Total Synthesis of (–)-Lasonolide A

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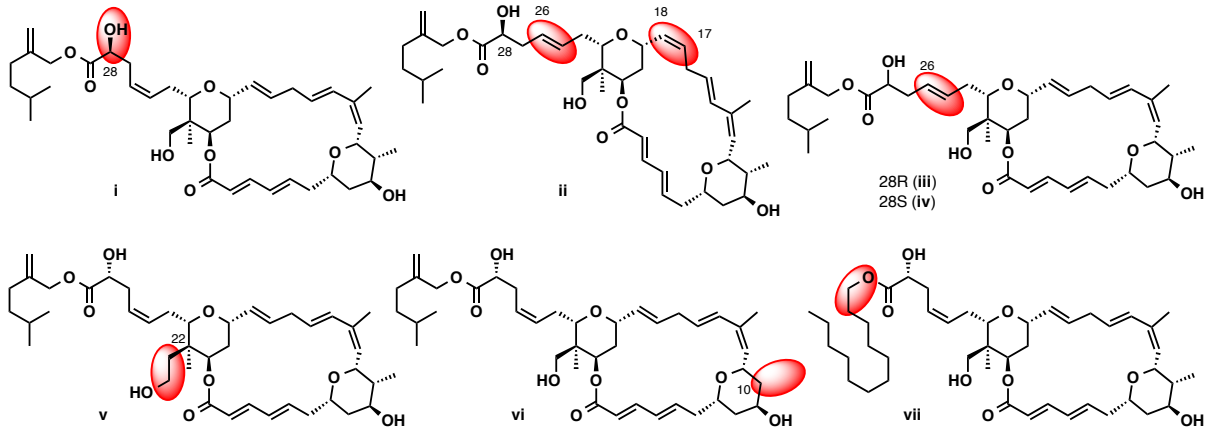
SUPPORTING INFORMATION

Table S1. Biological Activities of the Lasonolides and Analogs IC_{50} or GI_{50} (μM)

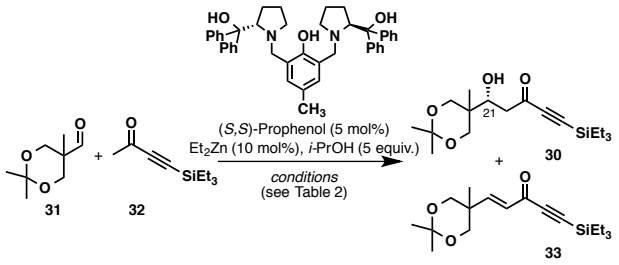


Entry	Structure	A-549	A-549	P388	PANC 1	NCI/ADR-RES	HCT-116	NCI-H460	ref
1	(–)-lasonolide A	0.0086	0.015	0.002	0.089	0.49	<0.003	<0.003	[1,2,3,4]
2	(+)-lasonolide A	-	6	-	-	-	3	2	[3]
3	lasonolide B	0.02	-	0.0004	-	-	-	-	[5]
4	lasonolide C	0.13	-	-	0.38	1.12	-	-	[2]
5	lasonolide D	4.5	-	-	4.89	>9	-	-	[2]
6	lasonolide E	0.31	0.007	-	0.57	>8	0.1	0.015	[2,4]
7	lasonolide F	>9	-	-	15.6	>9	-	-	[2]
8	lasonolide G	>6	-	-	>6	>6	-	-	[2]
9	i	-	2	-	-	-	0.04	0.02	[3]
10	ii	-	0.05	-	-	-	0.009	<0.003	[3]
11	iii	-	3.2	-	-	-	0.1	0.04	[3]
12	iv	-	>10	-	-	-	5	5	[3]
13	v	-	0.8	-	-	-	1.8	1	[4]
14	vi	-	0.1	-	-	-	0.045	0.065	[4]
15	vii	-	0.39	-	-	-	0.19	0.17	[4]

Table 1 summarizes known in vitro data for each analog (**i**–**vii**) as well as for lasonolides A-G.[5] In an effort to understand the structure activity relationships a rough comparison between the compounds can be deduced by analyzing the activities against the human lung carcinoma A-549 cell line. Firstly, the levorotatory and natural lasonolide A were significantly more active than the unnatural dextrorotatory compound (entries 1 and 2). Amongst the natural lasonolides (A-G), lasonolide A and B possessed the greatest cytotoxicity. Interestingly, lasonolide F, containing a carboxylic acid moiety at C28 was essentially inactive (entry 7). Taken together, these results imply that subtle structural differences in this portion of the molecule have dramatic effects on both potency and selectivity. For the synthetic analogs (entries 9-15) a 7-fold loss in potency was observed upon deleting the C10 methyl group (entry 14). Olefin geometries located at both the C17-C18 and C25-C26 positions had profound effects on activity. In each case where one of these geometries was altered (entries 9, 11, and 12) >100-fold loss of potency was observed. The geometric change at C17-C18 may indicate that a specific macrocyclic conformation may drive potency. Homologation of the C22 chain also significantly decreased potency by 50-fold. In this case, this decrease in potency could be the result of a change in small

molecule conformation or due to a disruption of a potential hydrogen bond critical for activity. Replacement of the C29 ester substituent to a lipophilic $C_{12}H_{25}$ chain (entry 15) also reduced activity, reinforcing the aforementioned hypothesis related to this portion of the molecule. Interestingly, it appears that the stereochemistry of the C28 alcohol has little influence on the overall biological activity, as the C28 epimer was only 3-fold less potent than lasonolide A.

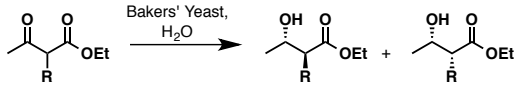
Table S2. Optimization Studies on the Asymmetric Aldol Reaction



Entry[a]	Conditions	Conv[b]	**30**[c]	ee[d]	**33**[c]
1	20 h, rt	ND	30%	ND	44%
2	20 h, 4°C	ND	56%	ND	27%
3	72 h, -20°C	84%	54%	99%	<10%
4[f]	72 h, -20°C	>90%	78%[e]	99%	ND

[a]Reactions were conducted using 1 equiv. of **31**, 3 equiv. **32**, and 1.5 equiv. by mass 4 Å MS, in THF (0.2 M). [b]Determined by ^{1}H NMR. [d]Yield determined by ^{1}H NMR using internal standard. [d]Determined by Chiral HPLC. [e]Isolated yield. [f]Work-up - direct filtration through celite. ND = not determined

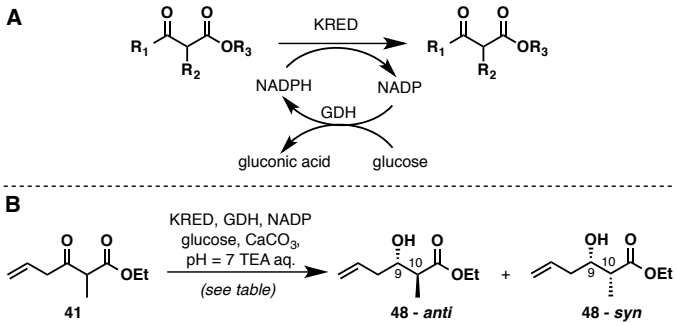
Table S3. Known Pre-treatment Effects on the Diastereoselectivity of Baker's Yeast Reductions



Entry	R	Cond. A[a,d]	Cond. B[b,d]	Cond. C[c,d]
1	Me	13 / 87	7 / 93	3 / 97
2	Et	34 / 66	20 /80	8 / 92
3	Pr	26 / 74	8 / 92	7 / 93
4	Allyl	70 / 30	35 / 65	4 / 96
5	Propargyl	34 / 66	14 / 86	6 / 94

[a] Cond. A: No Treatment. [b]Cond. B: 50 °C for 30 min. [c]Cond. C: 50°C for 30 min + MVK 60 mM. [d] ratio of *anti* (**50a**) : *syn* (**50b**).

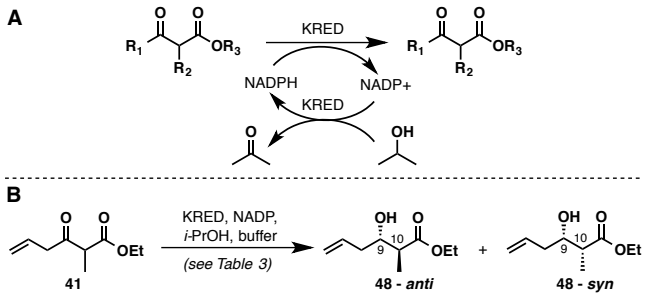
Table S4. Reduction with KRED with GDH as the Cofactor



Entry[a]	Enzyme	Time	Conv[b]	dr[c] (*anti*:*syn*)	ee (*anti*)[d]	ee (*syn*)[d]
1	KRH-CDX-006	3h	~95%	4 : 1	95%	>95%
2	KRH-CDX-009	20h	100%	1 : 2	-	-
3	KRH-CDX-012	20h	40%	1 : 1	-	-
4	KRH-CDX-016	20h	100%	2 : 1	-	-
5	KRH-CDX-041	20h	90%	1 : 1.5	>98%	89%

[a]Reactions were performed with 20 mg keto-ester, 10 mg of enzyme, 5 mg GDH in 1 mL 0.1 M triethanolamine pH = 7 aqueous buffer. [b]Conversion based on GC analysis of product / product + starting ketoester. [c]Based on GC analysis (*anti* : *syn*). [d]Favored enantiomer determined by conversion to known compounds (*vida infra)*.

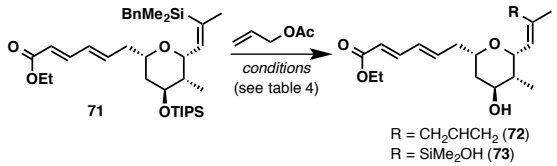
Table S5. Reduction with KRED with NADP as the Cofactor



Entry[a]	Enzyme	Buffer[b]	Time	Conv[c]	dr[d] (*anti*:*syn*)	ee (*anti*)[dfe]	ee (*syn*)[e,f]
1	CDX-001	**A**	3h	100%	1 : 1.5	>98%	84%
2	CDX-003	**A**	24h	~64%	2 : 1	-	-
3	CDX-008	**B**	4.5h	30%	1 : 1.9	-	-
4	CDX-019	**A**	24h	~50%	1.3 :1	-	-
5	CDX-022	**A**	24h	100%	1.3 :1	>98%	89%
6	CDX-023	**A**	24h	~90%	1.5 :1	-	-
7	**CDX-024**	**A**	**24h**	**100%**	**1 : 4**	**95%**	**>95%**
8	**CDX-024**	**B**	**68h**	**75%**	**1 : 4**	**>95%**	**>95%**
9	CDX-025	**A**	3h	~90%	1.4 : 1	80%	>98%
10	CDX-026	**A**	3h	~95%	1.4 : 1	91%	>98%
11	CDX-035	**B**	4.5h	37%	1 : 1.8	-	-
12	CDX-038	**A**	24h	100%	1.6 : 1	-	-
13	CDX-042	**B**	4.5h	40%	1 : 1.6	-	-
14	CDX-043	**B**	4.5h	37%	1 : 2	-	-
15	CDX-045	**A**	24h	75%	1 : 2.3	-	-
16	CDX-046	**B**	4.5h	8%	-	-	-
17	CDX-047	**B**	4.5h	53%	1 : 1.2	-	-
18	CDX-051	**B**	4.5h	9%	-	-	-
19	CDX-059	**B**	4.5h	51%	1 : 1.2	-	-
20	CDX-061	**B**	4.5h	39%	1 : 2	-	-
21	CDX-064	**B**	5h	62%	1 : 1.2	-	-
22	CDX-068	**B**	5.5h	87%	1 : 1.6	-	-
23	CDX-073	**B**	5.5h	75%	1 : 1.2	-	-
24	CDX-074	**B**	5.5h	81%	1 : 1.2	-	-
25	CDX-086	**B**	5.5h	39%	1 : 1.4	-	-
26	CDX-088	**B**	6h	79%	1 : 1.1	-	-
27	CDX-090	**B**	6h	56%	1 : 2.2	-	-
28	CDX-094	**B**	6h	55%	1 : 1.8	-	-
29	CDX-096	**B**	6h	19%	-	-	-
30	CDX-097	**B**	6h	71%	1 : 1.2	-	-

[a]Reactions were performed with 20 mg keto-ester, 5 mg of enzyme, 1 mg NADP in 0.5 mL IPA and 0.5 mL 0.1M buffer at ambient temperature. [b]**A:** TEA = triethanolamine; **B:** Phosphate (pH = 4.5). [c]Conversion based on GC analysis of product / product + starting ketoester. [d]Based on GC analysis (*anti* : *syn*). [e]Enantiomeric excess determined by Chiral cyclodex GC analysis. [f]Favored enantiomer determined by conversion to known compounds (*vida infra)*.

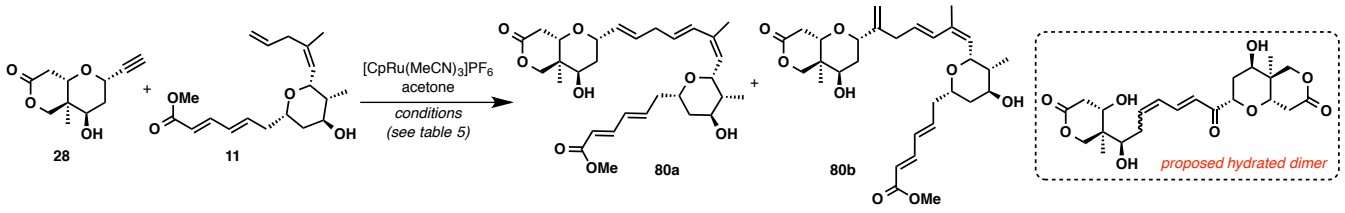
Table S6. Optimization Studies on the Hiyama Coupling



Entry[a]	Conditions	**72 : 73**	Yield
1	Pd_2dba_3•$CHCl_3$ (2 mol%), TBAF (4.2 equiv.) THF, 19h	1:1	75%[b]
2	Pd_2dba_3•$CHCl_3$ (4 mol%), TBAF (6.3 equiv.) THF, 3 d	1:1	44%[b]
3	Pd_2dba_3•$CHCl_3$ (10 mol%), TBAF (6.2 equiv.) THF, 18h	1:0	78%
4[c]	Pd_2dba_3•$CHCl_3$ (10 mol%), TBAF (6.3 equiv.) THF, 22h	1:0	85%

[a]All reactions were run using 8.0 equiv. allyl acetate, in THF (0.1 M) at rt. [b]Isolated as a mixture of **72** and **73**. [c]New bottle of TBAF solution.

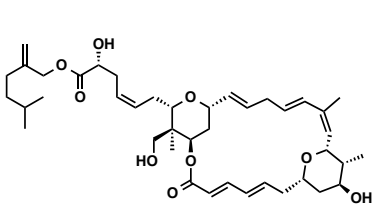
Table S7. Optimization Studies on the Intermolecular Ru-Catalyzed Alkene-Alkyne Coupling



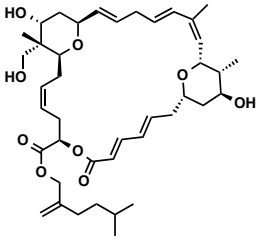
Entry [a]	**28** (equiv.)	**11** (equiv.)	Ru (mol%)	Temp (°C)	Time (h)	Conc. (M)	Conv. [b]	Yield [c]	**80a**:**80b**[b]
1	3	1	20	rt	1	0.06	50	N/A	2:1
2	3	1	20	rt/50	0.5/0.5	0.04	53	N/A	2:1
3	3	1	20	rt/50	0.25/0.75	0.02	70	N/A	2:1
4	3	1	20	rt/50	0.25/0.75	0.04	68	N/A	2:1
5	3	1	20	rt/50	0.25/0.75	0.12	35	31	2:1
6	3	1	60	rt/50	0.25/0.75	0.6	15	10	2:1
7	1	4.0	20	50	1	0.05	100	52	2:1
8	1	3.0	10	50	2.5	0.094	100	66	2:1

[a]All reactions were run under an atmosphere of nitrogen or argon using dry and degassed solvents. [b]Determined by ^{1}H NMR. [c]Isolated yield of the combined linear and branched isomers.

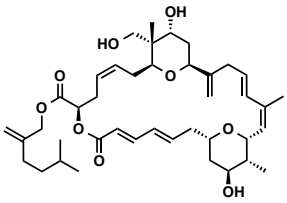
Table S7. Biological Testing of (–)-Lasonolide A and Analogs IC_{50} (nM)



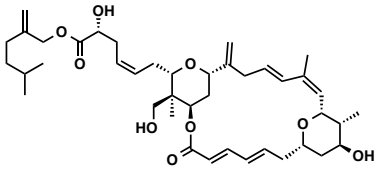
(–)-lasonolide A (1)



104



105



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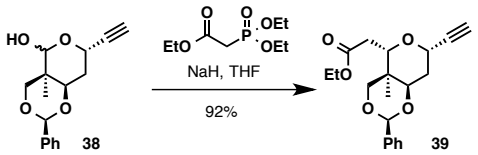
Cell Line	(–)-lasonolide A	**106**	**104**	**105**	Paclitaxel
A2058	16.6	>1000	>1000	>1000	2.6
Adr-Res	414.1	>1000	>1000	>1000	>100
BXPC3	148.1	>1000	>1000	>1000	10.6
DU145	29.2	>1000	>1000	>1000	6.0
HCT116	9.8	>1000	12.0	10.0	0.14
H460	20.7	>1000	>1000	>1000	6.3
MCF7	47.4	>1000	>1000	>1000	30.0
SK-BR-3	40.2	>1000	>1000	>1000	6.6
KPL-4	39.4	343.9	>1000	>1000	5.9

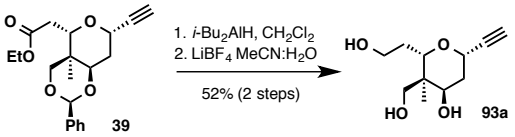
EXPERIMENTAL PROCEDURES

General methods. All reactions were carried out under an argon (for Pd-catalyzed reactions) or nitrogen atmosphere. All reagents were obtained commercially unless otherwise noted. Reactions were performed using glassware that was flame-dried under vacuum (~1 Torr). Air- and moisture-sensitive liquids and solutions were transferred via syringe or stainless steel cannula. Organic solutions were concentrated under reduced pressure (~15 Torr) by rotary evaporation. Solvents were purified by passage under 12 psi N_2 through activated alumina columns. Flash chromatography was performed with 0.040-0.063 μm Silica Gel. Compounds purified by chromatography were typically applied to the adsorbent bed using the indicated solvent conditions with a minimum amount of added dichloromethane as needed for solubility. Thin layer chromatography was performed on Whatman Partisil K6F Silica Gel 60 Å plates (250 μm). Visualization of the developed chromatogram was accomplished by fluorescence quenching or by staining with p-anisaldehyde, ninhydrin, or aqueous potassium permanganate. Nuclear magnetic resonance (NMR) spectra were acquired on either a Varian Mercury - 400 operating at 400 and 100 MHz, Varian Inova - 500 operating at 500 and 125 MHz, or Inova – 600 operating at 600 and 150 MHz for ^{1}H and ^{13}C, respectively, and are referenced internally according to residual solvent signals. Data for ^{1}H NMR are recorded as follows: chemical shift (δ, ppm), multiplicity (s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet), coupling constant (Hz), and integration. Data for ^{13}C NMR are reported in terms of chemical shift (δ, ppm). Infrared spectra were recorded on a Perkin Elmer Paragon 500 FT-IR spectrometer as thin films using NaCl or KBr salt plates and are reported in frequency of absorption. High performance liquid chromatography (HPLC) was performed on an Agilent Technologies 1200 series using Chiralcel columns. Optical rotations were measured on a Jasco DIP-1000 digital polarimeter using 5 cm glass cells with a Na 589 nm filter. High-resolution mass spectra were obtained from the Vincent Coates Foundation Mass Spectrometry Laboratory at Stanford University.



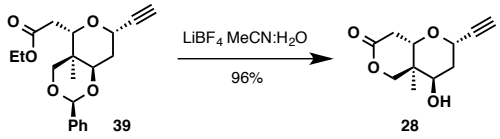
Ester 39. Triethylphosphonoacetate (3.36 mL, 16.95 mmol) was added carefully to a suspension of sodium hydride (washed with hexanes, 0.610 g, 15.26 mmol) in THF (30 mL) at 0 °C. The reaction was stirred for 5 min and then was warmed to rt and stirred for an additional 30 min (reaction should be clear). Lactol **38** (0.465 g, 1.69 mmol) in THF (12 mL total with rinses) was added and the reaction was then heated at 55 °C for 15 h. The reaction was cooled to rt and diluted with water and ethyl acetate. The aqueous layer was extracted with ethyl acetate (4 x 100 mL). The combined organic layers were washed with brine, dried with sodium sulfate, concentrated, and the residue was purified by flash column chromatography (silica, 10% → 25% ethyl acetate – hexanes) to give the desired product (0.533 g, 1.55 mmol, 92% yield). $[\alpha]_D^{23}$ -30 (*c* 0.61, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.53-7.50 (m, 2H), 7.42-7.34 (m, 3H), 5.52 (s, 1H), 4.84 (dd, J = 8.4, 4.4 Hz, 1H), 4.65 (dt, J = 12.0, 2.4 Hz, 1H), 4.21-4.14 (m, 2H), 3.91-3.87 (m, 2H), 3.54 (d, J = 14.4, 1H), 2.51 – 2.46 (m, 2H), 2.42 (d, J = 2.0 Hz, 1H), 2.17 (1H, ddd, J = 14.4, 12.0, 2.8 Hz), 1.96 (dt, J = 14.4, 2.8 Hz, 1H), 1.27 (t, J = 7.2 Hz, 3H), 0.87 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ (ppm): 171.16, 137.90, 129.19, 128.37, 126.23, 102.05, 82.60, 78.98, 73.08, 73.01, 72.87, 63.46, 60.65, 35.14, 34.49, 34.30, 14.39, 14.17. IR (KBr-film) ν (cm^{-1}): 2921,

2855, 1732, 1463, 1392, 1366, 1343, 1308, 1287, 1264, 1224, 1187, 1145, 1101, 1074, 1028. HRMS: (EI) calcd for $C_{20}H_{24}O_5$ $[M-H]^+$: 343.1543, found: 343.1545.

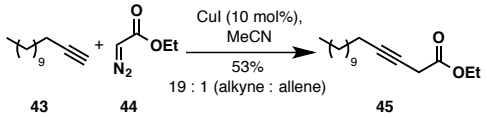


Triol 93a. Diisobutylaluminum hydride (1.2 M in toluene, 1.45 mL, 1.74 mmol) was added drop-wise to a solution of the ester **39** (0.150 g, 0.436 mmol) in dichloromethane (8.7 mL) at -78 °C. The reaction was warmed from -78 °C to rt over 1 h. Then a saturated aqueous solution of Rochelle's salts was added carefully and reaction was allowed to stir vigorously for 1 h. The reaction was diluted with water and dichloromethane. The aqueous layer was extracted dichloromethane (4 x 40 mL). The combined organic layers were dried with sodium sulfate, concentrated, and the residue was submitted to the next reaction without further purification

Lithium tetrafluoroborate (62 mg, 0.662 mmol) was added to a solution of the crude residue in acetonitrile (1.3 mL) and water (70 μL). The reaction was heated at 90 °C for 2 h. The reaction was cooled to rt and a saturated aqueous solution of sodium bicarbonate was added. The aqueous layer was extracted with dichloromethane (5 x 20 mL). The combined organic layers were dried with sodium sulfate, concentrated, and the residue was purified by flash column chromatography (silica, 50% → 80% → 100% ethyl acetate – hexanes) to give the desired product (49 mg, 0.229 mmol, 52% yield). $[\alpha]_D^{24}$-73.8 (*c* 1.0, CH_2Cl_2). ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 4.69 (bs, 1H), 4.62 (ddd, J = 12.0, 2.0, 2.0 Hz, 1H), 4.19 (dd, J = 10.0, 2.0 Hz, 1H), 3.91 (bs, 1H), 3.84 – 3.76 (m, 2H), 3.63 (d, J = 12.0 Hz, 1H), 3.56 (d, J = 12.0 Hz, 1H), 2.47 (d, J = 2.0 Hz, 1H), 2.09 – 2.03 (m, 1H), 1.78 – 1.74 (m, 1H), 1.72 – 1.58 (m, 2H), 0.79 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ (ppm): 83.1, 74.6, 73.1, 73.1, 69.6, 62.9, 60.2, 39.7, 36.8, 31.3, 15.1. IR (KBr-film) ν (cm^{-1}): 3251, 2919, 2892, 2846, 1411, 1371, 1317, 1024. HRMS: (ESI) calcd for $C_{11}H_{18}O_4Na$ $[M+Na]^+$: 237.1097, found: 237.1102.



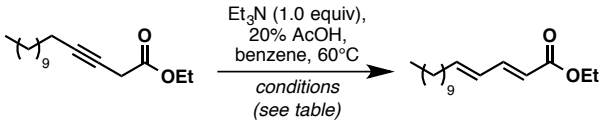
Lactone 28. Lithium tetrafluoroborate (0.610 g, 6.50 mmol) was added to a solution of ester **39** (0.160 g, 0.465 mmol) in acetonitrile (4.65 mL) and water (0.23 mL). The reaction was heated at 90 °C for 3 h. The reaction was cooled to rt and a saturated aqueous solution of sodium bicarbonate was added. The aqueous layer was extracted with dichloromethane (5 x 40 mL). The combined organic layers were dried with sodium sulfate, concentrated, and the residue was purified by flash column chromatography (silica, 20% → 50% → 80% → 100% ethyl acetate – hexanes) to give the desired product (93 mg, 0.446 mmol, 96% yield). $[\alpha]_D^{27}$-78 (*c* 1.0, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 4.66 (m, 1H), 4.44 (dd, 1H, *J* = 11.2, 0.8 Hz), 4.18 (dd, 1H, *J* = 11.6, 6.8 Hz), 3.97 (d, 1H, *J* = 11.2 Hz), 3.87 (t, 1H, *J* = 2.8 Hz), 2.93 (ddd, 1H, *J* = 18.0, 6.8, 0.8 Hz), 2.55 (dd, 1H, *J* = 18.4, 11.6 Hz), 2.53 (d, 1H, *J* = 2.0 Hz), 2.28 (ddd, 1H, *J* = 14.8, 12.4, 2.4 Hz), 1.82 (ddd, 1H, *J* = 14.8, 3.2, 3.2 Hz), 1.11 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 169.4, 81.8, 73.7, 73.1, 69.3, 68.6, 62.6, 36.5, 36.3, 33.6, 13.8. IR (KBr-film) ν (cm^{-1}): 3418, 3294, 2919, 1715, 1380, 1338, 1247, 1090, 1060, 999. HRMS: (ESI) calcd for $C_{11}H_{14}O_4Na$ $[M+Na]^+$: 233.0790, found: 233.0787.



43 44 45

Ester 45. The cross coupling procedure developed by Fu et al.[6] Tridecyne (5.0 g, 6.4 mL, 28 mmol) and ethyl diazoacetate (3.2 g, 2.9 mL, 28 mmol) were simultaneously added to a solution of copper iodide (0.270 g, 1.4 mmol) in anhydrous acetonitrile (40 mL). The resulting gently bubbling mixture was stirred at rt for 22 h. GC analysis shows approximately 60% conversion, which does not improve with time. The reaction was concentrated, and the residue was purified by flash column chromatography (silica, 1 → 2.5% ether in petroleum ether) to provide the desired product (53%) as a ~ 97.5 : 2.5 ratio of alkyne to allene as determined by ^{1}H NMR. ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 4.19 (q, J = 7.0 Hz, 2H), 2.24 (t, J = 1.5 Hz, 2H), 2.19 (tt, J = 6.9, 2.5 Hz, 2H), 1.50 (ddd, J = 15, 6.8, 6.8 Hz, 2H), 1.40-1.22 (m, 20H), 0.88 (t, J = 7.0 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ (ppm): 168.99, 83.61, 71.36, 61.37, 31.88, 29.60, 29.50, 29.32, 29.13, 28.83, 28.66, 26.07, 22.65, 18.74, 14.09. IR (KBr-film) ν (cm^{-1}): 2926, 2855, 1747, 1466, 1405, 1368, 1330, 1302, 1260, 1178, 1032, 722. HRMS: (EI) calcd for $C_{17}H_{30}O_2$ 266.2246 found 266.2247.

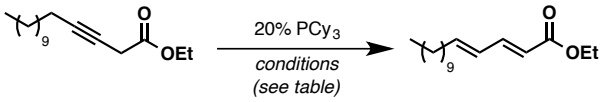
Phosphine Catalyst Optimization for the Isomerization of β-Ynoates to Dienoates



Entry[a]	*Addative*[b]	*conversion at 1h*[c]	*yield at 2d*[d]
1	none	0%	0%
2	20% DMAP	0%	decomp.
3	20% PPh_3	50%	81%
4	20% $P(o\text{-}MeOPh)_3$	71%	82%
5	20% $P(p\text{-}MeOPh)_3$	50%	73%
6	20% PPh_2Me	57%	84%
7	**20% PCy_3**	**72%**	**94%**
8	10% dppb	48%	82%

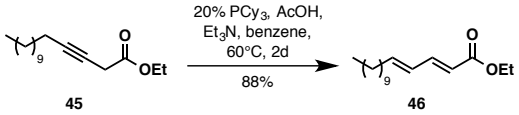
[a]Reactions conducted in benzene (0.2M) at 60°C for 2 days. [b]Equivalent to alkyne. [c]Conversion determined by GC relative product to staring alkyne. [d]Yield determined by ^{1}H NMR of pured dienoate.

Optimization of the Reaction Conditions for the Isomerization of Ynoate



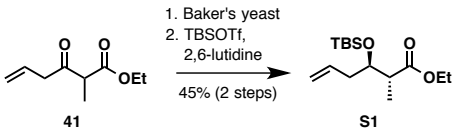
Entry[a]	Solvent	Et_3N[b]	AcOH[b]	Temperature	Time[c]	Yield[d]
1	benzene	1 equiv.	20%	80°C	24 h	97% (88%)[e]
2	benzene	40%	20%	80°C	24 h.	83%
3	MeCN	40%	20%	80°C	0.5 h	64%
4	MeCN	1equiv	20%	80°C	2.5 h	70%

[a] Reaction conducted in the indicated solvent (0.2M). [b] Equivalent to alkyne. [c] Time required for complete consumption of starting alkyne. [d] Yield determined by ^{1}H NMR of pure dienoate. [e] Isolated yield.



Dienoate 46. Tricyclohexylphosphine (22 mg, 76 μmol) was added to a solution of ester **45** (100 mg, 0.38 mmol), acetic acid (4.6 μL, 76 μmol) and triethylamine (50 μL, 0.38 mmol) in anhydrous benzene (2 mL). The reaction was stirred at 80°C under nitrogen for 1 d. The reaction was cooled to rt, concentrated and the residue was purified by flash column chromatography (silica, 5% ether in petroleum ether) to provide desired product (88 mg, 88%) %) with NMR Spectra corresponding to literature.[7] ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 7.26 (dd, J = 15.6, 8.0 Hz, 1H), 6.19-6.09 (m, 2H), 5.78 (d, J = 15.5 Hz, 1H), 4.20 (q, J = 7.5 Hz, 2H), 2.16 (q, J = 7.0 Hz, 2H), 1.43-1.26 (m, 19H), 0.88 (t, J = 7.5 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ (ppm): 167.31, 145.10, 144.78, 128.28, 119.09, 60.13, 32.98, 31.88, 29.57, 29.54, 29.41, 29.30, 29.15, 28.69, 22.66, 14.29, 14.09. IR (KBr-film) ν (cm^{-1}): 2925, 2855, 1716, 1644, 1618, 1466, 1368, 1303, 1258, 1191, 1138, 1038, 1000. HRMS: (EI) calcd for $C_{17}H_{30}O_2$ 266.2246 found 266.2237.

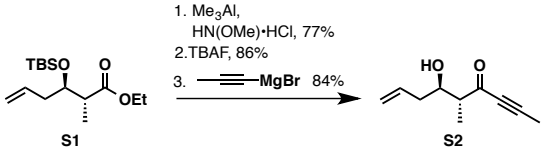
Baker's Yeast Reduction of β-Ketoester



Ester S1. Methylvinyl ketone (47 μL) was added to a suspension of Baker's yeast (11.8 g) in water (125 mL), and the suspension was stirred at 37 ºC for 30 min at which point dextrose (0.500 g) was added to the reaction. After another 10 min of stirring, keto-ester **41** (0.500 g, 2.9 mmol) was added to the yeast mixture. The gently bubbling mixture was stirred at 37 ºC for 2 d and dextrose (0.500 g) was added approximately every 12 h. The mixture was diluted with diethyl ether (100 mL) and water (500 mL). The mixture was sonicated for 1 – 2 h until the layers separated. The layers were separated, and the aqueous portion was extracted with diethyl ether (3 x 100 mL). The combined organic layers were dried with magnesium sulfate, passed through a plug of silica (eluting with diethyl ether 200 mL), and concentrated to provide the crude β – hydroxyl-ester (~0.400 g), which was used in the next step without further purification. ^{1}H NMR analysis shows 10 : 1 diastereoselectivity. Chiral cyclodex GC (105ºC to 90ºC by 1ºC / min) shows ~30% ee in favor of 17.40 over 17.90 min. ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 5.95–5.79 (m, 1H), 5.19–5.09 (m, 2H), 4.18 (qd, J = 7.1, 0.6 Hz, 2H), 3.76 (ddd, J = 7.5, 6.7, 4.4 Hz, 1H), 2.56 (quintet, J = 7 Hz, 1H), 2.32–2.42 (m, 1H), 2.27–2.17 (m, 1H), 1.28 (t, J = 7.2 Hz, 3H),

1.2 (m, 3H).

tert-Butyldimethylsilyl triflate (0.680 mL, 2.9 mmol) was added to a solution of the crude residue and 2,6-lutidine (0.380 mL, 3.2 mmol) in dichloromethane (5 mL) under nitrogen at -78ºC. The reaction was stirred for 30 min allowing the reaction to warm to -20ºC at which point all of the starting alcohol was consumed. The reaction was diluted with diethyl ether (100 mL). The organic layer was washed with phosphate buffer (0.5 M, pH=5, 3 x 50 mL), brine (1 x 50 mL), dried with magnesium sulfate, concentrated, and the residue was purified by flash column chromatography (silica, 3% diethyl ether in petroleum ether) to provide the desired product (0.380 g, 45% over 2 steps). $[\alpha]_D^{25}$-19 (*c* 0.72, $CHCl_3$, ~30% ee). ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 5.89 - 5.79 (m, 1H), 5.08 - 5.03 (m, 2H), 4.14-4.06 (m, 2H), 3.97 (dt, J = 7.0, 4.9 Hz, 1H), 2.60 (quintet, J = 7.1Hz, 1H), 2.32 - 2.18 (m, 2H), 1.24 (t, J = 7.2 Hz, 3H), 1.07 (d, J = 6.8 Hz, 3H), 0.86 (s, 9H), 0.05 (s, 3H), 0.02 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 174.89, 134.15, 117.31, 73.19, 60.14, 45.20, 38.09, 25.71, 17.96, 14.15, 12.37, -4.36, -5.03. IR (KBr-film) ν (cm^{-1}): 2956, 2936, 2858, 1738, 1475, 1464, 1376, 1257, 1179, 1127, 1084, 1055, 1001, 913, 838, 812. HRMS: (EI) calcd for $C_{15}H_{30}O_3Si$ 286.1964 found $[M\text{-}CH_3]^+$ calcd 271.1729 found 271.1731, $[M\text{-}C_3H_5]^+$ calcd 245.1573 found 245.1567, $[M\text{-}OC_2H_5]^+$ calcd 241.1624 found 241.1622, $[M\text{-}C_4H_9]^+$ calcd 229.1260 found 229.1260.

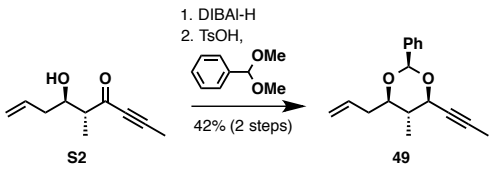


Ynone S2. The procedure of Luke et. al. was utilized for the synthesis of Weinreb amide. Trimethylaluminum (2.0 M in heptane, 1.2 mL, 2.4 mmol) was slowly added to a solution of *N*,*O*-Dimethylhydroxylamine hydrochloride (0.240 g, 2.5 mmol) in anhydrous benzene (5 mL) under nitrogen at 0ºC. The gently bubbling solution was allowed to warm to ambient temperature and stirred for 1h. This solution was cannulated into an anhydrous solution of ester **S1** (0.175 g, 0.61 mmol) in benzene (1 mL) at ambient temperature. The reaction was stirred at 40ºC for 4 h at which point all of the starting material was consumed by TLC. The reaction was cooled to rt and slowly poured into a stirring mixture of diethyl ether (50 mL) and phosphate buffer (0.5 M, pH = 6, 50 mL). After stirring the mixture for 30 min, the layers were separated. The organic layer was washed with 50% brine (1 x 15 mL brine + 15 mL water). The combined aqueous layers were back extracted with diethyl ether (1 x 50 mL). The combined organic portions were dried with magnesium sulfate, concentrated, and the residue purified by flash column chromatography (silica, 20% diethyl ether in petroleum ether) to provide the desired product (0.142 g, 77%). $[\alpha]_D^{23}$-32 (*c* 0.69, $CHCl_3$, ~30% ee). ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 5.96–5.86 (m, 1H), 5.09–5.04 (m, 2H), 4.01 (dt, J = 8.5, 4.1 Hz, 1H), 3.68 (s, 3H), 3.15 (s, 3H), 3.09 (bs, 1H), 2.37–2.31 (m, 1H), 2.31–2.22 (m, 1H), 0.99 (d, J = 6.8 Hz, 3H), 0.84 (s, 9H), 0.05 (s, 3H), -0.01 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 176.02, 133.87, 117.22, 72.93, 61.30, 39.93, 37.89, 31.80, 25.75, 17.99, 13.14, - 4.74, -4.95. IR (KBr-film) ν (cm^{-1}): 2930, 2857, 1664, 1466, 1414, 1388, 1256, 1070, 1001, 912, 838, 777.

Tetra-n-butylammonium fluoride (1M in THF, 0.67 mL, 0.67 mmol) was added to a solution of the substrate (0.100 g, 0.33 mmol) in THF (1 mL). The reaction was stirred at ambient temperature for 2 h. The reaction was

diluted with ethyl acetate (30 mL). The organic layer was washed with phosphate buffer (0.5 M, pH=5, 2 x 10 mL), brine (1 x 10 mL), dried with magnesium sulfate, concentrated, and the residue was purified by flash column chromatography (silica, 55% ethyl acetate in petroleum ether) to provided the desired product (53 mg, 86%). ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 5.88 (ddt, J = 17, 10, 7 Hz, 1H), 5.14–5.09 (m, 2H), 3.75–3.70 (m, 4H), 3.53–3.46 (m, 1H), 3.21 (s, 3H), 3.0–2.97 (m, 1H), 2.38–2.24 (m, 2H), 1.23 (d, J = 7.2 Hz, 3H).

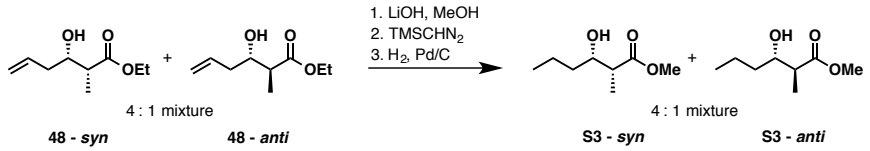
Propynylmagnesium bromide (0.5M in THF, 1.7mL, 0.85mmol) was added to a solution of the substrate (53 mg, 0.28 mmol) in THF (1 mL) at -78ºC under nitrogen. The reaction was allowed to warm to ambient temperature and stirred for 18 h. The reaction was slowly poured into a stirring mixture of diethyl ether (30 mL) and phosphate buffer (0.5 M, pH = 7, 15 mL). After stirring the mixture for 30 min, the layers were separated. The aqueous layer was extracted with diethyl ether (2 x 10 mL). The combined organic layers were washed with brine (1 x 10 mL), dried with magnesium sulfate, concentrated and the residue was purified by flash column chromatography (silica, 40% ether in petroleum ether) to provide the desired product (39 mg, 84%). $[\alpha]_D^{24}$+0.9 (*c* 0.6, $CHCl_3$, ~30% ee). ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 5.90–5.82 (m, 1H), 5.18–5.14 (m, 2H), 3.93–3.88 (m, 1H), 2.71 (quintet, J = 7.3 Hz, 1H), 2.41–2.36 (m, 2H), 2.20 (dtt, J = 14.2, 8.0, 1.0 Hz, 1H), 2.05 (s, 3H), 1.22 (d, J = 7.0 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ (ppm): 191.34, 134.01, 118.45, 91.73, 79.63, 71.84, 53.29, 38.55, 13.19, 4.20. IR (KBr-film) ν (cm^{-1}): 3455, 3077, 2978, 2918, 2849, 2218, 1668, 1540, 1458, 1435, 1256, 1178, 1075, 988, 940. HRMS: (EI) calcd for $C_{10}H_{14}O_2$, $[M\text{-}C_3H_5]^+$ 125.0598 found 125.0603.



Benzylidene Acetal 49. A precooled -78°C solution of diisobutylaluminum hydride (1M in hexanes, 0.15 mL, 0.15 mmol) in THF (2 mL) was added to solution of ynone **S2** (10 mg, 61 µmol) in anhydrous THF (2 mL) at -78ºC under nitrogen. The reaction was stirred at -78ºC for 3 h at which point the reaction was cannulated into a stirring mixture of ethyl acetate (10 mL), saturated Rochelle's salt (2 mL), and phosphate buffer (0.5 M, pH =5, 2 mL). The mixture was allowed to stir for 18 h at which point the layers were separated. The aqueous layer was extracted with ethyl acetate (2 x 3 mL). The combined organic layers were dried with magnesium sulfate, and concentrated. (^{1}H NMR analysis of the crude residue shows a 2.4 : 1 diastereoselectivity favoring the *syn*-diol.) The crude residue was purified by flash column chromatography (silica, 50% diethyl ether in petroleum ether) to provide the desired product. ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 5.92– 5.83 (m, 1H), 5.21 (d, J = 10 Hz, 1H), 5.20 (d, J = 17 Hz, 1H), 4.57–4.54 (m, 1H), 3.63 (td, J = 8.5, 3.1 Hz, 1H), 2.99 (bs, 1H), 2.58 (bs, 1H), 2.51–2.47 (m, 1H), 2.20 (dt, J = 14.7, 8.2 Hz, 1H), 1.88 (d, J = 2.1 Hz, 3H), 1.87–1.81 (m, 1H), 1.01 (d, J = 6.5 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ (ppm): 134.21, 118.87, 82.22, 78.71, 73.95, 66.63, 44.26, 39.54, 12.44, 3.61.

p-Toluenesulfonic acid monohydrate (1 mg) was added to a solution of substrate (12 mg, 71 µmol) and benzaldehyde dimethylacetal (16 µL, 0.11 mmol) in chloroform (0.3 mL). The reaction was stirred at ambient temperature for 6 h, at which point it was diluted with ethyl acetate (5 mL). The organic layer washed with saturated aqueous sodium bicarbonate (2 x 2 mL), dried with magnesium sulfate, concentrated and the residue

was purified by flash column chromatography (silica, 5% diethyl ether in petroleum ether) followed by concentration under high vacuum (<1 torr, 18 h) to provide the desired product (7.7 mg, 42%). $[\alpha]_D^{24}$+6 (*c* 0.3, $CHCl_3$, ~30% ee). ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 7.51 (d, J = 7.0 Hz, 2H), 7.36–7.31 (m, 3H), 5.98 (ddt, J = 17.1, 10.2, 7.0 Hz, 1H), 5.52 (s, 1H), 5.14–5.08 (m, 2H), 4.18 (dd, J = 10.3, 2.0 Hz, 1H), 3.52 (ddd, J = 10.0, 7.0, 3.2 Hz, 1H), 2.55–2.50 (m, 1H), 2.35 (dt, J = 14.6, 7.3 Hz, 1H), 1.94–1.80 (m, 4H), 0.98 (d, J = 7.0 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ (ppm): 138.08, 134.21, 128.75, 128.11, 126.32, 117.02, 100.78, 82.36, 81.65, 76.57, 73.61, 39.11, 37.10, 12.53, 3.73. IR (KBr-film) ν (cm^{-1}): 2921, 2850, 2243, 1458, 1402, 1336, 1309, 1215, 1173, 1139, 1112, 1070, 1029, 1005, 917, 757, 699. HRMS: (EI) calcd for $C_{17}H_{20}O_2$, $[M\text{-}H]^+$ 255.1379 found 255.1386.

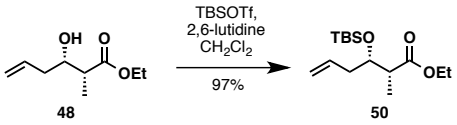


Esters S3-*syn* and S3-*anti*. Lithium hydroxide (1M in water, 1.3 mL, 1.3 mmol) was added to a solution of esters **48-*syn*** and **48-*anti*** (0.222 g, 1.30 mmol, 4:1 mixture of *syn:anti*) in methanol (0.5 mL), and the solution was stirred at rt for 3 h. The reaction was acidified using HCl (1M in water, 1.4 mL, 1.4 mmol) and saturated with solid sodium chloride. The aqueous layer was extracted with dichloromethane (6 x 3 mL). The combined organic layers were dried with magnesium sulfate, concentrated and the crude residue was used in the next step without further purification. ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 5.90-5.75 (m, 1H), 5.21-5.15 (m, 2H), 4.02 (ddd, J = 6.3, 6.3, 3.9 Hz, 1H), 3.78-3.74 (m, 1H), 2.67-2.59 (m, 1H), 2.31-2.26 (m, 2H), 1.26 (minor, d, J=7.2 Hz, 0.6H), 1.25 (major, d, J = 7.2 Hz, 2.4H).

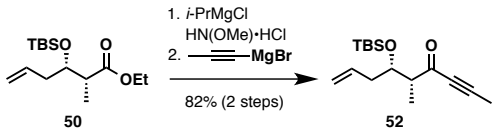
Trimethylsilyl diazomethane (2.0 M in hexanes, 3 mL, 6 mmol) was added drop-wise to a solution of the crude residue (from above) in methanol (3 mL) at 0°C until a yellow color persisted in the reaction. The reaction was quenched by the addition of acetic acid (2 drops) and concentrated. The crude residue was submitted to the next reaction without further purification. ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 5.88-5.75 (m, 1H), 5.18-5.11 (m, 2H), 3.97 (major, ddd, J = 6.9, 5.7, 3.9 Hz, 0.8H), 3.81-3.73 (minor, 0.2H), 3.72 (s, 3H), 2.58 (dddd, J = 6.9, 6.9, 6.9, 4.2 Hz, 1H), 2.32-3.19 (m, 2H), 1.22 (d, J = 6.9 Hz, 3H).

A suspension of the crude residue (from above), 10% Pd / C (60 mg) in methanol (3 mL) was stirred under an atmosphere of hydrogen for 12 h. The reaction was filtered through a pad of celite using diethyl ether, concentrated, and the residue was purified by flash column chromatography (silica, 40% diethyl ether in petroleum ether) to provide the desired *anti* and *syn* esters (1 : 4 ratio by GC). The diastereomers were not separable and spectra analysis was conducted on the mixture. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 3.91-3.86 (major, m, 0.8H), 3.70 (s, 3H), 3.7-3.63 (minor, m, 0.2H), 2.54-2.50 (m, 2H), 1.52-1.28 (m, 4H), 1.20-1.16 (m, 3H), 0.94-0.90 (m, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 176.60, 73.05 (minor), 71.42 (major), 51.77 (major), 51.69 (minor), 45.17 (minor), 44.16 (major), 36.84 (minor), 35.89 (major), 19.15 (major), 18.68 (minor), 14.30 (minor), 13.96 (major), 10.59. IR (KBr-film) ν (cm^{-1}): 3466, 2958, 2875, 1736, 1460, 1436, 1353, 1257, 1200, 1172, 1119, 1055, 1026, 986, 966, 892, 852. $[\alpha]_D^{24}$-8.1 (*c* 1.2, $CHCl_3$), 4 *syn* : 1 *anti*). ^{1}H NMR of the minor *anti* diastereomer corresponds to literature.[8] ^{1}H and ^{13}C NMR of the major *syn* diastereomer

corresponds to literature.[9]

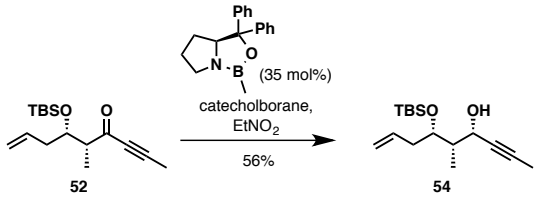


Ester 50. *tert*-Butyldimethylsilyl trifluoromethanesulfonate (3.69 g, 14.0 mmol) was added to a solution of the β-hydroxy ester **48** (1.72 g, 10.0 mmol) and 2,6-lutidine (1.71 g, 16.0 mmol) in dichloromethane (100 mL) at −78 °C. The reaction was allowed to warm to rt over 18 h. Then, phosphate buffer (pH = 4.5, 0.5 M, 50 mL) was added. The aqueous layer was extracted with dichloromethane (3 x 150 mL). The combined organic layers were dried with magnesium sulfate, concentrated and the residue was purified by flash column chromatography (silica, 10% diethyl ether – petroleum ether) to give the desired product (2.79 g, 9.7 mmol, 97% yield) as an inseparable mixture of diastereomers. ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 5.81 – 5.69 (m, 1H), 5.08 – 5.01 (m, 2H), 4.15 – 4.03 (m, 3H), 2.53 – 2.46 (m, 1H), 2.27 – 2.21 (m, 2H), 1.24 (dd, J = 7.2, 7.2 Hz, 3H), 1.11 (d, J = 6.9 Hz, 3H), 0.85 (s, 9H), 0.03 (s, 3H), 0.01 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm): 175.2, 134.4, 117.6,72.6, 60.4, 44.3, 40.1, 25.9, 18.1, 14.3, 11.1, -4.1, -4.8.

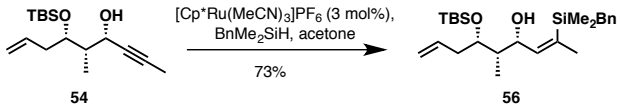


Ynone 52. Isopropylmagnesium chloride (2 M in THF, 15 mL, 30 mmol) was added to a solution of the ester **50** (2.86 g, 10.0 mmol) and *N*,*O*-Dimethylhydroxylamine hydrochloride (1.46 g, 15.0 mmol) in THF (2 mL) at -30 °C. The reaction is allowed to warm to -20 °C over 1 h, and then was monitored by TLC until completion. Once complete, saturated aqueous ammonium chloride was added. The aqueous layer was extracted with ethyl acetate (3 x 100 mL). The combined organic layers were washed with brine, dried with magnesium sulfate, concentrated, and the residue was submitted to the next reaction without further purification.

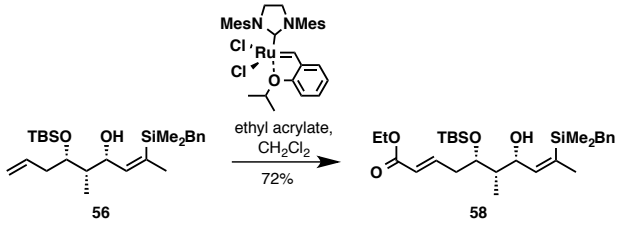
1-Propynylmagnesium bromide (0.5 M in THF, 26 mL, 13.0 mmol) was added to a solution of the crude substrate in THF (20 mL) at -78 °C. After 8 h the reaction is warmed to rt and stirred for an additional 1 h. Then 50 mL of phosphate buffer (pH = 4.5, 0.5 M) was added. The aqueous layer was extracted with diethyl ether (3 x 25 mL). The combined organic layers were dried with magnesium sulfate, concentrated, and the residue was purified by flash column chromatography (silica, 10% diethyl ether – petroleum ether) to give the desired product (2.28 g, 8.10 mmol, 82% yield) as an inseparable 3.4 : 1 mixture of diastereomers. $[\alpha]_D^{20}$13 (c 1.21, $CHCl_3$). ^{1}H NMR ($CDCl_3$ 300 MHz) δ(ppm): 5.90 – 5.75 (m, 1H), 5.08 – 5.01 (m, 2H), 4.12 (q, J = 5.1 Hz, 1H), 2.79 – 2.69 (m, 1H), 2.23 – 2.15 (m, 2H), 2.01 (s, 3H), 1.07 (d, J = 6.9 Hz, 3H), 0.85 (s, 9H), 0.05 (s, 3H), 0.04 (s, 3H). ^{13}C NMR ($CDCl_3$ 75 MHz) δ (ppm): 190.8, 134.2, 117.9, 90.7, 80.2, 72.0, 52.5, 40.3, 25.8, 18.1, 9.2, 4.2, -4.1, -4.7. IR (NaCl - film), ν (cm^{-1}): 3078, 2930, 2887, 2857, 2218, 1677, 1641, 1472, 1463, 1382, 1361, 1317, 1255, 1187, 1120, 1088, 1005, 914, 837, 811, 776, 734, 667. HRMS: (EI) calcd for $C_{13}H_{23}O_2Si$ $[M\text{-}C_2H_5]^+$ 239.1476 found 239.1469.



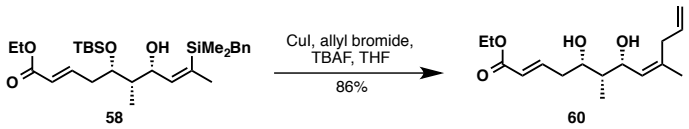
Propargyl Alcohol 54. (*S*)-(−)-2-Methyl-CBS-oxazaborolidine (1 M in toluene, 2.80 mL, 2.80 mmol) was added to a solution of ynone **52** (2.24 g, 8.0 mmol) in nitroethane (freshly distilled from calcium hydride, 40 mL) at rt. After 5 min the reaction was cooled to -78 °C, and catecholborane (freshly distilled, 4.76 g, 40.0 mmol) was added drop-wise to the reaction over 10 min. After addition, the reaction is allowed to stir at -78 °C for 4 h before being quenched carefully with phosphate buffer (pH = 4.5, 0.5 M) at the same temperature. After warming to rt, the aqueous layer was extracted with diethyl ether (3 x 200 mL). The combined organic layers were dried with magnesium sulfate, concentrated, and the residue was purified by flash column chromatography. At this stage the *syn* and *anti* diastereomers become separable. After 2 columns 1.27 g (4.5 mmol, 56% yield) of the desired product was isolated. $[\alpha]_D^{20}$17 (*c* 0.71, $CHCl_3$). ^{1}H NMR ($CDCl_3$ 300 MHz) δ(ppm): 5.74 – 5.65 (m, 1H), 5.08 – 5.00 (m, 2H), 4.33 (dd, J = 6.0, 2.4 Hz, 1H), 3.99 (ddd, J = 7.8 6.3, 3.0 Hz, 1H), 2.38 (bs, 1H), 2.32 – 2.26 (m, 2H), 1.84 (d, J = 2.1 Hz, 3H), 1.76 – 1.71 (m, 1H), 1.01 (d, J = 6.9 Hz, 3H), 0.86 (s, 9H), 0.07 (s, 3H), 0.06 (s, 3H). ^{13}C NMR ($CDCl_3$ 75 MHz) δ (ppm): 134.7, 117.3, 81.7, 74.4, 66.4, 43.0, 39.9, 25.9, 18.1, 8.1, 3.7, -3.8, -4.7. IR (NaCl - film), *v* (cm^{-1}): 3374, 3077, 2956, 2929, 2857, 2361, 1641, 1472, 1420, 1360, 1255, 1085, 1085, 1004, 912, 861, 809, 774, 670. HRMS: (EI) calcd for $C_{13}H_{25}O_2Si$ $[M\text{-}C_3H_5]^+$ 241.1624 found 241.1625.



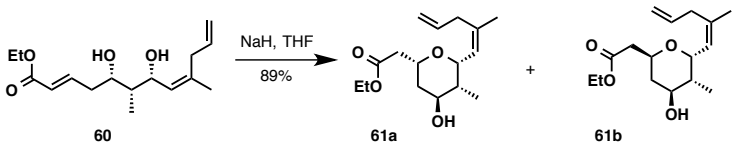
Vinyl Silane 56. $[Cp^*Ru(MeCN)_3]PF_6$ (66 mg, 0.13 mmol) was added to a solution of propargyl alcohol **54** (1.23 g, 4.37 mmol) and benzyldimethylsilane (0.851 g, 5.67 mmol) in acetone (9 mL) at -78 °C. After 10 min, the reaction was placed in a 0 °C ice bath and then was warmed from 0 °C to rt over 4.5 h. The reaction solution was directly subjected to flash column chromatography (silica, 5% diethyl ether – petroleum ether) to give the desired product (1.38 g, 3.20 mmol, 73% yield). $[\alpha]_D^{20}$-2 (*c* 1.01, $CHCl_3$). ^{1}H NMR ($CDCl_3$ 300 MHz) δ(ppm): 7.22 – 6.94 (m, 5H), 6.14 (dd, J = 9.0, 1.5 Hz, 1H), 5.64 – 5.54 (m, 1H), 5.07 – 4.97 (m, 2H), 4.28 (dd, J = 9.0,1.2 Hz, 1H), 3.88 – 3.82 (m, 1H), 2.79 (s, 1H), 2.26 – 2.21 (m, 2H), 2.21 – 2.10 (m, 2H), 1.71 (d, J = 1.8 Hz, 3H, 1.55 – 1.52 (m, 1H), 0.93 (d, J = 6.9 Hz, 3H), 0.88 (s, 9H), 0.11 (s, 3H), 0.10 (s, 3H), 0.09 (s, 3H), 0.09 (s, 3H). ^{13}C NMR ($CDCl_3$ 75 MHz) δ (ppm): 144.4, 140.1, 136.5, 134.3, 128.5, 128.4, 124.4, 117.8, 77.7, 74.5, 41.0, 39.9, 26.4, 261, 25.3, 18.2, 5.5, -1.4, -1.7, -3.3, -4.3. IR (NaCl - film), *v* (cm^{-1}): 3520, 3080, 3024, 2955, 2858, 1640, 1600, 1493, 1471, 1462, 1388, 1361, 1253, 1206, 1154, 1091, 1002, 938, 912, 835, 776, 698. HRMS: (EI) calcd for $C_{18}H_{37}O_2Si_2$ $[M\text{-}C_7H_7]^+$ 341.2332 found 341.2332.



Ester 58. Hoveyda-Grubbs 2nd generation catalyst (48 mg, 80 μmol) was added to a degassed solution of vinyl silane **56** (1.33 g, 3.10 mmol) and ethyl acrylate (2.45 g, 24.5 mmol) in dichloromethane (20 mL) at rt. Additional Hoveyda-Grubbs 2nd generation catalyst (30 mg, 50 μmol) was added at 4.5 h. After an additional 12 h the reaction was concentrated under reduced pressure. The residue was purified by flash column chromatography (silica, 5% → 10% diethyl ether – petroleum ether) to give the desired product (1.09 g, 2.22 mmol, 72%). $[\alpha]_D^{20}$ -26 (*c* 0.72, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.22 – 7.17 (m, 2H), 7.09 – 7.05 (m, 1H), 7.00 – 6.96 (m, 2H), 6.87 – 6.78 (m, 1H), 6.13 (dd, J = 9.2, 2.0 Hz, 1H), 5.85 (ddd, J = 15.6, 1.6, 1.6 Hz, 1H), 4.22 (dd, J = 9.2, 1.6 Hz, 1H), 4.15 (q, J = 7.2 Hz, 2H), 3.91 – 3.86 (m, 1H), 2.45 – 2.35 (m, 2H), 2.23 (bs, 1H), 2.2- - 2.15 (m, 2H), 1.74 (d, J = 1.6 Hz, 3H), 1.51 – 1.47 (m, 1H), 1.24 (t, J = 7.2 Hz, 3H), 0.92 (d, J = 7.2 Hz, 3H), 0.88 (s, 9H), 0.12 (s, 3H), 0.10 (s, 3H), 0.09 (s, 3H), 0.08 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 166.2, 144.5, 143.8, 139.9, 137.0, 128.3, 128.2, 124.3, 123.8, 76.0, 73.2, 60.4, 41.9, 38.0, 26.2, 25.9, 25.1, 18.0, 14.3, 6.4, -1.5, -1.9, -3.7, -4.4. IR (KBr-film) ν (cm^{-1}): 3517, 3060, 2955, 2858, 1723, 1657, 1600, 1548, 1493, 1463, 1452, 1390, 1368, 1318, 1256, 1207, 1173, 1092, 836, 775, 699. HRMS: (EI) calcd for $C_{21}H_{41}O_4Si_2$ $[M\text{-}CH_2Ph]^+$ 413.2544 found 413.2551.

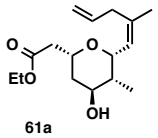


Alkene 60. Tetra-n-butylammonium fluoride (1 M in THF, 5.25 mL, 5.25 mmol) was added to a solution of the ester **58** (1.05 g, 2.10 mmol), copper iodide (0.79 g, 4.2 mmol) and allyl bromide (1.01 g, 8.40 mmol) in THF (10 mL). The reaction was heated at 40 °C for 12 h. Additional tetra-n-butylammonium fluoride (1 M in THF, 2.10 mL, 2.10 mmol) was added and the reaction was allowed to stir for an additional 1 h. Then 3.5% ammonium hydroxide solution (25 mL) was added and the reaction was diluted with diethyl ether. The aqueous layer was extracted with diethyl ether (3 x 100 mL). The combined organic layers were dried with magnesium sulfate, concentrated, and the residue was purified by flash column chromatography to give the desired product (0.51 g, 1.8 mmol, 86% yield). $[\alpha]_D^{20}$ -12 (*c* 0.71, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 6.91 (ddd, J = 15.6, 7.6, 7.6 Hz, 1H), 5.88 (ddd, J = 15.6, 1.6, 1.6 Hz, 1H), 5.80 – 5.70 (m, 1H), 5.36 (d, J = 8.8 Hz, 1H), 5.05 – 4.98 (m, 2H), 4.55 (dd, J = 8.4, 3.2 Hz, 1H), 4.16 (q, J = 7.2 Hz, 2H), 4.02 – 3.97 (m, 1H), 2.89 – 2.75 (m, 2H), 2.48 – 2.40 (m, 1H), 2.31 – 2.24 (m, 1H), 1.72 (d, J = 1.6 Hz, 3H), 1.55 – 1.47 (m, 1H), 1.26 (t, J = 7.2 Hz, 3H), 0.98 (d, J = 4.8 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 166.4, 145.4, 137.4, 135.9, 127.3, 123.7, 115.8, 64.3, 73.0, 60.4, 42.1, 38.0, 36.9, 23.8, 14.3, 5.5. IR (KBr-film) ν (cm^{-1}): 3419, 3078, 2977, 1715, 1652, 1445, 1369, 1268, 1211, 1168, 1044, 977, 913, 861. HRMS: (EI) calcd for $C_{13}H_{21}O_4$ $[M\text{-}C_2H_5]^+$ 241.1440 found 241.1459.



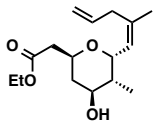
60 61a 61b

Tetrahydropyrans 61a and 61b. Sodium hydride (60% in oil, 1.8 mg, 45 µmol) was added to a solution of the alkene **60** (10.5 mg, 37.2 µmol) in THF (3.0 mL) at rt. After 30 min, phosphate buffer (pH 7.0, 1.0 M) was added and the reaction was further diluted diethyl ether. The aqueous layer was extracted with diethyl ether (3 x 25 mL). The combined organic layers were dried with magnesium sulfate, concentrated, and the residue was purified by flash column chromatography to give the desired product (9.3 mg, 33.1 µmol, 89%) as 1:1 mixture of diastereomers.



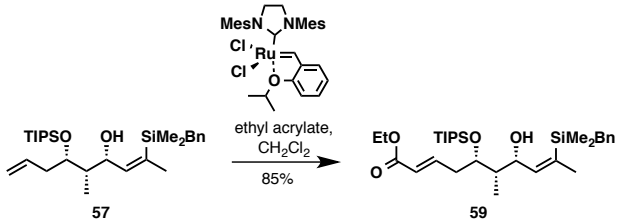
61a

$[\alpha]_D^{20}$ 32 (*c* 1.15, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 5.72 – 5.67 (m, 1H), 5.26 (d, J = 8.0 Hz, 1H), 5.02 – 4.95 (m, 2H), 4.65 (dd, J = 8.0, 2.0 Hz, 1H), 4.25 – 4.19 (m, 1H), 4.13 – 4.05 (m, 2H), 3.89 (bs, 1H), 2.83 (dd, J = 14.5, 6.5 Hz, 1H), 2.73 (dd, J = 14.0, 6.0 Hz, 1H), 2.55 (dd, J = 15.5, 7.0 Hz, 1H), 2.34 (dd, J = 15.5, 6.0 Hz, 1H), 1.68 (d, J = 1.5 Hz, 3H), 1.60 – 1.54 (m, 2H), 1.22 – 1.15 (m, 4H), 0.95 (d, J = 7.0 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 171.3, 136.9, 135.9, 124.9, 115.7, 71.3, 70.4, 68.9, 60.5, 41.4, 39.3, 37.1, 33.3, 23.5, 14.2, 11.3. IR (KBr-film) ν (cm^{-1}): 3459, 3078, 2973, 2919, 2730, 1731, 1715, 1694, 1686, 1636, 1463, 1445, 1372, 1296, 1296, 1162, 1055, 1029, 984, 911, 857, 761. HRMS: (EI) calcd for $C_{16}H_{26}O_4$ 282.1831 found 282.1817.



61b

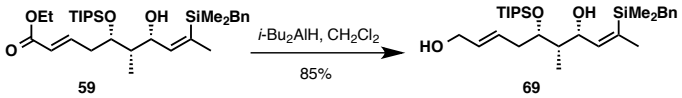
^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 5.70 – 5.65 (m, 1H), 5.30 (d, J = 8.4 Hz, 1H), 5.01 – 4.96 (m, 2H), 4.68 (dd, J = 7.6, 2.4 Hz, 1H), 4.24 (dq, J = 6.8, 2.4 Hz, 1H), 4.12 (d q, J = 7.2, 2.0 Hz, 3H), 3.92 – 3.85 (m, 1H), 2.86 (dd, J = 13.6, 4.0 Hz, 1H), 2.74 (dd, J = 15.2, 6.4 Hz, 1H), 2.56 (dd, J = 15.2, 6.8 Hz, 1H), 2.36 (dd, J = 15.2, 6.4 Hz, 1H), 1.68 (d, J = 1.2 Hz, 3H), 1.54 – 1.49 (m, 2H), 1.23 – 1.16 (m, 4H), 0.95 (d, J = 7.2 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 171.2, 141.8, 135.7, 120.6, 115.8, 73.5, 69.5, 66.4, 60.5, 41.4, 40.8, 36.7, 30.3, 23.8, 14.2, 12.8.



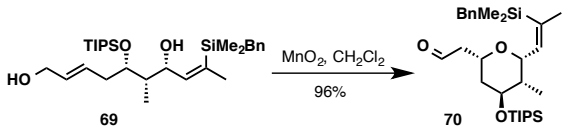
57 59

Ester 59. Hoveyda-Grubbs 2nd generation catalyst (62.6 mg, 0.10 mmol) was added to a degassed solution of the

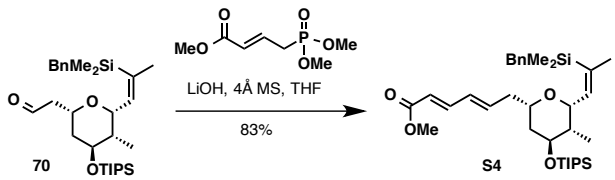
vinyl silane **57** (0.950 g, 2.0 mmol) and ethyl acrylate (2.13 mL, 20.0 mmol) in dichloromethane (29 mL) at rt. After 19 h the reaction was concentrated under reduced pressure. The residue was purified by flash column chromatography (silica, 5% → 7% ethyl acetate-hexanes) to give the desired product (0.933 g, 1.71 mmol, 85%) in greater than 10:1 *E*:*Z* selectivity. $[\alpha]_D^{20}$ -21 (*c* 1.0, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.19 – 7.16 (m, 2H), 7.06 – 7.02 (m, 1H), 6.97 - 6.95 (m, 2H), 6.77 – 6.71 (m, 1H), 6.12 (dd, J = 8.9, 1.6 Hz, 1H), 5.84 (dt, J = 15.6, 1.2 Hz, 1H), 4.31 (d, J = 8.4 Hz, 1H), 4.16 – 4.12 (m, 3H), 2.69 (d, J = 0.8 Hz, 1H), 2.56-2.44 (m, 2H), 2.16 (d, J = 2.0 Hz, 2H), 1.74 (d, J = 2.0 Hz, 3H), 1.54-1.48 (m, 1H), 1.23 (dd, J = 6.8 Hz, 3H), 1.07 – 1.02 (m, 21H), 0.96 (d, J = 7.2 Hz, 3H), 0.10 (s, 3H), 0.09 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): δ 166.0, 143.8, 143.7, 139.8, 137.0, 128.2, 128.1, 124.1, 123.8, 76.9, 73.9, 60.3, 51.8, 41.4, 37.8, 26.0, 25.0, 18.2, 18.1, 14.2, 13.2, 5.4, -1.7, -2.2. IR (KBr-film) ν (cm^{-1}): 3079, 2927, 2856, 1715, 1644, 1618, 1463, 1367, 1301, 1257, 1191, 1170, 1137, 1059, 1001, 957, 939, 911, 835, 774, 723, 667.



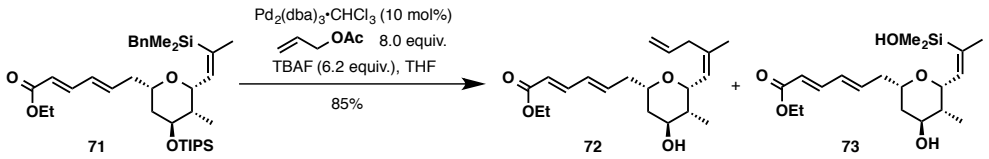
Allylic Alcohol 69. Diisobutylaluminum hydride (1.0M in Toluene, 0.80 mL, 0.80 mmol) was added to a solution of ester **59** (105 mg, 0.192 mmol) in dichloromethane (1.3 mL) at 0 °C. After 2 h, a saturated aqueous solution of sodium/potassium tartrate (5 mL) was added. The resulting solution was stirred for 30 min, and then diluted with ethyl acetate (5 mL). The aqueous layer extracted with ethyl acetate (2 × 10 mL). The combined organic layers were dried with sodium sulfate, concentrated and the residue was purified by flash column chromatography (silica, 10 → 25% ethyl acetate - petroleum ether) to give the desired product (83 mg, 85%). $[\alpha]_D^{27}$ 7.0 (*c* 0.48, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 7.20 (t, 2H, *J* = 7.6 Hz), 7.07 (t, 1H, *J* = 7.6 Hz), 7.00 (d, 2H, *J* = 7.6 Hz), 6.18 (dd, 1H, *J* = 9.2, 1.6 Hz), 5.70 (ddd, 1H, *J* = 15.2, 5.6, 5.6 Hz), 5.51 (m, 1H), 4.44 (dd, 1H, *J* = 8.8, 2.0 Hz), 4.11 (ddd, 1H, *J* = 8.4, 6.4, 2.0 Hz), 4.03 (d, 2H, *J* = 4.8 Hz), 3.07 (br s, 1H), 2.36 (t, 2H, *J* = 8.0 Hz), 2.21 (d, 1H, *J* = 13.6 Hz), 2.17 (d, 1H, *J* = 13.6 Hz), 1.74 (d, 3H, *J* = 1.6 Hz), 1.63 (m, 1H), 1.07 (m, 21H), 0.99 (d, 3H, *J* = 6.8 Hz), 0.12 (s, 3H), 0.08 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ (ppm): 144.1, 139.8, 136.5, 132.2, 128.2, 127.4, 124.2, 78.4, 74.8, 63.4, 40.6, 37.8, 26.2, 25.0, 18.2, 18.1, 13.3, 4.9, –1.8, –2.1. IR (KBr-film) ν (cm^{-1}): 3407, 2944, 2867, 1600, 1463, 1250, 1093, 1012, 829, 682. HRMS: (ESI) calcd for $C_{29}H_{52}O_3Si_2Na$ $[M+Na]^+$: 527.3353, found: 527.3339.



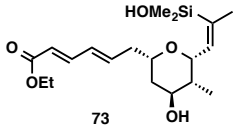
Aldehyde 70. Manganese dioxide (25.0 mg, 0.287 mmol) was added to a solution of allylic alcohol **69** (14.5 mg, 28.7 μmol) in dichloromethane (0.25 mL) at rt. After 1 h, additional manganese dioxide (12.5 mg, 0.144 mmol) was added. The reaction was stirred for 26 h and then filtered through a pad of Celite using dichloromethane (25 mL). The filtrate was concentrated under reduced pressure, and the residue was purified by flash column chromatography (silica, 5% → 10% ethyl acetate – hexanes) to give the desired product (14 mg, 27.6 μmol, 96%).



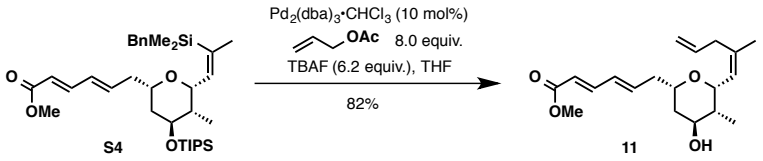
Dienoate S4. Lithium hydroxide (0.184 g, 4.38 mmol) was added to a suspension of aldehyde **70** (0.760 g, 1.51 mmol) trimethyl 4-phosphonocrotonate (0.912 g, 4.38 mmol) and 4 Å molecular sieves (flame dried, 8.4 g) in THF (84 mL). The reaction was heated at 70 °C for 18 h. After cooling to rt, the reaction was filtered through a plug of celite using ethyl acetate, concentrated, and the residue was purified by flash column chromatography (silica, 5% → 10% ethyl acetate – hexanes) to give the desired product (0.734 g, 1.25 mmol, 83% yield). $[\alpha]_D^{23}$39.8 (*c* 1.0, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.26 – 7.16 (m, 3H), 7.08 – 7.04 (m, 1H), 7.03 – 6.98 (m, 2H), 6.26 – 6.10 (m, 3H), 5.77 (d, J = 15.6 Hz, 1H), 4.64 (dd, J = 9.6, 2.4 Hz, 1H), 3.98 – 3.88 (m, 2H), 3.73 (s, 3H), 2.46 – 2.37 (m, 1H), 2.36 – 2.26 (m, 1H), 2.25 (d, J = 13.6 Hz, 1H), 2.19 (d, J = 13.6 Hz, 1H), 1.73 (d, J = 1.6 Hz, 3H), 1.73 – 1.64 (m, 1H), 1.62 – 1.52 (m, 1H), 1.44 (d, J = 14.0 Hz, 1H), 1.10 – 1.02 (m, 21H), 0.98 (d, J = 7.2 Hz, 3H), 0.12 (s, 3H), 0.11 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 167.7, 145.1, 141.0, 140.4, 139.9, 138.8, 130.4, 128.3, 128.2, 124.1, 119.3, 73.3, 71.5, 71.2, 51.5, 39.9, 39.7, 34.0, 26.2, 25.5, 18.3, 18.2, 12.4, 11.6, -1.8, -2.1. IR (KBr-film) ν (cm^{-1}): 2982, 2904, 2826, 1698, 1623, 1239, 1123, 1070, 1041, 985, 870, 818. HRMS: (ESI) calcd for $C_{34}H_{56}O_4Si_2Na$ $[M+Na]^+$: 607.3609, found: 607.3604.



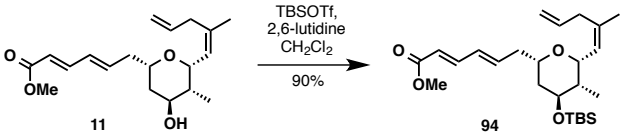
Alkene 72. Tetra-n-butylammonium fluoride (1M in THF (new bottle), 4.04 mL, 4.04 mmol) was added to a solution of dienoate **71** (0.390 g, 0.651 mmol) in THF (6.9 mL) followed by the addition of allyl acetate (0.560 mL, 5.21 mmol) and finally Pd_2dba_3•$CHCl_3$ (67.4 mg, 65.1 μmol) at rt. After 22 h saturated aqueous ammonium chloride was added and the reaction was diluted with ethyl acetate. The aqueous layer was extracted with ethyl acetate (3 x 50 mL). The combined organic layers were washed with brine, dried with sodium sulfate, concentrated, and the residue was purified by flash column chromatography (silica, 15% → 25% ethyl acetate - hexanes) to give the desired product (0.185 g, 0.553 mmol, 85% yield).



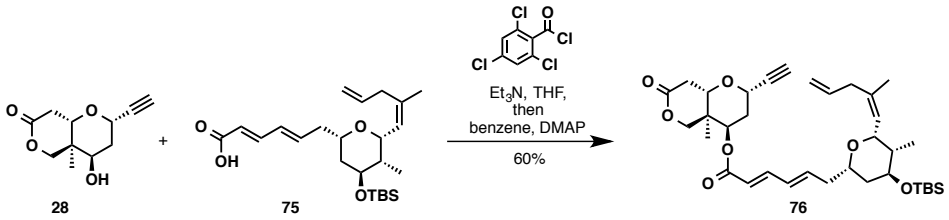
^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.24 (dd, 1H, *J* = 15.6, 10.8 Hz), 6.23 (dd, 1H, *J* = 15.2, 11.2 Hz), 6.11 (m, 1H), 5.97 (dd, 1H, *J* = 6.4, 1.6 Hz), 5.79 (d, 1H, *J* = 15.2 Hz), 4.74 (d, 1H, *J* = 5.6 Hz), 4.19 (q, 2H, *J* = 7.2 Hz), 3.96 (m, 2H), 3.11 (br s, 1H), 2.46 (m, 1H), 2.35 (m, 1H), 1.80 (t, 3H, *J* = 1.2 Hz), 1.65 (ddd, 2H, *J* = 14.4, 12.0, 2.8 Hz), 1.49 (m, 1H), 1.29 (t, 3H, *J* = 7.2 Hz), 0.95 (d, 3H, *J* = 7.2 Hz), 0.24 (s, 3H), 0.22 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 167.2, 144.4, 140.6, 139.0, 138.2, 130.9, 120.1, 73.9, 71.9, 70.3, 60.2, 39.6, 39.3, 33.0, 24.3, 14.3, 11.1, 0.5, 0.4. IR (KBr-film) ν (cm^{-1}): 3385, 2919, 1713, 1643, 1446, 1370, 1304, 1255, 1139, 1048, 1002, 874, 830, 776. HRMS: (ESI) calcd for $C_{19}H_{32}O_5SiNa$ $[M+Na]^+$: 391.1917, found: 391.1906.



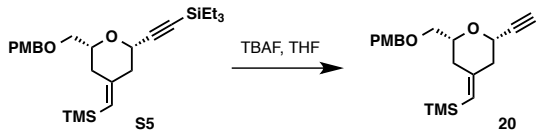
Alkene 11. Tetra-n-butylammonium fluoride (1M in THF (new bottle), 3.90 mL, 3.89 mmol) was added to a solution of dienoate **S4** (0.367 g, 0.627 mmol) in THF (6.6 mL) followed by the addition of allyl acetate (0.540 mL, 5.02 mmol) and finally Pd_2dba_3•$CHCl_3$ (65 mg, 62.7 µmol) at rt. After 14 h, saturated aqueous ammonium chloride was added and the reaction was diluted with ethyl acetate. The aqueous layer was extracted with ethyl acetate (4 x 50 mL). The combined organic layers were washed with brine, dried with sodium sulfate, concentrated, and the residue was purified by flash column chromatography (silica, 30% → 50% ethyl acetate - hexanes) to give the desired product (0.165 g, 0.515 mmol, 82% yield). $[\alpha]_D^{24}$ 59.1 (*c* 1.0, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.25 (dd, J = 15.2, 10.4 Hz, 1H), 6.25 – 6.12 (m, 2H), 5.78 (d, J = 15.2 Hz, 1H), 5.79 – 5.68 (m, 1H), 5.33 (d, J = 6.8 Hz, 1H), 5.07 – 4.68 (m, 2H), 4.66 (dd, J = 8.0, 2.4 Hz, 1H), 3.95 – 3.86 (m, 2H), 3.73 (s, 3H), 2.87 (dd, J = 14.8, 6.0 Hz, 1H), 2.76 (dd, J = 14.8, 6.4 Hz, 1H), 2.44 – 2.37 (m, 1H), 2.34 – 2.26 (m, 1H), 1.71 (d, J = 0.8 Hz, 3H), 1.71 – 1.52 (m, 3H), 1.47 (d, J = 14.0 Hz, 1H), 0.96 (d, J = 7.2 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 167.8, 145.1, 140.4, 136.8, 136.0, 130.4, 125.1, 119.3, 115.8, 71.5, 71.3, 70.6, 51.6, 39.8, 39.7, 37.2, 33.2, 23.6, 11.4. IR (KBr-film) ν (cm^{-1}): 3393, 2876, 1696, 1620, 1416, 1251, 1125, 1039, 988. HRMS: (ESI) calcd for $C_{19}H_{28}O_4Na$ $[M+Na]^+$: 343.1880, found: 343.1867.



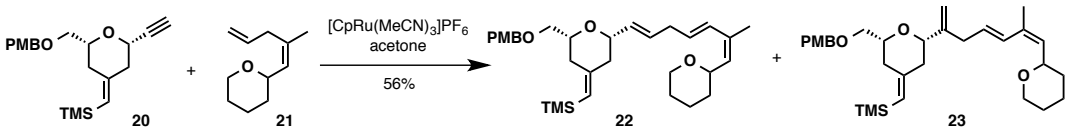
TBS Ether 94. *tert*-Butyldimethylsilyl trifluoromethanesulfonate (0.140 mL, 0.772 mmol) was added to a solution of alkene **11** (0.165 g, 0.515 mmol) and 2,6-lutidine (0.240 mL, 2.06 mmol) in dichloromethane (5.2 mL) at 0 °C. After 20 min, the reaction was warmed to rt and stirred for an additional 5 min. Saturated aqueous sodium bicarbonate was added and the reaction was diluted with dichloromethane. The aqueous layer was extracted with dichloromethane (4 x 40 mL). The combined organic layers were dried with sodium sulfate, concentrated, and the residue was purified by flash column chromatography (silica, 5% → 10% ethyl acetate - hexanes) to give the desired product (0.201 g, 0.464 mmol, 90% yield). $[\alpha]_D^{23}$ 55.8 (*c* 1.0, CH_2Cl_2). ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 7.26 (dd, J = 15.0, 10.5 Hz, 1H), 6.24 – 6.10 (m, 2H), 5.79 (d, J = 15.0 Hz, 1H), 5.77 – 5.68 (m, 1H), 5.31 (d, J = 8.5 Hz, 1H), 5.04 – 4.97 (m, 2H), 4.68 (d, J = 8.0 Hz, 1H), 3.93 – 3.84 (m, 1H), 3.81 (bs, 1H), 3.73 (s, 3H), 2.86 (dd, J = 14.5, 6.0 Hz, 1H), 2.71 (dd, J = 14.5, 6.5 Hz, 1H), 2.43 – 2.35 (m, 1H), 2.32 – 2.24 (m, 1H), 1.17 (s, 3H), 1.58 – 1.48 (m, 2H), 1.30 (d, J = 13.5 Hz, 1H), 0.91 (d, J = 7.5 Hz, 3H), 0.89 (s, 9H), 0.02 (s, 3H), 0.02 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ (ppm): 167.8, 145.2, 140.7, 136.0, 135.8, 130.2, 125.6, 119.2, 115.6, 71.5, 71.4, 70.9, 51.5, 40.2, 39.7, 37.1, 33.9, 25.8, 23.5, 18.1, 11.3, -4.8, -4.9. IR (KBr-film) ν (cm^{-1}): 2910, 2889, 2817, 1698, 1622, 1415, 1240, 1123, 1044, 988, 824, 764. HRMS: (ESI) calcd for $C_{25}H_{42}O_4SiNa$ $[M+Na]^+$: 457.2745, found: 457.2735.



Ester 76. To a solution of acid **75** (6.5 mg, 15.7 μmol) in THF (0.15 mL) were added triethylamine (2.6 μL, 18.8 μmol) and 2,4,6-trichlorobenzoyl chloride (2.6 μL, 16.5 μmol). The reaction was stirred at rt for 24 h, then filtered through a 2 mL M fritted Büchner funnel covered with a septum and a line of nitrogen flowing through. The filter cake was washed with dry benzene (2 mL), and the solvent was evaporated. The resultant colorless residue (newly formed crude anhydride) was dried under high vacuum for 40 min. In a separate vial containing lactone **28** (3.3 mg, 15.7 μmol) was added 4-dimethylaminopyridine (5.8 mg, 47.1 μmol) and benzene (0.20 μL). This solution was heated to reflux, and a solution of crude anhydride in benzene (0.20 mL) and added to this refluxing solution. The syringe was rinsed with benzene (2 × 0.20 mL) into the reaction mixture. After refluxing the solution for 4 h, the reaction was allowed to cool to rt. The reaction was quenched with water (2 mL) and diluted with ethyl acetate (2 mL). The layers were separated and the aqueous layer was extracted with ethyl acetate (3 × 2 mL). The combined organic layers were dried with sodium sulfate, concentrated and the residue was purified by flash column chromatography (silica, 15% → 25% ethyl acetate - petroleum ether) to give the desired product (5.8 mg, 60%). ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.29 (dd, 1H, J = 15.6, 12.5 Hz), 6.30–6.20 (m, 2H), 5.78 (d, 1H, J = 15.2 Hz), 5.73 (m, 1H), 5.32 (d, 1H, J = 8.0 Hz), 5.05–4.97 (m, 3H), 4.69 (dd, 1H, J = 8.0, 2.4 Hz), 4.55 (m, 1H), 4.11 (dd, 1H, J = 11.6, 6.8 Hz), 4.06 (d, 1H, J = 11.6 Hz), 3.98 (d, 1H, J = 11.2 Hz), 3.91 (m, 1H), 3.82 (m, 1H), 2.96 (dd, 1H, J = 18.4, 6.8 Hz), 2.87 (dd, 1H, J = 14.8, 6.4 Hz), 2.72 (dd, 1H, J = 14.0, 6.4 Hz), 2.60 (m, 1H), 2.54 (d, 1H, J = 2.4 Hz), 2.35 (m, 2H), 2.28 (ddd, 1H, J = 15.2, 12.0, 2.8 Hz), 1.99 (ddd, 1H, J = 15.2, 2.8, 2.8 Hz), 1.71 (d, 3H, J = 0.8 Hz), 1.61–1.51 (m, 2H), 1.31 (d, 1H, J = 14.0 Hz), 1.22 (s, 3H), 0.92 (d, 3H, J = 7.2 Hz), 0.90 (s, 9H), 0.031 (s, 6H). ^{13}C NMR (105 MHz, $CDCl_3$) δ (ppm): 168.6, 165.7, 146.8, 142.7, 136.0, 135.8, 129.7, 125.5, 117.8, 115.5, 81.1, 74.2, 72.1, 71.4, 70.8, 70.4, 69.8, 63.5, 40.1, 39.7, 37.0, 35.9, 33.9, 33.7, 33.0, 25.8, 23.4, 18.0, 13.7, 11.2, –4.9 (2). HRMS: (ESI) calcd for $C_{35}H_{52}O_7SiNa$ $[M+Na]^+$: 635.3353, found: 635.3361.

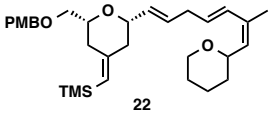


Alkene 20. Tetra-n-butylammonium fluoride (1 M in THF, 1.5 mL, 1.5 mmol) was added to a solution of the tetrahydropyran **S5** (512 mg, 1.5 mmol) in THF (3.7 mL) at 0 °C. After 15 min the reaction was warmed to rt and stirred for an additional 1h. The reaction was diluted with diethyl ether (50 mL) and water. The organic layer was washed water (2x), brine, dried with magnesium sulfate, concentrated, and the crude residue was purified by column chromatography (90:1- petroleum ether - diethyl ether). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.27 (d, J = 8.3 Hz, 2H), 6.87 (d, J = 8.6 Hz, 2H), 5.31 (t, J = 1.6 Hz, 1H), 4.54 (d, J = 11.7 Hz, 1H), 4.49 (d, J = 11.7 Hz, 1H), 4.12 (dt, J = 11.3, 2.4 Hz, 1H), 3.80 (s, 3H), 3.60 – 3.54 (m, 1H), 3.53 – 3.43 (m, 2H), 2.55 – 2.35 (m, 4H), 2.00 (ddt, J = 13.7, 11.4, 1.5 Hz, 1H), 0.09 (d, J = 0.5 Hz, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.13, 150.69, 130.18, 129.32, 125.08, 113.70, 82.42, 77.57, 73.19, 73.04, 72.55, 68.56, 55.24, 45.62, 36.28, 0.18.

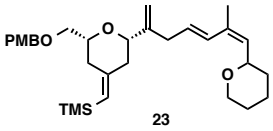


Dienes 22 and 23. Alkyne **20**[10] (34 mg, 0.10 mmol), alkene **21** (83 mg, 0.50 mmol), and $[CpRu(MeCN)_3]PF_6$ (4.3 mg, 10 μmol) were combined in a flame dried microwave vial under argon and dissolved in freshly distilled acetone (0.83 mL). The reaction is allowed to stir at rt for 4 h then 4 °C for 12 h. The reaction was concentrated under reduced pressure. The crude residue was purified by flash column chromatography (silica, 5→20% Et_2O in petroleum) to provide the desired products (28 mg, 56% yield) as a 4:1 mixture of linear and branched regioisomers as determined by ^{1}H NMR.

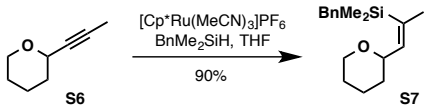
A small amount of the mixture of isomers was separated by preparative thin layer chromatography.



^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.27 (d, J = 8.4 Hz, 2H), 6.87 (d, J = 8.4 Hz, 2H), 6.42 (d, J = 15.6 Hz, 1H), 5.72 (dt, J = 15.5, 6.8 Hz, 1H), 5.56 (dd, J = 15.5, 6.2 Hz, 1H), 5.27 (bs, 2H), 4.52 (d, J = 3.8 Hz, 2H), 4.20 (t, J = 9.1 Hz, 1H), 3.99 (d, J = 10.5 Hz, 1H), 3.85 (m, 1H), 3.80 (s, 3H), 3.58–3.44 (m, 4H), 2.88 (t, J = 6.6 Hz, 2H), 2.44 (d, J = 13.5 Hz, 1H), 2.23–2.17 (m, 2H), 1.82 (s, 3H), 1.66-1.34 (m, 5H), 0.10 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 173.5, 159.1, 152.9, 134.2, 131.4, 130.36, 130.1, 130.0, 129.6, 129.4, 129.3, 128.1, 123.5, 113.7, 79.3, 29.6, 77.2, 73.7, 73.0, 72.8, 68.2, 55.3, 45.6, 36.6, 35.8, 32.3, 30.3, 25.7, 23.4, 20.5, 0.3.

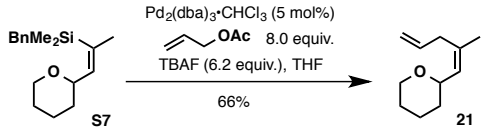


^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.27 (d, J = 8.9 Hz, 2H), 6.88 (d, J = 8.9 Hz, 2H), 6.44 (d, J = 15.2 Hz, 1H), 5.75 (dt, J = 15.7, 7.2 Hz, 1H), 5.28 (s, 1H), 5.27 (d, J = 10.4 Hz, 1H), 5.10 (s, 1H), 4.88 (s, 1H), 4.55 (s, 3H), 4.21 (ddd, J = 9.0, 8.0, 2.5 Hz, 1H), 3.98 (dq, J = 9.0, 8.0, 2.5 Hz, 1H), 3.8 (s, 3H), 3.62–3.45 (m, 6H), 3.02–2.85 (m, 3H), 2.47 (1h, d, J = 13.5 Hz), 2.28–2.17 (m, 3H), 1.55–1.35 (m, 6H), 0.10 (s, 9H).

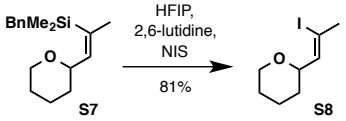


Vinyl Silane S7. $[Cp^*Ru(MeCN)_3PF_6]$ (12.7 mg, 30 μmol) was added to a solution of alkyne **S6** (0.40 mL, 3.0 mmol) and benzyldimethylsilane (0.575 mL, 3.6 mmol) in degassed acetone (6.0 mL) under an atmosphere of argon in a flame dried microwave vial at 0 °C. After 15 min, the reaction was warmed to rt and allowed to stir for 30 min. The reaction was concentrated under reduced pressure and the crude residue was purified by flash column chromatography (silica, 10% diethyl ether - petroleum ether) to provide the desired product (0.737 g, 90%). ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.21 (t, J = 7.6, 2H), 7.08 (t, J = 7.4, 1H), 7.02 (d, J = 8.2, 2H), 5.99 (dd, J = 8.7, 1.6, 1H), 3.97 (ddd, J = 11.4, 4.4, 1.8, 1H), 3.80-3.75 (m, 1H), 3.39 (td, J = 11.6, 2.4 Hz, 1H), 2.11

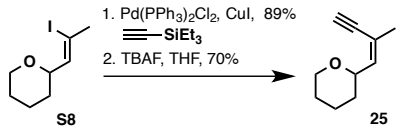
(d, J = 4.1 Hz, 2H), 1.75 (d, J=1.7 Hz, 3H), 1.63 – 1.32 (m, 6H), 0.15 (s, 3H), 0.12 (s, 3H).



Alkene 21. Tetra-n-butylammonium fluoride (1 M in THF, 15.8 mL, 15.8 mmol) was added to a solution of vinyl silane **S7** (0.700 g, 2.55 mmol) in THF (25.5 mL) followed by the addition of allyl acetate (1.11 mL, 10.2 mmol) and finally Pd_2dba_3•$CHCl_3$ (0.132 g, 0.128 mmol) at rt. After 18 h, the reaction was filtered through silica gel with ethyl acetate, pentane and diethyl ether. The filtrate was concentrated and the crude residue was purified by flash column chromatography (silica, 0% → 20% diethyl ether - petroleum ether) to provide the desired product (0.280 g, 66%). ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 5.76–5.72 (m, 1H), 5.25 (dd, J = 8.2, 0.7, 1H), 5.07–4.99 (m, 2H), 4.03–3.92 (m, 2H), 3.47 (td, J = 11.4, 2.3, 1H), 2.92–2.88 (m, 1H), 2.73 (dd, J = 14.6, 6.6, 1H), 1.88–1.78 (m, 1H), 1.69 (s, 3H), 1.63–1.35 (m, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 136.5, 135.9, 127.7, 115.6, 74.5, 68.2, 37.0, 32.4, 25.8, 23.4, 23.3. IR (KBr-film) ν (cm^{-1}): 2935, 2849, 1637, 1439, 1086, 1034.



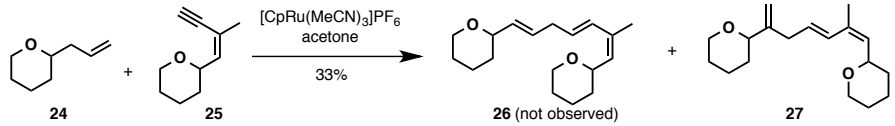
Vinyl Iodide S8. The iododesilylation procedure was developed by Zakarian et al.[11] N-iodosuccinimide (1.23 g, 5.5 mmol) was added to a solution of vinyl silane **S7** (1.0 g, 3.6 mmol) in hexafluoroisopropanol (12 mL) at 0 °C. After 4 min, the reaction was diluted with dichloromethane (50 mL) and water. The aqueous layer was extracted with dichloromethane (3 x 50 mL). The combined organic layers were washed with saturated sodium thiosulfate (2 x 10 mL), brine, dried with magnesium sulfate, concentrated, and the crude residue was purified by flash column chromatography (silica, 10% diethyl ether - petroleum ether) to give the desired product (0.731 g, 81%). ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 5.52 (dq, J = 7.4, 1.5 Hz, 1H), 3.97 (m, 1H), 3.90 (ddd, J = 10.4, 7.0, 2.3 Hz, 1H), 3.50 (td, J = 11.2, 2.5 Hz, 1H), 2.50 (d, J = 1.6 Hz, 3H), 1.85 (m, 1H), 1.69 (m, 1H), 1.62–1.47 (m, 3H), 1.41–1.30 (m, 1H).



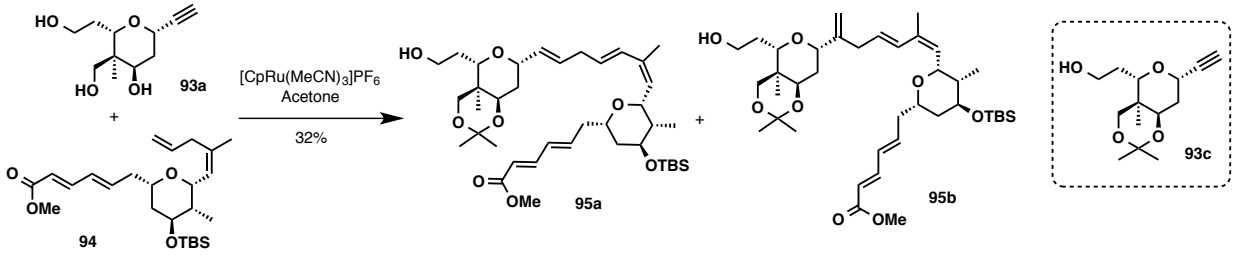
Alkyne 25. Triethylsilylacetylene (0.55 mL, 3.04 mmol) was added to a solution of vinyl iodide **S8** (0.700 g, 2.76 mmol), $Pd(PPh_3)_2Cl_2$ (19.4 mg, 28 µmol), and copper iodide (7.9 mg, 41 µmol) in triethylamine (9.2 mL) under an atmosphere of nitrogen at 50°C. After 1 h, the reaction was concentrated under reduced pressure and the crude residue was purified by flash column chromatography (silica, 10% diethyl ether - petroleum ether) to give the desired product (0.651 g, 89%). The product was submitted immediately to the next reaction.

Tetra-n-butylammonium fluoride (1M in THF, 2.5 mL, 2.5 mmol) was added drop-wise to a solution of the substrate (0.651 g, 2.5 mmol) in THF (6.2 mL) at 0 °C. After 15 min, the reaction was warmed to rt and stirred

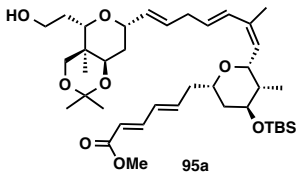
for an additional 1 h. The reaction was diluted with diethyl ether and water. The aqueous layer was extracted with diethyl ether (2 x 50 mL). The combined organic layer were washed with brine, dried with magnesium sulfate, concentrated, and the crude residue was purified by flash column chromatography (silica, 5% diethyl ether - petroleum ether) to give the desired product (0.257 g, 70% yield) as a 10:1 mixture of olefin isomers, favoring the *Z*-olefin, as confirmed by nOe analysis. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 5.78 (dq, J = 8.0, 0.6 Hz, 1H), 4.25 (ddd, J = 10.8, 8.4, 2.4 Hz, 1H), 3.96 (dd, J = 12.0, 4.0 Hz, 1H), 3.48 (td, J = 11.2, 2.4 Hz, 1H), 3.12 (s, 1H), 1.85 (d, J = 1.6 Hz, 3H), 1.85–1.80 (m, 1H), 1.66–1.31 (m, 5H). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 139.8, 118.4, 82.1, 81.7, 76.7, 68.2, 31.2, 25.7, 23.2, 23.0. IR (KBr-film) ν (cm^{-1}): 3293, 2937, 2849, 1204, 1086, 1035, 899.



Diene 27. Alkene **24** (15.1 mg, 0.12 mmol), alkyne **25** (15.0 mg, 0.10 mmol), and $[CpRu(MeCN)_3]PF_6$ (4.3 mg, 10 µmol) were combined in a flame dried microwave vial under an atmosphere of argon and dissolved in freshly distilled acetone (0.2 mL) at rt. After 2h, the reaction was concentrated under reduced pressure and the crude residue was purified by flash column chromatography (silica, 10% diethyl ether - petroleum ether) to give the branched product (8.9 mg, 33% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 5.63 (dd, *J* = 15.5, 8.0 Hz, 1H), 5.52 (dd, *J* = 15.7, 5.9 Hz, 1H), 5.22 (dd, *J* = 8.8, 1.5 Hz, 1H), 4.91 (d, *J* = 1.8 Hz, 1H), 4.80 (s, 1H), 4.04 – 3.86 (m, 3H), 3.82 – 3.72 (m, 1H), 3.52 – 3.35 (m, 2H), 2.83 (d, *J* = 6.9 Hz, 2H), 1.78 (d, *J* = 1.4 Hz, 3H), 1.67 – 1.33 (m, 12H).

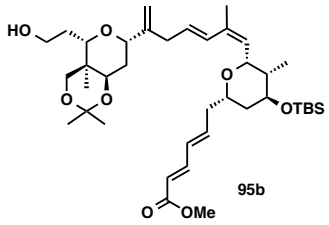


Dienes 95a and 95b. $[RuCp(MeCN)_3]PF_6$ (4.3 mg, 9.8 µmol) was added to a flame-dried vial and purged with argon. The vial was placed in a 55 °C bath and immediately a solution of alkene **94** (85 mg, 0.196 mmol) and alkyne **93a** (14 mg, 65 µmol) in acetone (degassed, 1.4 mL, total with rinses) was added drop-wise. After 2 h 10 min the reaction was allowed to cool to rt and then filtered through a short plug of silica (ethyl acetate, 25 mL). The filtrate was concentrated *in vacuo* and the residue was purified by flash column chromatography (silica, 10% → 30% → 40% → 50% → 80% ethyl acetate – hexane) to give the desired product (14.5 mg, 21 µmol, 32%) as a 3.2:1 mixture of the linear to branched isomer. Alkene **93c** (1.6 mg, 5.7 µmol) and alkene **94** (26.6 mg, 61.2 µmol) were recovered. The mixture of isomers was separated by preparative thin layer chromatography (50% ethyl acetate – hexane) to obtain the linear (11.0 mg, 16 µmol, 25%) and the branched (1.8 mg, 2.6 µmol, 4%) isomer.



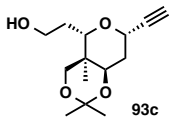
95a

$[\alpha]_D^{23}$ +23.0 (*c* 1.00, $CHCl_3$). ^{1}H NMR (600 MHz, $CDCl_3$) δ (ppm): 7.29 – 7.27 (m, 1H), 6.36 (d, J = 15.0 Hz, 1H), 6.23 – 6.15 (m, 2H), 5.79 (d, J = 15.0 Hz, 1H), 5.68 – 5.62 (m, 2H) 5.45 (dd, J = 15.5, 6 Hz, 1H), 5.31 (d, J = 7.8 Hz, 1H), 4.91 (d, J = 7.8 Hz, 1H), 4.39 (dd, J = 9.6, 3.0 Hz, 1H), 4.30 (dd, J = 10.8, 6.6 Hz, 1H), 3.93 – 3.86 (m, 3H), 3.83 – 3.78 (m, 2H), 3.73 (s, 3H), 3.55 (d, J = 12.6 Hz, 1H), 3.50 (d, J = 13.2 Hz, 1H), 2.82 – 2.78 (m, 2H), 2.41 – 2.37 (m, 1H), 2.33 – 2.29 (m, 1H), 1.82 (s, 3H), 1.78 – 1.55 (m, 4H), 1.59 – 1.53 (m, 4H), 1.44 (s, 3H), 1.43 (s, 3H), 0.93 (s, 9H), 0.89 (d, J = 7.8 Hz, 3H), 0.79 (s, 3H), 0.06 (s, 3H), 0.04 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ (ppm): 168.1, 145.5, 140.9, 132.9, 131.4, 130.5, 129.3, 128.64, 128.57, 119.5, 98.9, 73.2, 72.1, 71.8, 71.3, 71.1, 66.5, 63.2, 51.8, 40.7, 39.9, 36.5, 34.7, 34.1, 33.9, 30.8, 29.8, 26.2, 20.8, 19.1, 18.4, 15.2, 11.5, 6.9, 6.1, -4.5, -4.6. IR (KBr-film) ν (cm^{-1}): 3358, 2913, 1698, 1623, 1417, 1359, 1240, 1180, 1126, 1044, 825, 764. HRMS: (ESI) calcd for $C_{39}H_{64}O_8SiNa$ $[M+Na]^+$: 711.4263, found: 711.4272.



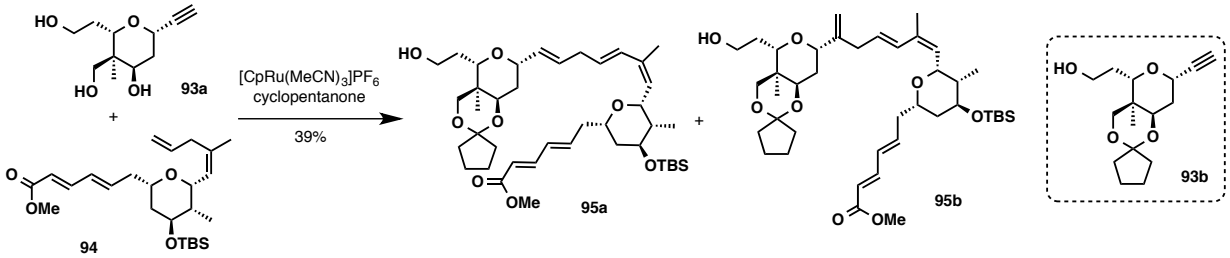
95b

$[\alpha]_D^{23}$ +32.8 (*c* 0.19, $CHCl_3$). ^{1}H NMR (600 MHz, $CDCl_3$) δ (ppm): 7.29 – 7.25 (m, 1H), 6.39 (d, J = 15.6 Hz, 1H), 6.24 – 6.15 (m, 2H), 5.79 (d, J = 15.6 Hz, 1H), 5.74 – 5.68 (m, 1H), 5.32 (d, J = 7.8 Hz, 1H), 5.06 (s, 1H), 4.92 (dd, J = 8.4, 2.4 Hz, 1H), 4.84 (s, 1H), 4.40 (dd, J = 9.6, 3.0 Hz, 1H), 4.28 (d, J = 11.4 Hz, 1H), 3.93 – 3.78 (m, 5H), 3.74 (s, 3H), 3.56 (d, J = 12.6 Hz, 1H), 3.51 (d, J = 12.6 Hz, 1H), 2.90 – 2.79 (m, 2H), 2.41 – 2.38 (m, 1H), 2.33 – 2.29 (m, 1H), 1.84 (s, 3H), 1.82-1.45 (m, 11H), 1.43 (s, 3H), 0.93 (s, 9H), 0.90 (d, J = 7.2 Hz, 3H), 0.80 (s, 3H), 0.05 (s, 3H), 0.04 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 167.8, 148.5, 145.2, 140.6, 132.8, 130.3, 129.1, 128.9, 128.3, 119.3, 110.9, 98.7, 75.0, 72.0, 71.6, 71.1, 71.0, 66.2, 62.8, 51.5, 40.5, 39.7, 36.2, 34.6, 33.9, 32.6, 30.7, 29.8, 29.6, 25.9, 20.6, 18.8, 18.1, 15.0, 11.2, -4.7, -4.9. IR (KBr-film) ν (cm^{-1}): 3367, 2911, 2887, 2817, 1697, 1622, 1441, 1415, 1359, 12389, 1179, 1145, 1125, 1044, 990, 958, 824, 764.

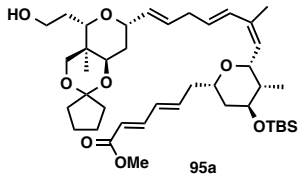


93c

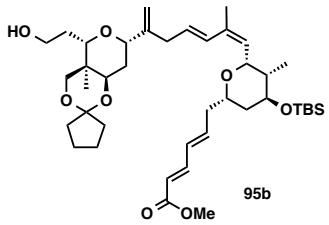
$[\alpha]_D^{23}$ -57.2 (*c* 1.00, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 4.59 (d, J = 12 Hz, 1H), 4.33 (dd, J = 6.5 Hz, 1H), 3.89 – 3.85 (m, 2H), 3.82 – 3.79 (m, 1H), 3.54 (d, J = 12.6 Hz, 1H), 3.49 (d, J = 12.6 Hz, 1H), 2.43 (d, J = 2 Hz, 1H), 2.11 – 2.05 (m, 1H), 1.75 – 1.69 (m, 3H), 1.43 (s, 3H), 1.41 (s, 3H), 0.81 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ (ppm): 99.0, 83.0, 76.6, 73.2, 71.5, 66.3, 63.3, 62.3, 34.6, 34.4, 31.2, 29.7, 18.9, 15.0. IR (KBr-film) ν (cm^{-1}): 3578, 2894, 2839, 1440, 1362, 1236, 1213, 1181, 1144, 1079, 1044. HRMS: (ESI) calcd for $C_{14}H_{22}O_4Na[M+Na]^+$: 277.1410, found: 277.1416.



Dienes 95a and 95b. $[RuCp(MeCN)_3]PF_6$ (3.7 mg, 8.5 µmol) was added to a flame-dried vial and purged with argon. The vial was placed in a 55 °C bath and immediately a solution of alkene **94** (73.6 mg, 0.170 mmol) and alkyne **93a** (12.1 mg, 56.4 µmol) in cyclopentanone (degassed, 1.2 mL, total with rinses) was added drop-wise. After 2 h 10 min the reaction was allowed to cool to rt and then filtered through a short plug of silica (ethyl acetate, 25 mL). The filtrate was concentrated *in vacuo* and the residue was purified by flash column chromatography (silica, 10% → 30% → 40% → 50% ethyl acetate – hexane) to give the desired product (12.5 mg, 17.5 µmol, 31%) and the undesired branched product (3.3 mg, 4.6 µmol, 8.2%) (3.8:1 mixture of the linear). Alkene **94** (53 mg, 0.122 mmol, 85%) and alkyne **93a** – as its cyclopentanone ketal (4.1 mg, 14.6 µmol, 26%) were recovered.

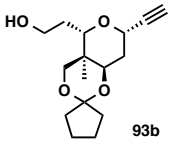


$[\alpha]_D^{23}$ +35.0 (*c* 1.0, $CHCl_3$). ^{1}H NMR (600 MHz, $CDCl_3$) δ (ppm): 7.29 – 7.24 (m, 1H), 6.37 (d, J = 15.6 Hz, 1H), 6.24 – 6.15 (m, 2H), 5.79 (d, J = 15.6 Hz, 1H), 5.68 – 5.62 (m, 2H), 5.45 (dd, J = 15.6 Hz, 6.0 Hz, 1 H), 5.31 (d, J = 7.8 Hz, 1H), 4.91 (dd, J = 8.4, 1.8 Hz, 1H), 4.45 (dd, J = 10.2, 3.6 Hz, 1H), 4.31 (d, J = 10.2, 6.0 Hz, 1H), 3.93 – 3.87 (m, 2H), 3.83 (d, J = 2.4 Hz, 1H), 3.82 – 3.78 (m, 1H), 3.75 – 3.74 (m, 1H), 3.74 (s, 3H), 3.55 (d, J = 12.6 Hz, 1H), 3.44 (d, J = 12.6 Hz, 1H), 2.82 – 2.78 (m, 2H), 2.41 – 2.37 (m, 1H), 2.33 – 2.29 (m, 1H), 1.82 (s, 3H), 1.94 – 1.24 (m, 19H), 0.93 (s, 9H), 0.90 (d, J = 7.2 Hz , 3H), 0.06 (s, 3H), 0.05 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ (ppm): 167.8, 145.2, 140.7, 132.7, 131.2, 130.3, 130.2, 129.1, 128.4, 128.3, 119.2, 110.7, 73.5, 72.9, 71.6, 71.1, 70.9, 67.7, 62.9, 51.6, 40.5, 40.2, 39.7, 36.3, 34.5, 33.9, 33.8, 30.6, 30.5, 29.8, 25.9, 24.5, 22.7, 20.6, 18.1, 15.0, 11.2, -4.7, -4.8. IR (KBr-film) ν (cm^{-1}): 3361, 2913, 2817, 1696, 1622, 1415, 1318, 1240, 1176, 1125, 1092, 1044, 990, 825. HRMS: (ESI) calcd for $C_{41}H_{66}O_8SiNa[M+Na]^+$: 737.4419, found: 737.4423.

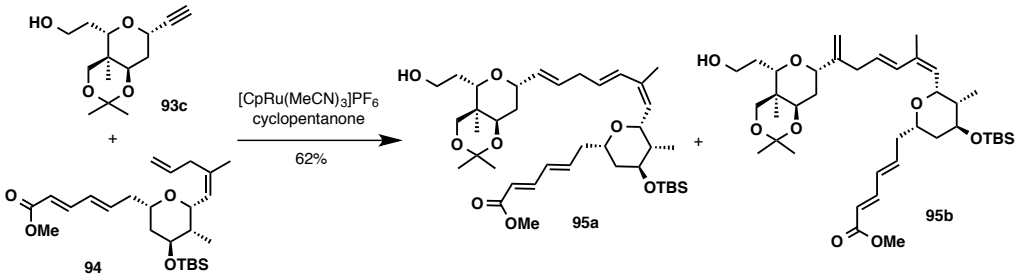


$[\alpha]_D^{23}$ +15.5 (*c* 0.10, $CHCl_3$). ^{1}H NMR (600 MHz, $CDCl_3$) δ (ppm): 7.29 – 7.25 (m, 1H), 6.39 (d, J = 15.6 Hz, 1H), 6.24 – 6.14 (m, 2H), 5.79 (d, J = 15.0 Hz, 1H), 5.74 – 5.69 (m, 1H), 5.31 (d, J = 8.4 Hz, 1H), 5.06 (s, 1H), 4.92 (dd, J = 8.4, 2.0 Hz, 1H), 4.84 (s, 1H), 4.46 (dd, J = 12.2, 3.6 Hz, 1H), 4.27 (d, J = 10.8 Hz, 1H), 3.94 – 3.72 (m, 5H), 3.74 (s, 3H), 3.56 (d, J = 12.6 Hz, 1H), 3.45 (d, J = 12.6 Hz, 1H), 2.89 – 2.80 (m, 2H), 2.42 – 2.38

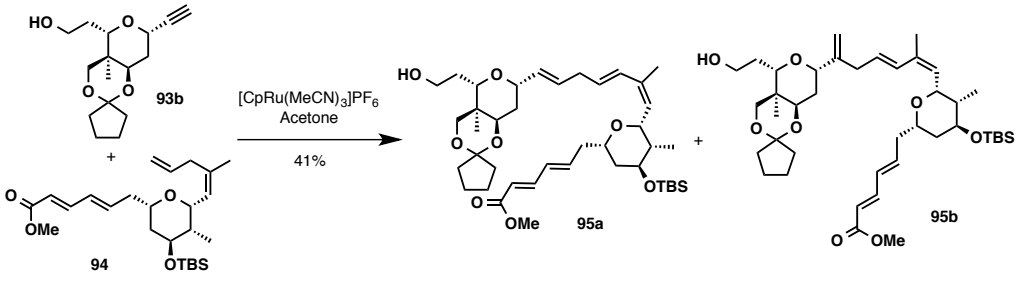
(m, 1H), 2.33 – 2.29 (m, 1H), 1.96 – 1.60 (m, 16H), 1.85 (s, 3H), 0.93 (s, 9H), 0.90 (d, J = 7.2 Hz, 3H), 0.79 (s, 3H), 0.07 (s, 3H), 0.05 (s, 3H). IR (KBr-film) ν (cm^{-1}): 3520, 3483, 3438, 3332, 2886, 1422, 1058. HRMS: (ESI) calcd for $C_{41}H_{66}O_8SiNa[M+Na]^+$: 737.4419, found: 737.4413.



$[\alpha]_D^{23}$ -62.2 (c 1.00, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 4.59 (d, J = 12.0 Hz, 1H), 4.37 (dd, J = 6.4 Hz, 1H), 3.90 – 3.84 (m, 1H), 3.81 – 3.76 (m, 1H), 3.74 (s, 1H), 3.54 (d, J = 12.4 Hz, 1H), 3.42 (d, J = 12.4 Hz, 1H), 2.42 (d, J = 2 Hz, 1H), 2.39 – 2.28 (m, 1H), 2.11 – 2.03 (m, 1H), 1.90 – 1.82 (m, 4H), 1.76 – 1.59 (m, 7H), 0.79 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 110.9, 83.0, 76.5, 73.2, 73.1, 67.7, 63.4, 62.2, 40.3, 34.6, 34.5, 31.2, 30.7, 24.7, 22.8, 14.9. IR (KBr-film) ν (cm^{-1}):3354, 2919, 2834, 1445, 1317, 1133, 1092, 1060, 1032. HRMS: (ESI) calcd for $C_{16}H_{24}O_4$ $[M+Na]^+$: 303.1567, found: 303.1567.

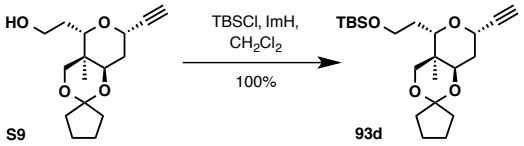


Dienes 95a and 95b. $[RuCp(MeCN)_3]PF_6$ (2.0 mg, 4.6 μmol) was added to a flame-dried vial and purged with argon. The vial was placed in a 55°C bath and immediately a solution of alkene **94** (40.0 mg, 92 μmol) and alkyne **93c** (7.8 mg, 30.7 μmol) in cyclopentanone (distilled over CaH_2 and degassed, 0.65 mL, total with rinses) was added drop-wise. After 2 h 10 min the reaction was allowed to cool to rt and then filtered through a short plug of silica (ethyl acetate, 25 mL), the filtrate was concentrated *in vacuo* and the residue was purified by flash column chromatography (silica, 10% → 30% → 50% ethyl acetate – hexane) to give the desired product (12.9 mg, 19 μmol, 62%) as a 3:1 mixture of the linear to branched isomer. Alkene **94** (31.8 mg, 73 μmol) was recovered. The mixture of isomers was separated by preparative thin layer chromatography (50% ethyl acetate – hexane) to obtain the linear (3.5 mg, 5.1 μmol, 17%) and the branched (1 mg, 1.5 μmol, 5%) isomers along with a mixed fraction (4.9 mg, 7.1 μmol, 23%).

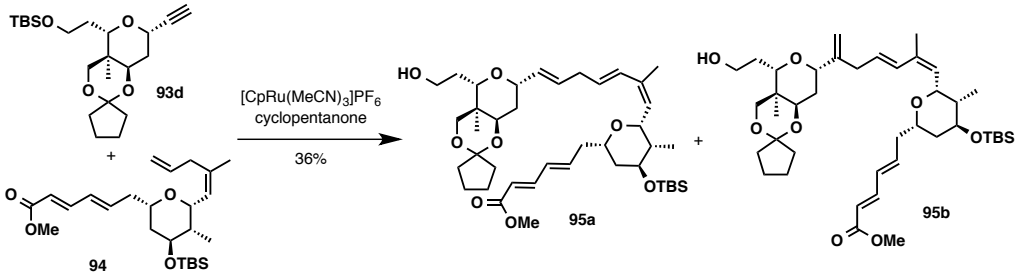


Dienes 95a and 95b. $[RuCp(MeCN)_3]PF_6$ (2.1 mg, 4.8 μmol) was added to a flame-dried vial and purged with argon. The vial was placed in a 55°C bath and immediately a solution of alkene **94** (41.3 mg, 95 μmol) and alkyne **93b** (8.9 mg, 32 μmol) in acetone (degassed, 0.67 mL, total with rinses) was added drop-wise. After 2 h

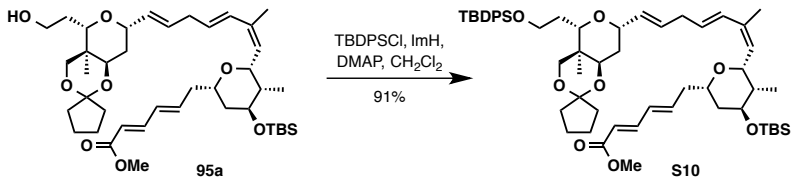
10 min the reaction was allowed to cool to rt and then filtered through a short plug of silica (ethyl acetate, 25 mL). The filtrate was concentrated *in vacuo* and the residue was purified by flash column chromatography (silica, 10% → 30% → 40% → 50% ethyl acetate – hexane) to give the desired product (9.2 mg, 13 µmol, 41%) as a 3.7:1 mixture of the linear to the branched isomer. Alkene **94** (26.6 mg, 61 µmol) and alkyne **93b** (1.6 mg, 5.7 µmol) were both recovered. The mixture of isomers could be separated by preparative thin layer chromatography (50% ethyl acetate – hexane) to obtain the linear (8.0 mg, 11 µmol, 35%) and the branched (1.0 mg, 1.4 µmol, 4%) isomers.



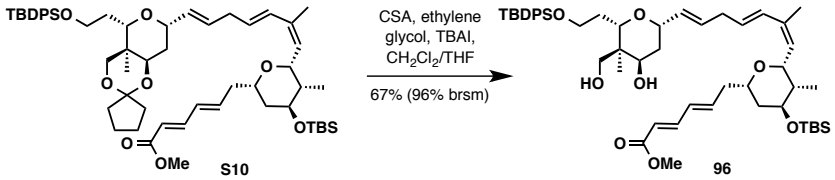
TBS Ether 93d. *tert*-Butyldimethylsilyl chloride (5.4 mg, 36 µmol) was added to a mixture of alcohol **S9** (10 mg, 36 µmol) and imidazole (6.1 mg, 90 µmol) in dichloromethane (0.4 mL) at rt. After 45 min, saturated aqueous sodium bicarbonate was added. The aqueous layer was extracted with dichloromethane (3 x 15 mL). The combined organic extract were dried with magnesium sulfate, concentrated *in vacuo* and the residue was purified by flash column chromatography (silica, 30% ethyl acetate – hexane) to give the desired product (14.4 mg, 36 µmol, 100%). $[\alpha]_D^{23}$ -64.8 (*c* 1.00, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 4.54 – 4.50 (m, 1H), 4.32 (d, J = 9.5 Hz, 1H), 3.79 -3.74 (m, 3H), 3.58 (d, J = 15.5 Hz, 1H), 3.40 (d, J = 12.5 Hz, 1H), 2.43 (d, J = 2 Hz, 1H), 2.08 – 2.04 (m, 1H), 1.90 – 1.82 (m, 3H), 1.75 – 1.59 (m, 7H), 1.55 – 1.48 (m, 1H), 0.90 (s, 9H), 0.76 (s, 3H), 0.08 (s, 3H), 0.06 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 110.6, 83.4, 73.1, 72.5, 72.2, 67.6, 63.1, 59.9, 40.1, 34.7, 34.3, 32.2, 30.6, 26.1, 24.6, 22.7, 18.4, 14.7, -5.2, -5.3. IR (KBr-film) ν (cm^{-1}): 3266, 2962, 2890, 2818, 1444, 1317, 1237, 1173, 1136, 1092, 1032, 963, 825, 765. HRMS: (ESI) calcd for $C_{22}H_{38}O_4SiNa[M+Na]^+$: 417.2432, found: 417.2429.



Dienes 95a and 95b. $[RuCp(MeCN)_3]PF_6$ (2.3 mg, 5.4 µmol) was added to a flame-dried vial and purged with argon. The vial was placed in a 55°C bath and immediately a solution of alkene **94** (47.4 mg, 0.109 mmol) and alkyne **93d** (14.4 mg, 36 µmol) in cyclopentanone (distilled over CaH_2 and degassed, 0.77 mL, total with rinses) was added drop-wise. After 2 h 10 min the reaction was allowed to cool to rt and then filtered through a short plug of silica (ethyl acetate, 25 mL). The filtrate was concentrated *in vacuo* and the residue was purified by flash column chromatography (silica, 10% → 30% → 40% ethyl acetate – hexane) to give the desired product (9.1 mg, 13 µmol, 36%) as a 3.7:1 mixture of the linear to the branched isomer. Alkene **94** (40 mg, 92 µmol) was recovered. The mixture of isomers could be separated by preparative thin layer chromatography (50% ethyl acetate – hexane) to obtain the linear (4.6 mg, 6.4 µmol, 18%) and branched (1 mg, 1.4 µmol, 4%) isomers.

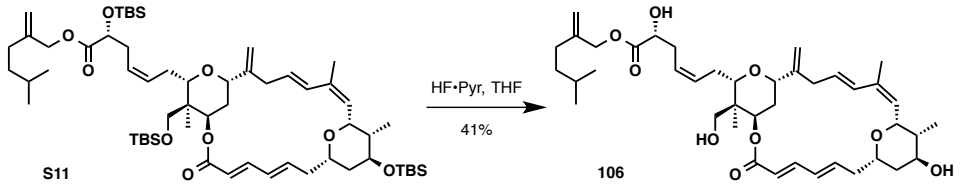


TBDPS Ether S10. *tert*-Butylchlordiphenylsilane (12 µL, 46.2 µmol) was added to a solution of diene **95a** (10.0 mg, 14.0 µmol), imidazole (9.4 mg, 0.138 mmol), and 4-dimethylaminopyridine (0.7 mg, 6.2 µmol) in dichloromethane (1.1 mL) at 0°C. After 30 min, the reaction was warmed to rt and stirred for an additional 30 min. The reaction was diluted with water and dichloromethane. The aqueous layer was extracted with dichloromethane (4 x 20 mL). The combined organic layers were dried with sodium sulfate, concentrated, and the residue was purified by flash column chromatography (silica, 100% dichloromethane (to remove silanol), then 10% ethyl acetate – hexane) to give the desired product (12.1 mg, 12.7 µmol, 91% yield). $[\alpha]_D^{23}$ 30.1 (*c* 1.00, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 7.73 – 7.66 (m, 4H), 7.42 – 7.29 (m, 6H), 7.27 (dd, J = 15.5, 10 Hz, 1H), 6.38 (d, J = 15.0 Hz, 1H), 6.24 – 6.13 (m, 2H), 5.79 (d, J = 15.5 Hz, 1H), 5.69 – 5.59 (m, 2H), 5.46 (dd, J = 15.5, 6.0 Hz, 1H), 5.32 (d, J = 7.5 Hz, 1H), 4.95 – 4.92 (m, 1H), 4.54 (d, J = 10.0 Hz, 1H), 4.22 (dd, J = 10.5, 5.0 Hz, 1H), 3.95 (m, 2H), 3.85 (m, 3H), 3.37 (s, 3H), 3.62 (d, J = 12.0 Hz, 1H), 3.43 (d, J = 12.0 Hz, 1H), 2.88 – 2.79 (m, 2H), 2.43 – 2.37 (m, 1H), 2.34 – 2.28 (m, 1H), 1.83 (s, 3H), 1.94 – 1.25 (m, 16 H), 1.06 (s, 9H), 0.92 (s, 9H), 0.90 (d, J = 7.0 Hz, 3H), 0.73 (s, 3H), 0.05 (s, 3H), 0.04 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 167.8, 145.2, 140.6, 135.7, 135.6, 134.4, 134.1, 132.7, 131.7, 130.3, 129.6, 129.4, 129.4, 128.3, 128.1, 127.7, 127.6, 119.2, 110.6, 73.8, 72.4, 71.6, 71.1, 71.1, 70.9, 67.7, 60.5, 51.6, 40.5, 40.2, 39.7, 36.5, 34.4, 33.9, 32.1, 30.7, 27.0, 25.9, 24.7, 22.8, 20.6, 19.4, 18.1, 14.9, 11.2, -4.7, -4.8. IR (KBr-film) ν (cm^{-1}): 2913, 2889, 2817, 1697, 1622, 1450, 1409, 1240, 1175, 1124, 1094, 989, 953. HRMS: (ESI) calcd for $C_{57}H_{85}O_8Si_2Na$ $[M+Na]^+$: 953.5777, found: 953.5761.

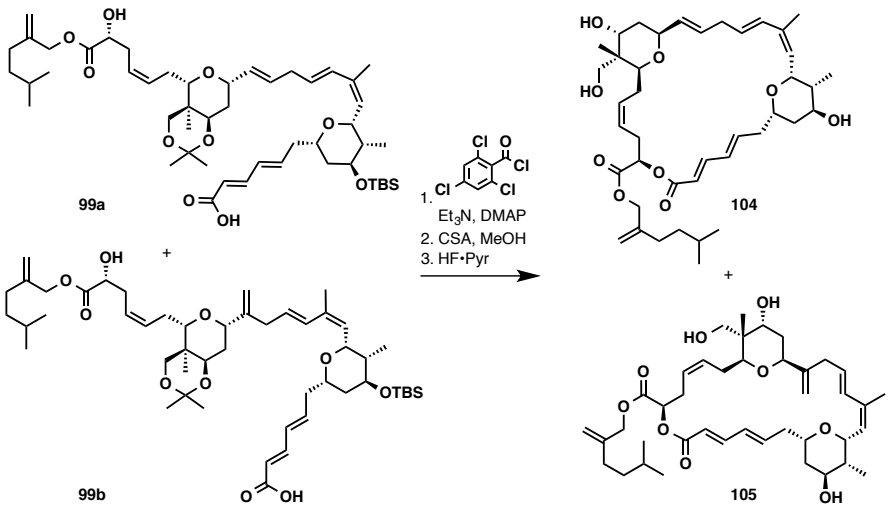


Diol 96. Tetrabutylammonium iodide (0.9 mg, 2.44 µmol) and camphorsulfonic acid (0.6 mg, 2.44 µmol) were added sequentially to a solution of ketal **S10** (12.1 mg, 12.69 µmol) and ethylene glycol (7 µL, 0.125 mmol) in THF (0.6 mL) and dichloromethane (1.2 mL) at rt. After 3 h 30 min, a saturated aqueous solution of sodium bicarbonate was added. The aqueous layer was extracted with ethyl acetate (5 x 20 mL). The combined organic layers were washed with brine, dried with sodium sulfate, concentrated, and the residue was purified by flash column chromatography (silica, 10% → 30% → 50% ethyl acetate – hexane) to give the desired product (7.5 mg, 8.4 µmol, 67% yield) and recovered starting material (3.5 mg, 3.67 µmol, 29% yield). $[\alpha]_D^{23}$ 11.4 (*c* 0.75, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 7.68 – 7.66 (m, 4H), 7.42 – 7.34 (m, 6H), 7.26 (dd, J = 15.6, 10.2 Hz, 1H), 6.39 (d, J = 15.0 Hz, 1H), 6.24 – 6.13 (m, 2H), 5.79 (d, J = 15.0 Hz, 1H), 5.70 – 5.61 (m, 2H), 5.48 (dd, J = 15.0, 5.4 Hz, 1H), 5.32 (d, J = 7.8 Hz, 1H), 4.31 – 4.23 (m, 2H), 3.96 – 3.78 (m, 5H), 3.73 (s, 3H), 3.71 (d, J = 12.0 Hz, 1H), 3.60 (d, J = 12.0 Hz, 1H), 3.43 (bs, 1H), 2.86 – 2.80 (m, 2H), 2.74 (bs, 1H), 2.39 (ddd, J = 14.4, 6.6, 6.6 Hz, 1H), 2.31 (ddd, J = 14.4, 6.6, 6.6 Hz, 1H), 1.83 (s, 3H), 1.80 – 1.54 (m, 6H), 1.32 (d, J = 13.2 Hz, 1H), 1.05 (s, 9H), 0.92 (s, 9H), 0.90 (d, J = 6.6 Hz, 3H), 0.79 (s, 3H), 0.05 (s, 3H), 0.04 (s, 3H). ^{13}C NMR (100

MHz, $CDCl_3$) δ (ppm): 168.0, 145.4, 140.9, 135.8, 135.7, 133.9, 133.7, 133.1, 131.6, 130.4, 130.1, 129.8, 129.8, 129.4, 128.4, 128.4, 127.90, 127.88, 119.3, 75.1, 72.7, 71.1, 71.4, 71.2, 71.0, 70.3, 61.7, 51.7, 40.5, 40.1, 39.8, 36.6, 36.4, 34.0, 32.6, 27.1, 26.0, 20.7, 19.4, 18.3, 15.5, 11.4, -4.6, -4.7. IR (KBr-film) ν (cm^{-1}): 3364, 2888, 1696, 1621, 1410, 1239, 1093, 824, 694. HRMS: (ESI) calcd for $C_{52}H_{78}O_8Si_2Na[M+Na]^+$: 909.5127, found: 909.5133.



(–)-*iso*-Lasonolide A 106. Hydrogen fluoride-pyridine (0.150 mL) was added to a solution of (–)-TBS-*iso*-lasonolide A **S11** (4.4 mg (of a 1.9:1 mixture of isomers) 4.23 μmol) in THF (0.25 mL) and pyridine (0.25 mL) in a plastic vial at rt. After 20 h, the reaction was carefully quenched with a saturated aqueous solution of sodium bicarbonate, and the reaction with diluted with ethyl acetate. The aqueous layer was extracted with ethyl acetate (5 x 20 mL). The combined organic layers were washed with brine, dried with sodium sulfate, concentrated, and the residue was purified by flash column chromatography (silica, 10% → 50% → 80% ethyl acetate – hexanes) and then further purified by preparative HPLC (econosil 250 x 10 mm; heptane/isopropanol 93:7:0; flow rate 5 mL/min; detection at 220 nm) to give (–)-*iso*-lasonolide A (**106**) (0.8 mg, 1.14 μmol, 41% yield). ^{1}H NMR ($CDCl_3$ 600 MHz) δ (ppm): 7.32–7.26 (m, 1H), 6.60 (d, J = 13.8 Hz, 1H), 6.29–6.21 (m, 2H), 5.76–5.66 (m, 2H), 5.70 (d, J = 16.2 Hz, 1H), 5.52–5.48 (m, 1H), 5.37 (d, J = 6.6 Hz, 1H), 5.24 (s, 1H), 5.09 (s, 1H), 5.03 (s, 1H), 4.98 (bs, 1H), 4.97 (s, 1H), 4.73 (d, J = 6.6 Hz, 1H), 4.62 (s, 2H), 4.28–4.23 (m, 1H), 4.11 (d, J = 10.8 Hz, 1H), 4.02–3.96 (m, 2H), 3.61 (d, J = 7.8 Hz, 1H), 3.42–3.38 (m, 1H), 3.38–3.32 (m, 1H), 3.22–3.16 (bs, 1H), 3.05 (dd, J = 14.4, 4.2 Hz, 1H), 2.90–2.83 (m, 2H), 2.62–2.56 (m, 1H), 2.51–2.46 (m, 1H), 2.32 (dd, J = 5.4 Hz, 2H), 2.24–2.08 (m, 3H), 2.06 (dd, J = 7.8 Hz, 2H), 1.89–1.84 (m, 1H), 1.82 (s, 3H), 1.74–1.25 (m, 7H), 1.13 (s, 3H), 1.04 (d, J = 6.6 Hz, 3H), 0.90 (d, J = 6.6 Hz, 6H). ^{13}C NMR ($CDCl_3$ 125 MHz) δ (ppm): 174.2, 168.0, 148.7, 147.8, 145.6, 143.8, 138.5, 131.5, 131.1, 128.7, 128.1, 125.3, 124.7, 117.9, 112.7, 112.2, 78.1, 75.5, 74.1, 72.5, 70.8, 70.3, 70.1, 67.9, 65.6, 41.9, 40.3, 38.8, 38.7, 36.7, 33.8, 33.5, 32.6, 31.1, 28.1, 27.8, 22.6, 21.1, 15.3, 11.6. IR (NaCl - film) ν (cm^{-1}): 3385, 2914, 2880, 2811, 1715, 1666, 1620, 1443, 1413, 1361, 1241, 1185, 1143, 1034. HRMS: (ESI) calcd for $C_{41}H_{60}O_9Na$ $[M+Na]^+$ 719.4130 found 719.4124.

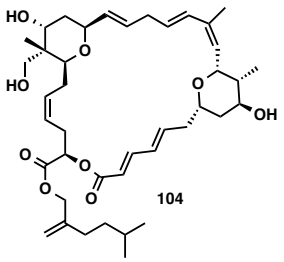


Lasonolide Analogs 104 and 105. A "stock solution" of 2,4,6-trichlorobenzoylchloride (27 µL, 0.172 mmol) and triethylamine (48 µL, 0.344 mmol) in THF (4.5 mL) was prepared in a flame-dried vial.

In a separate flask containing the neat secoacids **99a** and **99b** (15.4 mg, 17.7 µmol, 3:1 mixture of **99a**:**99b**) was added the "stock solution" (1.45 mL) at rt. After 3 h, the reaction was filtered through a plug of cotton, using THF, and concentrated. The crude residue was immediately dissolved in benzene (7.9 mL) and added drop-wise, over 25 min, to a solution of 4-dimethylaminopyridine (21.6 mg, 0.177 mmol) in benzene (1.0 mL) at 90 °C. After addition of the substrate was complete, the reaction was allowed to stir at 90 °C for an additional 1 h. The reaction was cooled to rt and directly subjected to flash column chromatography (silica, 5% ethyl acetate-hexanes) to deliver the desired compounds (8.2 mg, 9.63 µmol, 54% yield) as an inseparable mixture (3:1 linear to branched) of isomers which was used directly in the next reaction.

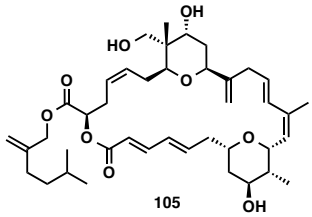
Camphorsulfonic acid (6.7 mg, 28.9 µmol) was added to a solution of the substrate (8.2 mg, 9.63 µmol) in methanol (2.14 mL) at rt. After 4 h, the methanol was removed under reduced pressure. The residue was diluted with ethyl acetate and water. The aqueous layer was extracted with ethyl acetate (4 x 20 mL). The combined organic layers were washed with brine, dried with sodium sulfate, concentrated, and the residue was submitted to the next reaction without further purification.

Hydrogen fluoride-pyridine (0.150 mL) was added to a solution of the crude substrate in THF (0.25 mL) and pyridine (0.25 mL) in a plastic vial at rt. After 20 h, the reaction as carefully quenched with a saturated aqueous solution of sodium bicarbonate, and the reaction with diluted with ethyl acetate. The aqueous layer was extracted with ethyl acetate (5 x 20 mL). The combined organic layers were washed with brine, dried with sodium sulfate, concentrated, and the residue was purified by flash column chromatography (silica, 10% → 50% → 80% ethyl acetate – hexanes) and then further purified by preparative HPLC (econosil 250x10 mm; heptane/isopropanol 93:7:0; flow rate 5 mL/min; detection at 220 nm) to give the branched isomer (1.2 mg, 1.72 µmol, 39% yield) and the linear isomer (3.3 mg, 4.74 µmol, 36% yield).



104

$[\alpha]_D^{24}$ +13.2 (c 0.33 in $CHCl_3$). ^{1}H NMR ($CDCl_3$ 600 MHz) δ (ppm): 7.30–7.23 (m, 1H), 6.60 (d, J = 15.0 Hz, 1H), 6.28 (dd, J = 15.6, 10.8 Hz, 1H), 6.21 (ddd, J = 15.6, 5.4 Hz, 1H), 5.85–5.79 (m, 1H), 5.78 (d, J = 15.6 Hz, 1H), 5.68–5.61 (m, 1H), 5.43–5.34 (m, 2H), 5.19 (dd, J = 10.8, 3.6 Hz, 1H), 5.01 (s, 1H), 4.99 (s, 1H), 4.93 (s, 1H), 4.88 (s, 1H), 4.78 (d, J = 6.6 Hz, 1H), 4.62 (d, J = 13.2 Hz, 1H), 4.56 (d, J = 13.2 Hz, 1H), 4.23 (d, J = 12.0 Hz, 1H), 4.08–4.02 (m, 2H), 4.02–3.97 (m, 2H), 3.68 (s, 2H), 3.09 (dd, J = 15.0, 6.0 Hz, 1H), 2.85–2.74 (m, 3H), 2.70–2.62 (m, 2H), 2.38–2.30 (m, 2H), 2.28–2.21 (m, 1H), 2.14–2.08 (m, 1H), 2.04 (dd, J = 7.8 Hz, 2H), 2.07–1.98 (m, 1H), 1.92–1.85 (m, 1H), 1.86 (s, 3H), 1.74–1.19 (m, 7H), 1.04 (d, J = 7.2 Hz, 3H), 0.89 (d, J = 6.6 Hz, 6H), 0.86 (s, 3H). ^{13}C NMR ($CDCl_3$ 125 MHz) δ (ppm): 172.0, 170.2, 149.0, 146.2, 141.6, 131.6, 130.8, 130.1, 129.6, 129.1, 127.6, 127.0, 125.4, 125.0, 118.8, 112.3, 75.6, 75.4, 73.0, 71.9, 71.6, 70.8, 70.1, 70.0, 67.7, 40.5, 38.8, 38.7, 36.7, 35.0, 34.1, 31.0, 29.8, 29.4, 27.8, 27.7, 22.6, 21.1, 15.8, 11.5. IR (NaCl - film) ν (cm^{-1}): 3364, 2914, 2882, 2812, 1693, 1621, 1442, 1359, 1241, 1162, 1116, 1077, 1031. HRMS: (ESI) calcd for $C_{41}H_{60}O_9Na$ $[M+Na]^+$ 719.4130 found 719.4129.

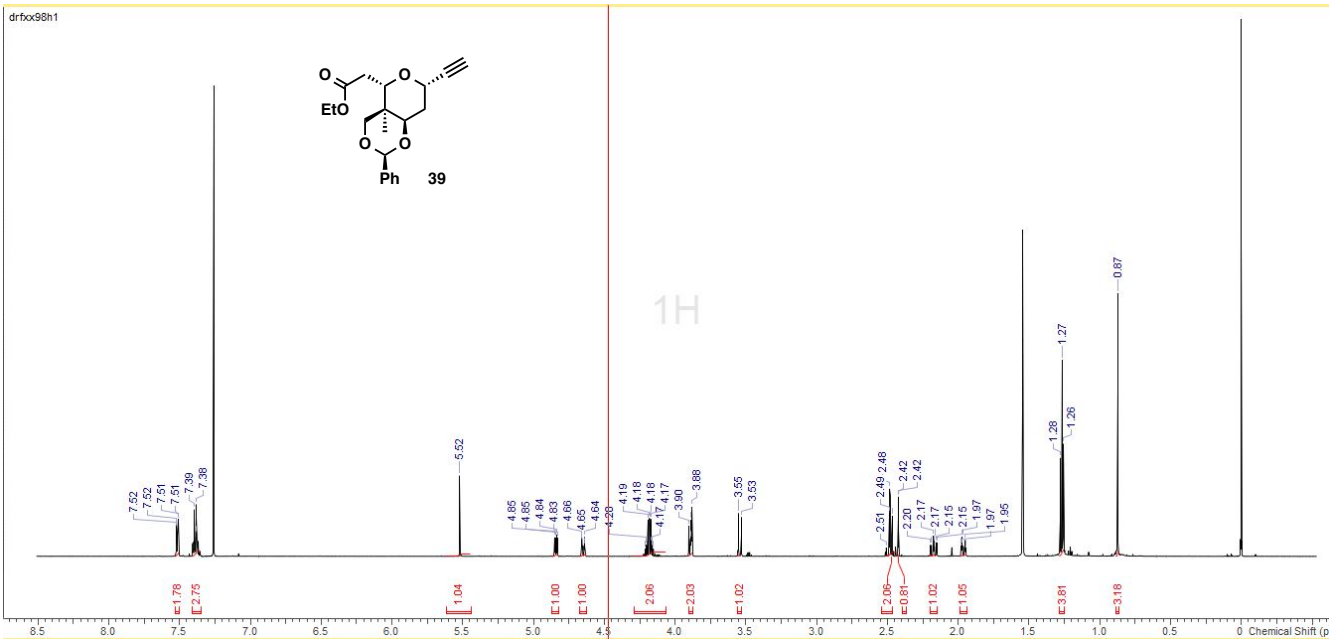


105

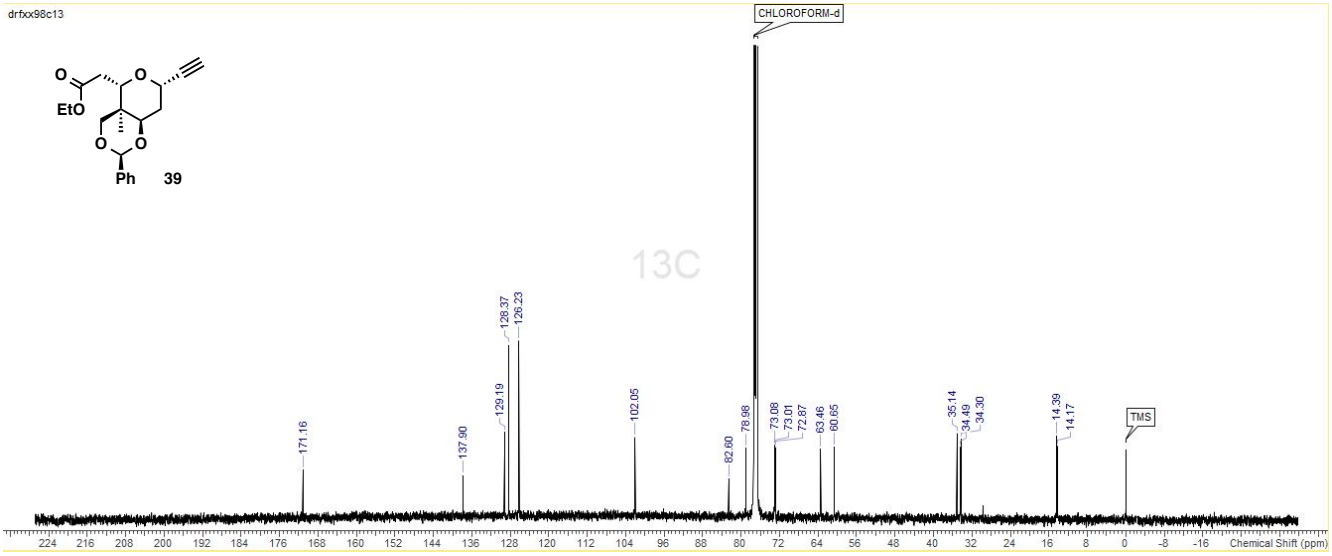
$[\alpha]_D^{24}$ -41.4 (c 0.33 in $CHCl_3$). ^{1}H NMR ($CDCl_3$ 600 MHz) δ (ppm): 7.32 (dd, J = 15.0, 10.2 Hz, 1H), 6.50 (d, J = 15.6 Hz, 1H), 6.33 (ddd, J = 15.6, 7.2 Hz, 1H), 6.24 (dd, J = 15.0, 10.8 Hz, 1H), 5.82 (d, J = 15.6 Hz, 1H), 5.74–5.66 (m, 3H), 5.47 (dd, J = 15.0, 4.8 Hz, 1H), 5.46–5.40 (m, 1H), 5.31 (d, J = 7.2 Hz, 1H), 5.19 (dd, J = 9.6, 4.2 Hz, 1H), 5.01 (s, 1H), 4.93 (s, 1H), 4.76 (dd, J = 7.8, 1.8 Hz, 1H), 4.60 (AB J = 18.6, 12.6 Hz, 2H), 4.25 (dd, J = 12.0, 5.4 Hz, 1H), 4.04 (dd, J = 10.2, 2.4 Hz, 1H), 4.00–3.92 (m, 3H), 3.64 (s, 2H), 2.84 (dd, J = 6.0 Hz, 2H), 2.82–2.74 (m, 1H), 2.66–2.58 (m, 1H), 2.36–2.31 (m, 1H), 2.22–2.10 (m, 3H), 2.04 (dd, J = 7.8 Hz, 2H), 1.86 (s, 3H), 1.80 (ddd, J = 14.4, 12.0, 3.0 Hz, 1H), 1.75–1.70 (m, 1H), 1.67–1.17 (m, 6H), 1.01 (d, J = 6.6 Hz, 3H), 0.88 (d, J = 7.2 Hz, 6H), 0.83 (s, 3H). ^{13}C NMR ($CDCl_3$ 125 MHz) δ (ppm): 170.3, 166.6, 146.5, 143.8, 142.8, 136.3, 130.8, 130.5, 129.7, 129.6, 129.3, 129.2, 126.2, 125.5, 118.6, 112.3, 75.3, 74.9, 73.1, 72.1, 72.0, 70.8, 70.6, 70.1, 67.6, 40.4, 39.4, 39.2, 36.7, 36.6, 36.5, 34.2, 31.0, 29.8, 27.8, 27.6, 22.6, 20.9, 15.6, 11.5. IR (NaCl - film) ν (cm^{-1}): 3368, 2917, 2883, 2814, 1693, 1619, 1442, 1358, 1243, 1168, 1117, 1074, 1011, 790. HRMS: (ESI) calcd for $C_{41}H_{60}O_9Na$ $[M+Na]^+$ 719.4130 found 719.4129.

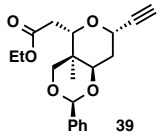
COPIES OF SPECTRA

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



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

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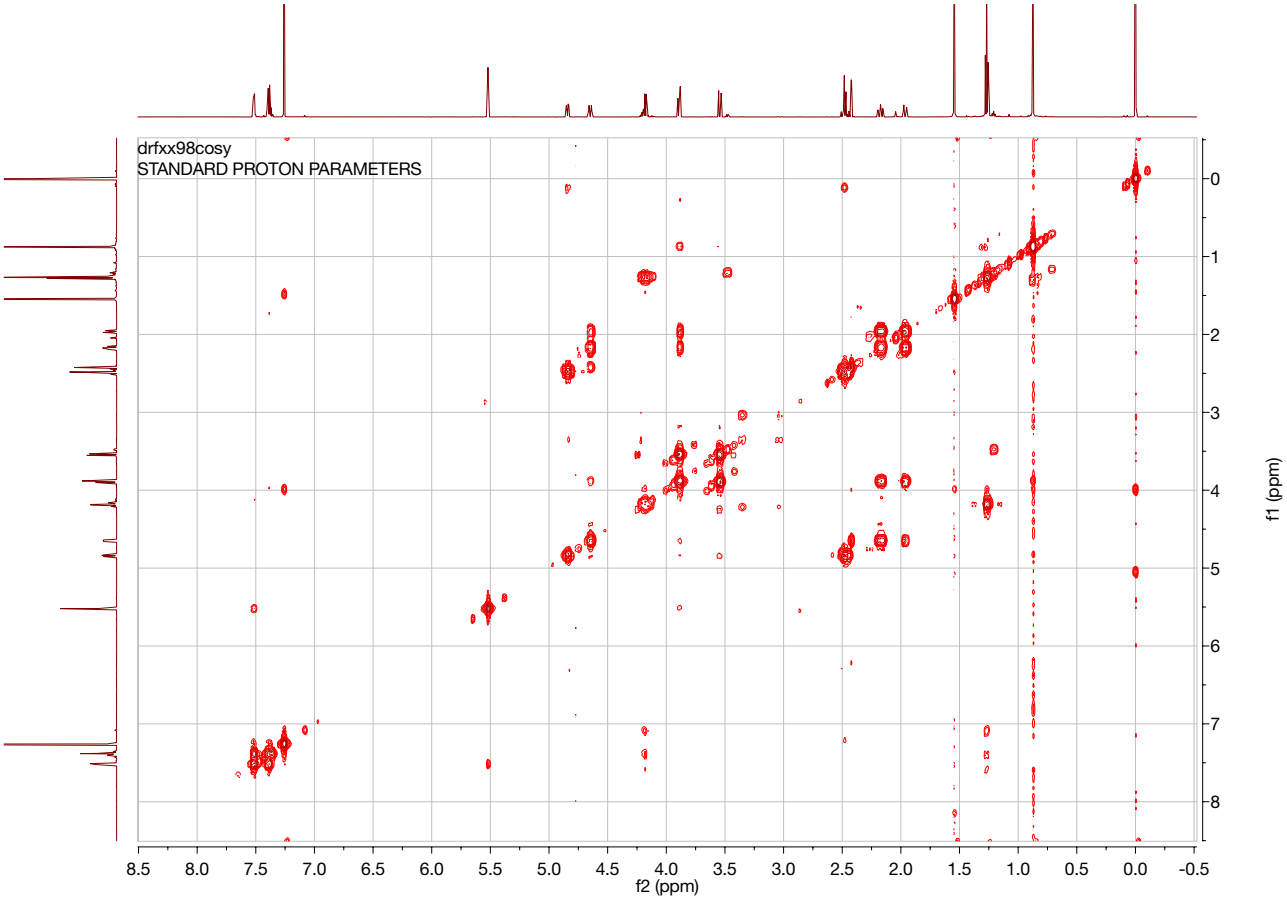
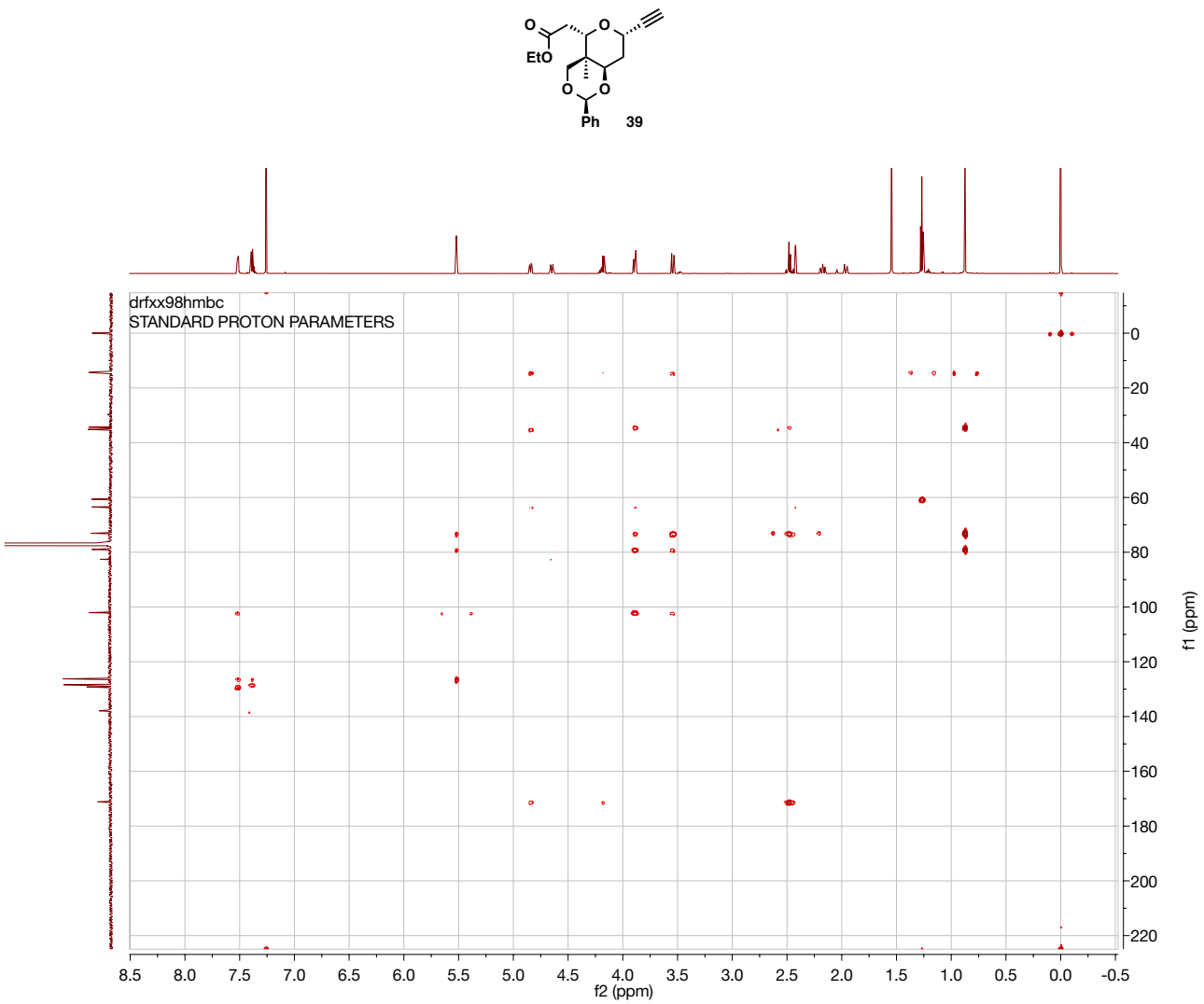
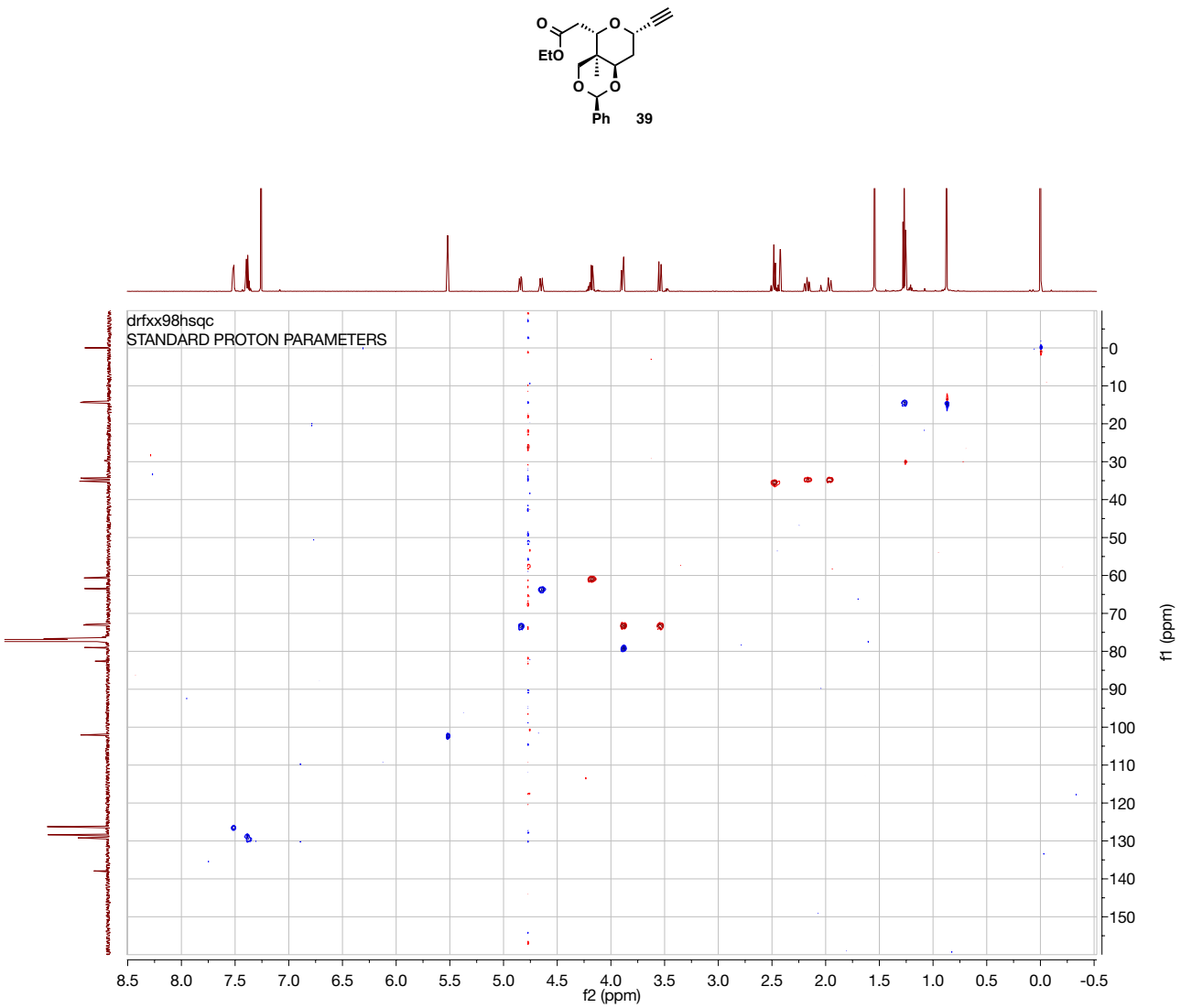
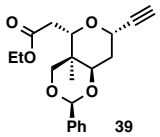
EtO
O
O
O
Ph

39

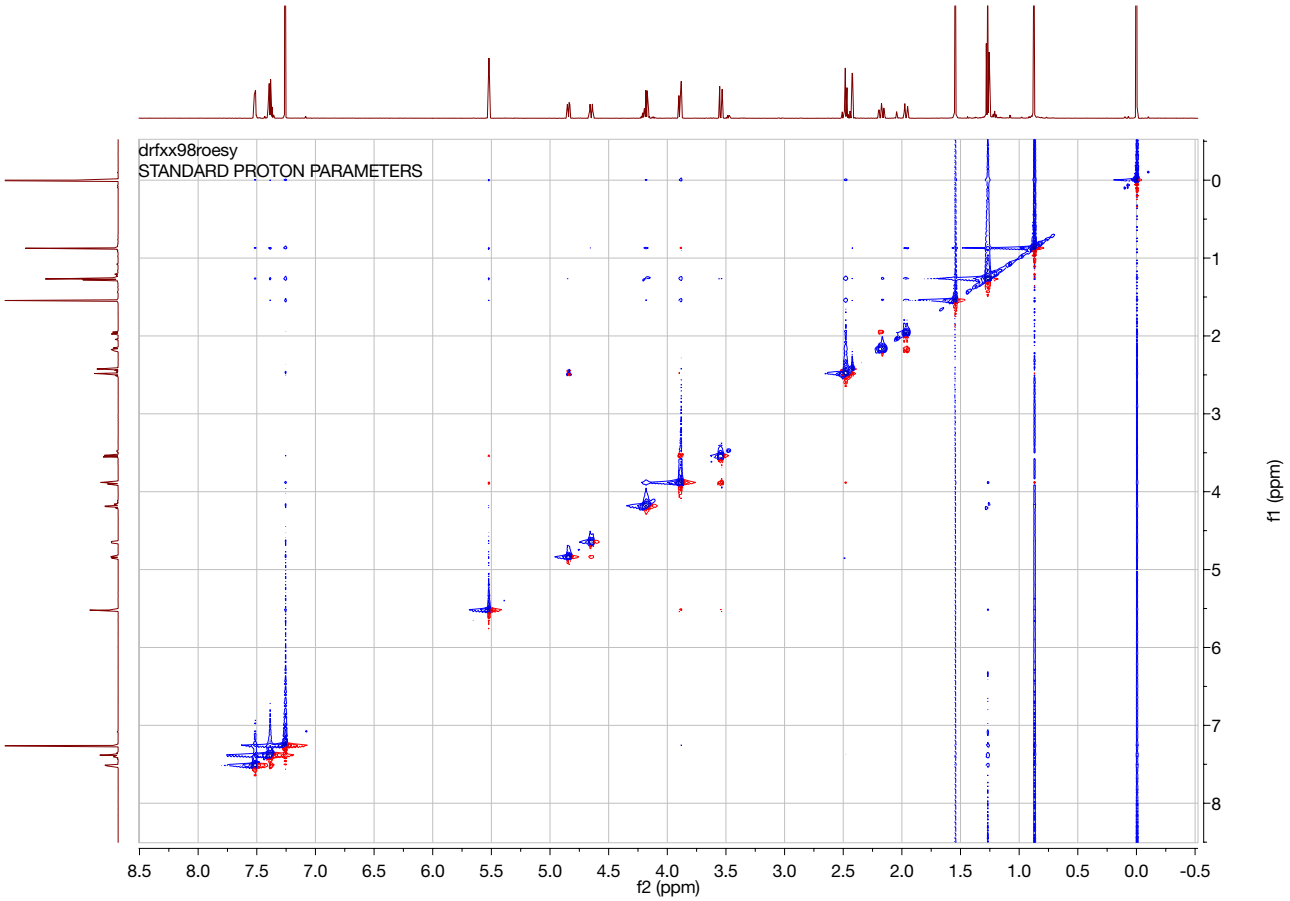

drfxx98cosy
STANDARD PROTON PARAMETERS
f2 (ppm)
f1 (ppm)

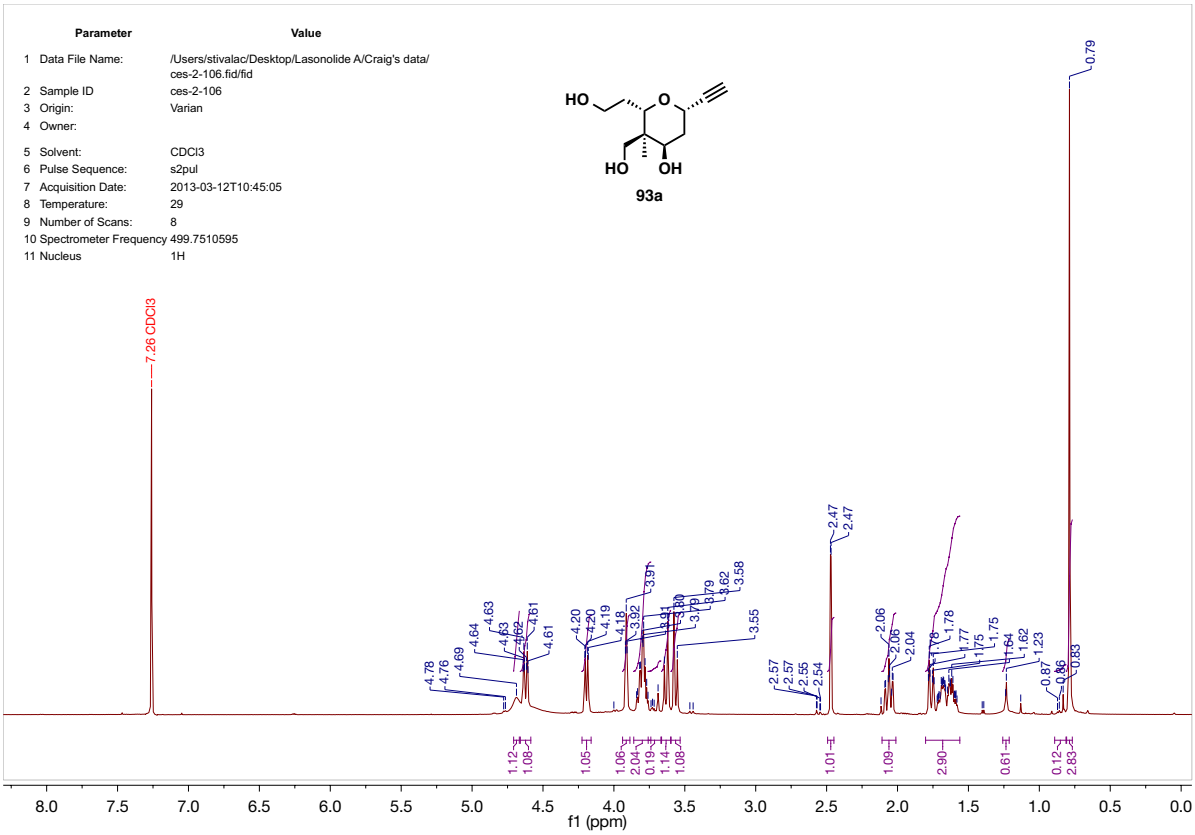

O
EtO
O
O
O
Ph
39
drfxx98hmbc
STANDARD PROTON PARAMETERS
f2 (ppm)
f1 (ppm)

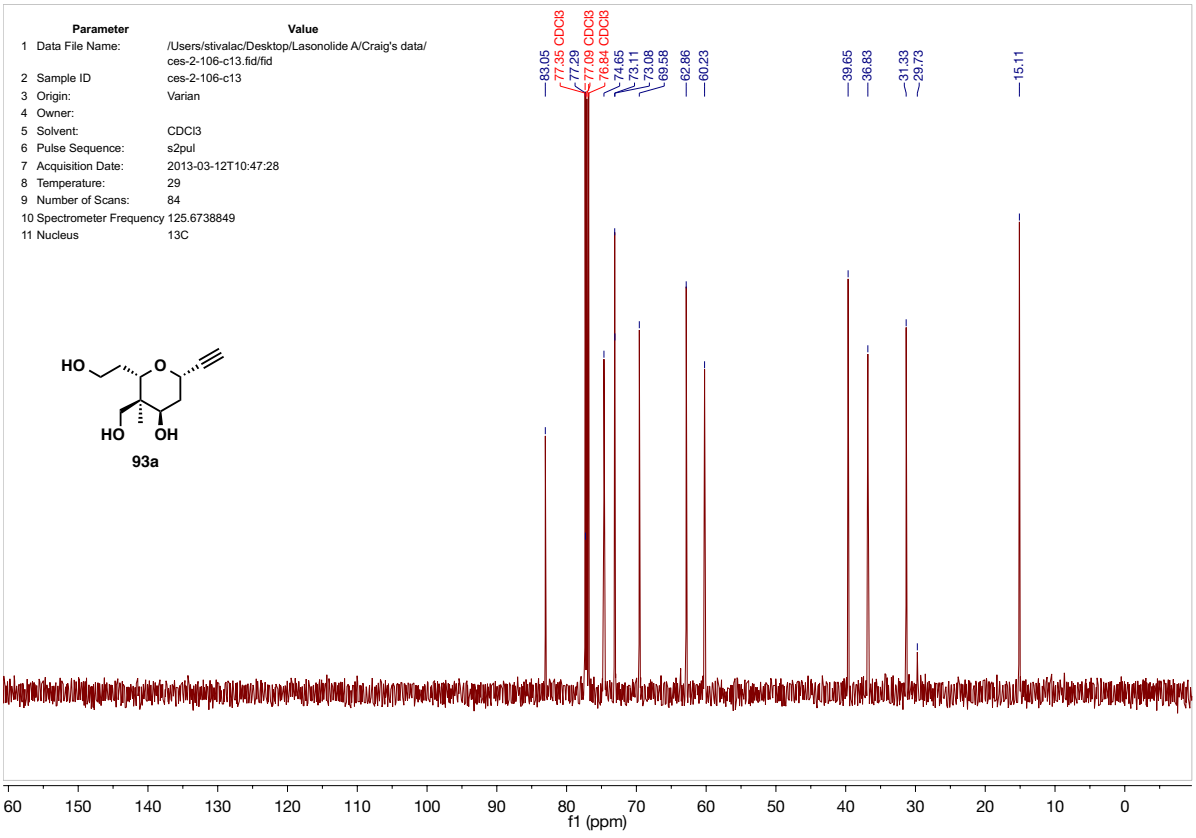

O
EtO
O
O
O
Ph
39
drfxx98hsqc
STANDARD PROTON PARAMETERS
f2 (ppm)
f1 (ppm)

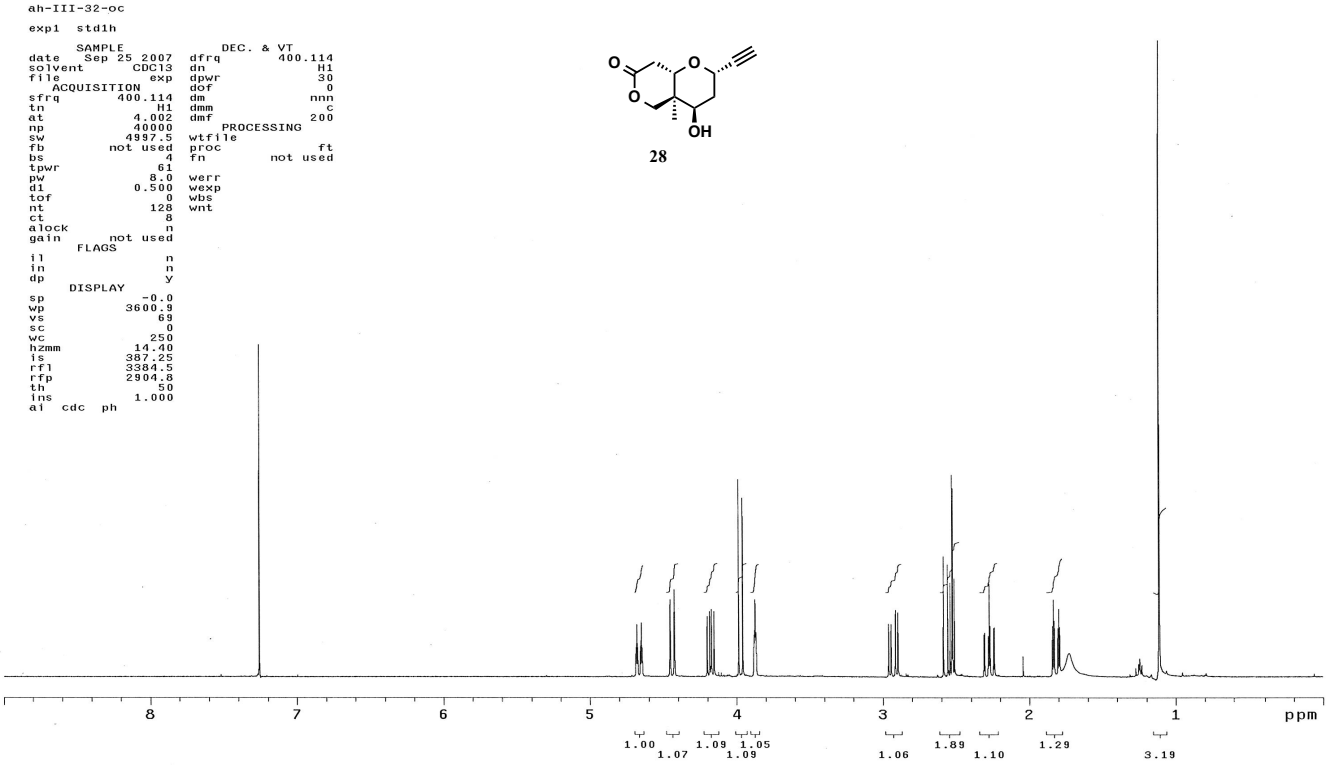

O
EtO
O
O
O
Ph

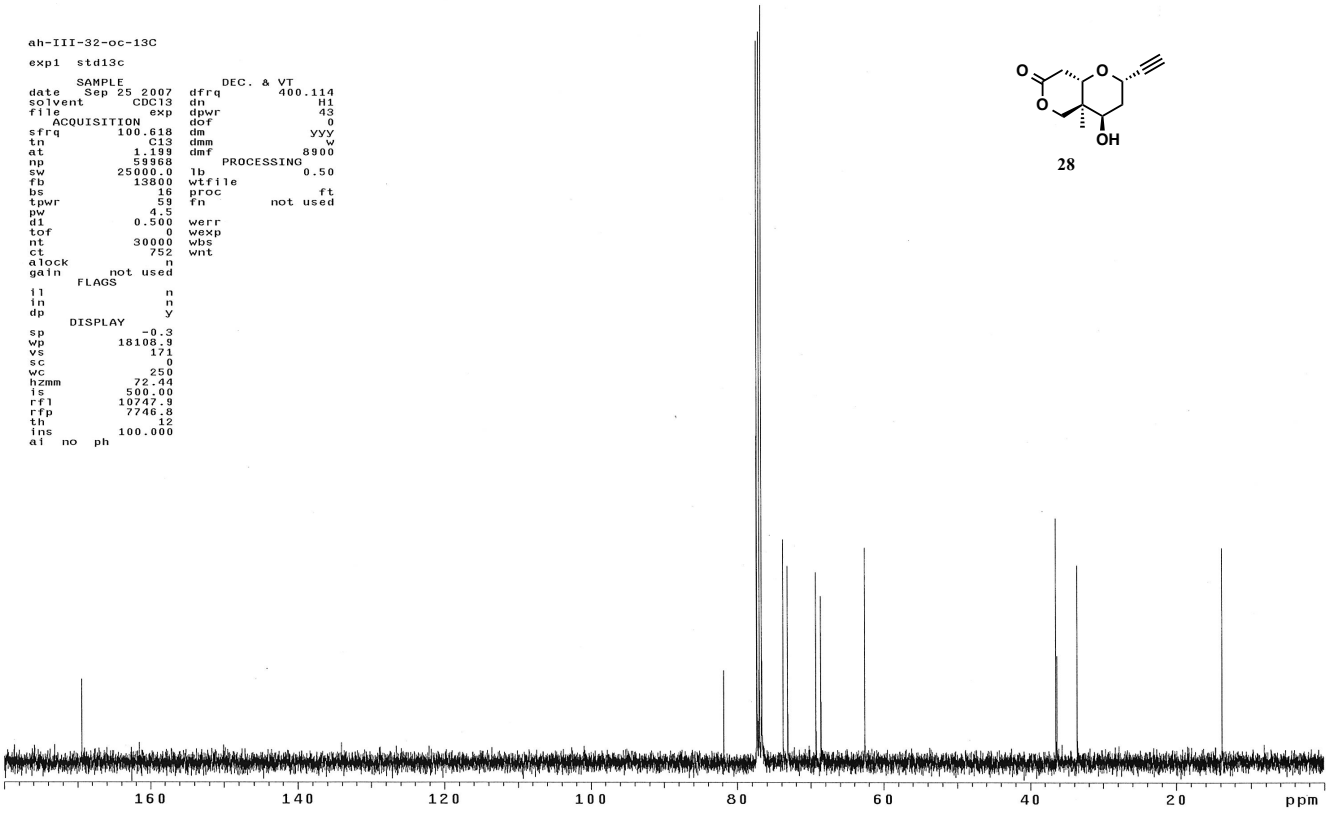
39


drfxx98roesy
STANDARD PROTON PARAMETERS
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f2 (ppm)
0 1 2 3 4 5 6 7 8
f1 (ppm)

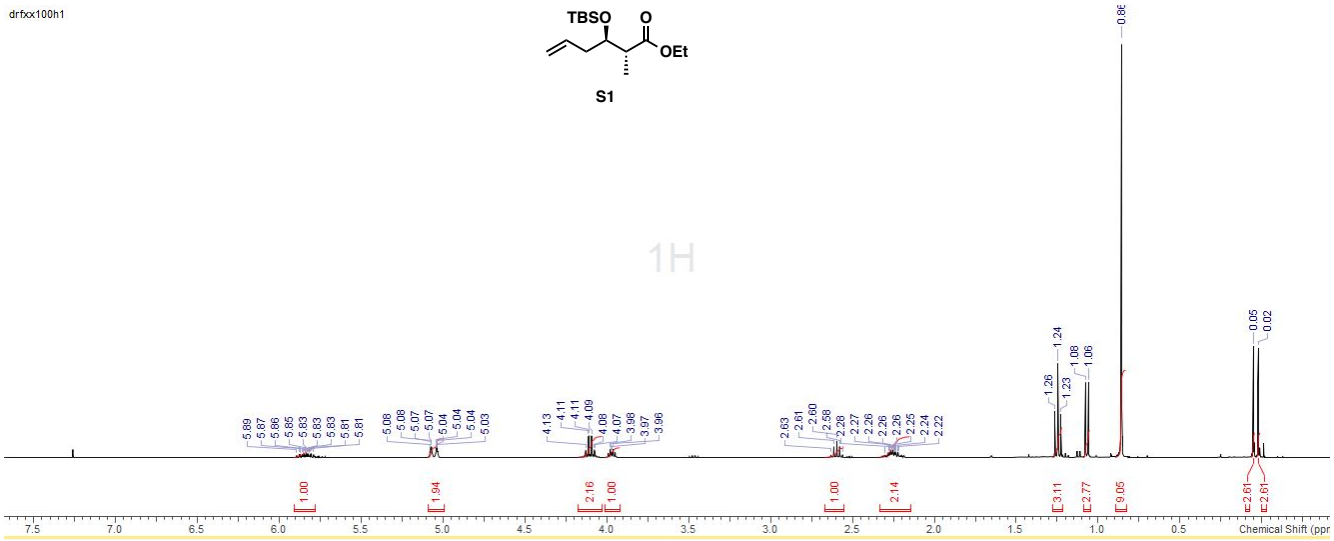

Parameter
Value
1 Data File Name: /Users/stivalac/Desktop/Lasonolide A/Craig's data/ces-2-106.fid/fid
2 Sample ID ces-2-106
3 Origin: Varian
4 Owner:
5 Solvent: CDCl3
6 Pulse Sequence: s2pul
7 Acquisition Date: 2013-03-12T10:45:05
8 Temperature: 29
9 Number of Scans: 8
10 Spectrometer Frequency 499.7510595
11 Nucleus 1H
HO
O
HO
OH
93a
7.26 CDCl3
0.79
f1 (ppm)


Parameter
Value
1 Data File Name: /Users/stivalac/Desktop/Lasonolide A/Craig's data/ces-2-106-c13.fid/fid
2 Sample ID ces-2-106-c13
3 Origin: Varian
4 Owner:
5 Solvent: CDCl3
6 Pulse Sequence: s2pul
7 Acquisition Date: 2013-03-12T10:47:28
8 Temperature: 29
9 Number of Scans: 84
10 Spectrometer Frequency 125.6738849
11 Nucleus 13C
HO
O
HO
OH
93a
77.35 CDCl3
77.09 CDCl3
76.84 CDCl3
f1 (ppm)

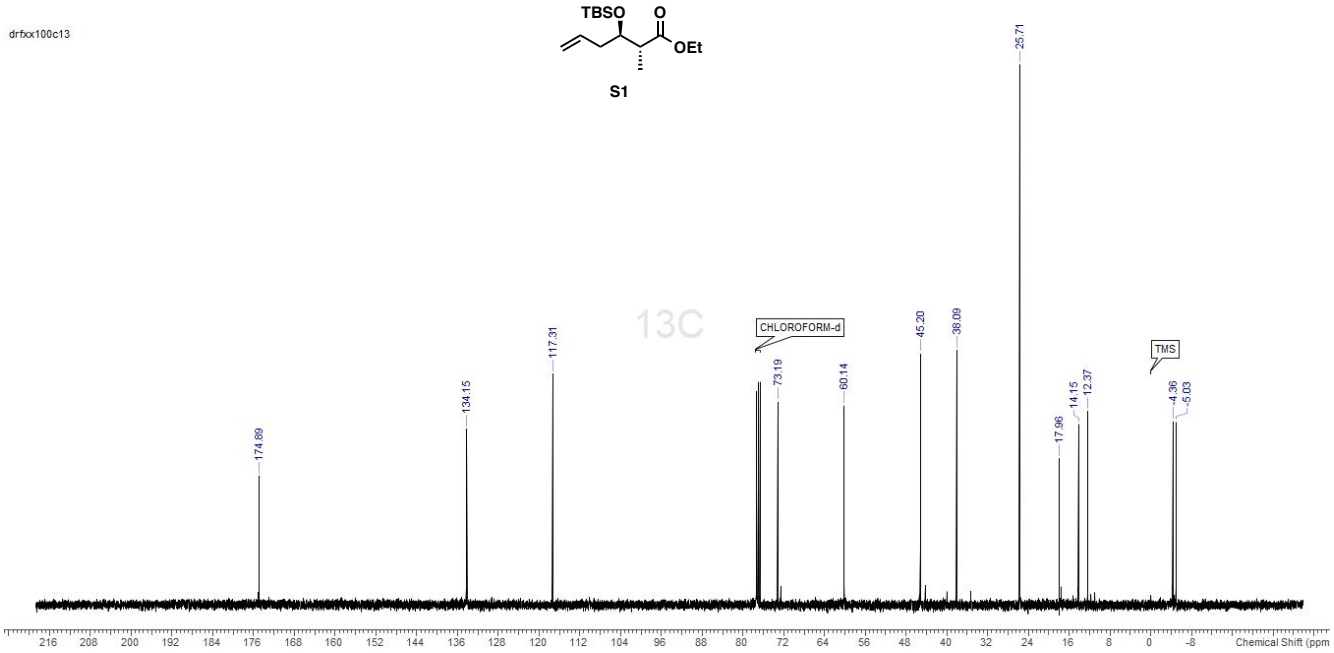

ah-III-32-oc
exp1 std1h
SAMPLE
date Sep 25 2007
solvent CDCl3
file exp
ACQUISITION
sfrq 400.114
tn H1
at 4.002
np 40000
sw 4997.5
fb not used
bs 4
tpwr 61
pw 8.0
d1 0.500
tof 0
nt 128
ct 8
alock n
gain not used
FLAGS
il n
in n
dp y
DISPLAY
sp -0.0
wp 3600.9
vs 69
sc 0
wc 250
hzmm 14.40
is 387.25
rfl 3384.5
rfp 2904.8
th 50
ins 1.000
ai cdc ph
DEC. & VT
dfrq 400.114
dn H1
dpwr 30
dof 0
dm nnn
dmm c
dmf 200
PROCESSING
wtfile
proc ft
fn not used
werr
wexp
wbs
wnt
O
O
O
OH
28
8
7
6
5
4
3
2
1
ppm
1.00
1.07
1.09
1.09
1.05
1.06
1.89
1.10
1.29
3.19


ah-III-32-oc-13C
exp1 std13c
SAMPLE
date Sep 25 2007
solvent CDCl3
file exp
ACQUISITION
sfrq 100.618
tn C13
at 1.199
np 59968
sw 25000.0
fb 13800
bs 16
tpwr 59
pw 4.5
d1 0.500
tof 0
nt 30000
ct 752
alock n
gain not used
FLAGS
il n
in n
dp y
DISPLAY
sp -0.3
wp 18108.9
vs 171
sc 0
wc 250
hzmm 72.44
is 500.00
rfl 10747.9
rfp 7746.8
th 12
ins 100.000
ai no ph
DEC. & VT
dfrq 400.114
dn H1
dpwr 43
dof 0
dm yyy
dmm w
dmf 8900
PROCESSING
lb 0.50
wtfile
proc ft
fn not used
werr
wexp
wbs
wnt
O
O
O
OH
28
160
140
120
100
80
60
40
20
ppm

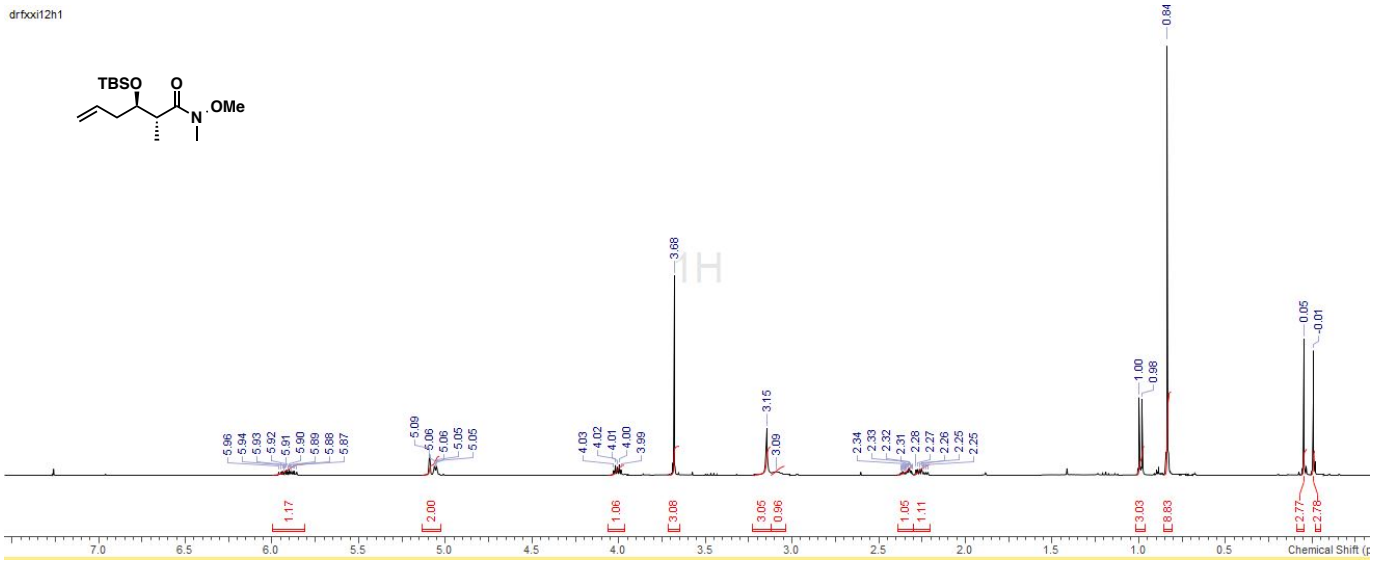
^{1}H NMR (400 MHz, $CDCl_3$)



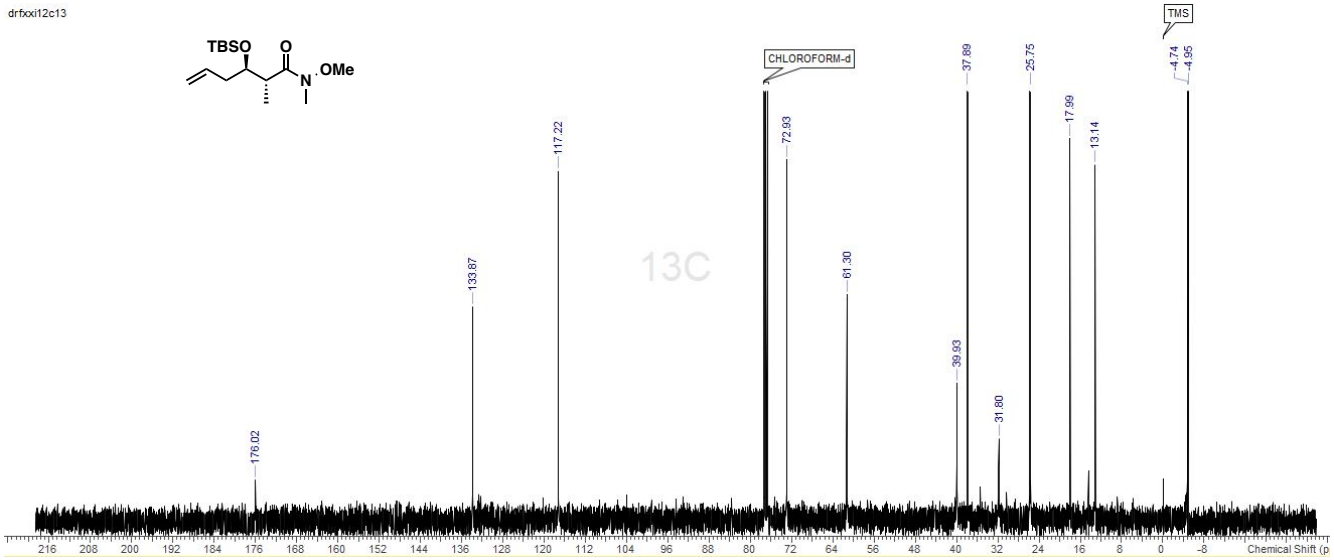
^{13}C NMR (100 MHz, $CDCl_3$)



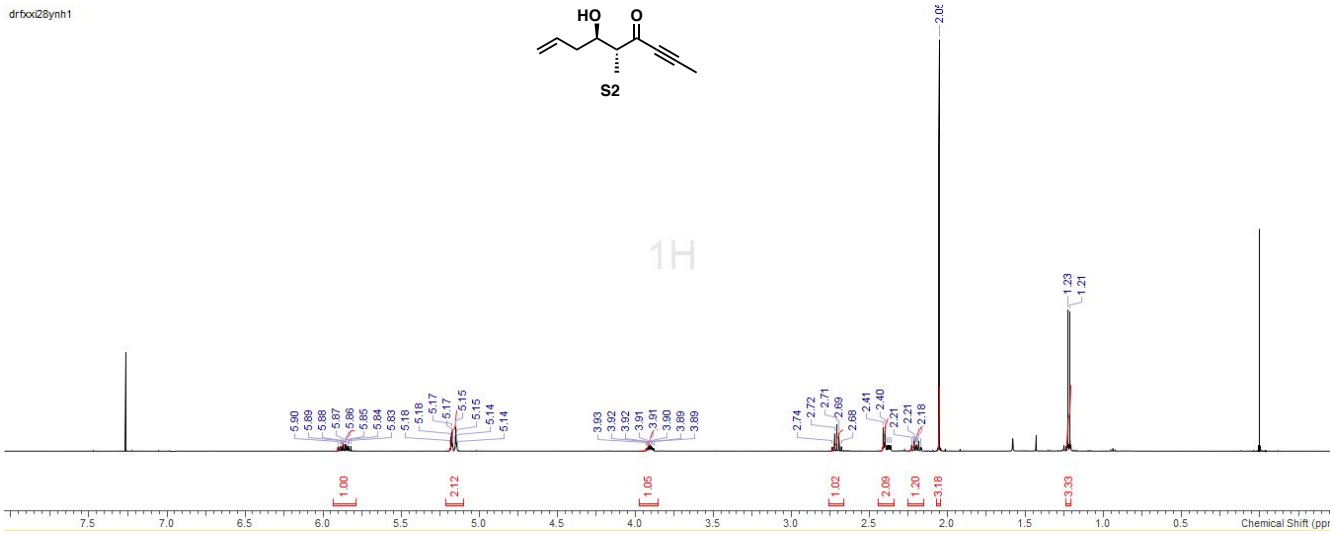
^{1}H NMR (500 MHz, $CDCl_3$)



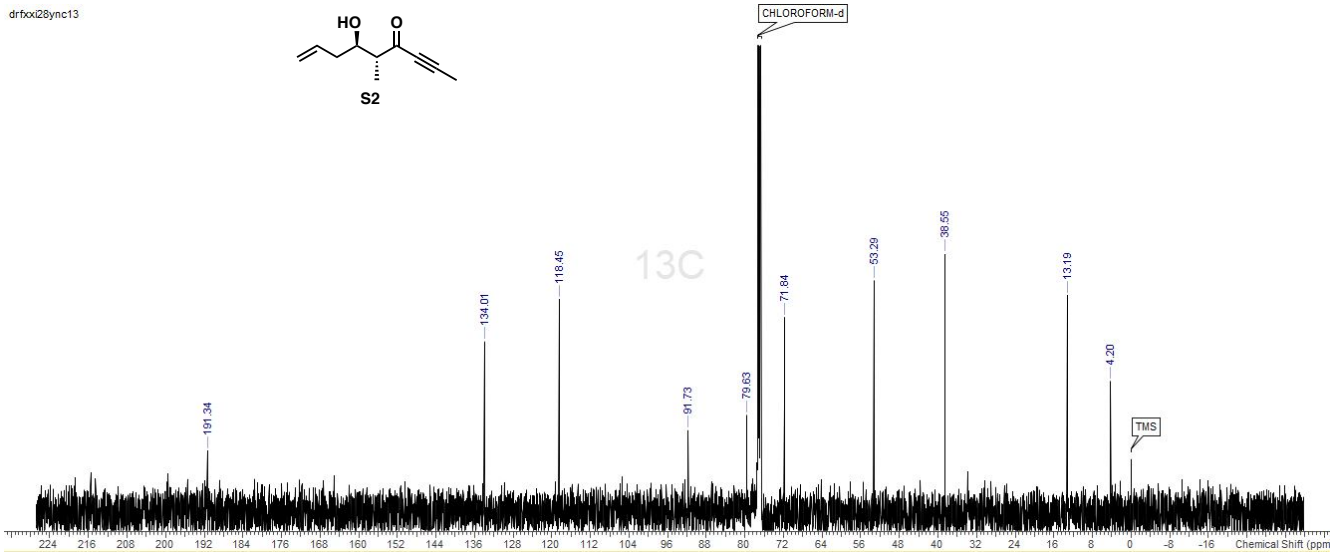
^{13}C NMR (100 MHz, $CDCl_3$)



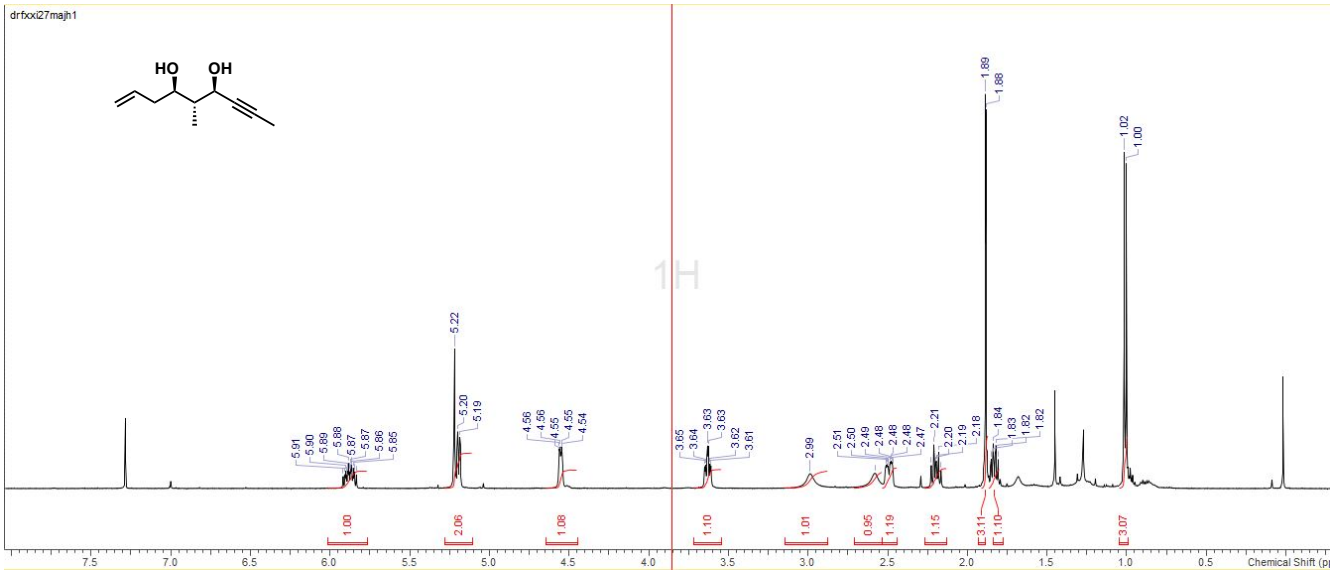
^{1}H NMR (500 MHz, $CDCl_3$)



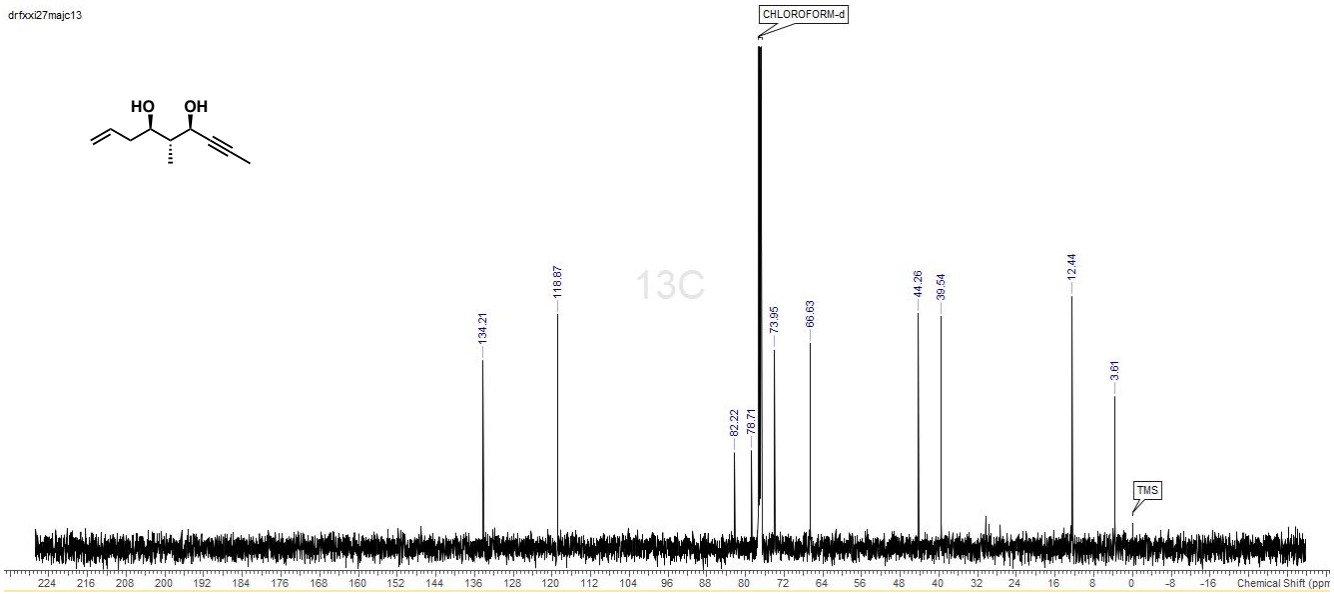
^{13}C NMR (125 MHz, $CDCl_3$)



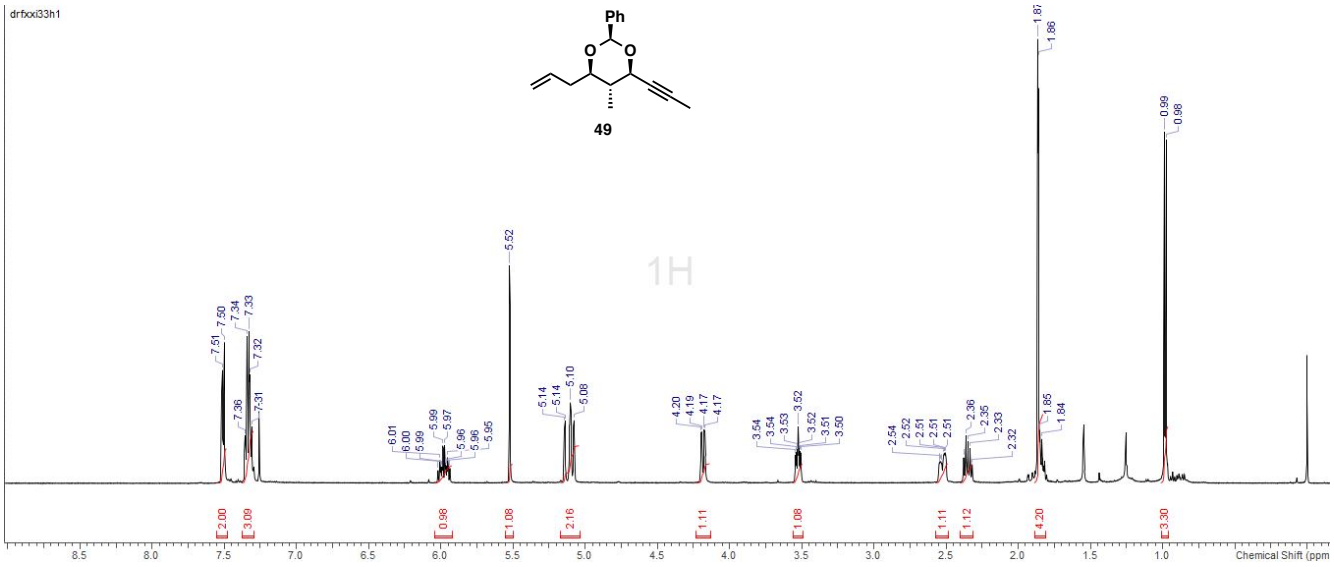
^{1}H NMR (500 MHz, $CDCl_3$)



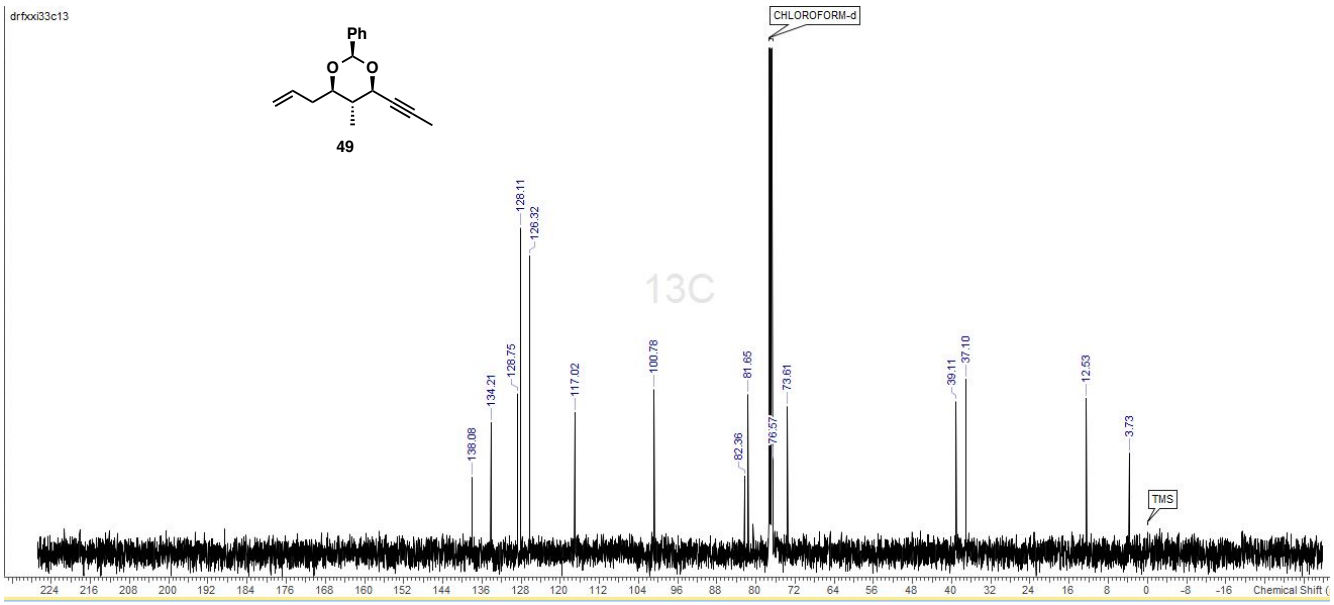
^{13}C NMR (125 MHz, $CDCl_3$)



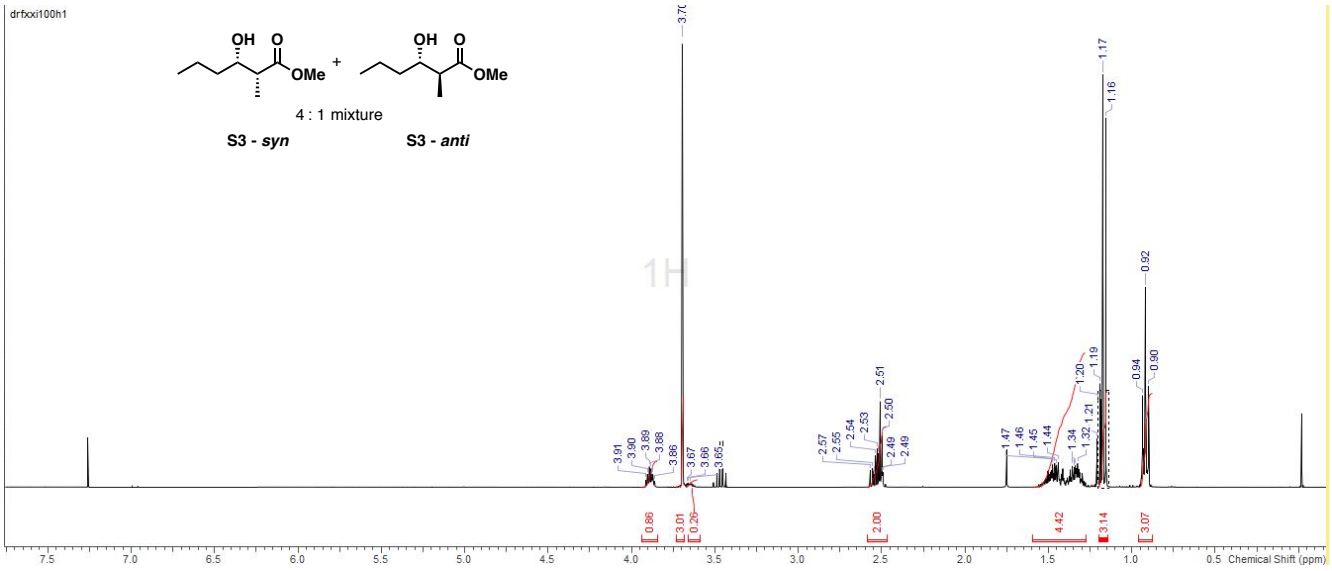
^{1}H NMR (500 MHz, $CDCl_3$)



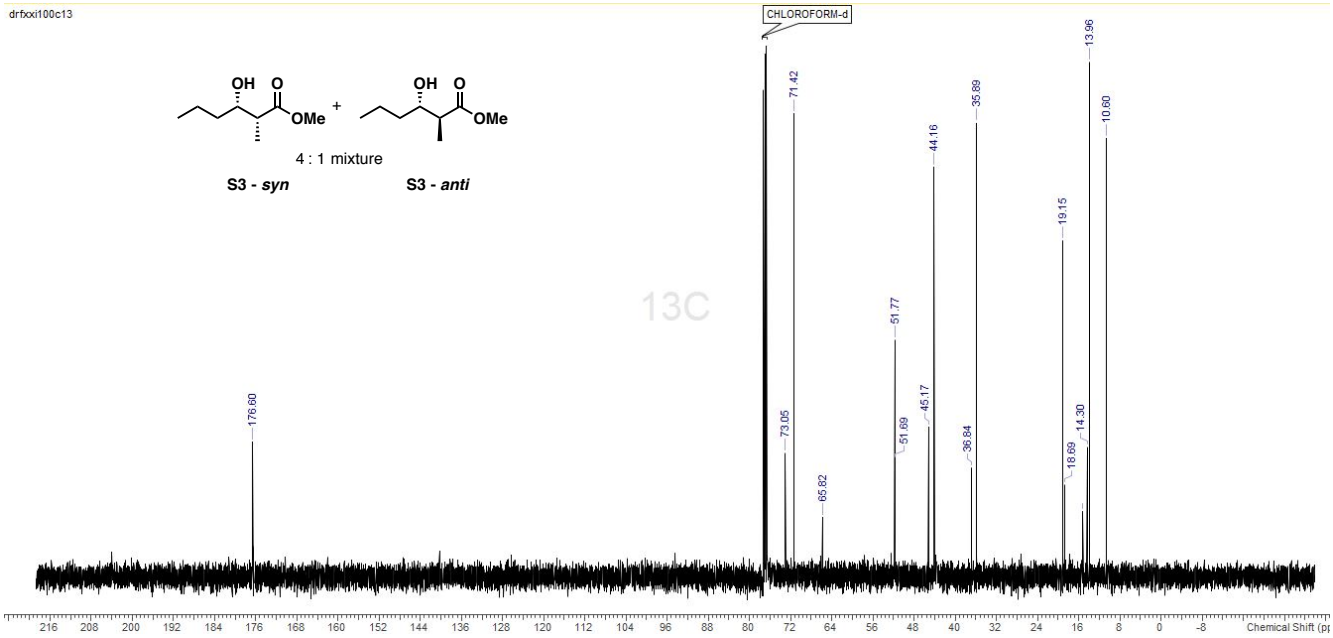
^{13}C NMR (125 MHz, $CDCl_3$)

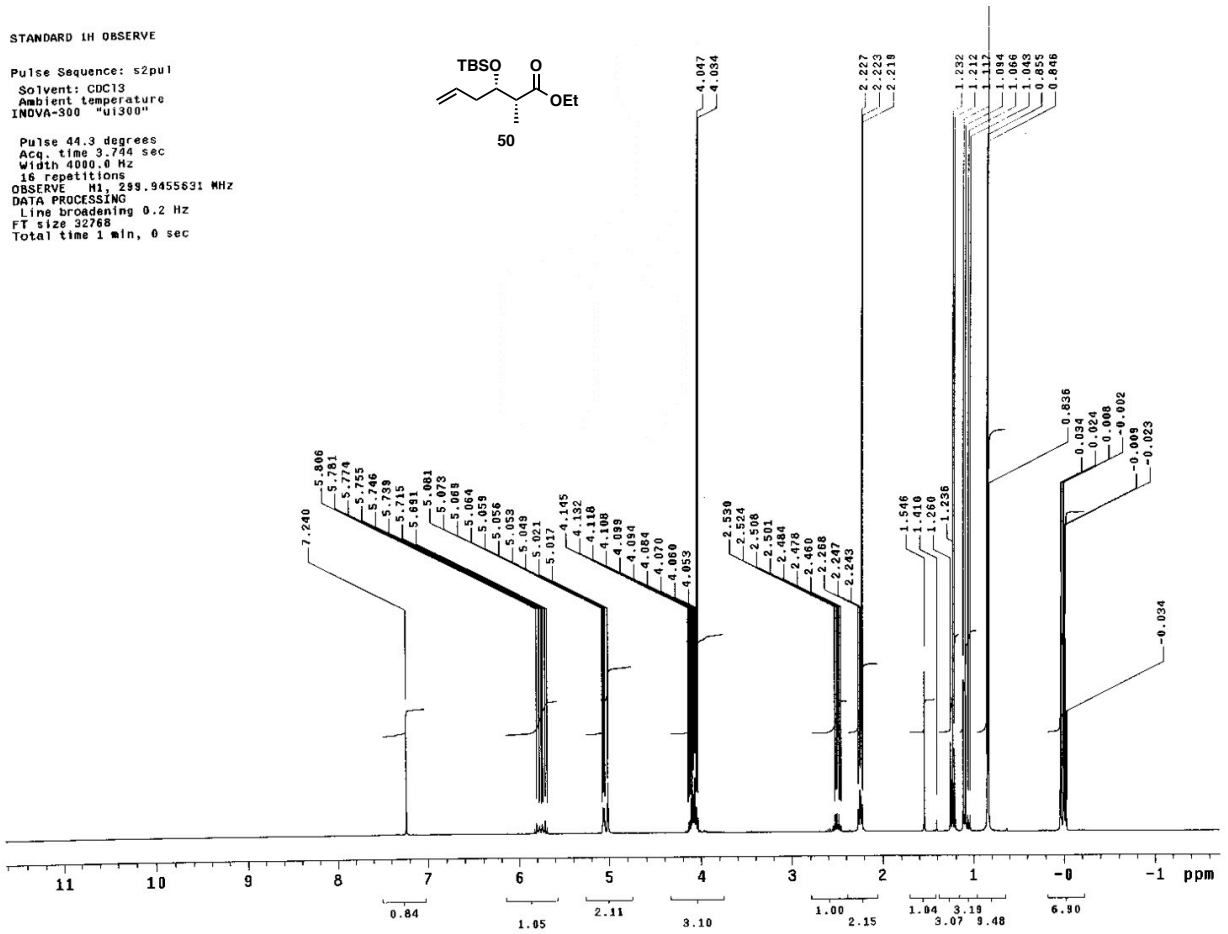


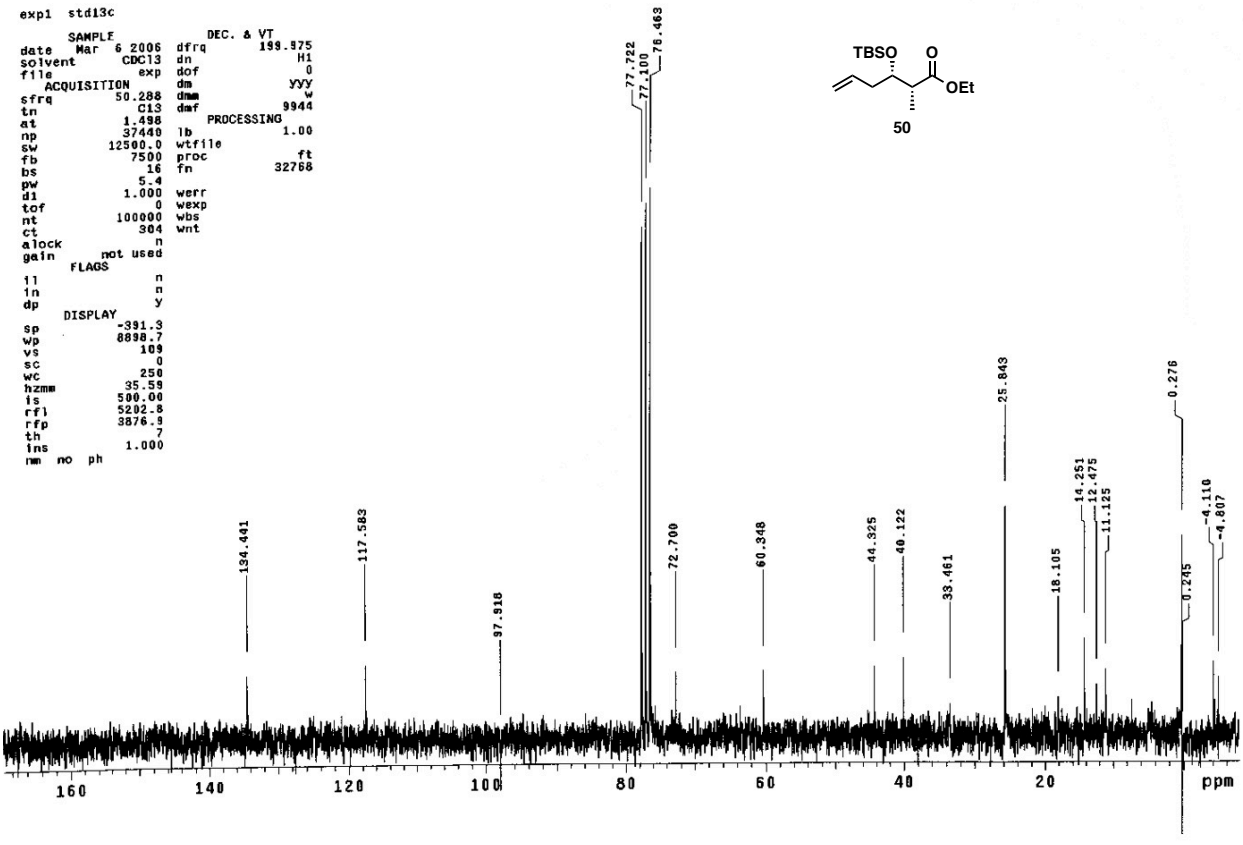
^{1}H NMR (400 MHz, $CDCl_3$)

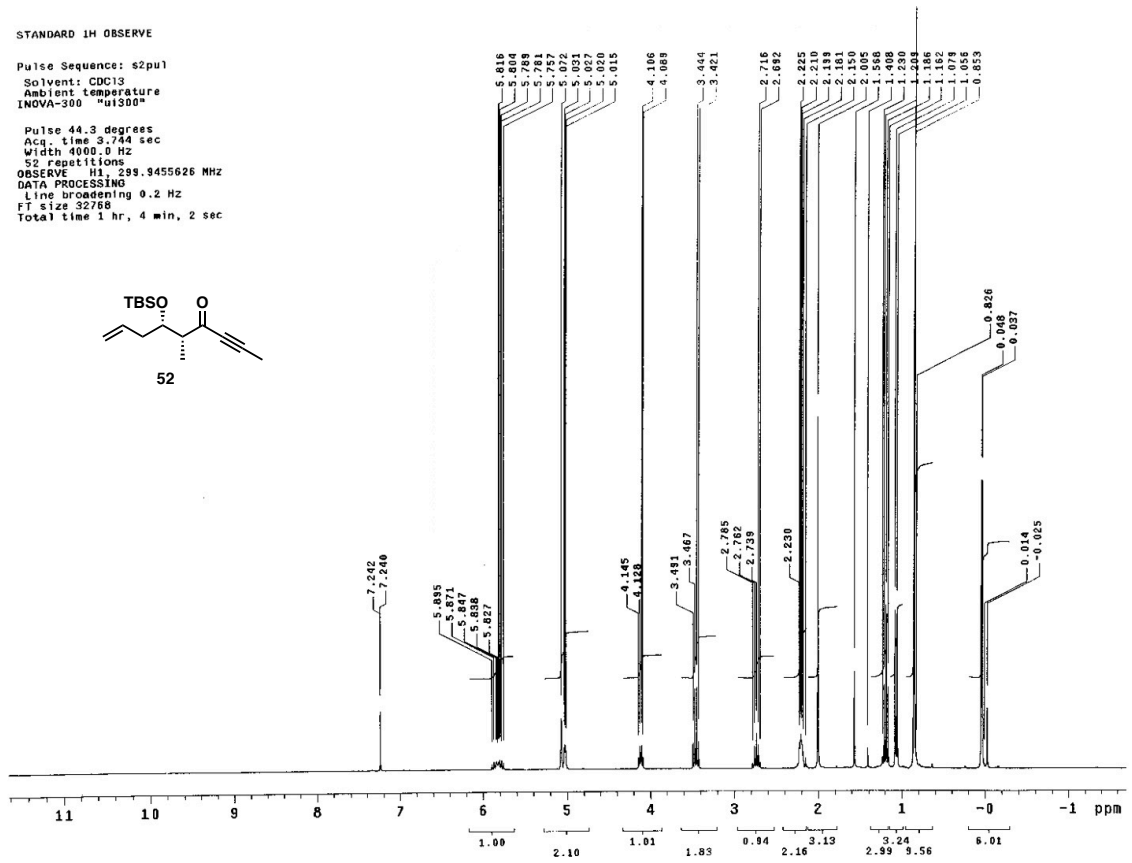


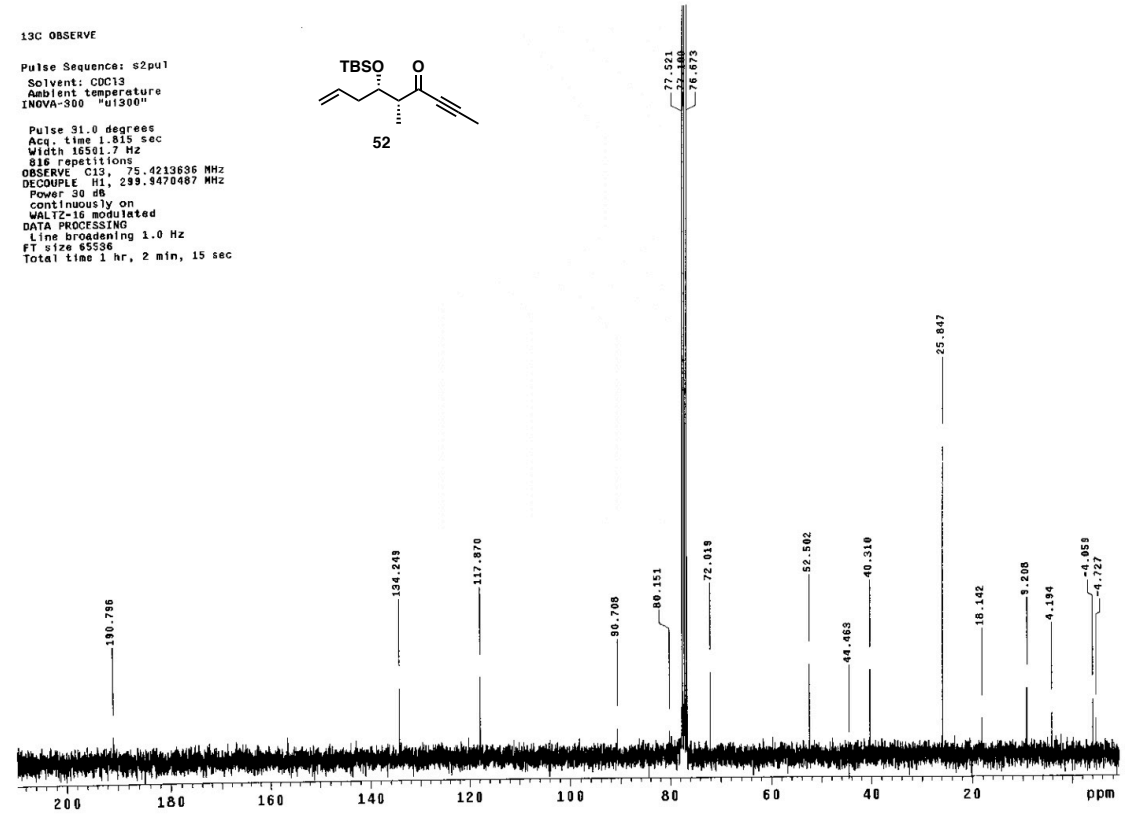
^{13}C NMR (100 MHz, $CDCl_3$)

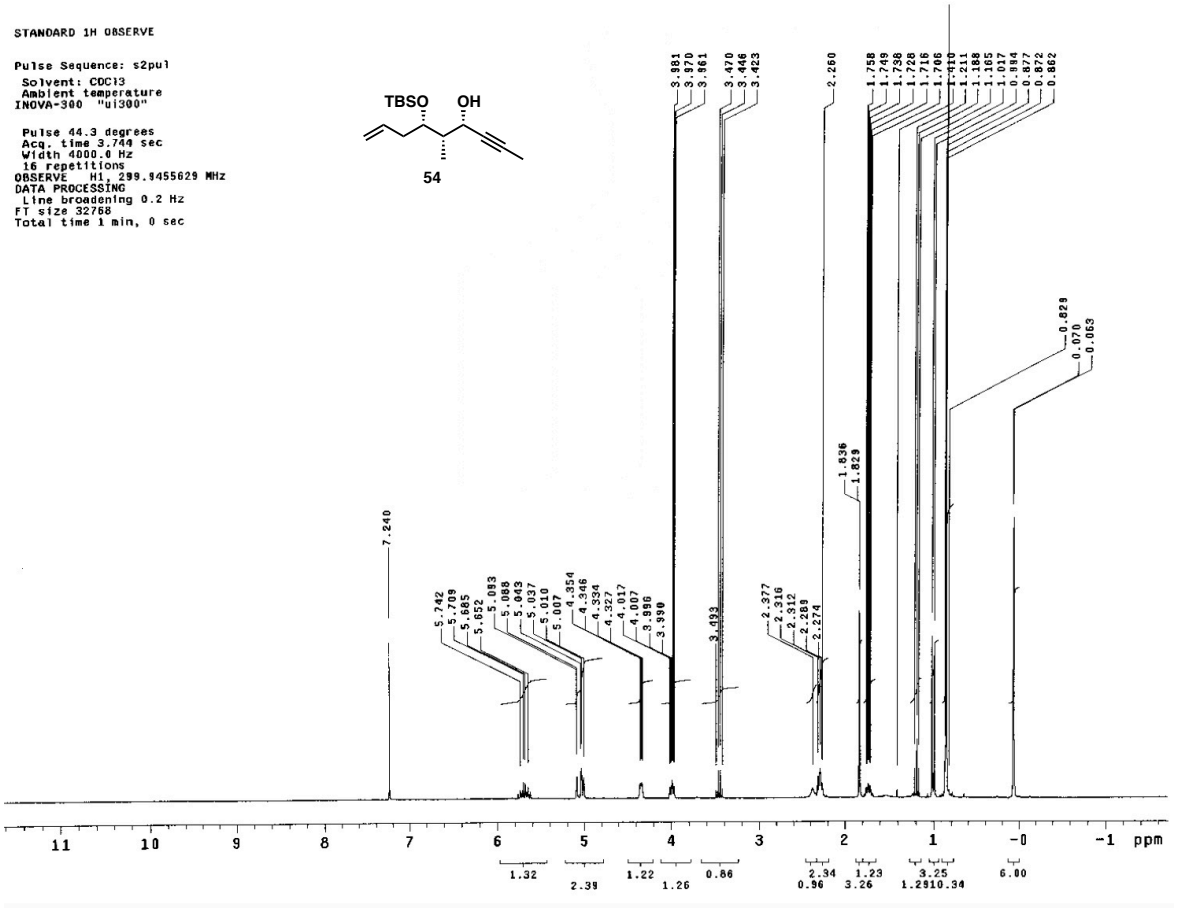


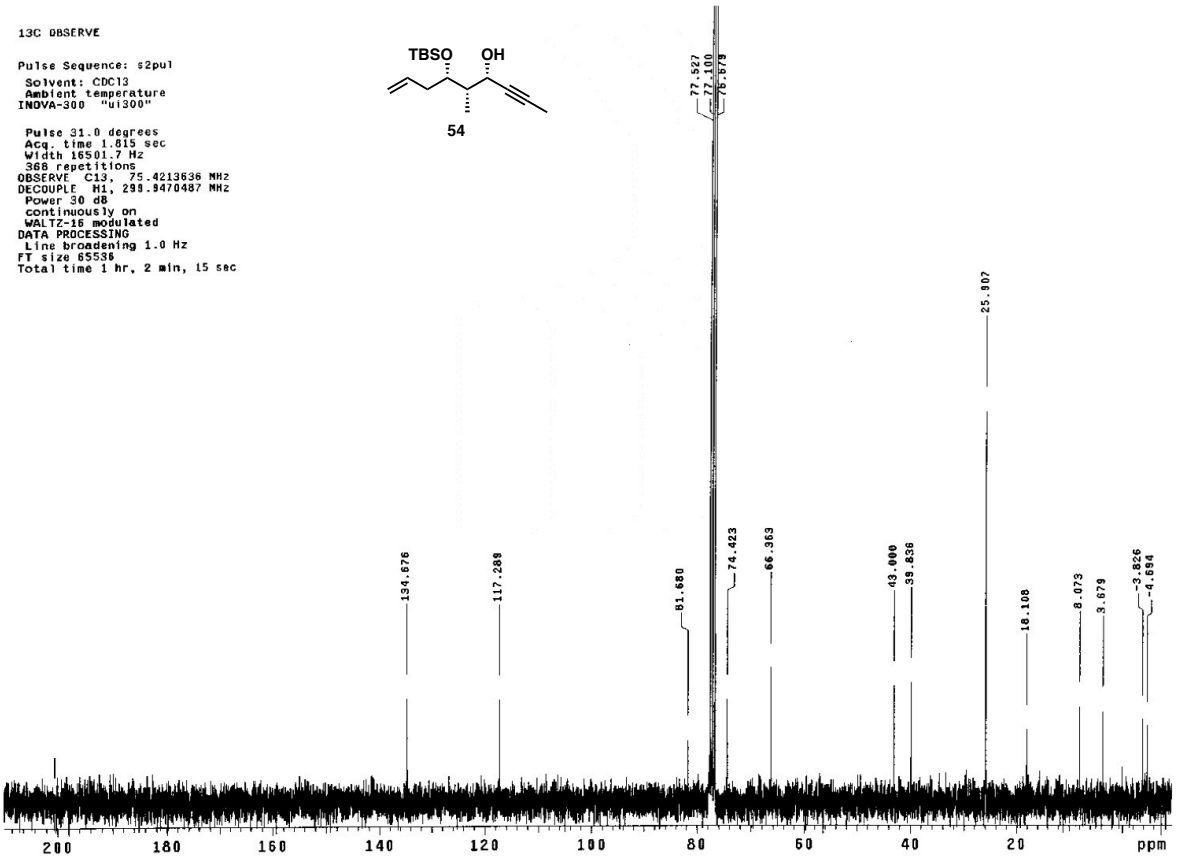

STANDARD 1H OBSERVE
Pulse Sequence: s2pul
Solvent: CDCl3
Ambient temperature
INOVA-300 "ui300"
Pulse 44.3 degrees
Acq. time 3.744 sec
Width 4000.0 Hz
16 repetitions
OBSERVE H1, 299.9455631 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 32768
Total time 1 min, 0 sec
TBSO
O
OEt
50
ppm

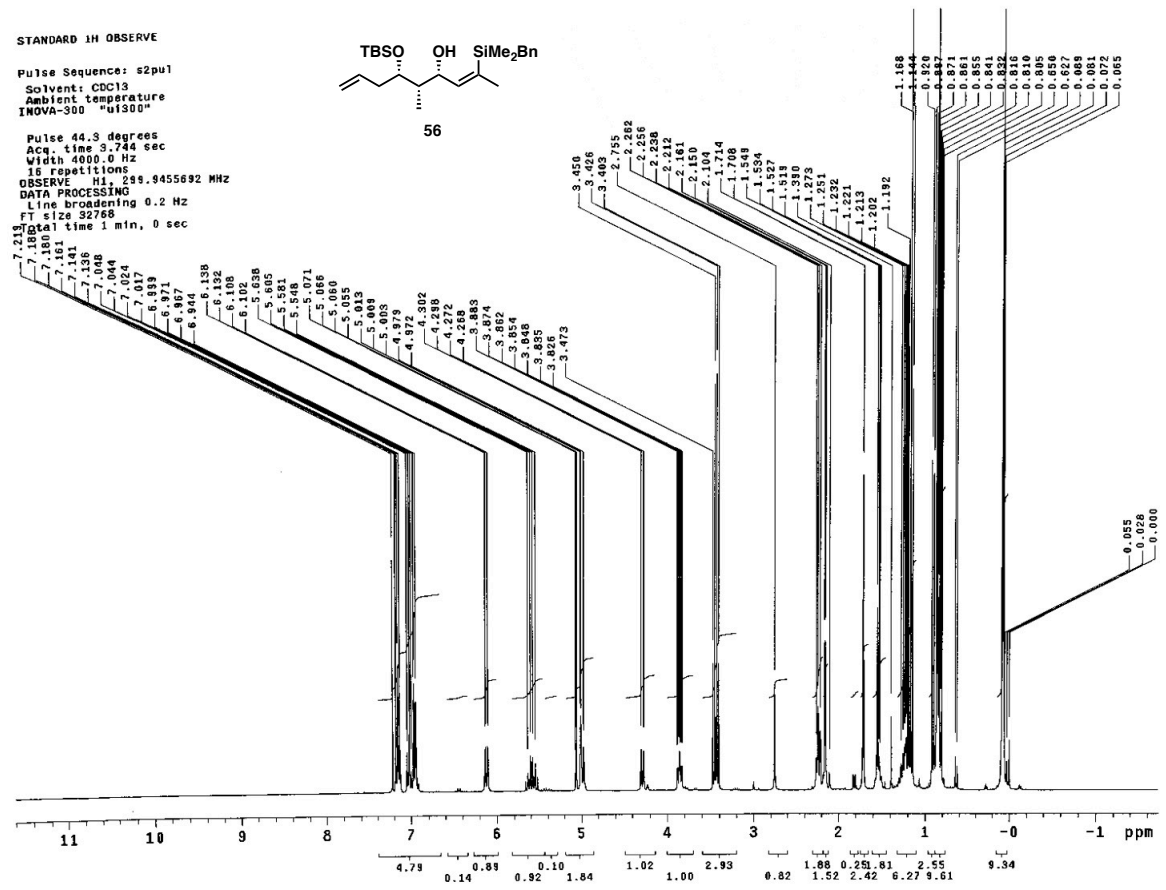

exp1 std13c
SAMPLE
date Mar 6 2006
solvent CDCl3
file exp
ACQUISITION
sfrq 50.288
tn C13
at 1.498
np 37440
sw 12500.0
fb 7500
bs 16
pw 5.4
d1 1.000
tof 0
nt 100000
ct 304
alock n
gain not used
FLAGS
il n
in n
dp y
DISPLAY
sp -391.3
wp 8898.7
vs 109
sc 0
wc 250
hzmm 35.59
is 500.00
rfl 5202.8
rfp 3876.9
th 7
ins 1.000
DEC. & VT
dfrq 199.975
dn H1
dof 0
dm yyy
dmm w
dmf 9944
PROCESSING
lb 1.00
wtfile
proc ft
fn 32768
werr
wexp
wbs
wnt
TBSO
O
OEt
50
ppm

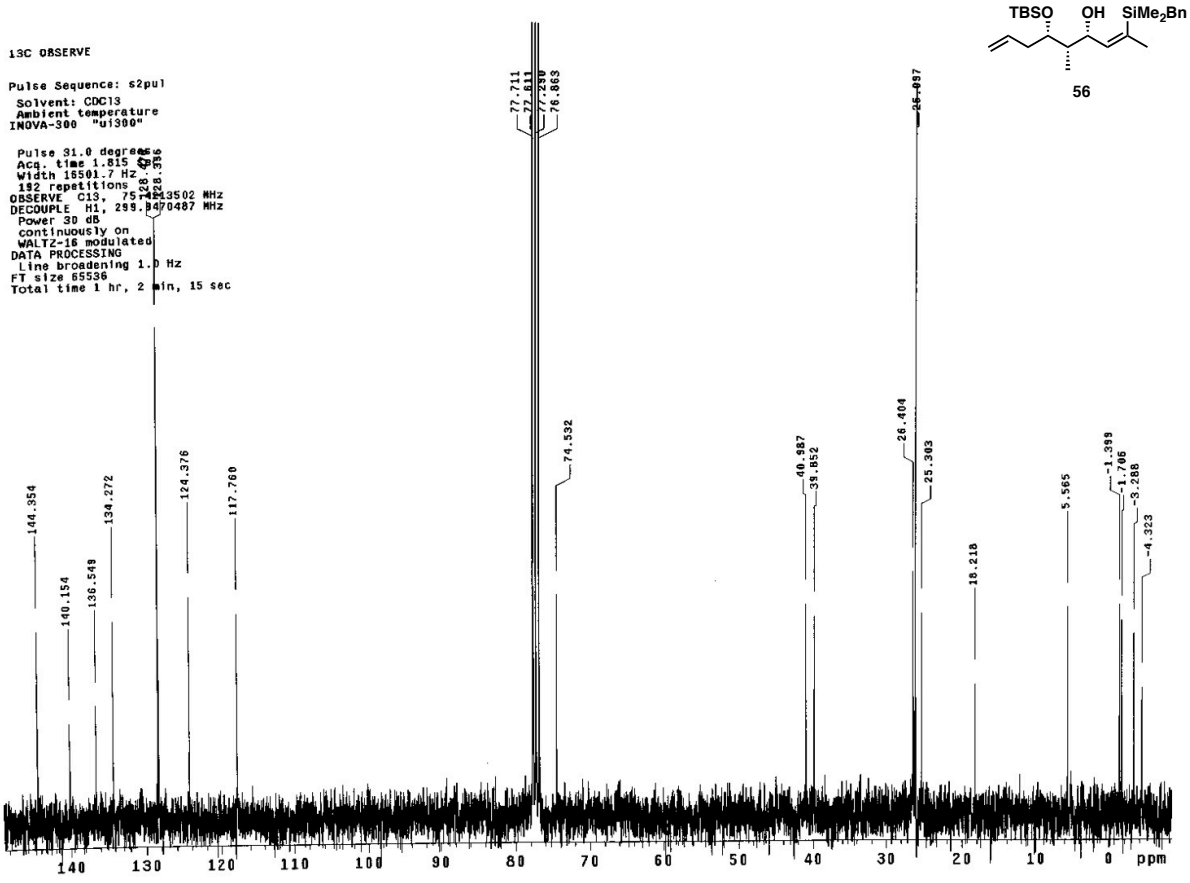

STANDARD 1H OBSERVE
Pulse Sequence: s2pul
Solvent: CDCl3
Ambient temperature
INOVA-300 "ui300"
Pulse 44.3 degrees
Acq. time 3.744 sec
Width 4000.0 Hz
52 repetitions
OBSERVE H1, 299.9455626 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 32768
Total time 1 hr, 4 min, 2 sec
TBSO
O
52
ppm

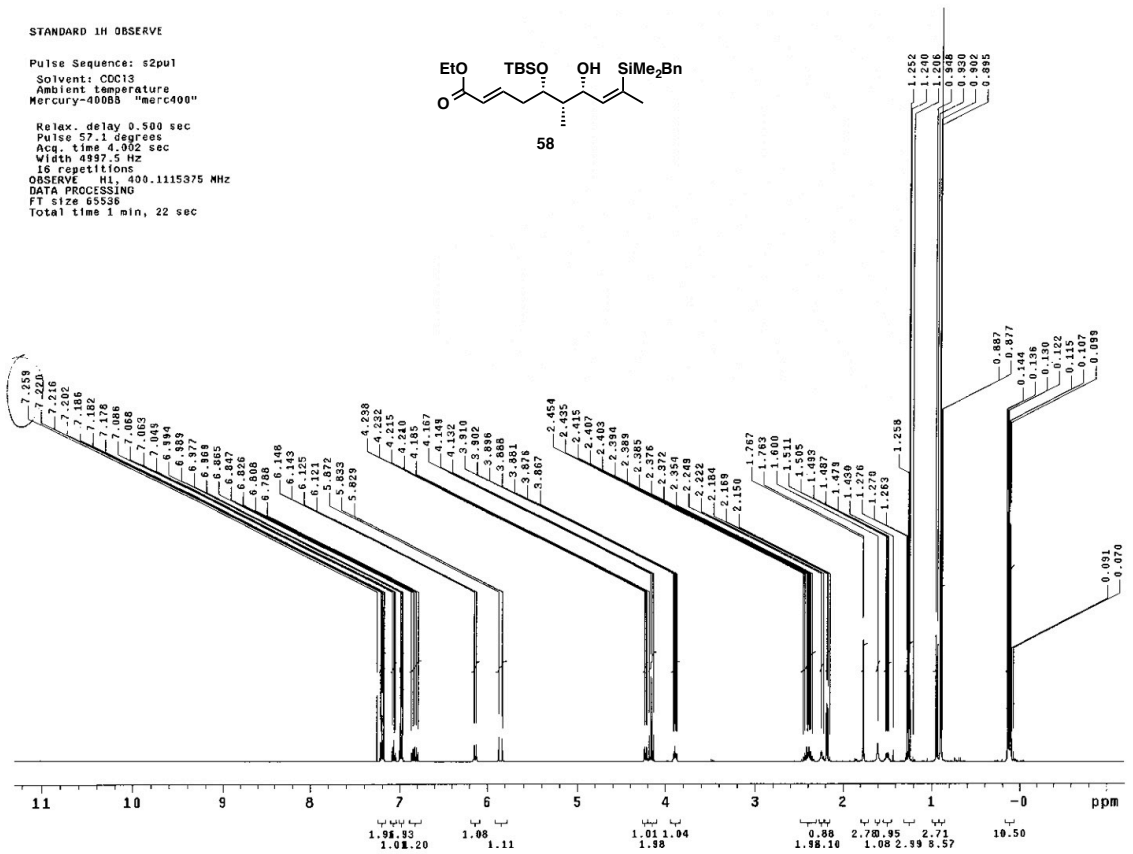

13C OBSERVE
Pulse Sequence: s2pul
Solvent: CDCl3
Ambient temperature
INOVA-300 "ui300"
Pulse 31.0 degrees
Acq. time 1.815 sec
Width 16501.7 Hz
816 repetitions
OBSERVE C13, 75.4213636 MHz
DECOUPLE H1, 299.9470487 MHz
Power 30 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 65536
Total time 1 hr, 2 min, 15 sec
TBSO
O
52
ppm

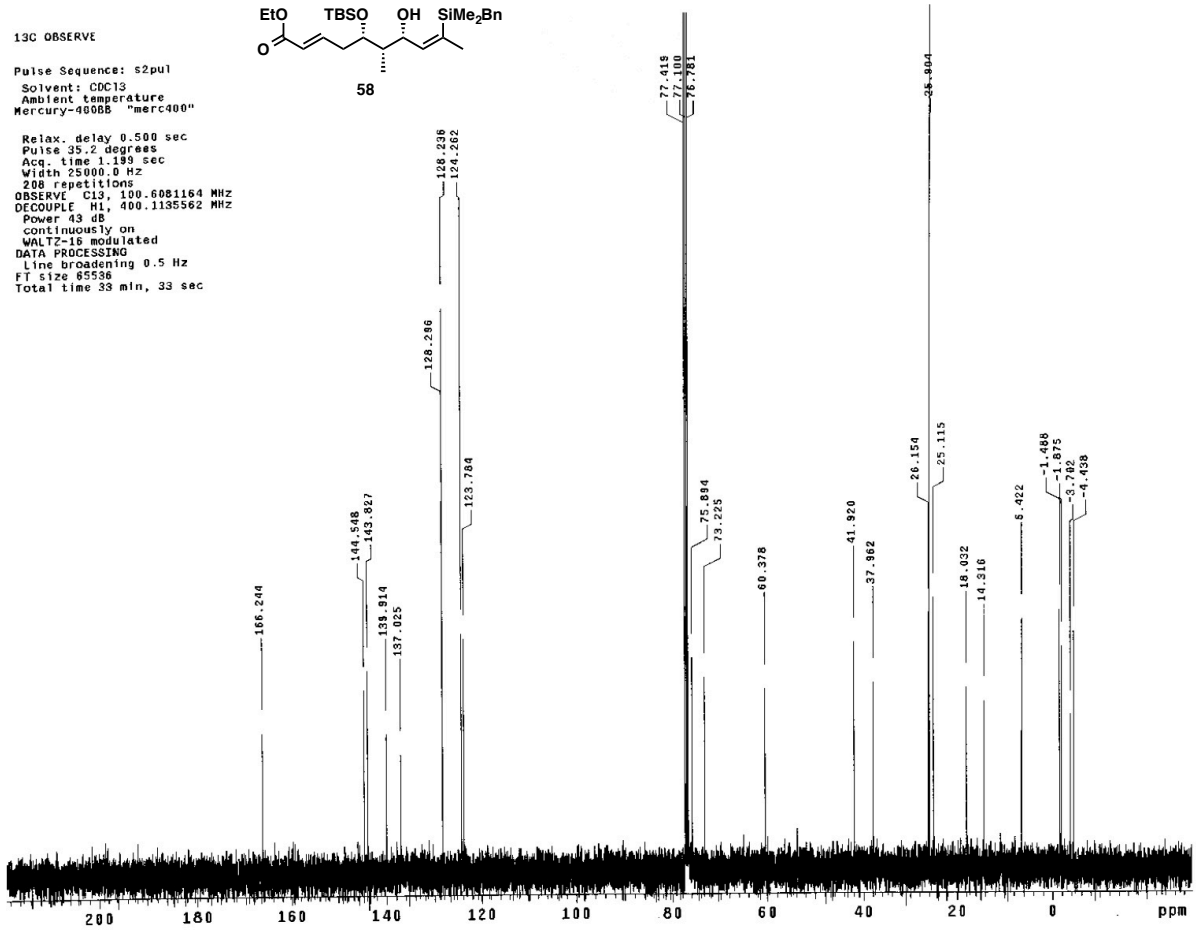

STANDARD 1H OBSERVE
Pulse Sequence: s2pul
Solvent: CDCl3
Ambient temperature
INOVA-300 "ui300"
Pulse 44.3 degrees
Acq. time 3.744 sec
Width 4000.0 Hz
16 repetitions
OBSERVE H1, 299.9455629 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 32768
Total time 1 min, 0 sec
TBSO
OH
54
ppm

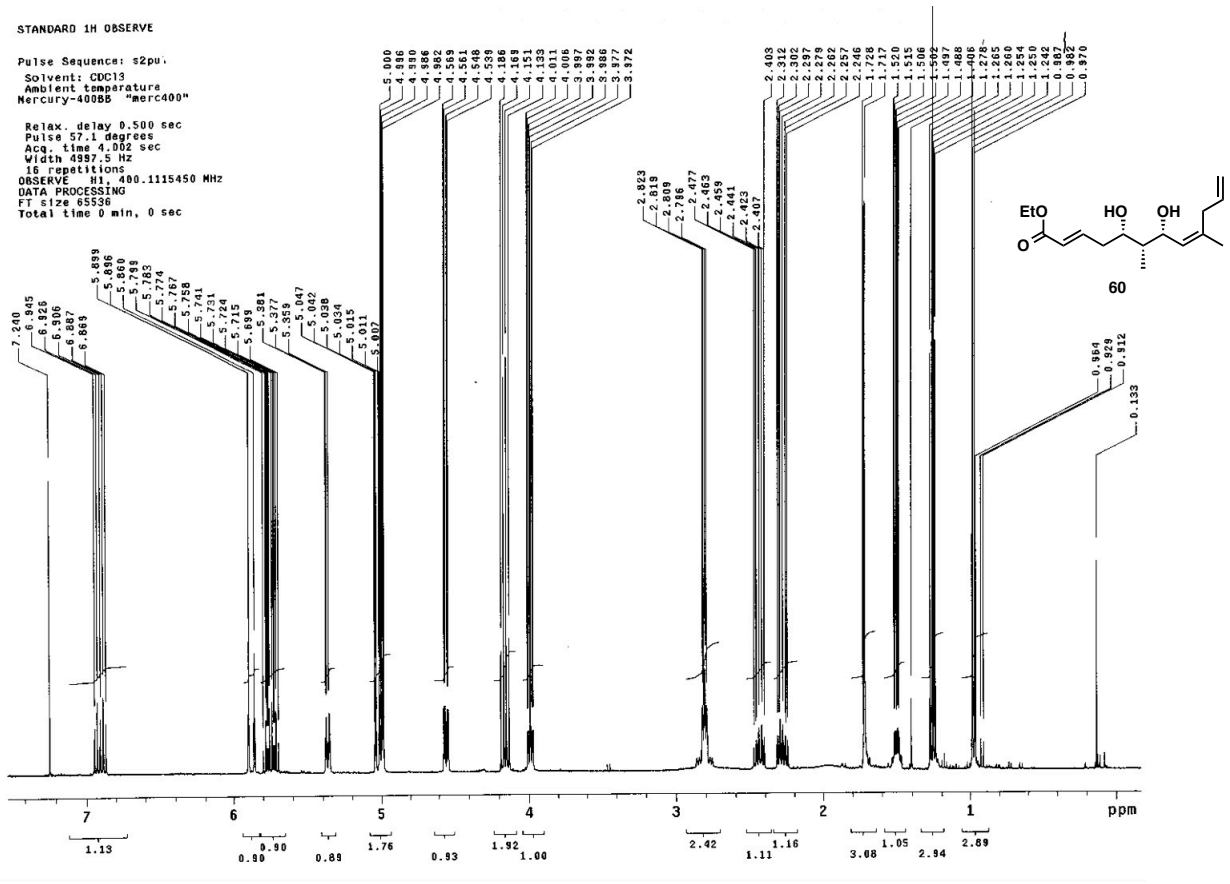

13C OBSERVE
Pulse Sequence: s2pul
Solvent: CDCl3
Ambient temperature
INOVA-300 "ui300"
Pulse 31.0 degrees
Acq. time 1.615 sec
Width 16501.7 Hz
368 repetitions
OBSERVE C13, 75.4213636 MHz
DECOUPLE H1, 299.9470487 MHz
Power 30 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 65536
Total time 1 hr, 2 min, 15 sec
TBSO
OH
54
ppm

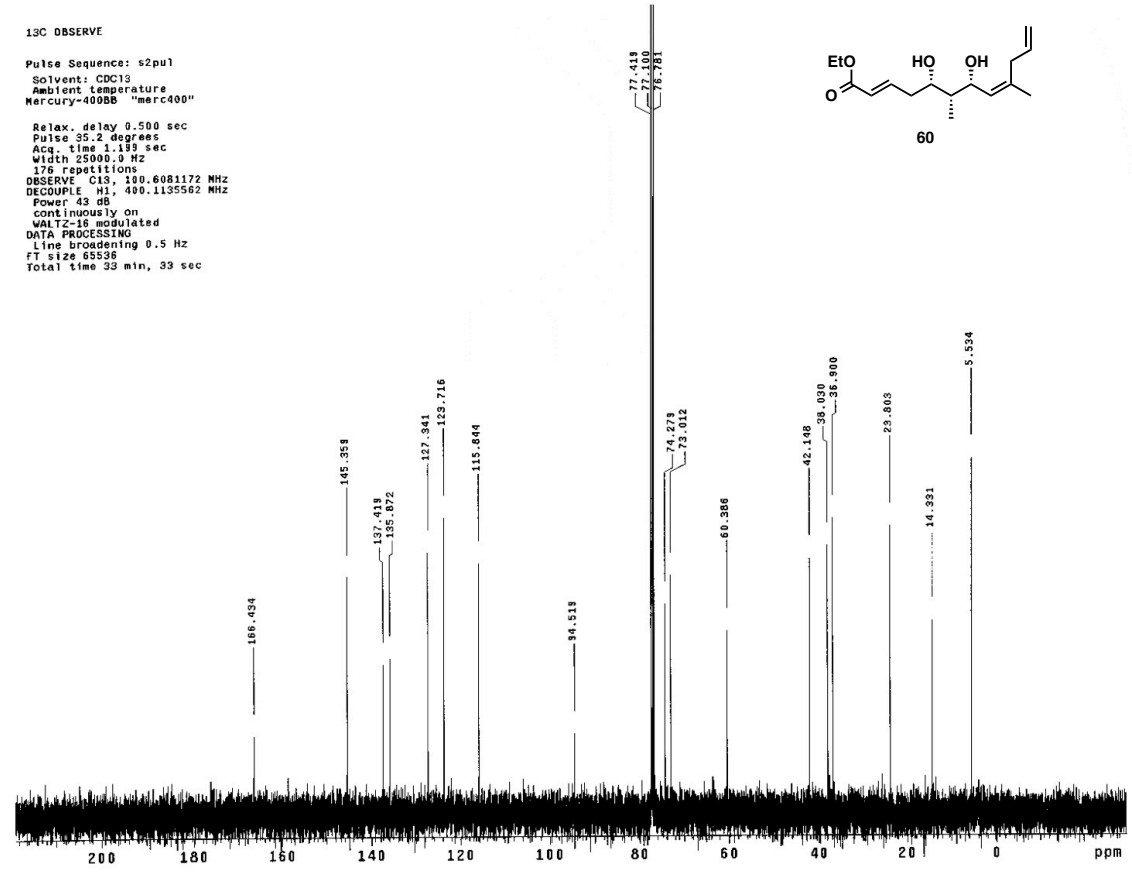

STANDARD 1H OBSERVE
Pulse Sequence: s2pul
Solvent: CDCl3
Ambient temperature
INOVA-300 "ui300"
Pulse 44.3 degrees
Acq. time 3.744 sec
Width 4000.0 Hz
16 repetitions
OBSERVE H1, 299.9455692 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 32768
Total time 1 min, 0 sec
TBSO OH SiMe2Bn
56
ppm

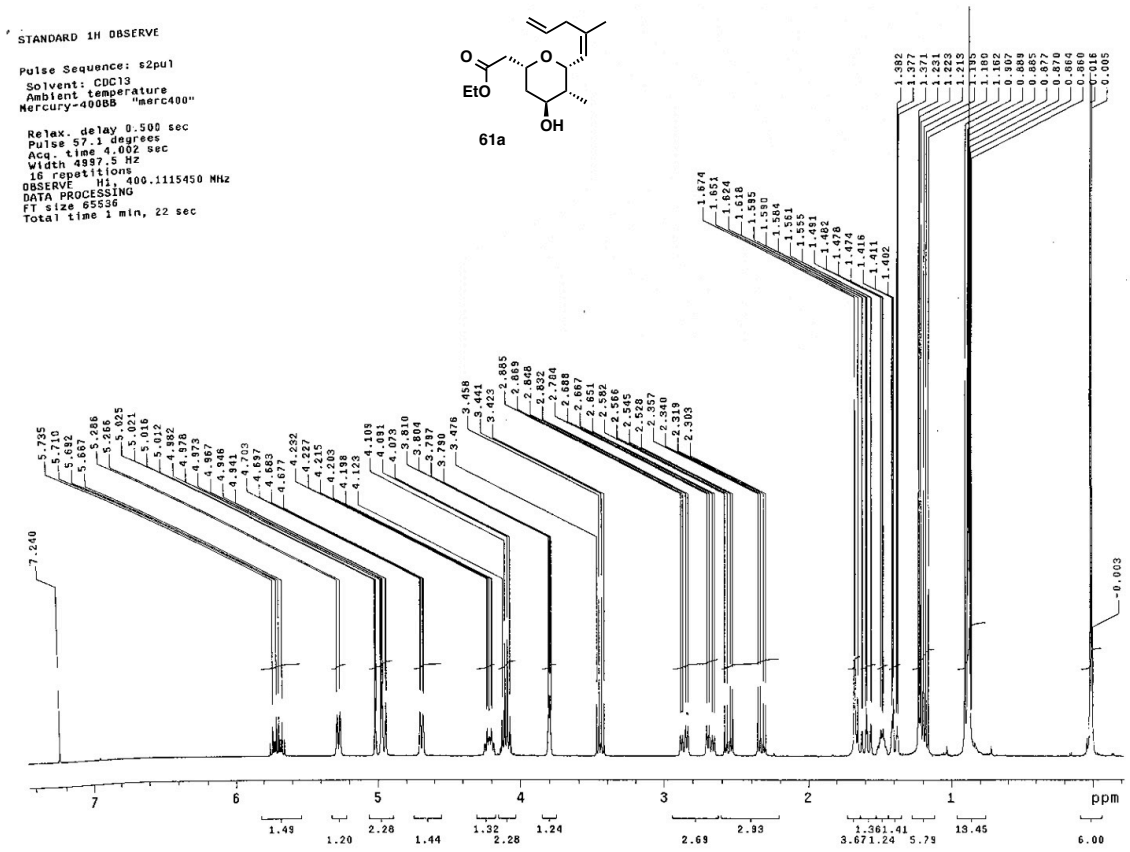

13C OBSERVE
Pulse Sequence: s2pul
Solvent: CDCl3
Ambient temperature
INOVA-300 "ui300"
Pulse 31.0 degrees
Acq. time 1.815 sec
Width 18501.7 Hz
192 repetitions
DECOUPLE H1, 299.9470487 MHz
Power 30 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 65536
Total time 1 hr, 2 min, 15 sec
TBSO OH SiMe2Bn
56
ppm

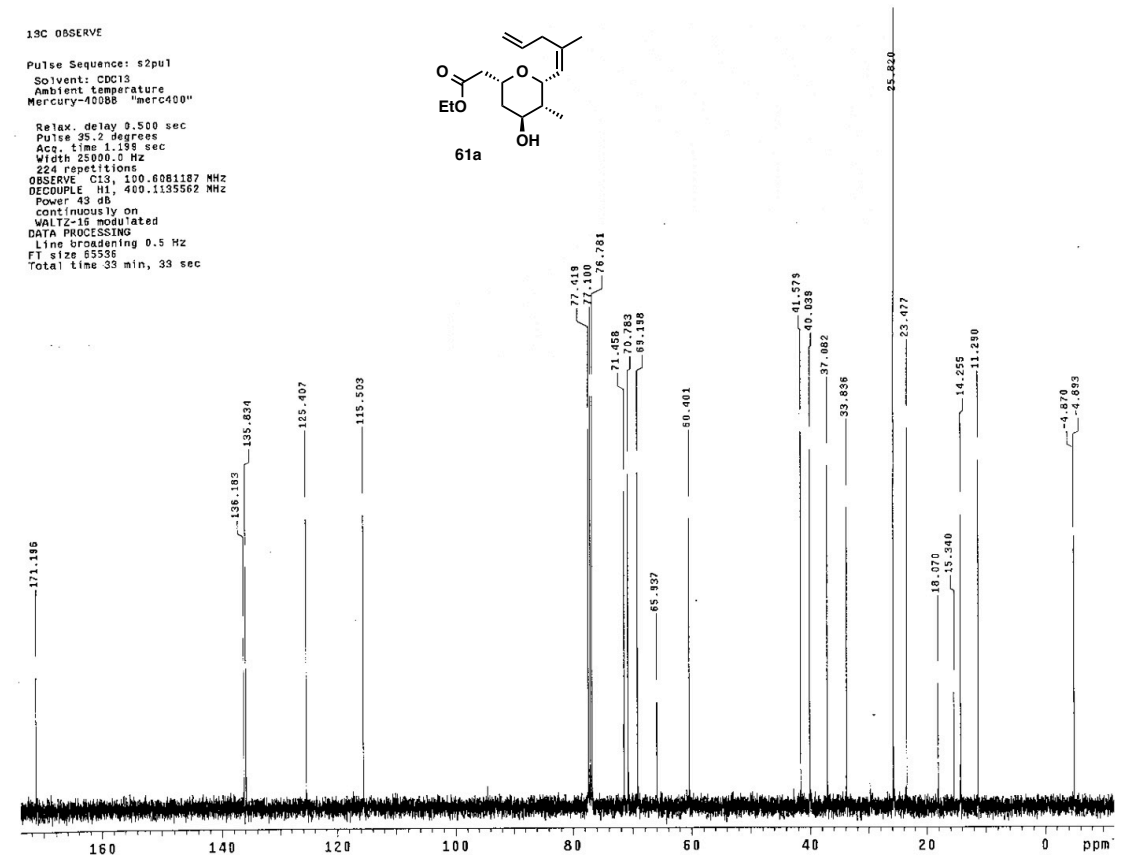

STANDARD 1H OBSERVE
Pulse Sequence: s2pul
Solvent: CDCl3
Ambient temperature
Mercury-400BB "merc400"
Relax. delay 0.500 sec
Pulse 57.1 degrees
Acq. time 4.002 sec
Width 4997.5 Hz
16 repetitions
OBSERVE H1, 400.1115375 MHz
DATA PROCESSING
FT size 65536
Total time 1 min, 22 sec
EtO
TBSO
OH
SiMe2Bn
58
ppm

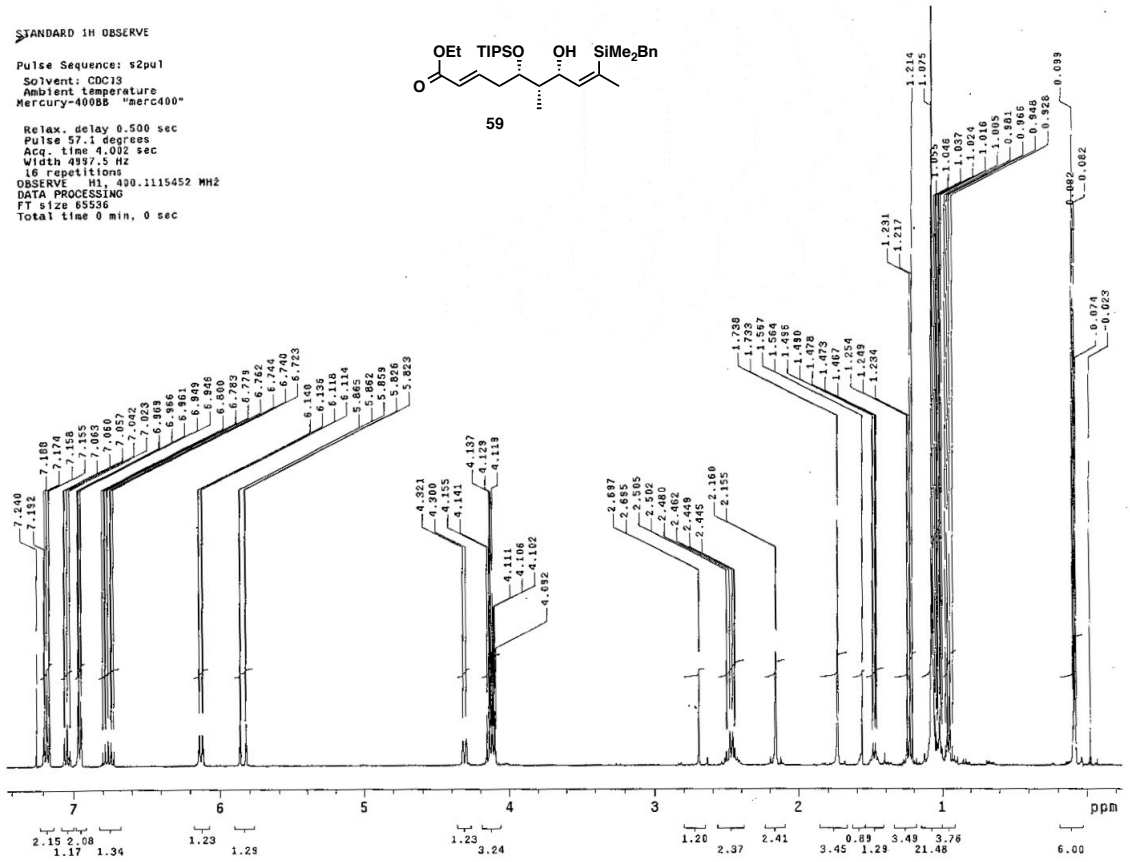

13C OBSERVE
Pulse Sequence: s2pul
Solvent: CDCl3
Ambient temperature
Mercury-400BB "merc400"
Relax. delay 0.500 sec
Pulse 35.2 degrees
Acq. time 1.199 sec
Width 25000.0 Hz
208 repetitions
OBSERVE C13, 100.6081164 MHz
DECOUPLE H1, 400.1135562 MHz
Power 43 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 33 min, 33 sec
EtO
TBSO
OH
SiMe2Bn
58
ppm


STANDARD 1H OBSERVE
Pulse Sequence: s2pul
Solvent: CDCl3
Ambient temperature
Mercury-400BB "merc400"
Relax. delay 0.500 sec
Pulse 57.1 degrees
Acq. time 4.002 sec
Width 4997.5 Hz
16 repetitions
OBSERVE H1, 400.1115450 MHz
DATA PROCESSING
FT size 65536
Total time 0 min, 0 sec
EtO
HO
OH
O
60
ppm


13C OBSERVE
Pulse Sequence: s2pul
Solvent: CDCl3
Ambient temperature
Mercury-400BB "merc400"
Relax. delay 0.500 sec
Pulse 35.2 degrees
Acq. time 1.189 sec
Width 25000.0 Hz
176 repetitions
OBSERVE C13, 100.6081172 MHz
DECOUPLE H1, 400.1135562 MHz
Power 43 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
line broadening 0.5 Hz
FT size 65536
Total time 33 min, 33 sec
EtO
HO
OH
O
60
ppm


STANDARD 1H OBSERVE
Pulse Sequence: s2pul
Solvent: CDCl3
Ambient temperature
Mercury-400BB "merc400"
Relax. delay 0.500 sec
Pulse 57.1 degrees
Acq. time 4.002 sec
Width 4997.5 Hz
16 repetitions
OBSERVE H1, 400.1115450 MHz
DATA PROCESSING
FT size 65536
Total time 1 min, 22 sec
61a
ppm


13C OBSERVE
Pulse Sequence: s2pul
Solvent: CDCl3
Ambient temperature
Mercury-400BB "merc400"
Relax. delay 0.500 sec
Pulse 35.2 degrees
Acq. time 1.198 sec
Width 25000.0 Hz
224 repetitions
OBSERVE C13, 100.6081187 MHz
DECOUPLE H1, 400.1135562 MHz
Power 43 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 33 min, 33 sec
61a
ppm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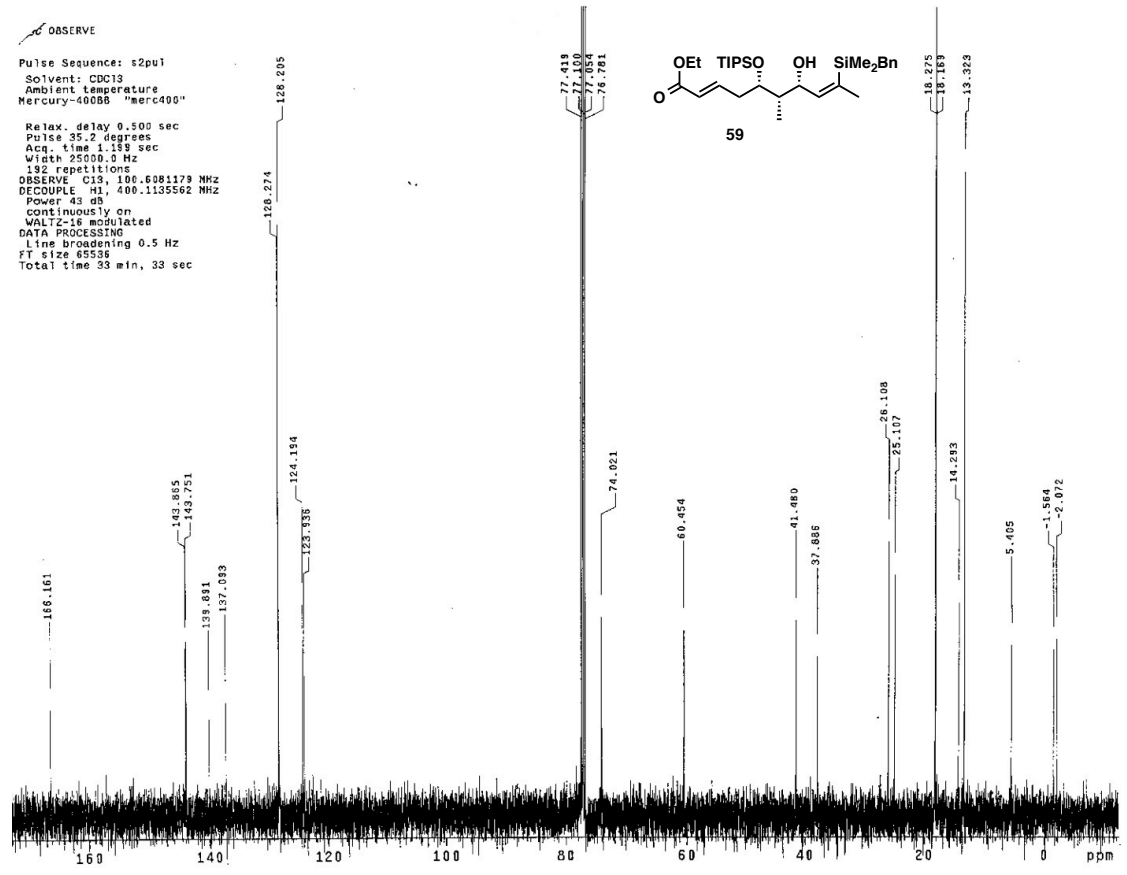
Solvent: CDCl3
Ambient temperature
Mercury-400BB "merc400"
Relax. delay 0.500 sec
Pulse 57.1 degrees
Acq. time 4.092 sec
Width 4997.5 Hz
16 repetitions
OBSERVE H1, 400.1115452 MHz
DATA PROCESSING
FT size 65536
Total time 0 min, 0 sec
OEt TIPSO OH SiMe2Bn
59
ppm


OBSERVE
Pulse Sequence: s2pul
Solvent: CDCl3
Ambient temperature
Mercury-400BB "merc400"
Relax. delay 0.500 sec
Pulse 35.2 degrees
Acq. time 1.199 sec
Width 25000.0 Hz
192 repetitions
OBSERVE C13, 100.6081179 MHz
DECOUPLE H1, 400.1135562 MHz
Power 43 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 33 min, 33 sec
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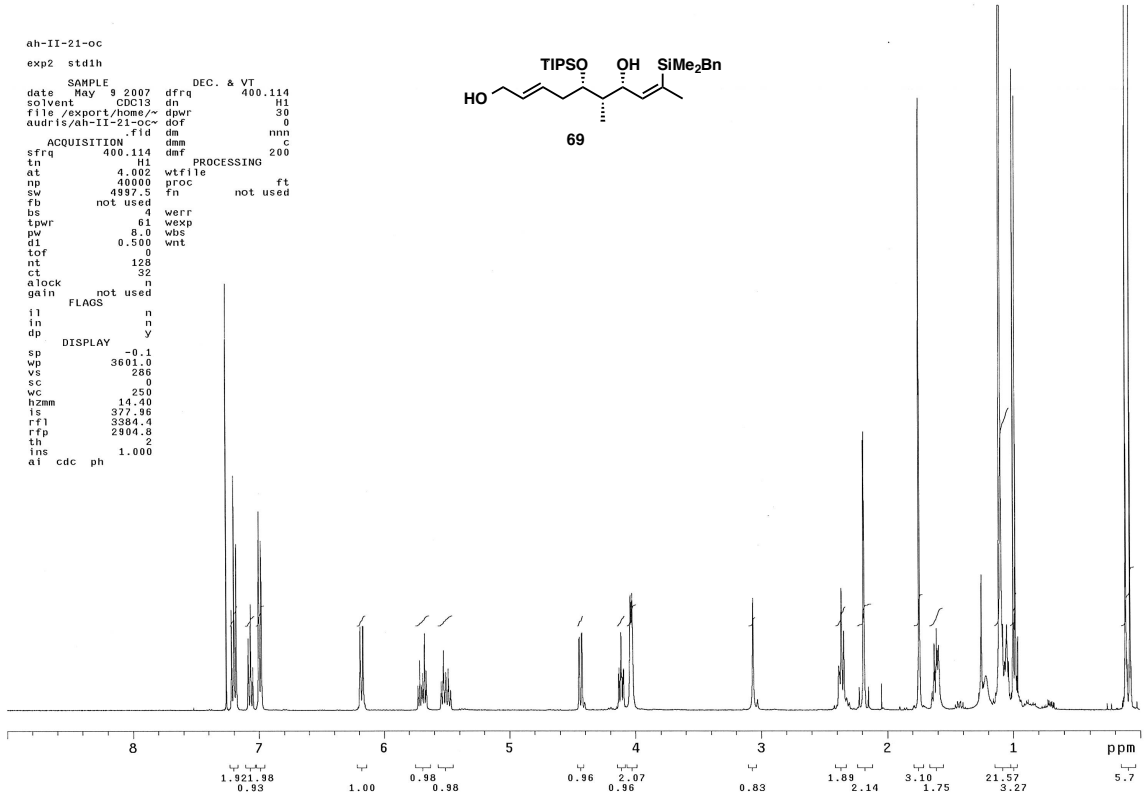
59
ppm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SAMPLE
date May 9 2007
solvent CDCl3
file /export/home/~
audris/ah-II-21-oc~
.fid
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np 40000
sw 4997.5
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tpwr 61
pw 8.0
d1 0.500
tof 0
nt 128
ct 32
alock n
gain not used
FLAGS
il n
in n
dp y
DISPLAY
sp -0.1
wp 3601.0
vs 286
sc 0
wc 250
hzmm 14.40
is 377.96
rfl 3384.4
rfp 2904.8
th 2
ins 1.000
ai cdc ph
DEC. & VT
dfrq 400.114
dn H1
dpwr 30
dof 0
dm nnn
dmm c
dmf 200
PROCESSING
wtfile
proc ft
fn not used
werr
wexp
wbs
wnt
TIPSO
OH
SiMe2Bn
HO
69
8
7
6
5
4
3
2
1
ppm
1.92 1.98
0.93
1.00
0.98
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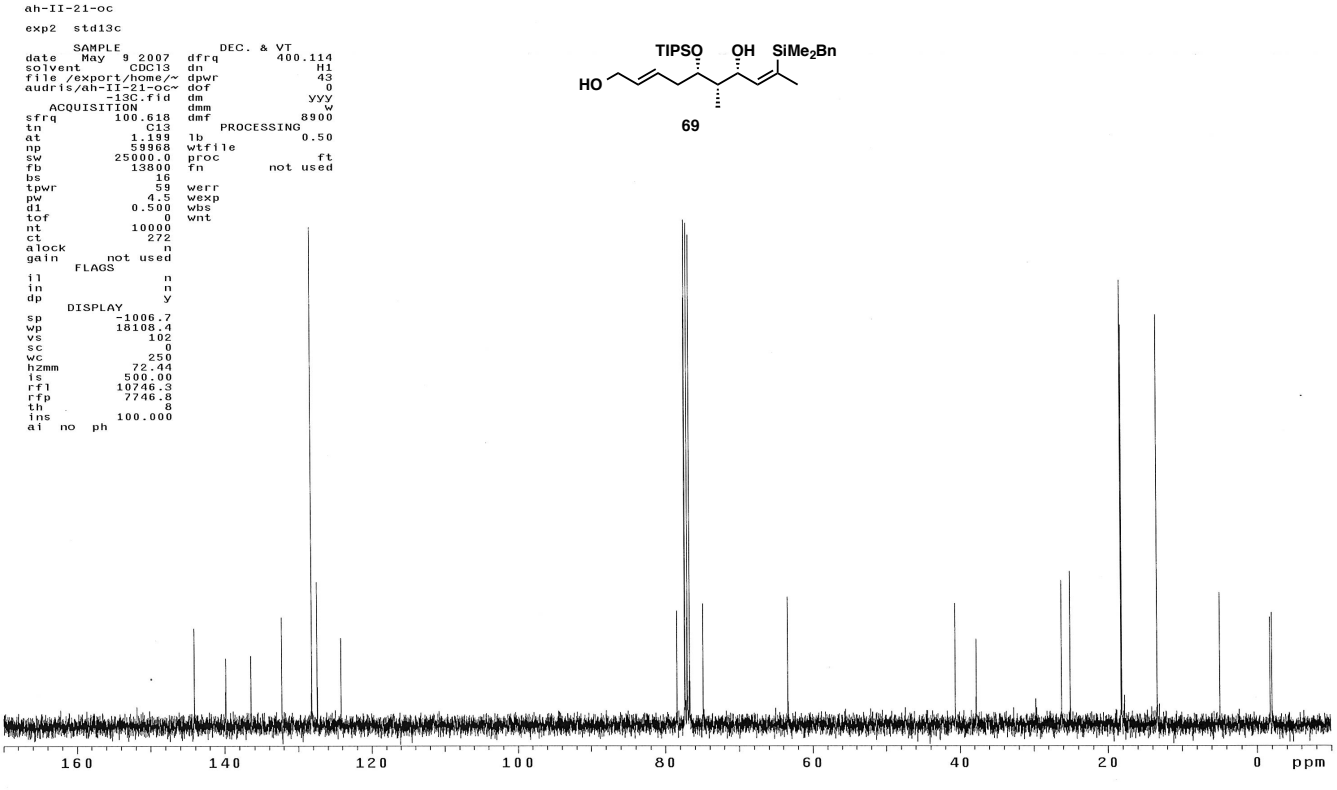
2.07
0.96
0.83
1.89
2.14
3.10
1.75
21.57
3.27
5.7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date May 9 2007
solvent CDCl3
file /export/home/~
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at 1.199
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d1 0.500
tof 0
nt 10000
ct 272
alock n
gain not used
FLAGS
il n
in n
dp y
DISPLAY
sp -1006.7
wp 18108.4
vs 102
sc 0
wc 250
hzmm 72.44
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rfl 10746.3
rfp 7746.8
th 8
ins 100.000
ai no ph
DEC. & VT
dfrq 400.114
dn H1
dpwr 43
dof 0
dm yyy
dmm w
dmf 8900
PROCESSING
lb 0.50
wtfile
proc ft
fn not used
werr
wexp
wbs
wnt
TIPSO
OH
SiMe2Bn
HO
69
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120
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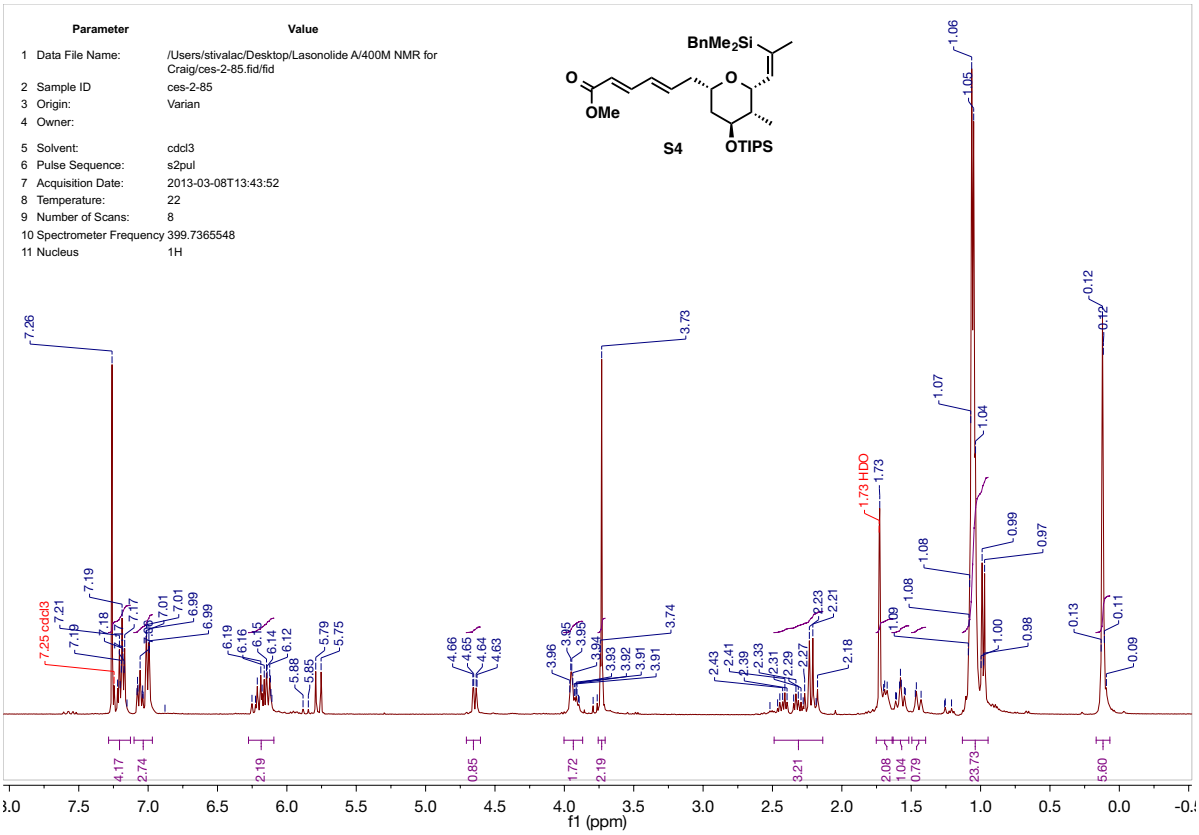
0
ppm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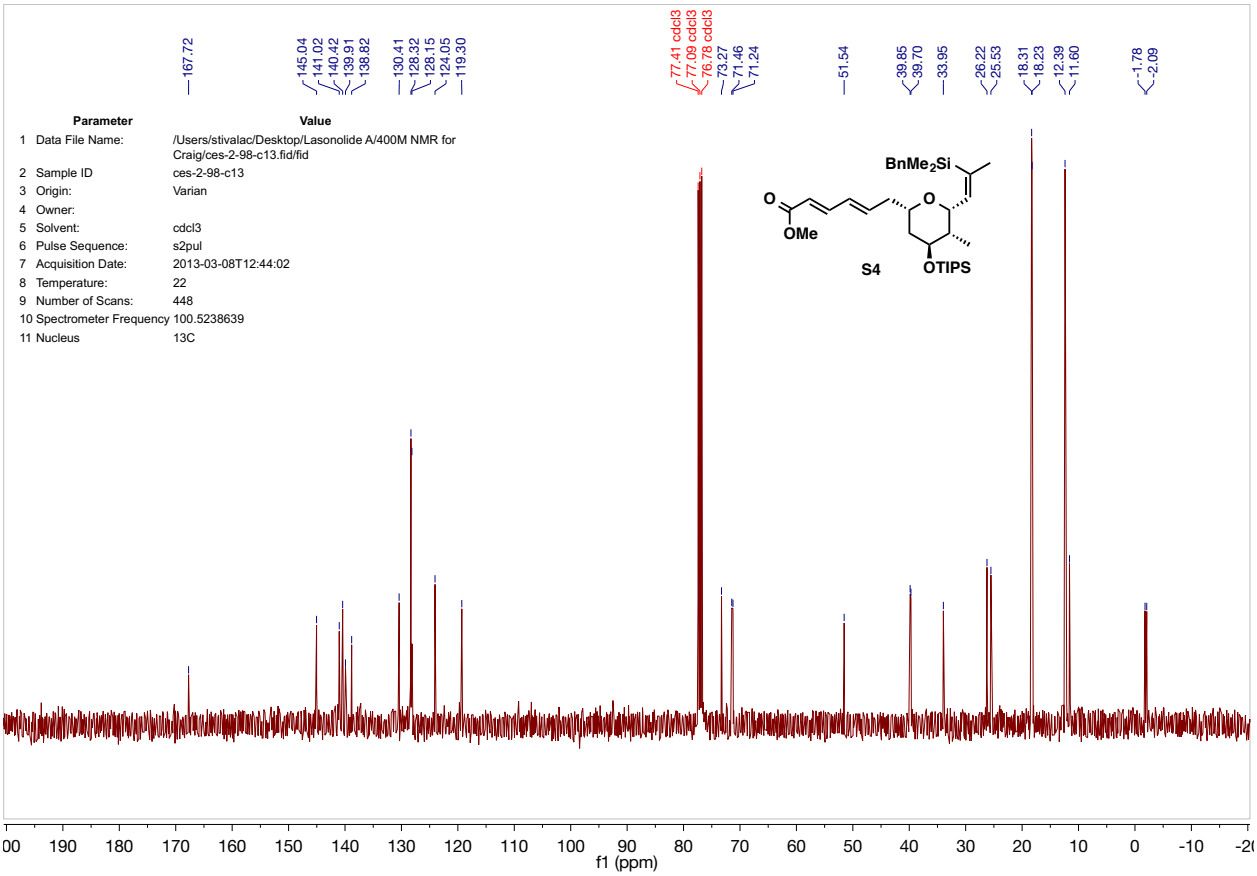
2 Sample ID ces-2-85
3 Origin: Varian
4 Owner:
5 Solvent: cdcl3
6 Pulse Sequence: s2pul
7 Acquisition Date: 2013-03-08T13:43:52
8 Temperature: 22
9 Number of Scans: 8
10 Spectrometer Frequency 399.7365548
11 Nucleus 1H
BnMe2Si
O
OMe
O
S4
OTIPS
f1 (ppm)


Parameter Value
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2 Sample ID ces-2-98-c13
3 Origin: Varian
4 Owner:
5 Solvent: cdcl3
6 Pulse Sequence: s2pul
7 Acquisition Date: 2013-03-08T12:44:02
8 Temperature: 22
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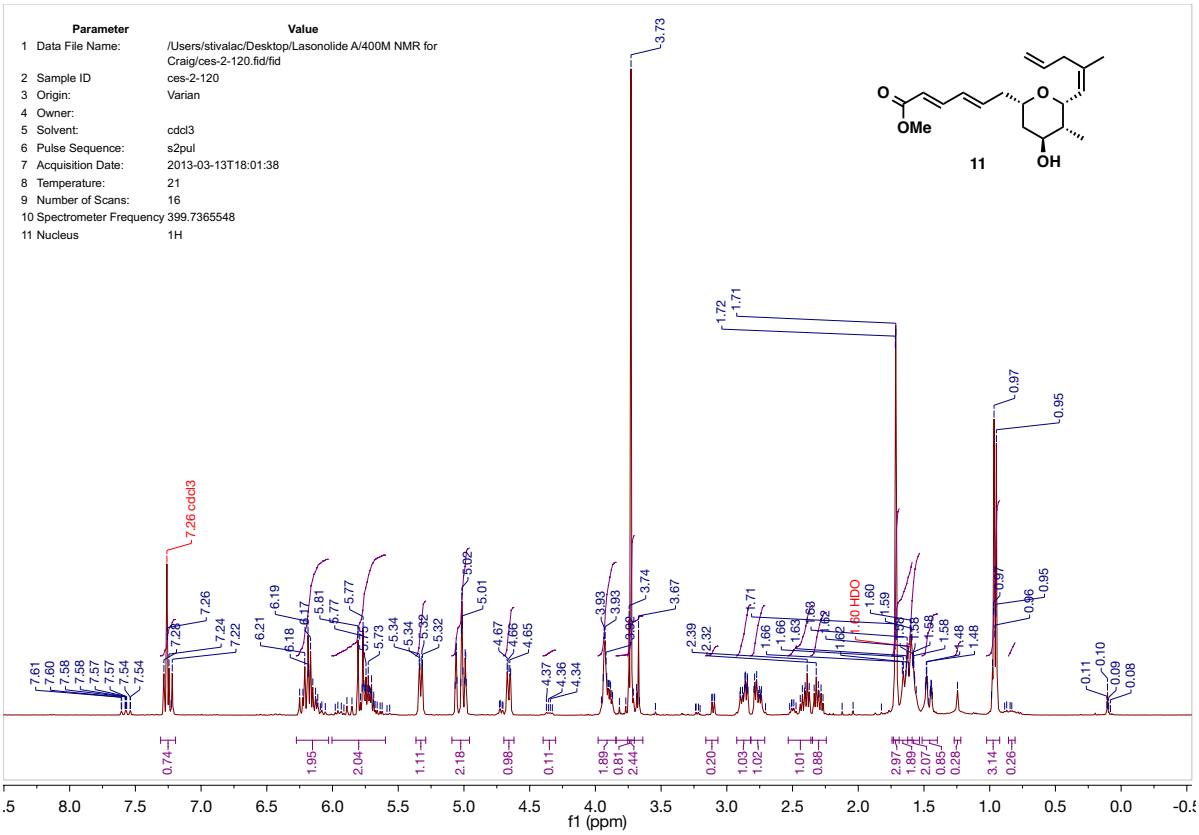
11 Nucleus 13C
BnMe2Si
O
OMe
O
S4
OTIPS
f1 (ppm)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4 Owner:
5 Solvent: cdcl3
6 Pulse Sequence: s2pul
7 Acquisition Date: 2013-03-13T18:01:38
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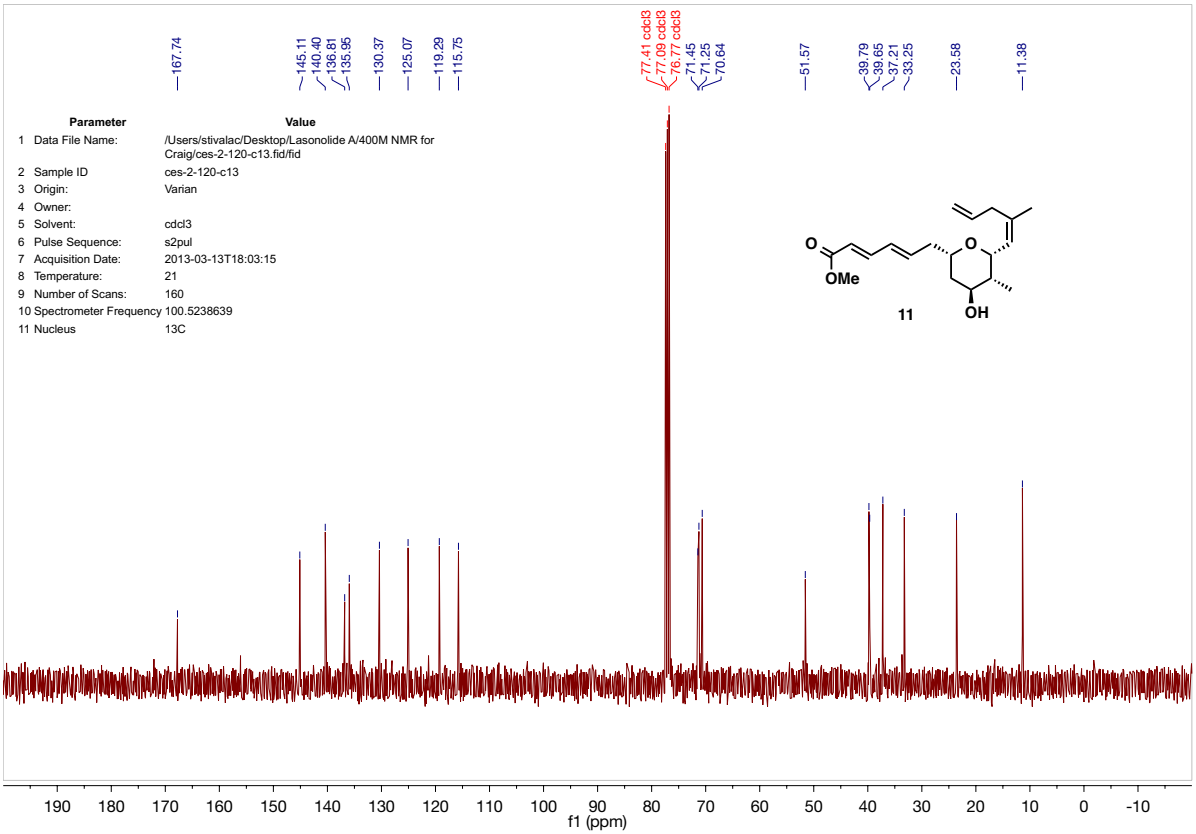
9 Number of Scans: 16
10 Spectrometer Frequency 399.7365548
11 Nucleus 1H
OMe
OH
11
f1 (ppm)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2 Sample ID ces-2-120-c13
3 Origin: Varian
4 Owner:
5 Solvent: cdcl3
6 Pulse Sequence: s2pul
7 Acquisition Date: 2013-03-13T18:03:15
8 Temperature: 21
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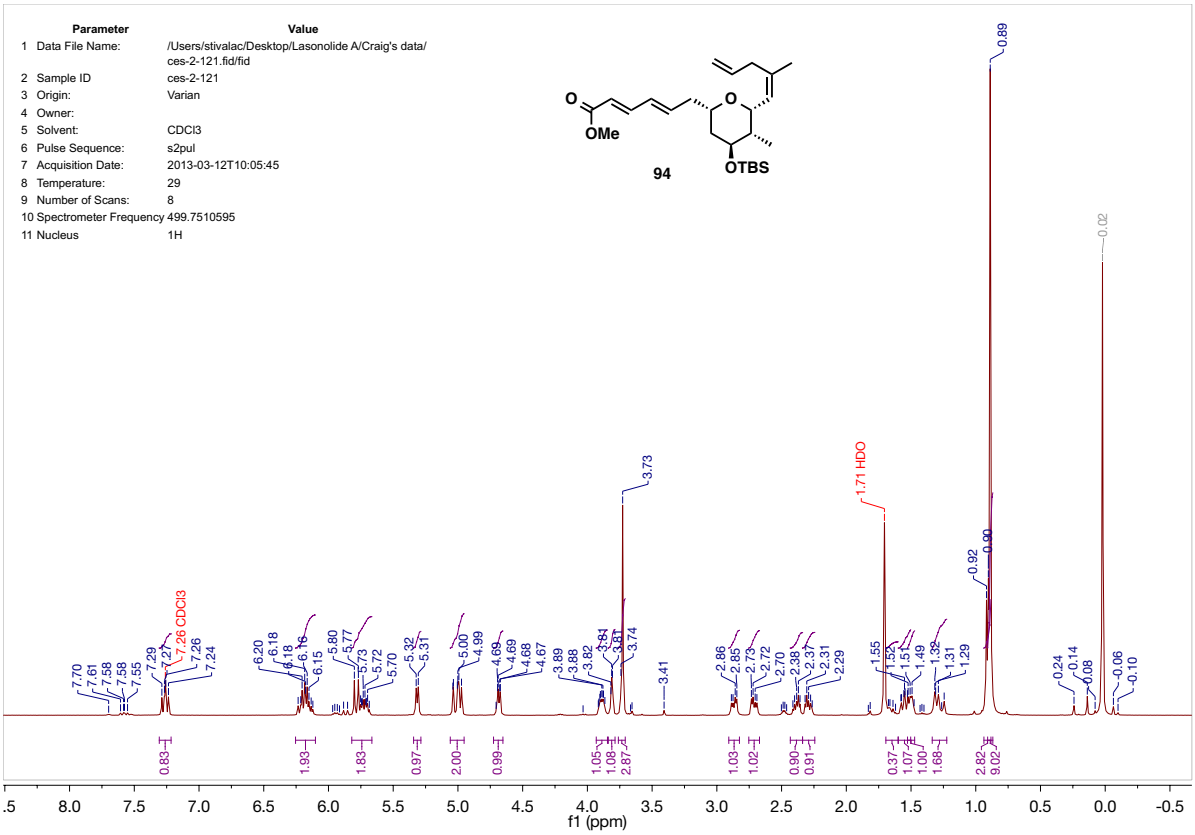
11 Nucleus 13C
OMe
OH
11
f1 (ppm)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4 Owner:
5 Solvent: CDCl3
6 Pulse Sequence: s2pul
7 Acquisition Date: 2013-03-12T10:05:45
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11 Nucleus 1H
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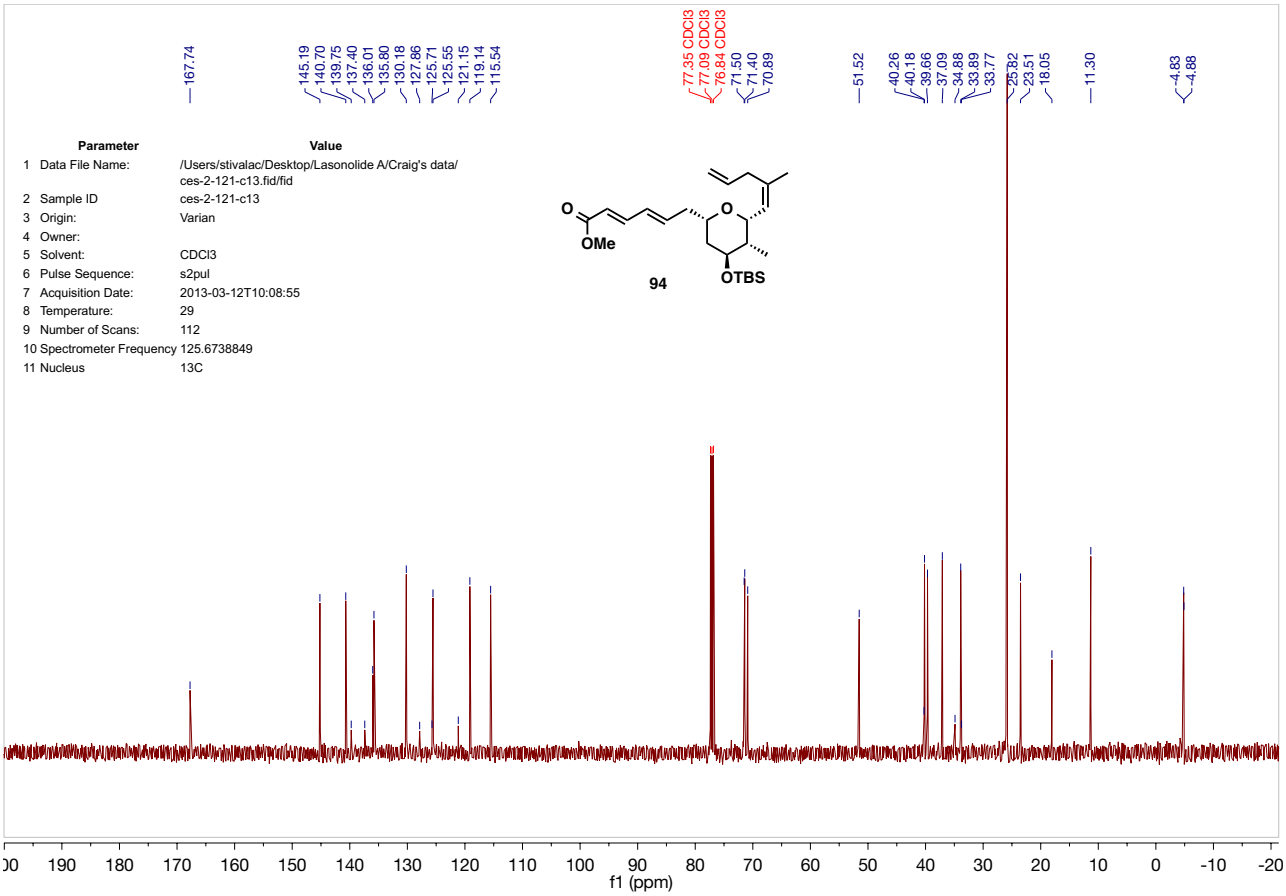
OTBS
94
f1 (ppm)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6 Pulse Sequence: s2pul
7 Acquisition Date: 2013-03-12T10:08:55
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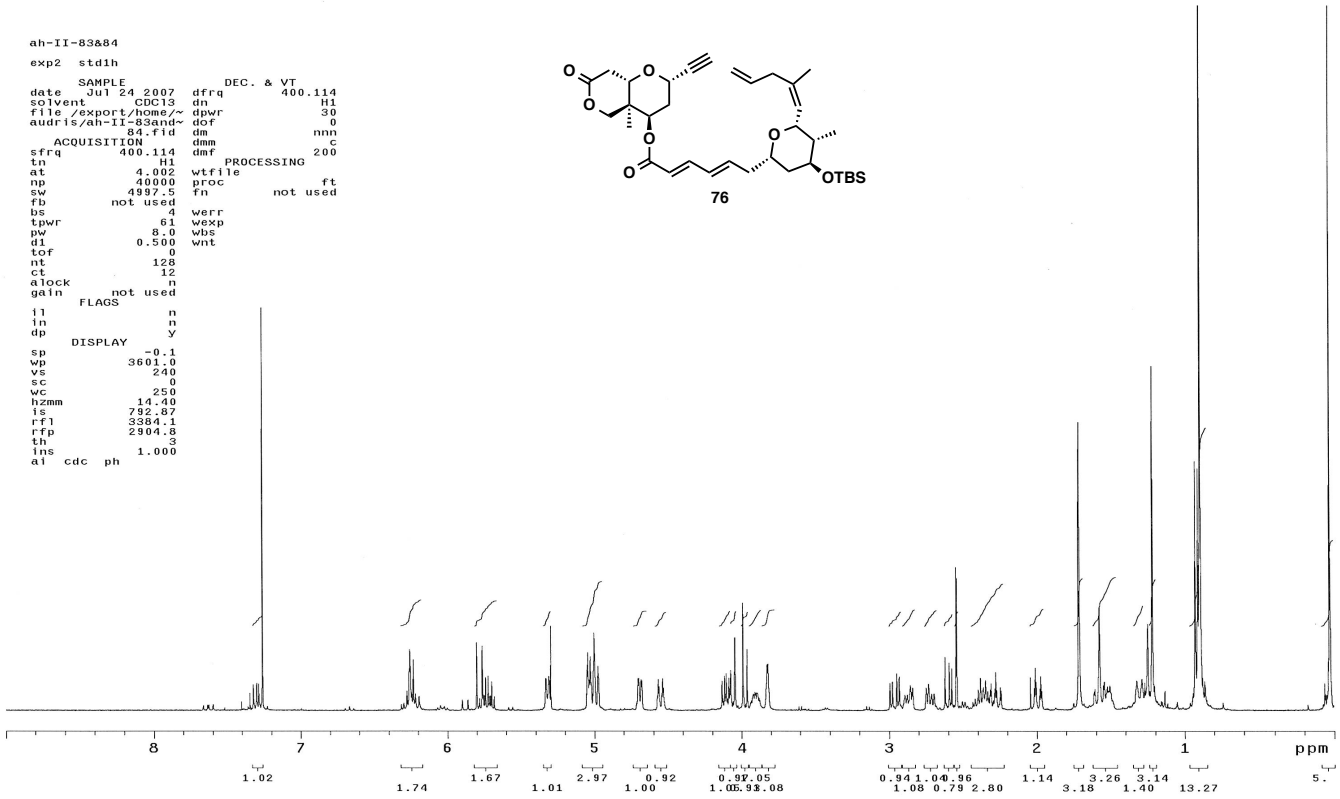
11 Nucleus 13C
OMe
OTBS
94
f1 (ppm)


ah-II-83&84
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date Jul 24 2007
solvent CDCl3
file /export/home/~
audris/ah-II-83and~
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pw 8.0
d1 0.500
tof 0
nt 128
ct 12
alock n
gain not used
FLAGS
il n
in n
dp y
DISPLAY
sp -0.1
wp 3601.0
vs 240
sc 0
wc 250
hzmm 14.40
is 792.87
rfl 3384.1
rfp 2904.8
th 3
ins 1.000
ai cdc ph
DEC. & VT
dfrq 400.114
dn H1
dpwr 30
dof 0
dm nnn
dmm c
dmf 200
PROCESSING
wtfile
proc ft
fn not used
werr
wexp
wbs
wnt
OTBS
76
8
7
6
5
4
3
2
1
ppm
1.02
1.74
1.67
1.01
2.97
0.92
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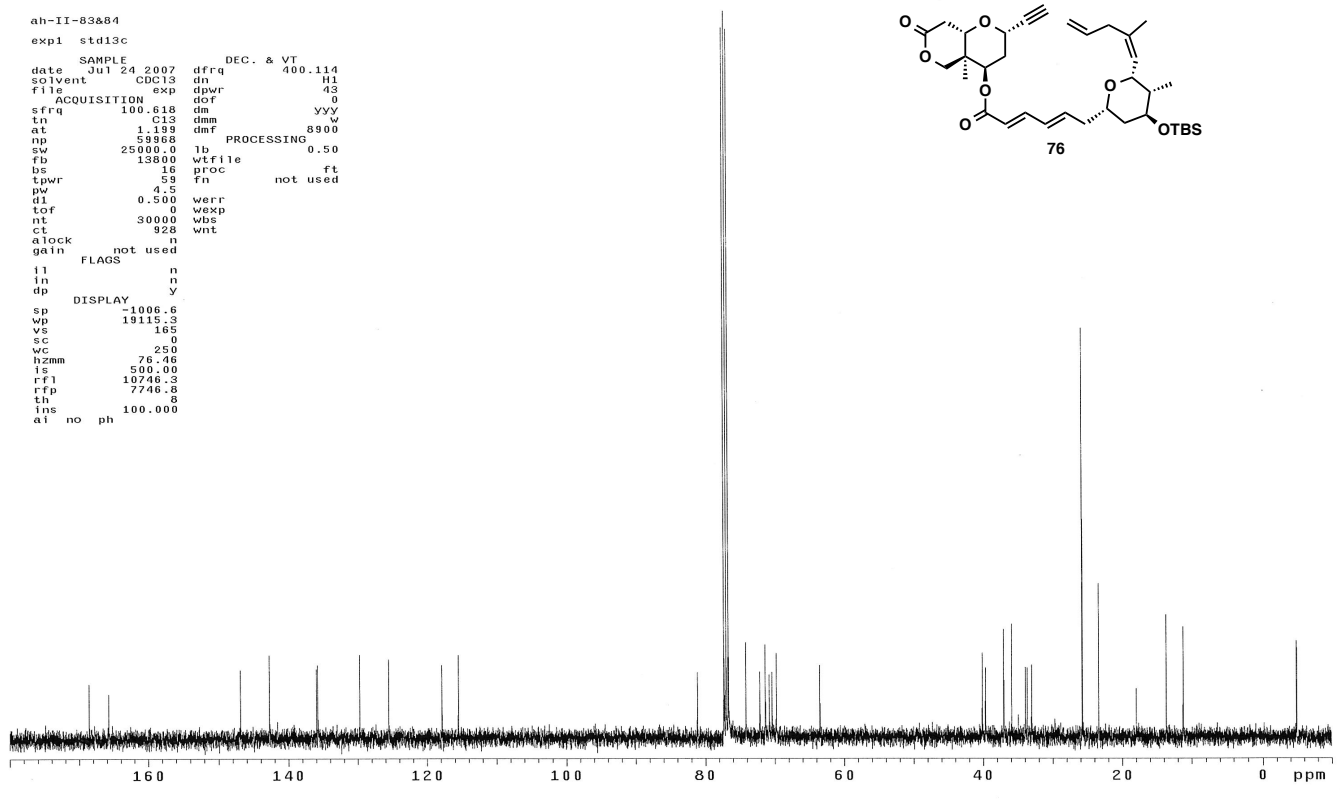
3.18
3.14
1.40
13.27
5.


ah-II-83&84
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date Jul 24 2007
solvent CDCl3
file exp
ACQUISITION
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at 1.199
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sw 25000.0
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bs 16
tpwr 59
pw 4.5
d1 0.500
tof 0
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ct 928
alock n
gain not used
FLAGS
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in n
dp y
DISPLAY
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DEC. & VT
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wtfile
proc ft
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werr
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60
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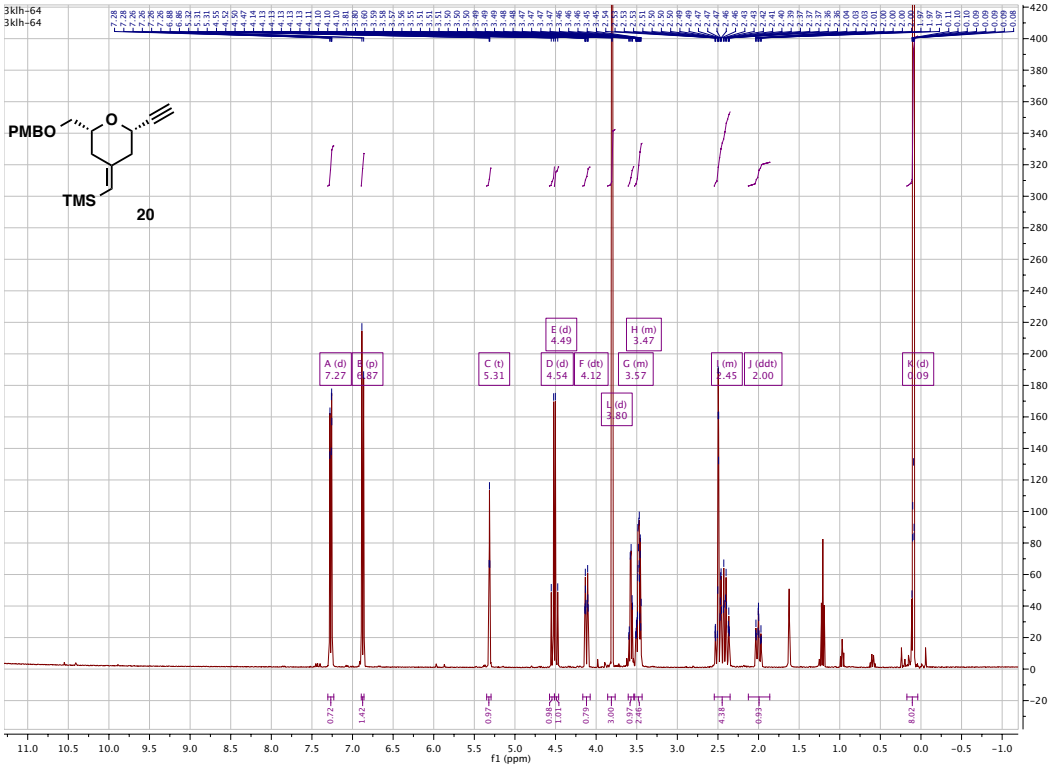
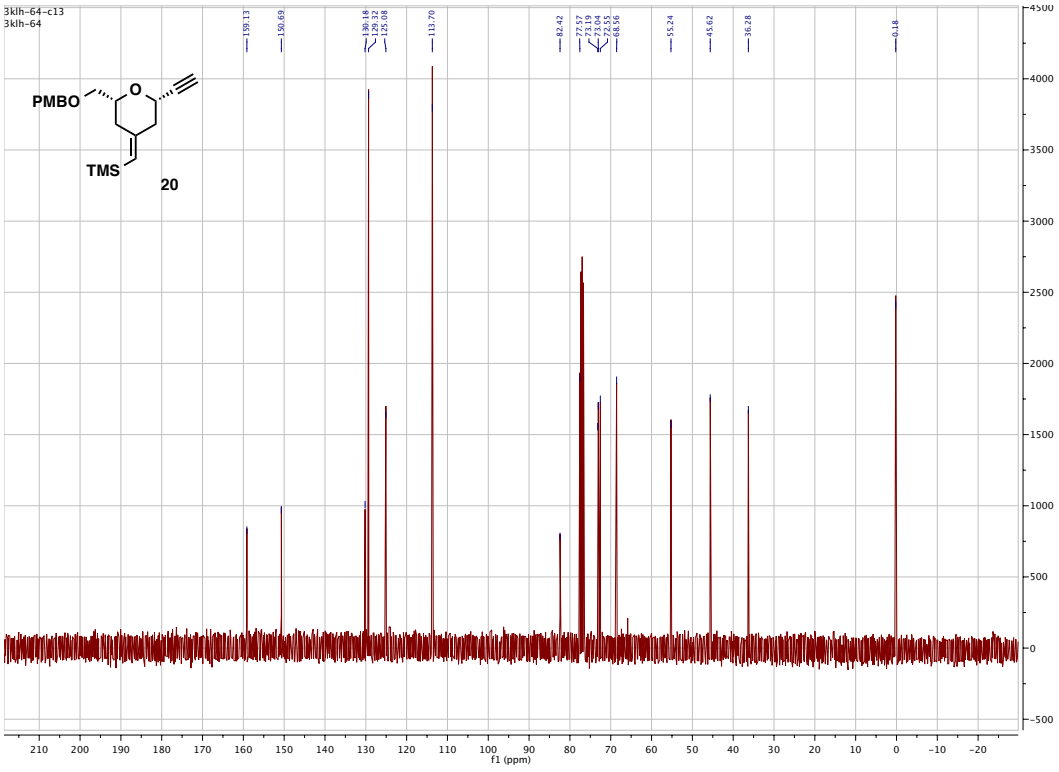
20
0
ppm

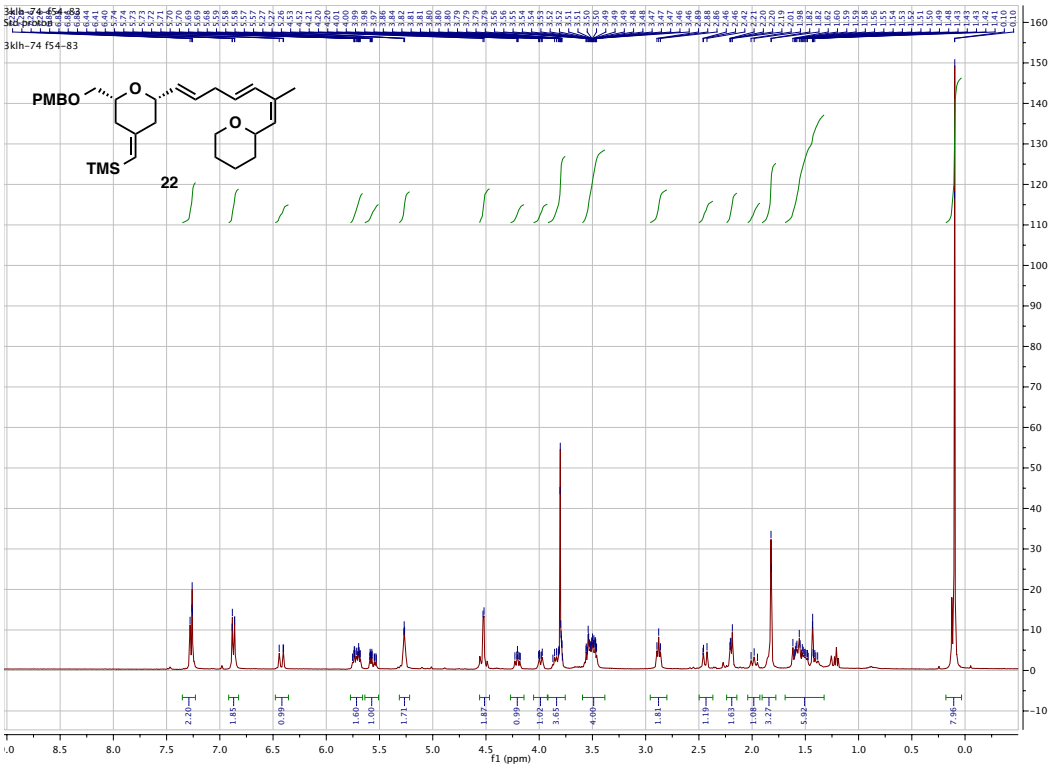
^{1}H NMR (400 MHz, $CDCl_3$)



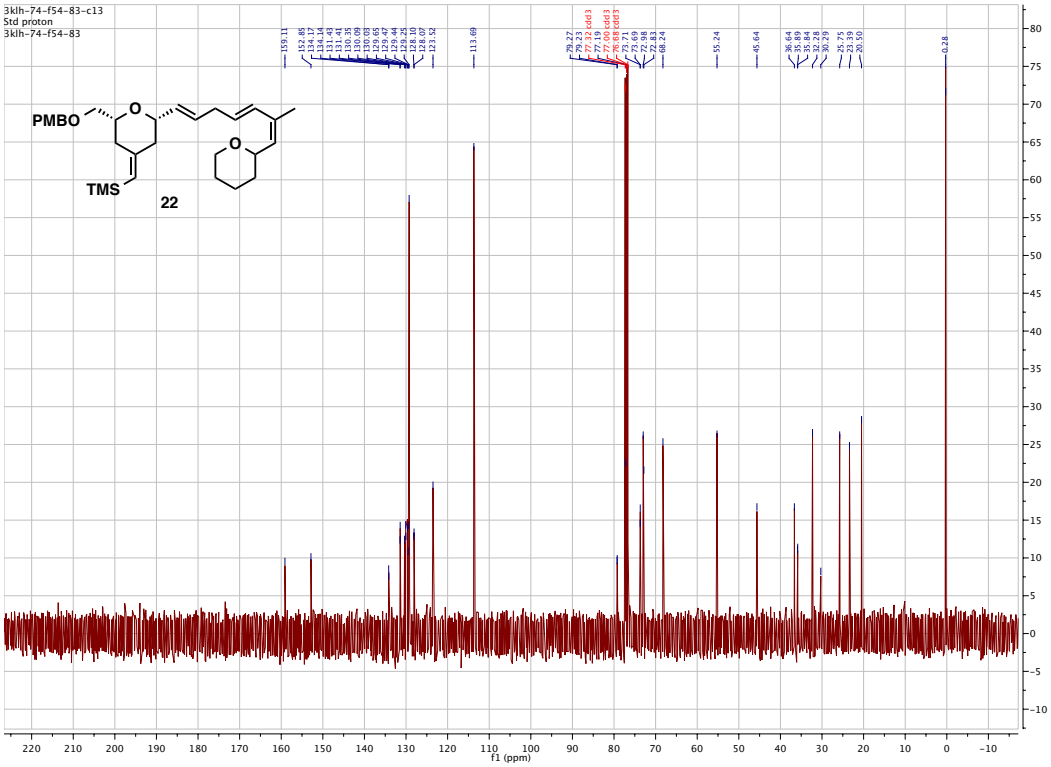
^{13}C NMR (100 MHz, $CDCl_3$)



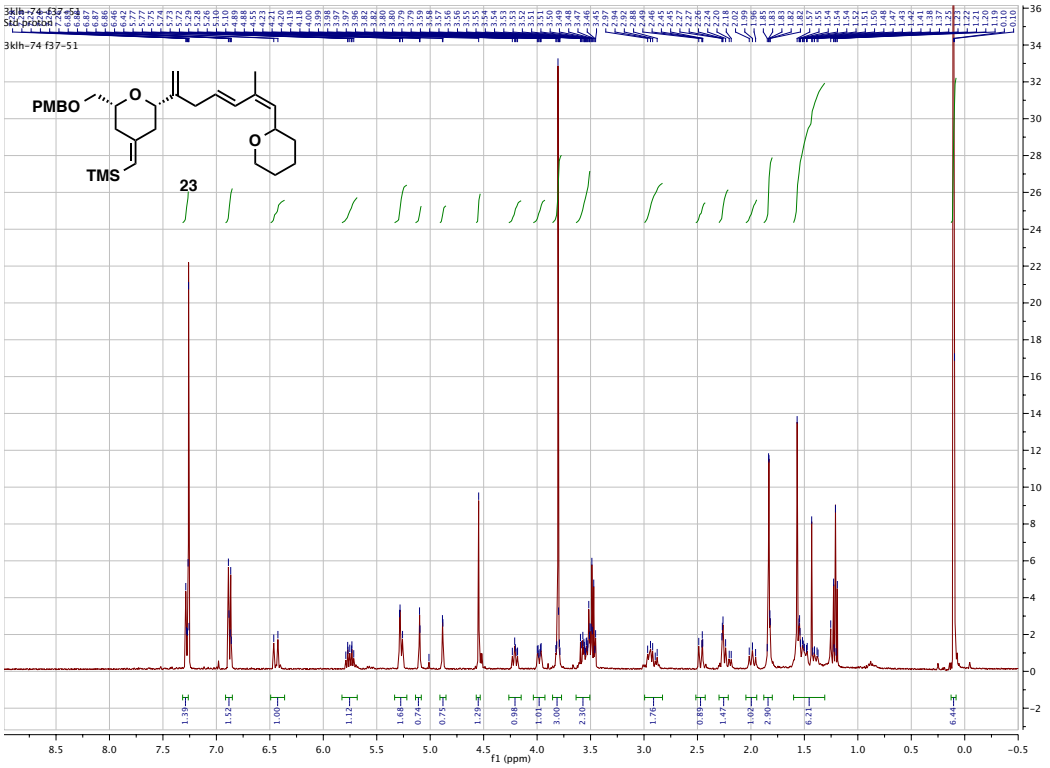
^{1}H NMR (400 MHz, $CDCl_3$)



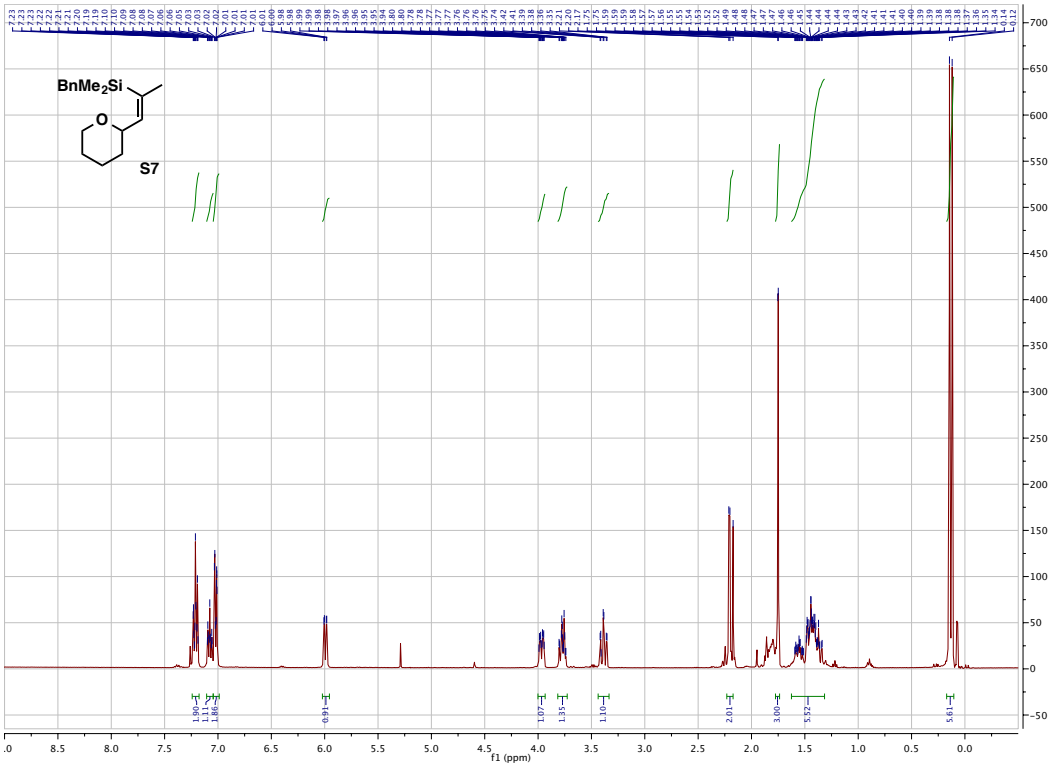
^{13}C NMR (100 MHz, $CDCl_3$)



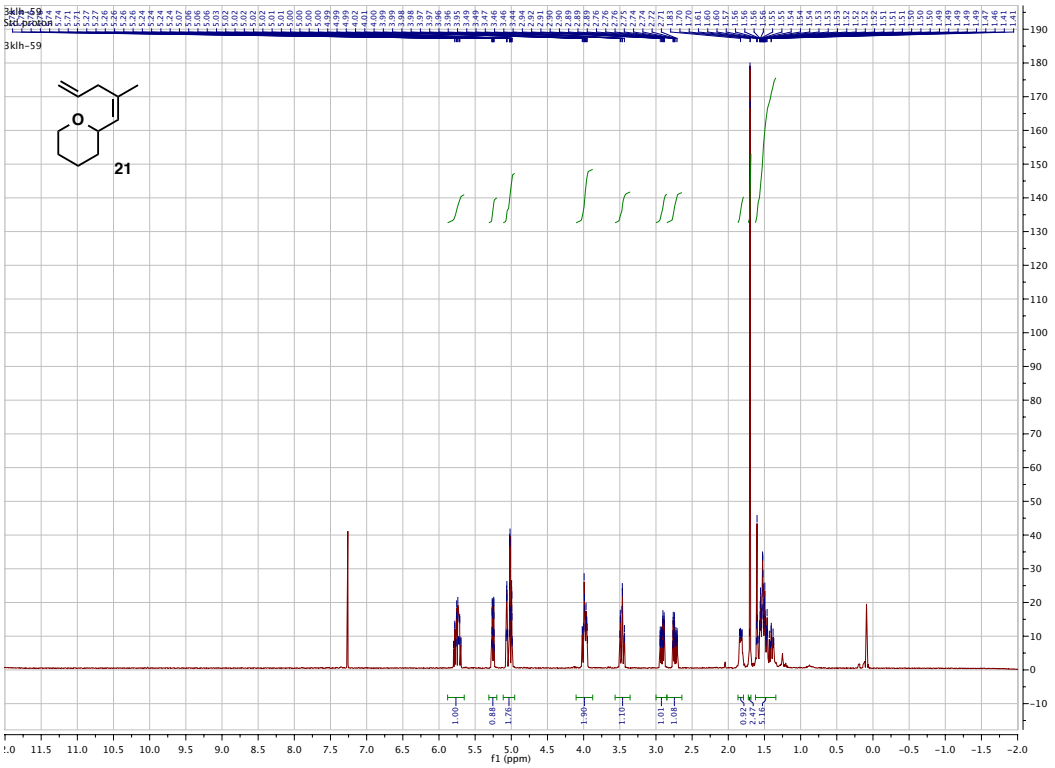
^{1}H NMR (400 MHz, $CDCl_3$)



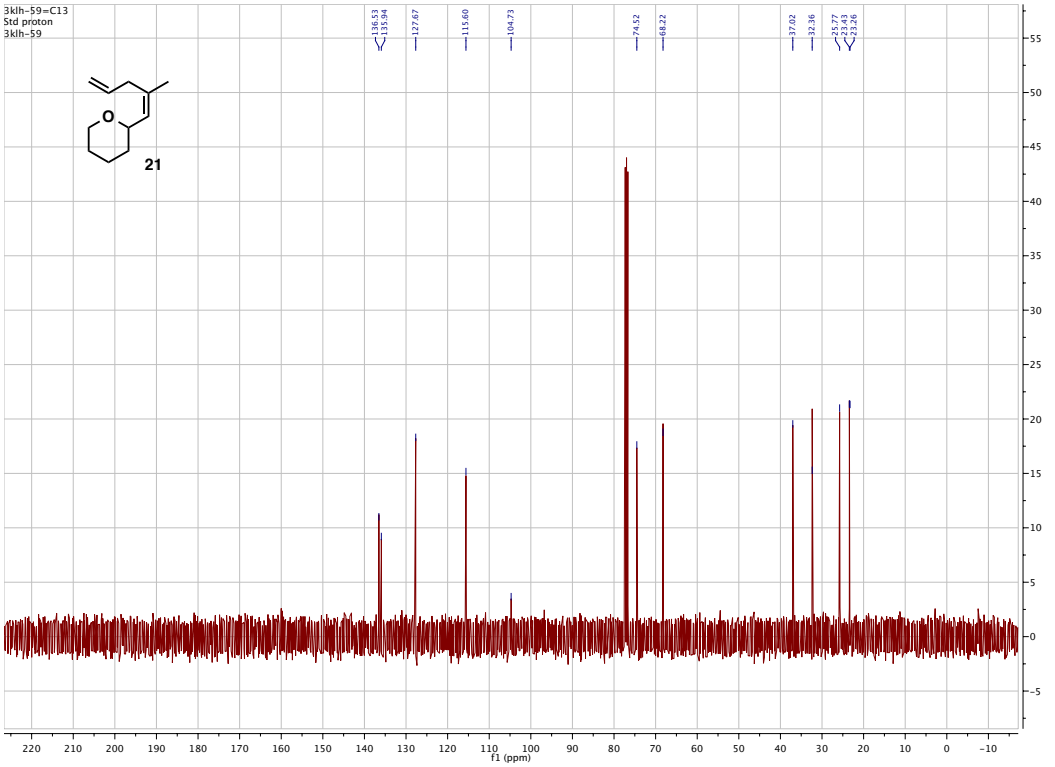
^{1}H NMR (400 MHz, $CDCl_3$)



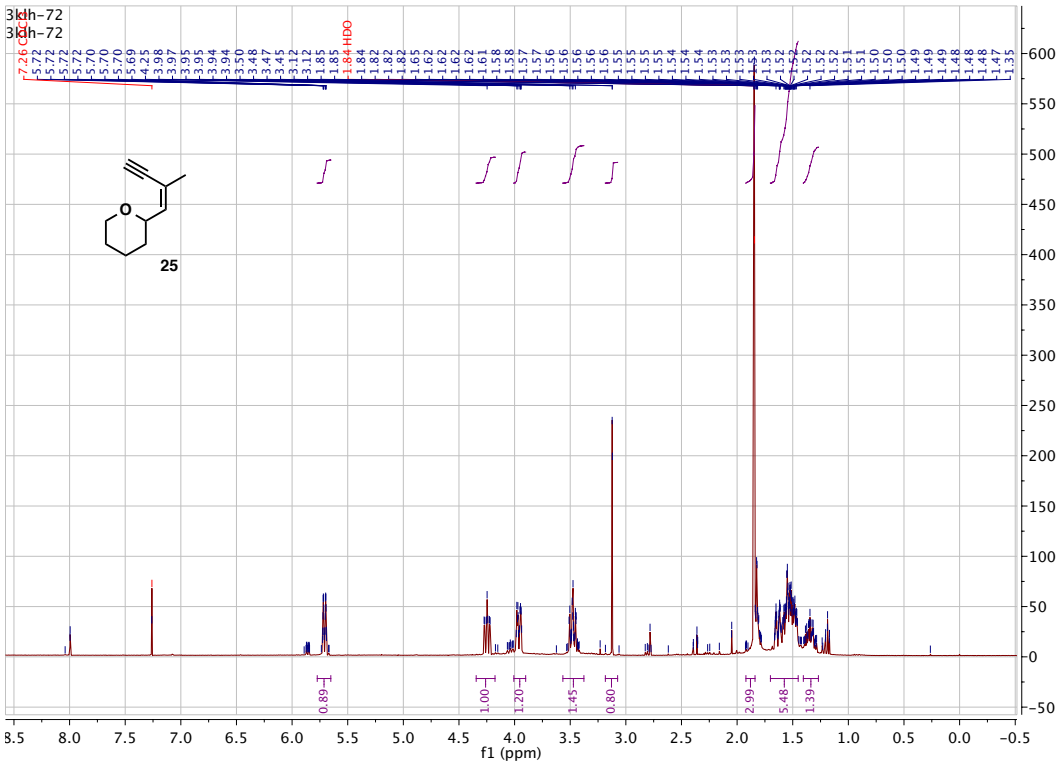
^{1}H NMR (400 MHz, $CDCl_3$)



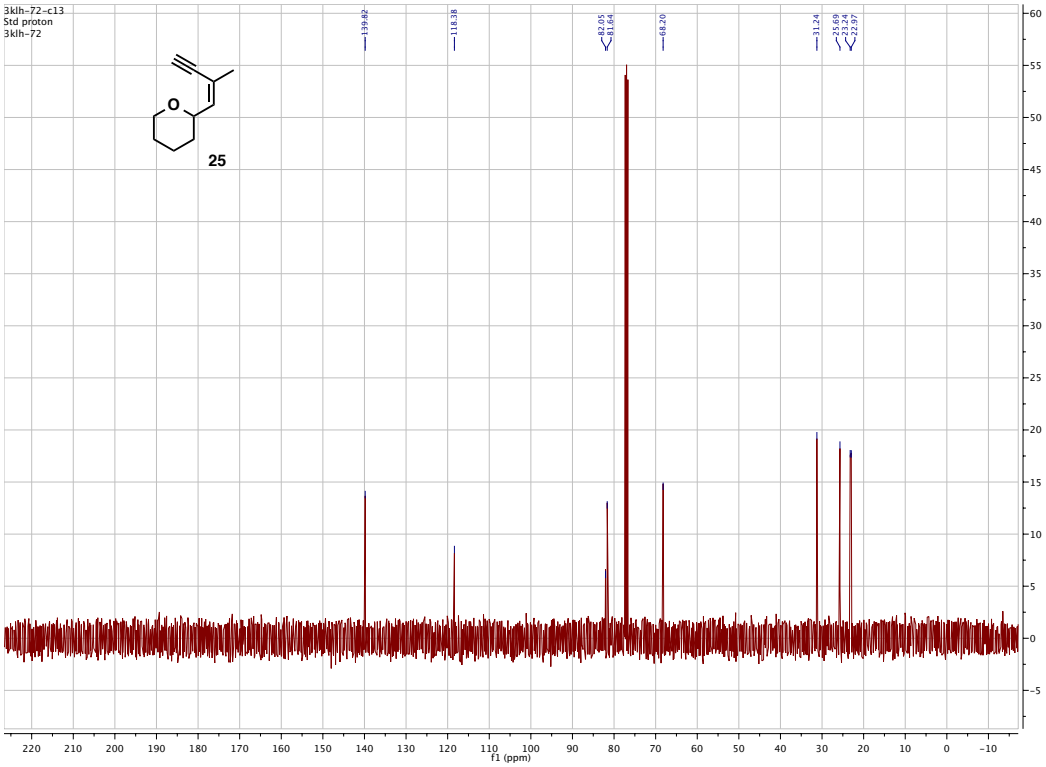
^{13}C NMR (100 MHz, $CDCl_3$)



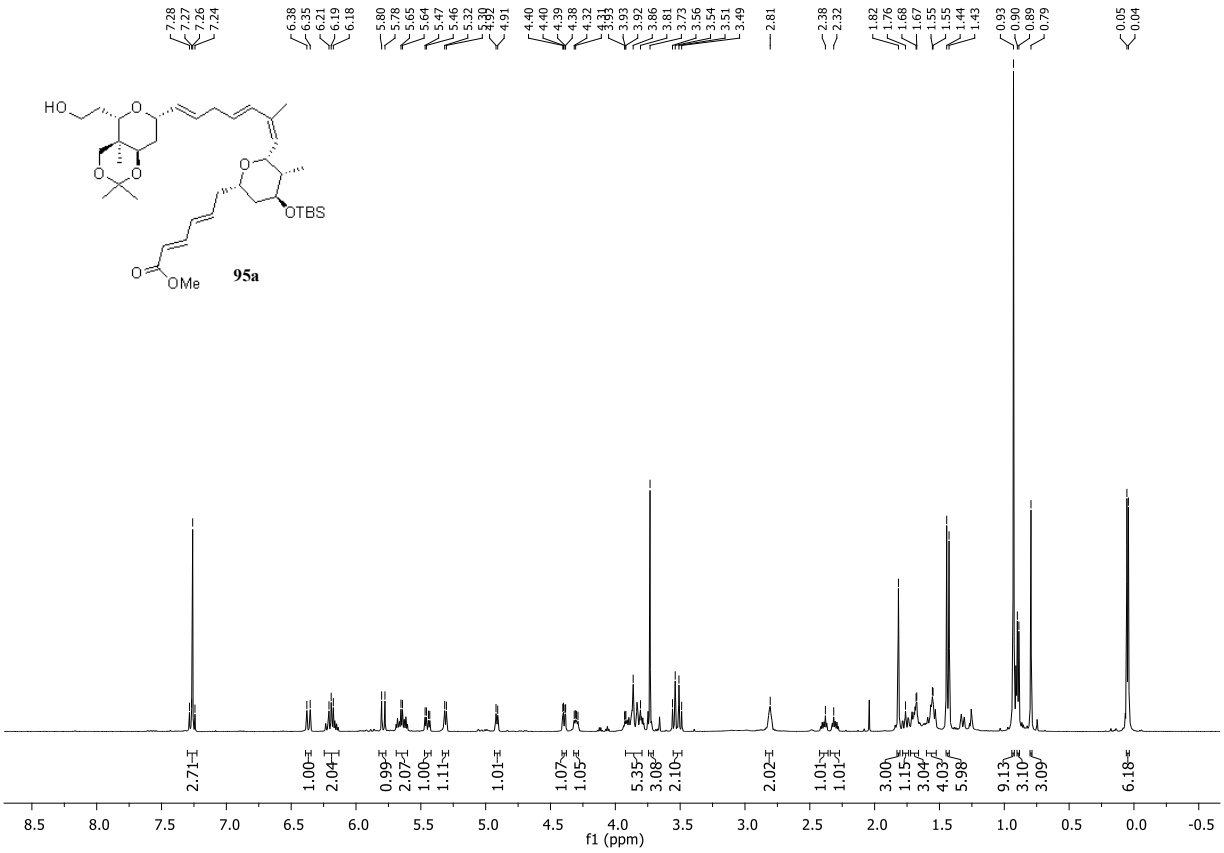
^{1}H NMR (400 MHz, $CDCl_3$)



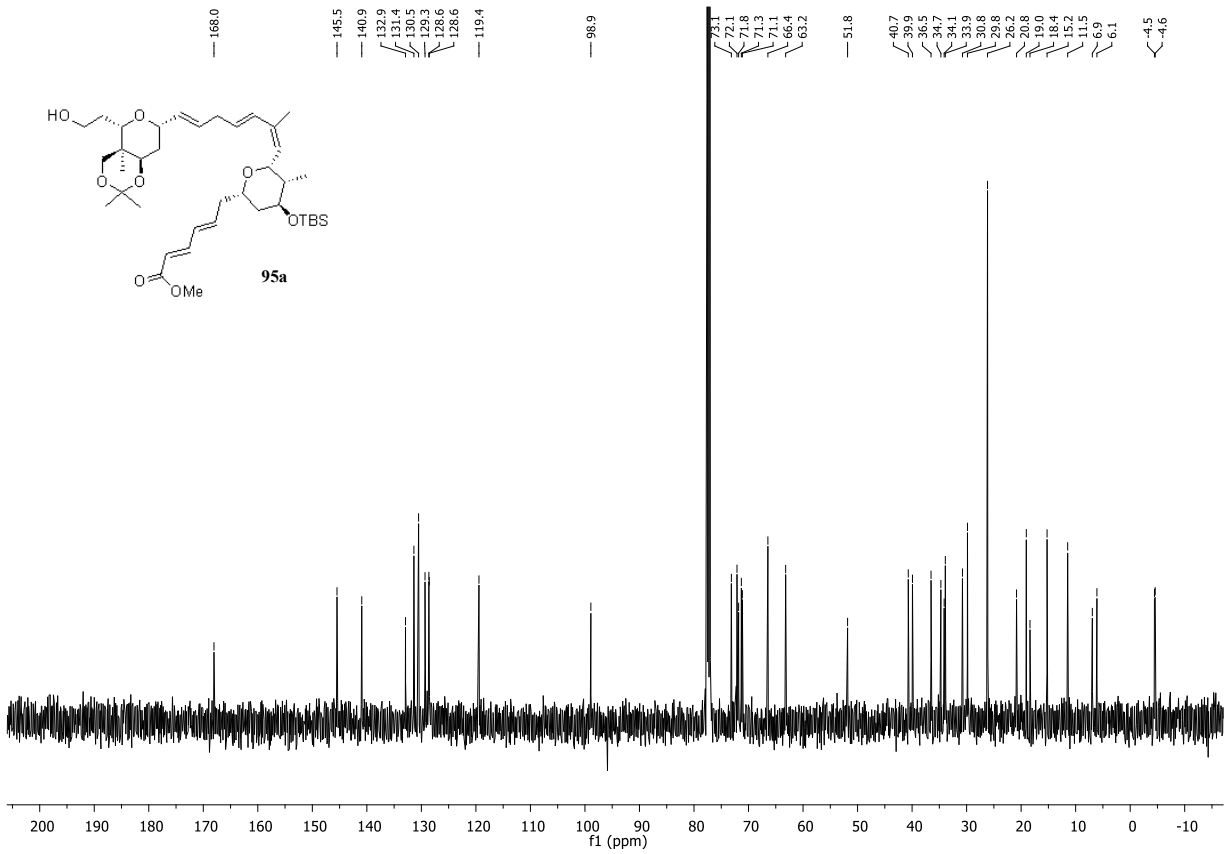
^{13}C NMR (100 MHz, $CDCl_3$)



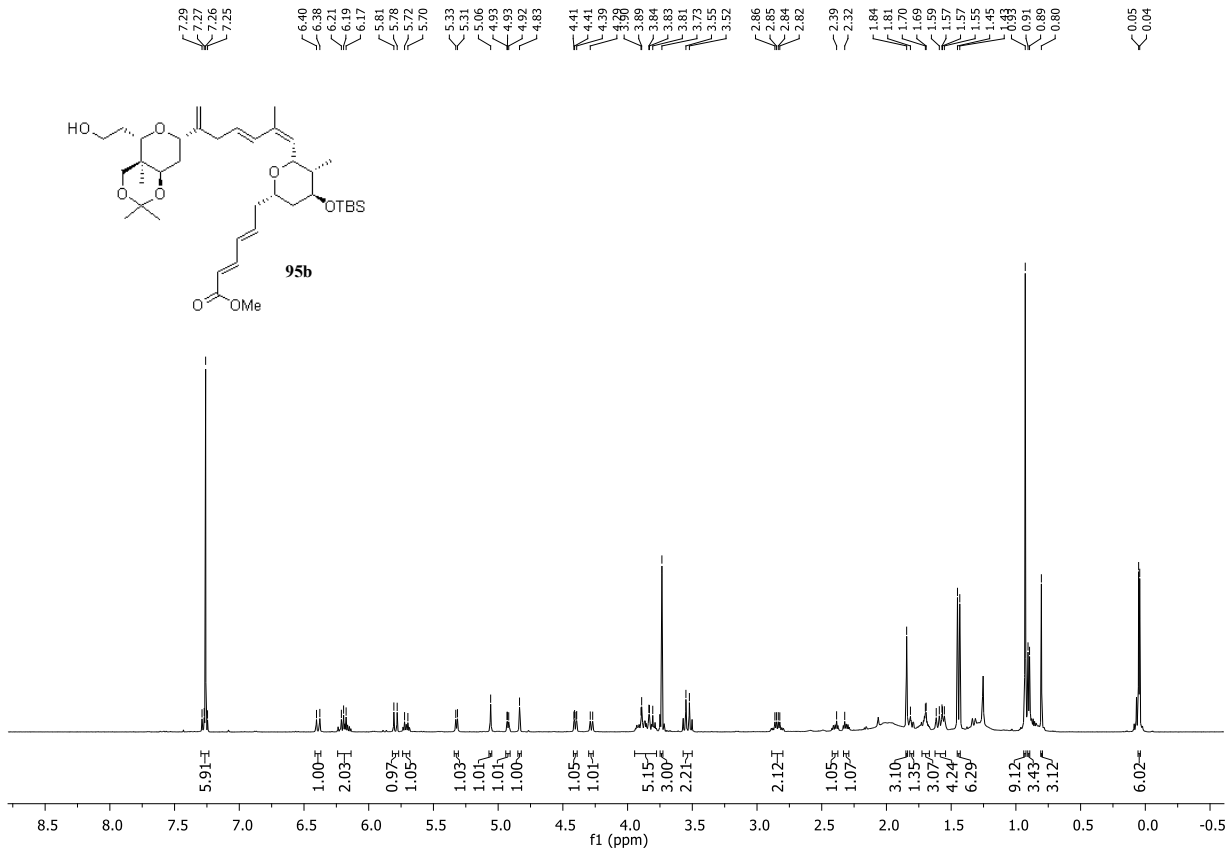
^{1}H NMR (600 MHz, $CDCl_3$)



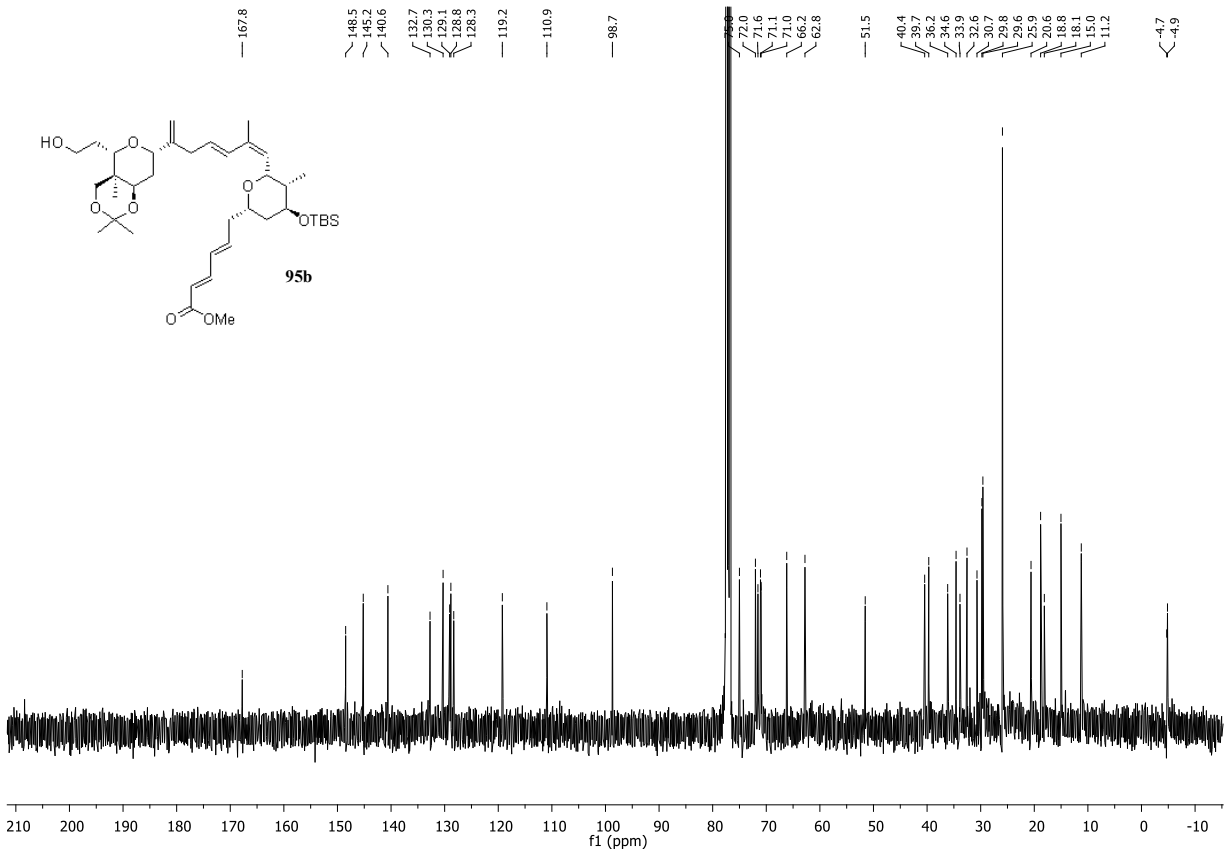
^{13}C NMR (125 MHz, $CDCl_3$)



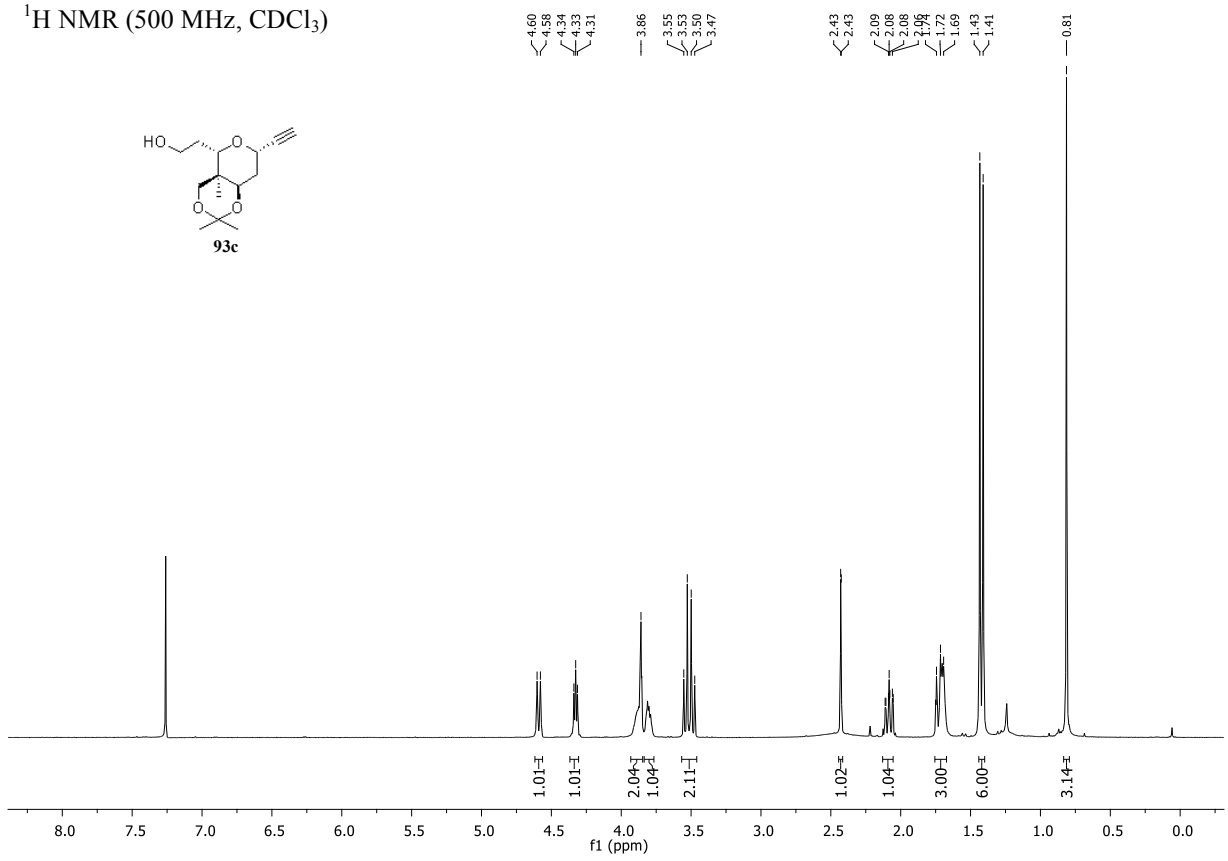
^{1}H NMR (600 MHz, $CDCl_3$)



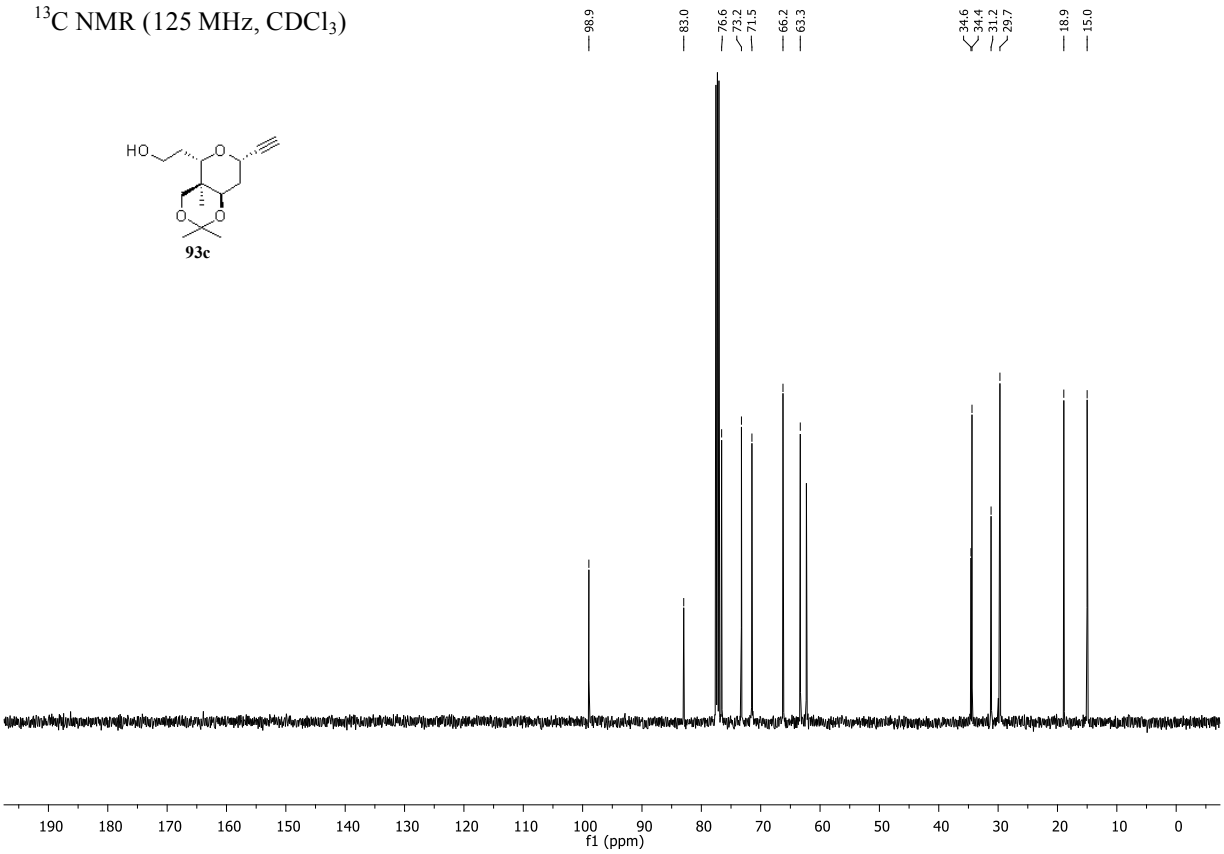
^{13}C NMR (100 MHz, $CDCl_3$)



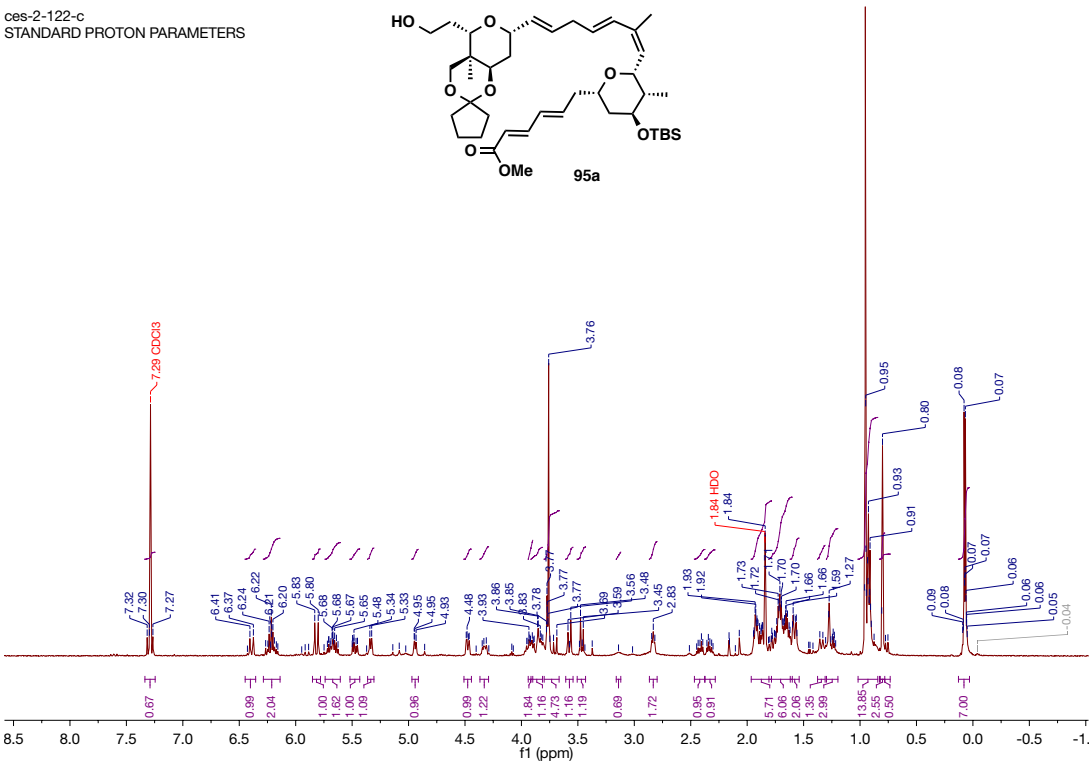
^{1}H NMR (500 MHz, $CDCl_3$)



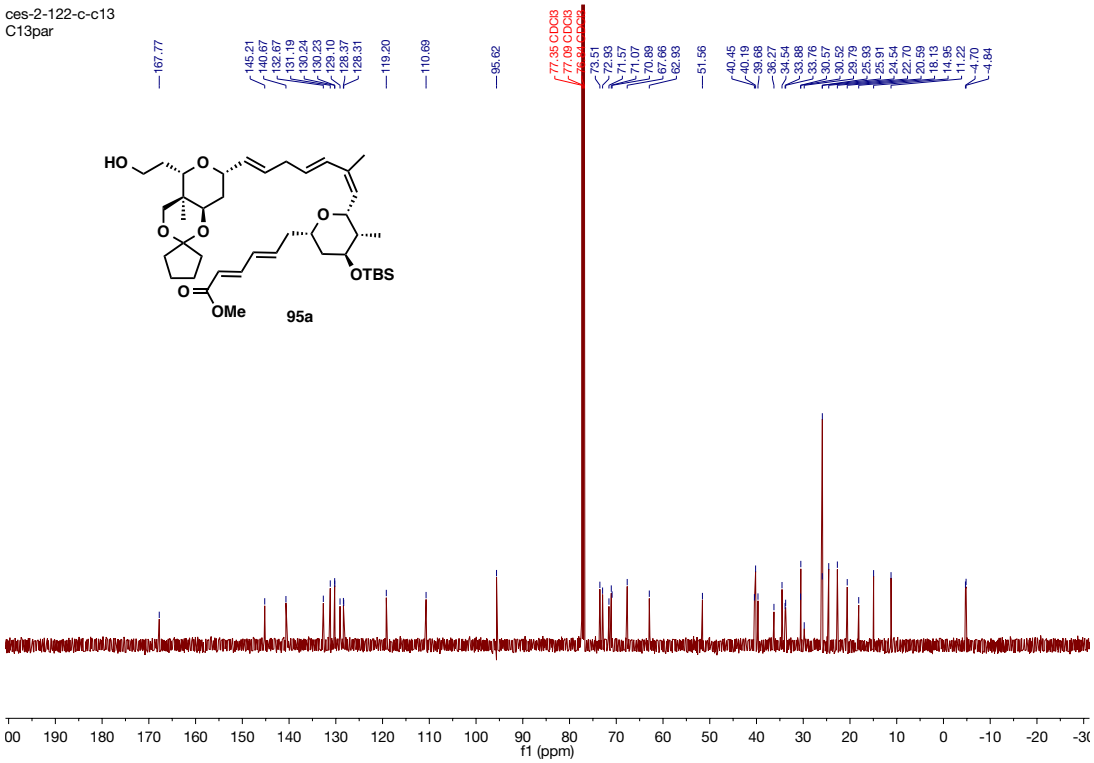
^{13}C NMR (125 MHz, $CDCl_3$)



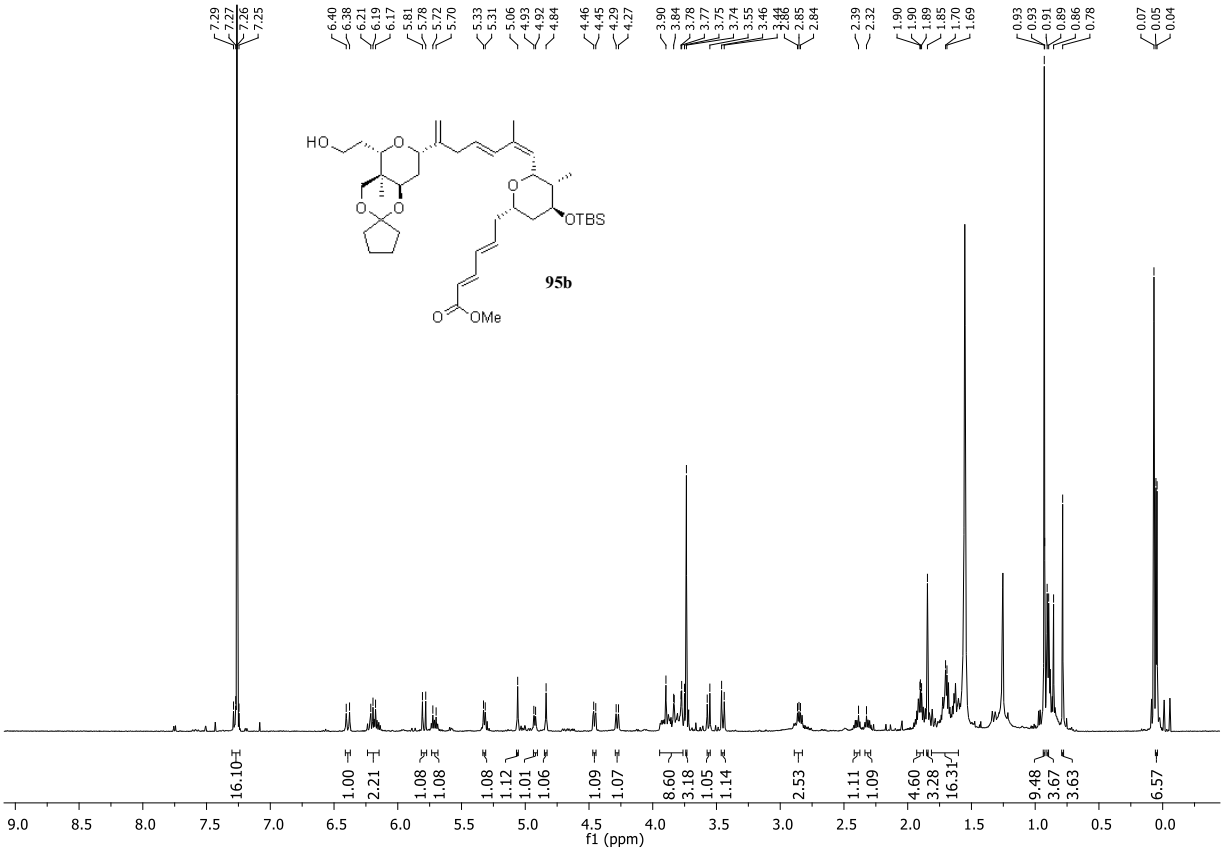
^{1}H NMR (600 MHz, $CDCl_3$)



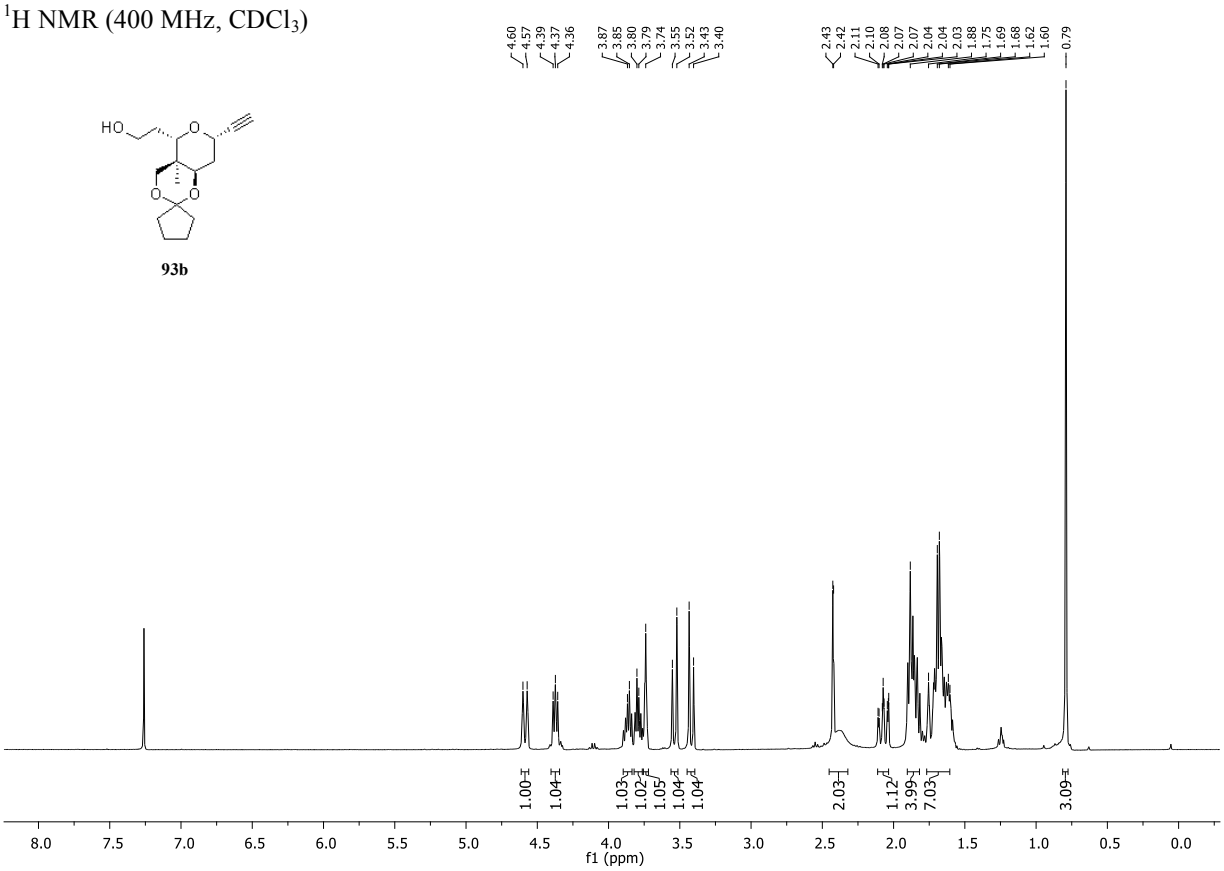
^{13}C NMR (125 MHz, $CDCl_3$)



^{1}H NMR (600 MHz, $CDCl_3$)

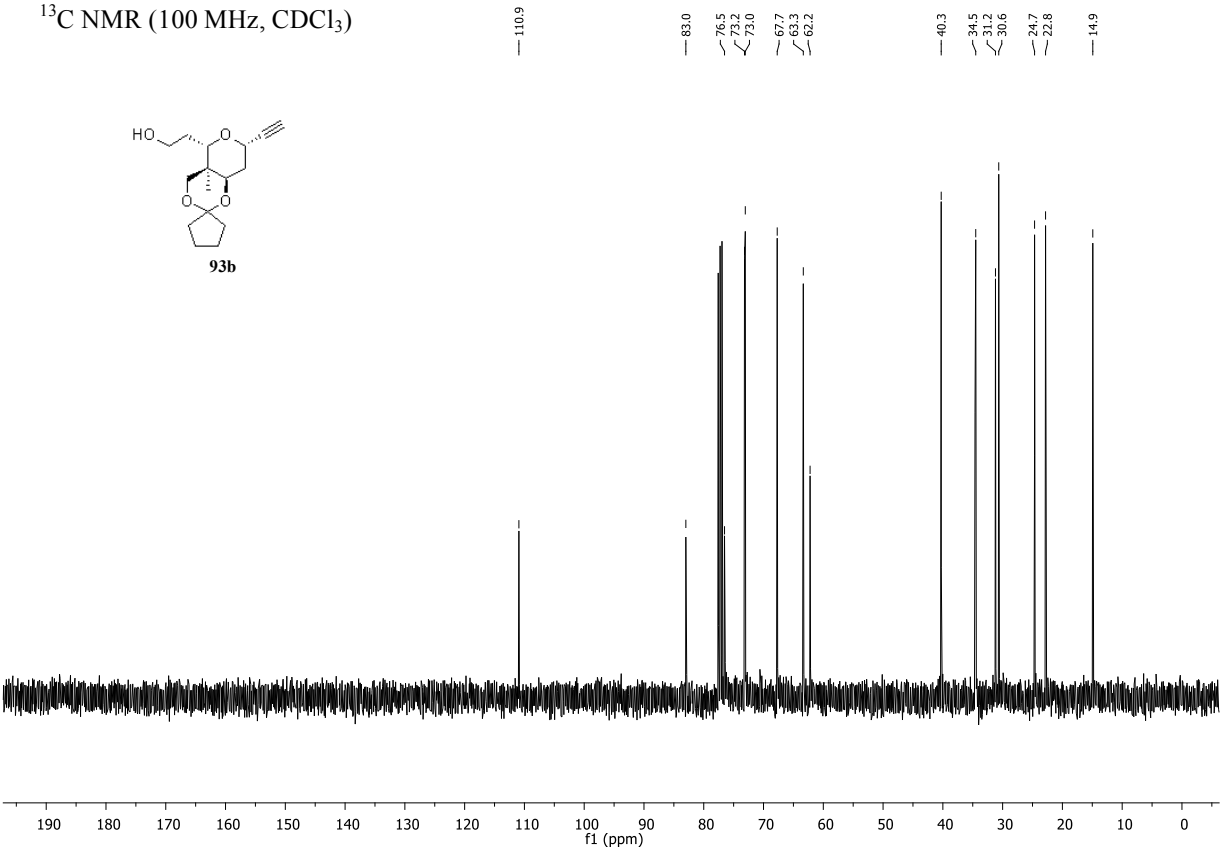


^{1}H NMR (400 MHz, $CDCl_3$)



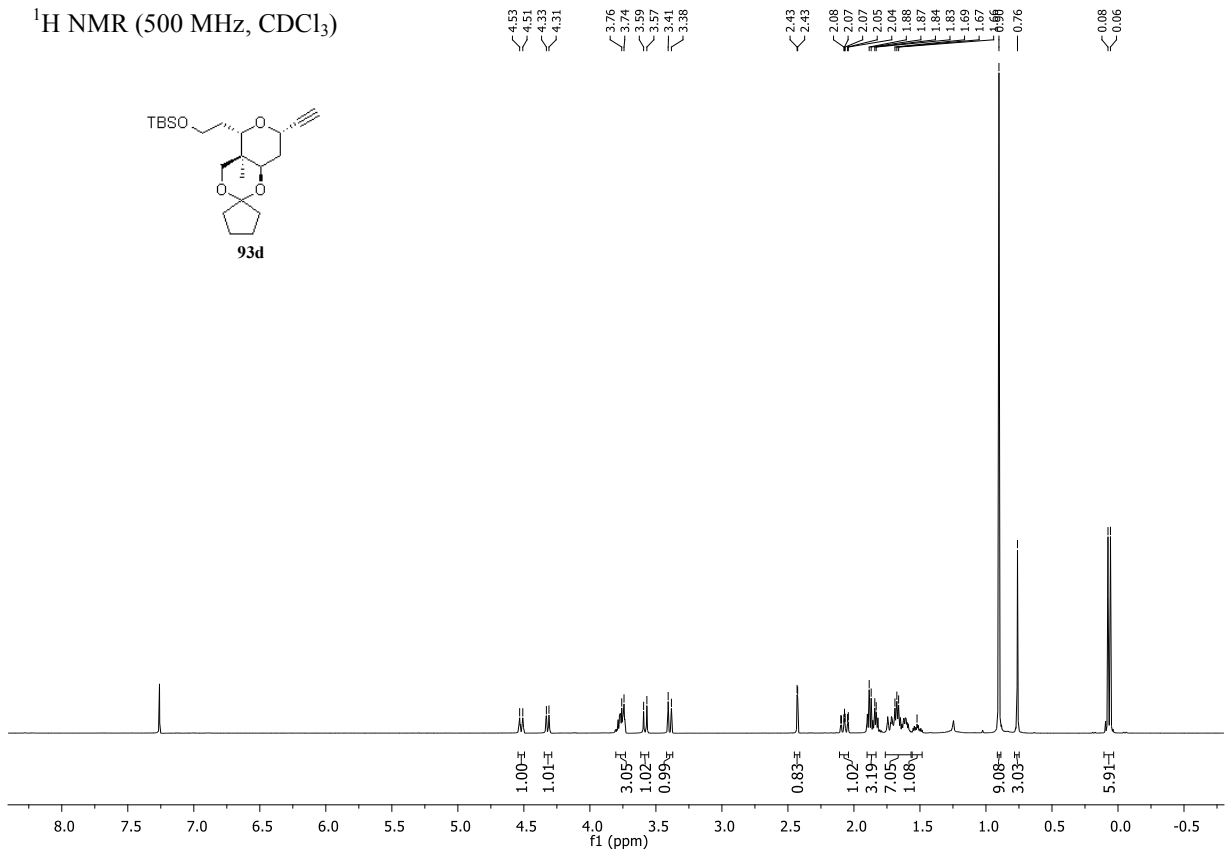
93b

^{13}C NMR (100 MHz, $CDCl_3$)

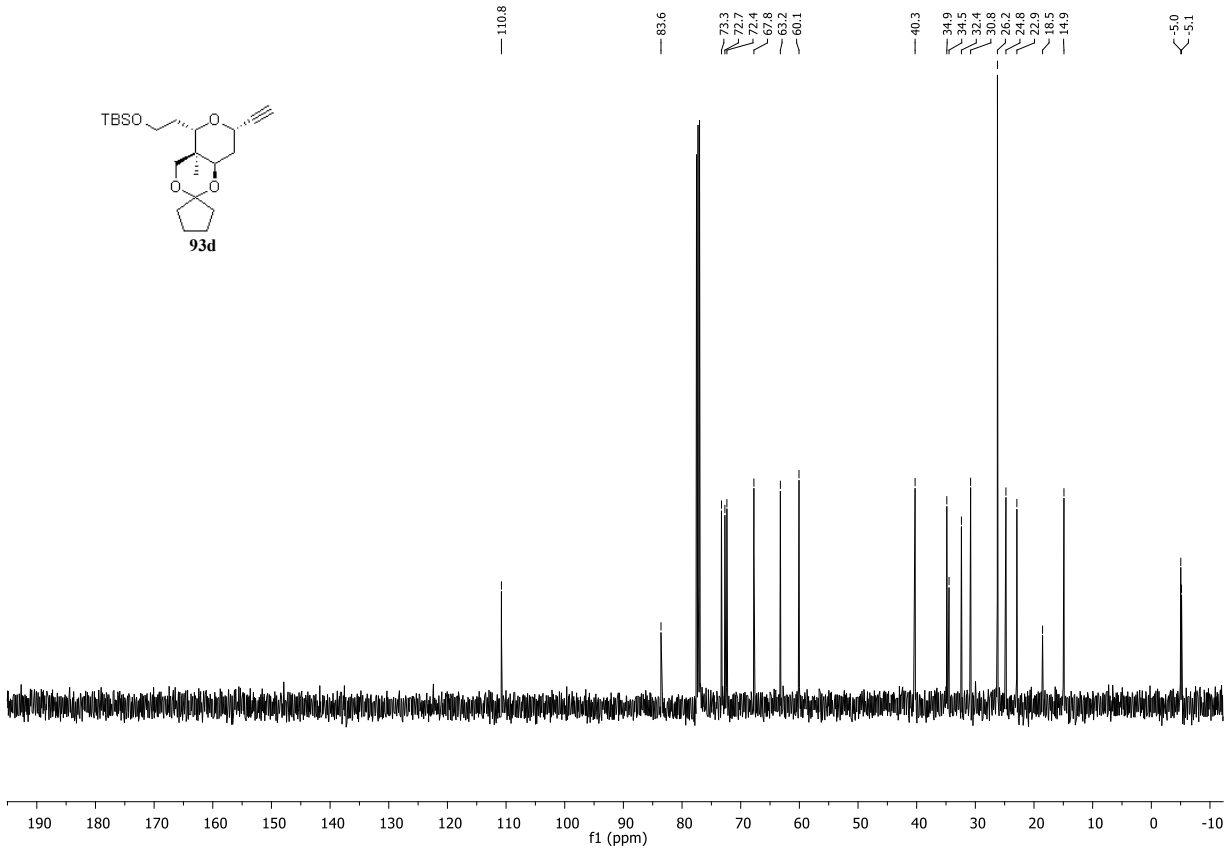


93b

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

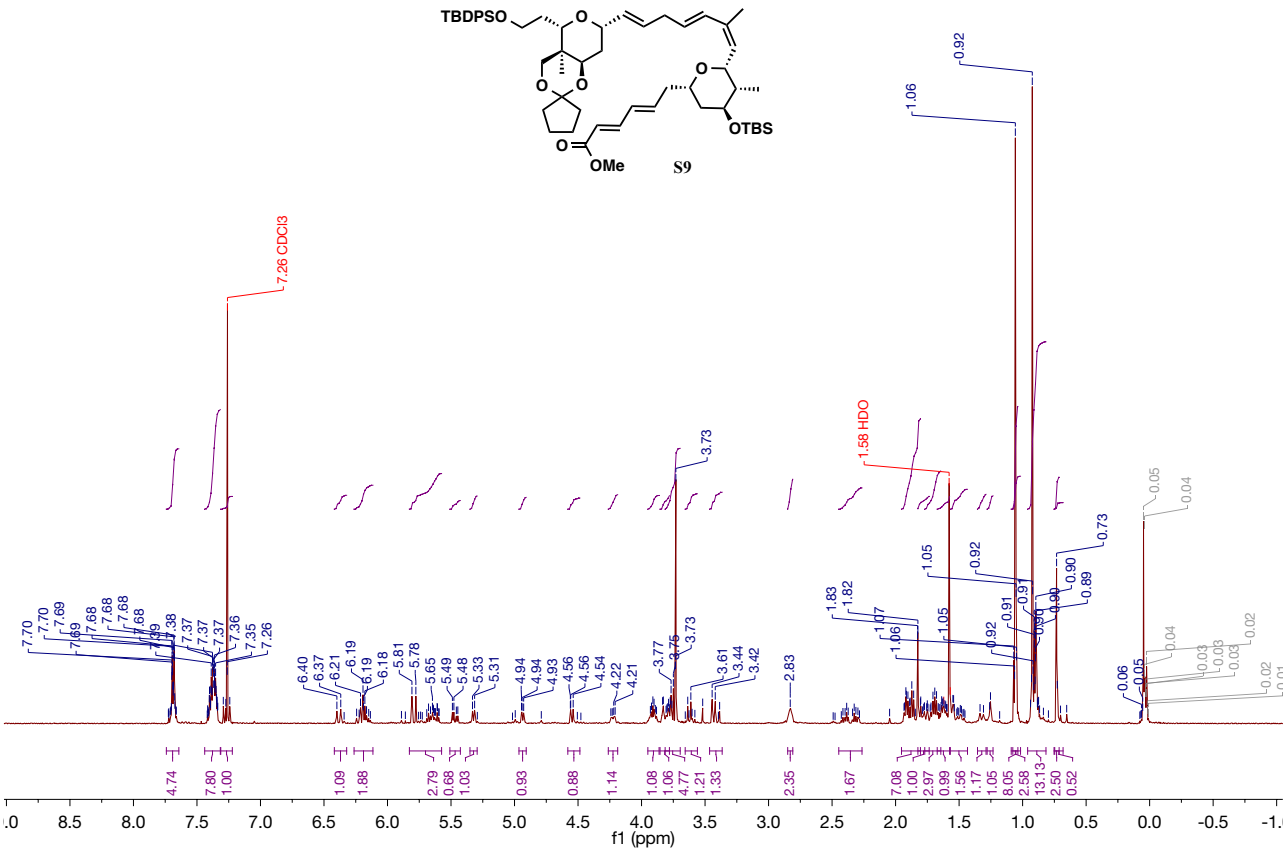


^{13}C NMR (125 MHz, $CDCl_3$)

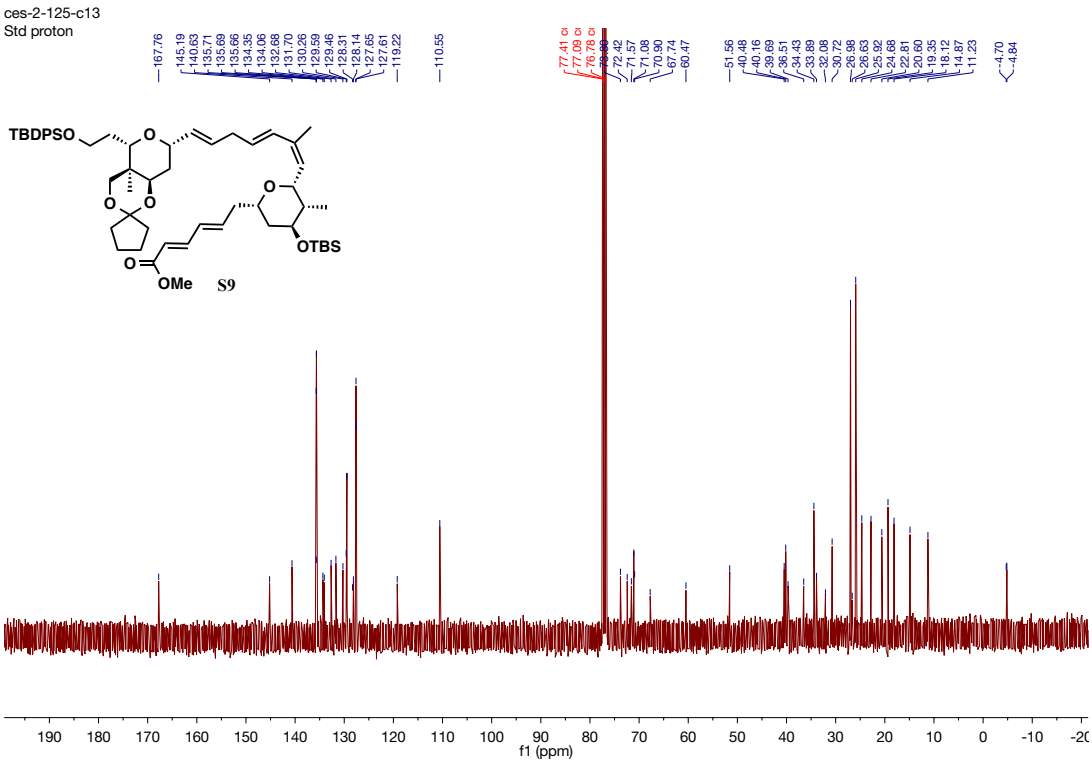


ces-2-125
STANDARD PROTON PARAMETERS

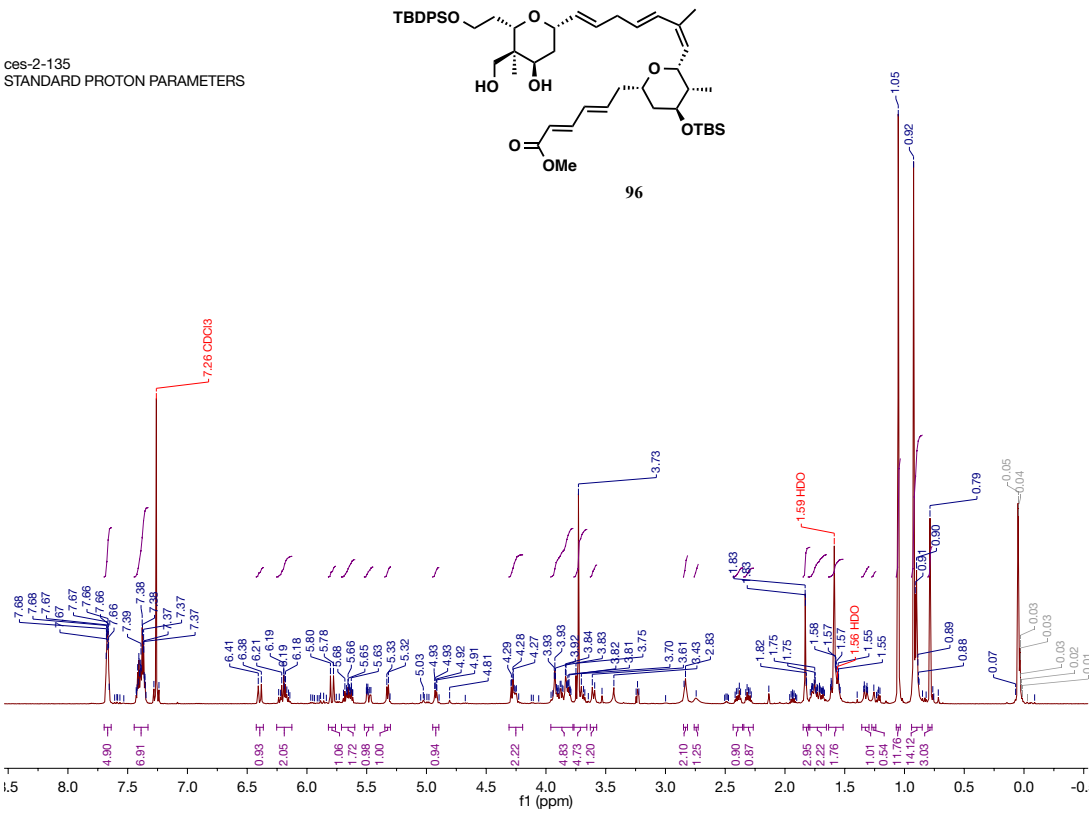
^{1}H NMR (500 MHz, $CDCl_3$)



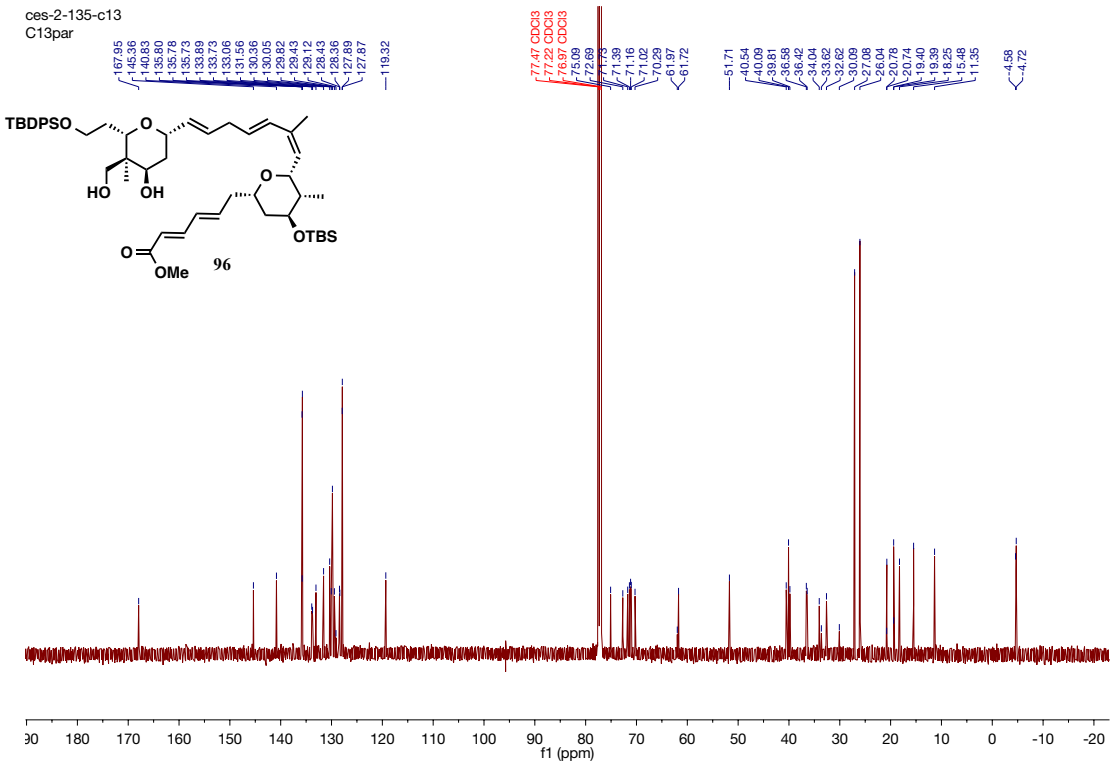
^{13}C NMR (100 MHz, $CDCl_3$)



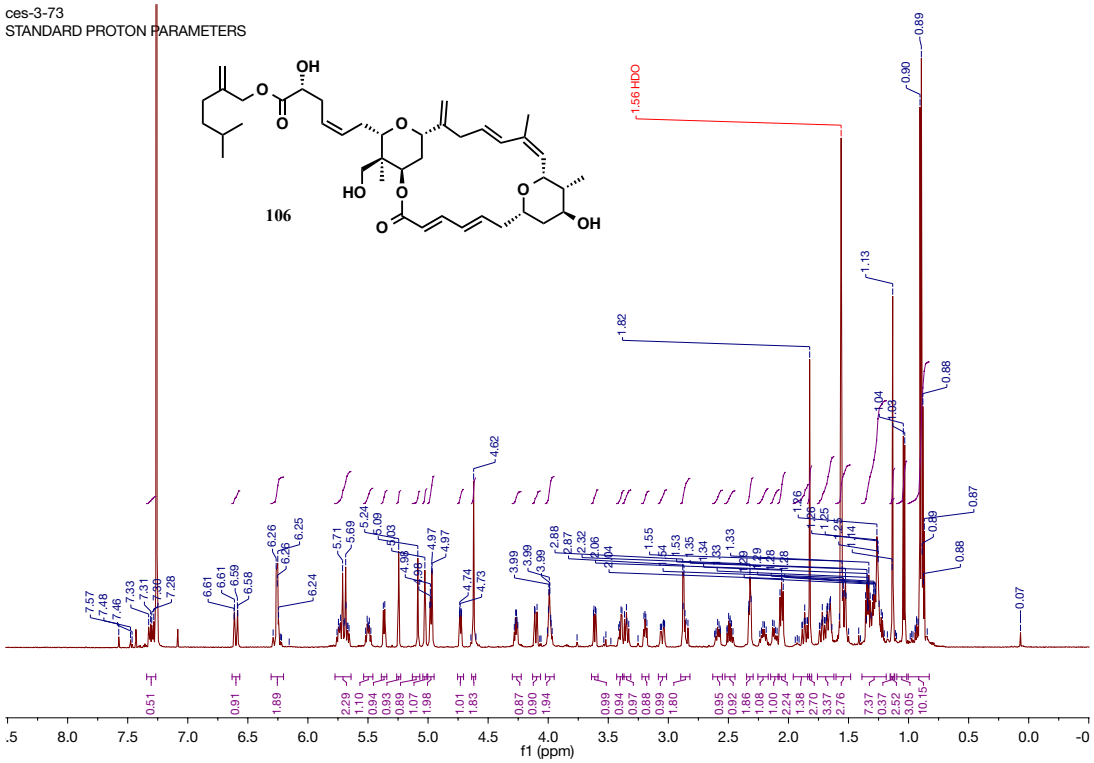
^{1}H NMR (500 MHz, $CDCl_3$)



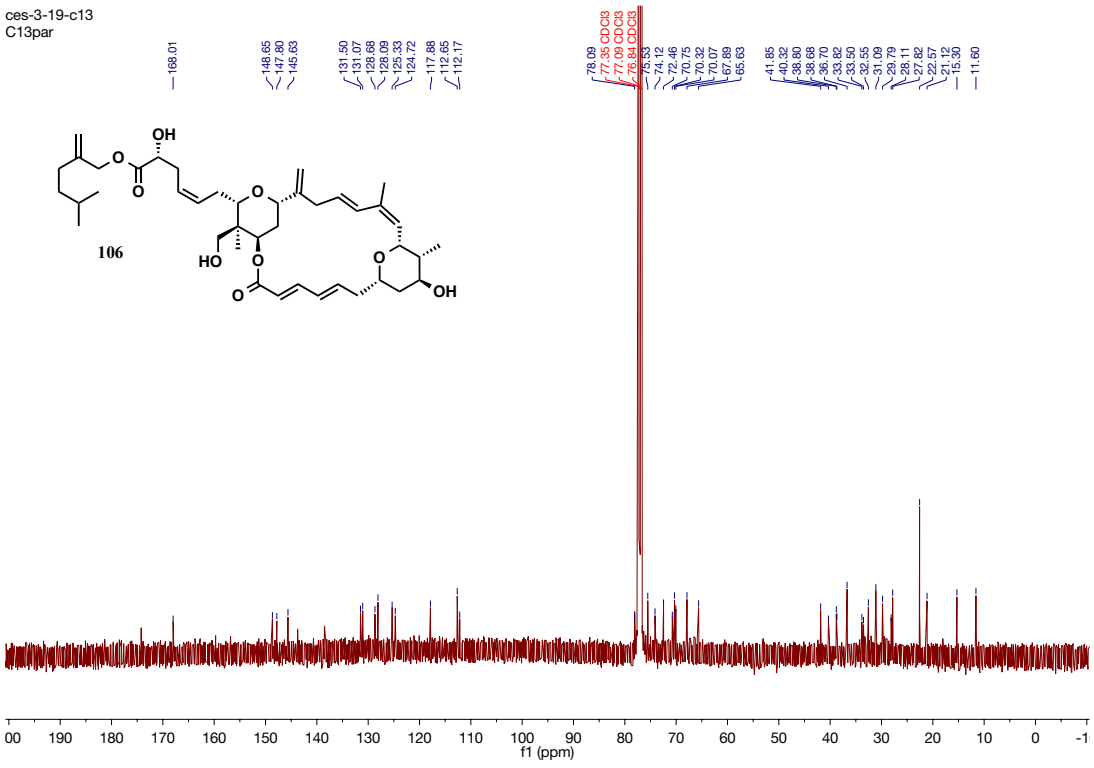
^{13}C NMR (100 MHz, $CDCl_3$)



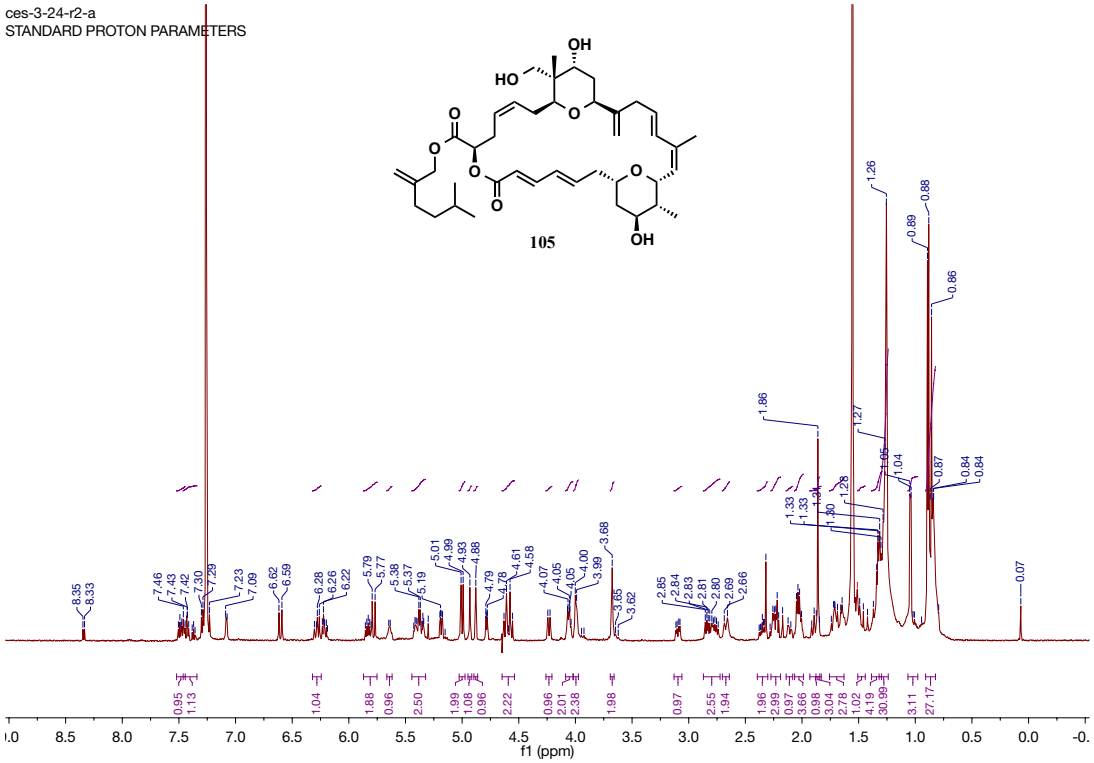
^{1}H NMR (600 MHz, $CDCl_3$)



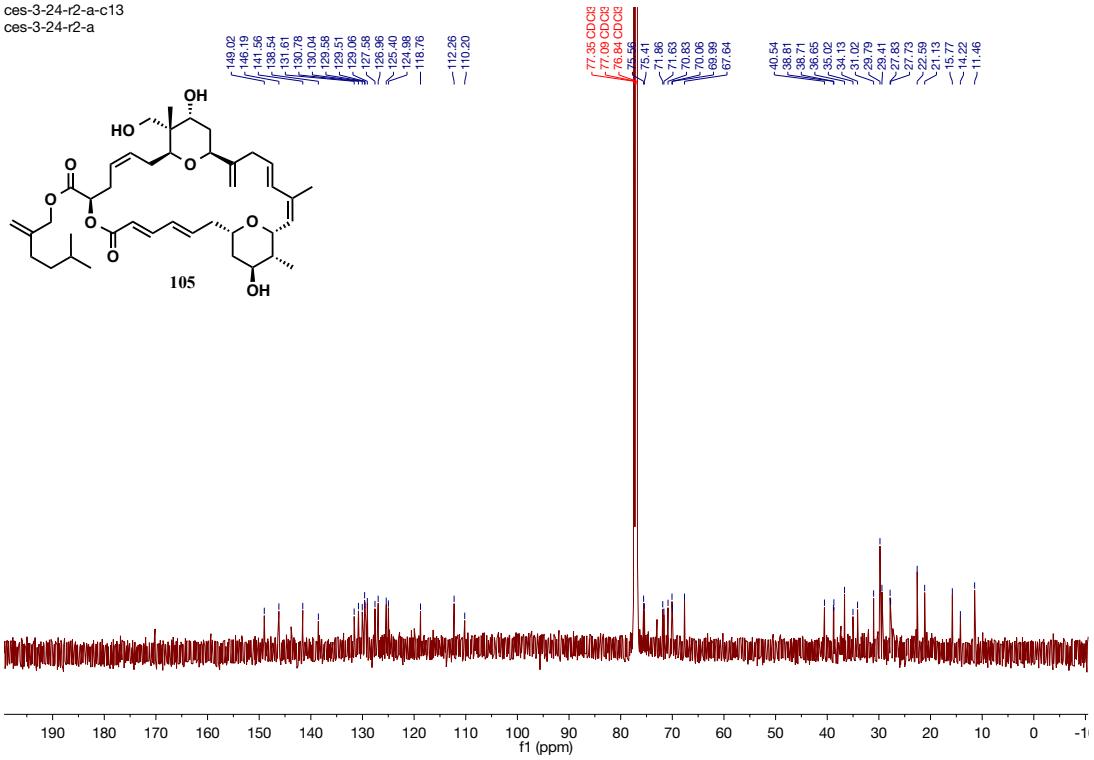
^{13}C NMR (125 MHz, $CDCl_3$)



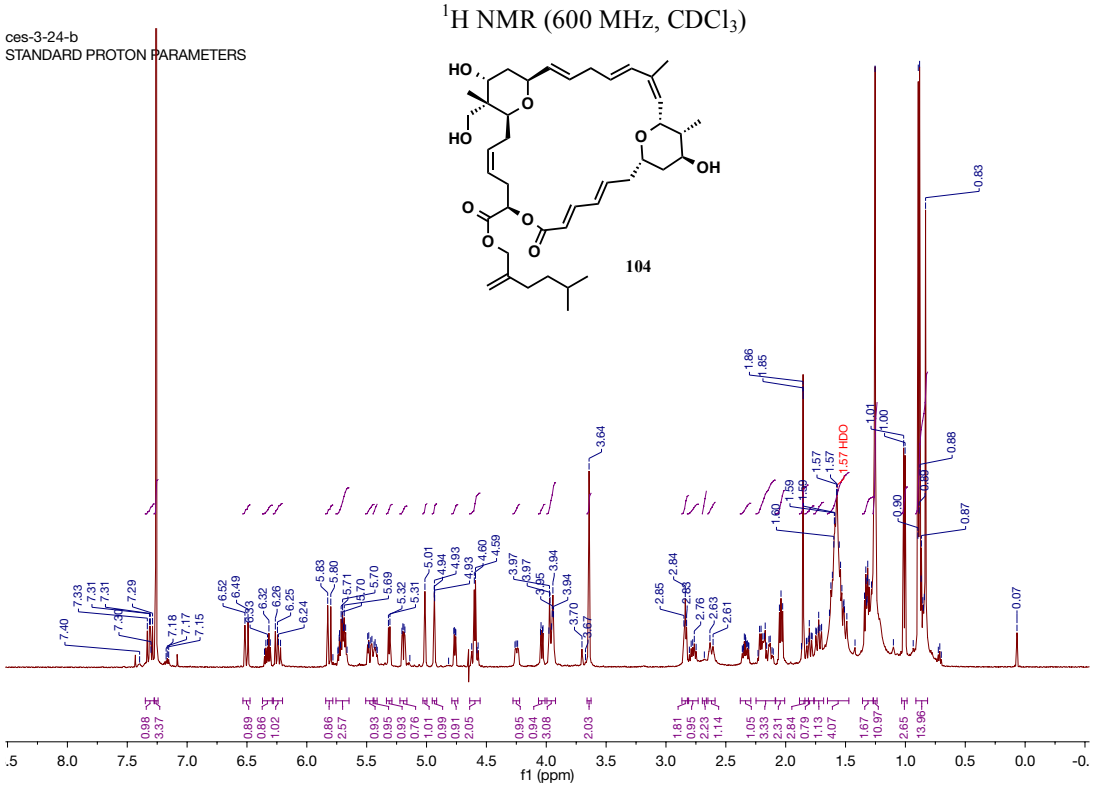
^{1}H NMR (600 MHz, $CDCl_3$)



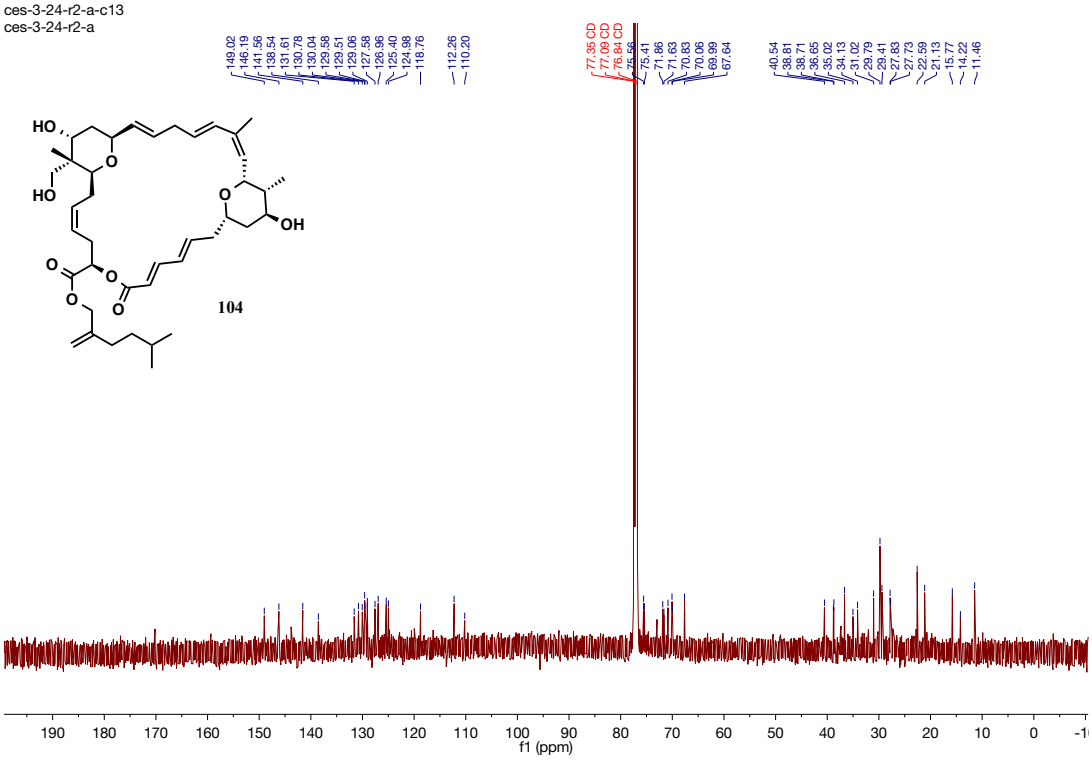
^{13}C NMR (125 MHz, $CDCl_3$)



^{1}H NMR (600 MHz, $CDCl_3$)



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



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