H_b$$CH_3$), 1.73 (dd, *J* = 6.3, 1.6 Hz, 3H, CH=CHCH_3), 1.58 (ddq, *J* = 13.4, 7.4, 7.4 Hz, 1H, $CH_a$$H_b$$CH_3$), and 0.92 (t, *J* = 7.4 Hz, 3H, CH_2CH_3).

^{13}C NMR ($CDCl_3$, 75 MHz): δ 175.0, 152.1, 135.4, 129.7, 129.4, 129.1, 128.6, 127.5, 66.0, 55.3, 48.2, 37.9, 25.7, 18.3, and 11.8.

TLC: R_f = 0.45 in 4:1 hexanes:EtOAc.

GCMS (5029021): t_R= 12.525 min, *m/z* 287 (M^+, 36), 258 (10), 178 (10), 111 (100), 91 (23), 83 (26), 67 (18), and 55 (49).

(2*R*,3*E*)-2-Ethyl-3-pentenoic acid (19)



SI-24 ***19***

Alkene **SI-24** (13 g, 45.3 mmol) was dissolved in THF/water (340 mL/113 mL) and cooled to 0 ºC. LiOH (90.6 mL, 2 M in H_2O, 181.2 mmol) and 30% aqueous H_2O_2 solution (37 ml, 362 mmol) were added. The mixture was stirred for 14 h, at which time all starting material had disappeared by TLC. Aqueous Na_2SO_3 was added, and the organic volatiles were removed *in vacuo* to leave an auqeous layer that was extracted with CH_2Cl_2 to remove non-acidic byproducts. The aqueous layer was acidified to pH 1 with 10% HCl and extracted with Et_2O. The organic layers were dried over Na_2SO_4 and concentrated *in vacuo* to give the crude carboxylic acid **19** (5.77 g, 99%) as a clear colorless oil.

^{1}H NMR ($CDCl_3$, 300 MHz; *E*-isomer): δ 9.34 (br s, 1H, CO_2H), 5.61 (dqd, *J* = 15.3, 6.3, 0.5 Hz, 1H, CH=C*H*CH_3), 5.42 (ddq, *J* = 15.3, 8.6, 1.5 Hz, 1H, C*H*=$CHCH_3$), 2.89 (ddd, *J* = 8.1, 7.5, 7.5 Hz, 1H, C*H*CH=$CHCH_3$), 1.78 (ddq, *J* = 13.5, 7.5, 7.4 Hz, 1H, C$H_a$$H_b$$CH_3$), 1.70 (dd, *J* = 6.5, 1.5 Hz, 3H, CH=CHCH_3), 1.56 (ddq, *J* = 13.5, 7.5, 7.4 Hz, 1H, $CH_a$$H_b$$CH_3$), and 0.91 (t, *J*

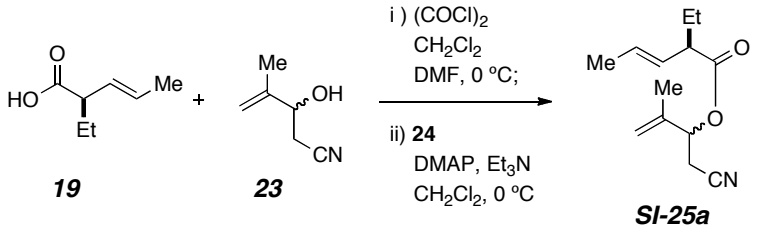
= 7.4 Hz, 3H, CH_2CH_3).

^{13}C NMR ($CDCl_3$, 125 MHz): δ 181.6, 128.7, 128.3, 50.9, 25.7, 18.1, and 11.7.

TLC: R_f = 0.01 in 4:1 hexanes:EtOAc.

GCMS (5029021): t_R= 5.60 min, *m/z* 128 (M^+, 10), 113 (8), 99 (73), 83 (60), and 55 (100).

(*2R*)- and (*2S*)-1-Cyano-3-methyl-3-buten-2-yl (2*R*,3*E*)-2-Ethyl-3-pentenoate (SI-25a)



Carboxylic acid **19** (1.51 g, 11.8 mmol) was dissolved in CH_2Cl_2 (15 mL, 0.8 M) and cooled to 0 ºC. Oxalyl chloride (3.04 mL, 35.4 mmol) and catalytic DMF (45 µL, 0.59 mmol) were added to the mixture. After being stirred for 2 h the reaction mixture was concentrated *in vacuo* to afford a crude acid chloride, which was redissolved in CH_2Cl_2 (59 mL, 0.2 M). DMAP (144 mg, 1.18 mmol), (±)-3-hydroxy-4-methyl-4-pentenenitrile[8,9] (**23**, 1.70 g, 15.3 mmol), and Et_3N (4.9 mL, 35.4 mmol) were added to the reaction mixture, which then was stirred for 2 h at room temperature. The reaction was quenched with H_2O and aqueous NH_4Cl and the mixture extracted with EtOAc. The combined organic layers were dried over Na_2SO_4 and concentrated *in vacuo* to give the crude product. MPLC (15:1 hexanes:EtOAc) afforded ester **SI-25a** (2.12 g, 81 %) as an inseparable diastereomeric mixture.

^{1}H NMR ($CDCl_3$, 500 MHz; as a mixture of diastereomers): δ 5.61 (dq, *J* = 15.2, 6.5 Hz, 1H, CH=C*H*CH_3), 5.43 (ddq, *J* = 15.2, 8.5, 1.6 Hz, 1H, C*H*=$CHCH_3$), 5.38-5.34 (m, 1H, CO_2CH), 5.15-5.12 (m, 1H, C=CH_aH_b), 5.08-5.06 (m, 1H, C=CH_aH_b), 2.93 (dt, *J* = 8.0, 7.5 Hz, 1H, COC*H*CH_2CH_3), 2.74 (m, 2H, CH_2CN), 1.80 (ddq, *J* = 14.6, 7.4, 7.4 Hz, 1H, C$H_aH_bCH_3$), 1.79 (br s, 3H, H_2C=CCH_3, one diastereomer), 1.77 (br s, 3H, H_2C=CCH_3, one diastereomer), 1.70 (dd, *J* = 6.4, 1.7 Hz, 3H, CH=CHCH_3, one diastereomer), 1.69 (dd, *J* = 6.4, 1.5 Hz, 3H, CH=CHCH_3, one diastereomer), 1.57 (ddq, *J* = 15.0, 7.5, 7.5 Hz, 1H, CH_aH_bCH$_3$), and 0.91 (t, *J* = 7.4 Hz, 3H, CH_2CH_3).

^{13}C NMR ($CDCl_3$, 125 MHz, as a mixture of two diastereomers): δ 173.3, 140.2, 129.0, 128.0,

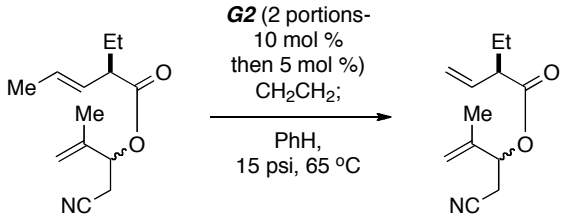
115.03, 115.00, 71.3, 51.0, 50.9, 25.8, 25.7, 22.53, 22.46, 18.46, 18.41, 18.04, 18.02, and 11.8.

TLC: R_f= 0.60 in 4:1 hexanes:EtOAc.

GCMS (5029021): t_R= 8.89 and 9.04 min, *m/z* 221 (M^+), 192 (2), 127 (25), 99 (20), 94 (25), 83 (100), 67 (37), and 55 (97).

HRMS (ESI/TOF): Calcd for $C_{13}H_{19}NO_2Na^+$: 244.1308. Found: 244.1319.

(*2R*)- and (*2S*)-1-Cyano-3-methyl-3-buten-2-yl (2*R*)-2-Ethyl-3-butenoate (SI-25b)



SI-25a ***SI-25b***

Ester **SI-25a** (100 mg, 0.452 mmol) and **G2** (38.4 mg, 0.0452 mmol) in benzene (45 mL, 0.01 M) were placed in a Fischer-Porter tube. The tube was evacuated and back-filled and pressurized with 15 atm of ethylene gas. The tube was heated to 65 ºC, and after 3 h a second portion of **G2** (19.2 mg, 0.0251 mmol) was added. The tube was repressurezed and heated for 8 h at 65 ºC, at which time the reaction was judged complete by GCMS analysis. The resultant mixture was cooled to room temperature, filtered through a plug of silica gel (6:1 hexanes:EtOAc), and concentrated *in vacuo* to give terminal alkene **SI-25b** (*ca.* 95 mg, quantitative).

^{1}H NMR ($CDCl_3$, 500 MHz; as a mixture of diastereomers): δ 5.82 (ddd, *J* = 16, 9, 9 Hz, 1H, C*H*=CH_2), 5.80 (ddd, *J* = 16, 9, 9 Hz, 1H, C*H*=CH_2), 5.37 (br m, 1H, CO_2CH), 5.18 (d, *J* = 16.1 Hz, 1H, CH=C$H_{trans}H_{cis}$), 5.17 (d, *J* = 10.5 Hz, 1H, CH=$CH_{trans}H_{cis}$), 5.14 and 5.13 (br s, 1H, C=CH_aH_b), 5.06 and 5.05 (m, 1H, C=CH_aH_b), 3.00 (dt, *J* = 7.6, 7.5 Hz, 1H, COC*H*CH_2CH_3), 2.74 (br m, 2H, CH_2CN), 1.8-1.7 (m, 4H, H_2C=CCH_3 and $CH_aH_bCH_3$), 1.55-1.65 (m, 1H, $CH_aH_bCH_3$), and 0.93 (t, *J* = 7.4 Hz, 3H, CH_2CH_3).

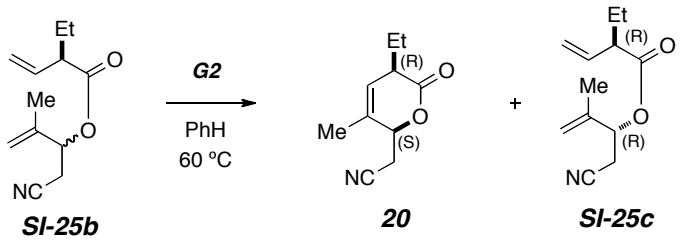
^{13}C NMR ($CDCl_3$, 125 MHz; as a mixture of diasteromers): δ 172.3, 139.9, 139.8, 135.0, 134.9, 128.0, 117.62, 117.61, 114.68, 114.63, 111.28, 111.26, 71.0, 51.53, 51.47, 35.3, 34.8, 26.7, 26.6, 26.06, 26.04, 25.9, 25.00, 24.93, 22.24, 22.15, 18.05, 18.02, 11.27, and 11.24.

TLC: R_f= 0.75 in 2:1 hexanes:EtOAc.

GCMS (5029021): t_R= 8.41 min, *m/z* 207 (M^+), 178 (2), 111 (6), 94 (30), 69 (100), and 67 (47).

HRMS (ESI/TOF): Calcd for $C_{12}H_{17}NO_2Na^+$: 230.1151. Found: 230.1164.

[(2*S*,5*R*)-5-Ethyl-3-methyl-6-oxo-5,6-dihydro-2*H*-pyran-2-yl]acetonitrile (20)



SI-25b ***20*** ***SI-25c***

Terminal alkene **SI-25b** (*ca.* 452 μmmol) and **G2** (19.0 mg, 22.4 μmol) were dissolved in benzene and warmed to 60 ºC. After 4 h a second portion of **G2** (18.0 mg, 21.2 μmol) was added. After 30 h a third portion of **G2** (11.5 mg, 13.6 μmol) was added and stirring was continued for 24 h. The reaction mixture was cooled to room temperature and concentrated *in vacuo*. The resultant mixture was filtered through a plug of silica gel (3:1 hexanes: EtOAc) and concentrated *in vacuo*. MPLC (2:1 hexanes:EtOAc) afforded the unreacted ester **SI-25c** and the more polar lactone **20** (36.5 mg, 40%).

Characterization data for lactone **20**:

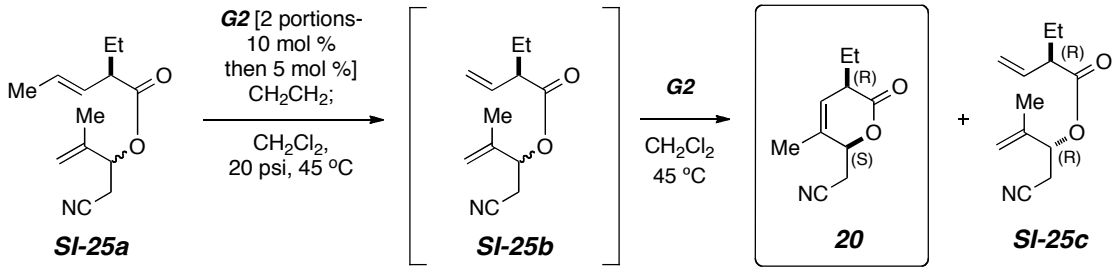
^{1}H NMR ($CDCl_3$, 300 MHz): δ 5.67 (ddq, *J* = 4, 1.5, 1.5 Hz, 1H, C*H*=CCH$_3$), 5.03 (br ddd, *J* = 4, 4, 4 Hz, 1H, CO_2CH), 3.00 (nfom, 1H, COC*H*CH$_2$CH$_3$), 2.98 (dd, *J* = 17.2, 4.3 Hz, 1H, C*H*$_a$H$_b$CN), 2.82 (dd, *J* = 17.2, 4.3 Hz, 1H, CH$_a$*H*$_b$CN), 1.96-1.84 (nfom, 2H, C*H*$_a$*H*$_b$CH$_3$), 1.83 (br s, 3H, HC=CC*H*$_3$), and 1.03 (t, *J* = 7.4 Hz, 3H, CH$_2$C*H*$_3$). **^{13}C NMR** ($CDCl_3$, 75 MHz; for lactone **20**): δ 170.3, 128.8, 124.4, 115.8, 77.2, 40.6, 26.9, 24.2, 18.4, and 11.2.

TLC: R_f = 0.18 in 2:1 hexanes:EtOAc.

GCMS (5029021): t_R = 9.79 min, *m/z* 179 (M^+), 151 (30), 139 (25), 135 (20), 120 (15), 111 (100), 95 (37), and 55 (30).

HRMS (ESI/TOF): Calcd for $C_{10}H_{13}NO_2Na^+$: 202.0838. Found: 202.0855.

One-pot procedure for the preparation of 20 from SI-25a.

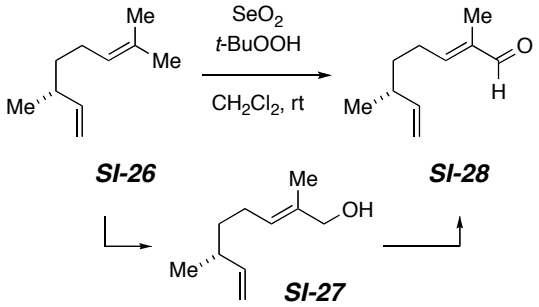


SI-25a ***SI-25b*** ***20*** ***SI-25c***

Ester **SI-25a** (100 mg, 452 μmmol) and **G2** (38.4 mg, 45.2 μmol) were dissolved in $CHCl_3$ (9

mL, 0.05 M) and the mixture was sparged with N_2 for 5 min. The N_2 atmosphere in the vessel was exchanged with one atmosphere of ethylene gas. The mixture was refluxed while maintaining 1 atm of CH_2CH_2. After 24 h a second portion of **G2** (19 mg, 22.6 mmol) was added and the mixture was stirred at reflux for 26 h. A third portion of **G2** (11 mg, 13.6 μmol) was added and the mixture was stirred at refux for 24 h. The solution was cooled to room temperature and concentrated *in vacuo*. The resultant mixture was filtered through a plug of silica gel (1:3 hexanes: EtOAc) and concentrated *in vacuo*. MPLC (2:1 hexanes:EtOAc) afforded ester (**SI-25c**) and the more polar lactone **20** (25 mg, 31%).

(6*R*,2*E*)-2,6-Dimethyl-2,7-octadienal (SI-28)



Selenium dioxide (8.03 g, 72.3 mmol) was placed in a 500 mL flask and CH_2Cl_2 (145 mL, 2.5 M) was added. *t*-BuOOH (207 mL, 70% solution in H_2O, 1.45 mol) and (-)-β-citronellene (**SI-26,** 50 g, 362 mmol) were added to a suspension of the reaction mixture at room temperature. This mixture was stirred at room temperture for 72 h, concentrated *in vacuo* to half its volume, and filtered. The filtrate was washed with a mixture of Na_2SO_3 (60 mg)/water (500 mL) and the aqueous layer was extracted with Et_2O. The combined organic layers were washed with aqueous $NaHCO_3$ and brine and dried over Na_2SO_4. The resulting solution was concentrated *in vacuo* to give a crude product. Flash chromatography (20:1 hexanes:EtOAc) afforded aldehyde **SI-28** (30 g, 55%) as a clear colorless oil.

^{1}H NMR ($CDCl_3$, 300 MHz): δ 9.40 (s, 1H, C*H*O), 6.49 [tq, J = 7.4, 1.3 Hz, 1H, C*H*=C(CH_3)CHO], 5.68 (ddd, *J* = 17.0, 10.4, 7.8 Hz, 1H, C*H*=CH_2), 5.00 (ddd, *J* = 17.1, 1.8, 1.0 Hz, CH=CH_{trans}H$_{cis}$), 4.98 (ddd, *J* = 10.2, 1.8, 0.9 Hz, 1H, CH=CH$_{trans}H_{cis}$), 2.34 [app q, *J* = 7.6 Hz, 2H, CH_2CH=C(CH_3)CHO], 2.17 [app. septet, *J* = 6.7 Hz, 1H, (CH_3)C*H*CH=CH_2], 1.74 [dd, *J* = 1.2, 1.0 Hz, 3H, CH=C(CH_3)CHO], 1.53-1.42 [nfom, 2H, CH_2CH(CH_3)], and 1.04 [d, J = 6.7

Hz, 3H, $(CH_3)CHCH=CH_2$].

^{13}C NMR ($CDCl_3$, 75 MHz): δ 195.5, 155.0, 143.8, 139.5, 113.7, 37.9, 35.3, 27.0, 20.5, and 9.4.

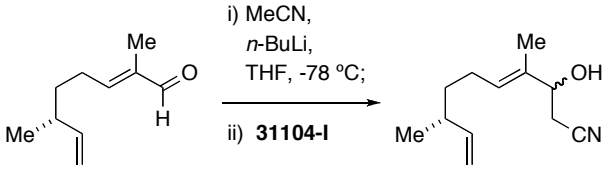
GCMS (5025015): t_R = 6.81 min. *m/z*: 151 $(M-H)^+$, 137 (27), 123 (37), 109 (26), 97 (27), 95 (88), 84 (100), 69 (48), 67 (72), and 55 (74).

TLC: R_f = 0.25 in 20:1 hexanes:EtOAc.

The intermdiate alcohol **SI-27** was detected in aliquots of the reaction mixture that were analyzed by GCMS at intermediate times.

GCMS (5025015, alcohol): t_R = 6.97 min. *m/z*: 154 (M^+), 136 (24), 123 (45), 121 (45), 107 (44), 97 (43), 93 (50), 84 (47), 81 (98), and 79 (60).

(*3R*,8*R*,4*E*)- and (*3S*,8*R*,4*E*)-3-Hydroxy-4,8-dimethyl-4,9-decadienenitrile (SI-29)



SI-28 ***SI-29***

Acetonitrile (2.86 mL, 54.8 mmol) was dissolved in THF (137 mL, 0.2 M) and cooled to -78 ºC. *n*-BuLi (20.6 mL, 2.0 M in hexane, 41.1 mmol) was added dropwise and the reaction mixture was stirred for 2 h. Aldehyde **SI-28** (4.17 g, 27.4 mmol) was added to the resulting orange-pink colored mixture. After 1.5 h the reaction mixture was quenched with aqueous NH_4Cl at -78 ºC and gradually warmed to room temperature. The mixture was extracted with EtOAc, and the combined organic layers were washed with $NaHCO_3$ and brine, dried over $MgSO_4$, filtered, and concentrated *in vacuo* to give the crude product. Flash chromatography (4:1 hexanes:EtOAc) afforded a racemic alcohol **SI-29** (4.68 g, 90%) as a clear colorless oil.

^{1}H NMR ($CDCl_3$, 500 MHz; as a mixture of diastereomers): δ 5.67 (ddd, *J* = 17.1, 10.3, 7.9 Hz, 1H, $CH=CH_2$), 5.55 [t, *J* = 7.2 Hz, 1H, $CH_2CH=C(CH_3)$], 4.97 (d, *J* = 17.2 Hz, 1H, $CH=CH_{trans}H_{cis}$), 4.94 (d, *J* = 10.3 Hz, 1H, $CH=CH_{trans}H_{cis}$), 4.36 (t, *J* = 6.4 Hz, 1H, $CHOH$), 2.62 (dd, *J* = 16.6, 6.9 Hz, 1H, CH_aH_bCN), 2.57 (dd, *J* = 16.6, 6.0 Hz, 1H, CH_aH_bCN), 2.13 [app. septet, *J* = 6.9 Hz, 1H, $(CH_3)CHCH=CH_2$], 2.07-1.98 [m, 2H, $CH_2CH=C(CH_3)$], 1.64 [s, 3H,

CH=C(C*H*$_3$)], 1.36 [app q, *J* = 7.5 Hz, 2H, C*H*$_2$CH(CH$_3$)], and 1.00 [d, *J* = 6.8 Hz, 3H, (C*H*$_3$)CHCH=CH$_2$].

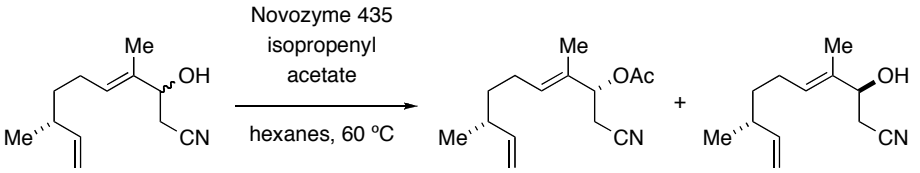
^{13}C NMR ($CDCl_3$, 125 MHz; as a mixture of diastereomers): δ 144.4, 134.1, 129.28, 129.22, 117.6, 113.12, 113.10, 73.41, 73.37, 37.6, 36.2, 25.5, 24.6, 20.42, 20.38, 11.56, and 11.53.

TLC: R_f = 0.25 in 4:1 hexanes:EtOAc.

GCMS (5029021): t_R = 11.3 min. *m/z*: 193 (M^+, 12), 176 (5), 160 (23), 146 (12), 135 (22), 120 (22), 107 (18), 93 (25), 79 (32), 69 (100), and 55 (30).

HRMS (ESI/TOF): Calcd for $C_{12}H_{19}NONa^+$: 216.1359. Found: 216.1360.

(3*S*,8*R*,4*E*)-3-Hydroxy-4,8-dimethyl-4,9-decadienenitrile (15)



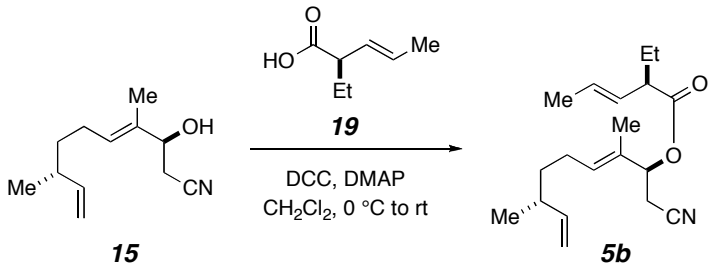
SI-29 ***SI-30*** ***15***

Racemic nitrile **SI-29** (8.6 g, 44.6 mmol) and isopropenyl acetate (74.3 mL, 0.6 M) were dissolved in hexanes (223 mL, 0.2 M). Novozyme 435 (2.58 g, 30% wt) was added and the suspension was heated at 65 ºC until (usually 3.5 days) the ratio between the desired alcohol **15** and the acetate **SI-30** was *ca.* 48:52, which was judged by integration of ^{1}H NMR spectra of aliquots. The suspension was filtered and the solids washed with hexanes. The filtrate was concentrated *in vacuo* to give the crude product. Flash chromatography (4:1 to 3:1 hexanes:EtOAc) afforded acetate **SI-30** and the more polar alcohol (*S*)-**15** (3.84 g, 45%) as a colorless oil.

15: $[\alpha]_D^{24}$ = -9.3º (c = 0.4, CH_2Cl_2).

TLC (for acetate **SI-30**): R_f = 0.45 in 4:1 hexanes:EtOAc.

(2*S*,7*R*,3*E*)-1-Cyano-3,7-dimethyl-3,8-nonadien-2-yl (2*R*,3*E*)-2-Ethylpent-3-enoate (5b)



Carboxylic acid **19** (500 mg, 3.91 mmol) and alcohol **15** (790 mg, 4.10 mmol) were dissolved in CH_2Cl_2 (20 mL, 0.2 M) and cooled to 0 ºC. DMAP (96 mg, 0.782 mmol) was added and the solution was stirred for 10 min at 0 ºC. DCC (1.05 g, 5.08 mmol) in CH_2Cl_2 (6 mL, therefore total concentration of the reaction would be 0.15 M) was added and the mixture was warmed to room temperature. After being sitrred for 17 h the reaction mixture was diluted with hexanes and filtered through Celite®. The filtrate was concentrated *in vacuo* to give a crude product. MPLC (20:1 hexanes:EtOAc) afforded ester **5b** (970 mg, 82 %).

^{1}H NMR ($CDCl_3$, 500 MHz; as a mixture of *E*/*Z*): δ 5.66 (ddd, *J* = 17.3, 10.3, 7.7 Hz, 1H, CH_2=C*H*C), 5.65-5.52 (m, 2H, CH=C*H*CH_3, CH_2C*H*=C), 5.41 (ddq, *J* = 15.1, 8.2, 1.5 Hz, 1H, C*H*=$CHCH_3$), 5.32 (dd, *J* = 6.3, 6.3 Hz, 1H, CO_2C*H*), 5.00-4.90 (m, 2H, CH=C$H_{trans}H_{cis}$), 2.90 (ddd, *J* = 8.2, 7.5, 7.5 Hz, 1H, COC*H*CH_2CH_3), 2.73 (dd, *J* = 16.8, 6.4 Hz, 1H, C$H_a$$H_b$CN), 2.66 (dd, *J* = 16.8, 6.3 Hz, 1H, $CH_a$$H_b$CN), 2.16 [m, 3H, ($CH_3$)C*H*CH=$CH_2$, C$H_2$CH=C($CH_3$)], 1.76 (ddq, *J* = 13.5, 7.4, 7.4 Hz, 1H, C$H_a$$H_b$$CH_3$), 1.693 (d, *J* = 6.3 Hz, 3H, CH=CHCH_3, one isomer), 1.688 (d, *J* = 6.3 Hz, 3H, CH=CHCH_3, one isomer), 1.644 (s, 3H, H_2C=CCH_3, one isomer), 1.641 (s, 3H, H_2C=CCH_3, one isomer), 1.55 (ddq, *J* = 13.4, 7.3, 7.3 Hz, 1H, $CH_a$$H_b$$CH_3$), 1.36 (m, 2H, C$H_2$CH($CH_3$)], 0.98 [d, *J* = 6.7, 3H, (CH_3)CHCH=CH_2], and 0.89 (t, *J* = 7.4 Hz, 3H, CH_2CH_3).

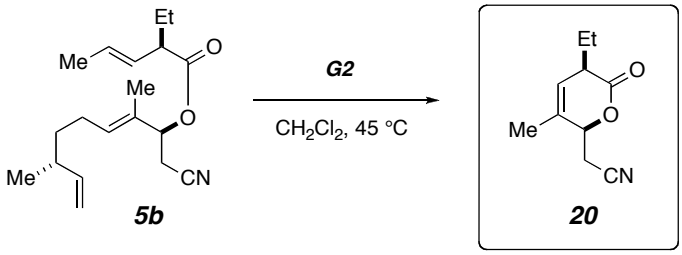
^{13}C NMR ($CDCl_3$, 75 MHz; as a mixture of *E*/*Z*): δ 173.3, 173.1, 144.36, 144.33, 131.03, 130.97, 130.1, 128.8, 128.30, 128.21, 127.71, 127.64, 116.46, 116.41, 113.14, 113.12, 73.30, 73.24, 51.01, 50.98, 37.6, 36.0, 25.9, 25.8, 25.7, 25.5, 22.6, 22.5, 20.4, 18.1, 12.18, 12.14, 11.75, and 11.69.

TLC: R_f = 0.70 in 4:1 hexanes:EtOAc.

GCMS (5029021): t_R = 11.68 and 11.71 min. *m/z*: 303 (M^+), 193 (14), 176 (10), 135 (23), 120 (23), 107 (12), 99 (12), 93 (20), 83 (100), 67 (18), and 55 (75).

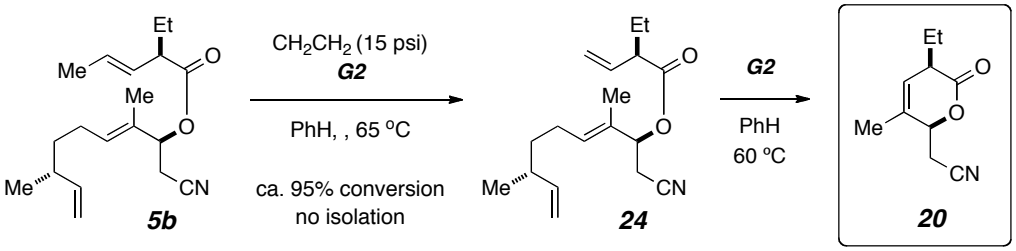
HRMS (ESI/TOF): Calcd for $C_{19}H_{29}NO_2Na^+$: 326.2091. Found: 326.2113.

(2*S*,5*R*)-5-Ethyl-5,6-dihydro-3-methyl-6-oxo-2*H*-pyran-2-acetonitrile (20)



Ester **5b** (1.0 g, 3.30 mmol) and **G2** (280 mg, 330 μmol) were dissolved in CH_2Cl_2 (330 mL, 0.01 M) and warmed to 45 ºC. After 10 h a second portion of **G2** (197 mg, 231 μmol) was added and the mixture was stirred at 45 °C for 25 h. A third portion of **G2** (170 mg, 198 μmol) was added and the mixture was stirred for 12 h. The solution was cooled to room temperature and concentrated *in vacuo*. The resultant mixture was filtered through a plug of silica gel (1:1 hexanes: EtOAc) and concentrated *in vacuo*. MPLC (2:1 hexanes:EtOAc) afforded lactone **20** (411 mg, 70%).

(2*S*,5*R*)-5-Ethyl-5,6-dihydro-3-methyl-6-oxo-2*H*-pyran-2-acetonitrile (20)



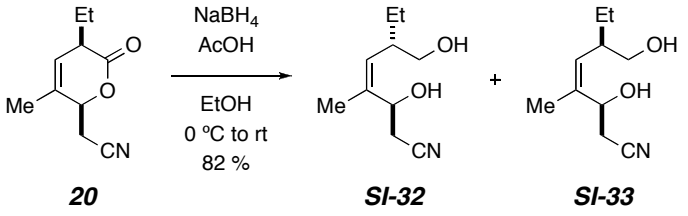
Ester **5b** (1.37 g, 4.52 mmol) and **G2** (153 mg, 180 mmol) in benzene (230 mL, 0.02 M) were placed in a Fischer-Porter tube. The tube was evacuated and filled with ethylene gas to set 15 psi as a final pressure. The tube was stirred in a 65 °C oil bath and after 4.5 h a second portion of **G2** (77 mg, 90 μmol) was added. The ethylene atmosphere was reestablished and the mixture was stirred for 12 h at 65 °C. A third portion of **G2** (57 mg, 67 μmol) was added and the mixture was again placed under ethylene and stirred at 65 °C, at which time no **5b** remained, as judged by GCMS analysis. The resultant mixture was cooled to room temperature, filtered through a plug of silica gel (6:1 hexanes:EtOAc), and concentrated *in vacuo* to give terminal alkene **24** (1.30 g, quantitative, *ca.* 95 % purity by GCMS), which was used directly in the next reaction.

TLC: R_f = 0.70 in 4:1 hexanes:EtOAc.

GCMS (5029021): t_R = 11.3 min. *m/z*: 289 (M^+), 193 (11), 174 (5), 160 (25), 146 (13), 135 (20), 120 (23), 107 (21), 97 (23), 93 (25), 81 (26), 79 (30), 69 (100), and 55 (27).

Terminal alkene **SI-31** (1.30 g, 4.50 mmol) and **G2** (150 mg, 180 μmol) were dissolved in benzene (230 mL, 0.02 M) and warmed to 60 ºC. After 13 h a second portion of **G2** (75.0 mg, 90.0 μmol) was added. After being stirred at 60 °C for 12 h the reaction mixture was cooled to room temperature and concentrated *in vacuo*. The resultant mixture was filtered through a plug of silica gel (3:1 hexanes: EtOAc) and concentrated *in vacuo*. Purification by MPLC (2:1 hexanes:EtOAc) afforded lactone **20** (220 mg, 30%).

(3*S*,6*S*,4*Z*)-3-Hydroxy-6-(hydroxymethyl)-4-methyl-4-octenenitrile (SI-32) and (3*S*,6*R*,4*Z*)-3-Hydroxy-6-(hydroxymethyl)-4-methyl-4-octenenitrile (SI-33)



20 ***SI-32*** ***SI-33***

Lactone **20** (100 mg, 0.559 mmol) was dissolved in EtOH (6 mL, 0.1 M), AcOH (16 μL, 0.279 mmol) was added, and the mixture was cooled to 0 ºC. $NaBH_4$ (85 mg, 2.23 mmol) was added in one portion and the mixture was warmed to room temperature. After being stirred for 1 h aqueous NH_4Cl was added and the mixture was extracted with EtOAc. The combined extracts were washed with brine and concentrated *in vacuo* to give the crude product. MPLC (1:2 hexanes:EtOAc) afforded diol **SI-33** (83.2 mg, 82%) as a clear colorless oil.

^{1}H NMR ($CDCl_3$, 500 MHz): δ 5.10 [d, *J* = 10.1 Hz, 1H, C*H*=C(CH_3)], 4.84 [dd, *J* = 7.0, 7.0 Hz, 1H, CH=C(CH_3)C*H*OH], 4.3 (br s, 1H, O*H*), 3.68 (dd, *J* = 10.1, 4.1 Hz, 1H, CHC$H_a$$H_b$OH), 3.28 (dd, *J* = 10.1, 10.1 Hz, 1H, CHC$H_a$$H_b$OH), 2.98 (br s, 1H, *OH*), 2.69 (dd, *J* = 16.6, 7.8 Hz, 1H, C$H_a$$H_b$CN), 2.58-2.48 (m, 1H, HOCH_2C*H*), 2.51 (dd, *J* = 16.6, 6.2 Hz, 1H, C$H_a$$H_b$CN), 1.79 [d, *J* = 1.4 Hz, 3H, CH=C(CH_3)], 1.37 (dqd, *J* = 14.8, 7.4, 5.0 Hz, 1H, C$H_a$$H_b$$CH_3$), 1.21 (dqd, *J* = 14.8, 7.5, 7.5 Hz, 1H, C$H_a$$H_b$$CH_3$), and 0.87 (t, *J* = 7.5 Hz, 3H, CH_2CH_3).

^{13}C NMR ($CDCl_3$, 125 MHz): δ 137.3, 133.2, 118.0, 65.9, 65.5, 42.0, 24.7, 23.1, 17.6, and 11.9.

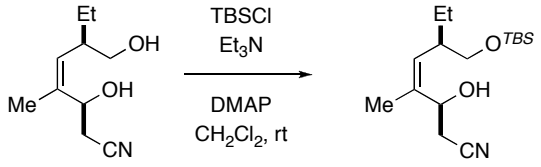
TLC: R_f = 0.65 in 1:3 hexanes:EtOAc for desired diol **SI-33**.

HRMS (ESI/TOF): Calcd for $C_{10}H_{17}NO_2Na^+$: 206.1151. Found: 206.1157.

The undesired diastereomeric diol **SI-32**, observed in this experiment at only trace levels, was isolated from experiments using $NaBH_4$ in EtOH and has the following characteristics: **^{1}H NMR** ($CDCl_3$, 500 MHz): δ 5.12 [dd, *J* = 10.5, 1.2 Hz, 1H, CH=C(CH_3)], 4.77 [dd, *J* = 6.6, 6.6 Hz, 1H, CH=C(CH_3)C*H*OH], 3.66 (ddd, *J* = 10.2, 4.6, 4.6 Hz, 1H, CHC$H_a$$H_b$OH), 3.34 (ddd, *J* = 10.2, 10.2, 2.0 Hz, 1H, CHC$H_a$$H_b$OH), 2.88 (br s, 1H, *OH*), 2.74-2.66 (m, 1H, HOCH_2C*H*), *2*.69 (dd, *J* = 16.6, 7.0 Hz, 1H, C$H_a$$H_b$CN), 2.65 (dd, *J* = 16.6, 6.3 Hz, 1H, C$H_a$$H_b$CN), 1.81 [d, *J* = 1.4 Hz, 3H, CH=C(C*H*$_3$)], 1.76 (br s, 1H, O*H*), 1.43 (dqd, *J* = 13.8, 7.5, 4.9 Hz, 1H, C$H_a$$H_b$$CH_3$), 1.21 (dqd, *J* = 13.7, 7.4, 7.4 Hz, 1H, C$H_a$$H_b$$CH_3$), and 0.87 (t, *J* = 7.5 Hz, 3H, CH_2C*H*$_3$).

TLC: R_f = 0.70 in 1:3 hexanes:EtOAc.

(3*S*,6*R*,4*Z*)-6-[(*tert*-Butyldimethylsilyloxy)methyl]-3-hydroxy-4-methyl-4-octenenitrile (SI-34)



SI-33 ***SI-34***

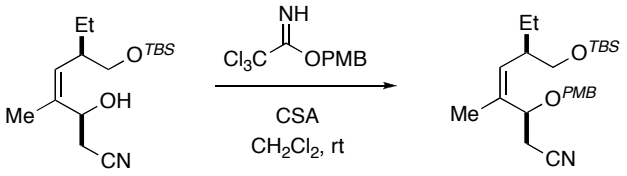
Diol **SI-33** (421 mg, 2.30 mmol) was dissolved in CH_2Cl_2 (23 mL, 0.1 M). Et_3N (634 μL, 4.55 mmol), DMAP (28 mg, 0.227 mmol), and TBSCl (411 mg, 2.73 mmol) were added successively to the reaction mixture. After being stirred for 17 h at ambient temperature the reaction mixture was quenched by the addition of aqueous NH_4Cl and the resulting mixture was extracted with EtOAc. The combined extracts were washed with brine and concentrated *in vacuo*. Purification by MPLC (6:1 hexanes:EtOAc) afforded TBS ether **SI-34** (681 mg, 99%) as a clear colorless oil. **^{1}H NMR** ($CDCl_3$, 500 MHz): δ 5.08 [d, *J* = 10.3 Hz, 1H, C*H*=C(CH_3)], 4.79 [ddd, *J* = 7.1, 7.1, 1.8 Hz, 1H, CH=C(CH_3)C*H*OH], 3.65 [dd, *J* = 9.5, 4.3 Hz, 1H, CHC$H_a$$H_b$(OTBS)], 3.24 [dd, *J* = 9.6, 9.6 Hz, 1H, CHC$H_a$$H_b$(OTBS)], 3.18 (d, *J* = 1.9 Hz, 1H, CH=C(CH_3)CHO*H*), 2.67 (dd, *J* = 16.5, 7.3 Hz, 1H, C$H_a$$H_b$CN), 2.58-2.50 (m, 1H, HOCH_2C*H*), 2.55 (dd, *J* = 16.5, 6.9 Hz, 1H, C$H_a$$H_b$CN), 1.80 [s, *J* = 1.5 Hz, 3H, CH=C(C*H*$_3$)], 1.38 (dqd, *J* = 13.4, 7.4, 4.8 Hz, 1H, C$H_a$$H_b$$CH_3$), 1.16 (ddq, *J* = 13.4, 8.9, 7.3 Hz, 1H, C$H_a$$H_b$$CH_3$), 0.89 [s, 9H, (C*H*$_3$)$_3$CSi($CH_3$)$_2$], 0.88 (t, *J* = 7.5 Hz, 3H, CH_2C*H*$_3$), and 0.07 [s, 6H, (CH_3)$_3$CSi(C*H*$_3$)$_2$].

^{13}C NMR ($CDCl_3$, 125 MHz): δ 136.9, 134.2, 118.0, 67.0, 65.5, 42.4, 26.2, 24.6, 22.6, 18.8, 18.0, 12.0, -5.21, and -5.28.

TLC: R_f = 0.45 in 3:1 hexanes:EtOAc.

HRMS (ESI/TOF): Calcd for $C_{16}H_{31}NO_2SiNa^+$: 320.2016. Found: 320.2021.

(3*S*,6*R*,4*Z*)-6-[(*tert*-Butyldimethylsilyloxy)methyl]-3-(4-methoxyphenylmethoxy)-4-methyl-4-octenenitrile (17)



SI-34 ***17***

TBS ether **SI-34** (1.13 g, 3.803 mmol), *d*-10-camphorsulfonic acid (176 mg, 0.761 mmol), and *p*-methoxybenzyl trichloroacetamide (5.88 g, 20.9 mmol)[10] were dissolved in CH_2Cl_2 (22.5 mL, 0.17 M). After the mixture had been stirred for 24 h, a solid had precipitated. The liquid portion was transferred to a separatory funnel and EtOAc and $NaHCO_3$ were added. The white solid was washed with pentane (3 times) and these washings were added to the separatory funnel. The aqueous layer was extracted with EtOAc, and the combined organic layers were washed with brine and concentrated *in vacuo*. Purification by MPLC (15:1 hexanes:EtOAc) afforded PMB ether **17** (1.22 g, 77%) as a pale yellow oil.

^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.28 (br d, *J* =8.7 Hz, 2H, MeOArH_aH_b), 6.88 (br d, *J* = 8.6 Hz, 2H, MeOArH_aH_b), 5.33 [dd, *J* = 10.6, 1.4 Hz, 1H, C*H*=C(CH_3)], 4.56 [dd, *J* = 8.6, 5.2 Hz, 1H, CH=C(CH_3)C*H*(OPMB)], 4.46 (d, *J* = 11.2 Hz, 1H, ArCH_aH_bO), 4.26 (d, *J* = 11.2 Hz, 1H, ArCH_aH_bO), 3.81 (s, 3H, OCH_3), 3.52 [dd, *J* = 9.7, 6.1 Hz, 1H, CHCH_aH_b(OTBS)], 3.51 [dd, *J* = 9.7, 6.3 Hz, 1H, CHCH_aH_b(OTBS)], 2.74 (dd, *J* = 16.7, 8.6 Hz, 1H, CH_aH_bCN), 2.45 (dd, *J* = 16.7, 5.2 Hz, 1H, CH_aH_bCN), 2.45-2.38 [m, 1H, C*H*CH_2(OTBS)], 1.73 [d, *J* = 1.4 Hz, 3H, CH=C(CH_3)], 1.54 (dqd, *J* = 14.9, 7.4, 5.2 Hz, 1H, C$H_aH_b$$CH_3$), 1.18 (dqd, *J* = 13.5, 7.5, 7.5 Hz, 1H, $CH_aH_b$$CH_3$), 0.89 [s, 9H, (C$H_3$)$_3$CSi($CH_3$)$_2$], 0.83 (t, *J* = 7.5 Hz, 3H, CH_2CH_3), and 0.04 [s, 6H, (CH_3)$_3$CSi(CH_3)$_2$].

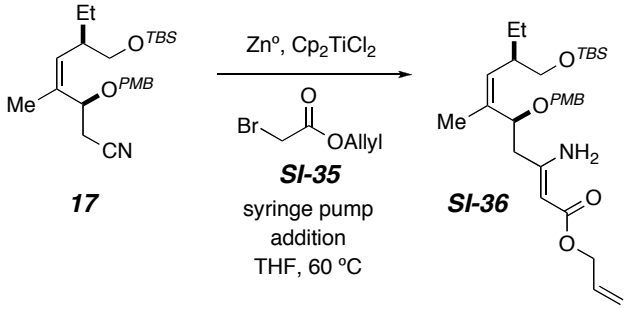
^{13}C NMR ($CDCl_3$, 125 MHz): δ 159.5, 135.1, 132.7, 130.0, 129.6, 117.9, 114.1, 72.2, 70.2, 66.8, 55.5, 41.9, 26.2, 24.8, 23.2, 18.7, 17.4, 11.9, -5.11, and -5.14.

TLC: R_f = 0.75 in 3:1 hexanes:EtOAc.

GCMS (5029021): t_R = 14.5 min. *m/z*: 402 [$(M\text{-}Me)^+$, 10], 360 (20), 199 (22), 121 (100), 107 (7), 89 (9), and 73 (12).

HRMS (ESI/TOF): Calcd for $C_{24}H_{39}NO_3SiNa^+$: 440.2591. Found: 440.2593.

2-Propenyl (2*Z*,4S,7*R*,6*Z*)-3-Amino-8-[(*tert*-butyldimethylsilyloxy)methyl]-5-(4-methoxyphenylmethoxy)-6-methyl-2,6-decadienoate (SI-36)



Nitrile **17** (408 mg, 978 μmol) was dissolved in THF (3.9 mL, 0.25 M). Zinc dust (1.30 g, 19.6 mmol) and Cp_2TiCl_2 (12.2 mg, 48.9 μmol) were added. Allyl bromoester **SI-35** (3 drops) was added to the reaction mixture. The reaction vessel was warmed and kept in an oil bath at 60 °C. Additional allyl bromoester **SI-35** (1.75 g, 9.78 mmol, see below for preparation) was added by syringe pump for 5 h at 60 ºC. The reaction mixture was cooled to room temperature and diluted with pentane. The mixture was filtered through a pad of silica gel and the filtrate was evaporated *in vacuo* to afford a crude enamino ester **SI-36** (quantitative) that was directly used for next reaction. A portion was purified for analytical purposes using MPLC (6:1 hexanes:EtOAc) to afford enamino ester **SI-36** as a light-yellowish oil.

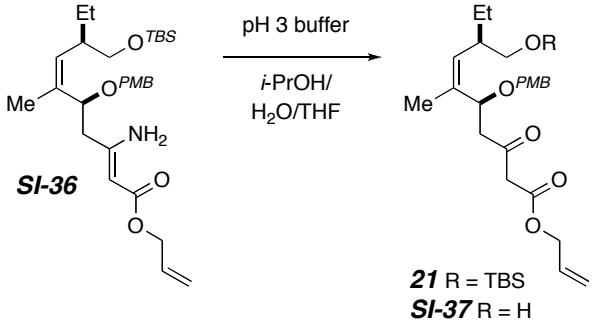
^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.78 (br s, 1H, NH_aH_b), 7.23 (d, *J* = 8.6 Hz, 2H, MeOArH_aH_b), 6.87 (d, *J* =8.6 Hz, 2H, MeOArH_aH_b), 5.96 (ddt, *J* = 17.2, 10.4, 5.6 Hz, 1H, C*H*=CH_2), 5.71 (br s, 1H, NH_aH_b), 5.31 (ddt, *J* = 17.2, 1.6, 1.6 Hz, 1H, CH=C$H_{trans}H_{cis}$), 5.20 (ddt, *J* = 10.4, 1.4, 1.4 Hz, 1H, CH=$CH_{trans}H_{cis}$), 5.19 [d, *J* = 10.4 Hz, 1H, C(CH_3)=C*H*], 4.57 (ddd, *J* = 5.6, 1.4, 1.4 Hz, 2H, CH_2CH=CH_2), 4.48 [dd, *J* = 9.9, 2.0 Hz, 1H, C*H*(OPMB)], 4.48 [s, 1H, NH_2C=C*H*C(O)], 4.39 (d, *J* = 10.8 Hz, 1H, ArCH_aH_b), 4.18 (d, *J* = 10.8 Hz, 1H, ArCH_aH_b), 3.81 (s, 3H, OCH_3), 3.49 [dd, *J* = 6.4, 3.0 Hz, 2H, CH_2(OTBS)], 2.62 [dd, *J* = 14.6, 9.9 Hz, 1H, CH(OPMB)CH_aH_b], 2.46 [m, 1H, C*H*CH_2(OTBS)], 2.05 [dd, *J* = 14.5, 2.1 Hz, 1H, CH(OPMB)CH_aH_b], 1.74 [d, *J* =

1.4 Hz, 3H, CH=C(C*H*$_3$)], 1.56 (dqd, *J* = 13.4, 7.5, 4.5 Hz, 1H, C*H*$_a$H$_b$CH$_3$), 1.11 (ddq, *J* = 13.5, 8.9, 7.5 Hz, 1H, CH$_a$*H*$_b$CH$_3$), 0.88 [s, 9H, (C*H*$_3$)$_3$CSi(CH$_3$)$_2$], 0.83 (t, *J* = 7.5 Hz, 3H, CH$_2$C*H*$_3$), and 0.02 [s, 6H, (CH$_3$)$_3$CSi(C*H*$_3$)$_2$].

TLC: R_f = 0.75 in 3:1 hexanes:EtOAc.

HRMS (ESI/TOF): Calcd for $C_{29}H_{47}NO_5SiNa^+$: 540.3116. Found: 540.3135.

2-Propenyl (4*S*,7*R*,6*Z*)-8-[(*tert*-Butyldimethylsilyloxy)methyl]-5-(4-methoxyphenylmethoxy)-6-methyl-3-oxo-6-decenoate (21)



The crude enaminoester **SI-36** was dissolved in THF (9.8 mL, 0.1 M), water (5 mL, 0.2 M), and *i*-PrOH (20 mL, 0.049 M). pH 3 Buffer (30 mL, 0.033 M citric acid/potassium phosphate) was added and the reaction mixture was stirred for 22 h and then extracted with EtOAc. The combined extracts were washed with brine, dried over $MgSO_4$, filtered, and concentrated *in vacuo* to afford a crude mixture of the ß-keto ester **21** and the ß-keto ester alcohol **SI-37** (that was detected in the ESI-MS), which was used directly for next reaction.

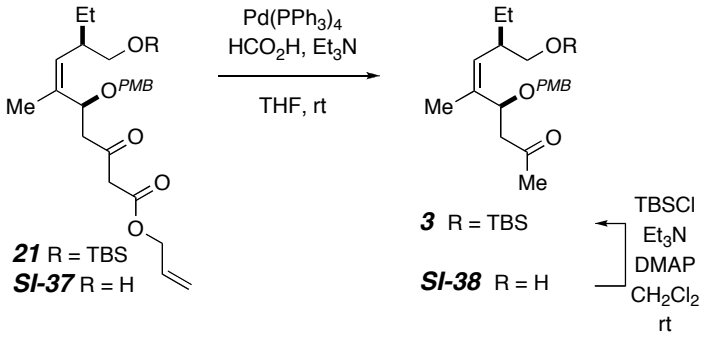
^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.22 (d, *J* = 8.6 Hz, 2H, MeOAr*H*$_a$H$_b$), 6.85 (d, *J* =8.6 Hz, 2H, MeOArH$_a$*H*$_b$), 5.89 (ddt, *J* = 17.2, 10.5, 5.8 Hz, 1H, C*H*=CH$_2$), 5.33 (ddt, *J* = 17.2, 1.5, 1.5 Hz, 1H, CH=C*H*$_{trans}$H$_{cis}$), 5.24 (ddt, *J* = 10.4, 1.3, 1.3 Hz, 1H, CH=CH$_{trans}$*H*$_{cis}$), 5.20 [dd, *J* = 10.5, 1.3 Hz, 1H, C(CH$_3$)=C*H*], 4.77 [dd, *J* = 10.1, 2.9 Hz, 1H, C*H*(OPMB)], 4.61 (ddd, *J* = 5.8, 1.4, 1.4 Hz, 2H, C*H*$_2$CH=CH$_2$), 4.35 (d, *J* = 10.9 Hz, 1H, ArC*H*$_a$H$_b$), 4.18 (d, *J* = 10.9 Hz, 1H, ArCH$_a$*H*$_b$), 3.79 (s, 3H, OC*H*$_3$), 3.50 [s, 2H, C(O)C*H*$_2$CO$_2$], 3.49 (m, 2H, C*H*$_2$OTBS), 3.02 [dd, *J* = 15.3, 10.1 Hz, 1H, CH(OPMB)C*H*$_a$H$_b$], 2.51 [ddddd, *J* = 10.6, 8.8, 6.0, 6.0, 4.6 Hz, 1H, C*H*CH$_2$(OTBS)], 2.41 [dd, *J* = 15.4, 2.9 Hz, 1H, CH(OPMB)C*H*$_a$H$_b$], 2.05 [dd, *J* = 14.5, 2.1 Hz, 1H, CH(OPMB)CH$_a$*H*$_b$], 1.72 [d, *J* = 1.3 Hz, 3H, CH=C(C*H*$_3$)], 1.55 (dqd, *J* = 13.6, 7.5, 4.6 Hz,

1H, C*H*$_a$H$_b$CH$_3$), 1.11 (ddq, *J* = 13.6, 8.6, 7.5 Hz, 1H, CH$_a$*H*$_b$CH$_3$), 0.89 [s, 9H, (C*H*$_3$)$_3$CSi(CH$_3$)$_2$], 0.79 (t, *J* = 7.5 Hz, 3H, CH$_2$C*H*$_3$), 0.032 [s, 3H, (CH$_3$)$_3$CSi(CH$_3$)(C*H*$_3$)], and 0.029 [s, 3H, (CH$_3$)$_3$CSi(CH$_3$)(C*H*$_3$)].

TLC: R_f = 0.75 in 3:1 hexanes:EtOAc.

HRMS (ESI/TOF): Calcd for $C_{29}H_{46}O_6SiNa^+$: 541.2956. Found: 541.2982.

(4*S*,7*R*,5*Z*)-7-[(*tert*-Butyldimethylsilyloxy)methyl]-4-(4-methoxyphenylmethoxy)-5-methyl-5-nonen-2-one (3)



The β-keto ester **21** (*ca.* 978 μmol) was dissolved in THF (9,8 mL, 0.1 M) and cooled to 0º C. *i*-Pr$_2$EtN (2.04 mL, 11.7 mmol) and HCO$_2$H (457 μL, 9.78 mmol, 88% pure) were added to the reaction mixture. After 5 min Pd(PPh$_3$)$_4$ (33.9 mg, 0.0293 mmol) was added to the mixture in one portion. The mixture was warmed to room temperature, stirred for 12 h, and concentrated *in vacuo*. The residue was filtered through a pad of SiO$_2$ with the aid of 1:1 hexanes:EtOAc and the filtrate was reconcentrated *in vacuo*. Purification by MPLC (4:1 hexanes:EtOAc) afforded ketone **3** (220 mg, 52% over three steps) and the ketone alcohol **SI-38** (68 mg, 22%), each as a light-yellowish oil.

^{1}H NMR (CDCl$_3$, 500 MHz): δ 7.22 (d, *J* =8.6 Hz, 2H, MeOAr*H*$_a$H$_b$), 6.85 (dd, *J* = 8.6 Hz, 2H, MeOArH$_a$*H*$_b$), 5.18 [dd, *J* = 10.5, 1.4 Hz, 1H, C*H*=C(CH$_3$)], 4.78 [dd, *J* = 9.9, 3.0 Hz, 1H, CH=C(CH$_3$)C*H*(OPMB)], 4.35 (d, *J* = 11.0 Hz, 1H, ArC*H*$_a$H$_b$O), 4.19 (d, *J* = 11.0 Hz, 1H, ArCH$_a$*H*$_b$O), 3.79 (s, 3H, OC*H*$_3$), 3.51 [dd, *J* = 9.7, 6.1 Hz, 1H, CHC*H*$_a$H$_b$(OTBS)], 3.49 [dd, *J* = 9.7, 6.3 Hz, 1H, CHCH$_a$*H*$_b$(OTBS)], 2.93 [dd, *J* = 15.5, 10.0 Hz, 1H, C*H*$_a$H$_b$C(O)CH$_3$], 2.52 [ddddd, *J* = 10.7, 8.7, 6.2, 6.2, 4.5 Hz, 1H, C*H*CH$_2$(OTBS)], 2.29 [dd, *J* = 15.5, 3.0 Hz, 1H, CH$_a$*H*$_b$C(O)CH$_3$], 2.14 [s, 1H, C(O)C*H*$_3$], 1.73 [d, *J* = 1.4 Hz, 3H, CH=C(C*H*$_3$)], 1.55 (dqd, *J* =

13.4, 7.5, 4.7 Hz, 1H, CH_aH$_b$CH$_3$), 1.11 (ddq, *J* = 13.6, 8.9, 7.4 Hz, 1H, CH$_a$$H_bCH_3$), 0.89 [s, 9H, (C$H_3$)$_3$CSi(CH$_3$)$_2$], 0.79 (t, *J* = 7.5 Hz, 3H, CH$_2$CH_3), 0.031 [s, 3H, (CH$_3$)$_3$CSi(CH$_3$)(CH_3)], and 0.029 [s, 3H, (CH$_3$)$_3$CSi(CH$_3$)(CH_3)].

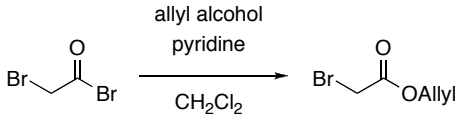
^{13}C NMR (CDCl$_3$, 125 MHz): δ 206.9, 159.2, 134.8, 132.4, 130.8, 129.5, 113.8, 73.2, 70.1, 67.0, 55.4, 48.1, 41.7, 31.1, 26.3, 24.8, 18.6, 18.1, 11.9, -5.15, and -5.18.

TLC: R_f = 0.55 in 6:1 (x2) hexanes:EtOAc for ketone **3**. R_f = 0.05 in 6:1 (x2) hexanes:EtOAc for the ketoalcohol **SI-38**.

HRMS (ESI/TOF): Calcd for $C_{24}H_{39}NO_3SiNa^+$: 457.2745. Found: 457.2781.

The ketoalcohol **SI-38** (68 mg, 0.213 mmol), Et$_3$N (6.6 µL, 425 µmol), DMAP (trace), and TBSCl (38.4 mg, 255 µmol) were dissolved in CH$_2$Cl$_2$ (1.75 mL, 0.12 M). After 12 h aqueous NaHCO$_3$ was added and the mixture was extracted with EtOAc. The combined organic layers were washed with brine and concentrated *in vacuo*. Purification by MPLC (6:1 hexanes:EtOAc) afforded ketone **3** (41 mg, 45%) as a clear oil. Including the TBS reprotection of **SI-38**, the total yield of ketone **3** from nitrile **17** was 61%.

Allyl Bromoethanoate (SI-35)



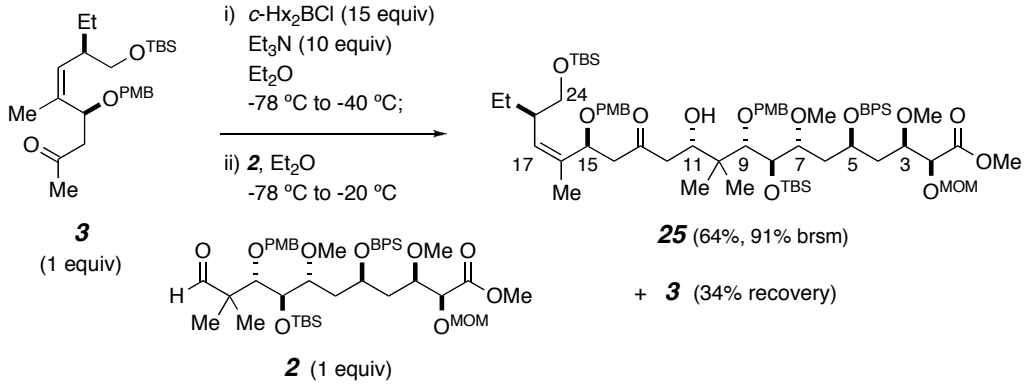
SI-39 ***SI-35***

Bromoacetyl bromide (**SI-39**, 12.9 mL, 149 mmol) was dissolved in CH$_2$Cl$_2$ (124 mL, 1.2 M) and cooled to 0 ºC. Pyridine (12.6 mL, 156 mmol) and allyl alcohol (10.6 mL, 156 mmol) were successively added to the reaction mixture. After 14 h aqueous NaHCO$_3$ was added and the mixture was extracted with EtOAc. The combined organic layers were washed with brine, dried over Na$_2$SO$_4$, filtered, and concentrated *in vacuo* to afford allyl bromoacetate (**SI-35**, 20 g, 75%) as a light-yellowish oil, which was used directly in the modified Blaise reaction.

^{1}H NMR (CDCl$_3$, 300 MHz): δ 5.93 (ddt, *J* = 17.2, 10.4, 5.8 Hz, 1H, CH=CH$_2$), 5.38 (ddt, *J* = 17.2, 1.5, 1.4 Hz, 1H, CH=CH_aH$_b$), 5.30 (ddt, *J* = 10.4, 1.5, 1.3 Hz, 1H, CH=CH$_a$$H_b$), 4.68 (ddd *J* = 5.8, 1.4, 1.3 Hz, 2H, CH_2CH=CH$_2$), and 3.87 (s, 2H, BrCH_2).

GCMS (5022014) : t_R = 5.00 min, *m/z* 180/178 (<1, M$^+$), 123/121 (100, M$^+$-allylO$^•$), 99 (88, M$^+$-HBr), 95/93 (53, BrCH$_2^+$), 85 (53, M$^+$-BrCH$_2^•$), 58 (75, C$_3$H$_6$O$^+$), and 57 (90, C$_3$H$_5$O$^+$).

Methyl (2*S*,3*R*,5*S*,7*R*,8*R*,9*S*,11*S*,15*S*,16*Z*,18*R*)-8-(*tert*-Butyldimethylsilyloxy)-18-[(*tert*-butyldimethylsilyloxy)methyl]-5-(*tert*-butyldiphenylsilyloxy)-11-hydroxy-3,7-dimethoxy-9,15-bis(4-methoxyphenylmethoxy)-2-(methoxymethoxy)-10,10,16-trimethyl-13-oxo-16-icosenoate (25)



Triethylamine (894 µL, 6.42 mmol) was dissolved in Et_2O (10.7 mL, 0.05 M) in a screw-capped culture tube fitted with a septum and under an argon atmosphere, and the solution was cooled to -78 °C. Dicyclohexylchloroborane (c-Hx_2BCl, 937 µL, 4.28 mmol, neat) and ketone **3** (232 mg, 535 µmol) in Et_2O (2.0 mL) were added in sequence, and the reaction mixture was stirred for 30 min at -78 ºC and warmed to -40 ºC. After 1 h the mixture was recooled to -78 ºC. Aldehyde **2** (449 mg, 508 µmol) in Et_2O (7.0 mL) was added slowly, the septum was replaces with a Teflon-lined screw cap, and the reaction mixture was stirred for 2 h. The mixture was warmed to -20 ºC and stored in a freezer (-20 ºC) for 12 h. The reaction was judged complete by TLC analysis. The reaction tube was placed in a 0 ºC bath, a solution of premixed MeOH-pH 7 buffer (3:1, 34 mL) was added, and the mixture was stirred for 10 min. Additional MeOH-pH 7 buffer (2:1, 17 mL) and H_2O_2 (9.0 mL, 30% in water) were added, and the mixture was stirred for 2.5 h at room temperature. The resultant mixture was extracted with Et_2O, and the combined extracts were washed with aqueous $NaHCO_3$ and brine, dried over $MgSO_4$, filtered and concentrated *in vacuo*. Purification by MPLC (5:1 hexanes:EtOAc) afforded the aldol adduct **25** (430 mg, 64.5%) and unreacted ketone **3** (80.0 mg, 34.4%), each as a clear colorless oil.

^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.72 (dd, *J* = 8.0, 1.5 Hz, 2H, *Ar-TBDPS*), 7.61 (dd, *J* = 8.0, 1.4 Hz, 2H, *Ar-TBDPS*), 7.38-7.25 (m, 6H, *Ar-TBDPS*, 2H, *Ar-PMB*), 7.19 (d, *J* = 8.7 Hz, 2H, *Ar-PMB*), 6.85 (d, *J* = 8.7 Hz, 2H, *Ar-PMB*), 6.82 (d, *J* = 8.7 Hz, 2H, *Ar-PMB*), 5.18 (dd, *J* = 10.4, 1.3 Hz, 1H, *H17*), 4.86 (d, *J* = 11.1 Hz, 1H, ArCH_aH_b), 4.80 (dd, *J* = 10.1, 2.8 Hz, 1H, *H15*),

4.52 (d, J = 7.0 Hz, 1H, OCH_aH$_b$OCH$_3$), 4.44 (d, J = 7.0 Hz, 1H, OCH$_a$$H_bOCH_3$), 4.37 (d, J = 11.1 Hz, 1H, ArCH$_a$$H_b$), 4.34 (d, J = 10.9 Hz, 1H, ArCH_aH$_b$), 4.24 (dd, J = 1.6, 1.6 Hz, 1H, *H8*), 4.21-4.17 (m, 1H, *H5*), 4.18 (d, J = 10.9 Hz, 1H, ArCH$_a$$H_b$), 4.06 (dd, J = 6.4, 5.8 Hz, 1H, *H11*), 3.84 (d, J = 3.1 Hz, 1H, *H2*), 3.78 (s, 3H, ArOCH_3), 3.77 (s, 3H, ArOCH_3), 3.71 (ddd, J = 10.2, 2.0, 2.0 Hz, *H7*), 3.63 (s, 3H, CO$_2$CH_3), 3.56 (d, J = 1.6 Hz, 1H, *H9*), 3.54 (ddd, J = 9.4, 3.1, 3.1 Hz, 1H, *H3*), 3.50 (d, J = 6 Hz, 2H, *H24*), 3.20 (s, 3H, OCH_3), 3.11 (s, 3H, OCH_3), 3.05 (s, 3H, OCH_3), 2.95 (dd, J = 15.7, 10.1 Hz, *H14a*), 2.56 (d, J = 6 Hz, 2H, *H12*), 2.58-2.49 (m, 1H, *H18*), 2.26 (dd, J = 15.6, 2.7 Hz, *H14b*), 2.05-1.90 [m, 3H, *H4a, H6a, H4b (or H6b)*], 1.72 (d, J = 1.4 Hz, 3H, *H23*), 1.55 (dqd, J = 13.5, 7.5, 4.5 Hz, 1H, *H19a*), 1.45 (ddd, J = 13.7, 9.6, 3.1 Hz, 1H, *H4b or H6b*), 1.10 (dqd, J = 13.6, 7.5, 5.6 Hz, 1H, *H19b*), 1.02 (s, 9H, (CH$_3$)$_2$SiC(CH_3)$_3$), 0.94 (s, 9H, (CH$_3$)$_2$SiC(CH_3)$_3$), 0.93 [s, 3H, C(CH_3)(CH$_3$)], 0.88 (s, 9H, Ph$_2$SiC(CH_3)$_3$), 0.88 [s, 3H, C(CH_3)(CH$_3$)], 0.78 (t, J = 7.5 Hz, 3H, CH$_2$CH_3), 0.100 [s, 3H, (CH$_3$)$_3$CSi(CH_3)(CH$_3$)], 0.080 [s, 3H, (CH$_3$)$_3$CSi(CH$_3$)(CH_3)], 0.029 [s, 3H, (CH$_3$)$_3$CSi(CH_3)(CH$_3$)], and 0.027 [s, 3H, (CH$_3$)$_3$CSi(CH$_3$)(CH_3)].

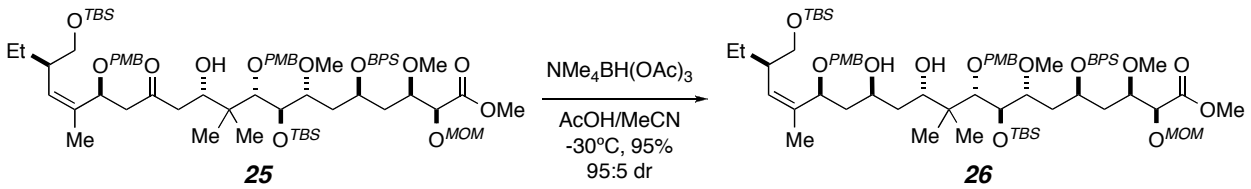
^{13}C NMR (CDCl$_3$, 125 MHz): δ 209.8, 171.1, 159.1, 159.0, 136.2, 136.1, 135.1, 134.6, 133.9, 132.5, 131.0, 130.5, 129.51, 129.45, 129.31, 129.2, 127.5, 127.3, 113.7, 113.7, 96.4, 89.3, 79.4, 79.0, 77.5, 75.2, 73.8, 73.0, 72.5, 70.0, 68.6, 66.9, 60.4, 58.6, 57.0, 56.1, 55.2, 51.7, 47.9, 46.1, 41.9, 41.7, 40.9, 38.5, 27.1, 26.2, 26.1, 24.7, 22.3, 21.1, 19.7, 19.4, 18.5, 18.3, 18.0, 14.3, 11.9, -4.18, -4.53, -5.22, and -5.25.

TLC: R$_f$ = 0.45 in 6:1 (x3) hexanes:EtOAc for the aldol adduct **25**.

R$_f$ = 0.75 in 6:1 (x3) hexanes:EtOAc for the recovered ketone **3**.

HRMS (ESI/TOF): Calcd for $C_{73}H_{116}O_{15}Si_3Na^+$: 1339.7514. Found: 1339.754.

Methyl (2*S*,3*R*,5*S*,7*R*,8*R*,9*S*,11*S*,13*S*,15*S*,16*Z*,18*R*)-8-(*tert*-Butyldimethylsilyloxy)-18-[(*tert*-butyldimethylsilyloxy)methyl]-5-(*tert*-butyldiphenylsilyloxy)-11,13-dihydroxy-3,7-dimethoxy-9,15-bis(4-methoxyphenylmethoxy)-2-(methoxymethoxy)-10,10,16-trimethyl-16-icosenoate (26)



25 ***26***

$Me_4NBH(OAc)_3$ (300 mg, 1.14 mmol) was dissolved in MeCN (1.1 mL, 0.1 M) and AcOH (1.1 μmol, 0.1 M) and stirred for 30 min at room temperature. The mixture was cooled to -30 ºC and ketone **25** (150 mg, 114 μmol) in MeCN (2.28 mL, 0.05 M) was added. After 2 h an aqueous solution of Rochelle's salt was added and the mixture was stirred for 5 min. CH_2Cl_2 was added to the resultant mixture and aqueous $NaHCO_3$ was added with care. The mixture was extracted with CH_2Cl_2, and the combined extracts were washed with $NaHCO_3$ and brine, dried over $MgSO_4$, and concentrated *in vacuo*. Purification by MPLC (4:1 hexanes:EtOAc) afforded the diol **26** (137 mg, 91%) as a clear colorless oil.

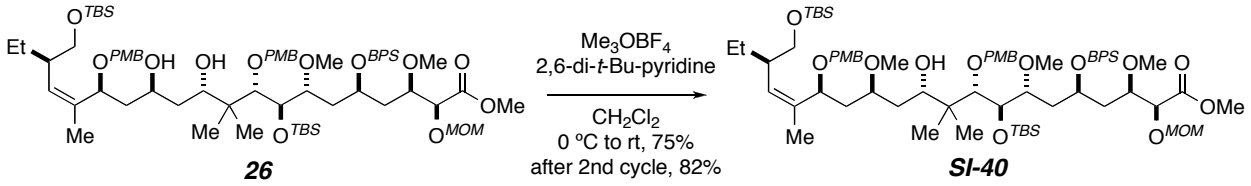
^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.72 (dd, *J* = 8.0, 1.5 Hz, 2H, *Ar-TBDPS*), 7.60 (dd, *J* = 8.0, 1.4 Hz, 2H, *Ar-TBDPS*), 7.38-7.24 (m, 6H, *Ar-TBDPS*, 2H, *Ar-PMB*), 7.124 (d, *J* = 8.7 Hz, 2H, *Ar-PMB*), 6.862 (d, *J* = 8.7 Hz, 2H, *Ar-PMB*), 6.860 (d, *J* = 8.7 Hz, 2H, *Ar-PMB*), 5.18 (dd, *J* = 10.3, 1.3 Hz, 1H, *H17*), 4.94 (d, *J* = 11.1 Hz, 1H, ArCH_aH$_b$), 4.56 (dd, *J* = 10.4, 2.8 Hz, 1H, *H15*), 4.52 (d, *J* = 7.0 Hz, 1H, OCH_aH$_b$OCH$_3$), 4.429 (d, *J* = 7.0 Hz, 1H, OCH$_a$$H_bOCH_3$), 4.425 (d, *J* = 11.0 Hz, 1H, ArCH$_a$$H_b$), 4.41 (d, *J* = 11.0 Hz, 1H, ArCH_aH$_b$), 4.31 (dd, *J* = 1.2, 1.2 Hz, 1H, *H8*), 4.23-4.18 (m, 1H, *H5*), 4.20 (d, *J* =10.9 Hz, 1H, ArCH$_a$$H_b$), 4.17-4.11 (m, 1H, *H13*), 3.94 (s, 1H, C11-O*H*), 3.87 (d, *J* = 10.0 Hz, 1H, *H11*), 3.82 (d, *J* = 3.1 Hz, 1H, *H2*), 3.80 (s, 3H, ArOCH_3), 3.78 (s, 3H, ArOCH_3), 3.78-3.74 (m, 1H, *H7*), 3.62 (s, 3H, CO_2CH_3), 3.56 (d, *J* = 1.2 Hz, 1H, *H9*), 3.53 (ddd, *J* = 9.3, 3.0, 3.0 Hz, 1H, *H3*), 3.50 (app d, *J* = 6.3 Hz, 2H, *H24a, H24b*), 3.19 (s, 3H, OCH_3), 3.11 (s, 3H, OCH_3), 3.02 (s, 3H, OCH_3), 2.54 (ddddd, *J* = 10.3, 8.9, 6.4, 6.4, 4.9 Hz, 1H, *H18*), 2.05-1.89 (m, 4H, *H4a, H6a, H12a, H14a*), 1.71 (d, *J* = 1.3 Hz, 3H, *H23*), 1.58-1.47 (m, 3H, *H12a, H14b(or12b), H19a*), 1.43-1.37 (m, 2H, *H4b(or 6b)* and *H12b(or 14b)*), 1.10 (dqd, *J* = 13.3, 7.5, 5.8 Hz, 1H, *H19b*), 0.99 [s, 9H, $(CH_3)_2SiC(CH_3)_3$], 0.98 [s, 3H, $C(CH_3)(CH_3)$], 0.93 [s, 9H, $(CH_3)_2SiC(CH_3)_3$], 0.894 [s, 9H, $Ph_2SiC(CH_3)_3$], 0.886 [s, 3H, $C(CH_3)(CH_3)$], 0.78 (t, *J* = 7.5 Hz, 3H, CH_2CH_3), 0.10 [s, 3H, $(CH_3)_3CSi(CH_3)(CH_3)$], 0.07 [s, 3H, $(CH_3)_3CSi(CH_3)(CH_3)$], and 0.03 [s, 6H, $(CH_3)_3CSi(CH_3)(CH_3)$].

^{13}C NMR ($CDCl_3$, 125 MHz): δ 171.2, 159.4, 159.1, 136.3, 136.2, 135.4, 135.1, 134.0, 132.5, 131.1, 130.3, 129.6 (2), 129.40, 129.35, 127.7, 127.4, 114.1, 113.8, 96.5, 91.1, 79.5, 79.1, 78.4, 77.6, 75.4, 73.8, 73.7, 70.0, 69.9, 68.6, 67.0, 58.7, 57.0, 56.2, 55.45, 55.40, 51.8, 42.0, 41.8, 41.2, 40.4, 38.5, 38.0, 27.3, 26.28, 26.21, 24.9, 22.4, 19.5, 19.0, 18.7, 18.4, 17.9, 12.0, -4.11, -4.37, -5.07, and -5.11.

TLC: R_f = 0.17 in 4:1 hexanes:EtOAc.

HRMS (ESI/TOF): Calcd for $C_{73}H_{118}O_{15}Si_3Na^+$: 1341.7671. Found: 1341.770.

Methyl (2*S*,3*R*,5*S*,7*R*,8*R*,9*S*,11*S*,13*S*,15*S*,16*Z*,18*R*)-8-(*tert*-Butyldimethylsilyloxy)-18-[(*tert*-butyldimethylsilyloxy)methyl]-5-(*tert*-butyldiphenylsilyloxy)-11-hydroxy-3,7,13-trimethoxy-9,15-bis(4-methoxyphenylmethoxy)-2-(methoxymethoxy)-10,10,16-trimethyl-16-icosenoate (SI-40)



Diol **26** (80 mg, 60.6 μmol) was dissolved in CH_2Cl_2 (3.0 mL, 0.02 M) and cooled to 0 ºC. 2,6-di-*tert*-Butylpyridine (327 μL, 1.46 mmol) and Meerwein's salt ($Me_3O^+BF_4^-$, 179 mg, 1.21 mmol) were added to the solution. After 5 h aqueous $NaHCO_3$ was added and the mixture was extracted with Et_2O. The combined extracts were washed with brine, dried over $MgSO_4$, filtered, and concentrated *in vacuo*. The resultant mixture was passed through a pad of SiO_2 using, first, 6:1 hexanes:EtOAc to remove 2,6-di-*tert*-butylpyridine containing contaminants as a yellow band and, then, 1:1 hexanes:EtOAc to give a crude material. Purification by MPLC (4:1 hexanes:EtOAc) afforded the alcohol **SI-40** (67.5 mg, 83%) and the more polar starting diol **26** (9.0 mg, 11%), each as a clear colorless oil.

^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.72 (dd, *J* = 8.0, 1.5 Hz, 2H, *Ar-TBDPS*), 7.61 (dd, *J* = 8.0, 1.4 Hz, 2H, *Ar-TBDPS*), 7.38-7.25 (m, 6H, *Ar-TBDPS*, 4H, *Ar-PMB*), 6.86 (d, *J* = 8.4 Hz, 2H, *Ar-PMB*), 6.85 (d, *J* = 8.5 Hz, 2H, *Ar-PMB*), 5.16 (dd, *J* = 10.1, 1.2 Hz, 1H, *H17*), 4.89 (d, *J* = 11.1 Hz, 1H, ArCH_aH$_b$), 4.53 (d, *J* = 7.0 Hz, 1H, OCH_aH$_b$OCH$_3$), 4.44 (d, *J* = 7.0 Hz, 1H, OCH$_a$$H_bOCH_3$), 4.40 (d, *J* = 11.1 Hz, 1H, ArCH$_a$$H_b$), 4.38 (d, *J* = 11.2 Hz, 1H, ArCH_aH$_b$), 4.35 (dd, *J* = 10.0, 2.8 Hz, 1H, *H15*), 4.29 (dd, *J* = 1.4, 1.4 Hz, 1H, *H8*), 4.20 (dddd, *J* = 9.9, 9.3, 3.2, 2.6 Hz, 1H, *H5*), 4.16 (d, *J* = 11.1 Hz, 1H, ArCH$_a$$H_b$), 3.83 (d, *J* = 3.1 Hz, 1H, *H2*), 3.79 (s, 3H, ArOCH_3), 3.78-3.73 (m, 2H, *H13, H7*), 3.77 (s, 3H, ArOCH_3), 3.63-3.61 (m, 1H, *H11*), 3.62 (s, 3H, CO_2CH_3), 3.54-3.47 (m, 4H, *H3, H9, H24a, H24b*), 3.30 (s, 3H, C13-OCH_3), 3.20 (s, 3H, OCH_3), 3.12 (s, 3H, OCH_3), 3.03 (s, 3H, OCH_3), 2.47 (ddddd, *J* = 10, 8, 6, 6, 6 Hz, 1H, *H18*), 2.15 (ddd, *J* = 14.1, 9.8, 4.1 Hz, 1H, *H14a*), 2.04-1.90 (m, 4H, *H4a, H6a, H12a*), 1.69 (d, *J* = 1.3 Hz, 3H, *H23*), 1.61-1.49 [m, 4H, *H6b(or 4b), H12b, H14b, H19a*], 1.42 [ddd, *J* = 16.7, 9.6, 2.9 Hz, 1H, *H4b(or 6b)*], 1.10 (app ddq, *J* = 13.5, 7.5, 7.5 Hz, 1H, *H19b*), 1.00 [s, 9H, $(CH_3)_2SiC(CH_3)_3$], 0.95 [s, 9H, $(CH_3)_2SiC(CH_3)_3$], 0.89 [s, 9H, $Ph_2SiC(CH_3)_3$], 0.88 [s, 3H,

C(C*H*$_3$)(CH$_3$)], 0.87 [s, 3H, C(C*H*$_3$)(CH$_3$)], 0.83 (t, *J* = 7.5 Hz, 3H, CH$_2$C*H*$_3$), 0.11 [s, 3H, (CH$_3$)$_3$CSi(C*H*$_3$)(CH$_3$)], 0.08 [s, 3H, (CH$_3$)$_3$CSi(CH$_3$)(C*H*$_3$)], and 0.03 [s, 6H, (CH$_3$)$_3$CSi(C*H*$_3$)(C*H*$_3$)].

^{13}C NMR (CDCl$_3$, 125 MHz): δ 171.2, 159.2, 159.1, 136.3, 136.2, 136.0, 135.4, 134.1, 131.7, 131.3, 131.0, 129.7, 129.6, 129.4 (2), 127.6, 127.4, 113.9, 113.7, 96.5, 90.6, 79.5, 79.1, 77.6, 76.8, 75.4, 73.9, 73.4, 73.3, 69.7, 68.6, 66.9, 58.7, 57.0, 56.8, 56.2, 55.38, 55.36, 51.8, 42.4, 41.6, 41.1, 38.5, 37.4, 35.2, 27.2, 26.3, 26.2, 24.9, 22.1, 19.45, 19.35, 18.6, 18.4, 18.1, 12.0, -4.11, -4.45, -5.08, and -5.12.

TLC: R$_f$ = 0.25 in 4:1 hexanes:EtOAc for the product **SI-40**.

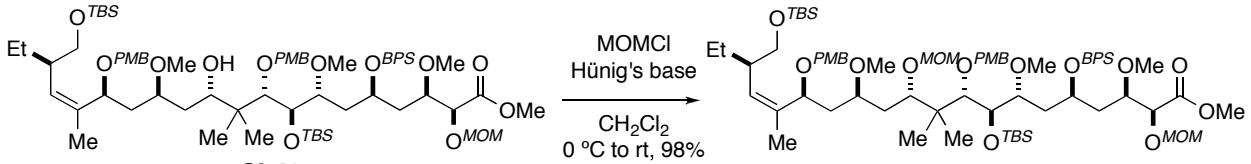
R$_f$ = 0.17 in 4:1 hexanes:EtOAc for the diol **26**.

R$_f$ = 0.62 in 4:1 hexanes:EtOAc (x3 elution) for the product **SI-40**.

R$_f$ = 0.55 in 4:1 hexanes:EtOAc (x3 elution) for the diol **26**.

HRMS (ESI/TOF): Calcd for $C_{74}H_{120}O_{15}Si_3Na^+$: 1355.7727. Found: 1355.786.

Methyl (2*S*,3*R*,5*S*,7*R*,8*R*,9*S*,11*S*,13*R*,15*S*,16*Z*,18*R*)-8-(*tert*-Butyldimethylsilyloxy)-18-[(*tert*-butyldimethylsilyloxy)methyl]-5-(*tert*-butyldiphenylsilyloxy)-3,7,13-trimethoxy-2,11-bis(methoxmethoxy)-9,15-bis(4-methoxyphenylmethoxy)-10,10,16-trimethyl-16-icosenoate (SI-41)



SI-40 ***SI-41***

Alcohol **SI-40** (60 mg, 45.0 μmol) was dissolved in CH_2Cl_2 (2.25 mL, 0.02 M) and cooled to 0 ºC. *i*-Pr$_2$NEt (196 μL, 1.12 mmol) and MOMCl (145 μL, 900 μmol, *ca.* 50% purity) were added and the reaction mixture was warmed to room temperature. After 12 h aqueous $NaHCO_3$ was added and the mixturer was extracted with Et_2O. The combined extracts were washed with brine, dried over $MgSO_4$, filtered, and concentrated *in vacuo*. MPLC (4:1 hexanes:EtOAc) afforded the MOM ether **SI-41** (61 mg, 98%) as a clear colorless oil.

^{1}H NMR (CDCl$_3$, 500 MHz): δ 7.70 (dd, *J* = 8.0, 1.4 Hz, 2H, *Ar-TBDPS*), 7.58 (dd, *J* = 8.0, 1.4 Hz, 2H, *Ar-TBDPS*), 7.38-7.24 (m, 6H, *Ar-TBDPS*, 4H, *Ar-PMB*), 6.849 (d, *J* = 8.7 Hz, 2H, *Ar-*

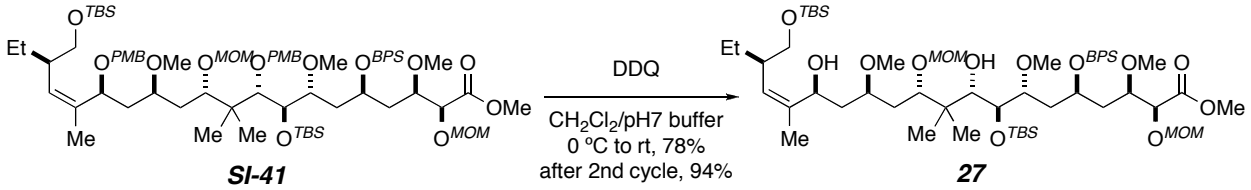
PMB), 6.845 (d, *J* = 8.7 Hz, 2H, *Ar-PMB*), 5.14 (dd, *J* = 10.3, 1.1 Hz, 1H, *H17*), 4.85 (d, *J* = 10.7 Hz, 1H, ArCH_aH$_b$), 4.65 (d, *J* = 7.0 Hz, 1H, OCH_aH$_b$OCH$_3$), 4.63 (d, *J* = 7.0 Hz, 1H, OCH$_a$$H_bOCH_3$), 4.52 (d, *J* = 7.0 Hz, 1H, OCH_aH$_b$OCH$_3$), 4.48 (d, *J* = 11.1 Hz, 1H, ArCH_aH$_b$), 4.42 (d, *J* = 7.0 Hz, 1H, OCH$_a$$H_bOCH_3$), 4.37 (d, *J* = 11.1 Hz, 1H, ArCH_aH$_b$), 4.33 (dd, *J* = 10.3, 2.0 Hz, 1H, *H15*), 4.24 (s, 1H, *H8*), 4.24-4.19 (m, 1H, *H5*), 4.15 (d, *J* = 11.1 Hz, 1H, ArCH$_a$$H_b$), 3.83-3.77 (m, 3H, *H2, H7, H11*), 3.77 (s, 6H, ArOCH_3), 3.67 (br app t, *J* = 9.5 Hz, 1H, *H13*), 3.62 (s, 3H, CO$_2$CH_3), 3.52-3.46 (m, 4H, *H3, H9, H24a, H24b*), 3.32 (s, 3H, OCH_3), 3.28 (s, 3H, C11-MOM-OCH_3), 3.19 (s, 3H, C13-OCH_3), 3.12 (s, 3H, OCH_3), 3.00 (s, 3H, OCH_3), 2.45 (ddddd, *J* = 10.5, 8.8, 5.9, 5.9, 4.4 Hz, 1H, *H18*), 2.23 (ddd, *J* = 13.9, 10.5, 3.2 Hz, 1H, *H14a*), 2.02-1.95 (m, 2H, *H4a, H12a*), 1.90 (ddd, *J* = 13.4, 9.4, 3.5 Hz, 1H, *H6a*), 1.74 (d, *J* = 1.2 Hz, 3H, *H23*), 1.73-1.53 (m, 3H, *H6b, H12b, H19a*), 1.36 (m, 2H, *H4b, H14b*), 1.12 (ddq, *J* =13.5, 7.8, 7.8 Hz, 1H, *19b*), 1.01 [s, 3H, C(CH_3)(CH$_3$)], 0.98 [s, 9H, Ph$_2$SiC(CH_3)$_3$], 0.95 [s, 3H, C(CH$_3$)(CH_3)], 0.92 [s, 9H, (CH$_3$)$_2$SiC(CH_3)$_3$], 0.89 [s, 9H, (CH$_3$)$_2$SiC(CH_3)$_3$], 0.82 (t, *J* = 7.4 Hz, 3H, CH$_2$CH_3), 0.063 [s, 3H, (CH$_3$)$_3$CSi(CH_3)(CH$_3$)], 0.055 [s, 3H, (CH$_3$)$_3$CSi(CH$_3$)(CH_3)], 0.034 [s, 3H, (CH$_3$)$_3$CSi(CH_3)(CH$_3$)], and 0.031 [s, 3H, (CH$_3$)$_3$CSi(CH$_3$)(CH_3)].

^{13}C NMR (CDCl$_3$, 125 MHz): δ 171.2, 159.0, 158.8, 136.4, 136.3, 136.2, 135.4, 134.2, 131.9, 131.4, 131.3, 129.5, 129.3, 129.21, 129.16, 127.6, 127.3, 113.8, 113.6, 99.2, 96.4, 87.7, 79.4, 79.1, 77.7, 75.1, 74.8, 73.8, 73.7, 73.3, 69.8, 68.6, 67.1, 58.7, 56.5, 56.2, 56.1, 55.9, 55.38, 55.34, 51.8, 43.3, 41.8, 41.3, 38.2, 37.7, 35.3, 27.3, 26.24, 26.21, 24.9, 21.9, 20.5, 19.5, 18.7, 18.4, 18.1, 12.2, -4.02, -4.51, -5.07, and -5.11.

TLC: R$_f$ = 0.6 in 4:1 (X2) hexanes:EtOAc.

HRMS (ESI/TOF): Calcd for C$_{76}$H$_{124}$O$_{16}$Si$_3$Na$^+$: 1399.8089. Found: 1399.810.

Methyl (2*S*,3*R*,5*S*,7*R*,8*R*,9*S*,11*S*,13*R*,15*S*,16*Z*,18*R*)-8-(*tert*-Butyldimethylsilyloxy)-18-[(*tert*-butyldimethylsilyloxy)methyl]-5-(*tert*-butyldiphenylsilyloxy)-9,15-dihydroxy-3,7,13-trimethoxy-2,11-bis(methoxmethoxy)-10,10,16-trimethyl-16-icosenoate (27)



SI-41 ***27***

Bis-PMB ether **SI-41** (211 mg, 153 μmol) was dissolved in CH_2Cl_2 (7.7 mL, 0.02 M) and pH7

phosphae buffer (7.7 mL, 0.02 M) was added. This mixture was cooled to 0 ºC and stirred for 30 min. DDQ (87 mg, 383 μmol) was added and after 3 h an additional portion of DDQ (24 mg, 107 μmol) was added. After an addditional 2.5 h aqueous $NaHCO_3$ was added and the mixture was extracted with Et_2O. The combined extracts were washed with brine, dried over $MgSO_4$, filtered, and concentrated *in vacuo*. Purification by MPLC (2:1 hexanes:EtOAc) afforded starting bis-PMB ether **SI-41** and the more polar diol **27** (153 mg, 78%). Resubjection of **SI-41** to the same reaction conditions afforded additional diol **27** (29 mg, 14%); total yield (182 mg, 94%).

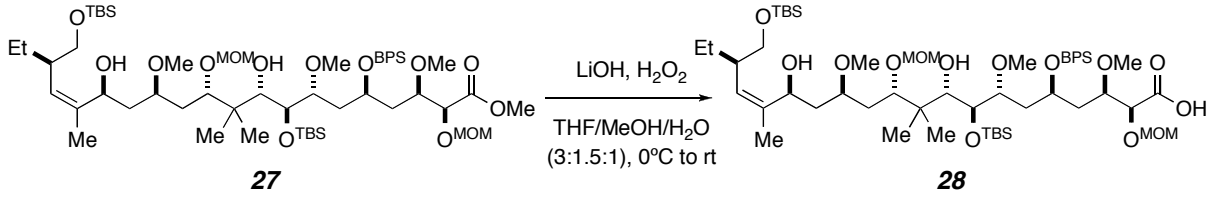
^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.74 (dd, *J* =8.0, 1.6 Hz, 2H, *Ar-TBDPS*), 7.67 (dd, *J* =8.0, 1.5 Hz, 2H, *Ar-TBDPS*), 7.41-7.30 (m, 6H, *Ar-TBDPS*), 4.94 (dd, *J* = 10.2, 1.0 Hz, 1H, *H17*), 4.70 (d, *J* = 6.8 Hz, 1H, $OCH_aH_bOCH_3$), 4.66 (d, *J* = 6.8 Hz, 1H, $OCH_aH_bOCH_3$), 4.56 (d, *J* = 6.9 Hz, 1H, $OCH_aH_bOCH_3$), 4.56-4.53 (m, 1H, *H15*), 4.47 (d, *J* = 6.9 Hz, 1H, $OCH_aH_bOCH_3$), 4.11-4.06 (m, 1H, *H5*), 3.92 (d, *J* = 5.9 Hz, 1H, *H8*), 3.83 (d, *J* = 3.0 Hz, 1H, *H2*), 3.68-3.63 (m, 3H, *H3, H13, H7 or H11*), 3.67 (s, 3H, CO_2CH_3), 3.56 (dd, *J* = 9.6, 5.1 Hz, 1H, *H24a*), 3.56-3.54 (m, 1H, *H11 or H7*), 3.42 (d, *J* = 3.2 Hz, 1H, O*H*), 3.395 (s, 3H, OCH_3), 3.392 (s, 3H, OCH_3), 3.39-3.36 (m, 1H, *H9*), 3.31 (dd, *J* = 9.3, 8.7 Hz, 1H, *H24b*), 3.26 (s, 3H, OCH_3), 3.128 (s, 3H, OCH_3), 3.122 (s, 3H, OCH_3), 2.67 (s, 3H, O*H*), 2.53 (ddddd, *J* = 10.0, 9.1, 5.4, 5.4, 4.7 Hz, 1H, *H18*), 2.10 (ddd, *J* = 14.1, 9.6, 4.4 Hz, 1H, *H14a*), 1.94 (ddd, *J* = 13.6, 8.3, 4.8 Hz, 1H, *H4a or H6a*), 1.83-1.79 (m, 2H, *H6a or H4a, H4b or H6b*), 1.76 (d, *J* =1.3 Hz, 3H, *H23*), 1.66-1.156 (m, 3H, *H12a, H12b, H6b or H4b*), 1.44 (dqd, *J* = 14.2, 7.5, 4.8 Hz, 1H, *H19a*), 1.35 (ddd, *J* = 14.0, 8.6, 4.0 Hz, 1H, *H14b*), 1.13 (dqd, *J* = 14.5, 7.5, 3.8 Hz, 1H, *H19b*), 1.05 [s, 9H, $Ph_2SiC(CH_3)_3$], 1.01 [s, 3H, $C(CH_3)(CH_3)$], 0.92 [s, 3H, $C(CH_3)(CH_3)$], 0.884 [s, 9H, $(CH_3)_2SiC(CH_3)_3$], 0.876 [s, 9H, $(CH_3)_2SiC(CH_3)_3$], 0.86 (t, *J* = 7.4 Hz, 3H, CH_2CH_3), 0.09 [s, 3H, $(CH_3)_3CSi(CH_3)(CH_3)$], 0.054 [s, 3H, $(CH_3)_3CSi(CH_3)(CH_3)$], 0.050 [s, 3H, $(CH_3)_3CSi(CH_3)(CH_3)$], and 0.04 [s, 3H, $(CH_3)_3CSi(CH_3)(CH_3)$]. (Resonances due to EtOAc are also present at δ 4.11, 2.05, and 1.23.)

^{13}C NMR ($CDCl_3$, 125 MHz): δ 171.3, 139.7, 136.3, 136.2, 135.0, 134.0, 130.7, 129.6, 129.5, 127.6, 127.5, 98.4, 96.5, 83.1, 80.2, 79.0, 77.7, 77.3, 76.6, 73.7, 69.1, 67.1, 66.0, 58.6, 56.7, 56.6, 56.3, 55.8, 51.8, 42.2, 42.1, 39.9, 38.0, 37.9, 37.0, 29.8, 27.2, 26.4, 26.2, 24.7, 19.4, 18.8, 18.7, 18.6, 18.5, 12.1, -2.94, -5.14, -5.25, and -5.26. (Resonances due to EtOAc are also present at δ 171.3, 60.5, 21.2, and 14.3.)

TLC: R_f = 0.17 in 4:1 hexanes:EtOAc.

HRMS (ESI/TOF): Calcd for $C_{60}H_{108}O_{14}Si_3Na^+$: 1159.6939. Found: 1159.695.

(2*S*,3*R*,5*S*,7*R*,8*R*,9*S*,11*S*,13*R*,15*S*,16*Z*,18*R*)-8-(*tert*-Butyldimethylsilyloxy)-18-[(*tert*-butyldimethylsilyloxy)methyl]-5-(*tert*-butyldiphenylsilyloxy)-9,15-dihydroxy-3,7,13-trimethoxy-2,11-bis(methoxmethoxy)-10,10,16-trimethyl-16-icosenoic Acid (28)



27 ***28***

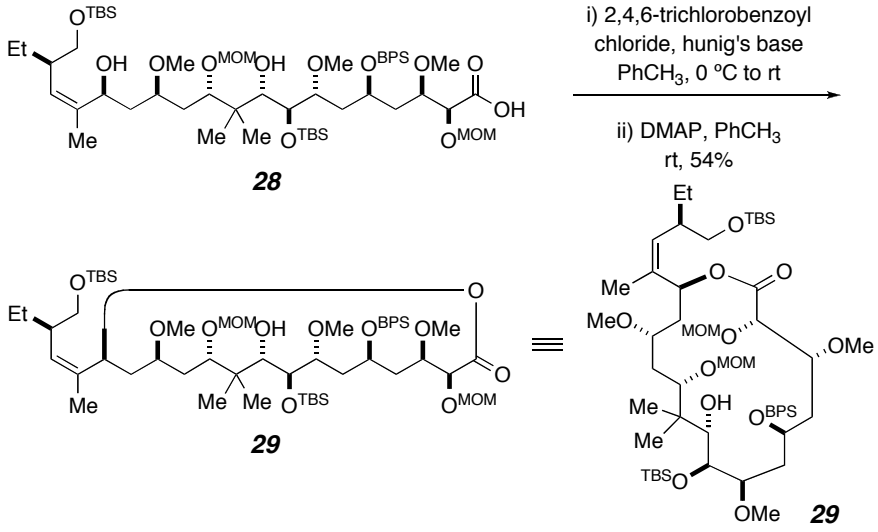
Ester **27** (37.8 mg, 33.2 μmol) was dissolved in THF/MeOH/water (1.25 mL/0.63 mL/0.42 mL, 0.014 M) and the solution was cooled to 0 ºC. LiOH (130 μL, 133 μmol, 1 M in H_2O) and H_2O_2 (27 μL, 30% in water, 266 μmol) were added and the solution was warmed to room temperature. After 48 h aqueous pH3 buffer was added and the mixture was extracted with EtOAc. The combined extracts were washed with brine, dried over $MgSO_4$, filtered, and concentrated *in vacuo* to afford acid **28**, which was used directly in the next reaction without further purification. **^{1}H NMR** ($CDCl_3$, 500 MHz): δ 7.73 (dd, *J* = 7.9, 1.5 Hz, 2H, *Ar-TBDPS*), 7.68 (dd, *J* = 8.0, 1.5 Hz, 2H, *Ar-TBDPS*), 7.41-7.31 (m, 6H, *Ar-TBDPS*), 4.94 (dd, *J* = 10.3, 1.0 Hz, 1H, *H17*), 4.70 (d, *J* = 6.8 Hz, 1H, $OCH_aH_bOCH_3$), 4.66 (d, *J* = 6.8 Hz, 1H, $OCH_aH_bOCH_3$), 4.60 (d, *J* = 6.8 Hz, 1H, $OCH_aH_bOCH_3$), 4.56-4.53 (dd, *J* = 9.9, 3.4 Hz, 1H, *H15*), 4.44 (d, *J* = 6.8 Hz, 1H, $OCH_aH_bOCH_3$), 4.05 (dddd, *J* = 12.9, 12.9, 5.2, 5.2, 1H, *H5*), 3.92 (d, *J* = 6.0 Hz, 1H, *H8*), 3.81 (d, *J* = 3.0 Hz, 1H, *H2*), 3.69 (ddd, *J* = 8.1, 4.7, 3.2 Hz, 1H, *H3*), 3.67-3.61 (m, 2H, *H13, H7*), 3.57 (dd, *J* = 9.6, 5.0 Hz, 1H, *H24a*), 3.55 (dd, *J* = 6.4, 2.2 Hz, 1H, *H11*), 3.394 (s, 3H, OCH_3), 3.391 (s, 3H, OCH_3), 3.37 (d, *J* = 5.9 Hz, 1H, *H9*), 3.31 (dd, *J* = 9.2, 9.0 Hz, 1H, *H24b*), 3.28 (s, 3H, OCH_3), 3.20 (s, 3H, OCH_3), 3.15 (s, 3H, OCH_3), 2.53 (ddddd, *J* = 9.5, 9.5, 9.5, 4.5, 4.5 Hz, 1H, *H18*), 2.09 (ddd, *J* = 14.1, 9.8, 4.5 Hz, 1H, *H14a*), 1.90 (ddd, *J* = 13.8, 7.9, 5.2 Hz, 1H, *H4a*), 1.85-1.78 (m, 1H, *H6a*), 1.76 (d, *J* =1.3 Hz, 3H, *H23*), 1.69 (ddd, *J* = 13.9, 7.7, 4.8 Hz, 1H, *H4b*), 1.64-1.58 (m, 3H, *H6b, H12a, H12b*) 1.45 (dqd, *J* = 14.6, 7.3, 4.3 Hz, 1H, *H19a*), 1.36 (ddd, *J* = 13.8, 8.2, 3.5 Hz, 1H, *H14b*), 1.13 (ddq, *J* = 13.4, 8.7, 7.3 Hz, 1H, *H19b*), 1.05 [s, 9H, $Ph_2SiC(CH_3)_3$], 1.00 [s, 3H, $C(CH_3)(CH_3)$], 0.90 [s, 3H, $C(CH_3)(CH_3)$], 0.88 [s, 9H, $(CH_3)_2SiC(CH_3)_3$], 0.87 [s, 9H, $(CH_3)_2SiC(CH_3)_3$], 0.86 (t, *J* = 7.5 Hz, 3H, CH_2CH_3), 0.08 [s, 3H, $(CH_3)_3CSi(CH_3)(CH_3)$], 0.051 [s, 6H, $(CH_3)_3CSi(CH_3)(CH_3)$, $(CH_3)_3CSi(CH_3)(CH_3)$], and 0.045 [s, 3H, $(CH_3)_3CSi(CH_3)(CH_3)$].

^{13}C NMR ($CDCl_3$, 125 MHz): δ 173.6, 139.8, 136.3, 136.2, 134.7, 134.2, 130.9, 129.7, 129.7, 127.66, 127.65, 98.5, 97.0, 83.1, 80.4, 78.8, 77.7, 76.9, 76.8, 73.7, 69.1, 67.2, 66.0, 58.7, 56.8, 56.7, 56.5, 55.9, 42.2, 42.1, 39.4, 38.0, 37.0, 29.9, 27.3, 26.7, 26.47, 26.3, 24.7, 19.5, 19.0, 18.79, 18.72, 18.65, 18.63, 18.58, 12.1, -2.82, -5.08, -5.19, and -5.20.

LCMS (Method: C_8 column, isocratic (90:10 methanol:water, 22 min, ES/APCI -/+): t_R = 1.3 min. $ESIMS_{neg}$ [$(M-H)^-$: 1121)].

TLC: R_f = 0.3 in 1:3 hexanes:EtOAc.

(3*S*,4*R*,6*S*,8*R*,9*R*,10*S*,12*S*,14*R*,16*S*)-9-(*tert*-Butyldimethylsilyloxy)-16-[(*R*,*Z*)-4-[(*tert*-butyldimethylsilyloxy)methyl]hex-2-en-2-yl]-6-(*tert*-butyldiphenylsilyloxy)-10-hydroxy-4,8,14-trimethoxy-3,12-bis(methoxymethoxy)-11,11-dimethyloxacyclohexadecane-2-one (29)



Acid **28** was dissolved in toluene (3.7 mL, 8.75 mM) and the solution was cooled to 0 ºC. *i*-Pr_2NEt (170 µL, 976 µmol) and 2,4,6-trichlorobenzoyl chloride (71 µL, 455 µmol) were added to the mixture. After 24 h this solution was added over 3 h by use of a syringe pump into a solution of toluene (39 mL, 0.84 mM) and DMAP (79.5 mg, 650 µmol) at room temperature. After 24 h aqueous $NaHCO_3$ was added and the mixture was extracted with EtOAc. The combined extracts were washed with brine, dried over $MgSO_4$, filtered, and concentrated *in vacuo*. Purification by flash chromatography (5:1 hexanes:EtOAc) afforded the lactone **29** (19.4 mg, 54%) as a clear colorless oil.

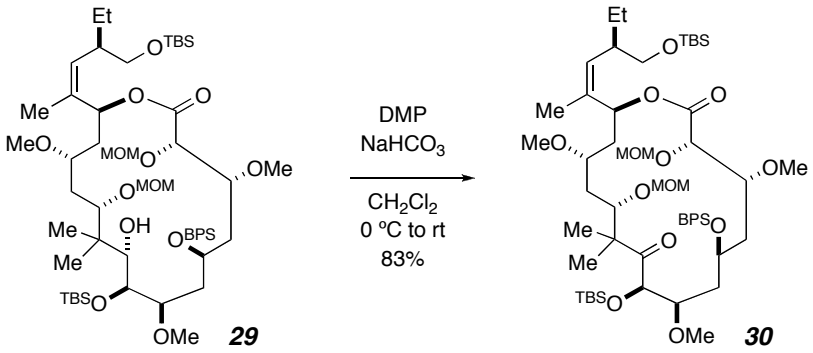
^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.78-7.75 (m, 4H, *Ar-TBDPS*), 7.40-7.31 (m, 6H, *Ar-TBDPS*), 5.78 (dd, *J* = 10.9, 2.5 Hz, 1H, *H15*), 4.98 (dd, *J* = 10.7, 0.8 Hz, 1H, *H17*), 4.68-4.62 (m, 4H, $OCH_aH_bOCH_3$), 4.11-4.06 (m, 1H, *H5*), 4.02 (br d, *J* = 4.8 Hz, 1H, *H2*), 3.90 (d, *J* = 8.8 Hz, 1H, *H8*), 3.79-3.71 (m, 3H, *H13, H24b,* O*H*), 3.44-3.40 (m, 1H, *H11*), 3.42 (s, 3H, OCH_3), 3.39-3.35 (m, 1H, *H24a*), 3.38 (s, 3H, OCH_3), 3.36 (s, 3H, OCH_3), 3.33 (s, 3H, OCH_3), 3.30-3.27 (m, 1H, *H3*), 3.25-3.24 (m, 1H, *H9*), 3.13-3.08 (m, 1H, *H7*), 2.95 (s, 3H, OCH_3), 2.50 (dddd, *J* = 12.5, 8.5, 8.5, 3.9 Hz, 1H, *H18*), 2.12-2.03 (m, 2H, *H12a, H14a*), 1.96-1.74 (m, 5H, *H4a, H6b, H4b or H6b, H14b, H19a*), 1.68-1.65 (m, 1H, *H6b or H4b*), 1.62 (d, 3H, *J* = 1.0 Hz, *H23*), 1.45-1.41 (m, 1H, *H12b*), 1.16 (dqd, *J* = 13.7, 7.5, 2.2 Hz, 1H, *H19b*), 1.09 [s, 12H, $Ph_2SiC(CH_3)_3$, $C(CH_3)(CH_3)$], 1.00 [s, 3H, $C(CH_3)(CH_3)$], 0.903 [s, 9H, $(CH_3)_2SiC(CH_3)_3$], 0.898 [s, 9H, $(CH_3)_2SiC(CH_3)_3$], 0.85 (t, *J* = 7.5 Hz, 3H, CH_2CH_3), 0.23 [s, 3H, $(CH_3)_3CSi(CH_3)(CH_3)$], 0.13 [s, 3H, $(CH_3)_3CSi(CH_3)(CH_3)$], 0.08 [s, 3H, $(CH_3)_3CSi(CH_3)(CH_3)$], and 0.06 [s, 3H, $(CH_3)_3CSi(CH_3)(CH_3)$]. (Resonances due to EtOAc are also present in this spectrum at δ 4.11, 2.05, and 1.23.)

^{13}C NMR ($CDCl_3$, 125 MHz): δ 168.9, 136.5, 136.3, 134.9, 134.4, 134.2, 130.2, 129.6, 129.4, 127.6, 127.4, 98.8, 96.3, 84.4, 79.3, 79.1, 78.5, 76.6, 76.0, 74.4, 68.83, 68.78, 65.6, 60.6, 57.7, 57.6, 56.3, 56.2, 55.6, 42.4, 42.0, 37.9, 34.2, 33.0, 29.92, 29.90, 27.4, 26.8, 26.2, 24.7, 21.3, 19.4, 18.5, 17.9, 14.4, 12.2, -2.16 (2), -5.12, and -5.14.

TLC: R_f = 0.67 in 3:1 hexanes:EtOAc.

HRMS (ESI/TOF): Calcd for $C_{59}H_{104}O_{13}Si_3Na^+$: 1127.6677. Found: 1127.673.

(3*S*,4*R*,6*S*,8*R*,9*R*,12*S*,14*R*,16*S*)-9-(*tert*-Butyldimethylsilyloxy)-16-[(*R*,*Z*)-4-[(*tert*-butyldimethylsilyloxy)methyl]hex-2-en-2-yl]-6-(*tert*-butyldiphenylsilyloxy)-4,8,14-trimethoxy-3,12-bis(methoxymethoxy)-11,11-dimethyloxacyclohexadecane-2,10-dione (30)



Lactone **29** (59 mg, 53.4 μmol) was dissolved in CH_2Cl_2 (2.67 mL, 0.02 M) and cooled to 0 ºC. Powdered $NaHCO_3$ (112 mg, 1.33 mmol) and Dess-Martin periodinane (226 mg, 534 μmol) were added to the reaction mixture. After 4 h aqueous $NaHCO_3$ was added and the mixture was extracted with EtOAc. The combined extracts were washed with brine, dried over $MgSO_4$, filtered, and concentrated *in vacuo*. Purification by MPLC (6:1 hexanes:EtOAc) afforded the ketone **30** (49.1 mg, 83%) as a clear colorless oil.

^{1}H NMR ($CDCl_3$, 500 MHz, slow rotation is in evidence for some resonances of protons in the C7-C11 region of the molecule): δ 7.76 (dd, *J* = 7.8, 1.6 Hz, 2H, *Ar-TBDPS*), 7.71 (dd, *J* = 7.9, 1.4 Hz, 2H, *Ar-TBDPS*), 7.42-7.31 (m, 6H, *Ar-TBDPS*), 5.64 (dd, *J* = 11.7, 1.9 Hz, 1H, *H15*), 4.94 (d, *J* = 10.7 Hz, 1H, *H17*), 4.79 (d, *J* = 7.1 Hz, 1H, $OCH_aH_bOCH_3$), 4.70-4.66 (m, 3H, $OCH_aH_bOCH_3$), 4.32 (br s, 1H, *H8*), 4.00-3.95 (m, 1H, *H5*), 3.99 (d, *J* = 2.5 Hz, *H2*), 3.91 (dd, *J* = 10.5, 2.2 Hz, 1H, *H11*), 3.81-3.79 (m, 1H, *H7*), 3.79 (dd, *J* = 9.9, 3.8 Hz, 1H, *H24a*), 3.61-3.57 (m, 1H, *H13*), 3.58 (s, 3H, OCH_3), 3.47 (s, 3H, OCH_3), 3.41 (s, 3H, OCH_3), 3.35 (dd, *J* = 9.9, 7.5 Hz, 1H, *H24b*), 3.34 (s, 3H, OCH_3), 3.09 (ddd, *J* = 5.6, 2.5, 2.5 Hz, 1H, *H3*), 2.53 (br s, 3H, OCH_3), 2.51-2.45 (m, 1H, *H18*), 1.87 (ddd, *J* = 15.3, 7.4, 2.2 Hz, 1H, *H14a*), 1.87 (ddd, *J* = 14.6, 11.4, 6.2 Hz, 1H, *H4a*), 1.78-1.68 (m, 2H, *H14b, H19a*), 1.65-1.58 (m, 2H, *H4b, H6a*), 1.50 (d, *J* = 0.9 Hz, *H23*), 3H, 1.43 [s, 3H, $C(CH_3)(CH_3)$], 1.35-1.21 (m, 2H, *H12a, H12b*), 1.29 [s, 3H, $C(CH_3)(CH_3)$], 1.15 (ddq, *J* = 13.4, 8.8, 7.4 Hz, 1H, *H19b*), 1.03 [s, 9H, $(CH_3)_2SiC(CH_3)_3$], 0.99 [s, 9H, $(CH_3)_2SiC(CH_3)_3$], 0.86 [s, 9H, $Ph_2SiC(CH_3)_3$], 0.81 (t, *J* = 7.5 Hz, 3H, CH_2CH_3), 0.18 [s, 3H, $(CH_3)_3CSi(CH_3)(CH_3)$], 0.12 [s, 3H, $(CH_3)_3CSi(CH_3)(CH_3)$], 0.02 [s, 3H, $(CH_3)_3CSi(CH_3)(CH_3)$], and 0.00 [s, 3H, $(CH_3)_3CSi(CH_3)(CH_3)$].

^{13}C NMR ($CDCl_3$, 125 MHz): δ 214.7, 168.7, 136.08, 136.05, 134.4, 134.2, 133.9, 129.9, 129.7, 129.5, 127.9, 127.7, 99.9, 96.9, 82.3, 80.6, 80.3, 78.4, 78.0, 74.2, 70.4, 69.6, 65.4, 56.9, 56.8, 56.4, 56.0, 52.5, 42.2, 38.4, 38.46, 38.43, 37.0, 34.4, 27.1, 26.3, 26.2, 25.9, 24.6, 19.6, 18.54, 18.49, 18.3, 12.1, -3.88, -4.92, -5.11, and -5.18.

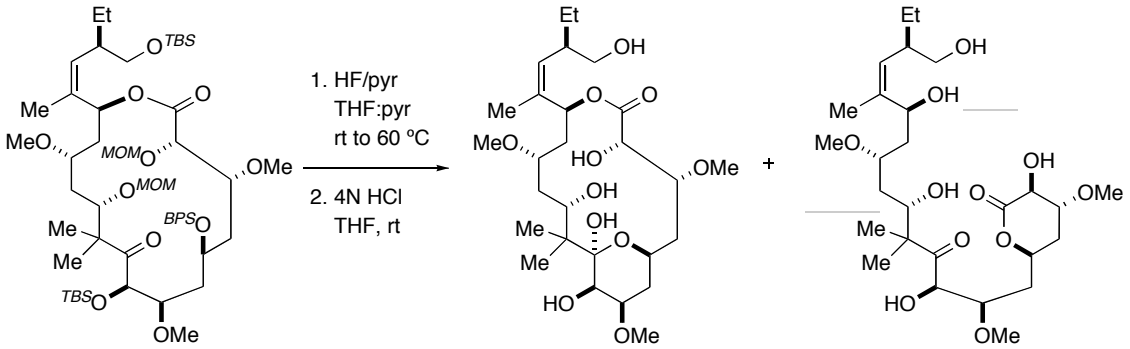
TLC: R_f = 0.55 in 4:1 hexanes:EtOAc.

HRMS (ESI/TOF): Calcd for $C_{59}H_{102}O_{13}Si_3Na^+$: 1125.6520. Found: 1125.652.

(1*R*,3*R*,4*S*,7*S*,9*S*,11*S*,13*R*,14*R*,15*R*)-4,11,13,14-Tetrahydroxy-7-[(*R*,*Z*)-4-(hydroxymethyl)hex-2-en-2-yl]-3,9,15-trimethoxy-12,12-dimethyl-6,17-dioxabicyclo[11.3.1]heptadecan-5-one (1)

and

(3*S*,4*R*,6*R*)-3-Hydroxy-4-methoxy-6-[(2*R*,3*R*,6*S*,8*R*,10*S*,13*R*,*Z*)-3,6,10-trihydroxy-13-(hydroxymethyl)-2,8-dimethoxy-5,5,11-trimethyl-4-oxopentadec-11-enyl]tetrahydro-2H-pyran-2-one (*iso*-1)



30 ***(+)-Peloruside A 1*** ***Isopeloruside A iso-1***

Ketone **30** (28.4 mg, 25.7 μmol) was placed in a plastic culture tube and THF (0.9 mL, 0.03 M), pyridine (1.4, 0.18 M), and HF•pyridine (270 μL of a 70% HF/30% pyridine solution) were added. After 1 h the solution was warmed to 60 ºC. After 48 h all three-silyl groups were cleaved, as judged by LCMS analysis of aliqouts. The solution was cooled to room temperature and aqueous $NaHCO_3$ solution was added with care. The mixture was extracted with EtOAc, and the combined extracts were washed with $CuSO_4$ (X2), water, and brine, and concentrated *in vacuo* to afford crude triol.

TLC: three spots converging to one with time (R_f= *ca.* 0.5-0.4) in 100:5 CH_2Cl_2:MeOH.

The sample of crude triol was dissolved in THF (6.8 mL, 4 mM) and aqueous HCl (4 N, 6.8 mL) was added and the solution was held at ambient tempertature. After 3 h aqueous $NaHCO_3$ was added with care and the mixture was extracted with EtOAc (x5) and then with a 1:1 mixture of $CHCl_3$/*i*-PrOH (x2). The comined extracts were washed with brine, dried over $MgSO_4$, filtered, and concentrated *in vacuo*. Purifcation by flash chromatography (a gradient from 100:4 to 100:5 CH_2Cl_2:MeOH) afforded (+)-peloruside A **1** (6.9 mg, 49%) and the more polar isopeloruside A ***iso*-1** (*ca.* 0.7 mg, 5.0%), each as a clear colorless oil.

Characterization data for peloruside A (1):

^{1}H NMR ($CDCl_3$, 800 MHz): δ 6.75 (s, 1H, C2-O*H*), 5.68 (d, *J* = 11.3, 1H, *H15*), 5.04 (d, *J* = 10.5 Hz, 1H, *H17*), 4.91-4.87 (m, 1H, *H11*), 4.53 (br s, 1H, O*H*), 4.43 (s, 1H, *H2*), 4.26 (dddd, *J* = 11.3, 11.3, 4.4, 2.7 Hz, 1H, *H5*), 4.23 (dd, *J* = 10.7, 5.4 Hz, 1H, *H3*), 4.02 (d, *J* = 2.8 Hz, 1H, *H8*), 3.99 (br d, *J* = 8.1 Hz, *H13*), 3.82 (ddd, *J* = 11.5, 5.1, 3.0 Hz, 1H, *H7*), 3.64 (dd, *J* = 10.7, 3.4 Hz, 1H, *H24a*), 3.48 (s, 3H, C13-OCH_3), 3.38 (s, 3H, C7-OCH_3), 3.36 (d, *J* =10.3 Hz, 1H, *H24b*), 3.30 (s, 3H, C3-OCH_3), 3.01 (br s, 1H, C24-O*H*), 2.74 (br s, 1H, O*H*), 2.61 (ddddd, *J* = 10.2, 9.4, 9.4, 5.4, 4.0 Hz, 1H, *H18*), 2.27 (br s, 1H, O*H*), 2.15 (dd, *J* = 15.3, 11.1 Hz, *H14a*), 2.13 (m, 1H, *H4a*), 2.07 (ddd, *J* = 15.4, 11.6, 4.8 Hz, 1H, *H12a*), 2.02 (dd, *J* = 15.5, 11.5 Hz, 1H, *H14b*), 1.78 (ddd, *J* = 12.5, 5.1, 2.2 Hz, 1H, *H6a*), 1.78 (m, 1H, *H4b*), 1.67 (d, *J* = 1.3 Hz, 3H, *H23*), 1.53 (ddd, *J* = 11.9, 11.5, 11.3 Hz, 1H, *H6b*), 1.43 (dqd, *J* = 13.5, 7.4, 4.5 Hz, 1H, *H19a*), 1.41 (m, 1H, *H12b*), 1.15 (ddq, *J* = 13.7, 9.4, 7.6 Hz, 1H, *H19b*), 1.12 (s, 3H, *H22*), 1.09 (s, 3H, *H21*), and 0.81 (t, *J* = 7.4 Hz, 3H, CH_2CH_3). The underlined resonances bear assignments that are supported by gCOSY and that are different from those in the original report of the structure of **1**.[11]

^{13}C NMR (chemical shifts deduced from gHMQC and gHMBC spectra, $CDCl_3$, 125 MHz): δ 174.1 (*C1*), 136.2 (*C16*), 131.0 (*C17*), 101.9 (*C9*), 78.2 (*C3*), 77.9 (*C13*), 75.9 (*C7*), 73.6 (*C11*), 70.9 (*C15*), 70.3 (*C2*), 66.9 (*C24*), 66.8 (*C8*), 63.5 (*C5*), 59.1 (*C13-OMe*), 56.1 (*C3-OMe*), 55.7 (*C7-OMe*), 43.5 (*C10*), 43.3 (*C18*), 35.7 (*C14*), 33.9 (*C12*), 32.5 (*C4*), 31.7 (*C6*), 24.6 (*C19*), 20.8 (*C22*), 17.5 (*C23*), 15.8 (*C21*), and 12.2 (*C20*).

TLC: R_f = 0.3 in 100:5 CH_2Cl_2:MeOH.

HRMS (ESI/TOF): Calcd for $C_{27}H_{48}O_{11}Na^+$: 571.3089. Found: 571.3085.

$[\alpha]_D^{24}$ = +15.9° (c = 0.345, $CDCl_3$).

Characterization data for *iso*-peloruside A (*iso*-1):

^{1}H NMR (chemical shift assignements guided by a COSY spectrum, $CDCl_3$, 500 MHz): δ 4.98 (dd, *J* = 10.1, 1.4 Hz, 1H, *H17*), 4.87 (d, *J* = 3.1 Hz, 1H, *H8*), 4.80-4.74 (m, 1H, *H5*), 4.68 (dd, *J* = 9.7, 3.5 Hz, 1H, *H15*), 4.30 (d, *J* = 6.4 Hz, 1H, *H2*), 4.08 (dd, *J* = 10.4, 0.9 Hz, 1H, *H11*), 3.99 (ddd, *J* = 10.5, 3.4, 2.4 Hz, 1H, *H7*), 3.65 (dd, *J* = 10, 4.5 Hz, 1H, *H24a*), 3.65 (m,1H, *H13*), 3.54 (nfom, 1H, *H3*), 3.46 (s, 3H, OCH_3), 3.45 (s, 3H, OCH_3), 3.38 (s, 3H, OCH_3), 3.24 (dd, *J* =10, 10 Hz, 1H, *H24b*), 2.60 (ddddd, *J* = 10.3, 9.4, 6.1, 4.9, 4.9 Hz, 1H, *H18*), 2.12 (ddd, *J* = 14.3, 9.6, 6.1 Hz, *H14a*), 1.97-1.94 (m, 1H, *H4a*), 1.85-1.70 (m, 3H, *H6a, H12a, H12b*), 1.68 (d, *J* = 1.4

Hz, 1H, *H23*), 1.63-1.55 (m, 3H, *H4b, H6b, H14b*), 1.39 (dqd, *J* = 13.4, 7.3, 4.9 Hz, 1H, *H19a*), 1.27 (s, 3H, *H21 or H22*), 1.19 (s, 3H, *H22 or H21*), 1.18-1.13 (m, 1H, *H19b*), and 0.87 (t, *J* = 7.4 Hz, 3H, $CH_2C\mathit{H_3}$).

TLC: R_f = 0.15 in 100:5 CH_2Cl_2:MeOH.

LCMS (ESI, MS/MS) : *m/z* 571.3 ($M+Na^+$) and from fragmentation of the 571.3 ion: 327.1 ($M+Na^+$- 244), 267 ($M+Na^+$-304), 125 ($M+Na^+$-304-142).

HRMS (ESI/TOF): Calcd for $C_{27}H_{48}O_{11}Na^+$: 571.3089. Found: 571.3005.

Supporting Information References

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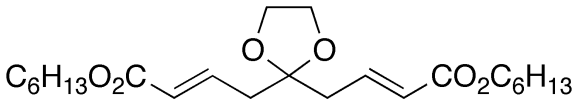
[9] Kopel, L. C. Ph.D. Thesis, University of Minnesota, Minneapolis, MN, 2008.

[10] "MPM (4-methoxybenzyl) protection of hydroxy functions under mild acidic conditions," Nakajima, N.; Horita, K.; Abe, R.; Yonemitsu, O. *Tetrahedron Lett.* **1988**, *29*, 4139-4142.

[11] "Peloruside A: A potent cytotoxic macrolide isolated from the new zealand marine sponge *Mycale* sp.," West, L. M.; Northcote, P. T.; Battershill, C. N. *J. Org. Chem.* **2000**, *65*, 445-449.



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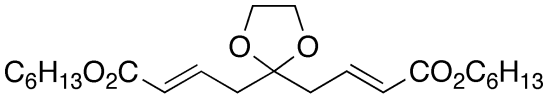

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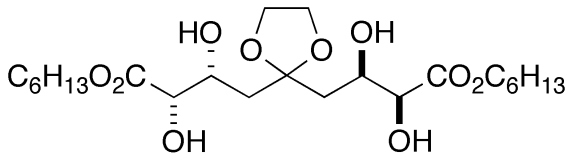

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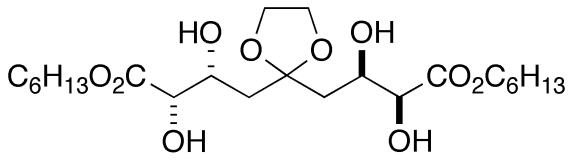
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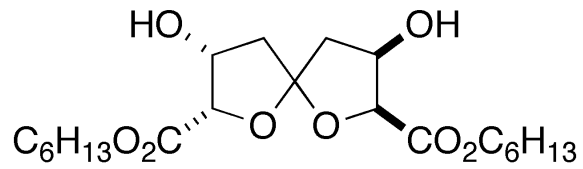

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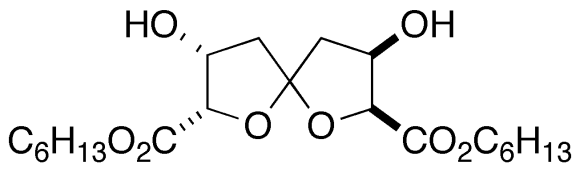
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$CO_2C_6H_{13}$

SI-3

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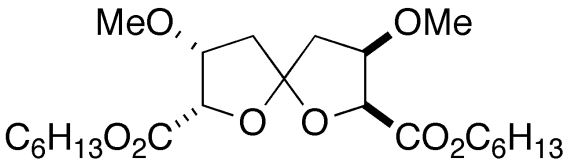

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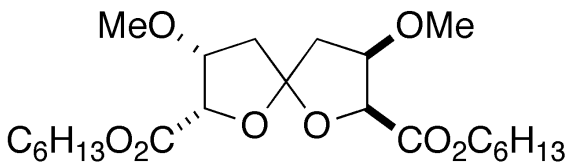
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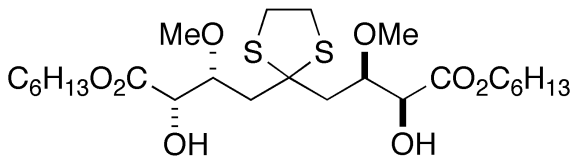

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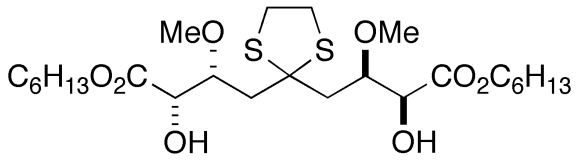
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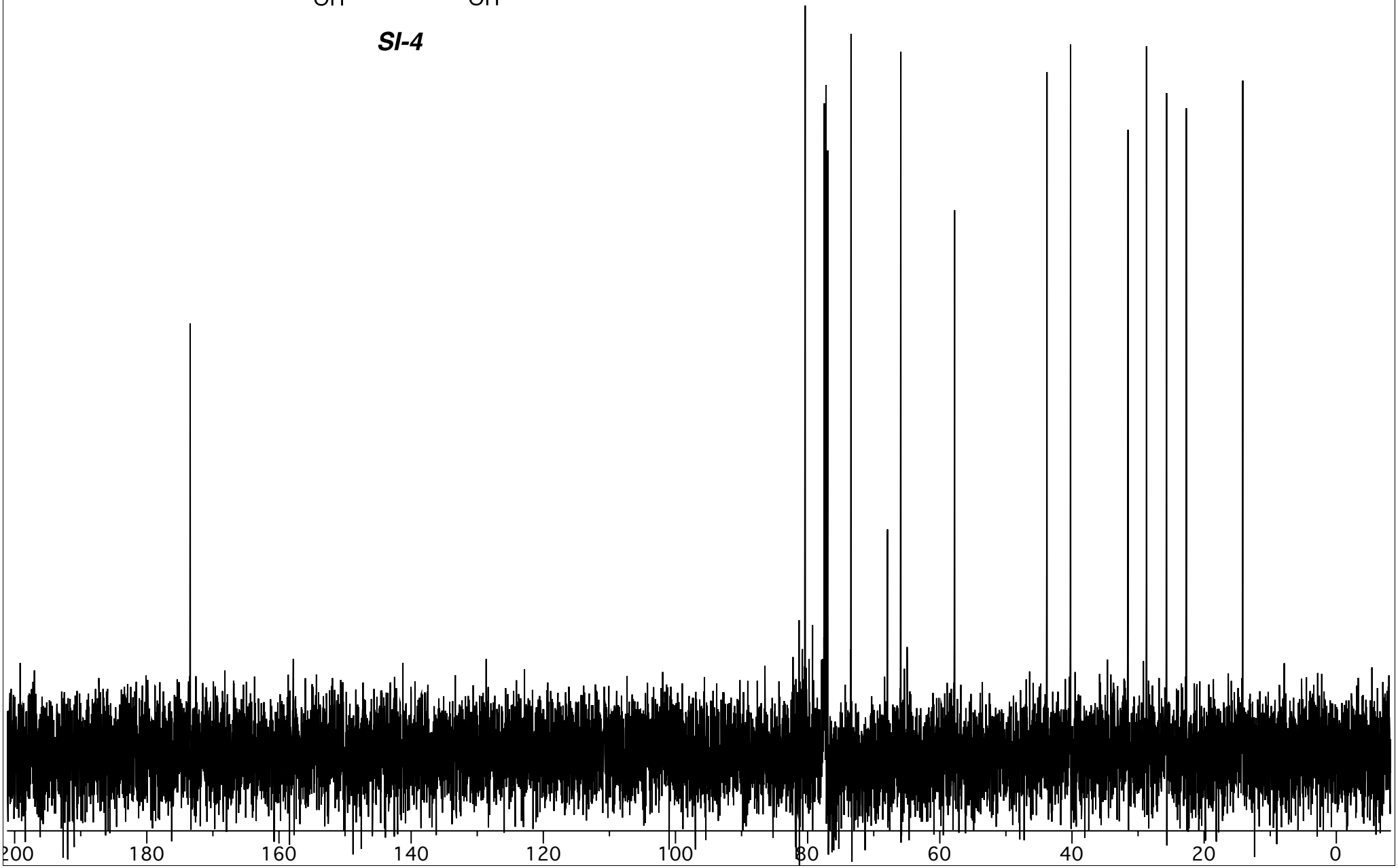
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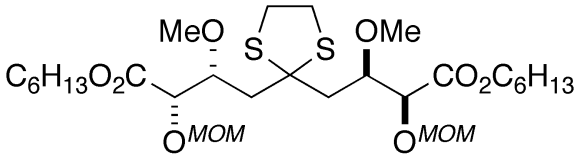

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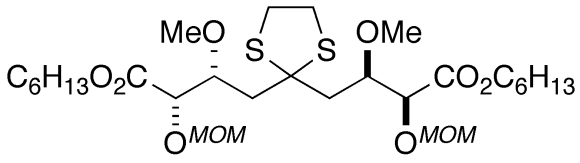
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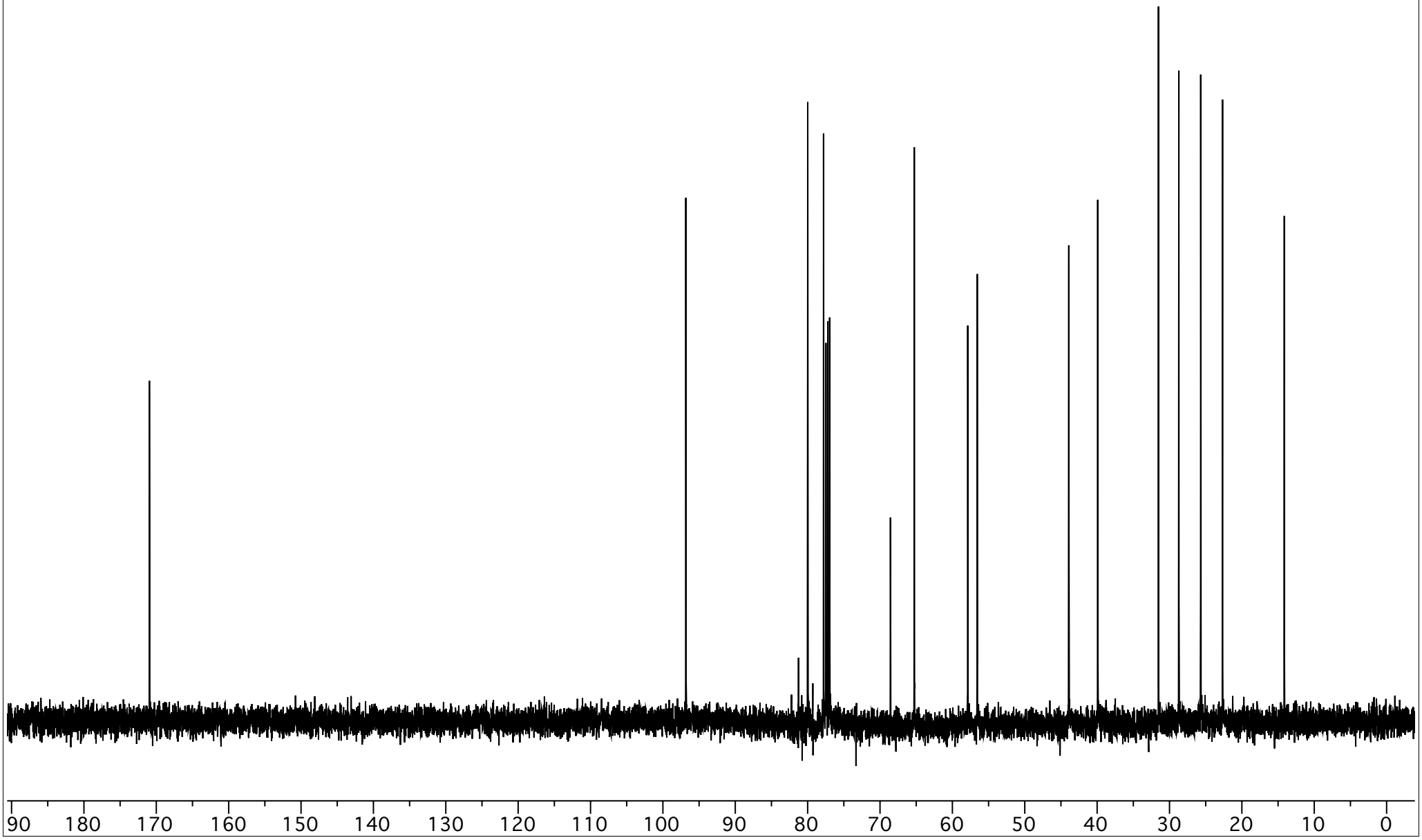
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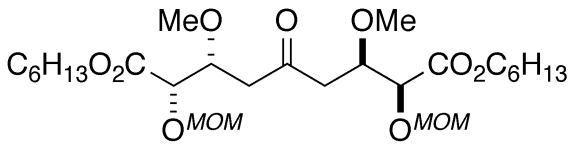

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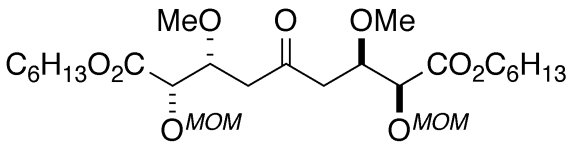
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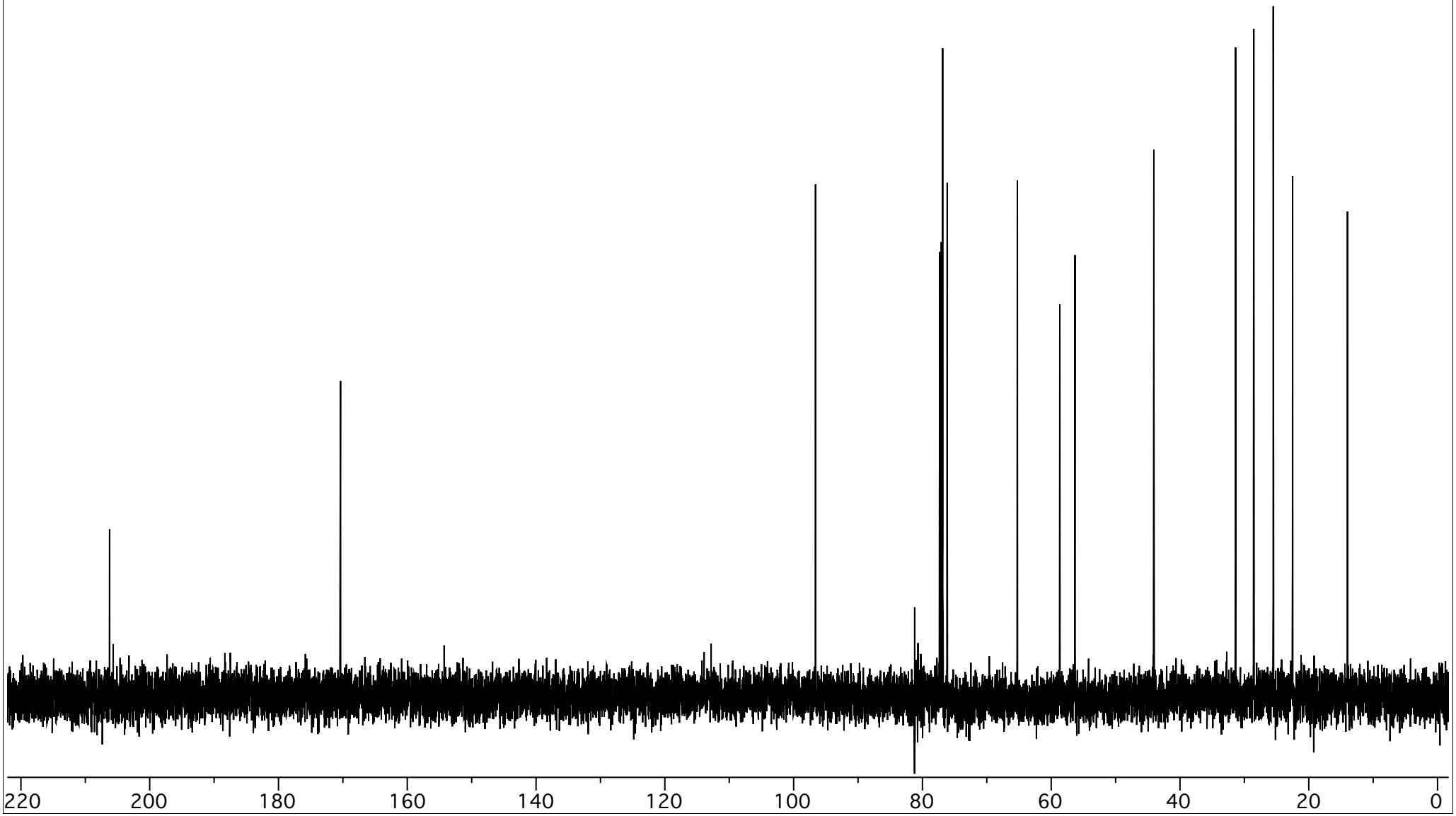
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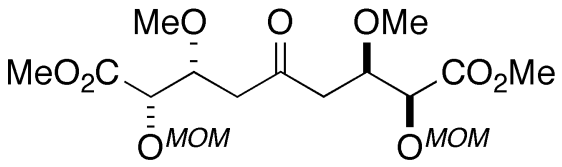

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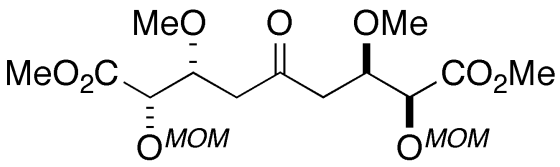
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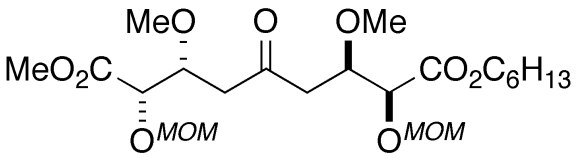

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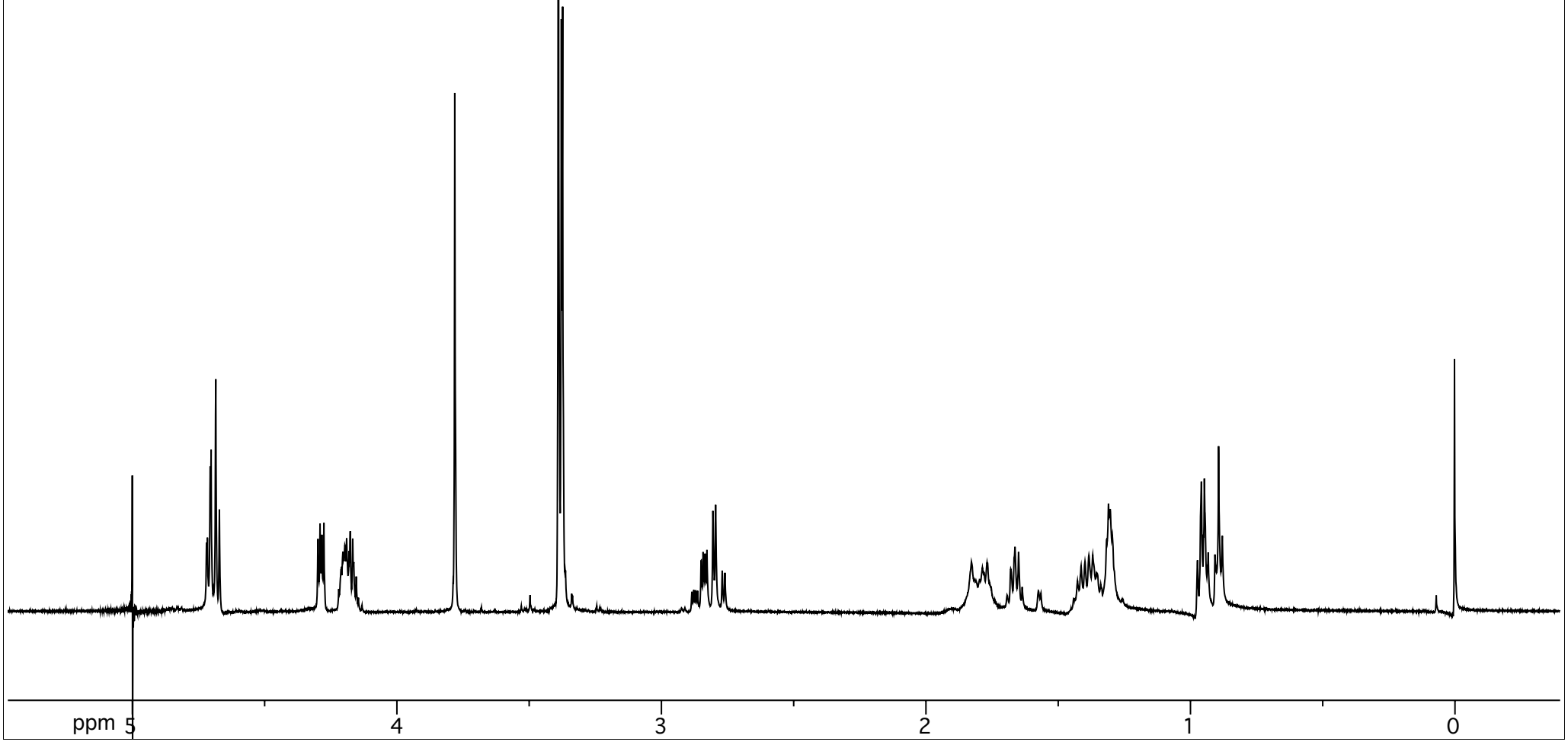

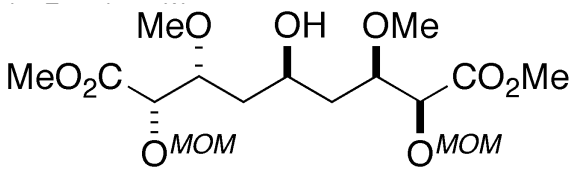

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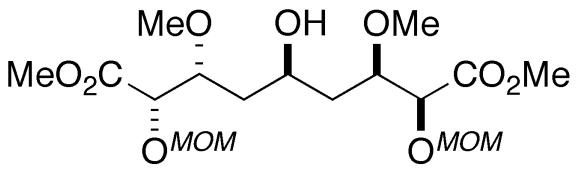
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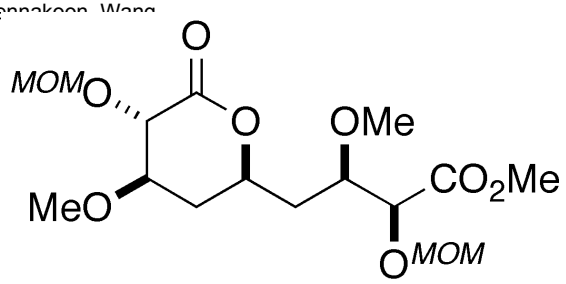

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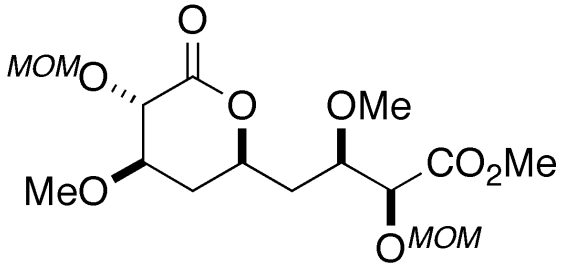
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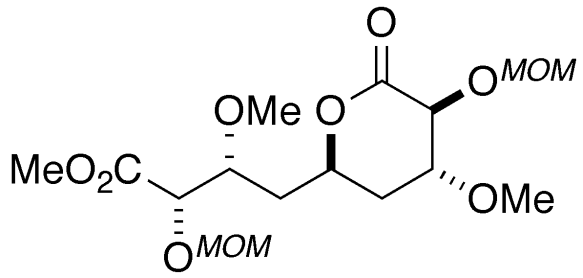

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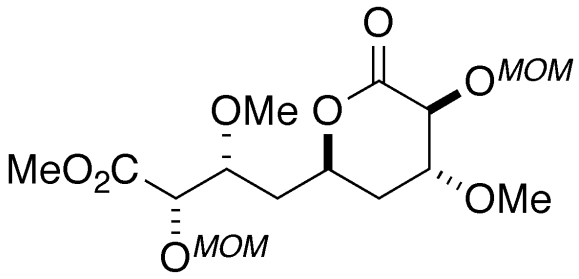
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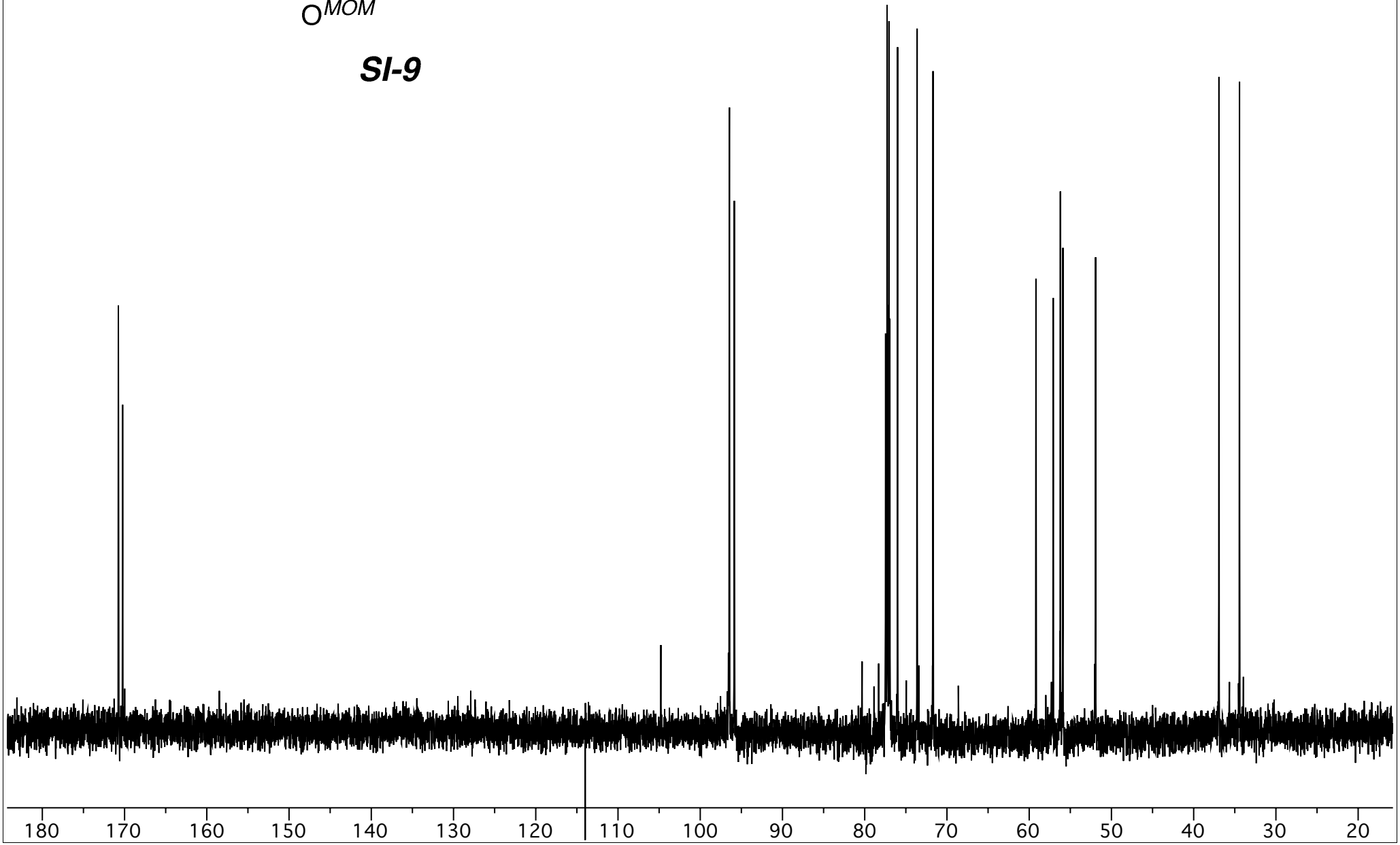
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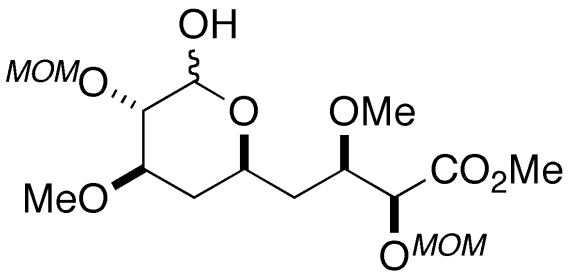

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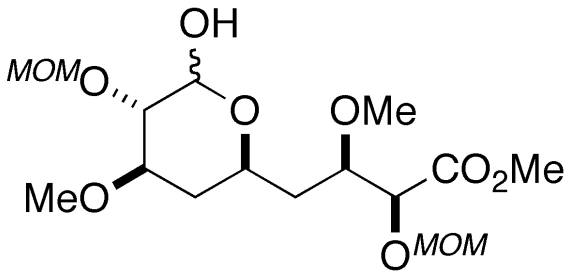
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SI-10

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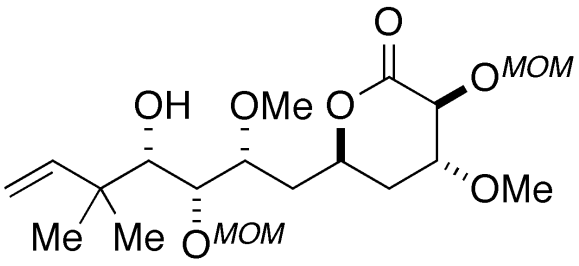

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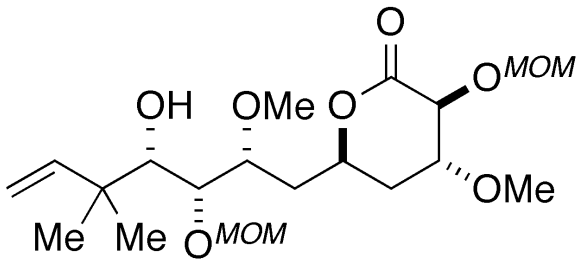
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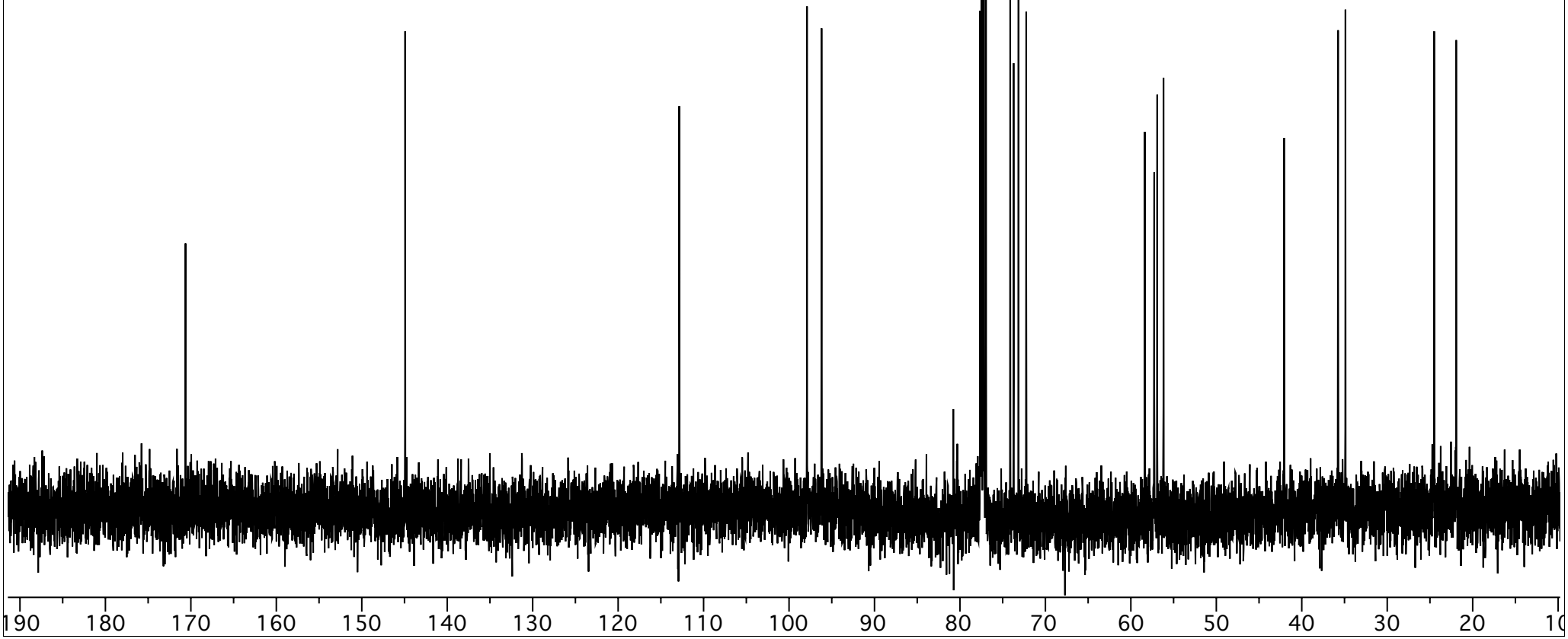
OMOM
OMe
Me
Me
OMOM

SI-11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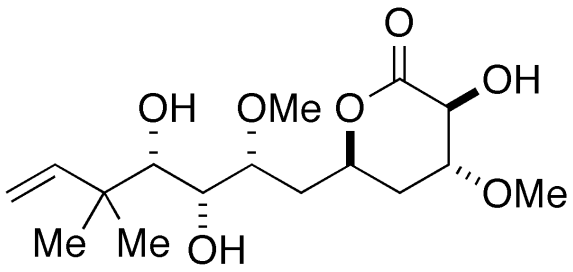
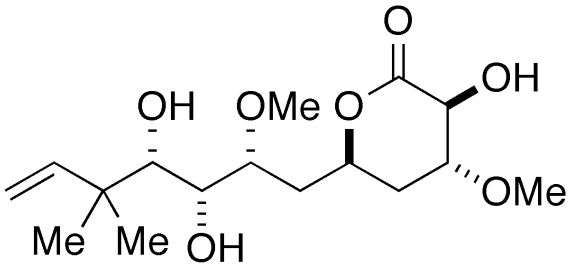
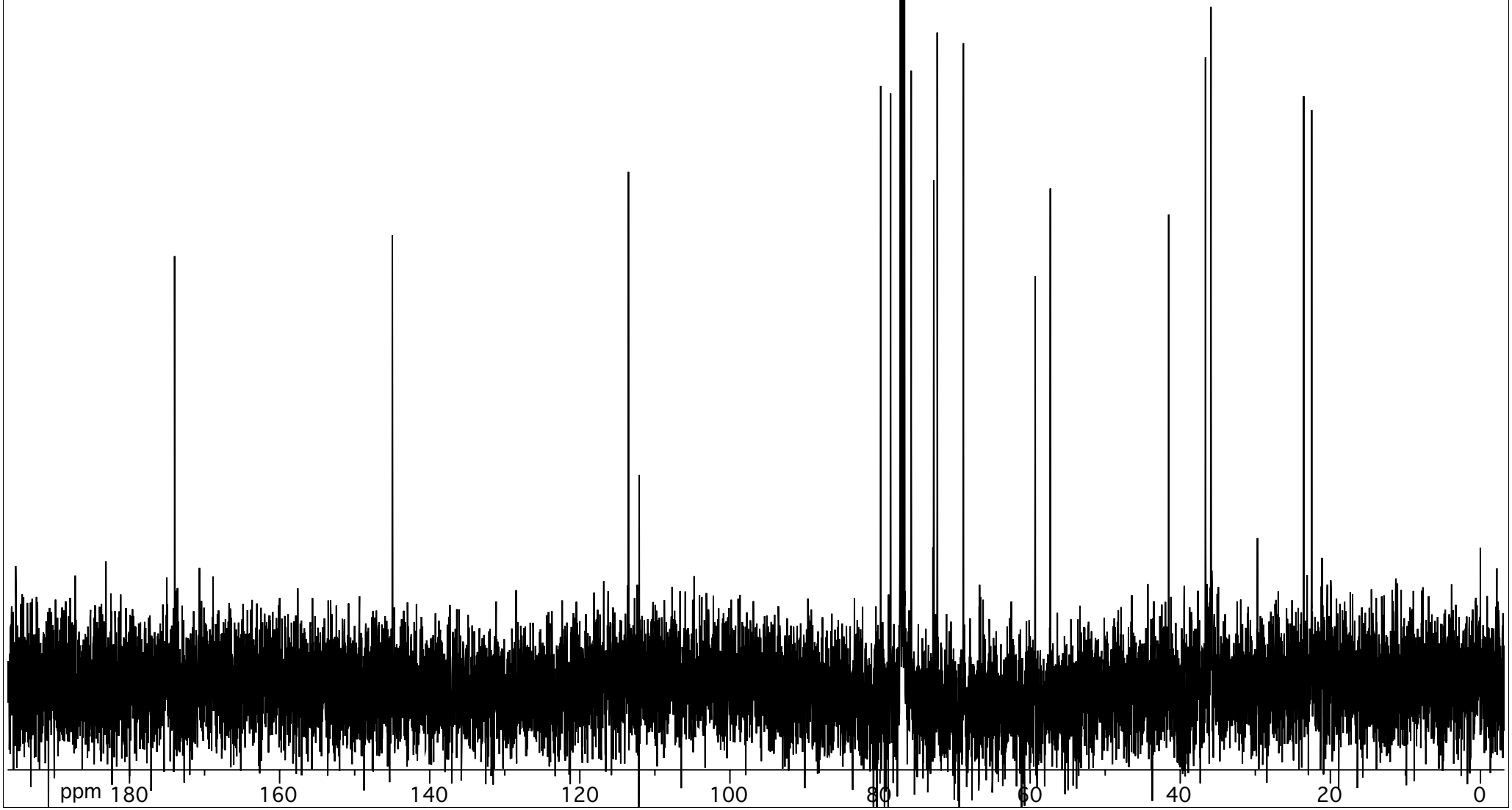
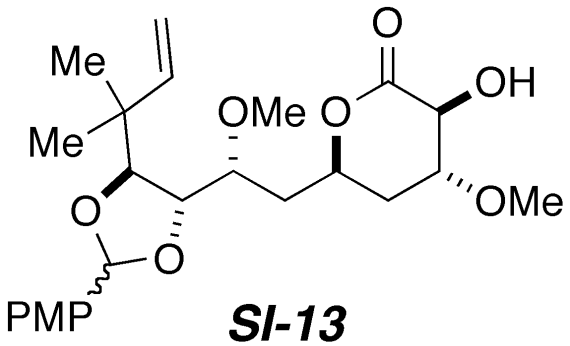


SI-12



SI-12





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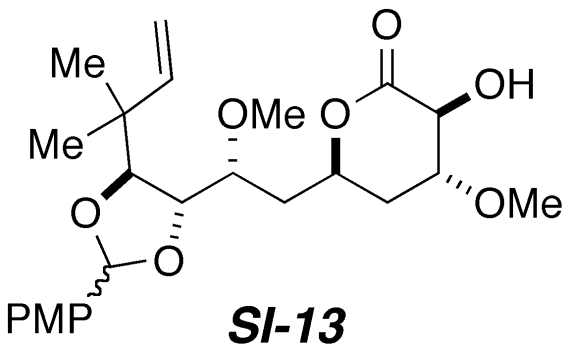
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Me
O
OMe
O
OH
OMe
O
O
PMP

SI-13

ppm
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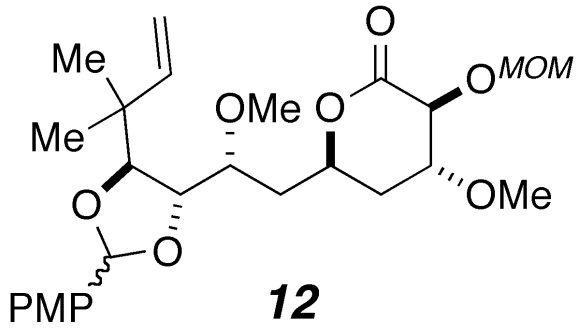

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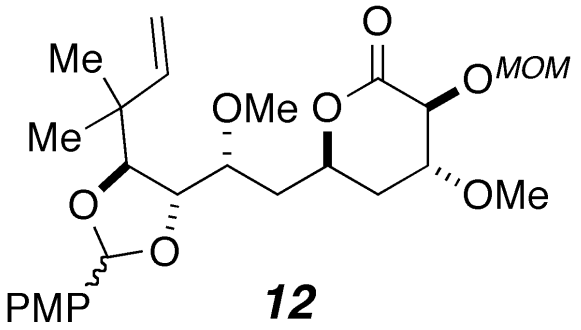
Me
Me
O
OMe
O
O
MOM
O
OMe
O
PMP

12

ppm
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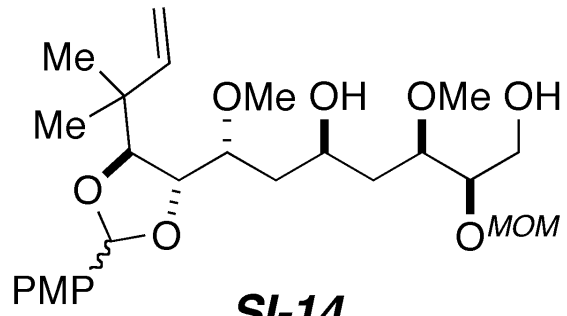
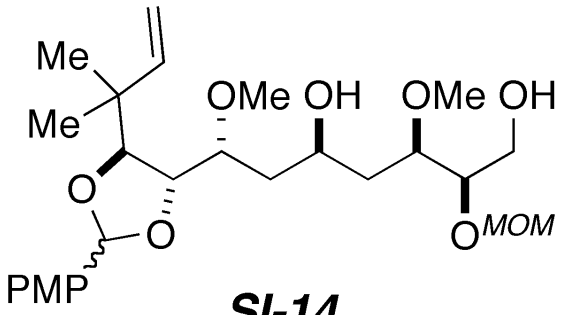


SI-14


Me
Me
OMe OH
OMe OH
O
O
O
MOM
PMP

SI-14

ppm 170
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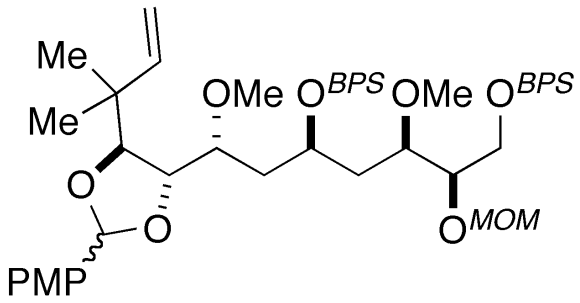
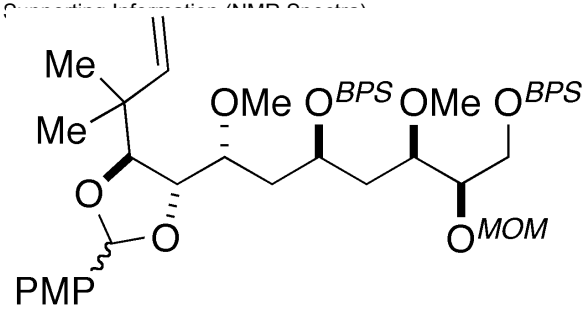
20



SI-15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OMe
O
BPS
OMe
O
BPS
O
O
O
MOM
PMP

SI-15

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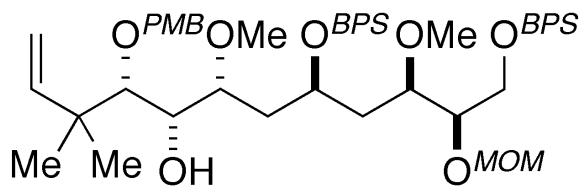
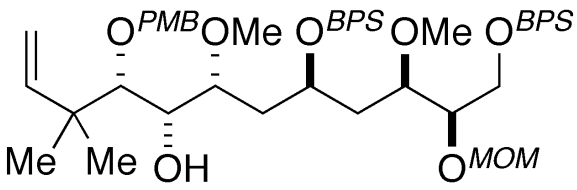


SI-16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OMe
O BPS
OMe
O BPS
Me
Me
OH
O MOM

SI-16

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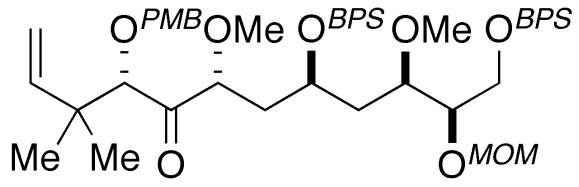

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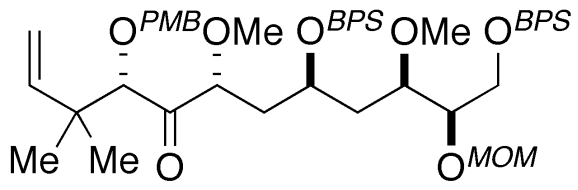
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OMe
O BPS
OMe
O BPS
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Me
O
O MOM

SI-17

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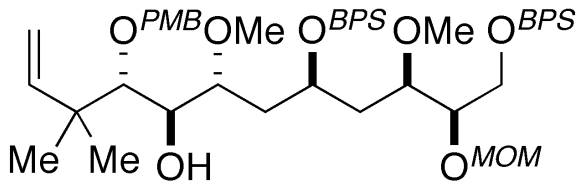
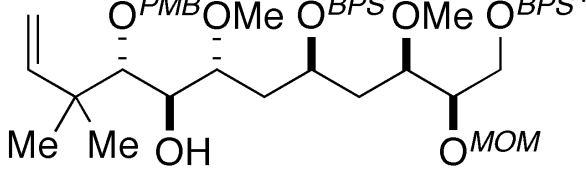


SI-18


O PMB
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O BPS
OMe
O BPS
Me
Me
OH
O MOM

SI-18

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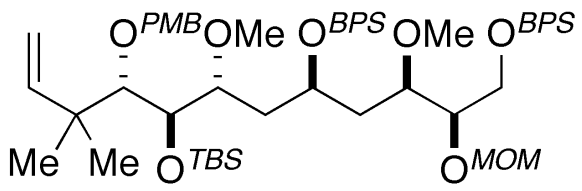

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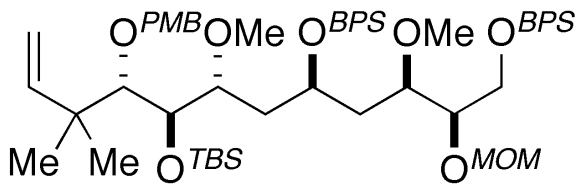
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Me
O TBS
O MOM

13

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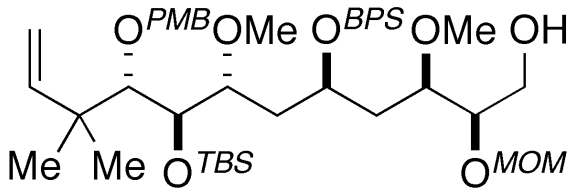
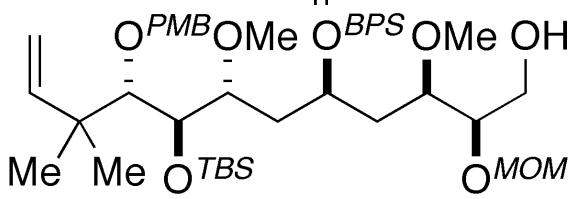


SI-19


O PMB
OMe
O BPS
OMe
OH
Me
Me
O TBS
O MOM

SI-19

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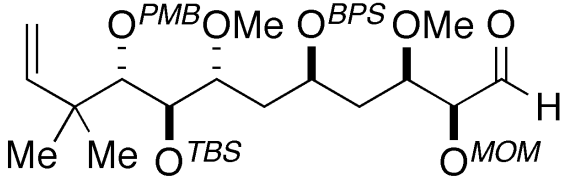
-10



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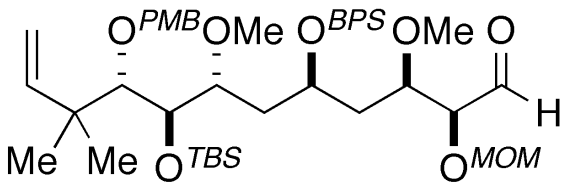
O PMB OMe O BPS OMe O
H
Me Me O TBS
O MOM

SI-20

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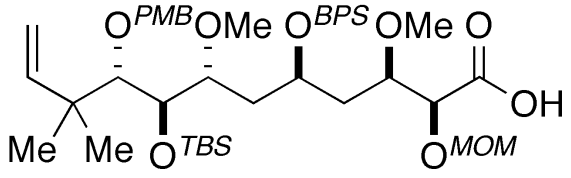
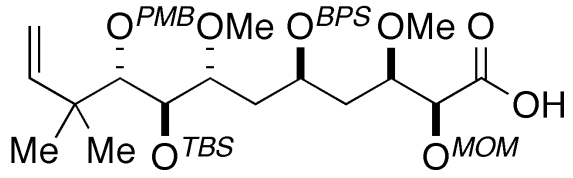


SI-21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OMe
O BPS
OMe
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OH
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Me
O TBS
O MOM

SI-21

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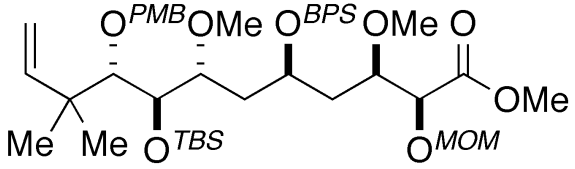
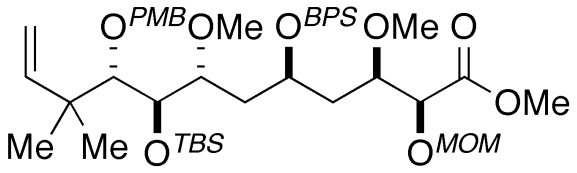


SI-22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O BPS
OMe
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OMe
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O TBS
O MOM

SI-22

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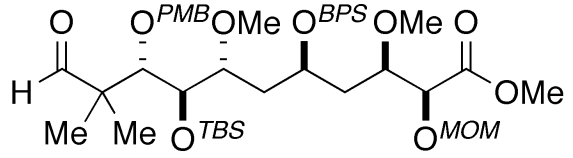

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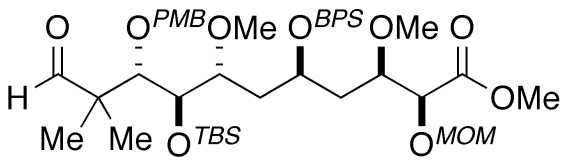
O
O PMB
OMe
O BPS
OMe
O
H
OMe
Me
Me
O TBS
O MOM

2

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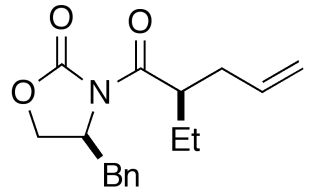

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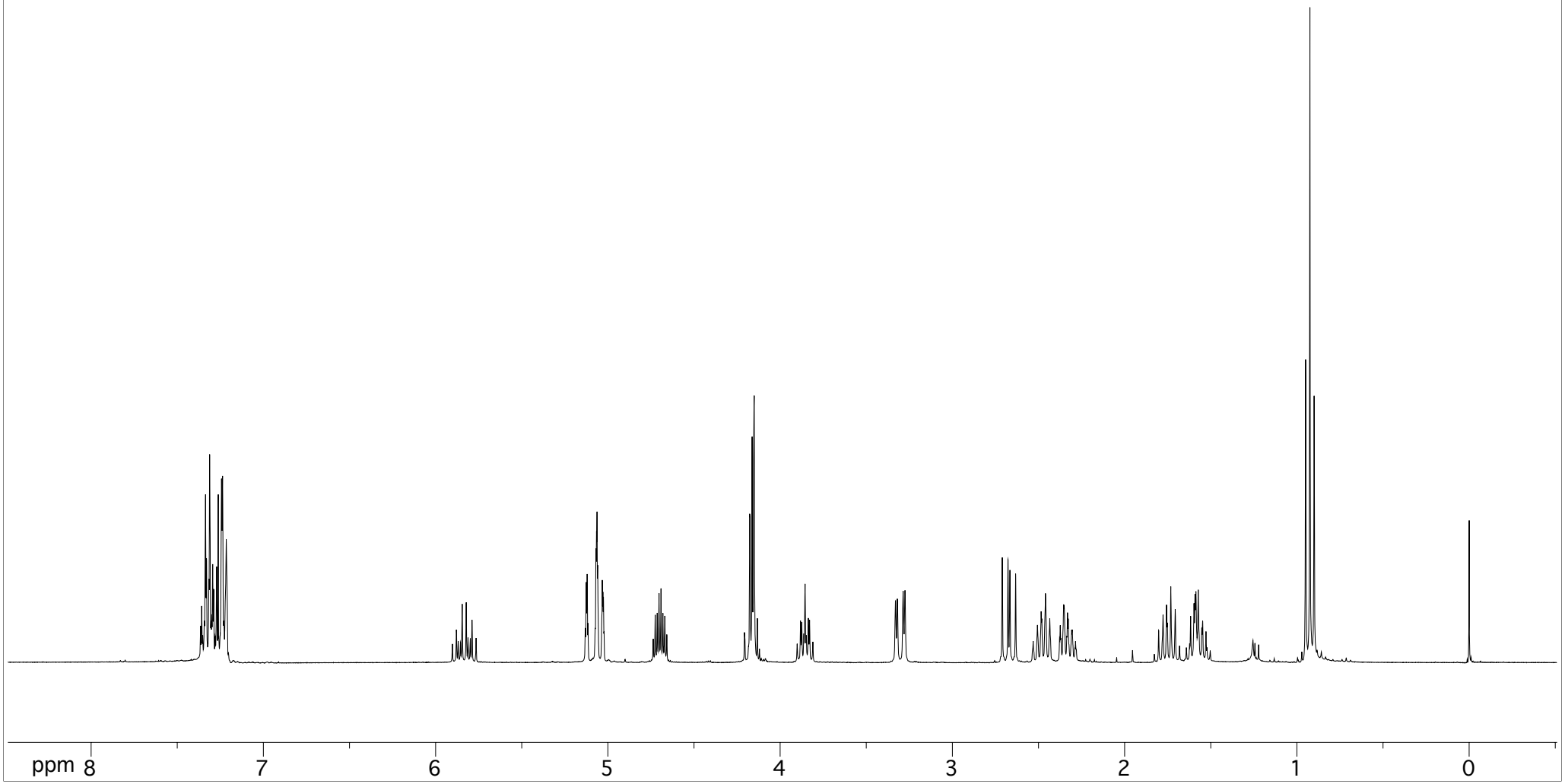

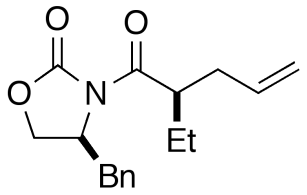

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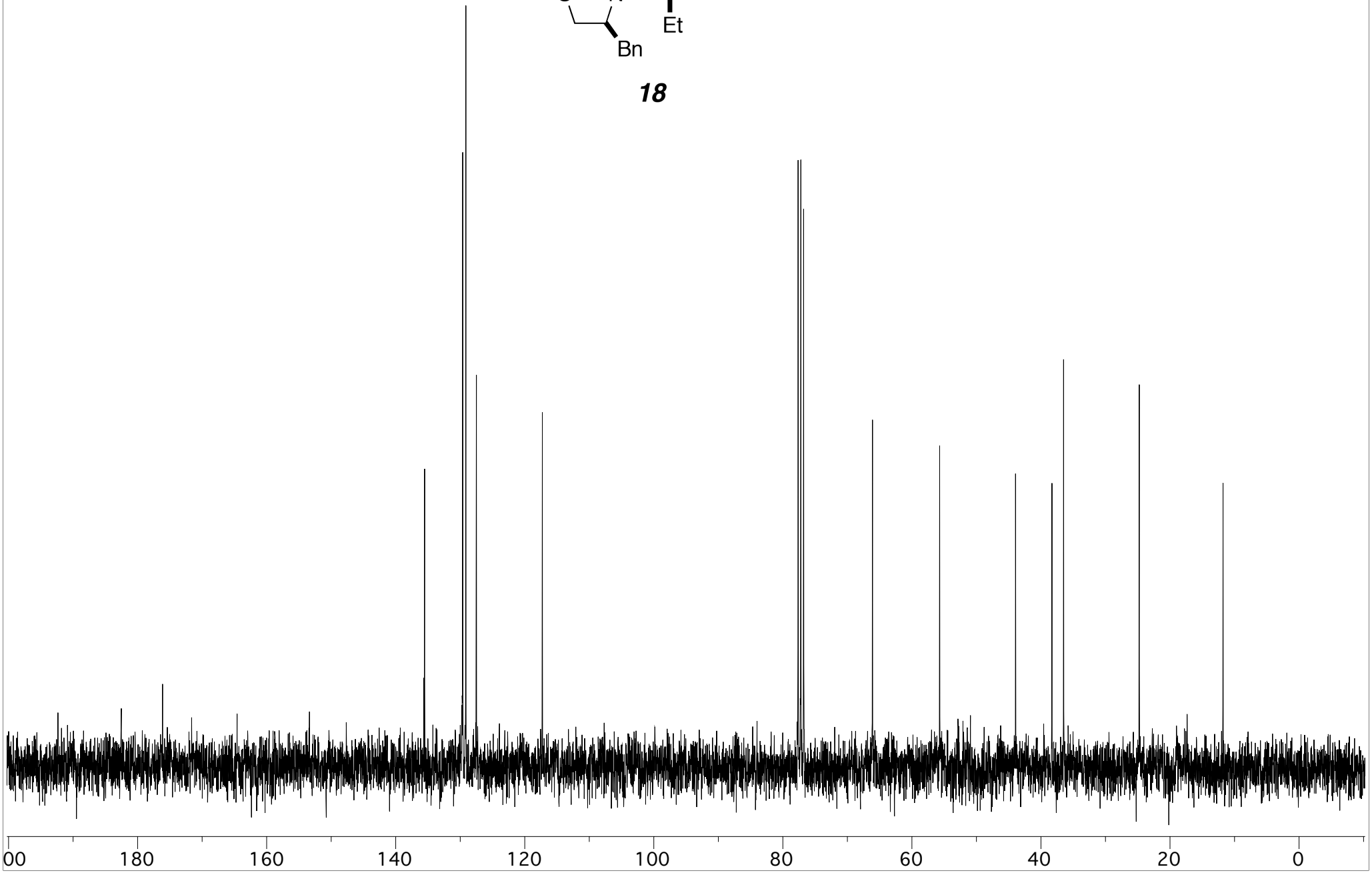
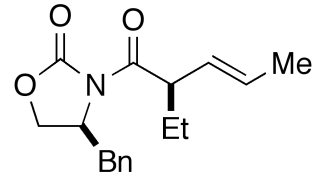
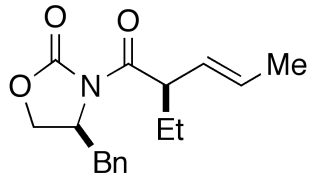
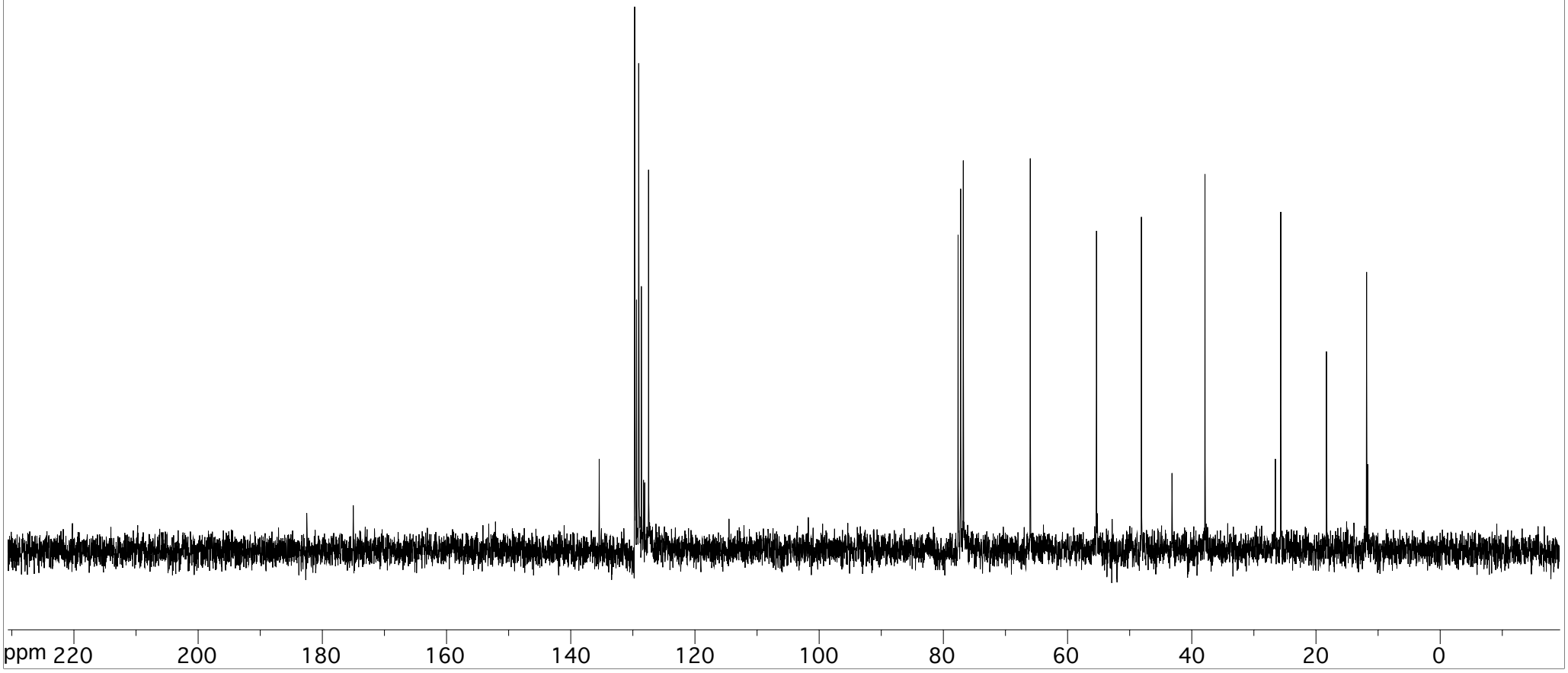


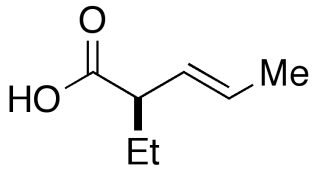


SI-24



SI-24





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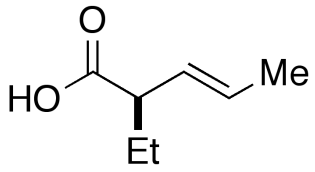

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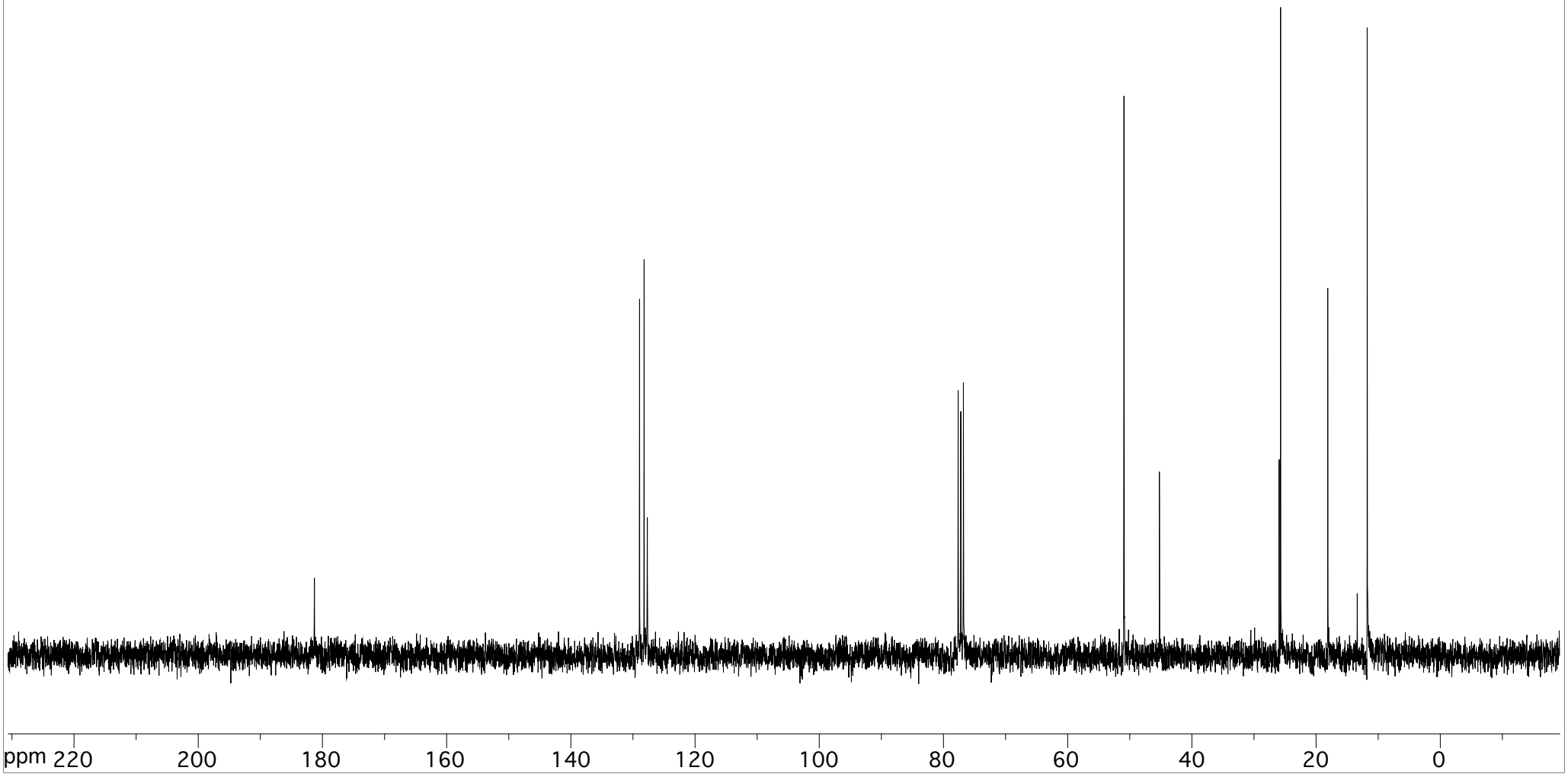
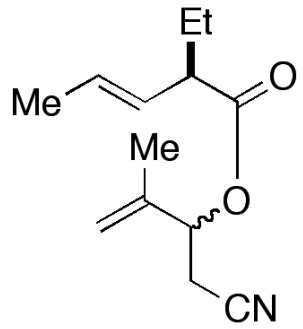
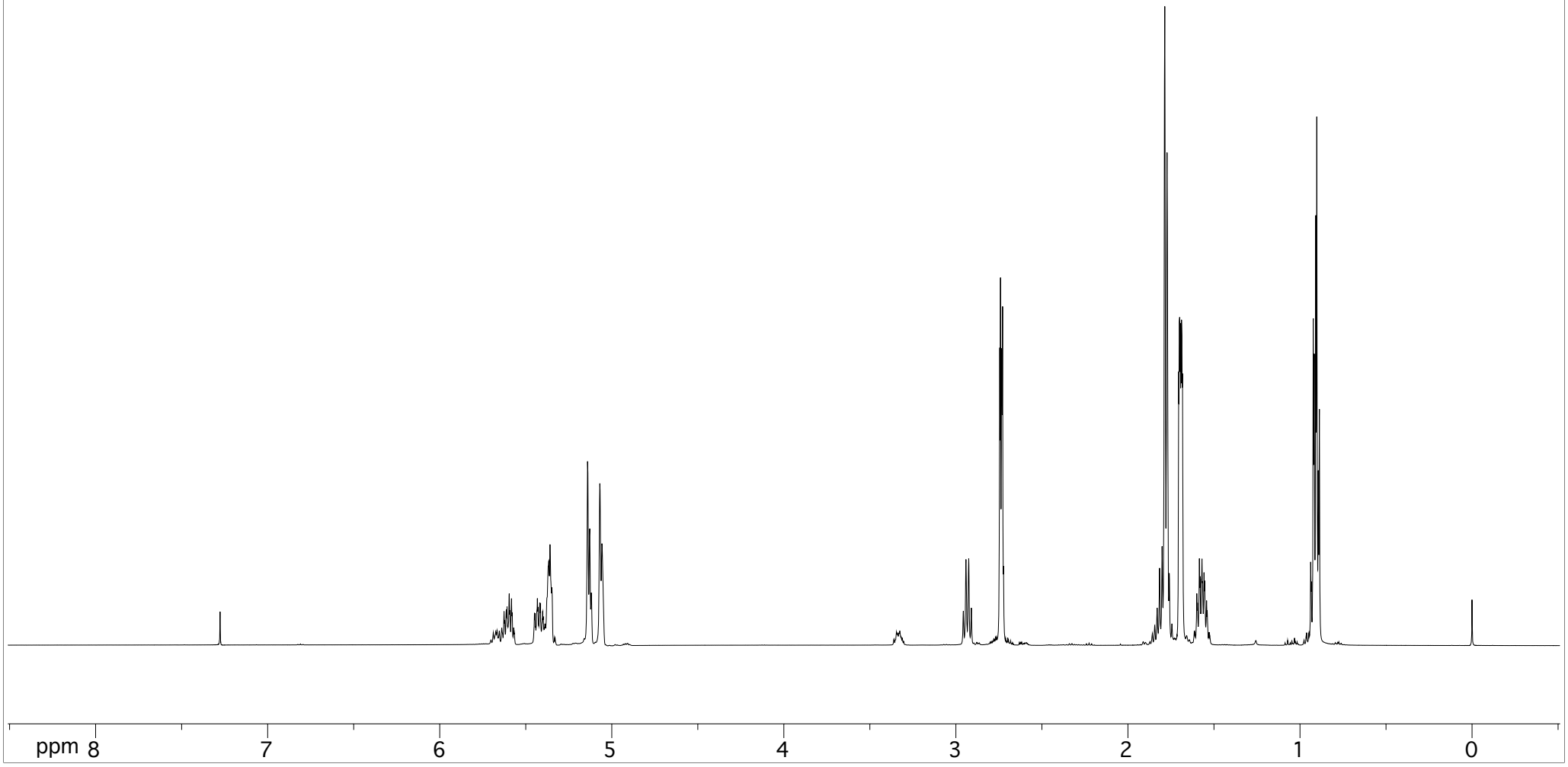
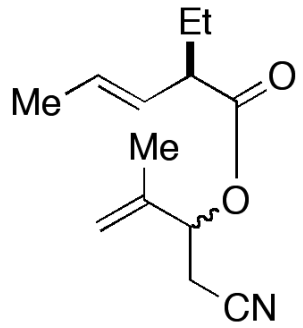


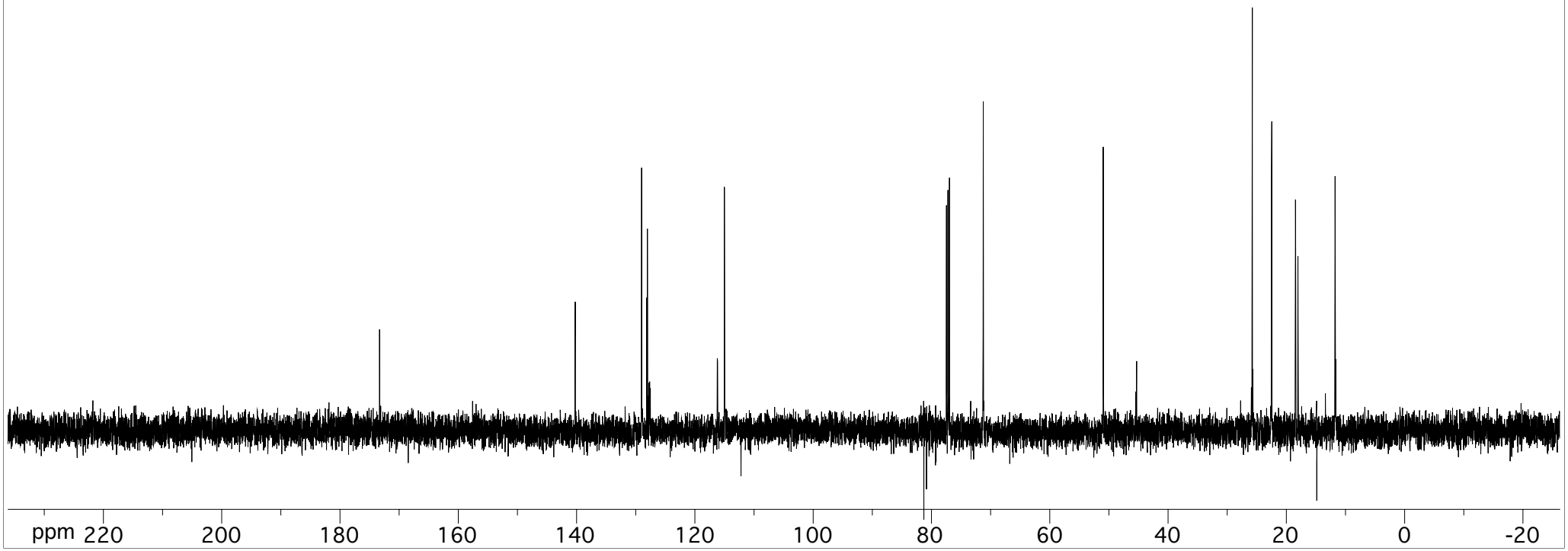


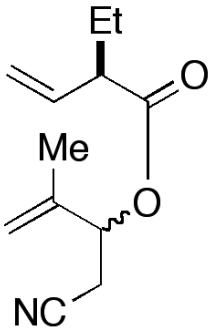
SI-25a



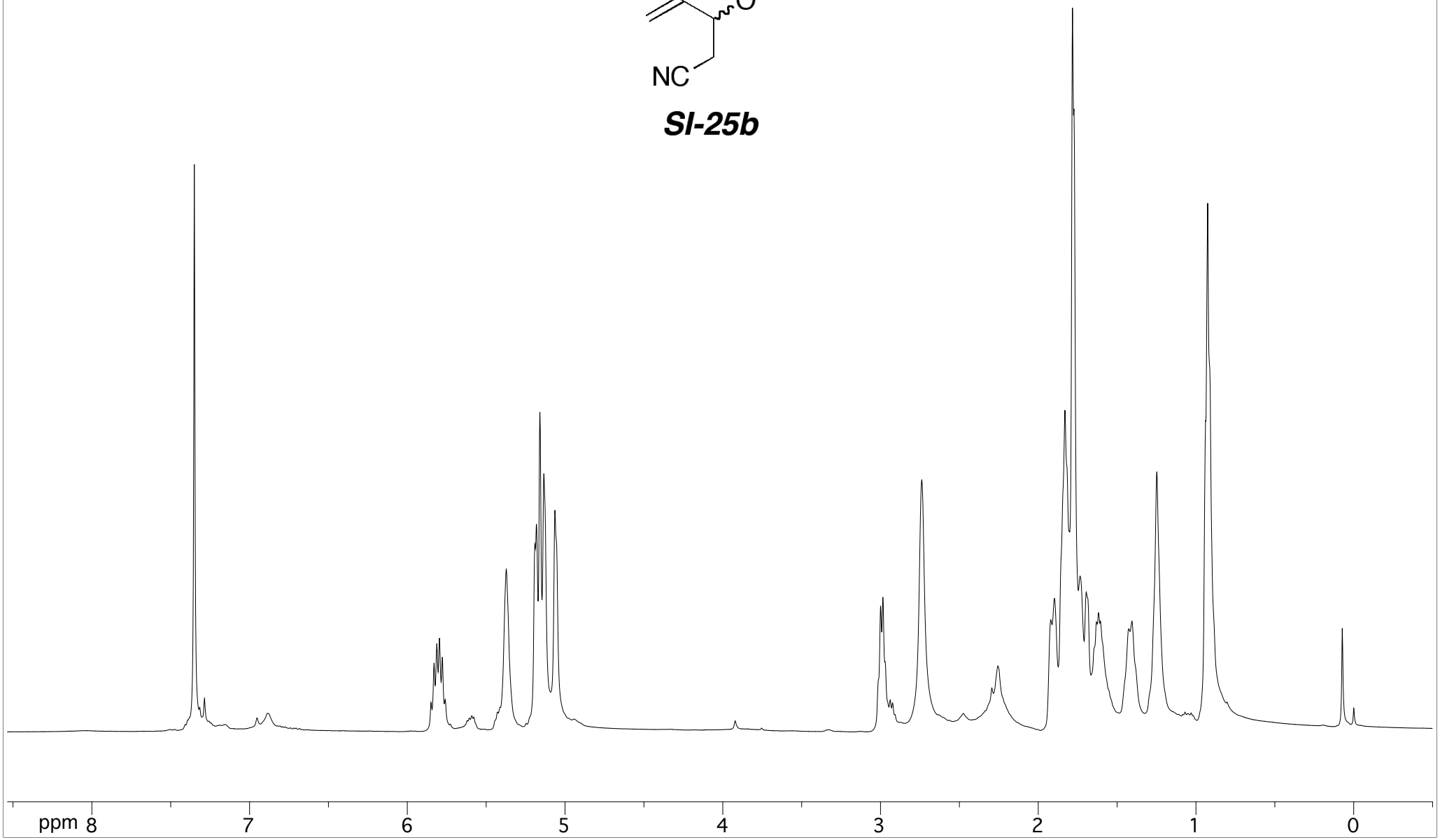


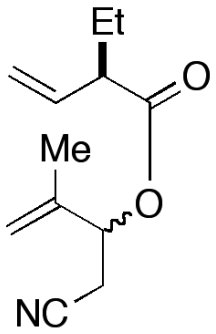
SI-25a



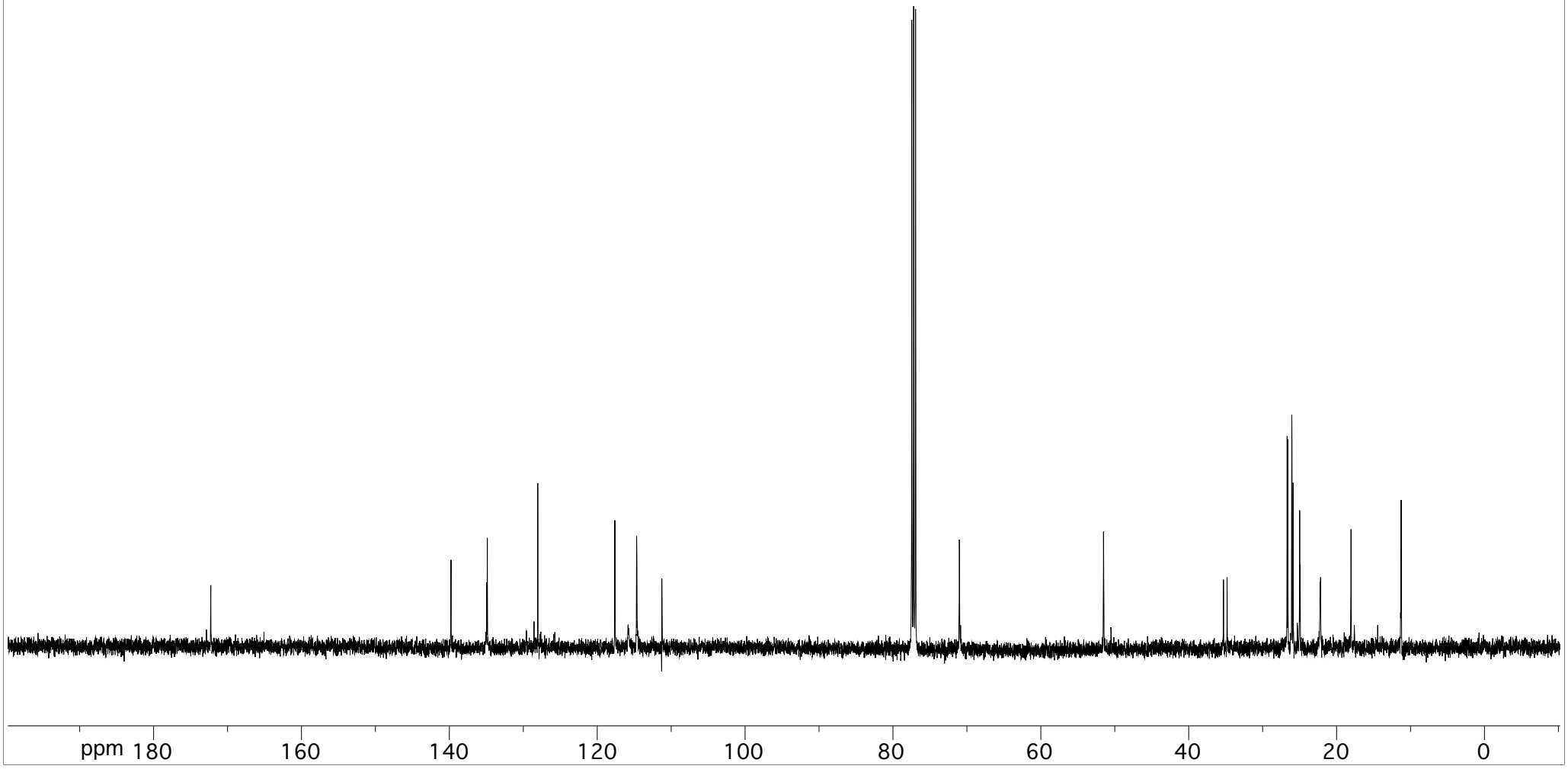


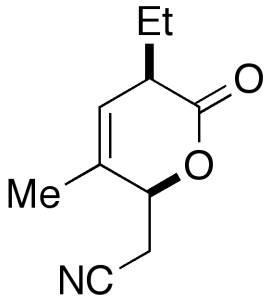
SI-25b





SI-25b





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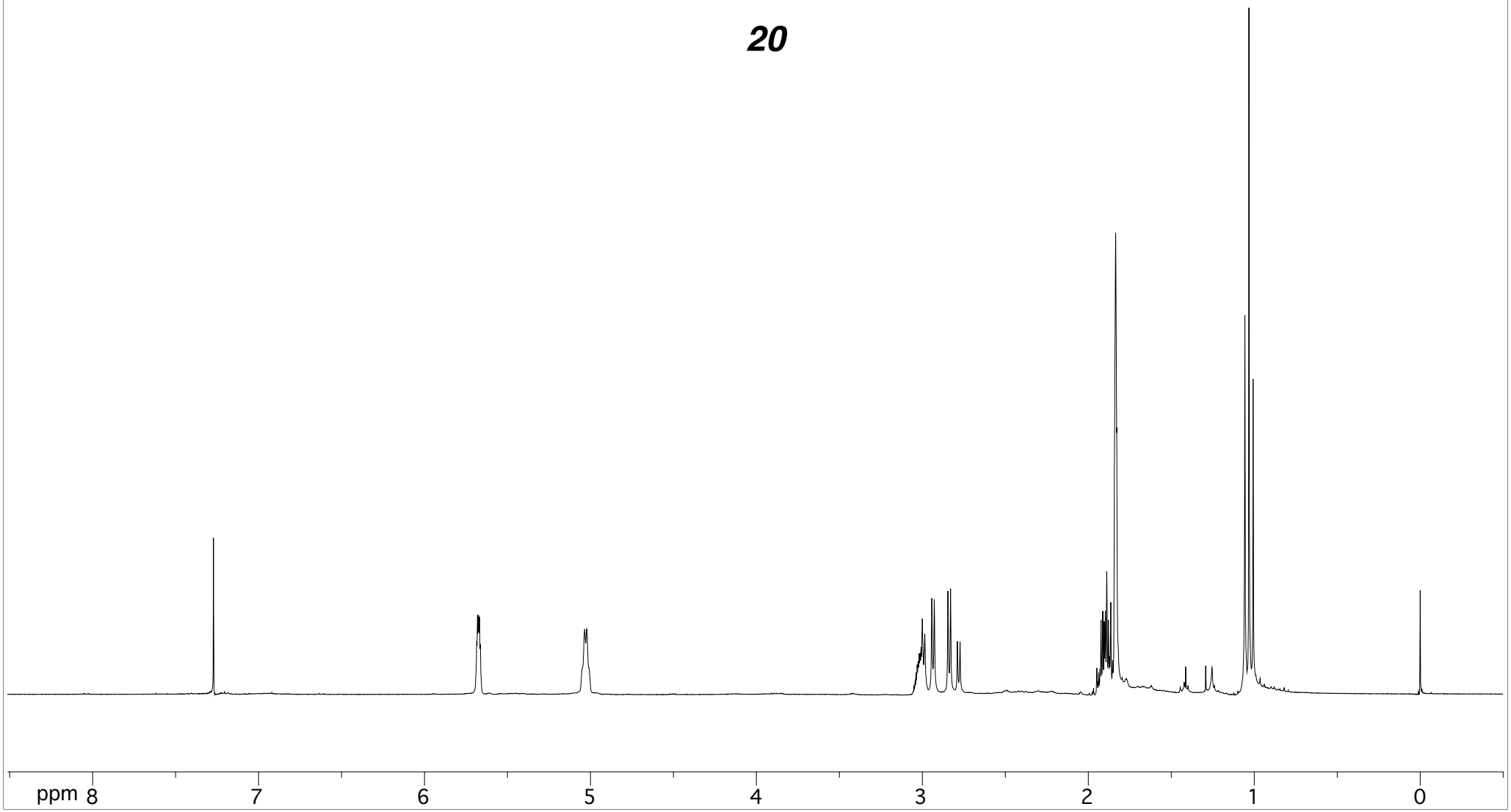

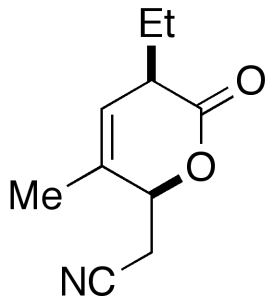

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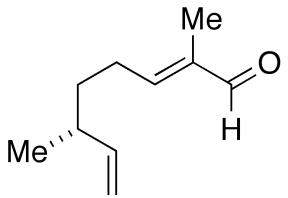

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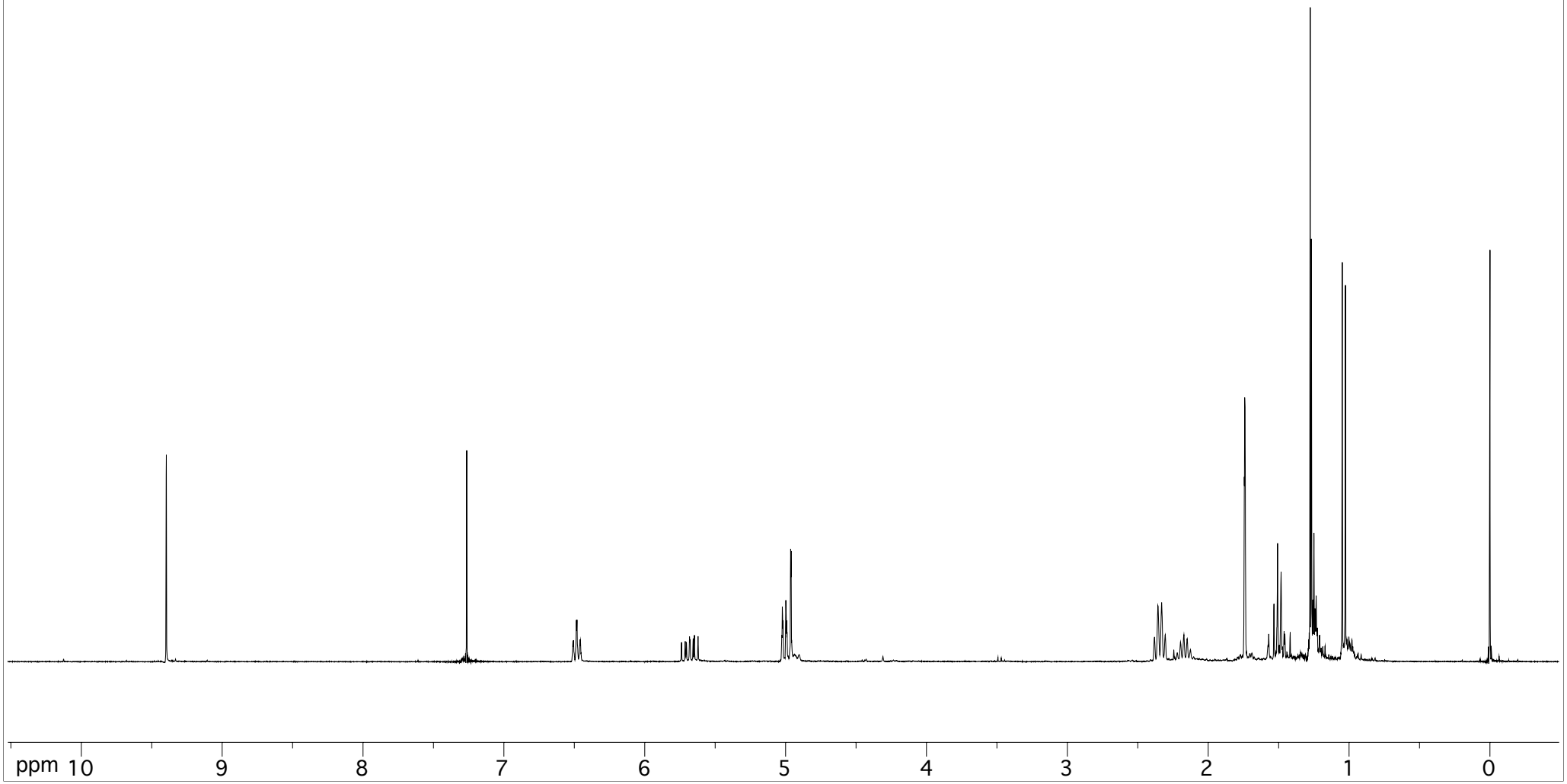

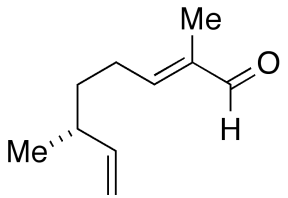

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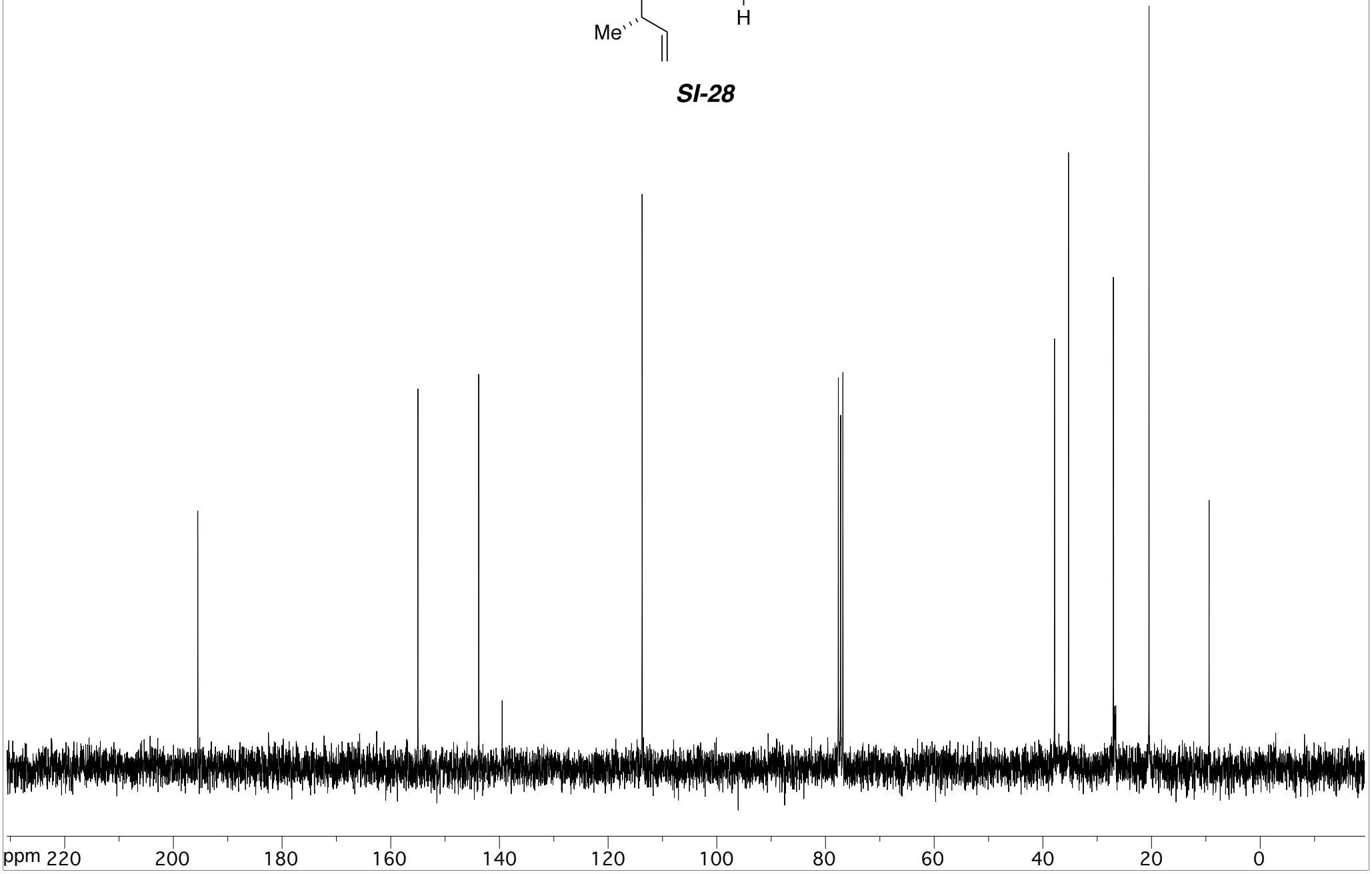

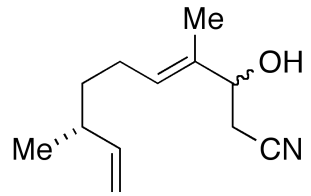

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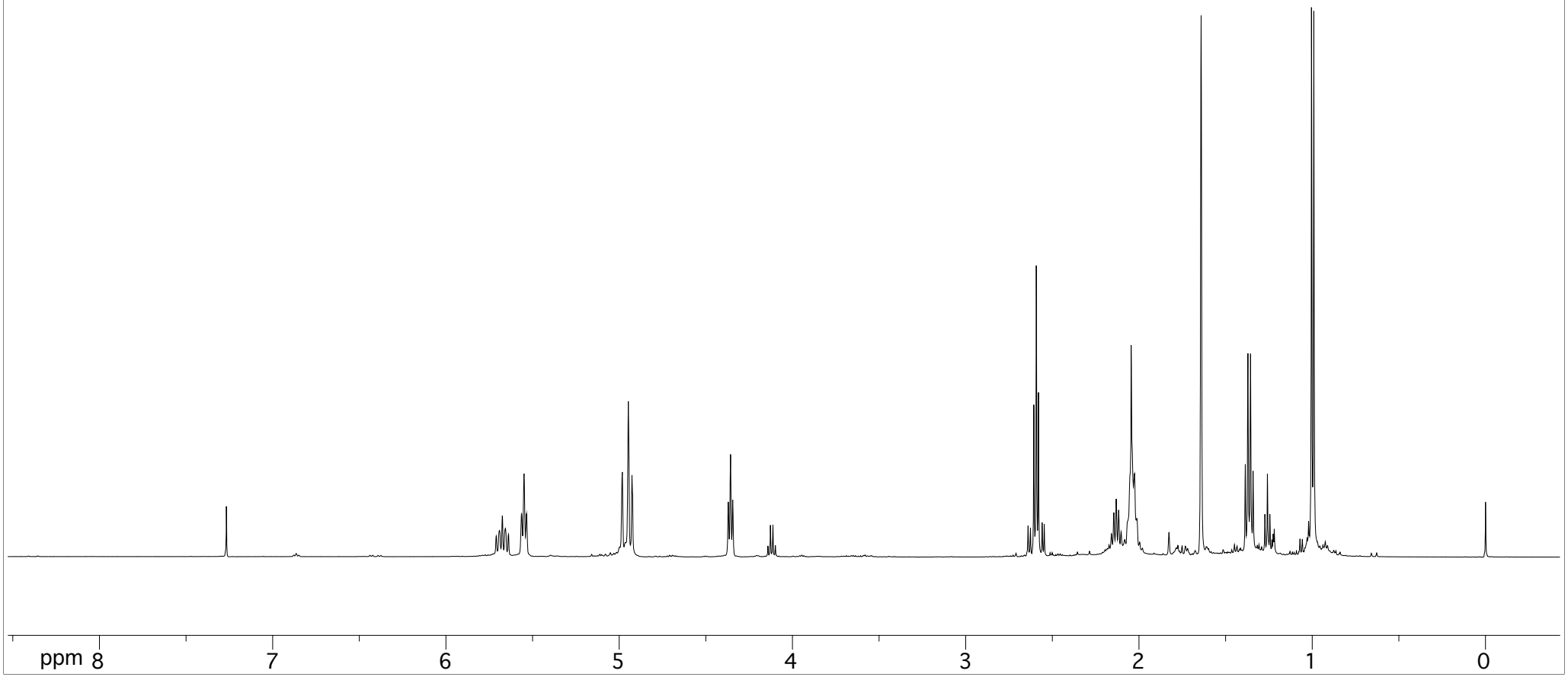
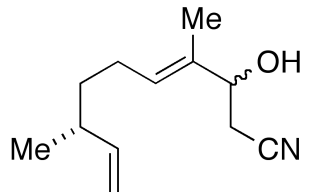
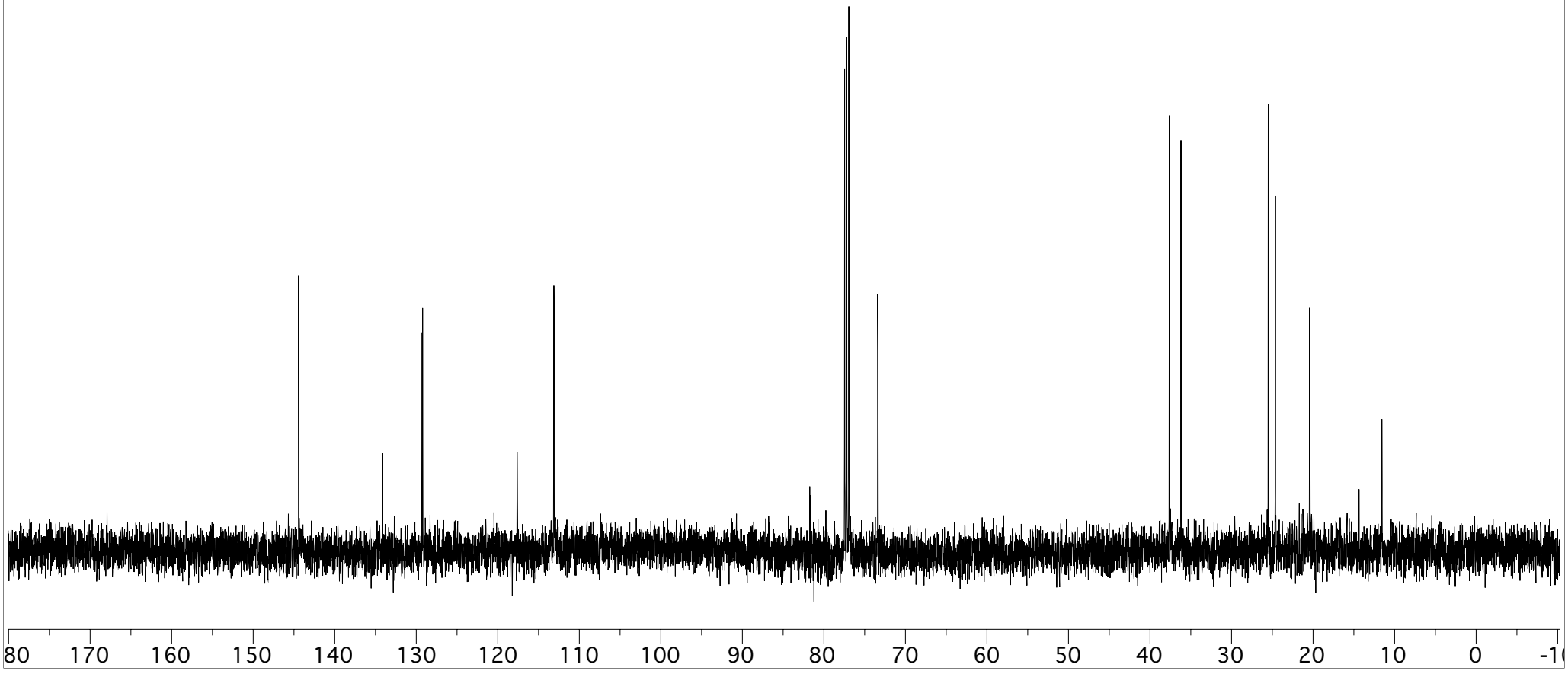



Me
OH
Me
CN

SI-29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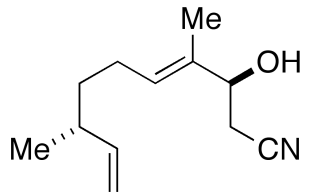

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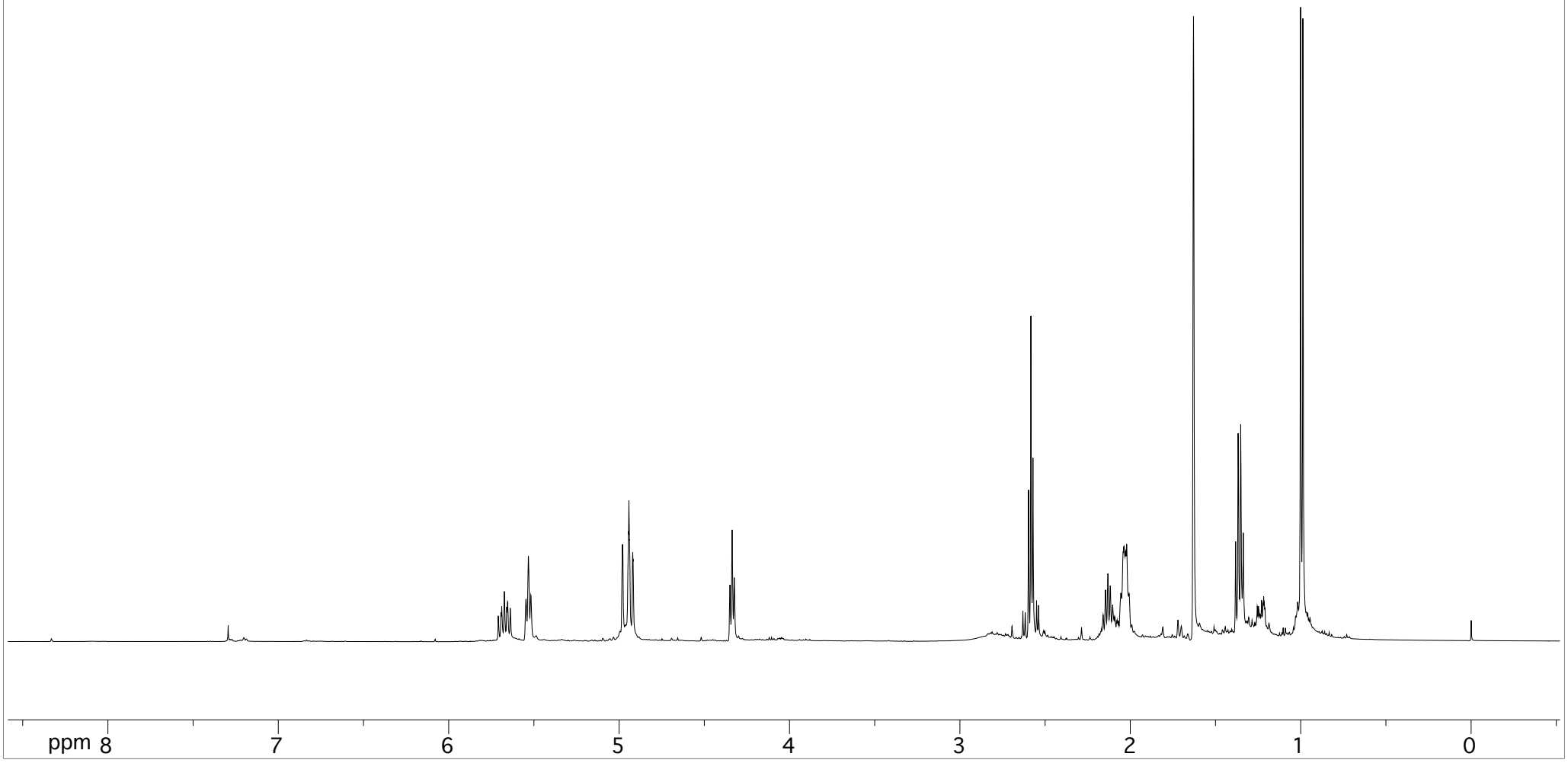

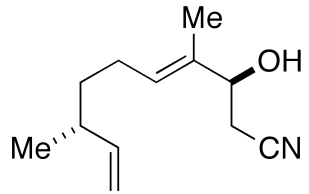
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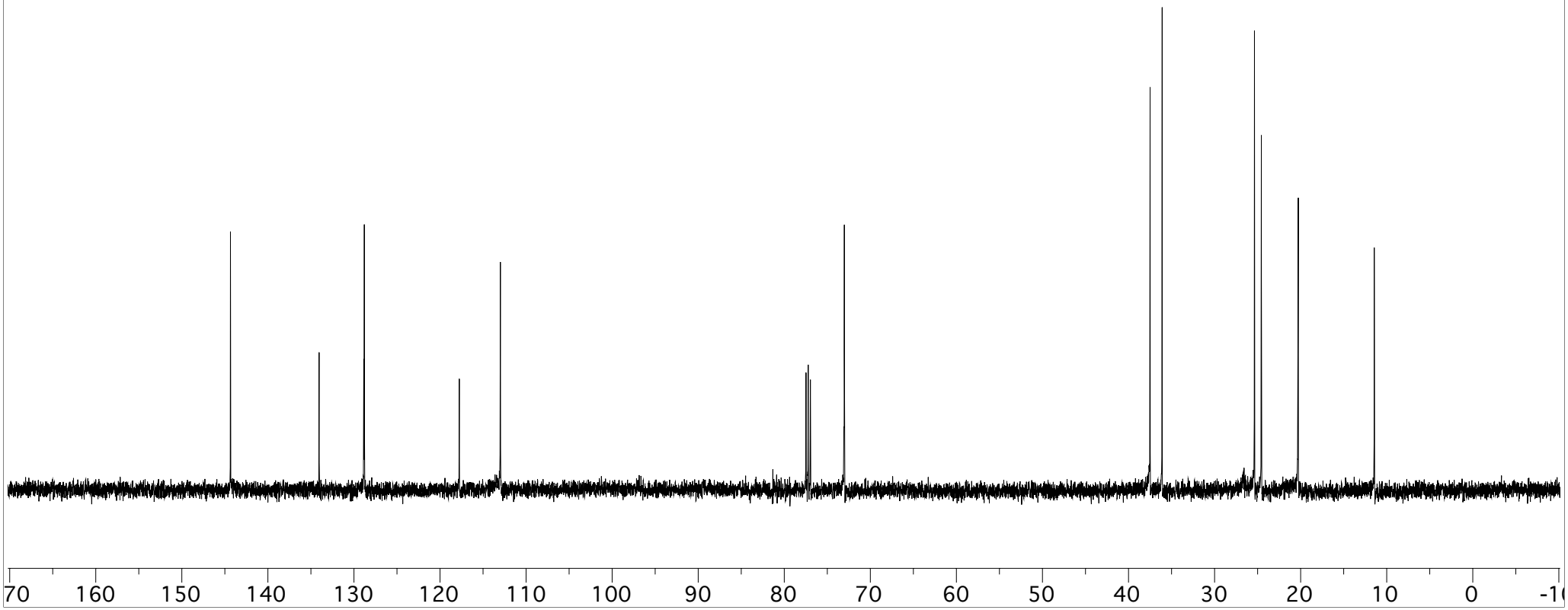
OH
Me
CN

15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10
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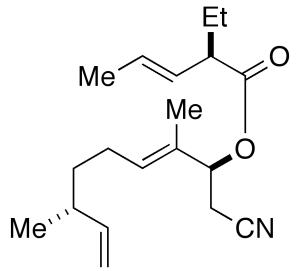

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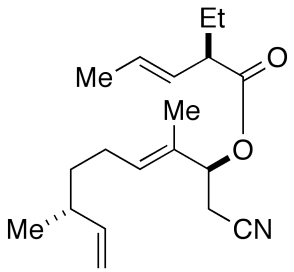
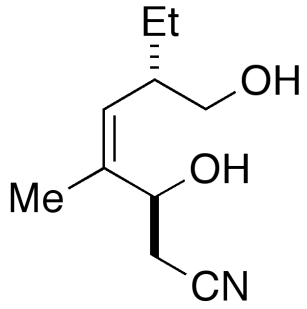


5b



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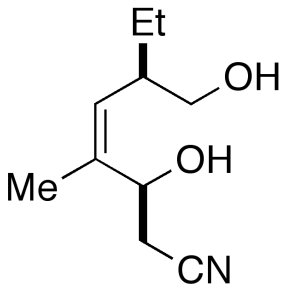

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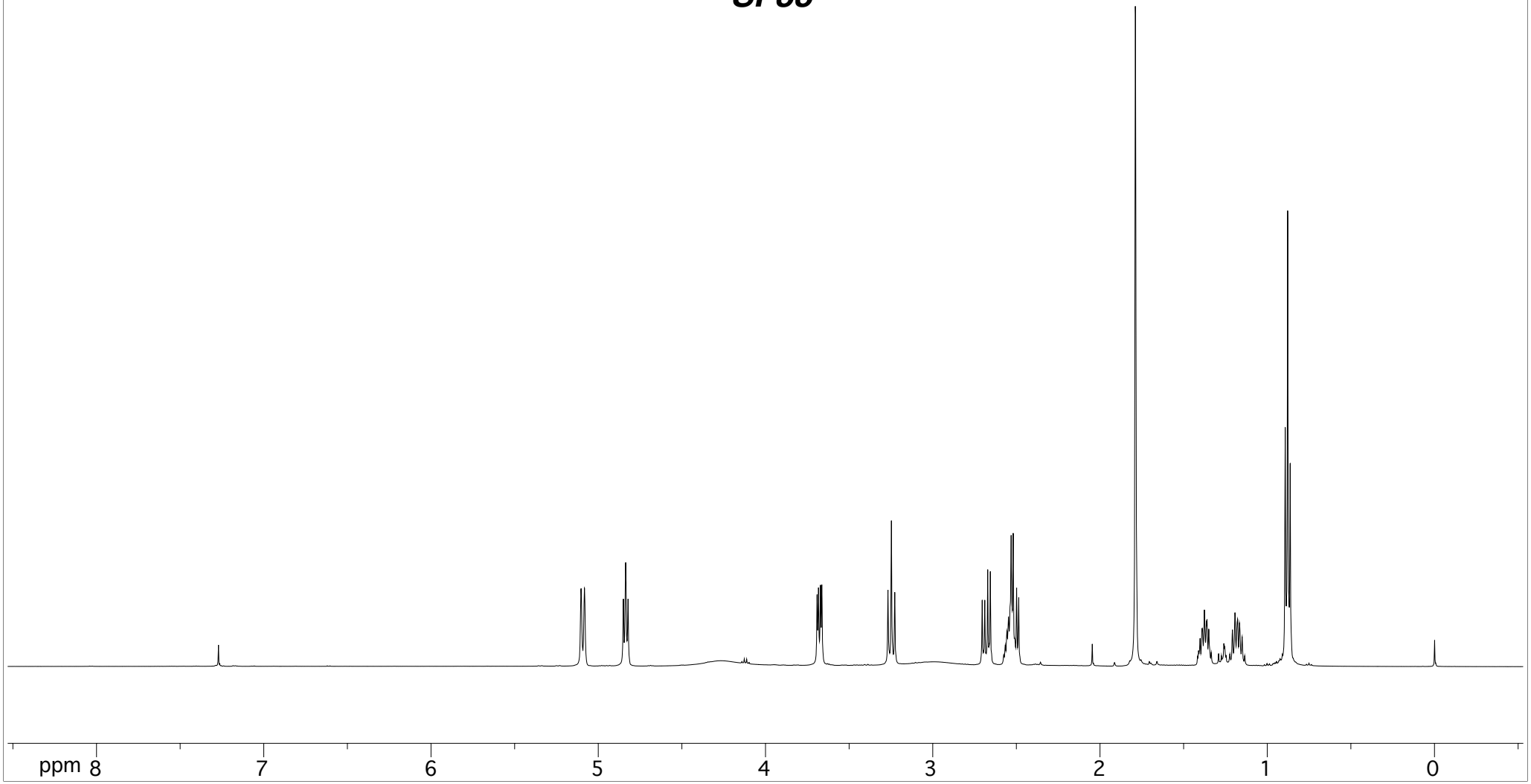

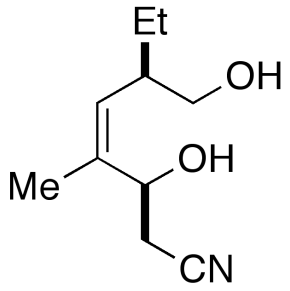

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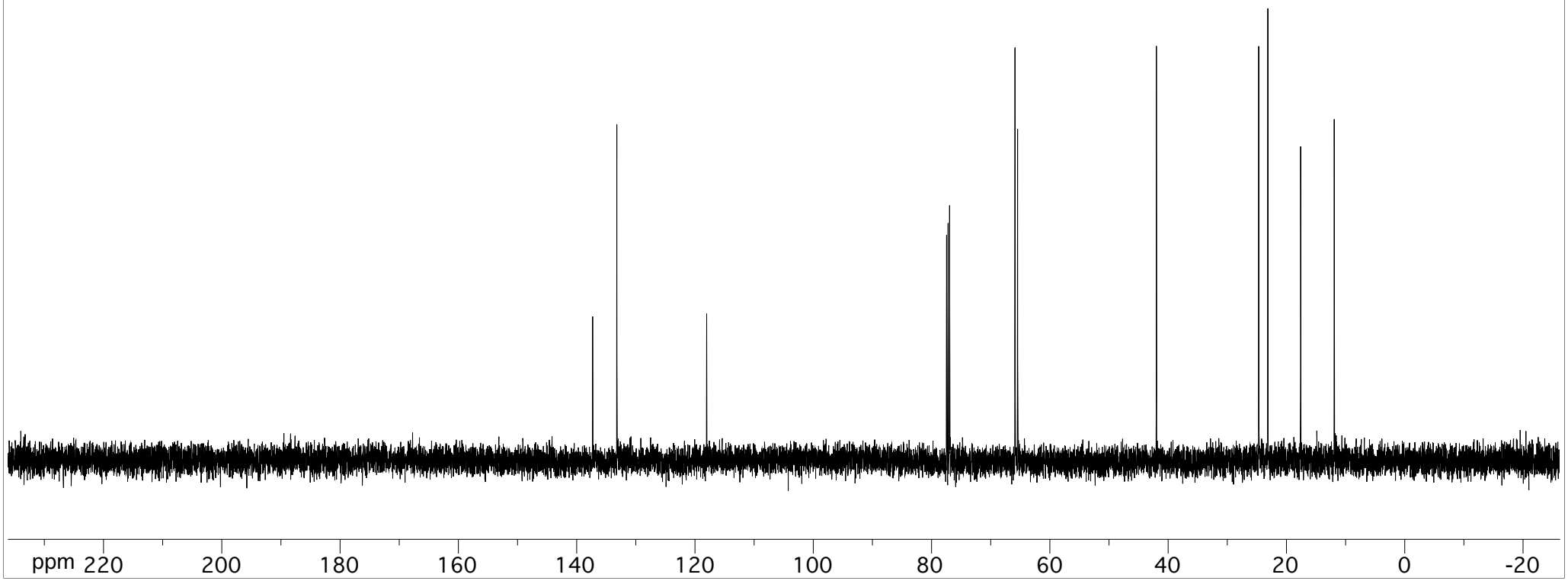

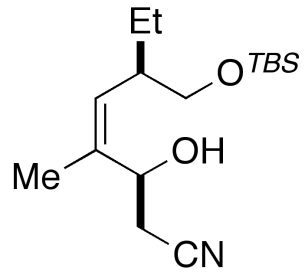

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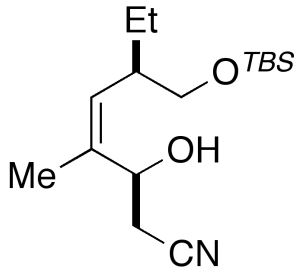
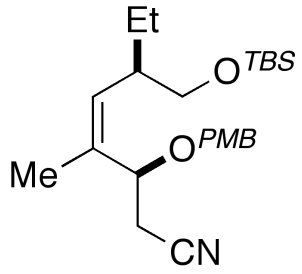


SI-34



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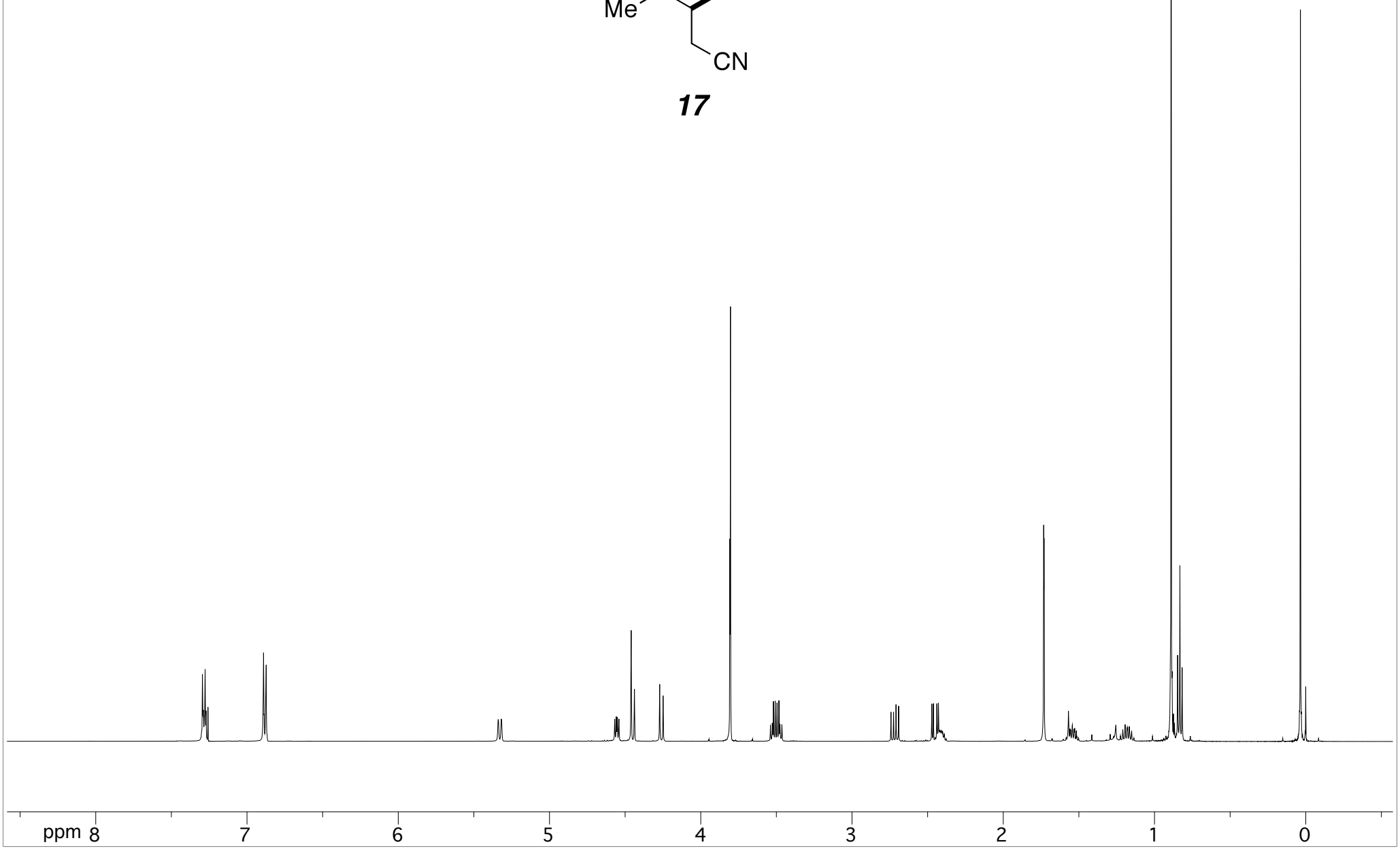

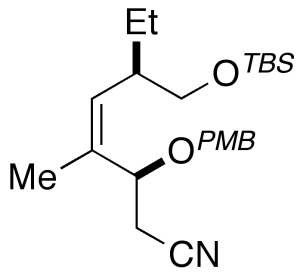

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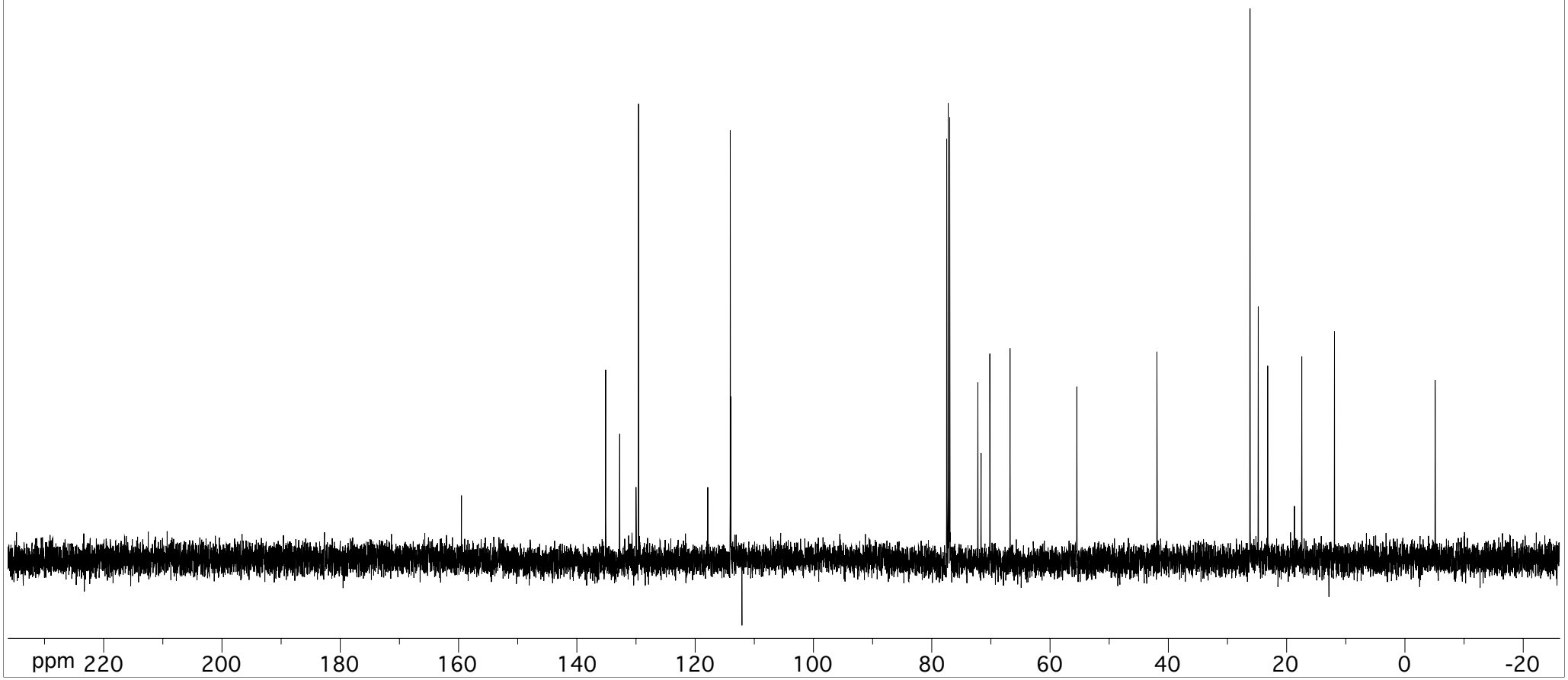

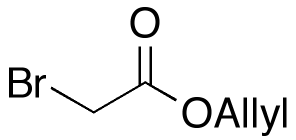

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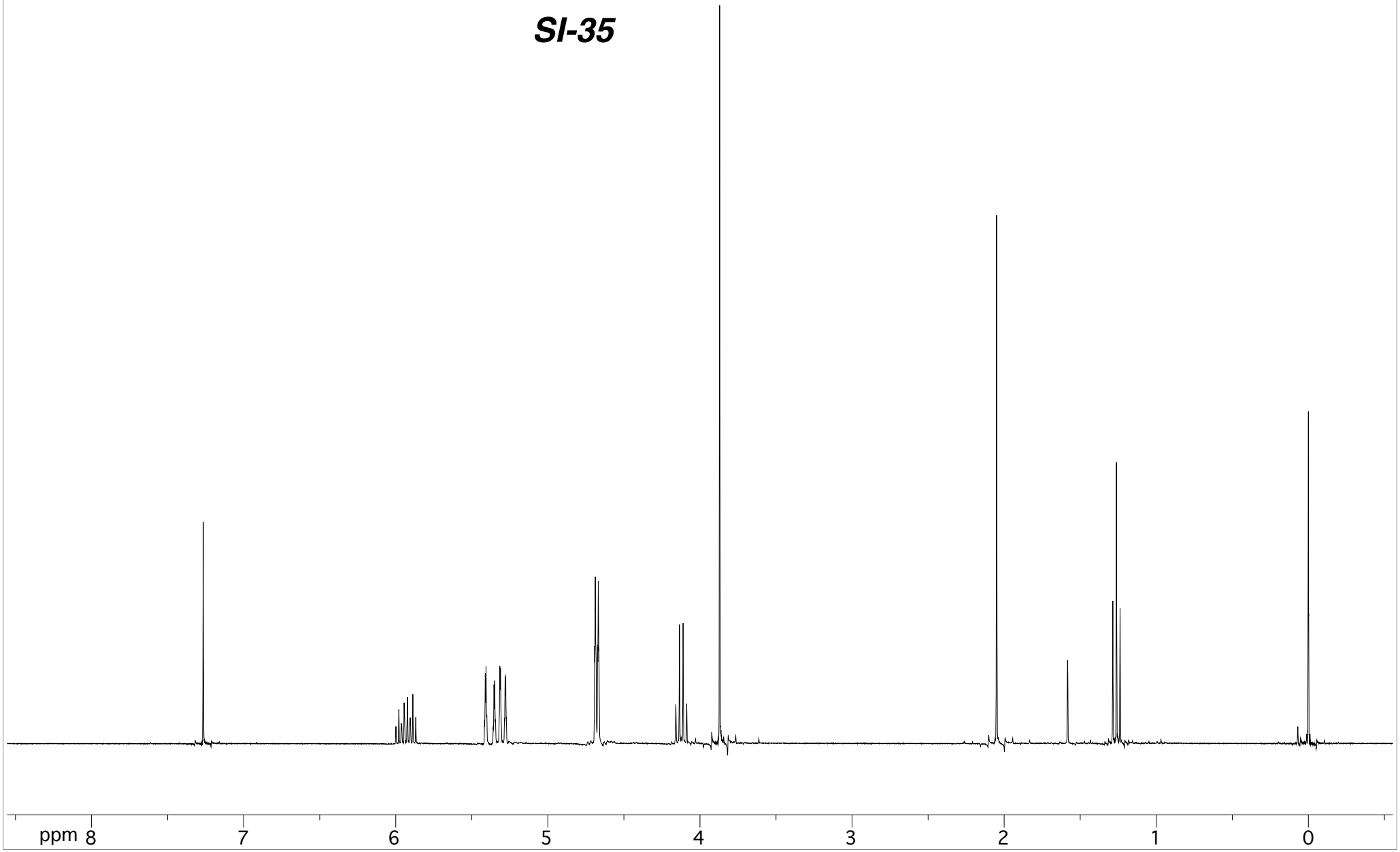

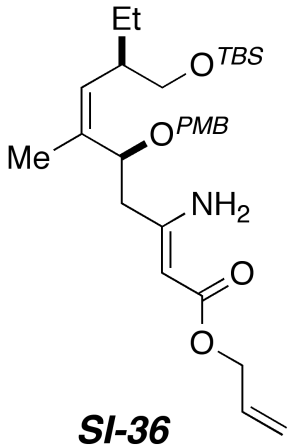

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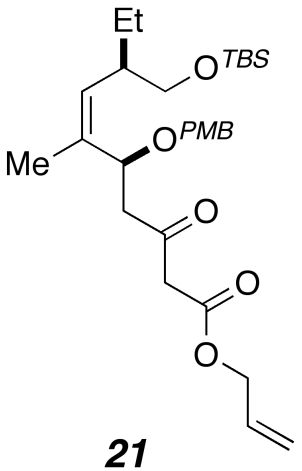

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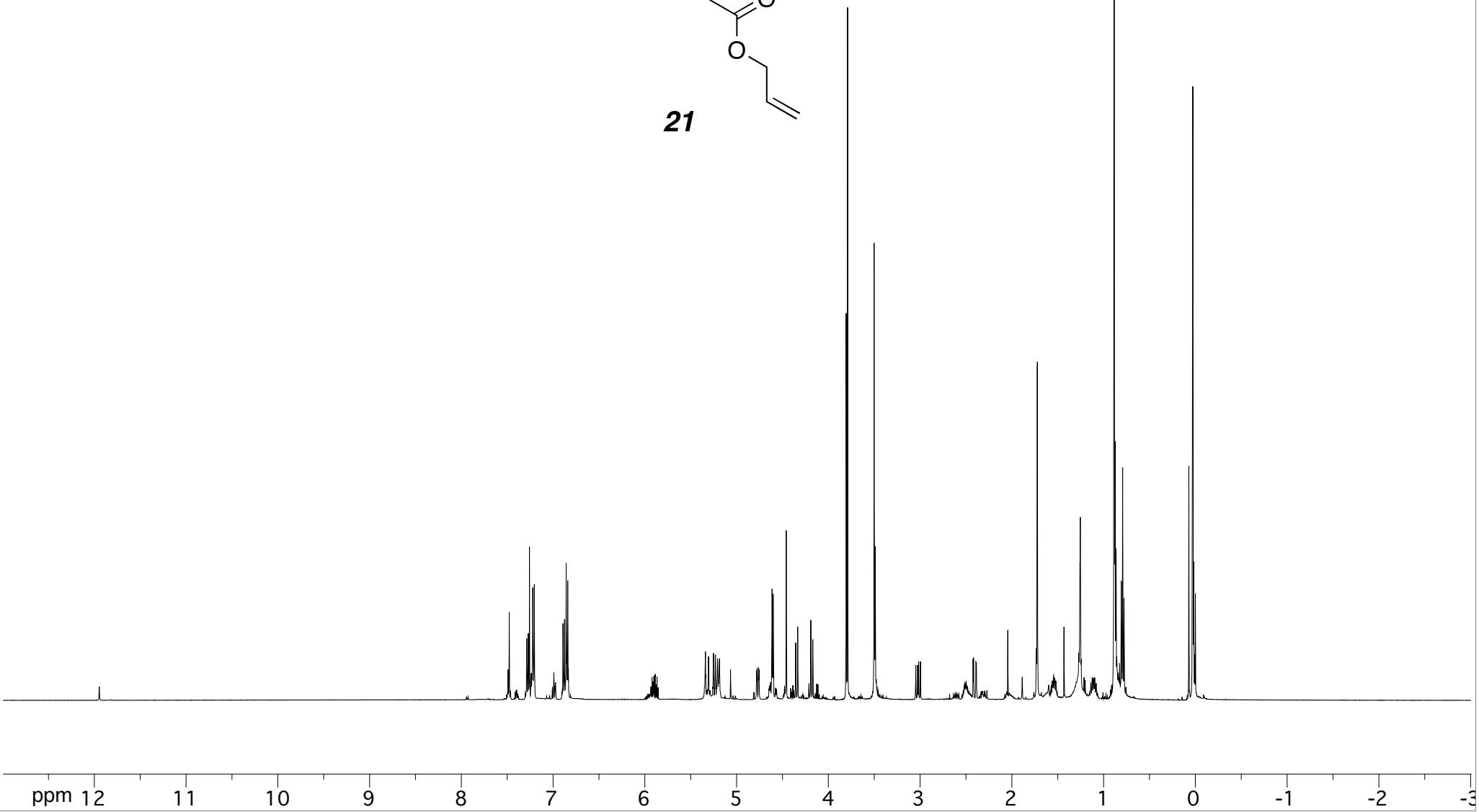

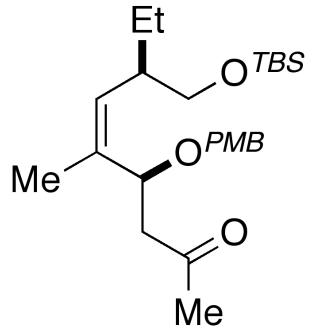

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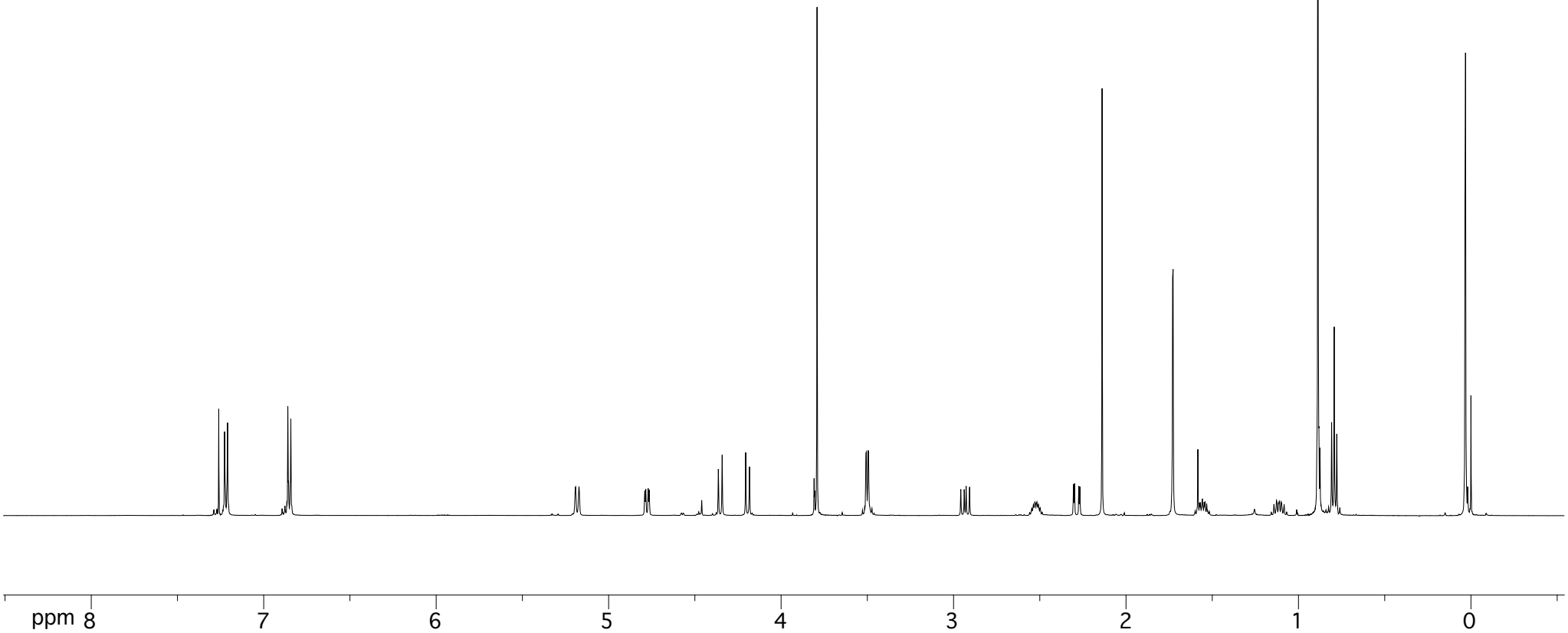
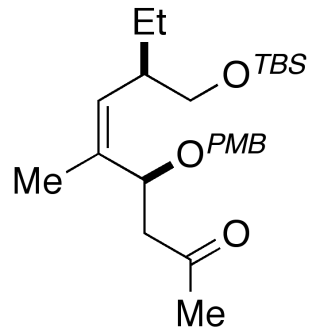
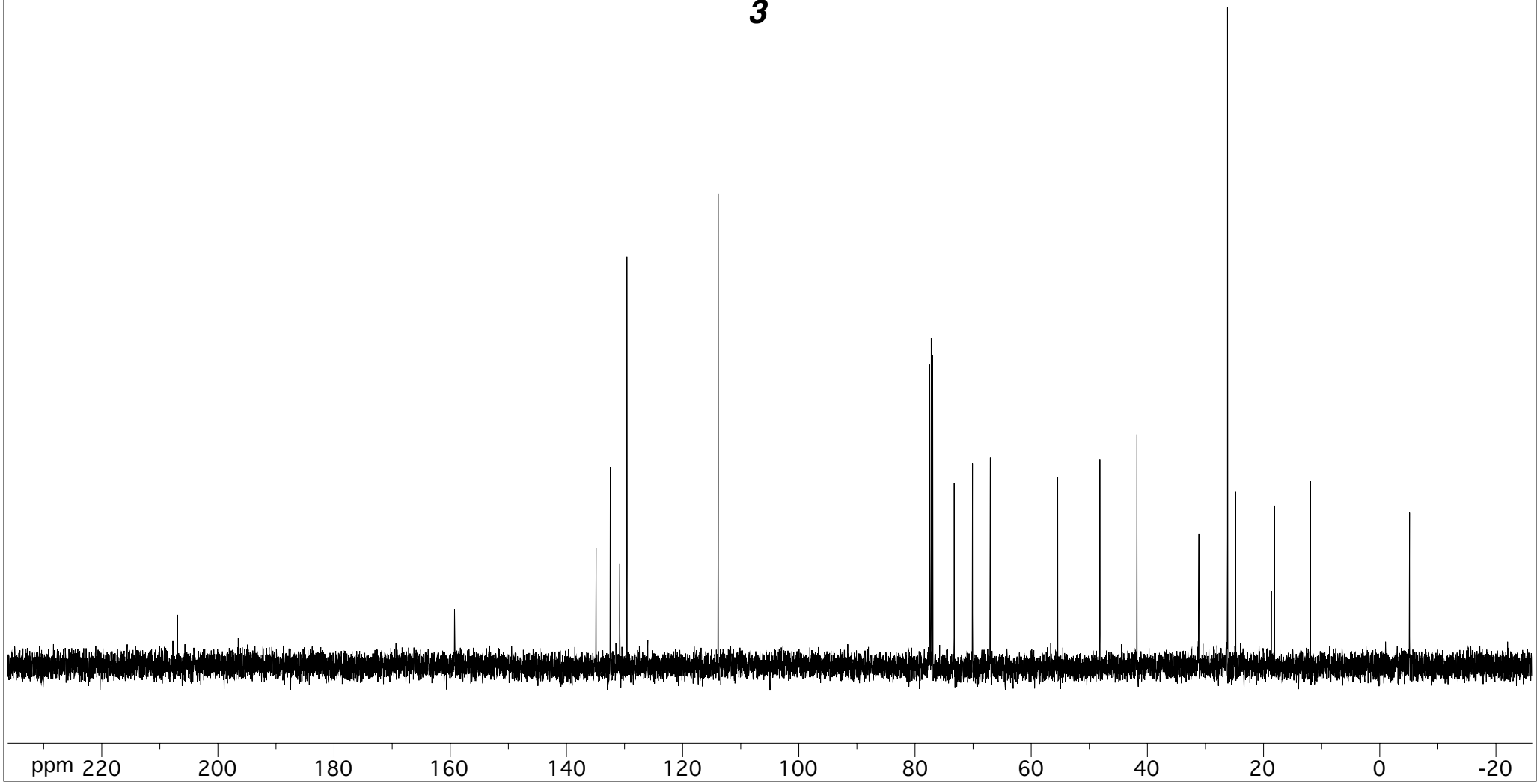



Et
O TBS
O PMB
Me
O
Me

3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100
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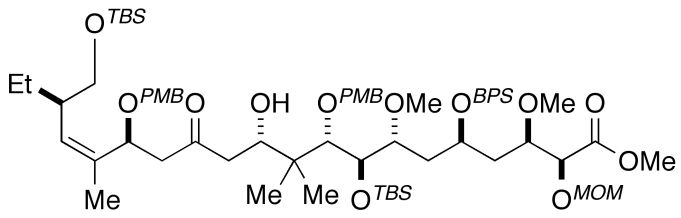
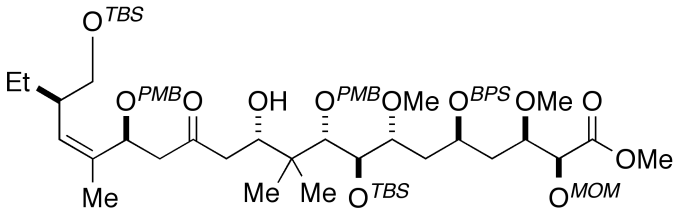
60
40
20
0
-20


O TBS
Et
O PMB O
OH
O PMB OMe O BPS OMe O
OMe
Me
Me Me O TBS
O MOM

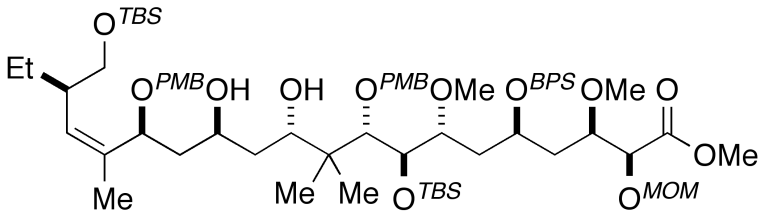
25

8
7
6
5
4
3
2
1
0


O TBS
Et
O PMB O
OH
O PMB OMe O BPS OMe O
OMe
Me
Me Me O TBS
O MOM

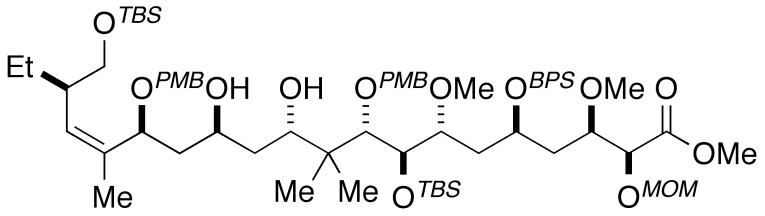
25

ppm 200
180
160
140
120
100
80
60
40
20
0


O TBS
Et
O PMB OH OH O PMB OMe O BPS OMe O
OMe
Me
Me Me O TBS
O MOM

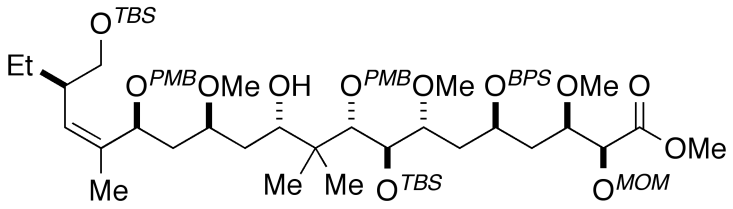
26

ppm 7
6
5
4
3
2
1
0


O TBS
Et
O PMB OH OH O PMB OMe O BPS OMe O
OMe
Me
Me Me O TBS
O MOM

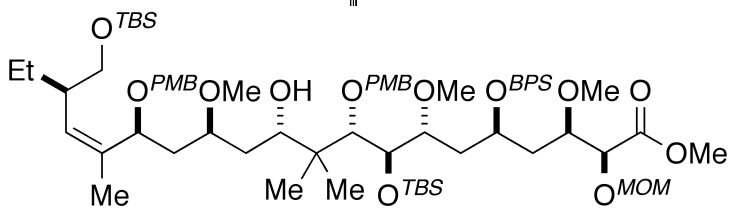
26

80 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -1


O TBS
Et
O PMB OMe OH
O PMB OMe O BPS OMe O
OMe
Me
Me Me O TBS
O MOM

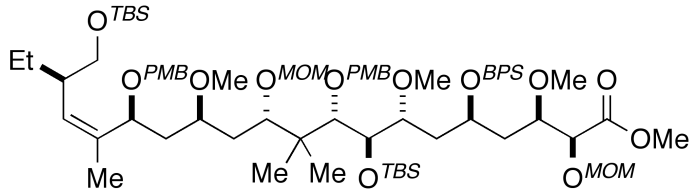
SI-40

8
7
6
5
4
3
2
1
0


O TBS
Et
O PMB OMe OH O PMB OMe O BPS OMe O
OMe
Me
Me Me O TBS
O MOM

SI-40

ppm 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0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Et
O PMB OMe O MOM O PMB OMe O BPS OMe O
OMe
Me
Me Me O TBS
O MOM

SI-41

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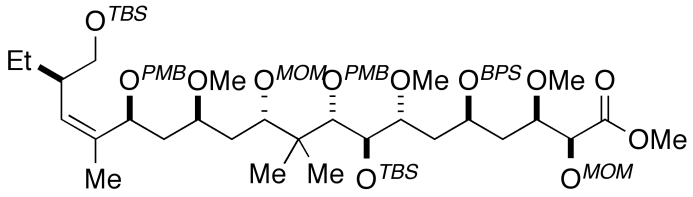
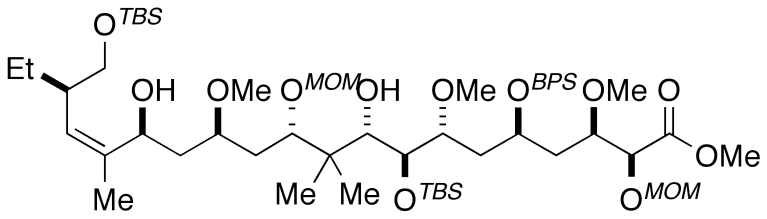
6
5
4
3
2
1
0


O TBS
Et
O PMB OMe O MOM O PMB OMe O BPS OMe O
OMe
Me
Me Me O TBS
O MOM

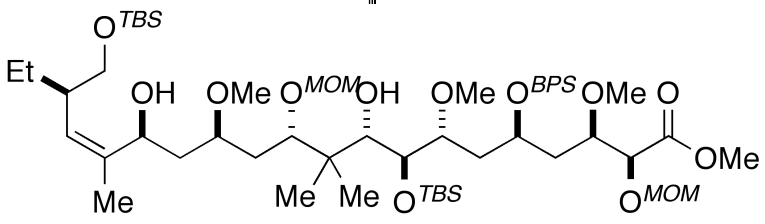
SI-41

ppm 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0


O TBS
Et
OH
OMe
O MOM
OH
OMe
O BPS
OMe
O
OMe
Me
Me
Me
O TBS
O MOM

27

ppm
7
6
5
4
3
2
1
0


O TBS
Et
OH
OMe
O MOM
OH
OMe
O BPS
OMe
O
OMe
Me
Me
Me
O TBS
O MOM

27

80
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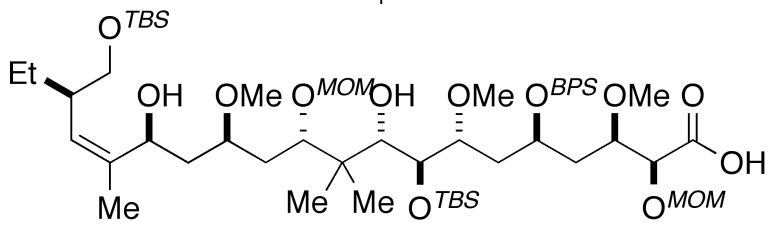
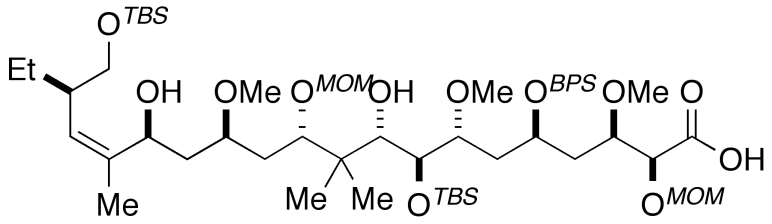
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-1


O TBS
Et
OH
OMe
O MOM
OH
OMe
O BPS
OMe
O
OH
Me
Me
Me
O TBS
O MOM

28

ppm
8
7
6
5
4
3
2
1
0


O TBS
Et
OH
OMe
O MOM
OH
OMe
O BPS
OMe
O
OH
Me
Me
Me
O TBS
O MOM

28

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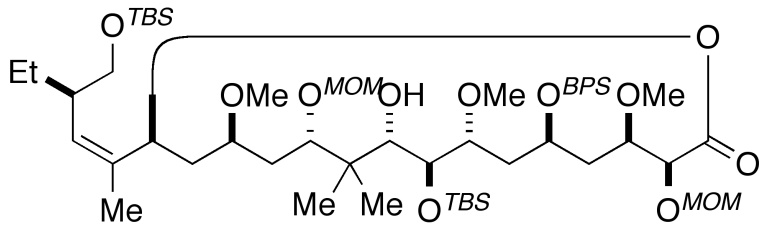
10
0
-1


O TBS
Et
O
OMe O MOM OH OMe O BPS OMe
O
Me
Me Me O TBS
O MOM

29

8
7
6
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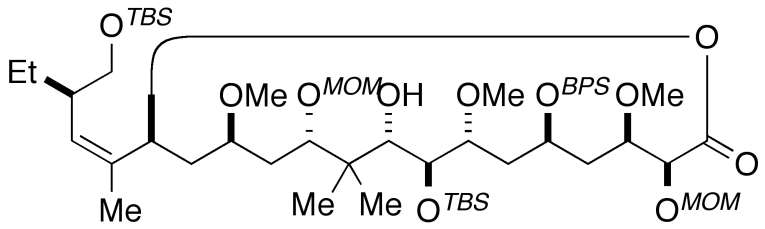
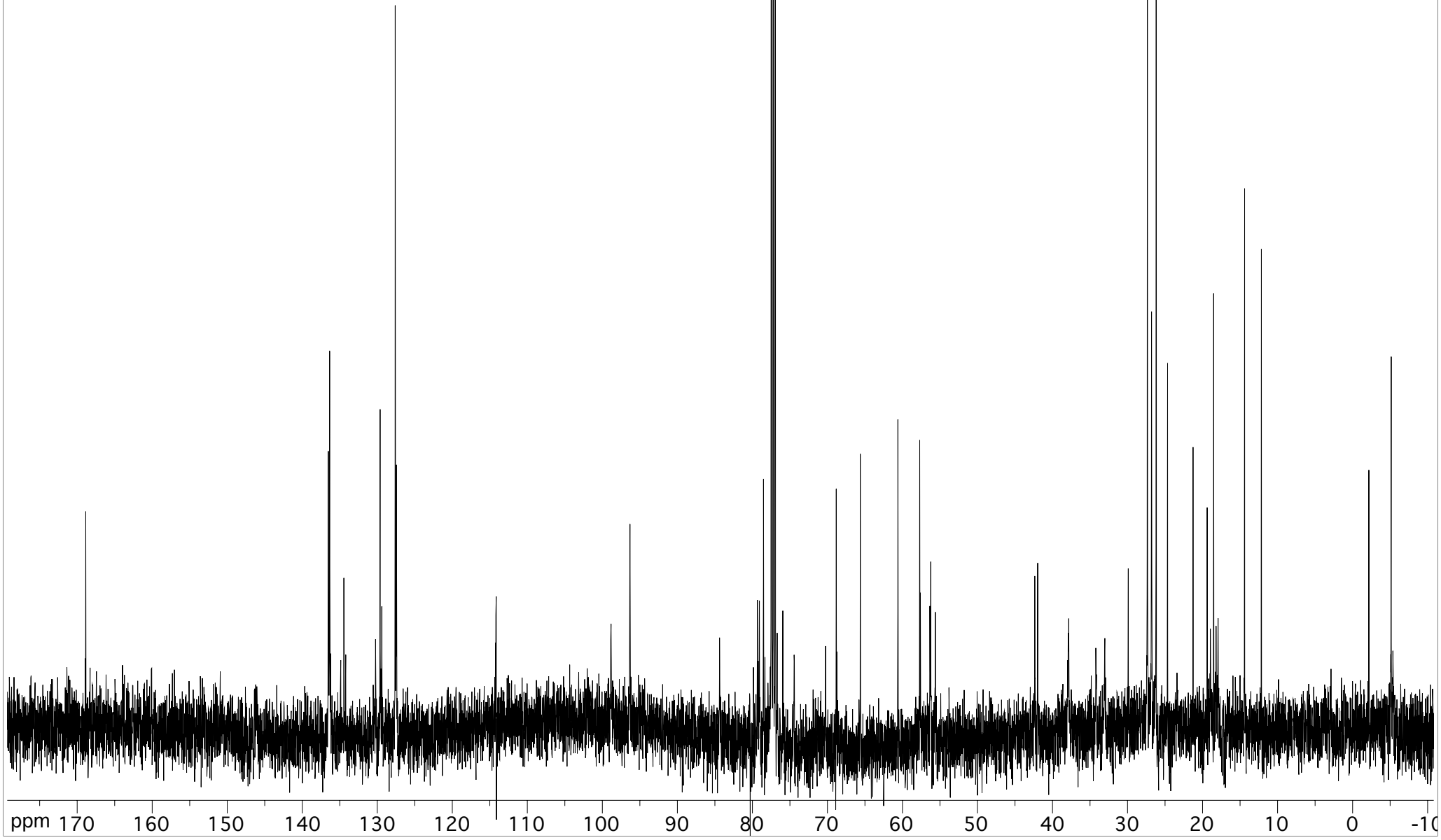
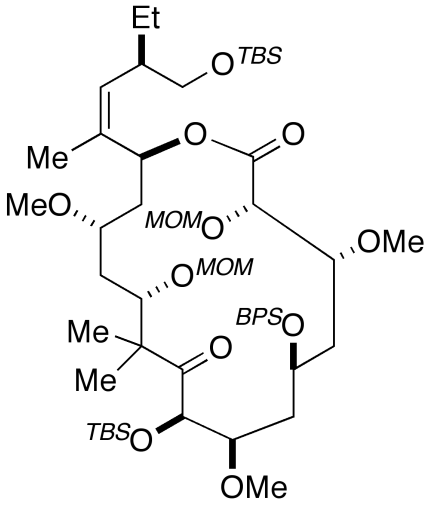
4
3
2
1
0

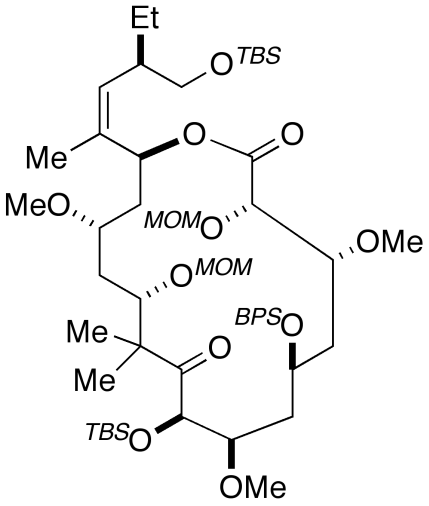

O TBS
Et
OMe O MOM OH OMe O BPS OMe
O
O
Me
Me Me O TBS
O MOM

29


ppm 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10

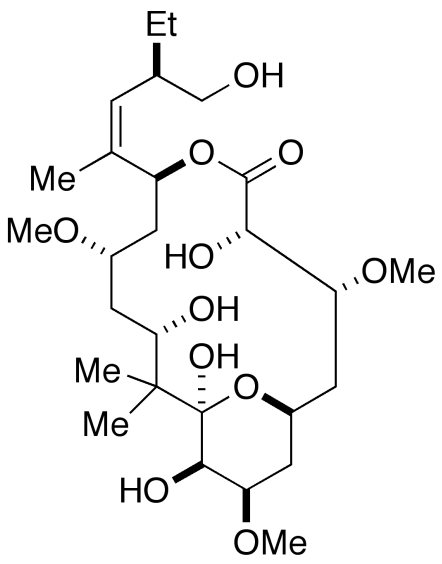


30


Et
O TBS
O
O
Me
MeO
MOM O
OMe
O MOM
BPS O
Me
O
Me
TBS O
OMe

30

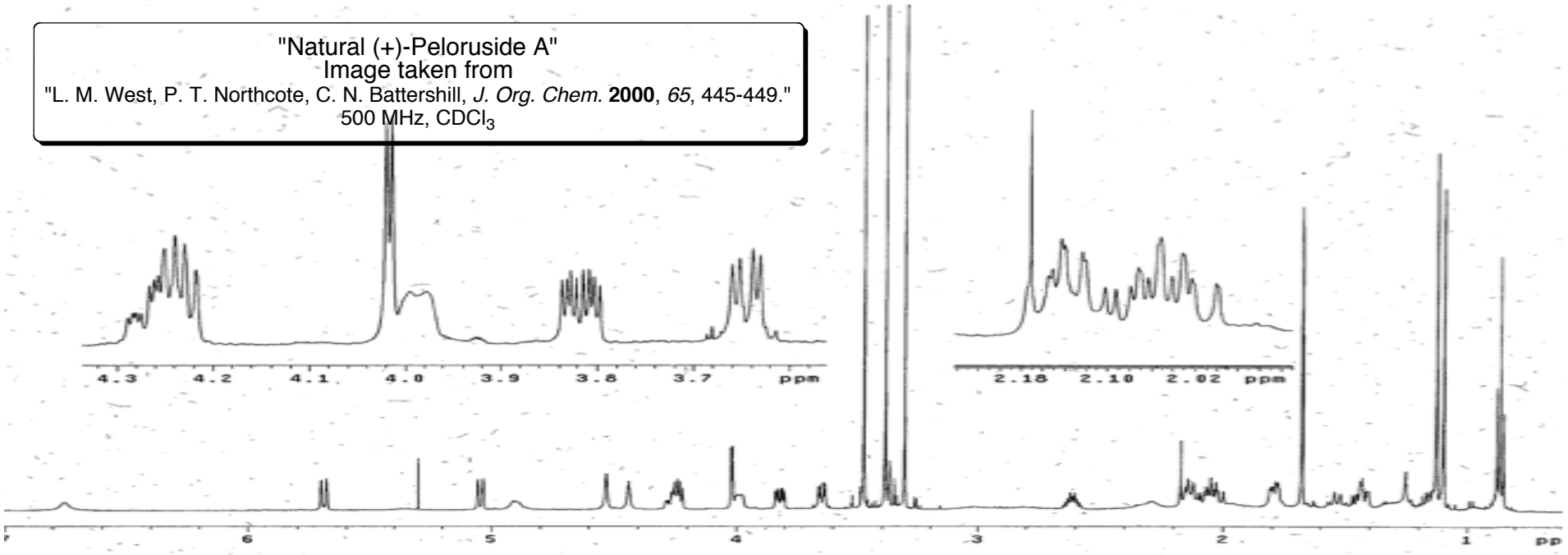
80
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-1



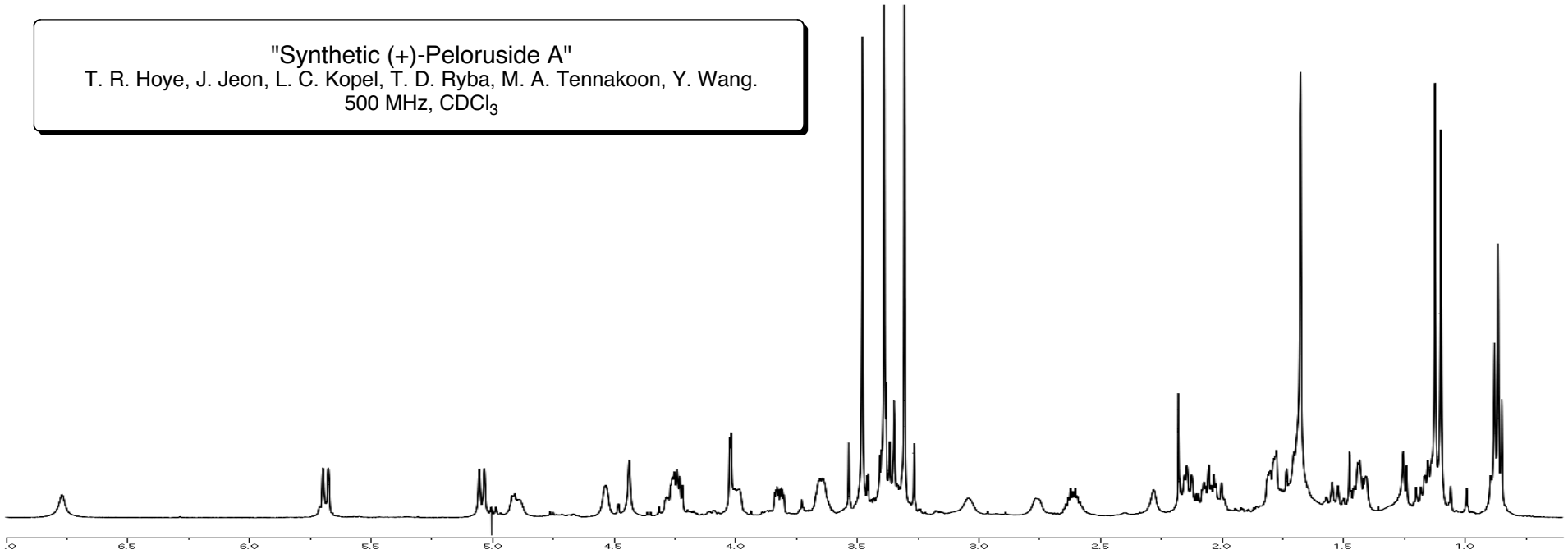
1

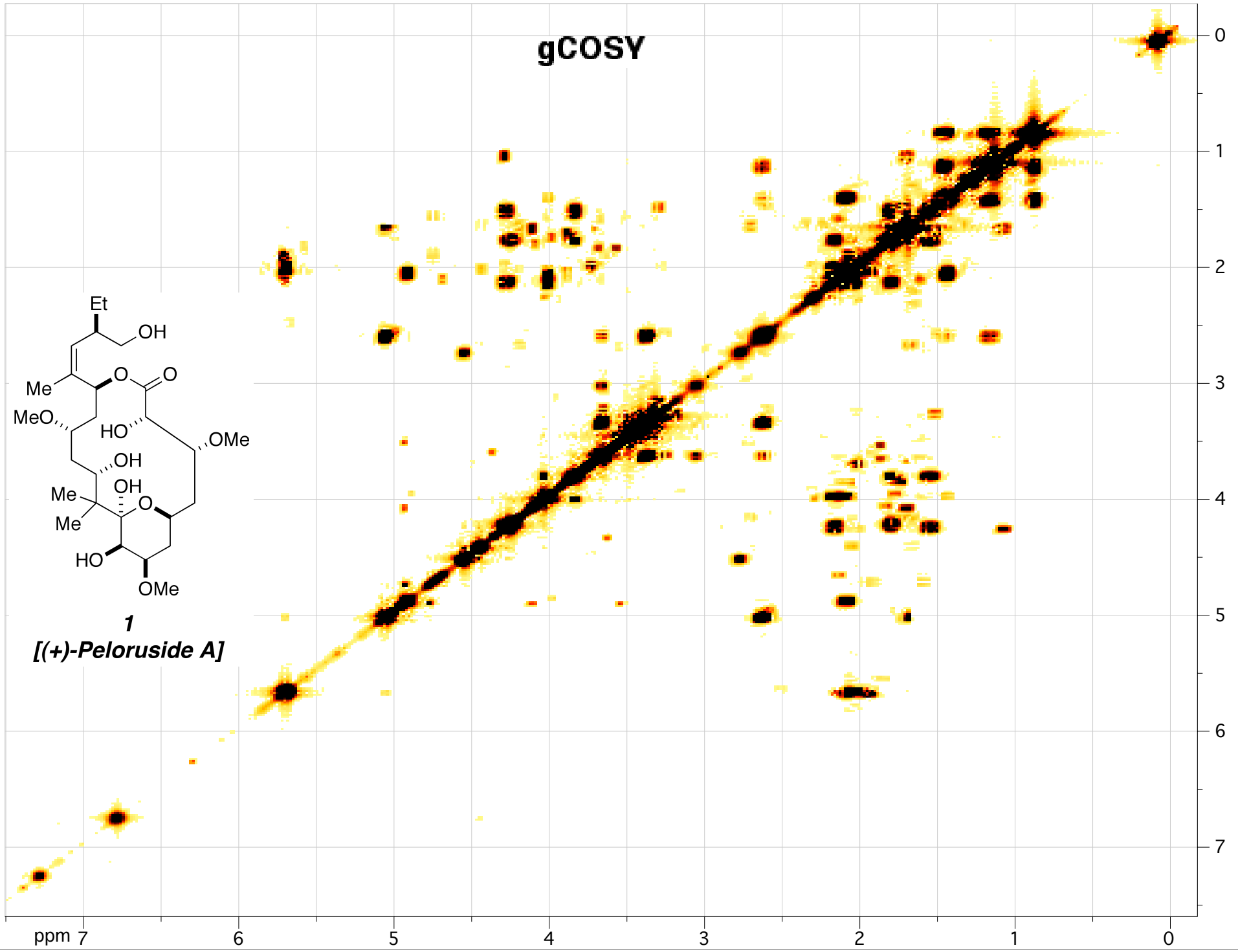
[(+)-Peloruside A]

"Natural (+)-Peloruside A"
Image taken from
"L. M. West, P. T. Northcote, C. N. Battershill, *J. Org. Chem.* **2000**, *65*, 445-449."
500 MHz, $CDCl_3$



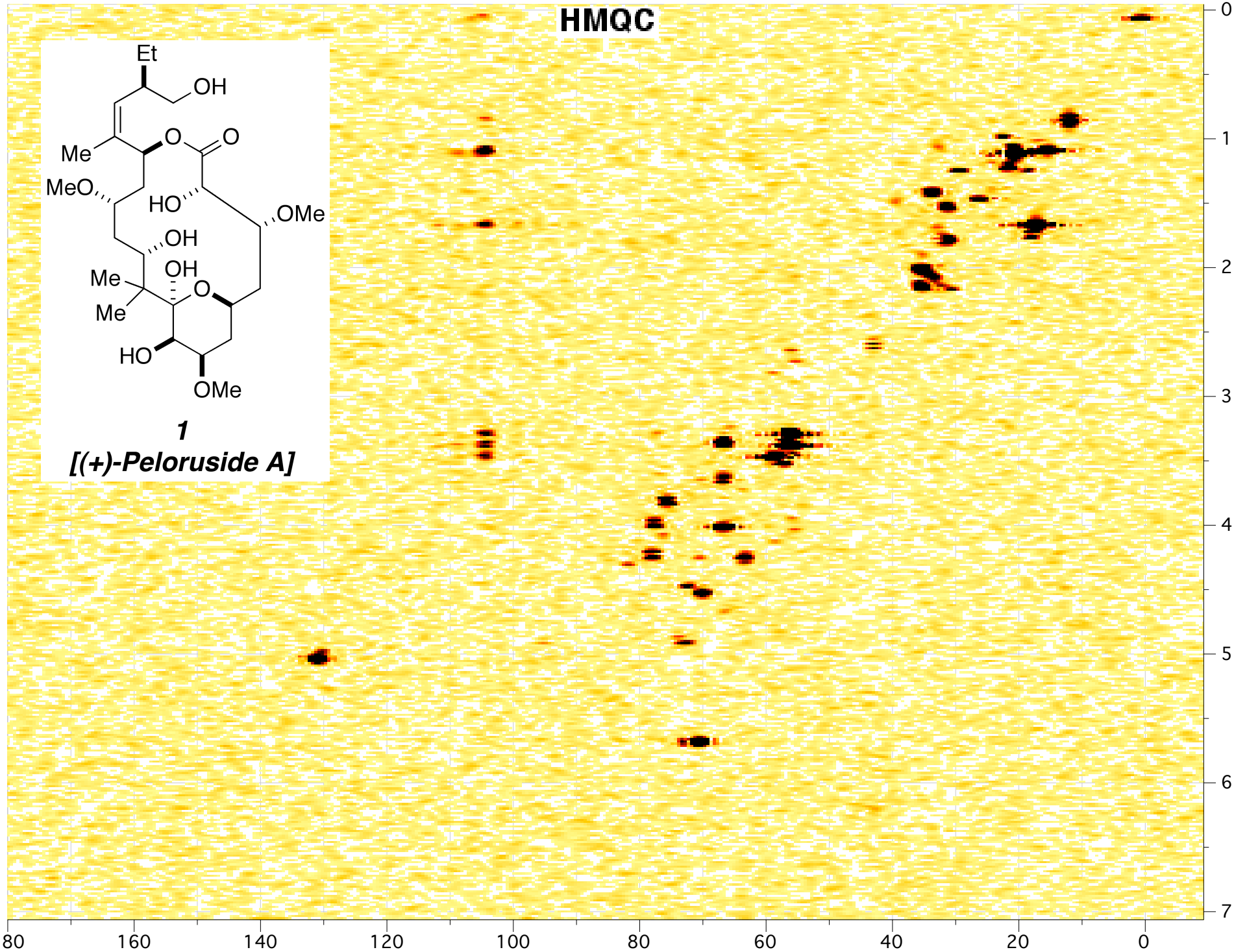
"Synthetic (+)-Peloruside A"
T. R. Hoye, J. Jeon, L. C. Kopel, T. D. Ryba, M. A. Tennakoon, Y. Wang.
500 MHz, $CDCl_3$

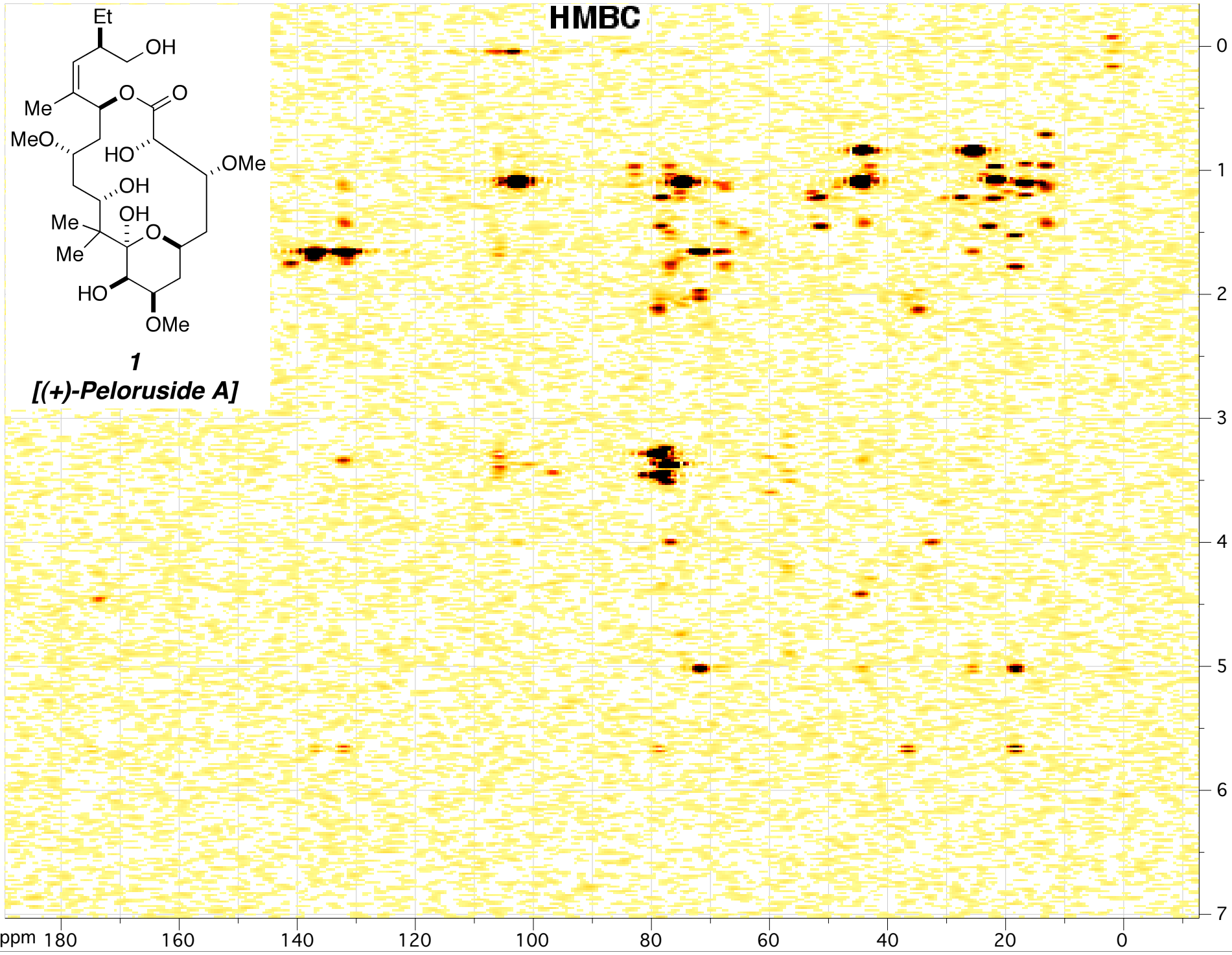


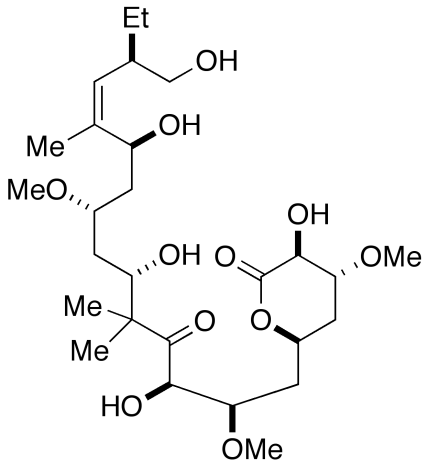


1

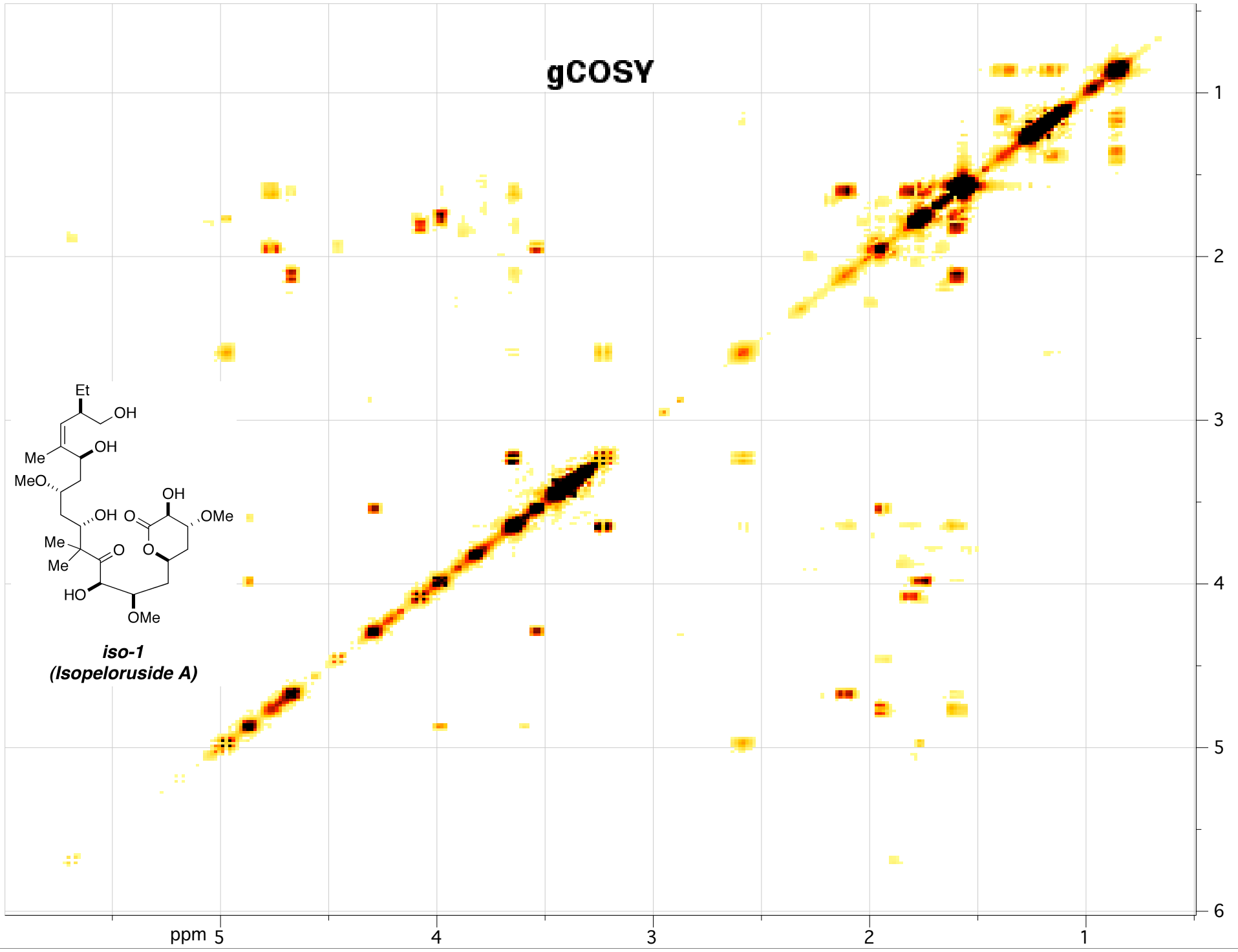
[(+)-Peloruside A]


HMQC
Et
OH
O
O
Me
MeO
HO
OMe
OH
OH
Me
O
Me
HO
OMe
1
[(+)-Peloruside A]
ppm
180
160
140
120
100
80
60
40
20
0
0
1
2
3
4
5
6
7


HMBC
Et
OH
O
O
Me
MeO
HO
OMe
OH
OH
Me
O
Me
HO
OMe
1
[(+)-Peloruside A]
ppm
180
160
140
120
100
80
60
40
20
0
0
1
2
3
4
5
6
7



iso-1
(Isopeloruside A)


gCOSY
Et
OH
Me
OH
MeO
OH
OH
O
OMe
Me
O
O
Me
HO
OMe
iso-1
(Isopeloruside A)
ppm
5
4
3
2
1
1
2
3
4
5
6