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Supporting Information

An Efficient and Scalable "Second Generation" Total Synthesis of the Marine Polyketide Limaol Endowed with Antiparasitic Activity

Stephan N. Hess and Alois Fürstner*

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Stephan N. Hess, and Alois Fürstner*

Max-Planck-Institut für Kohlenforschung, D-45470 Mülheim/Ruhr, Germany

fuerstner@kofo.mpg.de

Table of Content

General	S2
Substrates	S3
Conformational Aspects	S3
Intelligence Gathering and Route Scouting	S5
Dissecting the Spiroketalization	S12
Improved Preparation of the Northern Sector	S19
Revised Spirotricyclic Core	S24
Improved Fragment Coupling	S28
Completion of the "Second Generation" Total Synthesis of Limaol	S41
Copies of Spectra of New Compounds	S51
References	S83

General. All reactions were carried out under argon in glassware that was flame-dried under vacuum. The solvents were purified by distillation over the indicated drying agents and were transferred under Ar: THF, Et_2O (Mg/anthracene); hexanes, pentane, toluene (Na/K); NEt_3, diisopropylamine, diisopropylethylamine, 2,6-lutidine, pyridine, *tert*-butyl methyl ether, CH_2Cl_2, NMP, DMPU (CaH_2); MeOH (Mg, stored over 3Å MS); DMF, 1,4-dioxane, and CH_3CN were dried by an adsorption solvent purification system based on molecular sieves.

Thin layer chromatography (TLC): Macherey-Nagel precoated plates (POLYGRAM®SIL/UV254); Flash chromatography: Merck silica gel 60 (40-63 µm or 15-40 µm (referred to as "fine silica")) with pre-distilled or HPLC grade solvents.

NMR: Spectra were recorded on a Bruker AV 400 or Bruker AVIII 600 or AV600neo spectrometer in the solvents indicated; chemical shifts (δ) are given in ppm relative to TMS, coupling constants (*J*) in Hz. The solvent signals were used as references and the chemical shifts converted to the TMS scale ($CDCl_3$ at 7.26 and 77.16 ppm for ^1H and ^{13}C NMR spectroscopy, respectively; CD_2Cl_2 at 5.32 ppm and 53.84 ppm for ^1H and ^{13}C NMR spectroscopy, respectively; C_6D_6 at 7.16 ppm and 128.06 ppm for ^1H and ^{13}C NMR spectroscopy, respectively; CD_3OD at 4.87 and 3.31 ppm for ^1H NMR and 49.00 ppm for ^{13}C NMR spectroscopy, respectively). ^1H NMR data are reported as δ (ppm) (s = singlet, d = doublet, t = triplet, q = quartet, qui = quintet, m = multiplet or unresolved, br = broad signal, app = appearing as; coupling constant (*J*) in Hz; integration). ^{13}C NMR spectra were recorded with broadband ^1H decoupling. ^{119}Sn NMR spectra were recorded using Me_4Sn as external standard.

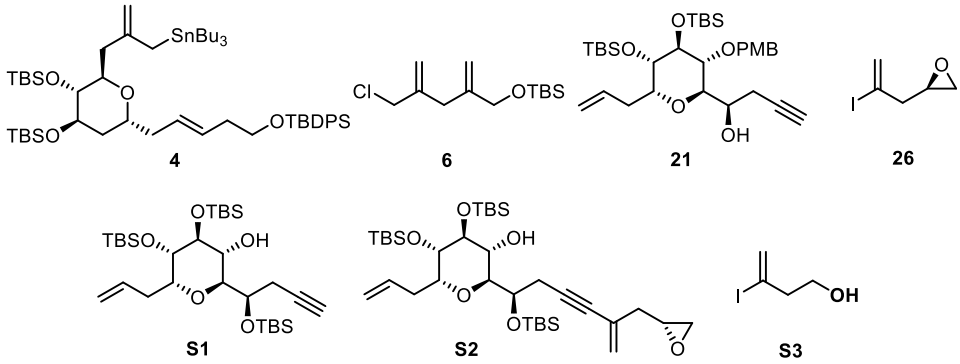
IR: Spectrum One (Perkin-Elmer) spectrometer, wavenumbers ($\tilde{\nu}$) in cm^{-1}.

MS (EI): Finnigan MAT 8200 (70 eV), ESIMS: ESQ 3000 (Bruker), accurate mass determinations: Bruker APEX III FT-MS (7 T magnet) or MAT 95 (Finnigan).

Substrates

Unless stated otherwise, all commercially available compounds (ABCR, Acros, Aldrich, Apollo Scientific, Strem, TCI) were used as received. $CuBr{\cdot}SMe_2$ was recrystallized from dimethylsulfide and stored under Argon.

The following compounds were prepared as described in the cited literature: **4**, **6**, **21**, **26**, **S1**, **S2**;[1] **S3**[2]



Conformational Aspects

The conformers of 2,4-dimethyl-1,4-pentadiene (**A**) were computed using ωB97X-D3 as functional and the

A

DEF2-TZVP basis-set and DEF2/J as auxiliary basis-set.[3,4,5] In the lowest-lying conformer (Figure S1), the two olefins are oriented in a "transoid" manner with a torsional angle of 171.7°; the planes spanned by the olefins are tilted against each other by 85.1°. The second lowest conformer is 0.853 $kcal{\cdot}mol^{-1}$ higher in energy (Figure S2); the olefins are also strongly twisted (torsional angle of 71.1°) and tilted (82.4°), such that the π-cloud are again positioned almost orthogonally to each other.

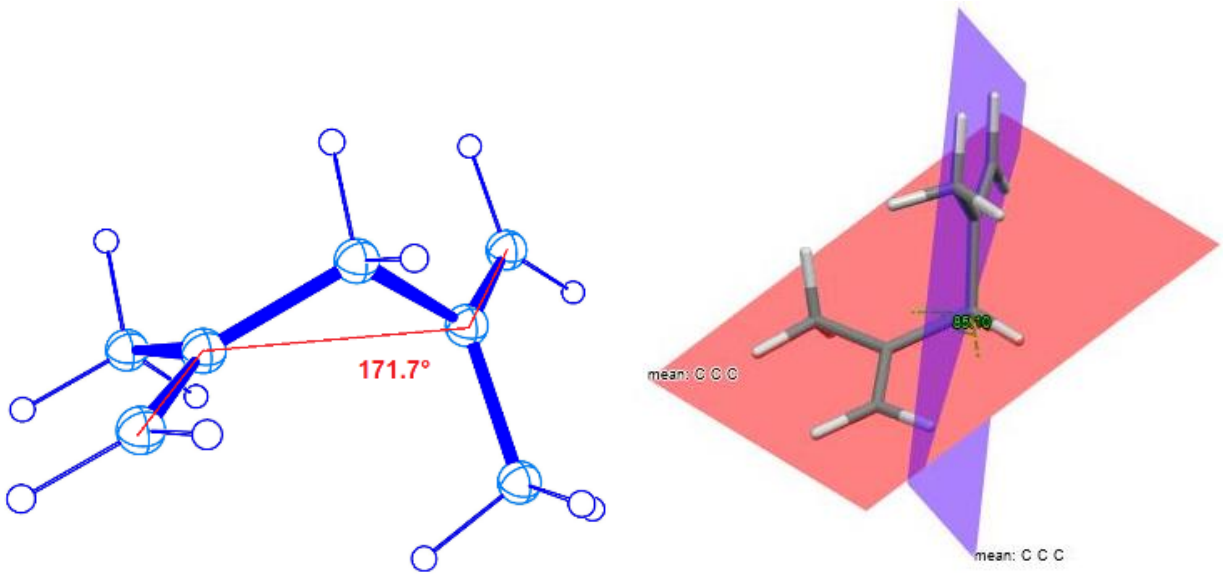


Figure S1. Computed structure of the lowest-energy conformer of **A**, in which the olefins are oriented in a transoid manner (torsional angle 171.7°) and the planes spanned by the olefins are tilted by 85.1°.

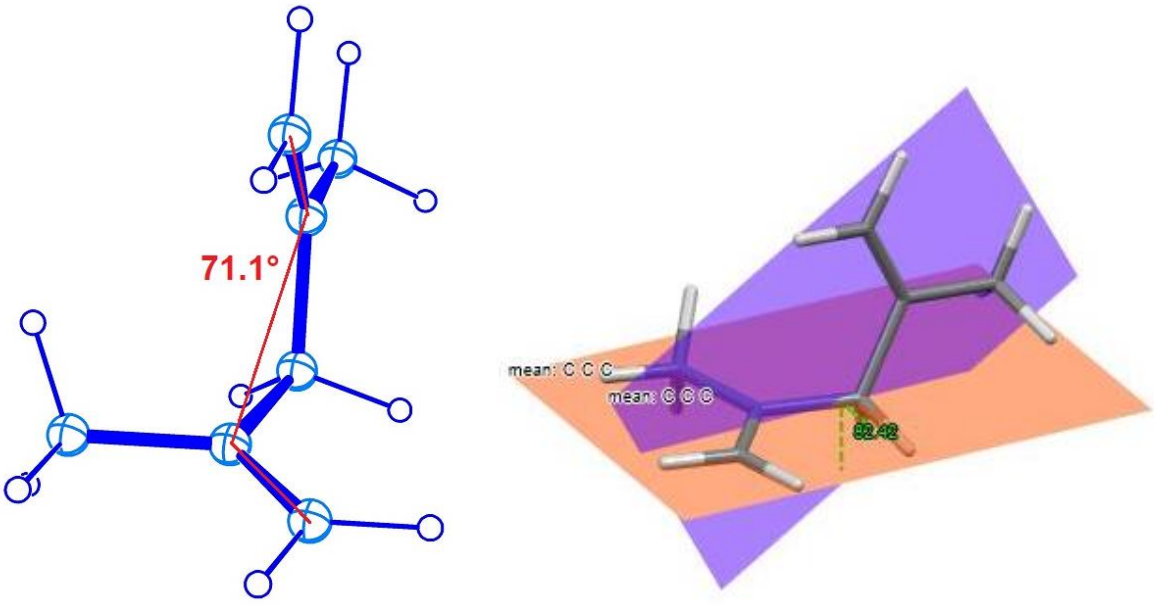
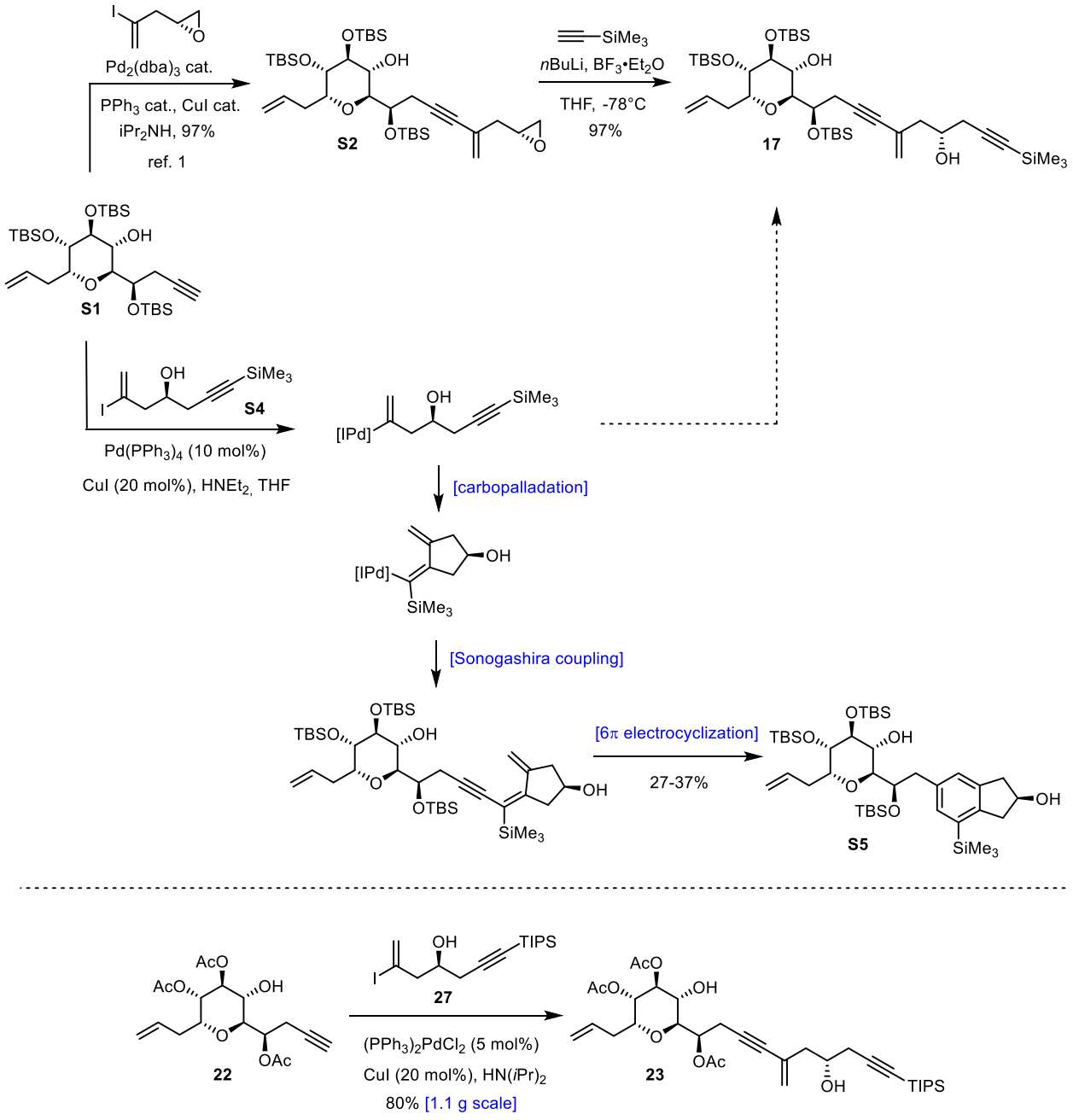


Figure S2. Second-lowest energy conformer of **A**, in which the olefins are twisted (torsional angle 71.1°) and the planes spanned by the olefins are tilted by 82.4°.

Intelligence Gathering and Route Scouting



Scheme S1. Route scouting during the preparation of the model compound **17**.

The attempted Sonogashira coupling of alkyne **S1** with alkenyl iodide **S4** bearing a TMS-capped alkyne entity resulted in the formation of the benzene derivative **S5**, which is best explained by fast carbopalladation of the alkenylpalladium species primarily formed followed by cross coupling and 6π electrocyclization. Therefore, the analogous TIPS-protected building block **27** was used for the preparation

of the actual substrate **23** used for the "second generation" synthesis of limaol as the bulky silyl group was expected to prevent the carbopalladation from occurring; this modification proved successful (see below).

Compound S5. Copper iodide (2.47 mg, 0.013 mmol), tetrakis(triphenylphosphine)palladium (7.51 mg, 0.0065 mmol) and diethylamine (0.2 mL) were added to a stirred solution of alkyne **S1** (38 mg, 0.065 mmol) and alkenyl iodide **S4** (24 mg, 0.078 mmol) in THF (1.5 mL). The resulting mixture was stirred for 1 h at ambient temperature before saturated aq. NH_4Cl (2 mL) was added. The aqueous phase was extracted with *tert*-butyl methyl ether (3 × 3 mL) and the combined organic layers were dried over $MgSO_4$, filtered and evaporated. Purification of the residue by flash chromatography (hexane/EtOAc 7:1) afforded the title compound as a colorless syrup (13.5 mg, 27%). $[\alpha]_D^{20}$ = +28.3 (c = 1.35, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 600 MHz): δ 7.17(s, 1H) 7.13 (s, 1H), 5.66 (m, 1H), 5.00 (m, 1H), 4.67 (dp, *J* = 3.5, 6.0, 6.0, 3.6 Hz, 1H) , 4.33 (m, 1H), 3.80 (t, *J* = 6.0 Hz, 1H), 3.76 (td, *J* = 7.0, 3.2, 7.0 Hz, 1H), 3.64 (q, *J* = 6.2 Hz, 1H), 3.59 (t, *J* = 6.2 Hz, 1H), 3.54 (dd, *J* = 3.2, 6.0 Hz, 1H), 3.22 (dd, *J* = 6.0,16.0 Hz, 1H), 3.14 (dd, *J* = 3.5, 16.1 Hz, 2H), 3.01 (dd, *J* = 4.5, 14.3 Hz, 1H), 2.94 (dd, *J* = 3.6, 16.0 Hz, 1H), 2.83 (dd, *J* = 3.5, 16.1 Hz, 1H), 2.75 (dd, *J* = 7.4, 14.3 Hz, 1H), 2.21 (t, *J* = 7.0, 7.0 Hz, 3H), 0.92 (s, 9H), 0.92 (s, 9H), 0.81 (s, 9H), 0.27 (s, 9H), 0.14 (s, 6H), 0.11 (s, 3H), 0.08 (s, 3H), -0.00 (s, 3H), -0.31 (s, 3H). ^{13}C NMR ($CDCl_3$, 151 MHz): δ 143.54, 139.83, 136.84, 135.53, 135.03, 134.06, 127.27, 116.82, 78.44, 74.60, 73.34, 73.21, 72.71, 72.31, 71.13, 43.41, 42.16, 41.33, 32.32, 26.11, 26.01, 25.95, 18.17, 18.11, 18.09, -0.73, -3.82, -3.93, -4.06, -4.18, -4.47, -4.62. IR (Film, cm^{-1}): 3522, 2953, 2929, 2857, 1472, 1403, 1361, 1250, 1091, 1005, 836, 777, 679. HRMS (EI) *m/z* calcd. for $C_{40}H_{76}O_6Si_4Na$ [M^+]: 787.4614; found 787.4611.

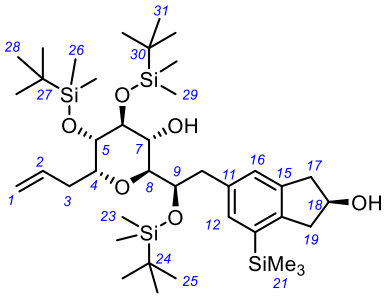


Table S1. Analysis of relevant NMR data of compound **S5**; arbitrary numbering scheme as shown in the insert.

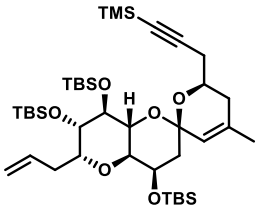
atom number	**^{1}H NMR** ($CDCl_3$, 600 MHz)			**^{13}C NMR** ($CDCl_3$, 150 MHz)	
	δ [ppm]	***J*** [Hz]	**COSY**	δ [ppm]	**HMBC**
1	4.99		2	116.8	3
2	5.66	7.0	1, 3	135.0	1, 3, 4
3	2.21	7.0, 7.0	2, 4	32.3	1, 2, 4, 5
4	3.76	7.0, 3.2, 7.0	3, 5	72.7	2, 3, 6, 8

atom number	**^{1}H NMR** ($CDCl_3$, 600 MHz)			**^{13}C NMR** ($CDCl_3$, 150 MHz)	
	δ [ppm]	***J*** [Hz]	**COSY**	δ [ppm]	**HMBC**
5	3.54	6.0, 3.2	4, 6	72.3	3, 6, 7
6	3.80	6.0	5, 7	73.2	4, 5, 7, 8, 22
7	3.64	6.2	6, 8	71.1	5, 6, 8, 22
8	3.59	6.2, 6.2	7, 9	78.4	4, 6, 10
9	4.33	6.2, 4.5, 7.4	8, 10	74.6	7. 8, 10
10	3.01	4.5, 14.3	9, 10’	41.3	8, 12, 16
	2.75	7.4, 14.3	9, 10		
11	--	--	--	136.9	9, 10
12	7.17			134.1	10
13	--	--	--	135.5	12, 19’,21
14	--	--	--	143.6	12, 16, 17, 19
15	--	--	--	139.8	17, 19
16	7.13			127.3	10, 17’
17	3.14	16.1, 3.5	17’, 18	42.2	16, 19
	2.83	16.1, 6.0	17, 18		
18	4.67	3.5, 3.6, 6.0, 6.0	17, 19	73.3	17, 19
19	3.22	16.0, 6.0	18, 19’	43.4	17
	2.94	16.0, 3.6	18, 19		

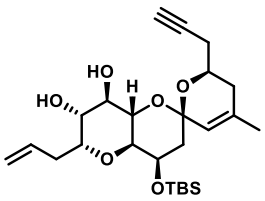
Compound 17. *n*-Butyllithium (1.6 M in hexanes, 2.2 mL, 3.5 mmol) was added dropwise to a stirred solution of trimethylsilylacetylene (0.53 mL, 3.8 mmol) in anhydrous THF (25 mL) at −78 °C. The resulting solution was stirred at this temperature for 20 min. Boron trifluoride etherate (0.43 mL, 3.5 mmol) was slowly added at −78 °C. After stirring at −78 °C for 5 min, a solution of epoxide **S2** (1.1 g, 1.6 mmol) in THF (2.0 mL, 2 × 1.5 mL wash) was added *via* cannula at −78 °C. After 1 h of stirring at this temperature, the reaction was quenched with brine (30 mL). The aqueous phase was extracted with *tert*-butyl methyl ether (3 × 20 mL) and the combined organic layers were dried over anhydrous Na_2SO_4, filtered, and concentrated. The residue was purified by flash chromatography (hexanes/EtOAc 20:1) to give the title compound as a colorless oil (1.2 g, 97%). $[\alpha]_D^{20}$ = +28.9 (c = 1.16, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 5.84 (ddt, *J* = 17.1, 10.1, 6.9 Hz, 1H), 5.36 (d, *J* = 2.0 Hz, 1H), 5.31 – 5.23 (m, 1H), 5.14 (dd, *J* = 17.2, 1.7 Hz, 1H), 5.13 – 5.05 (m, 1H), 4.13 (dt, *J* = 8.4, 4.4 Hz, 1H), 4.02 (d, *J* = 8.1 Hz, 1H), 3.84 – 3.75 (m, 2H), 3.70 – 3.51 (m, 3H), 3.41 (d, *J* = 5.8 Hz, 1H), 2.65 (dd, *J* = 17.3, 4.2 Hz, 1H), 2.57 (dd, *J* = 17.3, 4.6 Hz, 1H), 2.54 – 2.37 (m, 4H), 2.34 (ddd, *J* = 13.7, 7.6, 0.9 Hz, 1H), 2.31 –

2.20 (m, 2H), 0.92 (s, 9H), 0.90 (s, 9H), 0.90 (s, 9H), 0.16 (s, 12H), 0.13 (s, 9H), 0.10 (s, 3H), 0.09 (s, 3H); ^{13}C NMR ($CDCl_3$, 101 MHz): δ 135.1, 128.1, 123.3, 117.3, 103.1, 88.1, 87.7, 82.4, 76.3, 73.4, 73.2, 72.7, 72.6, 72.0, 68.3, 44.3, 32.5, 28.0, 26.3, 26.2, 25.9, 25.5, 18.4, 18.3, 18.2, 0.3, –3.7, –3.9, –3.9, –3.9, –4.2, –4.4; IR (film, cm^{-1}): 3518, 2954, 2930, 2897, 2858, 2177, 1472, 1251, 1125, 1096, 1029, 1005, 913, 837, 777, 681; HRMS (ESI) for $C_{40}H_{76}O_6Si_4Na$ $[M+Na]^{+:}$ calcd. 787.4611; found 787.4620.

Compound 18. (Acetonitrile)[(2-biphenyl)di-*tert*-butylphosphine]gold(I) hexafluoro-antimonate (**10**, 77 mg, 0.10 mmol)[6] and pyridinium *p*-toluenesulfonate (25 mg, 0.10 mmol) were added to a solution of enyne **17** (0.96 g, 1.2 mmol) in CH_2Cl_2 (12 mL). The mixture was stirred at room temperature for 1.5 h before the reaction was quenched with triethylamine (1.0 mL). Saturated aqueous NH_4Cl (20 mL) and *tert*-butyl methyl ether (30 mL) were introduced and the aqueous phase was extracted with *tert*-butyl methyl ether (3 × 10 mL). The combined organic fractions were washed with brine (20 mL), dried over anhydrous Na_2SO_4, filtered and concentrated. The residue was purified by flash chromatography (hexanes/*tert*-butyl methyl ether 80:1) to give the title compound as a pale yellow oil (0.71 g, 74%). $[\alpha]_D^{20}$ = +26.9 (c = 1.00, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 5.80 (ddt, *J* = 16.9, 10.2, 6.7 Hz, 1H), 5.18 (s, 1H), 5.09 (dd, *J* = 17.2, 1.9 Hz, 1H), 5.03 (dd, *J* = 10.2, 2.0 Hz, 1H), 4.12 (tdd, *J* = 8.8, 6.8, 4.2 Hz, 1H), 3.99 (q, *J* = 3.0 Hz, 1H), 3.92 – 3.78 (m, 2H), 3.68 – 3.55 (m, 2H), 3.29 (dd, *J* = 10.1, 2.8 Hz, 1H), 2.59 (dd, *J* = 16.6, 4.9 Hz, 1H), 2.47 – 2.39 (m, 2H), 2.30 (dd, *J* = 16.6, 9.0 Hz, 1H), 1.98 (dd, *J* = 17.2, 4.0 Hz, 1H), 1.93 – 1.88 (m, 1H), 1.84 (dd, *J* = 14.2, 3.0 Hz, 1H), 1.71 (s, 3H), 1.67 (dd, *J* = 14.3, 3.3 Hz, 1H), 0.91 (s, 9H), 0.91 (s, 9H), 0.87 (s, 9H), 0.15 (s, 9H), 0.12 (s, 3H), 0.08 (s, 3H), 0.05 (s, 6H), 0.01 (s, 3H), −0.01 (s, 3H); ^{13}C NMR ($CDCl_3$, 101 MHz): δ 135.7, 124.4, 116.2, 103.8, 95.4, 86.1, 76.3, 74.2, 73.2, 70.3, 68.7, 66.7, 65.7, 42.3, 34.3, 29.6, 27.1, 26.6, 26.4, 26.0, 22.9, 18.5, 18.4, 18.3, 0.3, −3.4, −3.6, −4.2, −4.2, −5.2; IR (film, cm^{-1}): 2955, 2928, 2887, 2856, 2183, 1473, 1463, 1383, 1361, 1250, 1204, 1130, 1091, 1037, 1005, 968, 912, 858, 837, 775, 674; HRMS (ESI) for $C_{40}H_{76}O_6Si_4Na$ $[M+Na]^{+:}$ calcd. 787.4611; found 787.4624.



Compound 19. A solution of TBAF (1 M in THF, 1 mL, 1.0 mmol) was added to a solution of compound **18** (76.5 mg, 0.1 mmol) in THF (1 mL) at 0 °C. The ice bath was removed and the mixture stirred at ambient temperature for 14 h. The reaction was quenched with aq. saturated NH_4Cl (2 mL), the aqueous phase was extracted with EtOAc (3 × 2 mL), the combined organic layers were dried over sodium sulfate and evaporated, and the residue was purified by flash chromatography (hexanes/EtOAc 3:2) to give the title compound as a colorless syrup (42.9 mg, 96%). ^{1}H NMR (600 MHz, $CDCl_3$): δ 5.83 (ddt, *J* = 17.0, 10.2, 6.7



Hz, 1H), 5.25 (h, *J* = 1.6 Hz, 1H), 5.12 (dq, *J* = 17.1, 1.6 Hz, 1H), 5.06 (ddt, *J* = 10.2, 2.0 Hz, 1H), 4.09 (m, 1H), 4.06 (m, 2H), 4.03 (q, *J* = 3.0 Hz, 1H), 3.76 (dd, *J* = 9.5, 5.8 Hz, 1H), 3.71 (t, *J* = 9.3 Hz, 1H), 3.28 (dd, *J* = 9.9, 2.8 Hz, 1H), 2.47 (m, 1H), 2.51 (ddd, *J* = 16.6, 6.2, 2.7 Hz, 1H), 2.44 (m, 3H), 2.34 (ddd, *J* = 16.6, 7.0, 2.7 Hz, 1H), 1.99 (m, 3H), 1.91 (dd, *J* = 14.4, 3.0 Hz, 1H), 1.74 (m, 4H), 0.88 (s, 9H), 0.01 (s, 3H), 0.01 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$): δ 137.4, 135.1, 123.8, 116.4, 95.6, 81.4, 75.0, 72.6, 72.3, 69.9, 69.6, 68.0, 66.3, 66.2, 60.4, 42.1, 34.2, 29.3, 25.7, 25.3, 22.8, 21.1, 18.3, 14.2, −4.4, −5.4; ^{29}Si NMR (119 MHz, $CDCl_3$) δ −17.5 ppm.

Compound 20. HF·pyridine (110 mg, 0.1 mmol) was added to a solution compound **19** (42.9 mg, 0.09 mmol) in THF (0.5 mL) in a Teflon flask and the resulting mixture was stirred for 2 d at ambient temperature. The reaction was quenched with saturated aq. $NaHCO_3$ (1 mL), the aqueous phase was extracted with EtOAc (3 × 1 mL), the combined organic layers were washed with saturated aq. NH_4Cl and brine (1 mL each), dried over sodium sulfate, filtered, and evaporated. The residue was purified by flash chromatography (hexanes/EtOAc 1:2 to 0:1) to give the title compound as a colorless syrup (9.1 mg, 28%). ^{1}H NMR (400 MHz, $CDCl_3$): 5.91 – 5.76 (m, 1H), 5.29 (dt, *J* = 2.7, 1.4 Hz, 1H), 5.17 – 5.02 (m, 2H), 4.23 (ddd, *J* = 11.3, 6.0, 4.1 Hz, 1H), 4.17 – 4.08 (m, 2H), 4.06 – 4.01 (m, 1H), 3.95 (dd, *J* = 10.3, 9.1 Hz, 1H), 3.87 (dd, *J* = 9.3, 6.0 Hz, 1H), 3.78 (t, *J* = 9.2 Hz, 1H), 3.57 (d, *J* = 9.9 Hz, 1H), 3.34 (dd, *J* = 10.3, 3.0 Hz, 1H), 2.68 (m, 2H), 2.59 – 2.29 (m, 4H), 2.13 – 2.06 (m, 2H), 2.02 – 1.92 (m, 2H), 1.85 (dd, *J* = 14.6, 3.2 Hz, 1H), 1.75 (d, *J* = 1.3 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$): 137.4, 134.7, 122.1, 116.7, 96.7, 80.2, 75.7, 72.3, 72.2, 70.8, 69.1, 68.4, 66.6, 66.4, 40.1, 34.4, 29.5, 25.1, 22.7.

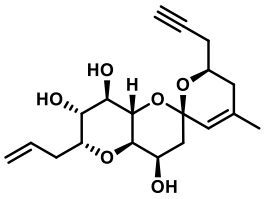
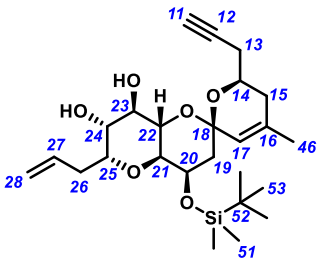
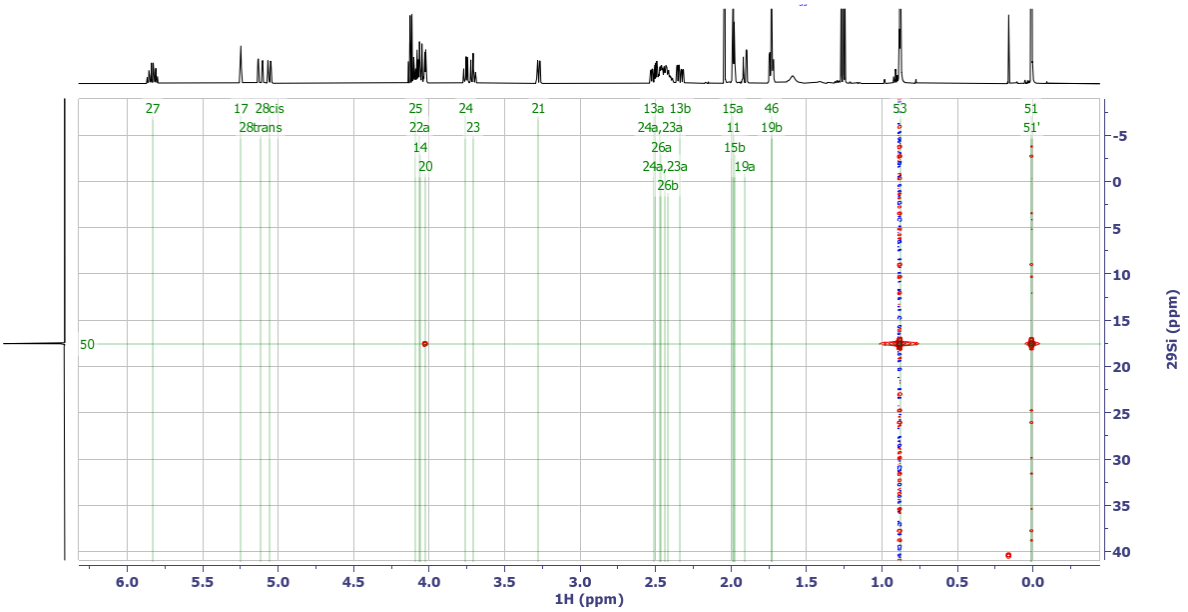


Table S2. Analysis of the NMR data of compound **19**; arbitrary numbering scheme as shown in the insert.



atom number	**^{1}H NMR** ($CDCl_3$, 600 MHz)			**^{13}C NMR** ($CDCl_3$, 150 MHz)	
	δ [ppm]	***J*** [Hz]	**COSY**	δ [ppm]	**HMBC**
11	1.98	2.8	13	69.9	13
12	--	--	--	81.4	11, 13, 14
13	2.51	16.6, 6.2, 2.7	11, 13b, 14	25.3	14, 15
	2.34	16.6, 7.0, 2.7	11, 13a, 14		
14	4.06		13, 15	66.3	13, 15, 46
15	1.97-2.00		14, 17, 46	34.2	13, 17, 46
16	--	--	--	137.4	14, 15, 46
17	5.25	1.6	15, 18, 19, 46	123.8	15, 19b
18	--	--	--	95.6	14, 17, 19, 20
19	1.91	14.4, 3.0	19b, 20	42.1	17, 20, 46
	1.73		19a, 20		
20	4.03	19, 21		66.2	19a, 20, 22a
21	3.28	9.9, 2.8	20, 21, 22a	69.6	19a, 20, 22a, 23, 25
22	4.06	9.5	21, 23	68.0	20, 21, 23, 24
23	3.71	9.3	22a, 24	72.6	21, 22a, 24, 25
24	3.76	9.5, 5.8	23, 25	72.3	23, 25, 26b
25	4.09	10.4, 5.8, 4.0	24, 26	75.0	21, 24, 26, 27
26	2.46		25, 26b, 27	29.3	24, 25, 27, 28
	2.42		25, 26a, 27		
27	5.83	17.0, 10.2, 6.7	26, 28	135.1	25, 26, 28trans
28	5.06 (cis)	10.2, 2.0	27, 28trans	116.4	26
	5.12 (trans)	17.1, 1.6	27, 28cis		
46	1.73		15, 17	22.8	15, 17
51	0.01			–4.4	51’
51’	0.01			–5.4	51
52	--	--	--	18.3	53
53	0.88			25.7	



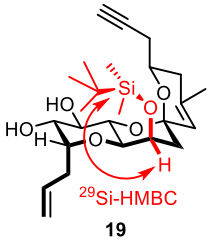


Figure S3. ^{29}Si HMBC spectrum ($CDCl_3$) allowing the identification of the residual silyl group in **19** as the C20-OTBS ether

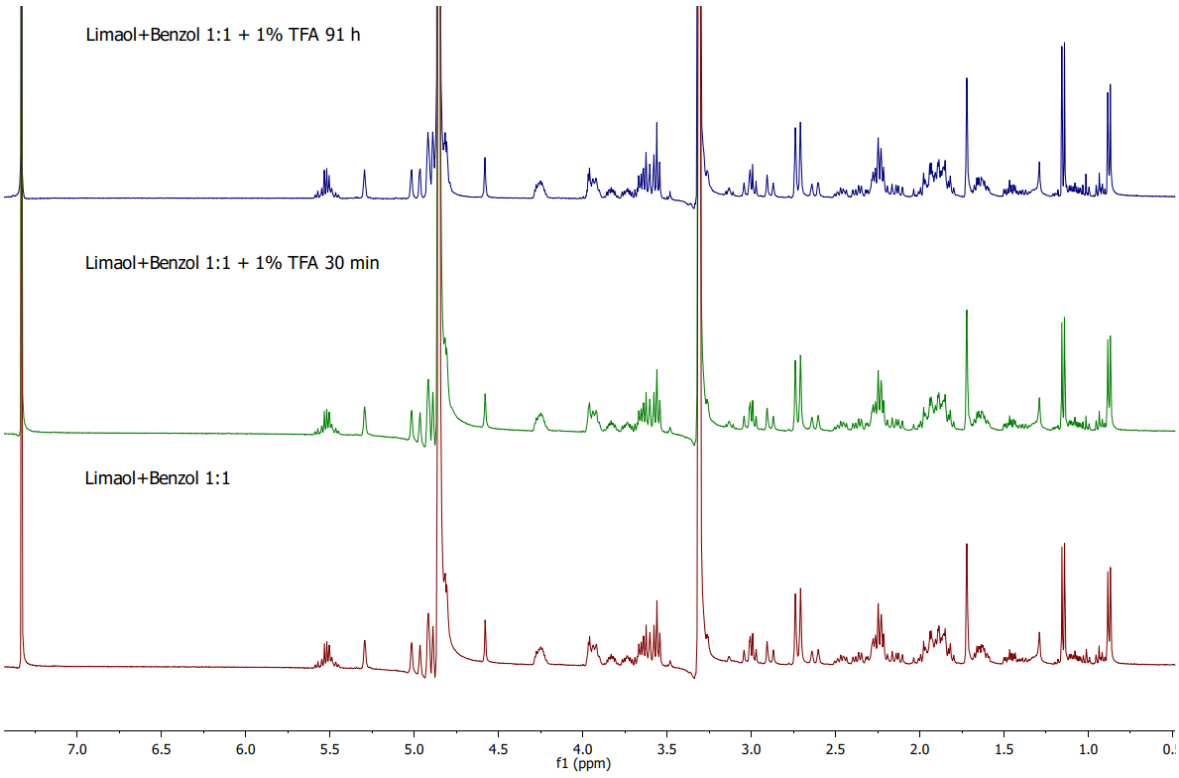


Figure S4 Stability test: ^{1}H NMR spectra of limaol (**1**) in [D_4]-MeOH in the presence of trifluoroacetic acid (1 mol%) after 30 min and after 91 h of storage at ambient temperature; C_6H_6 served as internal standard

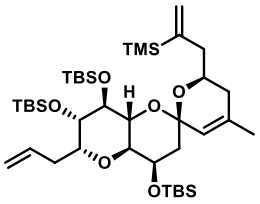
Dissecting the Spiroketalization

(*S*)-2-Iodo-6-(trimethylsilyl)hept-1-en-6-yn-4-ol (S6). 1,2-Dibromoethane (20 µL, 0.23 mmol) was added to a suspension of magnesium turnings (46 mg, 1.9 mmol) in THF (3 mL). The mixture was stirred at room temperature for 5 min before (1-bromovinyl)trimethylsilane (0.15 mL, 0.95 mmol) was added dropwise over 5 min, so as to maintain gentle reflux. The resulting mixture was filtered under argon and the filtrate was cooled to −40 °C. Copper(I) iodide (9.1 mg, 48 µmol) was added and the mixture was stirred at this temperature for 30 min. A solution of epoxide **26** (0.10 g, 0.48 mmol) in THF (0.5 mL, 2 × 0.2 mL washes) was added over 10 min at −40 °C. The mixture was warmed to 0 °C over 14 h. The reaction was quenched by adding saturated aq. NH_4Cl (8 mL), the aqueous phase was extracted with *tert*-butyl methyl ether (3 × 8 mL), and the combined organic layers were dried over anhydrous Na_2SO_4, filtered, and concentrated. The residue was purified by flash chromatography (hexanes/EtOAc 10:1) to give the title compound as a colorless oil (92 mg, 62%). $[\alpha]_D^{20}$ = +0.7 (c = 1.06, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 6.17 (q, *J* = 1.3 Hz, 1H), 5.84 (d, *J* = 1.4 Hz, 1H), 5.70 (dt, *J* = 2.8, 1.3 Hz, 1H), 5.52 (dt, *J* = 2.9, 0.7 Hz, 1H), 3.97 (dtq, *J* = 9.4, 5.0, 2.2 Hz, 1H), 2.60 – 2.49 (m, 2H), 2.45 (dddd, *J* = 13.7, 4.3, 1.5, 0.7 Hz, 1H), 2.26 (ddt, *J* = 13.7, 8.9, 0.9 Hz, 1H), 1.82 (d, *J* = 2.4 Hz, 1H), 0.14 (s, 9H); ^{13}C NMR ($CDCl_3$, 101 MHz): δ 149.0, 128.5, 128.4, 107.7, 68.2, 52.5, 43.7, –1.1; IR (film, cm^{-1}): 3428, 2954, 2906, 1616, 1406, 1351, 1283, 1248, 1208, 1161, 1110, 1046, 930, 896, 837, 758, 691, 660, 561, 518, 485; HRMS (ESI) for $C_{10}H_{19}OISiNa$ $[M+Na]^+$: calcd. 333.0142; found 333.0146.

Compound 40. Copper(I) iodide (23 mg, 0.12 mmol) was added to a solution of alkyne **S1** (0.48 g, 0.81 mmol) in degassed diisopropylamine (6 mL) and the resulting mixture stirred at room temperature for 10 min. A solution of alkenyl iodide **S6** (0.27 g, 0.87 mmol) in diisopropylamine (1 mL, 2 × 1 mL wash) was added, followed by triphenylphosphine (43 mg, 0.16 mmol) and tris(dibenzylideneacetone)dipalladium(0) (37 mg, 41 µmol). The mixture was stirred for 1 h at room temperature before the reaction was quenched at 0 °C with saturated aqueous NH_4Cl (20 mL). The mixture was diluted with *tert*-butyl methyl ether (20 mL), allowed to warm to room temperature, and the aqueous phase was extracted with *tert*-butyl methyl ether (3 × 15 mL). The combined organic extracts were washed with brine (20 mL), dried over anhydrous Na_2SO_4, and concentrated. The residue was purified by flash chromatography (hexanes/EtOAc 15:1) to afford the title compound as a colorless oil (0.60 g, 96%). $[\alpha]_D^{20}$ = +28.2 (c = 1.24, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 5.83 (ddt, *J* = 17.1, 10.2, 6.9 Hz, 1H), 5.69 (dd, *J* = 2.9, 1.4 Hz, 1H), 5.48 (d, *J* = 3.0 Hz, 1H), 5.35 (d, *J* = 2.1 Hz, 1H), 5.29 – 5.21 (m, 1H), 5.12 (dd, *J* =

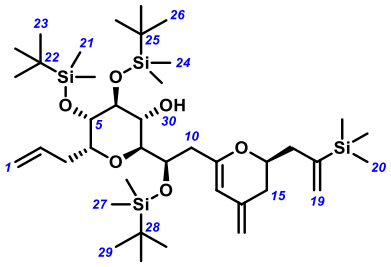
17.2, 1.8 Hz, 1H), 5.11 – 5.03 (m, 1H), 4.19 – 4.10 (m, 1H), 3.98 (tt, *J* = 8.7, 5.0 Hz, 1H), 3.84 – 3.74 (m, 2H), 3.62 (dt, *J* = 8.7, 5.8 Hz, 2H), 3.55 (dd, *J* = 6.3, 3.5 Hz, 1H), 3.37 (d, *J* = 5.7 Hz, 1H), 2.66 (dd, *J* = 17.3, 4.3 Hz, 1H), 2.55 (dd, *J* = 17.2, 4.9 Hz, 1H), 2.48 – 2.35 (m, 2H), 2.36 – 2.18 (m, 4H), 1.96 (d, *J* = 2.5 Hz, 1H), 0.92 (s, 9H), 0.90 (s, 9H), 0.89 (s, 9H), 0.15 (s, 3H), 0.13 (d, *J* = 1.4 Hz, 9H), 0.11 (s, 9H), 0.10 (s, 3H), 0.09 (s, 3H); ^{13}C NMR ($CDCl_3$, 101 MHz): δ 149.3, 135.1, 128.8, 127.7, 122.9, 117.2, 87.9, 82.7, 77.4, 76.6, 73.3, 73.1, 72.6, 71.8, 68.3, 45.2, 43.9, 32.6, 26.3, 26.2, 25.9, 25.4, 18.3, 18.2, 18.2, −1.2, −3.7, −3.9, −3.9, −4.0, −4.2, −4.4; IR (film, cm^{-1}): 3517, 2953, 2929, 2857, 1472, 1250, 1096, 835, 777, 682; HRMS (ESI) for $C_{40}H_{78}O_6Si_4Na$ $[M+Na]^+$: calcd. 789.4768; found 789.4777.

Compound 41. 2,6-Di-*tert*-butylpyridine (0.13 mL, 0.59 mmol) and (acetonitrile)[(2-biphenyl)di-*tert*-butylphosphine]gold(I) hexafluoroantimonate (**10**, 22 mg, 28 μmol)[6] were added to a solution of enyne **40** (0.43 g, 0.56 mmol) in CH_2Cl_2 (5.5 mL) at 0 °C. The mixture was stirred at 0 °C for 5 h and then filtered through Celite. The filtrate was concentrated to afford the corresponding enol ether **42** contaminated with residual pyridine base. The structure of this compound was elucidated by NMR spectroscopy using ^{1}H, ^{13}C, COSY, HSQC, HMBC, and NOESY experiments (see Table S3).



The residue was dissoved in acetic acid (5.5 mL) and the mixture stirred at room temperature for 30 min before it was diluted with *tert*-butyl methyl ether (20 mL) and cooled to 0 °C. Saturated aq. $NaHCO_3$ (10 mL) was added slowly and additional solid $NaHCO_3$ was introduced until gas evolution had ceased. The aqueous phase was extracted with *tert*-butyl methyl ether (3 × 8 mL) and the combined organic fractions were washed with brine (10 mL), dried over anhydrous Na_2SO_4, filtered, and concentrated. The residue was purified by flash chromatography (hexanes/*tert*-butyl methyl ether 100:1) to give the title compound as a pale yellow oil (0.38 g, 89%). $[\alpha]_D^{20}$ = +44.9 (c = 1.12, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 5.82 (ddt, *J* = 17.0, 10.3, 6.7 Hz, 1H), 5.77 – 5.71 (m, 1H), 5.42 (dd, *J* = 3.0, 1.3 Hz, 1H), 5.18 (p, *J* = 1.3 Hz, 1H), 5.09 (dd, *J* = 17.3, 1.8 Hz, 1H), 5.08 – 5.00 (m, 1H), 4.15 (ddt, *J* = 10.4, 8.8, 4.5 Hz, 1H), 4.01 (q, *J* = 3.0 Hz, 1H), 3.95 – 3.82 (m, 2H), 3.67 (t, *J* = 8.4 Hz, 1H), 3.61 (dd, *J* = 8.5, 4.9 Hz, 1H), 3.28 (dd, *J* = 10.0, 2.9 Hz, 1H), 2.54 (ddt, *J* = 15.3, 5.0, 1.8 Hz, 1H), 2.47 – 2.38 (m, 2H), 2.16 (dd, *J* = 15.2, 8.3 Hz, 1H), 1.91 – 1.69 (m, 4H), 1.72 – 1.63 (m, 5H), 0.92 (s, 9H), 0.89 (s, 8H), 0.88 (s, 7H), 0.11 (s, 3H), 0.09 (s, 12H), 0.07 (s, 3H), 0.05 (s, 3H), 0.02 (s, 3H), 0.01 (s, 4H); ^{13}C NMR ($CDCl_3$, 101 MHz): δ 148.2, 135.9, 135.6, 125.7, 124.4, 116.2, 95.0, 76.5, 74.2, 73.4, 70.7, 68.7, 66.8, 66.1, 42.5, 40.9, 34.9, 29.8, 26.5, 26.4, 26.1, 22.9, 18.7, 18.6, 18.4, −1.6, −3.5, −3.5, −3.7, −4.1, −4.3, −5.1; IR (film, cm^{-1}): 2953, 2928, 2857, 1472, 1250, 1205, 1090, 1038, 968, 836, 776, 671; HRMS (ESI) for $C_{40}H_{79}O_6Si_4$ $[M+H]^+$: calcd. 767.4948; found 767.4952.

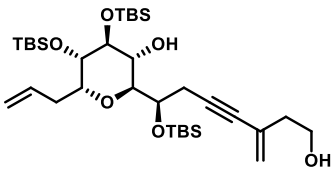
Table S3. Analysis of the NMR data of enol ether **42**; arbitrary numbering scheme as shown in the insert.



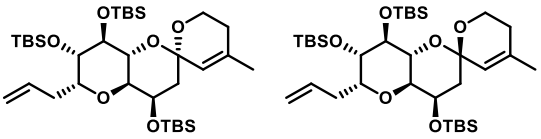
atom number	**^{1}H NMR** ($CDCl_3$, 500 MHz)			**^{13}C NMR** ($CDCl_3$, 126 MHz)	
	δ [ppm]	***J*** [Hz]	**COSY**	δ [ppm]	**HMBC**
1-*cis*	5.06	1.9 (1-*trans*), 10.3 (2)	2	116.9	
1-*trans*	5.1	17.2 (2), 1.9 (1-*cis*)	2		
2	5.82	17.2 (1-*trans*), 10.3 (1-*cis*)	1-*cis*, 1-*trans*, 3′, 3″	135.1	3′, 3″
3′	2.38	-	2, 4	32.4	1-*cis*, 1-*trans*
3″	2.26	-	2, 4		
4	3.83	9.8, 4.0, 4.0	3′, 3″, 5	72.7	5
5	3.55	5.8 (6)	4, 6	72.4	3′, 6
6	3.79	5.8 (5), 6.0 (7)	5, 7	73.3	5, 7
7	3.62	6.0 (8), 6.0 (30), 6.0 (6)	6, 8, 30	71	5, 6, 8
8	3.56	6.0 (7)	7, 9	78	7, 9, 10
9	4.35	-	8, 10′, 10″	70.7	8, 10″
10′	2.56	-	9	39.5	8, 12
10″	2.21	-	9		
11	-	-	-	154.3	10′, 10″, 12
12	5.32	-	-	104	10″, 14′, 14″
13	-	-	-	137.9	15′, 15″
14′	4.61	-	14″	105	12
14″	4.41	-	14′		
15′	2.38	-	16	34.5	12, 14′, 14″, 17′, 17″
15″	2.18	-	16		
16	4.06	-	15′, 15″, 17′, 17″	75.3	15′, 15″, 17′, 17″
17′	2.57	-	16	41.3	-
17″	2.35	-	16		
18	-	-	-	147.8	17′, 17″, 19′, 19″, 20, 20′, 20″
19′	5.65	-	19″	127.5	17′, 17″
19″	5.45	-	19′		
20	0.1	-	-	–1.38	18
21, 24, 27	0.06 – 0.14	-	-	–4.66 – –3.71	-
22, 25, 28	-	-	-	18.1 – 18.2	-

atom number	**^{1}H NMR** ($CDCl_3$, 500 MHz)			**^{13}C NMR** ($CDCl_3$, 126 MHz)	
	δ [ppm]	***J*** [Hz]	**COSY**	δ [ppm]	**HMBC**
23, 26, 29	0.86 – 0.93	-	-	25.9 – 26.1	-
30	3.07	6.0 (7)	7	-	-

Compound 43. A solution of copper(I) iodide (1.9 mg, 0.01 mmol), alkyne **S1** (15 mg, 0.026 mmol),[2] alkenyl iodide **S3** (7.6 mg, 0.039 mmol), tetrakis(triphenylphosphine)palladium (3.0 mg, 0.003 mmol) and di(*iso*-propyl)ethylamine (10 mg, 0.08 mmol) in toluene (0.25 mL) was stirred at room temperature for 20 h. The reaction was quenched at 0 °C with saturated aqueous NH_4Cl (1 mL). The mixture was diluted with *tert*-butyl methyl ether (2 mL), allowed to warm to room temperature, and the aqueous phase was extracted with *tert*-butyl methyl ether (3 × 1 mL). The combined organic extracts were washed with brine (1 mL), dried over anhydrous Na_2SO_4, and concentrated. The residue was purified by flash chromatography (hexanes/EtOAc 7:1) to afford the title compound as a colorless oil (12.2 mg, 73%). $[\alpha]_D^{20}$ = +271.3 (c = 1.22, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 5.85 (m, 1H), 5.35 (s, 1H), 5.26 (s, 1H), 5.11 (m, 2H), 4.14 (m, 1H), 3.79 (m, 4H), 3.61 (m, 3H), 3.44 (m, 1H), 2.61 (m, 2H), 2.39 (m, 3H), 2.25 (m, 1H), 1.61 (m, 1H), 0.92 (s, 9H), 0.90 (s, 18H), 0.13 (m, 18H); ^{13}C NMR ($CDCl_3$, 101 MHz): δ 135.0, 128. 5, 122.5, 117.1, 87.7, 82.2, 77.2, 73.2, 72.4, 60.8, 40.7, 32.5, 32.4, 31.8, 31.1, 26.1, 26.0, 25.7, 25.3, 18.2, 18.10, 18.07, −3.9, −4.0, −4.1, −4.4, −4.6; IR (film, cm^{-1}): 2953, 2929, 2895, 2857, 1472, 1254, 1096, 1040, 836, 777; HRMS (ESI) for $C_{34}H_{66}O_6Si_3Na$ $[M+Na]^+$: calcd. 677.4062; found 677.4059.



Compounds 44 and 45. $AgBF_4$ (0.54 mg, 0.0027 mmol) was added to a solution of compound **33** (6.0 mg, 0.009 mmol), pyridinium *p*-toluenesulfonate (0.23 mg, 0.0009 mmol) and triphenylphosphinegold chloride (0.28 mg, 0.0009 mmol) in tetrahydrofuran (0.2 mL) at 0°C. Stirring was continued at ambient temperature for 3 h before the mixture was diluted with *tert*-butyl methyl ether (2 mL) and the reaction was quenched with saturated aqueous $NaHCO_3$ (1 mL). The aqueous phase was extracted with *tert*-butyl methyl ether (3 x 1 mL), the combined organic layers were dried over $MgSO_4$ and evaporated, and the residue was purified by flash chromatography (hexanes/EtOAc 40:1 to 30:1) to afford compound **44** (3.0 mg, 50%) and compound **45** (2.1 mg, 35%) as a colorless oil each.



When the reaction was performed with the cationic gold complex **10** as the catalyst, the combined yield was 66% with a dr ≈ 3:1 (^{1}H NMR). For their spectroscopic data, see Tables S4 and S5

The stereochemcial assignment of the spiroacetal center was based on 2D NOESY data. The most indicative nOe's are as shown:

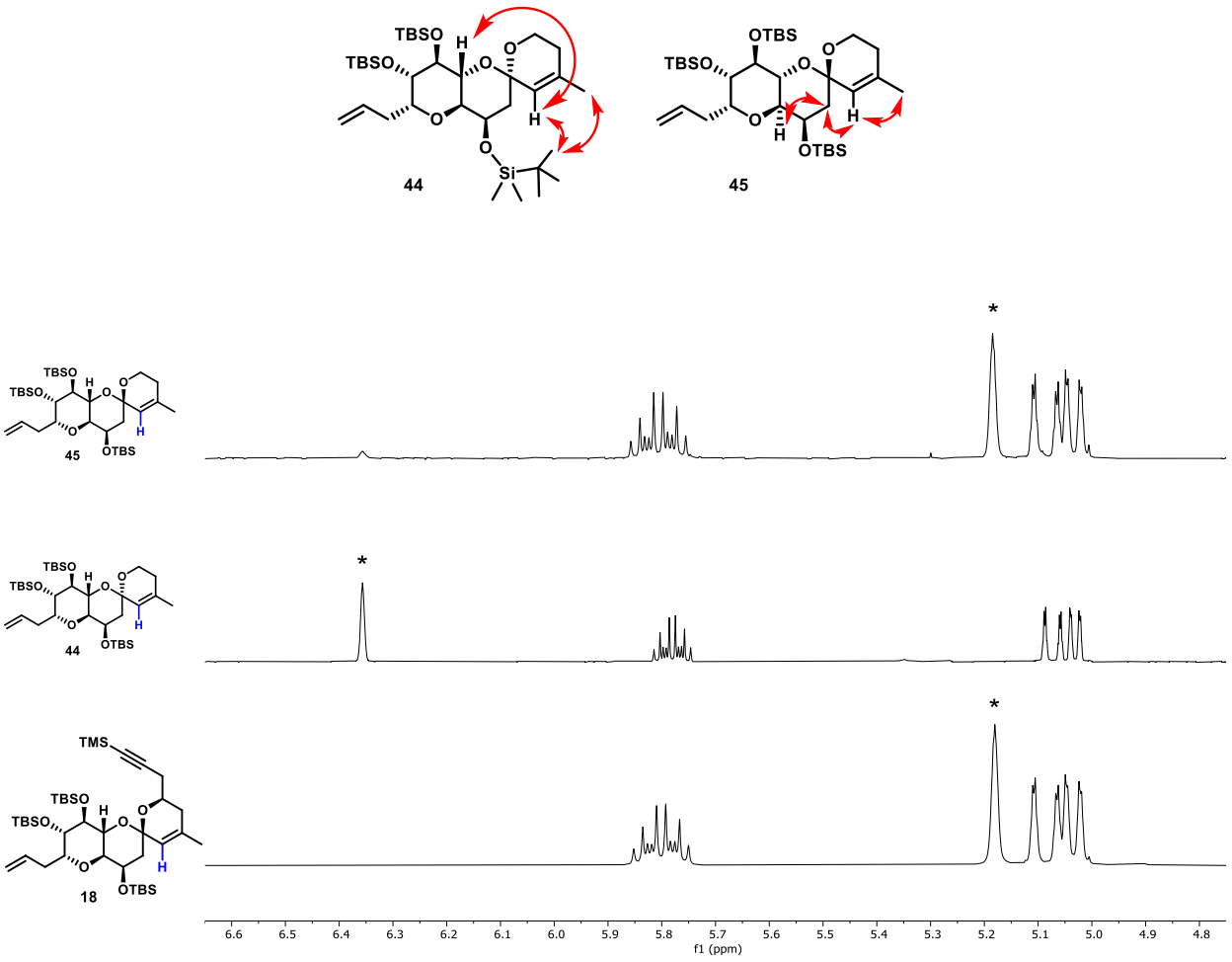
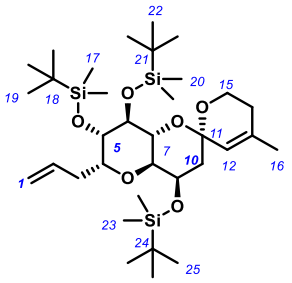


Figure S5. Comparison of the olefinic range (4.8-6.6 ppm) of the ^{1}H NMR spectra of compound **18** formed in the gold catalyzed step as a single diasteromer with those of the truncated spiroketals **44** (kinetic product) and **45** (thermodynamic product benefitting from a double-anomeric effect). The peaks marked with an asterisk correspond to the respective olefinic protons marked in blue.

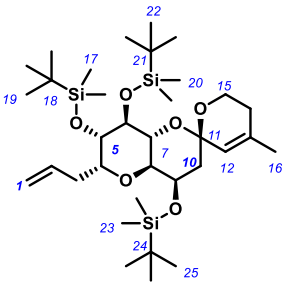
Table S4. Analysis of the NMR data of compound **44**; arbitrary numbering scheme as shown in the insert.



atom number	**^{1}H NMR** ($CDCl_3$, 600 MHz)			**^{13}C NMR** ($CDCl_3$, 150 MHz)	
	δ [ppm]	***J*** [Hz]	**COSY**	δ [ppm]	**HMBC**
1-*cis*	5.03	1.7 (1-*trans*), 10.2 (2)	2, 3	116.2	
1-*trans*	5.07	17.0 (2), 1.7 (1-*cis*), 1.7 (3)	2, 3		
2	5.78	17.0 (1-*trans*), 10.2 (1-*cis*), 6.8 (3)	1-*cis*, 1-*trans*, 3′, 3″	135.3	1-*trans*, 3, 4
3	2.41	6.8 (2), 1.7 (1-*trans*)	1, 2, 4	29.9	1-*cis*, 1-*trans*, 5
3″		-			
4	3.87	9.5, 5.1, 5.0	3	75.8	2, 3, 5
5	3.58	5.0 (4), 7.5 (6)	3, 4, 6	74.4	4, 6
6	3.68	7.5 (5), 8.0 (7)	5, 7	73.7	4, 5, 7, 8
7	3.64	9.8 (8), 8.0 (6)	6, 8a	71.6	5, 6, 8, 9
8	3.41	2.7 (9), 9.8 (7)	9	69.8	4, 7, 9, 10′
9	4.12	3.2 (10′), 3.2 (10″), 2.7 (8)	8, 10′, 10″	68.2	7, 10″
10′	1.89	3.2 (9), 14.1 (10″)	10″	43.0	-
10″	1.85	3.2 (9), 14.1 (10′)	9, 10′		
11	-	-	-	95.4	9, 10, 12, 15
12	6.36	-	14, 16	123.0	10, 14, 16
13	-	-	-	133.1	14, 15″, 16
14′	2.24	17.3 (14″)	12, 14″, 15	29.0	12, 15″, 16
14″	1.64	17.3 (14′), 3.6 (15′)	12, 14′, 15′		
15′	4.19	3.6 (14″), 11.0 (15″)	14, 15″	59.5	14′
15″	3.81	11.0 (15′), 6.4	14′, 15′		
16	1.67	-	12	22.9	12, 14″
17	0.10	-	-	–3.7	17′
17′	0.07	-	-	–4.6	17
18	-	-	-	18.2	17′, 17″, 19
19	0.91	-	18	26.2	-
20	0.13	-	-	–4.2	20′
20′	0.08	-	-	–3.2	20
21	-	-	-	18.1	20, 22

atom number	**^{1}H NMR** ($CDCl_3$, 600 MHz)			**^{13}C NMR** ($CDCl_3$, 150 MHz)	
	δ [ppm]	***J*** [Hz]	**COSY**	δ [ppm]	**HMBC**
22	0.87	-	-	25.9	-
23	0.08	-	-	–4.3	23’
23’	0.05	-	-	–5.4	23
24	-	-	-	18.3	23, 25
25	0.91	-	-	25.8	-

Table S5. Analysis of the NMR data of compound **45**; arbitrary numbering scheme as shown in the insert.

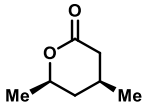


atom number	**^{1}H NMR** ($CDCl_3$, 600 MHz)			**^{13}C NMR** ($CDCl_3$, 150 MHz)	
	δ [ppm]	***J*** [Hz]	**COSY**	δ [ppm]	**HMBC**
1-*cis*	5.03	10.2 (2)	1-*trans*, 2	116.0	
1-*trans*	5.09	17.0 (2)	1-*cis*, 2		
2	5.81	17.0 (1-*trans*), 10.2 (1-*cis*)	1-*cis*, 1-*trans*, 3	135.7	1-*trans*, 3, 4
3	2.42	-	2, 4	29.4	1-*cis*, 1-*trans,* 2, 5
3’’		-			
4	3.89	10.0, 4.6, 4.6	3, 5	76.2	3, 5
5	3.62	-	4	74.1	3, 4, 6, 7
6	3.64	-	7	73.1	4, 5, 7
7	3.86	10.1 (8), 8.0	6, 8a	68.5	5, 6, 8, 9
8	3.29	2.8 (9), 10.1 (7)	7, 9	70.3	4, 9, 10’
9	4.00	2.9 (10’), 3.4 (10’’), 2.8 (8)	8, 10	66.6	7, 10’
10’	1.86	2.9 (9), 14.3 (10’’)	9	41.9	12
10’’	1.66	3.4 (9), 14.3 (10’)	9		
11	-	-	-	94.1	9, 10, 12, 15
12	5.18	-	16	124.7	14, 16
13	-	-	-	135.9	14, 15’, 16
14’	2.17	-	14’’, 15	29.0	12, 15’’, 16
14’’	1.63	-	14’, 15		
15’	3.97	11.3 (15’), 11.3, 4.0	14, 15’’	57.6	14’
15’’	3.63	11.3 (15’)	14’, 15’		
16	1.68	-	12	22.9	12, 14’’

atom number	**^{1}H NMR** ($CDCl_3$, 600 MHz)			**^{13}C NMR** ($CDCl_3$, 150 MHz)	
	δ [ppm]	***J*** [Hz]	**COSY**	δ [ppm]	**HMBC**
17	0.11	-	-	–3.7	17′
17′	0.08	-	-	–4.4	17
18	-	-	-	18.2	17, 19
19	0.91	-	18	26.3	-
20	0.06	-	-	–3.9	20′
20′	0.06	-	-	–3.6	20
21	-	-	-	18.3	20, 22
22	0.89	-	-	26.3	-
23	0.02	-	-	–4.3	23′
23′	0.00	-	-	–5.2	23
24	-	-	-	18.3	23, 25
25	0.88	-	-	25.7	24

Improved Preparation of the Northern Sector

(4*S*,6*R*)-4,6-Dimethyl-3,4,5,6-tetrahydro-2*H*-pyran-2-one (32). The compound was prepared according to a procedure by Schmid and co-workers.[7,8]



A freshly prepared solution of tetrafluoroboric acid (0.04 M in EtOH, 5.50 mL, 0.220 mmol) was added to a solution of [Ru((*S*)-MeO-BIPHEP)$(OAc)_2$] ((*S*)-**38**, 27.5 mg, 22.0 µmol)[9] in EtOH (12.5 mL) and the mixture was stirred at room temperature for 2 h. A solution of 4,6-dimethyl-2-pyrone (**31**, 1.37 g, 11.0 mmol) in EtOH (5.0 mL, 2 × 2.5 mL washes) was added to an oven-dried 150 mL-autoclave under argon equipped with a glass insert and a stirring bar. The catalyst solution (18.0 mL total volume) was added and complete transfer was ensured with EtOH washes (2 × 4.0 mL). The autoclave was closed, pressurized with 60 bar of H_2, and heated to 60 °C for 23 h. After cooling to room temperature, the residual gas was carefully released in a well-ventilated hood and the mixture was concentrated. The residue was purified by flash chromatography (fine silica, hexanes/*tert*-butyl methyl ether 1:1) to give the title compound as a colorless oil (961 mg, 68%). Purity and dr after flash chromatography were determined by GC-MS analysis to be 93% and 18:1, respectively (Figure S6). According to GC-MS analysis using a chiral stationary phase, the *ee* of the major diastereoisomer was determined to be 98% (Figure S7). The spectral data and specific rotation were in good agreement with the reported values.[8] $[\alpha]_D^{20}$ = +7.6 (c = 0.63, MeOH), literature: $[\alpha]_D^{20}$ = +6.6 (c = 0.56, MeOH); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 4.41 (dqd, *J* = 11.6, 6.3, 2.9

Hz, 1H), 2.67 (dd, *J* = 11.8, 1.9 Hz, 1H), 2.12 – 1.96 (m, 2H), 1.97 – 1.87 (m, 1H), 1.37 (d, *J* = 6.3 Hz, 3H), 1.30 – 1.13 (m, 1H), 1.03 (d, *J* = 6.3 Hz, 3H); ^{13}C NMR ($CDCl_3$, 101 MHz): δ 171.6, 77.4, 39.0, 38.0, 27.0, 22.0, 21.8.

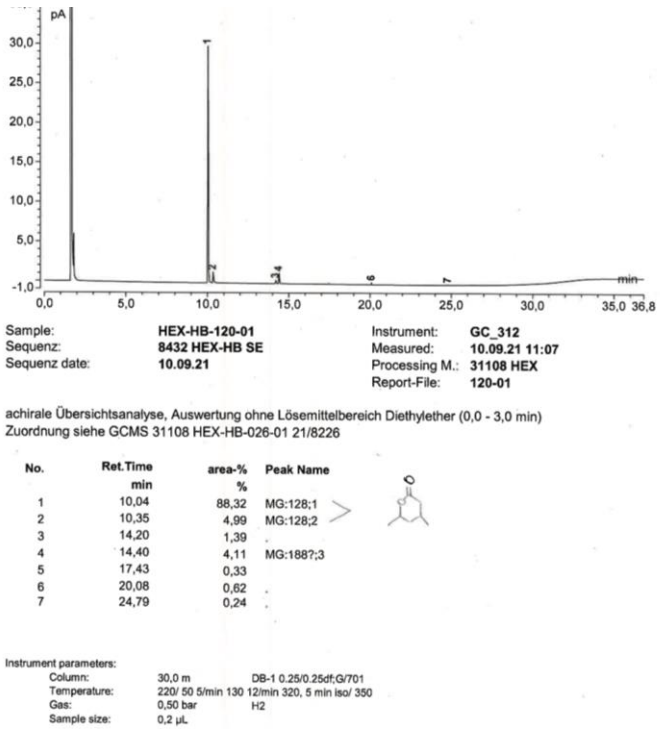


Figure S6. GC-MS analysis of compound **32** using an achiral stationary phase.

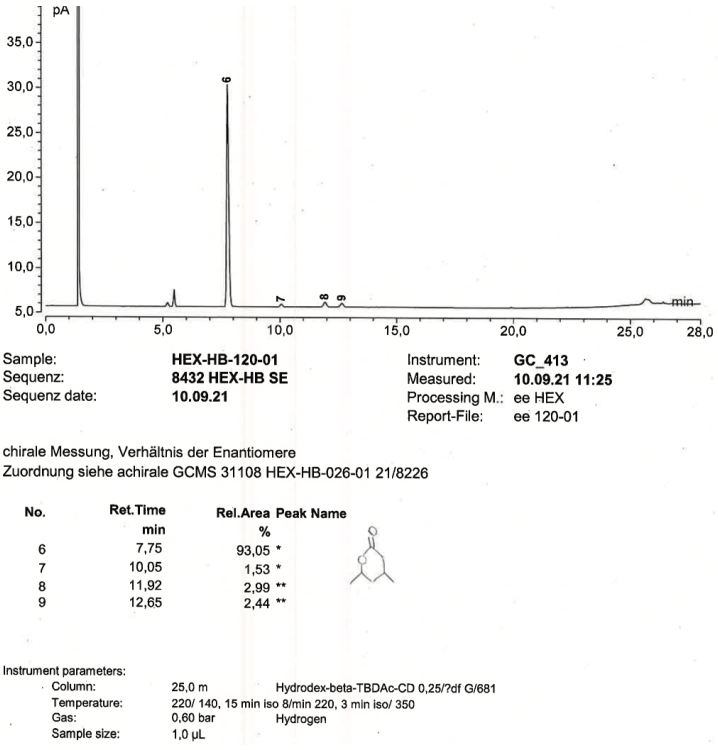
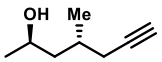


Figure S7. GC-MS analysis of compound **32** using a chiral stationary phase.

(2*R*,4*R*)-4-Methylhept-6-yn-2-ol (34).[10] A solution of CCl_4 (17.3 mL, 180 mmol) in THF (24 mL) was added

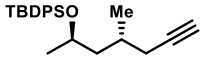


dropwise over the course of 4 h to a solution of lactone **32** (961 mg, 7.49 mmol) and triphenylphosphine (7.86 g, 30.0 mmol) in THF (96 mL) at reflux temperature. Once the addition was complete, the mixture was allowed to cool to ambient temperature. Water (60 mL) was added, the phases were separated, and the aqueous layer extracted with CH_2Cl_2 (3 × 40 mL). The combined organic phases were washed with saturated aq. $NaHCO_3$ (20 mL), dried over Na_2SO_4 and concentrated under reduced pressure to a total volume of ca. 10 mL. Pentane (50 mL) was added under vigorous stirring, the precipitate was filtered off, and the filtrate again reduced to a total volume of ca. 10 mL. This cycle of precipitation/evaporation was repeated three times before all volatile materials were evaporated and the solid residue was subjected to flash chromatography (pentane/Et_2O, 98:2) to furnish the dichloroolefin **33** as a colorless syrup (1.10 g, 75%). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 3.77 (dqd, *J* = 11.3, 6.2, 2.1 Hz, 1H), 2.81 (ddd, *J* = 14.3, 4.0, 1.9 Hz, 1H), 1.79 – 1.68 (m, 2H), 1.61 (dd, *J* = 14.3, 11.9 Hz, 1H), 1.32 (d, *J* = 6.2 Hz, 3H), 1.12 (dt, *J* = 13.7, 12.2 Hz, 1H), 1.00 (d, *J* = 6.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 101 MHz): δ 150.2, 104.2, 76.8, 40.8, 33.8, 29.2, 22.0, 21.8. *Note*: This compound decomposes upon storage and should be used without delay.

A solution of compound **33** in THF (15 mL) was added to a suspension of lithium sand (236 mg, 33.7 mmol) in THF (30 mL) at room temperature. The suspension was stirred at reflux temperature for 3 h before it was cooled to room temperature. The reaction was then carefully quenched with MeOH (3 mL) followed by aq. NH_4Cl (30 mL), and the mixture was extracted with diethyl ether (3 × 20 mL). The combined organic phases were washed with brine (30 mL), dried over Na_2SO_4, and concentrated. The residue was purified by flash chromatography (pentane/Et_2O 2:1) to afford the title compound as colorless liquid (531 mg, 75%, 56% over two steps). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 3.90 (qt, *J* = 10.1, 4.8 Hz, 1H), 2.25 – 2.08 (m, 2H), 1.97 (t, *J* = 2.7 Hz, 1H), 1.91 (dqd, *J* = 9.0, 6.4, 5.0 Hz, 1H), 1.59 (ddd, *J* = 14.1, 9.1, 5.0 Hz, 1H), 1.30 (ddd, *J* = 13.9, 9.0, 3.8 Hz, 1H), 1.26 – 1.23 (m, 1H), 1.22 (d, *J* = 6.2 Hz, 3H), 1.03 (d, *J* = 6.6 Hz, 3H); ^{13}C NMR ($CDCl_3$, 101 MHz): δ 83.2, 69.6, 66.1, 45.6, 29.3, 26.5, 24.6, 19.3.

Note: This compound was directly used in the next step due to its volatility.

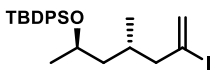
Compound 35. Imidazole (539 mg, 7.92 mmol) and TBDPSCl (1.55 mL, 5.94 mmol) were added to a solution of alcohol **34** (500 mg, 3.96 mmol) in DMF (10 mL). The mixture was stirred at room temperature for 18 h before the reaction was quenched with saturated aq. NH_4Cl (20 mL). The resulting mixture was extracted with *tert*-butyl methyl ether (3 × 20 mL) and the combined organic layers were washed with brine (30 mL), dried over Na_2SO_4, filtered and concentrated. The residue was purified by flash chromatography (hexanes/*tert*-butyl methyl ether 100:1) to afford the title compound as colorless liquid (1.28 g, 88%). The spectral data and specific rotation matched the recorded data of the previously synthesized material.[1]



$[\alpha]_D^{20}$ = +13.0 (c = 0.68, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.73 – 7.65 (m, 4H), 7.47 – 7.32 (m, 6H), 3.89 (app h, *J* = 5.9 Hz, 1H), 2.10 – 2.01 (m, 1H), 1.99 – 1.90 (m, 2H), 1.85 (app dq, *J* = 14.4, 6.5 Hz, 1H), 1.69 (app dt, *J* = 13.4, 6.5 Hz, 1H), 1.30 – 1.17 (m, 1H), 1.06 (m, 12H), 0.84 (d, *J* = 6.6 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 136.1, 135.1, 134.4, 129.7, 129.5, 127.7, 127.5, 83.3, 69.3, 67.8, 46.3, 29.0, 27.2, 26.3, 24.2, 19.5; IR (film, cm^{-1}): 3309, 3071, 2930, 2858, 1461, 1427, 1375, 1109, 1061, 702; HRMS (ESI) for $C_{24}H_{32}OSiNa$ $[M+Na]^+$: calcd. 387.2115; found 387.2111.

The further elaboration of **35** into the building block **2** followed the route described in ref. 1

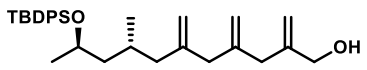
Compound 36. 9-I-9-BBN (1.51 mL, 1.0 M in hexane, 1.51 mmol) was added over the course of 1 h to a stirred solution of alkyne **35** (440 mg, 1.21 mmol) in anhydrous pentane (12 mL) at 0 °C. Once the addition was complete, stirring was continued at room temperature for 16 h. At this point, HOAc (268 mg, 4.47 mmol) was added and the mixture was stirred for another 1 h. The reaction was then quenched with aq. NaS_2O_3 (1 M) and $NaHCO_3$ until the mixture was colorless and showed a pH ≈ 7. The aqueous layer was extracted with *tert*-butyl methyl ether (3 × 20 mL), and the combined organic layers were washed with brine, dried over Na_2SO_4, filtered and concentrated. The residue was purified by flash chromatography (hexanes/Et_3N, 100:1) to give the title compound as a colorless liquid (524 mg, 88%). *Note*: It was critical to ensure that the silica was neutralized. $[\alpha]_D^{20}$ = 19.8 (c = 0.30, $CHCl_3$). ^{1}H NMR (C_6D_6, 400 MHz): δ 7.88 – 7.76 (m, 4H), 7.27 – 7.20 (m, 6H), 5.64 (d, *J* = 1.2 Hz, 1H), 5.58 – 5.52 (s, 1H), 3.99 – 3.89 (m, 1H), 2.19 – 2.00 (m, 2H), 1.78 (dd, *J* = 14.3, 7.7 Hz, 1H), 1.57 (ddd, *J* = 13.1, 8.1, 4.7 Hz, 1H), 1.23 (s, 9H), 1.08 (d, *J* = 6.1 Hz, 3H), 0.97 (ddd, *J* = 13.4, 8.8, 4.5 Hz, 1H), 0.66 (d, *J* = 6.5 Hz, 3H); ^{13}C NMR (C_6D_6, 100 MHz): δ 136.4, 135.3, 134.6, 130.0, 129.9, 126.5, 112.3, 67.8, 53.1, 46.5, 29.1, 27.5, 24.5, 19.6, 18.7; IR (film, cm^{-1}): 3070, 2962, 2929, 2857, 1616, 1427, 1110, 509; HRMS (ESI) for $C_{24}H_{33}OISiNa$ $[M+Na]^+$: calcd. 515.1238; found 515.1245.



Compound 37. *Preparation of the Organozinc Compound*: *t*BuLi (1.7 M in pentane, 1.31 mL, 2.23 mmol) was added dropwise over 20 min to a solution of alkenyl iodide **36** (524 mg, 1.06 mmol) in Et_2O (1.6 mL) at −78 °C. The resulting solution was stirred for 30 min at this temperature before a solution of zinc bromide (0.5 M in THF, 2.16 mL, 1.08 mmol) was added dropwise. After stirring for additional 15 min at −78 °C, the cooling bath was removed and the solution of the organozinc reagent allowed to warm to ambient temperature over the course of 30 min.

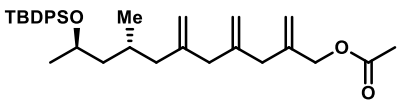
Negishi Cross-coupling Reaction/Deprotection: A flame-dried Schlenk tube was charged with allyl chloride **6** (265 mg, 1.01 mmol) and DMF (2.7 mL). The solution was degassed by purging with Argon for 15 min. $Pd(PPh_3)_4$ (61 mg, 53 µmol) was added followed by the solution of the organozinc reagent. The mixture was stirred at ambient temperature for 4 h before saturated NH_4Cl solution (10 mL) was added. The resulting mixture was extracted with *tert*-butyl methyl ether (3 × 10 mL). The combined organic layers were washed with brine, dried over Na_2SO_4, filtered and concentrated.

TBAF solution (1 M in THF, 1.17 mL, 1.17 mmol) was added to a solution of the crude material in THF (2 mL)



at 0 °C. The cooling bath was removed and the resulting mixture was stirred for 1.5 h. The reaction was quenched with saturated aq. NH_4Cl solution (5 mL) and the aqueous phase extracted with *tert*-butyl methyl ether (3 × 5 mL). The combined organic layers were washed with brine (10 mL), dried over Na_2SO_4, filtered and concentrated. The residue was subjected to flash chromatography (hexanes/*tert*-butyl methyl ether 6:1) to give the title compound as a colorless liquid (416 mg, 82% over two steps). $[\alpha]_D^{20}$ = −4.8 (c = 0.45, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.72 – 7.65 (m, 4H), 7.44 – 7.32 (m, 6H), 5.12 (s, 1H), 4.91 (s, 1H), 4.87 (s, 1H), 4.84 (s, 1H), 4.77 (s, 1H), 4.76 (s, 1H), 4.03 (s, 2H), 3.90 (app dq, *J* = 12.1, 6.0 Hz, 1H), 2.75 (s, 2H), 2.66 (s, 2H), 1.89 – 1.76 (m, 2H), 1.65 (m, 1H), 1.57 (ddd, *J* = 12.6, 8.0, 4.5 Hz, 1H), 1.04 (d, *J* = 2.2 Hz, 13H), 0.69 (d, *J* = 6.4 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 146.3, 145.6, 144.6, 136.0, 135.9, 135.0, 134.3, 129.5, 129.4, 127.5, 127.3, 113.8, 113.1, 111.8, 67.7, 65.4, 47.3, 43.6, 42.5, 39.5, 27.1, 27.0, 24.3, 19.5, 19.3; IR (film, cm^{-1}): 3330, 3071, 2962, 2928, 2857, 1638, 1428, 1375, 1110, 1060, 897; HRMS (ESI) for $C_{31}H_{44}O_2SiNa$ $[M+Na]^+$: calcd. 499.3003; found 499.3008.

Compound 2. Pyridine (30 µL, 0.37 mmol), acetic anhydride (44 µL, 0.47 mmol), and DMAP (3.8 mg,

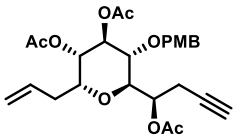


31 µmol) were sequentially added to a stirred solution of alcohol **37** (0.15 g, 0.31 mmol) in CH_2Cl_2 (4 mL) at 0 °C. The cooling bath was removed and the mixture stirred for 2 h at room temperature. The reaction was quenched with saturated aqueous NH_4Cl solution (4 mL) and the mixture diluted with *tert*-

butyl methyl ether (8 mL). The aqueous phase was extracted with *tert*-butyl methyl ether (3 × 4 mL). The combined organic fractions were washed with brine (4 mL), dried over anhydrous Na_2SO_4, filtered and concentrated. The residue was purified by flash chromatography (hexanes/EtOAc 20:1) to give the title compound as a colorless oil (0.15 g, 96%). $[\alpha]_D^{20}$ = −5.2 (c = 1.00, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.69 (ddd, *J* = 8.2, 6.8, 1.6 Hz, 4H), 7.47 – 7.32 (m, 6H), 5.12 (s, 1H), 5.02 – 4.95 (m, 1H), 4.86 (s, 2H), 4.79 – 4.73 (m, 2H), 4.49 (s, 2H), 3.90 (dqd, *J* = 8.1, 6.1, 4.6 Hz, 1H), 2.75 (s, 2H), 2.66 (s, 2H), 2.08 (s, 3H), 1.91 – 1.76 (m, 2H), 1.72 – 1.50 (m, 2H), 1.10 – 1.07 (m, 1H), 1.05 (s, 9H), 1.04 (d, *J* = 6.1 Hz, 3H), 0.69 (d, *J* = 6.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 170.8, 145.6, 143.9, 141.5, 136.1, 136.1, 135.1, 134.5, 129.6, 129.5, 127.6, 127.5, 114.6, 114.3, 113.2, 67.8, 66.3, 47.4, 43.8, 42.6, 39.7, 27.2, 27.1, 24.4, 21.1, 19.6, 19.5; IR (film, cm^{-1}): 3072, 2962, 2929, 2858, 1744, 1638, 1472, 1459, 1428, 1374, 1227, 1155, 1129, 1110, 1058, 1027, 996, 951, 899, 822, 741, 728, 703, 685, 612, 500; HRMS (ESI) for $C_{33}H_{46}O_3SiNa$ $[M+Na]^+$: calcd. 541.3108; found 541.3112.

Revised Spirotricyclic Core

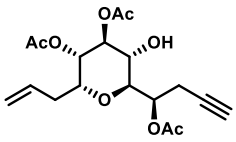
Compound S7. TBAF (22.6 mL, 1.0 M in THF, 22.6 mmol) was added to a solution of compound **21** (6.08 g, 10.3 mmol) in THF (80 mL) at 0 °C. The cooling bath was removed and the mixture was stirred at room temperature for 2 h. Water (80 mL) and EtOAc (80 mL) were introduced and the aqueous phase was extracted with EtOAc (3 × 40 mL). The combined organic layers were dried over anhydrous Na_2SO_4 and filtered. The solvent was evaporated and the residue was dissolved in CH_2Cl_2 (50 mL).



Pyridine (6.66 mL, 82.3 mmol), acetic anhydride (5.83 mL, 61.7 mmol), and DMAP (62.8 mg, 0.514 mmol) were added sequentially and the mixture was stirred at room temperature for 2 h. The reaction was quenched with saturated aqueous NH_4Cl (50 mL) and the aqueous phase was extracted with EtOAc (3 × 30 mL). The combined organic fractions were washed with brine (50 mL), dried over anhydrous Na_2SO_4, and filtered. After evaporation of the solvent, the residue was purified by flash chromatography (hexanes/EtOAc 3:1) to afford the title compound as a colorless oil (4.46 g, 89%). $[\alpha]_D^{20}$ = +40.7 (c = 0.95, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.26 (d, *J* = 8.4 Hz, 2H), 6.88 (d, *J* = 8.4 Hz, 2H), 5.77 (ddt, *J* = 17.1, 10.3, 7.0 Hz, 1H), 5.33 (dt, *J* = 17.4, 6.3 Hz, 2H), 5.16 – 5.06 (m, 2H), 4.88 (dd, *J* = 7.1, 4.2 Hz, 1H), 4.59 (q, *J* = 11.2 Hz, 2H), 4.02 (dt, *J* = 9.5, 4.5 Hz, 1H), 3.88 (t, *J* = 6.0 Hz, 1H), 3.79 (s, 3H), 3.52 (t, *J* = 6.2 Hz, 1H), 2.57 – 2.45 (m, 3H), 2.32 – 2.21 (m, 1H), 2.07 (s, 3H), 2.06 (s, 3H), 1.97 (t, *J* = 2.8 Hz, 1H), 1.95 (s, 3H); ^{13}C NMR ($CDCl_3$, 101 MHz): δ 170.3, 170.0, 169.9, 159.6, 133.4, 129.9, 129.5, 118.2, 114.1, 79.8, 73.4, 73.0, 72.7, 70.8, 70.6,

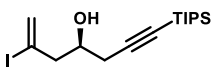
70.1, 69.7, 69.6, 55.4, 32.6, 21.2, 21.0, 20.9, 20.3; IR (film, cm^{-1}): 3279, 2937, 1743, 1613, 1514, 1430, 1370, 1303, 1230, 1175, 1096, 1034, 920, 823, 671, 665, 640, 603, 519, 483, 459; HRMS (ESI) for $C_{26}H_{32}O_9Na$ $[M+Na]^+$: calcd. 511.1939; found 511.1941.

Compound 22. Water (9.0 mL) and 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (2.90 g, 12.8 mmol) were



sequentially added to a solution of **S7** (4.46 g, 9.14 mmol) in CH_2Cl_2 (90 mL) at 0 °C. The mixture was stirred for 1 h at room temperature, diluted with water (60 mL) and extracted with EtOAc (3 × 50 mL). The combined organic fractions were washed with water (60 mL) and brine (60 mL), dried over anhydrous Na_2SO_4, and filtered. The solvent was evaporated and the crude product purified by flash chromatography (hexanes/EtOAc 3:2) to yield the title compound as a colorless oil (3.18 g, 95%). $[\alpha]_D^{20}$ = +59.9 (c = 1.00, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 5.74 (dddd, *J* = 16.7, 10.2, 7.4, 6.3 Hz, 1H), 5.31 (dt, *J* = 7.0, 5.3 Hz, 1H), 5.19 – 5.07 (m, 3H), 4.97 (dd, *J* = 8.6, 5.1 Hz, 1H), 4.13 (dt, *J* = 10.6, 4.7 Hz, 1H), 3.84 (dd, *J* = 8.1, 5.1 Hz, 1H), 3.71 (dd, *J* = 7.4 Hz, 1H), 2.91 – 2.85 (m, 1H), 2.66 (ddd, *J* = 17.1, 5.5, 2.7 Hz, 1H), 2.55 (ddd, *J* = 17.1, 6.9, 2.7 Hz, 1H), 2.51 – 2.42 (m, 1H), 2.33 – 2.21 (m, 1H), 2.09 (s, 3H), 2.06 (s, 3H), 2.05 (s, 3H), 1.98 (t, *J* = 2.7 Hz, 1H); ^{13}C NMR ($CDCl_3$, 101 MHz): δ 171.3, 170.3, 169.9, 133.3, 118.0, 79.7, 72.9, 72.7, 71.6, 70.7, 70.6, 70.0, 69.6, 31.5, 21.1, 21.0, 20.9, 20.0; IR (film, cm^{-1}): 3483, 3290, 2932, 1741, 1643, 1430, 1370, 1230, 1149, 1097, 1072, 1033, 995, 918, 671, 637, 604, 554, 535, 497, 473, 446, 424; HRMS (ESI) for $C_{18}H_{24}O_8Na$ $[M+Na]^+$: calcd. 391.1363; found 391.1366.

(*S*)-2-Iodo-7-(triisopropylsilyl)hept-1-en-6-yn-4-ol (27). *n*-Butyllithium (8.09 mL, 1.6 M in hexanes,



13.0 mmol) was added dropwise to a stirred solution of (triisopropylsilyl)acetylene (3.27 mL, 14.6 mmol) in anhydrous THF (60 mL) at −78 °C. The resulting solution was stirred at this temperature for 20 min. Boron trifluoride etherate (1.60 mL, 13.0 mmol) was added dropwise at −78 °C. After stirring at −78 °C for 5 min, a solution of epoxide **26** (1.70 g, 8.09 mmol) in THF (2.0 mL, 2 × 1.5 mL washes) was added *via* cannula at −78 °C. After 1 h of stirring at this temperature, the reaction was quenched with brine (60 mL). The aqueous phase was extracted with *tert*-butyl methyl ether (3 × 50 mL) and the combined organic layers were dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by flash chromatography (hexanes/EtOAc 12:1) to give the title compound as a colorless oil (3.13 g, 98%). $[\alpha]_D^{20}$ = −13.2 (c = 0.96, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 6.18 (q, *J* = 1.3 Hz, 1H), 5.85 (d, *J* = 1.4 Hz, 1H), 4.05 (dp, *J* = 8.0, 5.4 Hz, 1H), 2.75 (ddd, *J* = 14.3, 4.7, 1.3 Hz, 1H), 2.66 – 2.56 (m, 1H), 2.57 – 2.45 (m, 2H), 2.03 (d, *J* = 5.2 Hz, 1H), 1.07 (d, *J* = 3.2 Hz, 21H); ^{13}C NMR ($CDCl_3$, 101 MHz): δ 128.9, 106.5, 103.7, 84.6, 68.5, 51.6, 27.6, 18.8, 11.4; IR (film, cm^{-1}): 3394, 2942, 2892, 2864, 2172, 1617, 1462, 1421, 1383, 1188, 1117, 1072, 1057, 1025, 995, 898, 883, 677, 663,

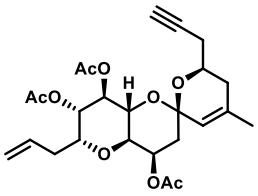
641, 596, 581, 509, 490, 457, 444, 409; HRMS (ESI) for $C_{16}H_{29}OISiNa$ $[M+Na]^+$: calcd. 415.0925; found 415.0926.

Compound 23. Copper(I) iodide (110 mg, 0.580 mmol) was added to a solution of alkyne **22** (1.07 g, 2.90 mmol) in degassed diisopropylamine (3 mL). The mixture was stirred at room temperature for 10 min. A solution of alkenyl iodide **27** (1.25 g, 3.19 mmol) in diisopropylamine (1 mL, 2 × 0.5 mL wash) was added, followed by bis(triphenylphosphine)-palladium(II) chloride (102 mg, 0.145 mmol). The mixture was stirred for 1.5 h at room temperature, before the reaction was quenched at 0 °C by addition of saturated aqueous NH_4Cl (25 mL). The mixture was diluted with EtOAc (25 mL) and warmed to room temperature, and the aqueous phase was extracted with EtOAc (3 × 15 mL). The combined organic extracts were washed with brine (25 mL), dried over anhydrous Na_2SO_4, and concentrated. The residue was purified by flash chromatography (hexanes/EtOAc 3:2) to afford the desired enyne as a pale yellow oil (1.47 g, 80%). $[\alpha]_D^{20}$ = +33.9 (c = 0.94, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 5.76 (dddd, *J* = 16.6, 10.2, 7.4, 6.3 Hz, 1H), 5.38 (d, *J* = 1.9 Hz, 1H), 5.33 (td, *J* = 6.5, 4.1 Hz, 1H), 5.31 – 5.25 (m, 1H), 5.21 – 5.04 (m, 3H), 5.01 (dd, *J* = 8.8, 5.3 Hz, 1H), 4.17 (dt, *J* = 10.7, 4.8 Hz, 1H), 4.07 – 3.96 (m, 1H), 3.89 – 3.76 (m, 2H), 3.11 (d, *J* = 5.7 Hz, 1H), 2.83 (dd, *J* = 17.1, 6.7 Hz, 1H), 2.64 (dd, *J* = 17.1, 6.3 Hz, 1H), 2.58 – 2.42 (m, 4H), 2.43 – 2.32 (m, 2H), 2.28 (dddt, *J* = 15.1, 6.0, 4.4, 1.4 Hz, 1H), 2.09 (s, 3H), 2.07 (s, 3H), 2.06 (s, 3H), 1.13 – 0.99 (m, 21H); ^{13}C NMR ($CDCl_3$, 101 MHz): δ 171.2, 170.2, 169.9, 133.3, 127.7, 123.9, 118.1, 104.2, 86.3, 84.1, 82.8, 73.0, 72.9, 71.8, 70.8, 70.2, 69.5, 69.0, 43.8, 31.4, 28.1, 21.2, 21.0, 20.9, 20.7, 18.8, 11.4; IR (film, cm^{-1}): 3458, 2943, 2865, 2171, 1745, 1464, 1430, 1369, 1230, 1163, 1073, 1031, 995, 916, 884, 676, 605, 526, 478, 447; HRMS (ESI) for $C_{34}H_{52}O_9SiNa$ $[M+Na]^+$: calcd. 655.3273; found 655.3274.

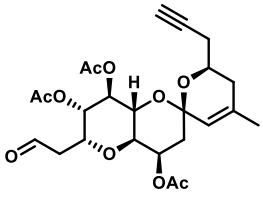
Compound 24. (Acetonitrile)[(2-biphenyl)di-*tert*-butylphosphine]gold(I) hexafluoro-antimonate (**10**, 36.0 mg, 46.5 µmol)[6] and pyridinium *p*-toluenesulfonate (11.7 mg, 46.5 µmol) were added to a solution of enyne **23** (1.47 g, 2.33 mmol) in CH_2Cl_2 (23 mL). The mixture was stirred at room temperature for 20 min and the reaction quenched with triethylamine (1.0 mL). Saturated aqueous NH_4Cl (30 mL) and EtOAc (40 mL) were added. The aqueous phase was extracted with EtOAc (3 × 20 mL) and the combined organic fractions were washed with brine (40 mL), dried over anhydrous Na_2SO_4, filtered and concentrated. The residue was purified by flash chromatography (hexanes/EtOAc 5:1) to give the title compound as a colorless oil (1.16 g, 79%). $[\alpha]_D^{20}$ = +19.3 (c = 1.07, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 5.74 (dddd, *J* = 17.5, 10.2, 7.4, 6.1 Hz,

1H), 5.30 (t, *J* = 9.8 Hz, 1H), 5.21 (d, *J* = 1.6 Hz, 1H), 5.17 – 5.06 (m, 3H), 5.03 (q, *J* = 3.1 Hz, 1H), 4.33 – 4.18 (m, 2H), 3.89 (ddt, *J* = 9.1, 7.8, 5.3 Hz, 1H), 3.53 (dd, *J* = 10.2, 3.1 Hz, 1H), 2.74 – 2.51 (m, 2H), 2.49 – 2.34 (m, 2H), 2.26 (dd, *J* = 15.3, 3.0 Hz, 1H), 2.07 (s, 3H), 2.04 (s, 3H), 2.03 (s, 3H), 2.01 – 1.93 (m, 2H), 1.74 (dd, *J* = 15.2, 3.2 Hz, 1H), 1.69 (d, *J* = 1.4 Hz, 3H), 1.11 – 0.97 (m, 21H); ^{13}C NMR ($CDCl_3$, 101 MHz): δ 171.0, 170.5, 170.0, 137.4, 133.5, 122.7, 117.7, 104.4, 95.5, 82.5, 73.3, 71.1, 70.7, 67.9, 67.8, 66.8, 66.7, 37.9, 34.4, 30.6, 27.0, 22.9, 21.5, 21.0, 20.9, 18.7, 11.4; IR (film, cm^{-1}): 2942, 2865, 2175, 1750, 1463, 1432, 1369, 1223, 1161, 1120, 1101, 1067, 1034, 995, 965, 917, 883, 847, 757, 677, 664, 603, 459, 422; HRMS (ESI) for $C_{34}H_{52}O_9SiNa$ $[M+Na]^+$: calcd. 655.3273; found 655.3274.

Compound S8. Silver(I) fluoride (432 mg, 3.41 mmol) was added to a solution of spiroketal **24** (1.44 g, 2.27 mmol) in acetonitrile (23 mL). The mixture was stirred at room temperature for 19 h. Saturated aqueous NH_4Cl (20 mL) was introduced and the biphasic mixture was vigorously stirred for 90 min. EtOAc (40 mL) was added and the suspension was filtered through a pad of Celite. The aqueous phase was extracted with EtOAc (3 × 20 mL) and the combined organic fractions were washed with brine (50 mL), dried over anhydrous Na_2SO_4, filtered and concentrated. The residue was purified by flash chromatography (hexanes/EtOAc 7:3) to give the title compound as a pale yellow foam (975 mg, 90%). $[\alpha]_D^{20}$ = +32.5 (c = 1.03, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 5.75 (dddd, *J* = 17.4, 10.2, 7.4, 6.2 Hz, 1H), 5.30 (t, *J* = 9.8 Hz, 1H), 5.23 (dt, *J* = 2.6, 1.3 Hz, 1H), 5.17 – 5.07 (m, 3H), 5.03 (q, *J* = 3.1 Hz, 1H), 4.35 (t, *J* = 10.0 Hz, 1H), 4.25 (ddd, *J* = 10.7, 5.9, 4.5 Hz, 1H), 3.94 – 3.85 (m, 1H), 3.54 (dd, *J* = 10.3, 3.1 Hz, 1H), 2.64 – 2.52 (m, 1H), 2.49 – 2.33 (m, 3H), 2.28 (dd, *J* = 15.3, 3.0 Hz, 1H), 2.10 (s, 3H), 2.06 (s, 3H), 2.05 – 2.01 (m, 4H), 1.93 (ddd, *J* = 10.3, 2.4, 1.2 Hz, 1H), 1.86 (dd, *J* = 17.1, 4.0 Hz, 1H), 1.75 (dd, *J* = 15.2, 3.2 Hz, 1H), 1.70 (s, 3H); ^{13}C NMR ($CDCl_3$, 101 MHz): δ 171.1, 170.5, 170.1, 137.4, 133.5, 122.9, 117.7, 95.6, 80.8, 73.2, 71.3, 70.5, 70.0, 67.9, 67.8, 66.9, 66.7, 37.9, 34.4, 30.6, 25.2, 22.8, 21.5, 21.1, 20.9; IR (film, cm^{-1}): 3279, 2933, 1737, 1681, 1643, 1431, 1370, 1223, 1119, 1101, 1066, 1034, 994, 966, 907, 864, 756, 666, 645, 605, 521, 466, 424; HRMS (ESI) for $C_{25}H_{32}O_9Na$ $[M+Na]^+$: calcd. 499.1939; found 499.1940.



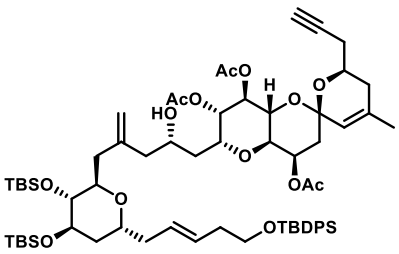
Compound 25. 2,6-Lutidine (379 µL, 3.26 mmol), osmium tetroxide (50.0 µL, 4% in water, 8.14 µmol) and sodium periodate (1.39 g, 6.51 mmol) were sequentially added to a stirred solution of spiroketal **S8** (776 mg, 1.63 mmol) in 1,4-dioxane/H_2O (3:1, 16 mL) at room temperature. The resulting mixture was stirred for 21 h before the reaction was quenched with saturated aqueous $Na_2S_2O_3$ (20 mL). The aqueous phase was extracted with EtOAc (3 × 20 mL) and the combined organic layers were washed with saturated aqueous



NH_4Cl (30 mL) and brine (30 mL), dried over Na_2SO_4 and concentrated. The residue was purified by flash chromatography (hexanes/EtOAc 1:1 to 1:2) to afford the desired aldehyde as a white foam (612 mg, 79%). $[\alpha]_D^{20}$ = +13.3 (c = 1.00, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 9.72 (dd, *J* = 2.4, 1.5 Hz, 1H), 5.26 – 5.13 (m, 3H), 5.05 (q, *J* = 3.1 Hz, 1H), 4.85 (dt, *J* = 7.8, 6.1 Hz, 1H), 4.38 (dd, *J* = 10.3, 9.4 Hz, 1H), 3.89 (dddd, *J* = 10.7, 6.9, 5.8, 3.8 Hz, 1H), 3.52 (dd, *J* = 10.3, 3.1 Hz, 1H), 2.93 – 2.77 (m, 2H), 2.49 – 2.34 (m, 2H), 2.25 (dd, *J* = 15.3, 3.0 Hz, 1H), 2.10 (s, 3H), 2.06 (s, 3H), 2.04 (d, *J* = 2.8 Hz, 1H), 2.01 (s, 3H), 1.94 – 1.91 (m, 1H), 1.90 – 1.83 (m, 1H), 1.76 (dd, *J* = 15.3, 3.3 Hz, 1H), 1.70 (s, 3H); ^{13}C NMR ($CDCl_3$, 101 MHz): δ 198.3, 170.9, 170.4, 169.9, 137.5, 122.7, 95.6, 80.8, 70.3 (two overlapping signals), 70.0, 69.1, 68.8, 67.5, 66.8, 66.4, 41.7, 37.9, 34.4, 25.2, 22.8, 21.4, 21.0, 20.8; IR (film, cm^{-1}): 3281, 2917, 1732, 1428, 1371, 1235, 1161, 1118, 1103, 1066, 1035, 994, 965, 904, 851, 756, 666, 648, 603, 521, 494, 466, 426; HRMS (ESI) for $C_{24}H_{30}O_{10}Na$ $[M+Na]^+$: calcd. 501.1731; found 501.1730.

Improved Fragment Coupling

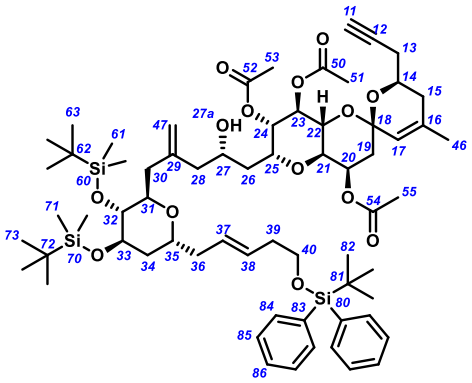
Compound 29. Boron tribromide (1.0 M in CH_2Cl_2, 1.26 mL, 1.26 mmol) was added to a solution of (*S*,*S*)-1,2-diphenyl-1,2-ethylene-diamine bis(toluenesulfonamide) ((*S*,*S*)-**28**; 654 mg, 1.26 mmol)[11] in CH_2Cl_2 (12 mL) at 0 °C. The mixture was stirred for 10 min at 0 °C and for 1 h at ambient temperature before all volatile materials were removed in high vacuum.



A solution of allyl stannane **4** (1.32 g, 1.30 mmol) in CH_2Cl_2 (3.0 mL) was added dropwise at 0 °C to a solution of the residue in CH_2Cl_2 (10 mL). After stirring for 17 h at ambient temperature, the mixture was cooled to −78 °C and a solution of aldehyde **25** (415 mg, 0.867 mmol) in CH_2Cl_2 (2.0 mL) was added dropwise over the course of 5 min. The mixture was stirred for 3 h before the reaction was quenched with aq. phosphate buffer (pH 7.4, 15 mL). Water (15 mL) was introduced and the aqueous phase was extracted with EtOAc (3 × 20 mL). The combined organic extracts were washed with brine (20 mL), dried over Na_2SO_4, filtered and concentrated. The residue was suspended in Et_2O (5 mL) and the colorless solid was filtered off to recover the chiral diamine ligand. The filtrate was evaporated and the residue purified by flash chromatography (fine silica, hexanes/EtOAc, 3:1) to give the title compound as a colorless oil (877 mg, 84%). A second fraction contained the diastereoisomer **S9** epimeric at C27 (163 mg, 16%).

Analytical and spectral data of the major diastereoisomer **29**: $[\alpha]_D^{20}$ = +19.6 (c = 1.00, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.70 – 7.63 (m, 4H), 7.44 – 7.34 (m, 6H), 5.52 – 5.34 (m, 2H), 5.26 – 5.19 (m, 2H), 5.15 (dd, *J* = 9.8, 5.8 Hz, 1H), 5.05 (q, *J* = 3.0 Hz, 1H), 4.96 (d, *J* = 1.8 Hz, 1H), 4.92 – 4.87 (m, 1H), 4.49 (ddd, *J* = 11.7, 5.7, 2.6 Hz, 1H), 4.38 (t, *J* = 9.8 Hz, 1H), 3.95 – 3.74 (m, 5H), 3.65 (t, *J* = 6.9 Hz, 2H), 3.53 (dd, *J* = 10.2, 3.0 Hz, 1H), 3.37 (dd, *J* = 3.8, 2.3 Hz, 1H), 2.67 (dd, *J* = 14.3, 9.1 Hz, 1H), 2.42 (tddt, *J* = 16.8, 12.5, 8.6, 4.3 Hz, 3H), 2.32 – 2.14 (m, 7H), 2.10 (s, 4H), 2.06 (s, 3H), 2.03 (s, 3H), 2.00 – 1.83 (m, 3H), 1.77 (ddd, *J* = 12.7, 8.5, 2.9 Hz, 2H), 1.69 (s, 3H), 1.67 – 1.56 (m, 2H), 1.46 – 1.36 (m, 1H), 1.04 (s, 9H), 0.94 – 0.85 (m, 18H), 0.05 (s, 3H), 0.04 (s, 6H), 0.02 (s, 3H); ^{13}C NMR ($CDCl_3$, 101 MHz): δ 171.0, 170.4, 170.0, 144.0, 137.4, 135.7, 134.2, 129.7, 129.2, 128.2, 127.8, 127.7, 122.9, 115.4, 95.6, 80.8, 77.1, 71.2, 70.9, 70.8, 70.7, 70.3, 70.1, 68.4, 67.9, 66.8, 66.7, 65.3, 64.1, 44.8, 38.7, 37.9, 37.6, 36.2, 34.4, 33.9, 32.1, 28.0, 27.0, 26.0, 25.2, 22.8, 21.5, 21.1, 21.0, 19.3, 18.2, 18.1, 17.7, 13.7, −4.3, −4.4, −4.4, −4.7; IR (film, cm^{-1}): 2954, 2929, 2895, 2857, 1753, 1471, 1462, 1428, 1380, 1366, 1239, 1160, 1094, 1069, 1036, 1006, 967, 836, 776, 742, 704, 613, 505, 489; HRMS (ESI) for $C_{66}H_{100}O_{14}Si_3Na$ $[M+Na]^+$: calcd. 1223.6313; found 1223.6305.

Table S6. Detailed analysis of the NMR data of compound **29**; arbitrary numbering scheme as shown in the insert.

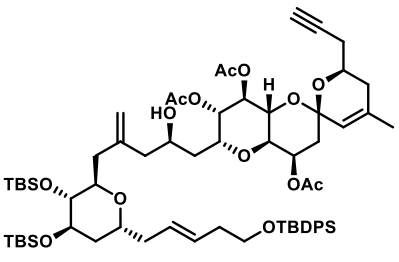


atom number	**^{1}H NMR** ($CDCl_3$, 600 MHz)				**^{13}C NMR** ($CDCl_3$, 151 MHz)/ **^{29}Si NMR** ($CDCl_3$, 119 MHz)	
	δ [ppm]	***J*** [Hz]	**COSY**	**NOESY**	δ [ppm]	**HMBC**
11	2.05	2.6	13a, 13b	-	69.9	13a, 13b
12	-	-	-	-	80.6	11, 13a, 13b, 14
13a	2.46	16.6, 6.8, 2.6	11, 13b, 14	-	25.1	11, 14, 15a
13b	2.39	16.6, 5.8, 2.7	11, 13a, 14	-		
14	3.91	10.5, 6.4, 3.5	13a, 13b, 15a, 15b	22	66.5	13a, 13b, 15a, 15b
15a	1.95	-	14, 15b, 17	46	34.2	13a, 13b, 17, 46
15b	1.87	17.0, 3.7	14, 15a, 17	46		
16	-	-	-	-	137.2	15a, 15b, 46
17	5.22	-	15a, 15b, 46	19a, 19b, 46	122.7	15a, 15b, 19b, 46

atom number	**^{1}H NMR** ($CDCl_3$, 600 MHz)				**^{13}C NMR** ($CDCl_3$, 151 MHz)/ **^{29}Si NMR** ($CDCl_3$, 119 MHz)	
	δ [ppm]	***J*** [Hz]	**COSY**	**NOESY**	δ [ppm]	**HMBC**
18	-	-	-	-	95.4	14, 17, 19a, 19b, 20, 22
19a	2.29	15.3, 3.0	19b, 20	17, 20	37.7	17
19b	1.76	15.3, 3.1	19a, 20	17, 20, 21, 23		
22	4.38	9.9	21, 23	14, 24	66.7	20, 21, 23, 24
23	5.22	9.7	22, 24	19b, 21, 26b	70.6	21, 22, 24, 25
24	5.15	9.8, 5.9	23, 25	22, 25	70.6	23, 25, 26a
25	4.50	11.7, 5.9, 2.6	24, 26a, 26b	24, 26b, 27, 27a	70.7	23, 24, 26a
26a	1.94	14.9, 11.4, 7.4	25, 26b, 27	21	32.0	24, 25, 28a, 28b
26b	1.61	-	25, 26a, 27	23, 25, 27		
27	3.87	-	26a, 26b, 28a, 28b	25, 26b, 28a, 28b, 47''	65.2	25, 26b, 28a, 28b
27a	2.26	-	-	25, 47''	-	-
28a	2.27	-	27, 28b, 47''	27, 31, 47''	44.6	26b, 30a, 30b, 47', 47''
28b	2.16	13.9, 9.1	27, 28a, 47''	27, 47''		
29	-	-	-	-	143.8	28a, 28b, 30a, 30b, 31, 47', 47''
30a	2.67	14.3, 9.2	30b, 31, 47'	31, 35, 47'	37.5	28a, 28b, 31, 32, 47', 47''
30b	2.41	14.7, 4.4	30a, 31, 47', 47''	31, 32, 47'		
31	3.78	10.9, 4.7, 2.2	30a, 30b, 32	28a, 30a, 30b, 32, 47''	76.9	30a, 30b, 33, 35
32	3.37	3.5, 2.3	31, 33, 34b	30b, 31, 33, 47', 61, 61'	71.1	30a, 30b, 31, 33, 34b
33	3.80	3.9	32, 34a, 34b	32, 34a, 34b	70.1	32, 34a, 34b
34a	1.77	-	33, 34b, 35	33	33.7	32, 36a, 36b
34b	1.40	13.5	32, 33, 34a, 35	33		
35	3.83	-	34a, 34b, 36a, 36b	30a, 36a, 36b, 37	65.2	31, 33, 34a, 36a, 36b, 37
36a	2.22	-	35, 36b, 37	35	38.5	35, 37, 38
36b	2.08	-	35, 36a, 37	35		
37	5.40	15.4, 7.2, 6.2, 1.0	36a, 36b, 38	35	128.0	35, 36a, 36b, 38, 39
38	5.46	15.1, 6.5	37, 39	40	129.1	36a, 36b, 37, 39, 40
39	2.26	-	38, 40	-	36.1	37, 38, 40
40	3.65	-	39	38	64.0	38, 39
46	1.70	-	17	15a, 15b, 17	22.7	15b
47'	4.96	1.8	30a, 30b, 47''	30a, 30b, 31, 32	115.3	28a, 28b, 30a, 30b
47''	4.89	2.0	28a, 28b, 30b, 47'	27, 27a, 28a, 28b		
50	-	-	-	-	170.3	23, 51

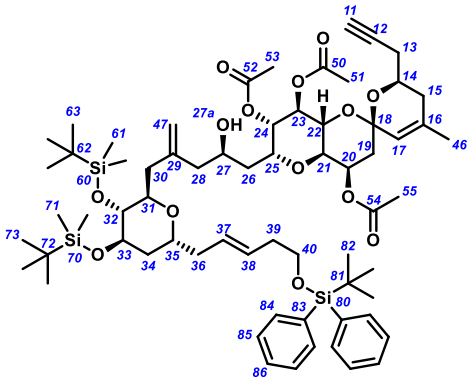
atom number	^{1}H NMR ($CDCl_3$, 600 MHz)				^{13}C NMR ($CDCl_3$, 151 MHz)/ ^{29}Si NMR ($CDCl_3$, 119 MHz)	
	δ [ppm]	*J* [Hz]	COSY	NOESY	δ [ppm]	HMBC
51	2.06	-	-	-	20.9	-
52	-	-	-	-	169.8	24, 53
53	2.03	-	-	-	20.8	-
54	-	-	-	-	170.9	20, 55
55	2.10	-	-	-	21.3	-
60	-	-	-	-	18.4	32, 61, 61’
61	0.04	-	-	32	−4.4	61’
61’	0.04	-	-	32	−4.6	61
62	-	-	-	-	18.0	61, 61’, 63
63	0.89	-	-	-	25.9	63
70	-	-	-	-	18.5	33, 71, 71’
71	0.05	-	-	-	−4.5	71’
71’	0.02	-	-	-	−4.9	71
72	-	-	-	-	18.0	71, 71’, 73
73	0.88	-	-	-	25.6	73
80	-	-	-	-	−4.8	40, 82, 84
81	-	-	-	-	19.2	82
82	1.04	-	-	-	26.8	82
83	-	-	-	-	134.0	84, 85
83’	-	-	-	-	134.0	84’, 85’
84	7.66	-	85	-	135.5	84,86
84’	7.66	-	85’	-	135.5	84’, 86’
85	7.37	-	84, 86	-	127.6	84, 85
85’	7.37	-	84’, 86’	-	127.6	84’, 85’
86	7.40	-	85	-	129.5	84
86’	7.40	-	85’	-	129.5	84’

Analytical and spectral data of the minor diastereoisomer **S9**: $[\alpha]_D^{20}$ = +12.1 (c = 1.00, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.69 – 7.63 (m, 4H), 7.45 – 7.33 (m, 6H), 5.52 – 5.33 (m, 2H), 5.26 (t, *J* = 9.7 Hz, 1H), 5.23 – 5.20 (m, 1H), 5.13 – 5.01 (m, 2H), 4.92 (s, 1H), 4.89 (s, 1H), 4.46 – 4.27 (m, 2H), 3.95 – 3.86 (m, 2H), 3.80 (dt, *J* = 7.1, 3.1 Hz, 3H), 3.75 (dd, *J* = 10.3, 3.0 Hz, 1H), 3.65 (t, *J* = 6.9 Hz, 2H), 3.32 (dd, *J* = 3.9, 2.2 Hz, 1H), 2.87 – 2.77 (m, 2H), 2.42 (qdd, *J*



= 16.6, 6.3, 2.7 Hz, 2H), 2.33 – 2.11 (m, 7H), 2.09 (s, 3H), 2.06 (s, 3H), 2.05 – 2.04 (m, 2H), 2.03 (s, 3H), 2.00 – 1.83 (m, 3H), 1.81 – 1.72 (m, 2H), 1.70 (s, 3H), 1.67 – 1.62 (m, 1H), 1.39 (dt, *J* = 14.0, 3.1 Hz, 1H), 1.04 (s, 9H), 0.92 – 0.85 (m, 18H), 0.07 – 0.03 (m, 9H), 0.02 (s, 3H); ^{13}C NMR ($CDCl_3$, 101 MHz): δ 171.0, 170.4, 170.0, 143.8, 137.3, 135.7, 134.2, 129.7, 129.0, 128.4, 127.7, 123.0, 115.3, 95.5, 80.9, 76.4, 73.4, 71.8, 71.2, 70.6, 70.3, 70.0, 68.7, 68.4, 67.7, 66.8, 66.7, 65.2, 64.1, 43.4, 38.6, 37.9, 36.9, 36.2, 34.4, 34.1, 32.1, 27.0, 26.1, 26.0, 26.0, 25.9, 25.3, 22.8, 21.5, 21.1, 20.9, 19.4, 18.2, 18.1, −4.4, −4.4, −4.6, −4.7; IR (film, cm^{-1}): 2953, 2929, 2894, 2857, 1751, 1472, 1428, 1380, 1366, 1238, 1094, 1068, 1036, 1006, 967, 836, 776, 741, 704, 506; HRMS (ESI) for $C_{66}H_{100}O_{14}Si_3Na$ $[M+Na]^+$: calcd. 1223.6313; found 1223.6314.

Table S7. Detailed analysis of the NMR data of the minor diastereomer **S9**; arbitrary numbering scheme as shown in the insert.



atom number	**^{1}H NMR** ($CDCl_3$, 600 MHz)				**^{13}C NMR** ($CDCl_3$, 151 MHz)/ **^{29}Si NMR** ($CDCl_3$, 119 MHz)	
	δ [ppm]	***J*** [Hz]	**COSY**	**NOESY**	δ [ppm]	**HMBC**
11	2.05	2.6	13a, 13b	-	69.9	13a, 13b
12	-	-	-	-	80.7	11, 13a, 13b, 14
13a	2.45	16.7, 6.9, 2.6	11, 13b, 14	-	25.1	11, 14, 15a
13b	2.39	16.6, 5.8, 2.6	11, 13a, 14	-		
14	3.90	-	13a, 13b, 15a, 15b	-	66.5	13a, 13b, 15a, 15b
15a	1.95	-	14, 15b, 17	46	34.2	13a, 13b, 17, 46
15b	1.87	17.2, 3.6	14, 15a, 17	46		
16	-	-	-	-	137.1	15a, 15b, 46
17	5.22	-	15a, 15b, 46	19a, 19b	122.8	15a, 15b, 19b, 46
18	-	-	-	-	95.4	14, 17, 19a, 19b, 20, 22
19a	2.26	15.3, 3.0	20	17, 20	37.7	17
19b	1.77	15.4, 3.2	20	17, 20, 21, 23		
20	5.04	3.0	19a, 19b, 21	19a, 19b, 21	67.6	19a, 21, 22
21	3.75	10.3, 3.0	20, 22	19b, 20, 23, 26a	68.2	19a, 20, 23, 25
22	4.36	10.0	21, 23	-	66.6	20, 21, 23, 24

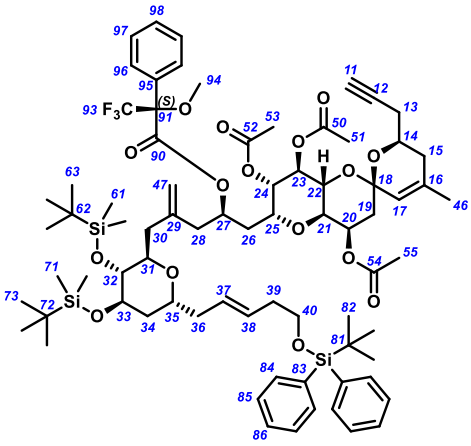
atom number	^{1}H NMR ($CDCl_3$, 600 MHz)				^{13}C NMR ($CDCl_3$, 151 MHz)/ ^{29}Si NMR ($CDCl_3$, 119 MHz)	
	δ [ppm]	*J* [Hz]	COSY	NOESY	δ [ppm]	HMBC
23	5.26	9.7	22, 24	19b, 21, 26b	70.4	21, 22, 24, 25
24	5.07	9.8, 5.9	23, 25	25	71.0	23, 25, 26a
25	4.35	-	24, 26a, 26b	24, 26b, 27, 28a	73.2	23, 24, 26a, 27, 31
26a	2.02	14.9, 11.4, 7.4	25, 26b, 27	21	31.9	24, 25, 27a
26b	1.67	-	25, 26a, 27	23, 25, 27		
27	3.90	-	26a, 26b, 28a, 28b	25, 26b, 27a, 47''	68.5	25, 26a, 26b, 28a, 28b
27a	2.84	-	-	27	-	-
28a	2.28	-	27, 47''	25, 31, 47''	43.2	30a, 47', 47''
28b	2.13	14.2, 9.3	27	47''		
29	-	-	-	-	143.6	28a, 28b, 30a, 30b, 31, 47', 47''
30a	2.82	14.6, 10.6	30b, 31	31, 32, 35, 47'		31, 32, 47', 47''
30b	2.22	14.7, 4.4	30a, 31, 47'	31, 47'		
31	3.82	10.9, 4.7, 2.2	30a, 30b, 32	28a, 30a, 30b, 32, 47'	76.2	30a, 30b, 33, 35
32	3.33	3.9, 2.3	31, 33	30a, 31, 33, 47', 61, 61'	71.6	30a, 30b, 31, 33, 34b
33	3.79	3.9	32	32, 34a, 34b	70.1	31, 32, 34b, 35
34a	1.76	-	34b	33	33.9	32, 36a, 36b
34b	1.39	-	34a	33		
35	3.81	-	-	30a, 36a, 36b, 37	65.0	31, 33, 34a, 36a, 36b, 37
36a	2.19	-	36b, 37	35	38.4	35, 37, 38
36b	2.06	-	36a, 37	35		
37	5.39	-	36a, 36b, 38	35	128.2	35, 36a, 36b, 38, 39
38	5.44	-	37, 39	40	128.9	36a, 36b, 37, 39, 40
39	2.26	-	38, 40	-	36.1	37, 38, 40
40	3.65	-	39	38	64.0	38, 39
46	1.70	-	17	15a, 15b	22.7	17
47'	4.92	-	30b	30a, 30b, 31, 32	115.1	28a, 28b, 30a, 30b
47''	4.89	-	28a	27, 28a, 28b		
50	-	-	-	-	170.2	23, 51
51	2.06	-	-	-	20.9	-
52	-	-	-	-	169.8	24, 53
53	2.03	-	-	-	20.8	-
54	-	-	-	-	170.8	20, 55
55	2.09	-	-	-	21.3	-

atom number	**^{1}H NMR** ($CDCl_3$, 600 MHz)				**^{13}C NMR** ($CDCl_3$, 151 MHz)/ **^{29}Si NMR** ($CDCl_3$, 119 MHz)	
	δ [ppm]	***J*** [Hz]	**COSY**	**NOESY**	δ [ppm]	**HMBC**
60	-	-	-	-	18.3	32, 61, 61', 63
61	0.04	-	-	-	−4.5	61'
61'	0.04	-	-	-	−4.6	61
62	-	-	-	-	18.1	61, 61', 63
63	0.88	-	-	-	25.9	63
70	-	-	-	-	18.5	33, 71, 71', 73
71	0.05	-	-	-	−4.6	71'
71'	0.02	-	-	-	−4.9	71
72	-	-	-	-	25.8	73
73	0.88	-	-	-	25.8	73
80	-	-	-	-	−4.8	40, 82, 84, 84', 85, 85'
81	-	-	-	-	19.2	82
82	1.04	-	-	-	26.8	82
83	-	-	-	-	134.0	84, 84', 85, 85'
83'	-	-	-	-	134.0	-
84	7.66	-	85	-	135.5	84, 86
84'	7.66	-	85'	-	135.5	84', 86'
85	-	-	-	-	127.6	85
85'	-	-	-	-	127.6	85'

Preparation of the (*S*)- and (*R*)-MTPA esters (S8) of the minor diastereomer S9. (*R*)-(−)-MTPA-Cl (4.2 mg, 17 µmol) and DMAP (0.20 mg, 1.7 µmol) were added to a stirred solution of **S9** (10 mg, 8.3 µmol) and pyridine (2.1 µL, 26 µmol) in CH_2Cl_2 (0.2 mL) at room temperature. Stirring was continued for 16 h before the reaction was quenched with H_2O (1 mL) and the mixture was diluted with EtOAc (2 mL). The aqueous phase was extracted with EtOAc (2 × 2 mL). The combined organic fractions were dried over anhydrous Na_2SO_4, filtered and concentrated. The residue was purified by flash chromatography (hexanes/EtOAc 4:1) to give (*S*)-**S10** as a pale yellow oil (9.3 mg, 79%).

(*R*)-**S10** was prepared analogously using (*S*)-(+)-MTPA-Cl.

Table S8. Analysis of the NMR data of (*S*)-**S10**; arbitrary numbering scheme as shown in the insert.

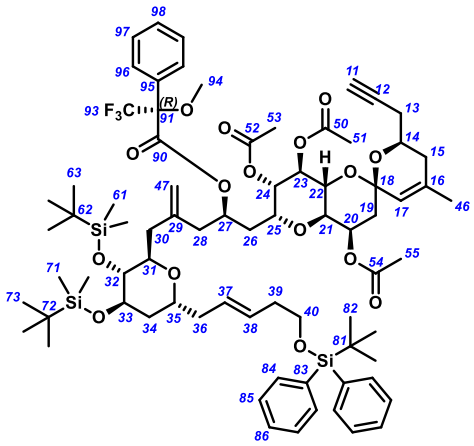


atom number	**^{1}H NMR** ($CDCl_3$, 600 MHz)				**^{13}C NMR** ($CDCl_3$, 151 MHz)/ **^{29}Si NMR** ($CDCl_3$, 119 MHz)	
	δ [ppm]	***J*** [Hz]	**COSY**	**NOESY**	δ [ppm]	**HMBC**
11	2.05	2.6	13a, 13b	22	69.9	13a, 13b
12	-	-	-	-	80.7	11, 13a, 13b, 14
13a	2.45	16.7, 6.8, 2.8	11, 13b, 14	-	25.1	11, 14, 15a
13b	2.39	16.7, 5.9, 2.7	11, 13a, 14	-		
14	3.91	10.8, 6.9, 5.9, 3.6	13a, 13b, 15a, 15b	-	66.5	13a, 13b, 15a
15a	1.95	-	14, 15b, 17	-	34.2	13a, 13b, 17, 46
15b	1.88	17.5, 3.6	14, 15a, 17	-		
16	-	-	-	-	137.2	15a, 15b, 46
17	5.25	-	15a, 15b, 46	-	122.8	15b, 46
18	-	-	-	-	95.5	14, 17, 19a, 19b, 20, 22
19a	2.30	15.3, 3.1	19b, 20	-	37.7	17
19b	1.78	15.3, 3.1	19a, 20	-		
20	5.10	3.1	19a, 19b, 21	19b, 21	67.9	19a, 21, 22
21	3.72	10.3, 3.0	20, 22	19b, 20, 23, 26a	68.4	19a, 20, 22, 23, 25
22	4.36	10.0	21, 23	11, 24, 55	66.6	21, 23, 24
23	5.19	9.6	22, 24	21	70.4	22, 24, 25, 51
24	5.09	9.7, 5.9	23, 25	22	70.6	23, 25, 53
25	4.16	11.1, 5.9, 3.5	24, 26a, 26b	-	70.8	24, 26a, 27
26a	2.17	-	25, 26b, 27	21	29.4	24, 27, 28
26b	1.83	-	25, 26a, 27	-		
27	5.34	-	26a, 26b, 28	47''	72.7	25, 26a, 28
28	2.41	-	27, 47''	31, 47''	39.0	26a, 27, 30a, 30b, 47', 47''
29	-	-	-	-	142.0	27, 28, 30a, 30b, 31, 47', 47''

atom number	**^{1}H NMR** ($CDCl_3$, 600 MHz)				**^{13}C NMR** ($CDCl_3$, 151 MHz)/ **^{29}Si NMR** ($CDCl_3$, 119 MHz)	
	δ [ppm]	***J*** [Hz]	**COSY**	**NOESY**	δ [ppm]	**HMBC**
30a	2.76	14.6, 9.9	30b, 31, 47'	47'	36.7	28, 31, 47', 47''
30b	2.28	-	30a, 31, 47'	32		
31	3.74	-	30a, 30b, 32	28, 32, 47'	76.4	30a, 30b, 33
32	3.33	3.9, 2.0	31, 33	30b, 31, 47'	71.2	30a, 31, 34b
33	3.79	-	32, 34a, 34b	34a, 34b	70.1	31, 32, 34b
34a	1.75	13.4, 10.4, 2.9	33, 34b, 35	33	33.7	34a, 34b
34b	1.38	14.4	33, 34a, 35	33		
35	3.79	-	34a, 34b, 36a, 36b	-	64.7	31, 34a, 36a, 36b, 37
36a	2.17	-	35, 36b, 37	-	38.6	37, 38
36b	2.05	-	35, 36a, 37	-		
37	5.39	-	36a, 36b, 38	-	128.3	35, 36a, 36b, 39
38	5.43	-	37, 39	-	128.7	36a, 36b, 39, 40
39	2.25	-	38, 40	-	36.1	37, 38, 40
40	3.64	7.0	39	-	64.0	38, 39
46	1.70	-	17	-	22.7	15b, 17
47'	4.89	-	30a, 30b	30a, 31, 32	115.7	28, 30a, 30b
47''	4.83	-	28	27, 28		
50	-	-	-	-	170.2	23, 51
51	2.06	-	-	-	20.9	-
52	-	-	-	-	169.7	24, 53
53	2.01	-	-	-	20.7	-
54	-	-	-	-	170.7	55
55	2.08	-	-	22	21.3	-
61	0.01, 0.02, 0.03, 0.04	-	-	-	−4.92, −4.68, −4.66, −4.61	-
61'	0.01, 0.02, 0.03, 0.04	-	-	-	−4.92, −4.68, −4.66, −4.61	-
62	-	-	-	-	17.94, 17.99	-
63	0.88, 0.88	-	-	-	25.83, 25.85	-
71	0.01, 0.02, 0.03, 0.04	-	-	-	−4.92, −4.68, −4.66, −4.61	-
71'	0.01, 0.02, 0.03, 0.04	-	-	-	−4.92, −4.68, −4.66, −4.61	-
72	-	-	-	-	17.94, 17.99	-
73	0.88, 0.88	-	-	-	25.83, 25.85	-
81	-	-	-	-	19.2	82
82	1.04	-	-	-	26.8	82
83	-	-	-	-	134.02, 134.03	84, 85

atom number	^{1}H NMR ($CDCl_3$, 600 MHz)				^{13}C NMR ($CDCl_3$, 151 MHz)/ ^{29}Si NMR ($CDCl_3$, 119 MHz)	
	δ [ppm]	*J* [Hz]	COSY	NOESY	δ [ppm]	HMBC
83'	-	-	-	-	134.02, 134.03	84', 85'
84	7.66	-	85	-	135.6	84, 86
84'	7.66	-	85'	-	135.6	84', 86'
85	7.37	-	84	-	127.6	85
85'	7.37	-	84'	-	127.6	85'
86	7.41	-	-	-	129.5	84
86'	7.41	-	-	-	129.5	84'
90	-	-	-	-	166.2	27
91	-	-	-	-	84.9	94, 96
92	-	-	-	-	122.7	-
94	3.42	1.30	-	-	55.9	-
95			Signals not found			
96	7.41	-	-	-	Signal not found	
97			Signals not found			
98			Signals not found			

Table S9. Analysis of the NMR data of (*R*)-**S10**; arbitrary numbering scheme as shown in the insert.

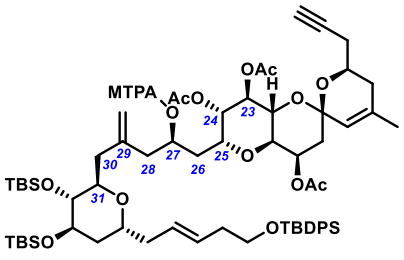


atom number	^{1}H NMR ($CDCl_3$, 600 MHz)				^{13}C NMR ($CDCl_3$, 151 MHz)/ ^{29}Si NMR ($CDCl_3$, 119 MHz)	
	δ [ppm]	*J* [Hz]	COSY	NOESY	δ [ppm]	HMBC
11	2.05	2.6	13a, 13b	22	69.9	13a, 13b
12	-	-	-	-	80.7	11, 13a, 13b, 14
13a	2.45	16.5, 6.8, 2.6	11, 13b, 14	-	25.1	11, 14, 15a
13b	2.39	16.7, 5.8, 2.7	11, 13a, 14	-		
14	3.89	-	13a, 13b, 15a, 15b	-	66.5	13a, 13b, 15a

atom number	**^{1}H NMR** ($CDCl_3$, 600 MHz)				**^{13}C NMR** ($CDCl_3$, 151 MHz)/ **^{29}Si NMR** ($CDCl_3$, 119 MHz)	
	δ [ppm]	***J*** [Hz]	**COSY**	**NOESY**	δ [ppm]	**HMBC**
15a	1.94	-	14, 15b, 17	-	34.2	13a, 13b, 17, 46
15b	1.87	17.2, 3.6	14, 15a, 17	-		
16	-	-	-	-	137.2	15a, 15b, 46
17	5.24		15a, 15b, 46	-	122.8	15b, 46
18	-	-	-	-	95.5	14, 17, 19a, 19b, 20, 22
19a	2.28	-	19b, 20	-	37.6	17
19b	1.76	-	19a, 20	20, 21		
20	5.07	3.1	19a, 19b, 21	19b, 21	67.8	19a, 21, 22
21	3.68	10.3, 3.0	20, 22	19b, 20, 23, 26a	68.4	19a, 20, 22, 23, 25
22	4.37	9.9	21, 23	11, 24, 55	66.6	21, 23, 24
23	5.20	9.7	22, 24	21	70.4	22, 24, 25, 51
24	5.12	9.8, 5.8	23, 25	22	70.6	23, 25, 53
25	4.22	10.7, 5.9, 3.6	24, 26a, 26b	-	70.8	24, 26a, 27
26a	2.20	-	25, 26b, 27	21	29.7	24, 27, 28
26b	1.93	-	25, 26a, 27	-		
27	5.30	-	26a, 26b, 28	47''	72.8	25, 26a, 28
28	2.35	-	27, 47''	31, 47''	38.9	26a, 27, 30a, 30b, 47', 47''
29	-	-	-	-	141.6	27, 28, 30a, 30b, 31, 47', 47''
30a	2.66	14.6, 9.7	30b, 31, 47'	47'	36.7	28, 31, 47', 47''
30b	2.25	-	30a, 31, 47'	32		
31	3.71	-	30a, 30b, 32	28, 32, 47'	76.4	30a, 30b
32	3.32	3.6, 1.7	31, 33	30b, 31, 47'	71.0	30a, 31, 34b
33	3.77	-	32, 34a, 34b	34a, 34b	70.1	31, 32, 34b
34a	1.73	-	33, 34b, 35	33	33.7	32, 36a, 36b
34b	1.36	14.4, 2.4, 4.4	33, 34a, 35	33		
35	3.75	-	34a, 34b, 36a, 36b	-	64.6	31, 34a, 36a, 36b, 37
36a	2.16	-	35, 36b, 37	-	38.7	37, 38
36b	2.04	-	35, 36a, 37	-		
37	5.38	-	36a, 36b, 38	-	128.3	36a, 36b, 39
38	5.43	-	37, 39	-	128.7	36a, 36b, 39, 40
39	2.25	-	38, 40	-	36.1	37, 38, 40
40	3.64	7.0	39	-	64.0	38, 39
46	1.70	-	17	-	22.7	15b, 17

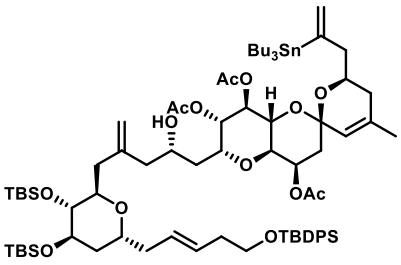
atom number	**^{1}H NMR** ($CDCl_3$, 600 MHz)				**^{13}C NMR** ($CDCl_3$, 151 MHz)/ **^{29}Si NMR** ($CDCl_3$, 119 MHz)	
	δ [ppm]	***J*** [Hz]	**COSY**	**NOESY**	δ [ppm]	**HMBC**
47'	4.76	-	30a, 30b	30a, 31, 32	115.6	28, 30a, 30b
47''	4.71	-	28	27, 28		
50	-	-	-	-	170.2	23, 51
51	2.06	-	-	-	20.9	-
52	-	-	-	-	169.7	24, 53
53	2.03	-	-	-	20.7	-
54	-	-	-	-	170.7	55
55	2.09	-	-	22	21.3	-
61	0.02, 0.03, 0.04	-	-	-	−4.93, −4.70, −4.66, −4.62	-
61'	0.02, 0.03, 0.04	-	-	-	−4.93, −4.70, −4.66, −4.62	-
62	-	-	-	-	17.95, 17.99	-
63	0.88, 0.88	-	-	-	25.83, 25.84	-
71	0.02, 0.03, 0.04	-	-	-	−4.93, −4.70, −4.66, −4.62	-
71'	0.02, 0.03, 0.04	-	-	-	−4.93, −4.70, −4.66, −4.62	-
72	-	-	-	-	17.95, 17.99	-
73	0.88, 0.88	-	-	-	25.83, 25.84	-
81	-	-	-	-	19.2	82
82	1.04	-	-	-	26.8	82
83	-	-	-	-	134.0	84, 85
83'	-	-	-	-	134.0	84', 85'
84	7.66	-	85	-	135.6	84, 86
84'	7.66	-	85'	-	135.6	84', 86'
85	7.37	-	84	-	127.6	85
85'	7.37	-	84'	-	127.6	85'
86	7.41	-	-	-	129.5	84
86'	7.41	-	-	-	129.5	84'
90	-	-	-	-	166.1	27
91	-	-	-	-	84.9	94, 96
92	-	-	-	-	122.7	-
94	3.42	1.3	-	-	55.9	-
95			Signals not found			
96	7.41	-	-	-	-	-
97			Signals not found			
98			Signals not found			

Table S10. Analysis of the Mosher esters **S10** according to Hoye and co-workers;[12] arbitrary numbering scheme as shown in the insert.



Atom number	(*S*)-268 δ [ppm]	(*R*)-268 δ [ppm]	Δδ [ppm]
31	3.74	3.71	+0.03
30a	2.76	2.66	+0.10
30b	2.28	2.25	+0.03
28	2.41	2.35	+0.06
27	5.34	5.30	+0.04
26a	2.17	2.20	−0.03
26b	1.83	1.93	−0.10
25	4.16	4.22	−0.06
24	5.09	5.12	−0.03
23	5.19	5.20	−0.01

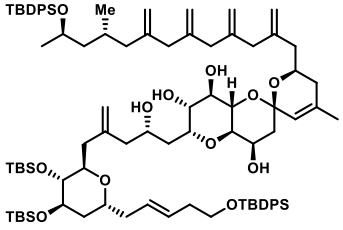
Compound 30. *n*-Butyllithium (1.6 M in hexanes, 2.39 mL, 3.83 mmol) was added to a solution of hexabutylditin (2.03 mL, 4.02 mmol) in THF (7.0 mL) at −20 °C. The mixture was stirred at this temperature for 15 min to give a pale yellow solution of tributylstannyllithium. This solution was cooled to −40 °C before solid copper(I) cyanide (171 mg, 1.91 mmol) was added in one portion. The mixture was cooled to −78 °C over 30 min. Methanol (1.55 mL, 38.3 mmol) and a solution of compound **29** (766 mg, 0.638 mmol) in THF (1.0 mL, 2 × 1.0 mL washes) were added sequentially at this temperature and the orange mixture was stirred at −78 °C for 2 h. The mixture was warmed to room temperature before sat. aq. NH_4Cl (15 mL), water (5 mL), and EtOAc (20 mL) were introduced. The aqueous phase was extracted with EtOAc (3 × 15 mL) and the combined organic extracts were washed with brine (20 mL), dried over Na_2SO_4, filtered and concentrated. The residue was purified by flash chromatography (hexanes/18% EtOAc + 1% NEt_3) to give the title compound as a colorless oil (762 mg, 80%). $[\alpha]_D^{20}$ = +22.7 (c = 1.00, CH_2Cl_2); ^{1}H NMR (CD_2Cl_2, 400 MHz): δ 7.67 (dt, *J* = 6.4, 1.7 Hz, 4H), 7.48 – 7.32 (m, 6H), 5.93 – 5.82 (m, 1H), 5.55 – 5.36 (m, 2H), 5.30 (dd, *J* = 2.7, 1.3 Hz, 1H), 5.27 – 5.18 (m, 2H), 5.09 – 5.01 (m, 2H),



4.96 (d, *J* = 1.9 Hz, 1H), 4.89 (d, *J* = 1.9 Hz, 1H), 4.48 (ddd, *J* = 11.7, 6.0, 2.6 Hz, 1H), 4.25 (t, *J* = 9.9 Hz, 1H), 3.95 (ddt, *J* = 9.8, 8.5, 4.9 Hz, 1H), 3.88 – 3.75 (m, 4H), 3.68 (t, *J* = 6.9 Hz, 2H), 3.51 (dd, *J* = 10.1, 3.1 Hz, 1H), 3.40 (dd, *J* = 3.7, 2.0 Hz, 1H), 2.76 (dd, *J* = 14.4, 9.4 Hz, 1H), 2.69 (dd, *J* = 14.8, 5.5 Hz, 1H), 2.41 – 2.14 (m, 8H), 2.10 (dd, *J* = 14.3, 7.6 Hz, 1H), 2.05 (s, 3H), 2.02 (s, 3H), 2.01 (s, 3H), 2.00 – 1.91 (m, 1H), 1.85 – 1.78 (m, 3H), 1.75 (td, *J* = 6.6, 2.9 Hz, 1H), 1.70 (d, *J* = 1.4 Hz, 3H), 1.62 – 1.47 (m, 7H), 1.45 – 1.39 (m, 1H), 1.39 – 1.26 (m, 7H), 1.04 (s, 9H), 0.96 – 0.87 (m, 33H), 0.09 – 0.06 (m, 9H), 0.04 (s, 3H); ^{13}C NMR (CD_2Cl_2, 101 MHz): δ 170.9, 170.6, 170.0, 150.6, 144.6, 138.2, 135.9, 134.5, 129.9, 129.3, 128.8, 128.0, 127.6, 122.9, 115.3, 95.6, 77.4, 71.6, 71.3, 71.0, 70.7, 70.6, 68.7, 68.1, 67.1, 65.5, 65.2, 64.5, 46.6, 45.1, 39.1, 38.5, 37.7, 36.5, 35.2, 34.2, 32.4, 29.5, 27.8, 27.8, 27.0, 26.1, 26.1, 23.0, 21.5, 21.2, 21.0, 19.5, 18.4, 18.3, 13.9, 9.9, 9.7, −4.4, −4.4, −4.5, −4.7; ^{119}Sn NMR (CD_2Cl_2, 149 MHz): δ −43.6; IR (film, cm^{-1}): 2954, 2928, 2856, 1754, 1471, 1463, 1428, 1378, 1364, 1236, 1090, 1070, 1006, 964, 939, 919, 836, 776, 740, 703, 688, 671, 613, 505; HRMS (ESI) for $C_{78}H_{128}O_{14}Si_3SnNa$ [M+Na]$^+$: calcd. 1515.7526; found 1515.7518.

Completion of the "Second Generation" Total Synthesis of Limaol

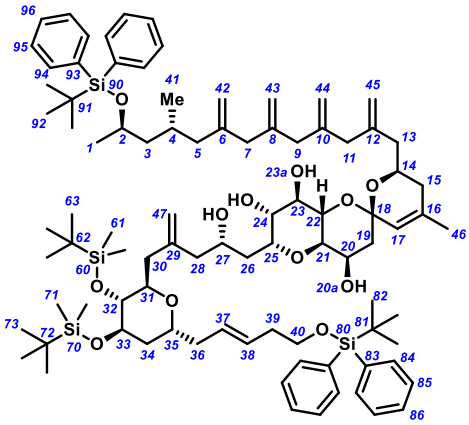
Compound 39. Tris(dibenzylideneacetone)dipalladium(0) (22.3 mg, 24.3 μmol) was added to a degassed solution of stannane **30** (726 mg, 0.486 mmol), acetate **2** (278 mg, 0.535 mmol), and lithium chloride (61.9 mg, 1.46 mmol) in DMF (1.0 mL) at room temperature. The solution was stirred at 60 °C for 20 h before the reaction was quenched with water (4 mL) and phosphate buffer (pH 7.4, 2 mL) at room temperature. The aqueous phase was extracted with EtOAc (3 × 8 mL) and the combined organic extracts were washed with brine (10 mL), dried over Na_2SO_4, filtered and concentrated to give a mixture of acetate regioisomers.



This residue was dissolved in THF (6.0 mL). MeOH (2.0 mL) and aq. NaOH (2.0 M, 2.0 mL, 4.0 mmol) were added and the mixture was stirred for 3 h at room temperature. The reaction was quenched with sat. aq. NH_4Cl (10 mL) and water (5 mL). The aqueous phase was extracted with EtOAc (3 × 15 mL) and the combined organic extracts were washed with brine (10 mL), dried over Na_2SO_4, filtered and concentrated. The crude product was purified by flash chromatography (fine silica, hexanes/EtOAc 7:3) to give the title compound as a colorless oil (521 mg, 70% over two steps). $[\alpha]_D^{20}$ = +38.7 (c = 1.00, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.72 – 7.64 (m, 8H), 7.44 – 7.32 (m, 12H), 5.42 (qt, *J* = 15.4, 6.4 Hz, 2H), 5.26 (s, 1H), 4.99 (s, 1H), 4.98 (s, 1H), 4.96 – 4.94 (m, 1H), 4.93 (d, *J* = 2.0 Hz, 1H), 4.90 (d, *J* = 1.9 Hz, 1H), 4.85 (s, 1H), 4.83 (s, 2H), 4.76 (d, *J* = 2.2 Hz, 1H), 4.74 (d, *J* = 2.3 Hz, 1H), 4.37 (q, *J* = 5.9 Hz, 1H), 4.16 (ddt, *J* = 10.7, 8.7, 4.2 Hz,

1H), 4.01 (dq, *J* = 9.8, 3.0 Hz, 1H), 3.96 – 3.71 (m, 9H), 3.70 – 3.60 (m, 3H), 3.35 (dd, *J* = 3.8, 2.3 Hz, 1H), 3.29 (dt, *J* = 6.5, 2.8 Hz, 1H), 2.93 (d, *J* = 14.8 Hz, 1H), 2.83 (d, *J* = 14.8 Hz, 1H), 2.77 (dd, *J* = 14.4, 10.0 Hz, 1H), 2.68 – 2.57 (m, 5H), 2.37 – 2.15 (m, 8H), 2.12 – 2.02 (m, 2H), 2.00 – 1.89 (m, 2H), 1.87 – 1.53 (m, 12H), 1.47 – 1.37 (m, 1H), 1.09 – 0.99 (m, 22H), 0.94 – 0.86 (m, 18H), 0.69 (d, *J* = 6.1 Hz, 3H), 0.18 – −0.03 (m, 12H); ^{13}C NMR ($CDCl_3$, 101 MHz): δ 145.8, 144.7, 144.6, 143.9, 143.3, 137.8, 136.1, 136.1, 135.7, 135.2, 134.5, 134.2, 129.7, 129.6, 129.5, 129.3, 128.2, 127.7, 127.6, 127.5, 122.4, 116.0, 114.4, 114.1, 113.1, 96.7, 75.0, 72.5, 72.0, 71.5, 70.4, 70.3, 68.3, 68.1, 67.8, 66.9, 65.8, 65.5, 64.1, 47.4, 45.0, 43.7, 42.6, 42.1, 41.4, 41.4, 40.3, 38.6, 37.6, 36.2, 35.4, 35.2, 34.0, 27.2, 27.1, 27.0, 26.0, 24.4, 23.0, 19.7, 19.5, 19.3, 18.2, 18.1, −4.3, −4.3, −4.4, −4.7; IR (film, cm^{-1}): 3456, 3072, 2954, 2929, 2896, 2857, 1638, 1472, 1462, 1428, 1379, 1361, 1255, 1177, 1109, 1090, 998, 958, 940, 895, 835, 776, 740, 702, 612, 505, 446, 420; HRMS (ESI) for $C_{91}H_{138}O_{12}Si_4Na$ [M+Na]$^+$: calcd. 1557.9158; found 1557.9150.

Table S11. Detailed analysis of the NMR data of compound **39**; arbitrary numbering scheme as shown in the insert.



atom number	**^{1}H NMR** ($CDCl_3$, 600 MHz)				**^{13}C NMR** ($CDCl_3$, 151 MHz)/ **^{29}Si NMR** ($CDCl_3$, 119 MHz)	
	δ [ppm]	*J* [Hz]	**COSY**	**NOESY**	δ [ppm]	**HMBC**
1	1.03	6.1	2	-	24.2	3b
2	3.89	-	1, 3a, 3b	41	67.7	1, 3a, 3b
3a	1.06	-	2, 3b, 4	-	47.3	1, 2, 4, 5a, 5b, 41
3b	1.57	13.0, 8.0, 4.4	2, 3a, 4	-		
4	1.82	-	3a, 3b, 5a, 5b, 41	-	27.0	2
5a	1.64	-	4, 5b, 42''	7, 42'', 43	43.6	3a, 3b, 4, 7, 42', 42''
5b	1.82	-	4, 5a, 42''	7, 42'', 43		
6	-	-	-	-	145.7	5a, 5b, 7, 41, 42', 42'', 43
7	2.63	-	42', 43	5a, 5b, 42', 43	42.5	5a, 5b, 9, 42', 42'', 43
8	-	-	-	-	144.6	7, 9, 42', 42'', 43, 44', 44''
9	2.63	-	43, 44', 44''	11a, 11b, 44''	41.3	7, 43, 44', 44''

atom number	**^{1}H NMR** ($CDCl_3$, 600 MHz)				**^{13}C NMR** ($CDCl_3$, 151 MHz)/ **^{29}Si NMR** ($CDCl_3$, 119 MHz)	
	δ [ppm]	***J*** [Hz]	**COSY**	**NOESY**	δ [ppm]	**HMBC**
10	-	-	-	-	144.4	9, 11a, 11b, 43, 44', 44'', 45', 45''
11a	2.83	14.6	11b, 44', 44'', 45''	9, 13b, 14, 22, 44', 45', 45''	42.0	9, 13a, 13b, 44', 44'', 45', 45''
11b	2.93	14.7	11a, 44', 45''	9, 13b, 14, 22, 44'		
12	-	-	-	-	143.1	11a, 11b, 13a, 13b, 14, 45', 45''
13a	2.21	-	13b, 14, 45'	44', 45'	41.2	11a, 11b, 15b, 45', 45''
13b	2.25	-	13a, 14, 45'	11a, 11b, 44', 45'		
14	4.15	-	13a, 13b, 15a, 15b	11a, 11b, 22, 44', 45'	65.6	13a, 13b, 15b, 45', 45''
15a	1.82	17.6, 3.6	14, 15b	-	35.3	13a, 13b, 17, 46
15b	1.93	17.1, 10.9	14, 15a, 17, 46	-		
16	-	-	-	-	137.7	15a, 15b, 46
17	5.26	-	15b, 46	19a, 46	122.3	15a, 15b, 46
18	-	-	-	-	96.6	17, 19a, 19b, 20
19a	1.81	15.5, 3.1	19b, 20	17, 20a, 21	40.2	17, 20a
19b	2.06	14.6, 3.3	19a, 20	20, 20a		
20	4.01	9.4, 3.1	19a, 19b, 20a, 21	19b, 21	66.7	19b, 20a, 22
20a	3.68	10.5	20	19a, 19b, 45', 45''	-	-
21	3.29	6.6, 2.8	20, 22	19a, 20, 26a, 26b	70.3	19b, 20, 22, 23, 25
22	3.74	-	21, 23	11a, 11b, 14, 23a, 45', 45''	68.1	20, 21, 23, 23a
23	3.74	-	22, 23a, 24	23a, 25	72.3	21, 22, 23a, 24, 25
23a	2.57	-	23	22, 23	-	-
24	3.77	-	23, 25	25	71.9	22, 23, 23a, 25, 26a, 26b
25	4.37	6.1	24, 26a, 26b	23, 24, 27	74.8	24, 26a, 26b
26a	1.79	-	25, 26b, 27	21	35.1	24, 25, 28a, 28b
26b	1.96	-	25, 26a, 27	21		
27	3.90	-	26a, 26b, 28a, 28b	25, 28b, 30b, 47''	67.9	25, 26a, 26b, 28a, 28b, 47', 47''
28a	2.19	-	27, 28b, 47''	47''	44.9	26a, 26b, 30a, 30b, 47', 47''
28b	2.30	-	27, 28a, 47''	27, 47''		
29	-	-	-	-	143.7	28a, 28b, 30a, 30b, 31, 47', 47''
30a	2.33	14.3, 5.0	30b, 31, 47'	32, 47'	37.5	28a, 28b, 31, 47', 47''
30b	2.76	14.3, 10.0	30a, 31, 47'	27, 32, 35, 47'		
31	3.80	-	30a, 30b, 32	36a, 47'	77.2	30a, 30b, 33
32	3.35	3.7, 2.5	31, 33	30a, 30b, 47'	71.4	30a, 30b, 31, 34a
33	3.79	3.8	32, 34a, 34b	31, 70	70.1	31, 32, 34a, 35

atom number	**^{1}H NMR** ($CDCl_3$, 600 MHz)				**^{13}C NMR** ($CDCl_3$, 151 MHz)/ **^{29}Si NMR** ($CDCl_3$, 119 MHz)	
	δ [ppm]	***J*** [Hz]	**COSY**	**NOESY**	δ [ppm]	**HMBC**
34a	1.40	13.4, 4.6, 2.7	33, 34b, 35	-	33.9	32, 36a, 36b
34b	1.77	13.1, 9.9, 2.8	33, 34a, 35	-		
35	3.83	9.2, 6.5, 2.4	34a, 34b, 36a, 36b	30b, 36a, 37, 47'	65.3	31, 34b, 36a, 36b, 37
36a	2.07	13.8, 7.0	35, 36b, 37, 38	31, 35, 38	38.5	34b, 37, 38
36b	2.20	13.3, 6.5	35, 36a, 37, 38	38		
37	5.38	15.4, 6.8, 1.2	36a, 36b, 38, 39	35	128.1	36a, 36b, 38, 39
38	5.45	15.4, 6.7, 1.2	36a, 36b, 37, 39	36a, 36b, 40	129.2	36a, 36b, 37, 39, 40
39	2.26	6.9	37, 38, 40	-	36.1	37, 38, 40
40	3.65	6.9	39	38	63.9	38, 39
41	0.68	6.2	4	2, 42''	19.6	3b, 4, 5a, 5b
42'	4.76	2.4	7, 42''	7	112.9	5a, 5b, 7
42''	4.74	2.3	5a, 5b, 42'	5a, 5b, 41		
43	4.83	-	7, 9	5a, 5b, 7	113.9	7, 9
44'	4.92	-	9, 11a, 11b, 44''	11a, 11b, 13a, 13b, 14	114.2	9, 11a, 11b
44''	4.84	-	9, 11a, 44'	9		
45'	4.98	1.8	13a, 13b, 45''	11a, 13a, 13b, 14, 20a, 22	115.9	11a, 11b, 13a, 13b
45''	4.97	1.9	11a, 11b, 45'	11a, 20a, 22		
46	1.72	-	15b, 17	17	22.8	15a, 17
47'	4.95	-	30a, 30b, 47''	30a, 30b, 31, 32, 35	115.9	28a, 28b, 30a, 30b
47''	4.90	-	28a, 28b, 47'	27, 28a, 28b		
60	-	-	-	-	18.5	32, 61, 61', 63
61	0.05	-	-	-	−4.5	61'
61'	0.04	-	-	-	−4.6	61
62	-	-	-	-	17.98, 18.05	61, 61', 63
63	0.89	-	-	-	25.86, 25.87	63
70	-	-	-	-	18.6	33, 71, 71', 73
71	0.05	-	-	-	−4.5	71'
71'	0.03	-	-	-	−4.9	71
72	-	-	-	-	17.98, 18.05	71, 71', 73
73	0.88	-	-	-	25.86, 25.87	73
80	-	-	-	-	−4.7	40, 82, 84, 84'
81	-	-	-	-	19.2	82
82	1.04	-	-	-	26.9	82
83	-	-	-	-	134.0	84, 85

atom number	**^{1}H NMR** ($CDCl_3$, 600 MHz)				**^{13}C NMR** ($CDCl_3$, 151 MHz)/ **^{29}Si NMR** ($CDCl_3$, 119 MHz)	
	δ [ppm]	***J*** [Hz]	**COSY**	**NOESY**	δ [ppm]	**HMBC**
83'	-	-	-	-	134.0	84', 85'
84	7.66	-	-	-	135.6	84, 86
84'	7.66	-	-	-	135.6	84', 86'
85	7.37	-	-	-	127.6	84, 85
85'	7.37	-	-	-	127.6	84', 85'
86	7.41	-	-	-	129.5	84
86'	7.41	-	-	-	129.5	84'
90	-	-	-	-	-6.9	2, 92, 94, 94'
91	-	-	-	-	19.3	92
92	1.05	-	-	-	27.1	92
93	-	-	-	-	134.3	94, 95
93'	-	-	-	-	135.0	94', 95'
94	7.70	-	-	-	135.9	94, 96
94'	7.68	-	-	-	136.0	94', 96'
95	7.36	-	-	-	127.5	94, 95
95'	7.36	-	-	-	127.3	94', 95'
96	7.41	-	-	-	129.5	94
96'	7.41	-	-	-	129.3	94'

Limaol (1). A solution of silyl ether **29** (521 mg, 0.339 mmol) in THF (1.0 mL, 2 × 0.5 mL wash) was added to a solution of TBAF trihydrate (2.14 g, 6.78 mmol) in THF (5.0 mL) at 0 °C. The cooling bath was removed and the mixture was stirred at room temperature for 22 h. The reaction was quenched with phosphate buffer (pH 7.4, 10 mL) and the aqueous phase was extracted with EtOAc (5 × 8 mL). The combined organic extracts were washed with brine (10 mL), dried over Na_2SO_4, filtered and concentrated. The residue was purified by flash chromatography (EtOAc/8% MeOH) to give the title compound as a white foam (278 mg, 99%). The analytical and spectral data matched the data previously obtained. $[\alpha]_D^{20}$ = +40 (c = 0.1, MeOH);[1] literature: $[\alpha]_D^{20}$ = +63 (c = 0.1, MeOH).[13] ^{1}H NMR (CD_3OD, 600 MHz): 5.58 – 5.44 (m, 2H), 5.29 (dq, *J* = 2.6, 1.4 Hz, 1H), 5.02 – 4.99 (m, 1H), 4.96 (d, *J* = 2.2 Hz, 1H), 4.92 – 4.90 (m, 3H), 4.89 – 4.87 (m, 2H), 4.86 (d, *J* = 2.0 Hz, 1H), 4.81 (d, *J* = 2.4 Hz, 1H), 4.80 (q, *J* = 1.2 Hz, 1H), 4.28 – 4.20 (m, 2H), 3.95 (q, *J* = 3.1 Hz, 1H), 3.96 – 3.88 (m, 2H), 3.82 (dqd, *J* = 9.0, 6.2, 3.9 Hz, 1H), 3.73 (ddd, *J* = 10.8, 8.2, 4.7 Hz, 1H), 3.66 (dd, *J* = 10.3, 9.0 Hz, 1H), 3.65 (dd, *J* = 9.3, 6.3 Hz, 1H), 3.60

(t, *J* = 9.1 Hz, 1H), 3.60 – 3.57 (m, 1H), 3.55 (t, *J* = 6.8 Hz, 2H), 3.26 (dd, *J* = 10.2, 2.9 Hz, 1H), 3.01 (d, *J* = 14.7 Hz, 1H), 2.98 (t, *J* = 8.4 Hz, 1H), 2.88 (d, *J* = 14.6 Hz, 1H), 2.73 (d, *J* = 2.3 Hz, 2H), 2.70 (s, 2H), 2.61 (d, *J* = 14.8 Hz, 1H), 2.50 – 2.42 (m, 1H), 2.36 (dd, *J* = 13.7, 6.5 Hz, 1H), 2.32 – 2.18 (m, 6H), 2.12 (dd, *J* = 15.1, 9.7 Hz, 1H), 2.01 – 1.78 (m, 9H), 1.71 (d, *J* = 1.2 Hz, 3H), 1.68 – 1.58 (m, 2H), 1.46 (ddd, *J* = 13.7, 9.1, 4.3 Hz, 1H), 1.14 (d, *J* = 6.1 Hz, 3H), 1.07 (ddd, *J* = 13.9, 9.1, 3.9 Hz, 1H), 0.87 (d, *J* = 6.4 Hz, 3H); ^{13}C NMR (CD_3OD, 151 MHz): δ 147.1, 146.1, 146.0, 145.5, 145.3, 138.4, 130.3, 129.9, 123.7, 115.8, 115.1, 114.7, 114.4, 113.8, 97.8, 77.1, 74.9, 73.7, 73.3, 73.1, 72.6, 70.5, 70.0, 70.0, 68.1, 66.8, 66.4, 66.1, 62.8, 47.6, 46.5, 45.0, 43.3, 43.2, 42.5, 42.3, 41.3, 39.1, 37.1, 36.5, 36.2, 35.9, 32.5, 28.2, 24.4, 22.8, 19.8; IR (Microscope, cm^{-1}): 3383, 2924, 2856, 1638, 1430, 1379, 1176, 1069, 996, 967, 895; HRMS (ESI) for $C_{47}H_{74}O_{12}Na$ $[M+Na]^+$: calcd. 853.5072; found 853.5075

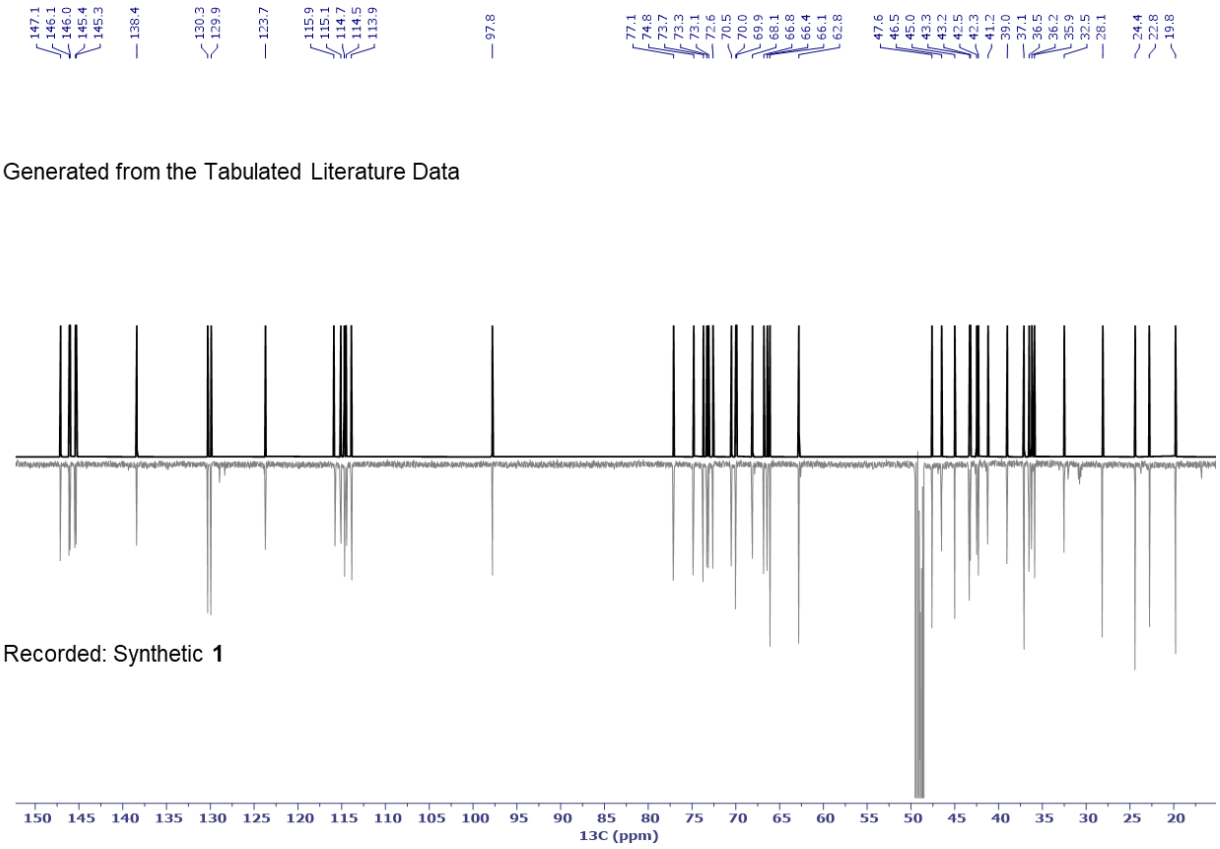
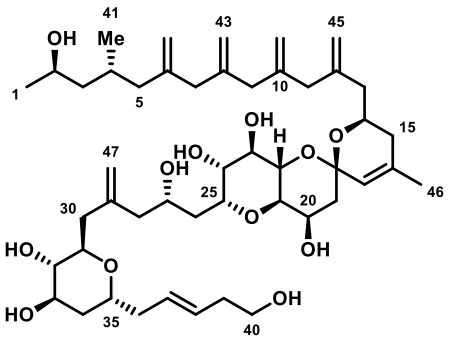


Figure S8. Visual comparison of the ^{13}C NMR data of authentic limaol (**1**) with those of synthetic **1 (**Note that the literature does ***not*** depict the ^{13}C NMR spectrum of limaol (**1**); the shown spectrum (up) was generated (MestReNova) by converting the tabulated ^{13}C NMR data (ref. [13]) into a formal spectrum; the intensity of the lines is arbitrarily set to be identical for all signals; for a tabular survey of the exact numbers, see Table S13

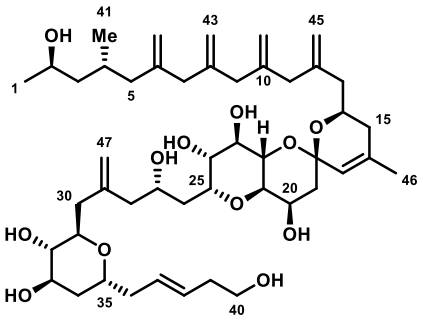
Table S12. Analysis of the NMR data of synthetic limaol (**1**); arbitrary numbering scheme as shown in the insert.



atom number	**^{1}H NMR** (CD_3OD, 600 MHz)				**^{13}C NMR** (CD_3OD, 151 MHz)	
	δ [ppm]	**m**	***J*** [Hz]	**COSY**	δ [ppm]	**HMBC**
1	1.14	d	6.1	2	24.4	3ab
2	3.82	dqd	9.0, 6.2, 3.9	1, 3ab	66.1	1, 3ab
3a	1.46	ddd	13.7, 9.1, 4.3	2, 3b, 4, 41	47.6	1, 5ab, 41
3b	1.07	ddd	13.9, 9.1, 3.9	2, 3a, 4, 41		
4	1.87	m	-	3ab, 5b, 41	28.2	3ab, 5ab, 41
5a	1.98	m	13.3, 5.8	5b, 41, 42′	45.0	3ab, 7, 41, 42′, 42′′
5b	1.82	m	13.2, 8.2	4, 5a, 41, 42′		
6	-	-	-	-	147.1	5ab, 7, 42′, 42′′
7	2.73	m	-	42′, 42′′, 43′	43.4	5ab, 9, 42′, 42′′, 43′, 43′′
8	-	-	-	-	146.1	7, 9, 43′, 43′′
9	2.70	m	-	43′, 43′′, 44′, 44′′	42.3	7, 11ab, 43′, 43′′, 44′, 44′′
10	-	-	-	-	146.0	9, 11ab, 44′, 44′′
11a	3.01	d	14.7	11b, 44′, 45′, 45′′	43.2	9, 13ab, 44′, 44′′, 45′, 45′′
11b	2.88	d	14.6	11a, 44′, 44′′, 45′′		
12	-	-	-	-	145.3	11ab, 13ab, 14, 45′, 45′′
13a	2.29	dd	14.0, 3.8	13b, 14, 45′	42.5	11ab, 45′, 45′′
13b	2.21	m	-	13a, 14, 45′		
14	4.24	m	-	13ab, 15ab	66.8	13ab, 15a
15a	1.93	m	-	14, 15b, 17, 46	36.2	13ab, 17, 46
15b	1.84	m	-	14, 15a, 46		
16	-	-	-	-	138.4	15ab, 46
17	5.29	m	-	15ab, 19a, 46	123.7	15ab, 46
18	-	-	-	-	97.8	17, 19ab, 20, 22
19a	1.94	m	-	17, 20	41.3	20
19b	1.86	m	-	20		
20	3.95	m	3.1	19ab, 21	68.1	19a, 22
21	3.26	dd	10.2, 2.9	20, 22	70.5	19a, 20, 22, 25
22	3.66	dd	10.3, 9.0	21	70.0	20, 21, 23
23	3.59	d	9.1	24	72.6	21, 22, 25

24	3.64	dd	9.3, 6.3	23, 25	73.1	23, 25
25	4.25	m	-	24, 26ab	74.9	24, 26a
26a	1.88	m	-	25, 26b, 27	32.5	22, 28ab
26b	1.62	m	-	25, 26a, 27		
27	3.92	m	-	26ab, 28ab	66.4	26b, 28ab
28a	2.36	dd	13.7, 6.5	27, 28b, 47''	46.5	30ab, 47', 47''
28b	2.23	m	-	27, 28a, 47''		
29	-	-	-	-	145.5	28ab, 30ab, 31, 47', 47''
30a	2.61	d	14.8	30b, 31, 47', 47''	39.1	28ab, 32, 47', 47''
30b	2.12	dd	15.1, 9.7	30a, 31, 47'		
31	3.59	m	-	30ab, 32	73.8	30ab, 32, 35
32	2.98	t	8.4	31, 33	77.1	30b, 31, 33, 34ab
33	3.73	ddd	10.8, 8.2, 4.7	32, 34ab	70.0	32, 34ab
34a	1.92	m	-	33, 34b, 35	36.5	32, 35, 36ab
34b	1.63	m	-	33, 34a, 35		
35	3.92	m	-	34ab, 36ab	73.3	34b, 36ab, 37
36a	2.46	m	-	35, 36b, 37	35.9	34b, 35, 37, 38
36b	2.25	m	-	35, 36a, 37		
37	5.48	m	-	36ab, 38	139.9	35, 36ab, 38
38	5.54	m	-	37, 39	130.3	36ab, 37, 40
39	2.23	m	-	38, 40	37.1	37, 38, 40
40	3.55	t	6.8	39	62.8	38, 39
41	0.87	d	6.4	3ab, 4, 5ab	19.8	3ab, 5ab
42'	4.81	d	2.4	5ab, 7	113.8	5ab, 7
42''	4.80	q	1.2	7		
43'	4.90	m	-	7, 9	114.7	7, 9
43''	4.88	m	-	9		
44'	5.01	m	-	9, 11ab, 44''	115.1	9, 11ab
44''	4.88	m	-	9, 11b, 44'		
45'	4.96	d	2.2	11a, 13ab, 45''	115.8	11ab, 13ab
45''	4.91	m	-	11ab, 45'		
46	1.71	d	1.2	15ab, 17	22.8	15b, 17
47'	4.91	m	-	30ab, 47''	114.4	28ab, 30ab
47''	4.86	d	2.0	28ab, 30a, 47'		

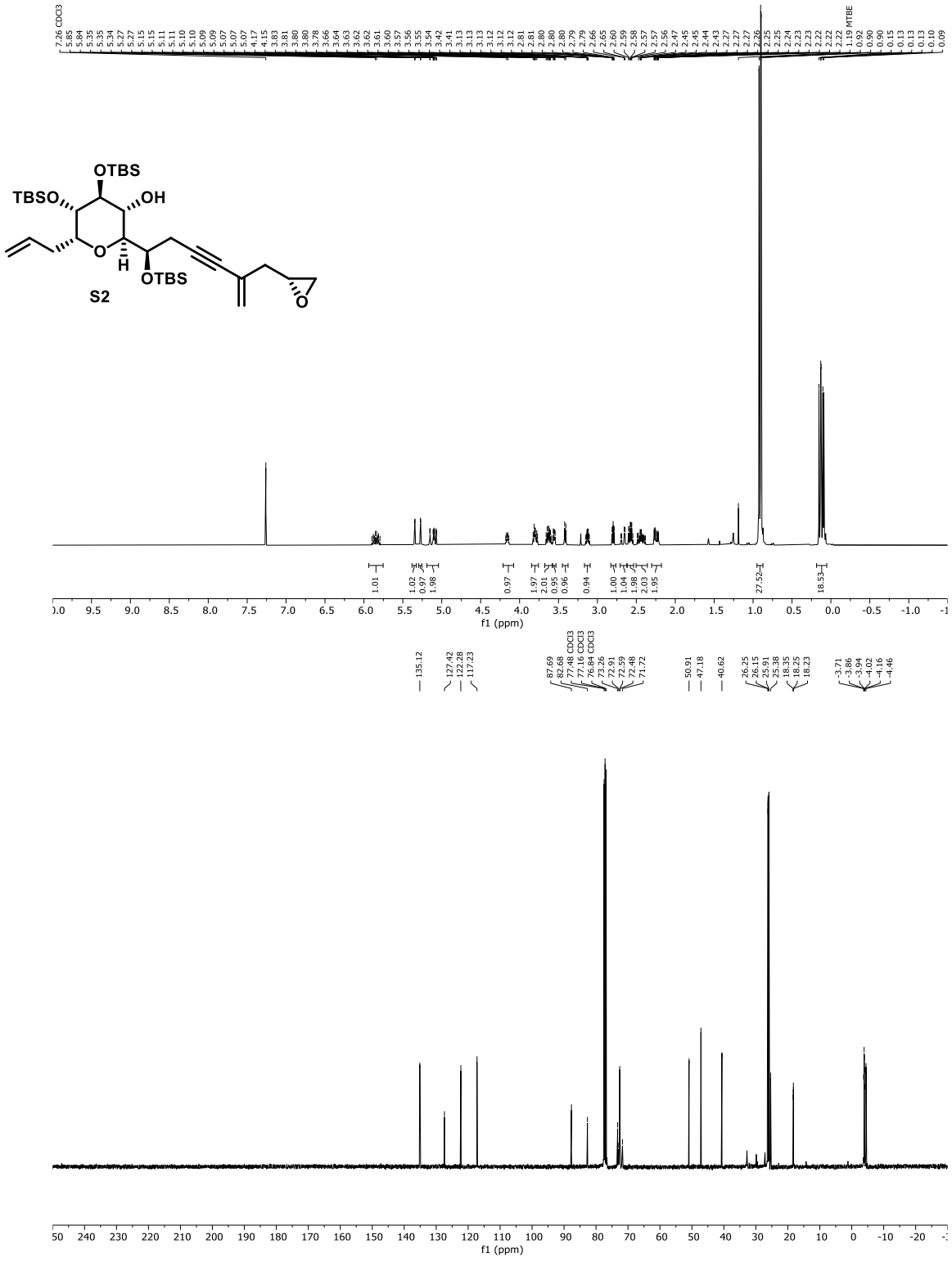
Table S13. Comparison of ^{13}C NMR data of synthetic **1** with authentic limaol.[13]

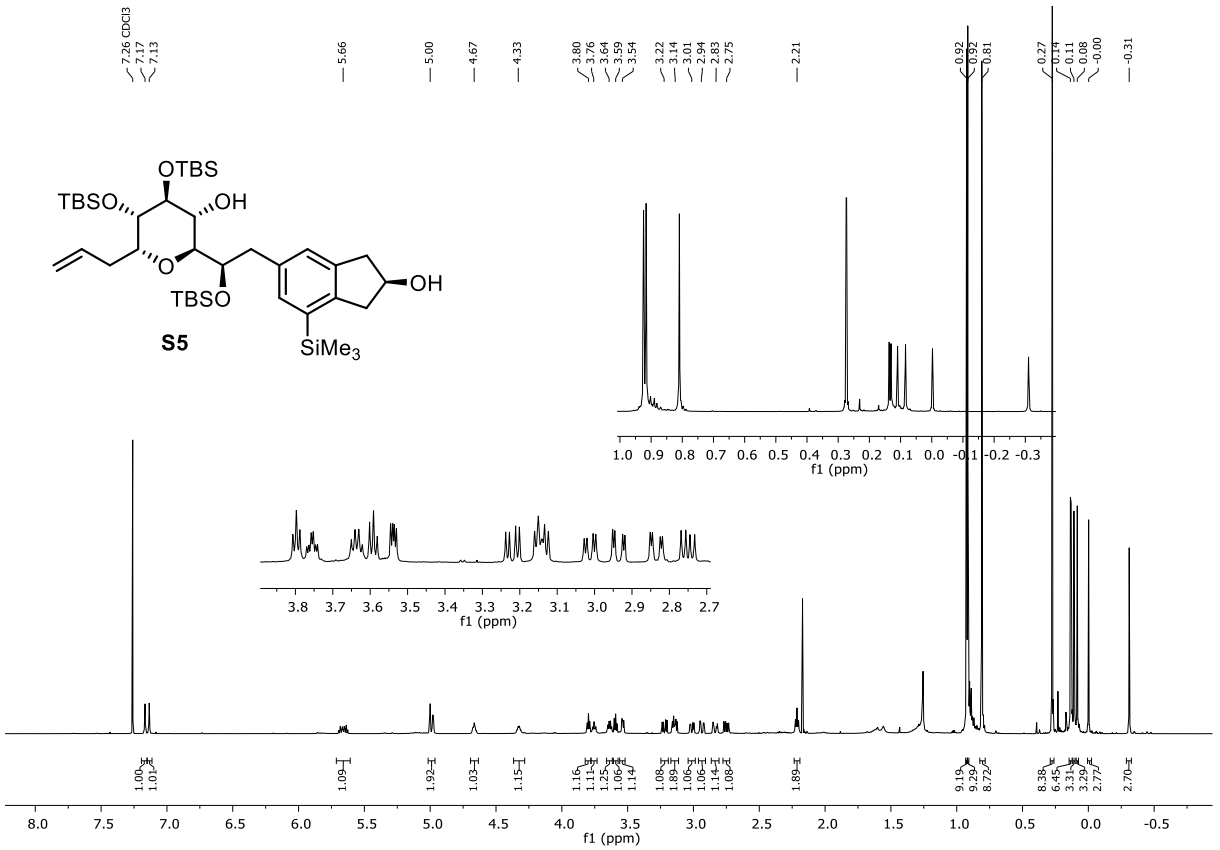


atom number	Limaol	Synthetic 1	Δδ
1	24.4	24.4	±0.0
2	66.1	66.1	±0.0
3	47.6	47.6	±0.0
4	28.1	28.2	−0.1
5	45.0	45.0	±0.0
6	147.1	147.1	±0.0
7	43.3	43.3	±0.0
8	146.1	146.1	±0.0
9	42.3	42.3	±0.0
10	146.0	146.0	±0.0
11	43.2	43.2	±0.0
12	145.3	145.3	±0.0
13	42.5	42.5	±0.0
14	66.8	66.8	±0.0
15	36.2	36.2	±0.0
16	138.4	138.4	±0.0
17	123.7	123.7	±0.0
18	97.8	97.8	±0.0
19	41.2	41.2	±0.0
20	68.1	68.1	±0.0
21	70.5	70.5	±0.0
22	69.9	70.0	−0.1
23	72.6	72.6	±0.0
24	73.1	73.1	±0.0
25	74.8	74.9	−0.1
26	32.5	32.5	±0.0
27	66.4	66.4	±0.0
28	46.5	46.5	±0.0
29	145.4	145.5	−0.1
30	39.0	39.1	−0.1
31	73.7	73.7	±0.0
32	77.1	77.1	±0.0

33	70.0	70.0	±0.0
34	36.5	36.5	±0.0
35	73.3	73.3	±0.0
36	35.9	35.9	±0.0
37	129.9	129.9	±0.0
38	130.3	130.3	±0.0
39	37.1	37.1	±0.0
40	62.8	62.8	±0.0
41	19.8	19.8	±0.0
42	113.9	113.8	+0.1
43	114.7	114.7	±0.0
44	115.1	115.1	±0.0
45	115.9	115.8	+0.1
46	22.8	22.8	±0.0
47	114.5	114.4	+0.1

Spectra of New Compounds (in the order they appear in the SI)

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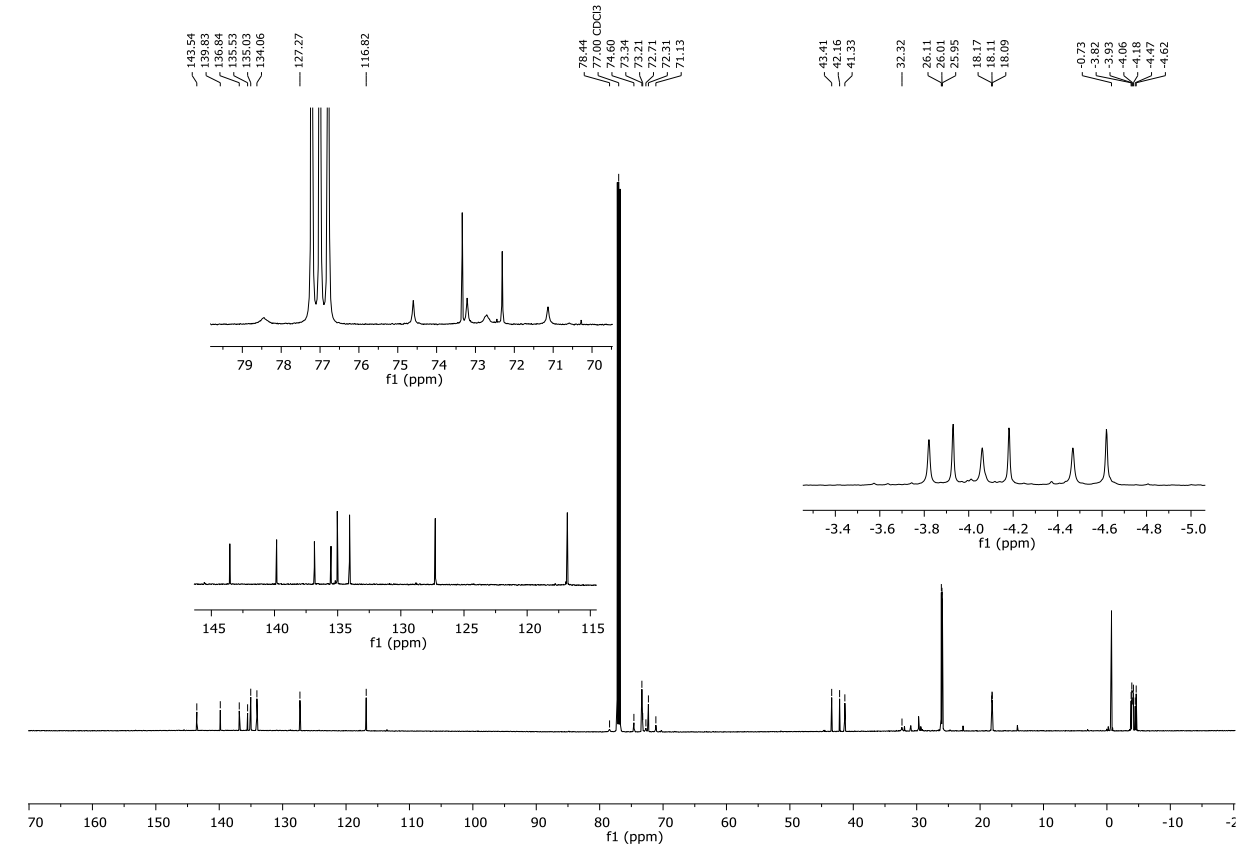
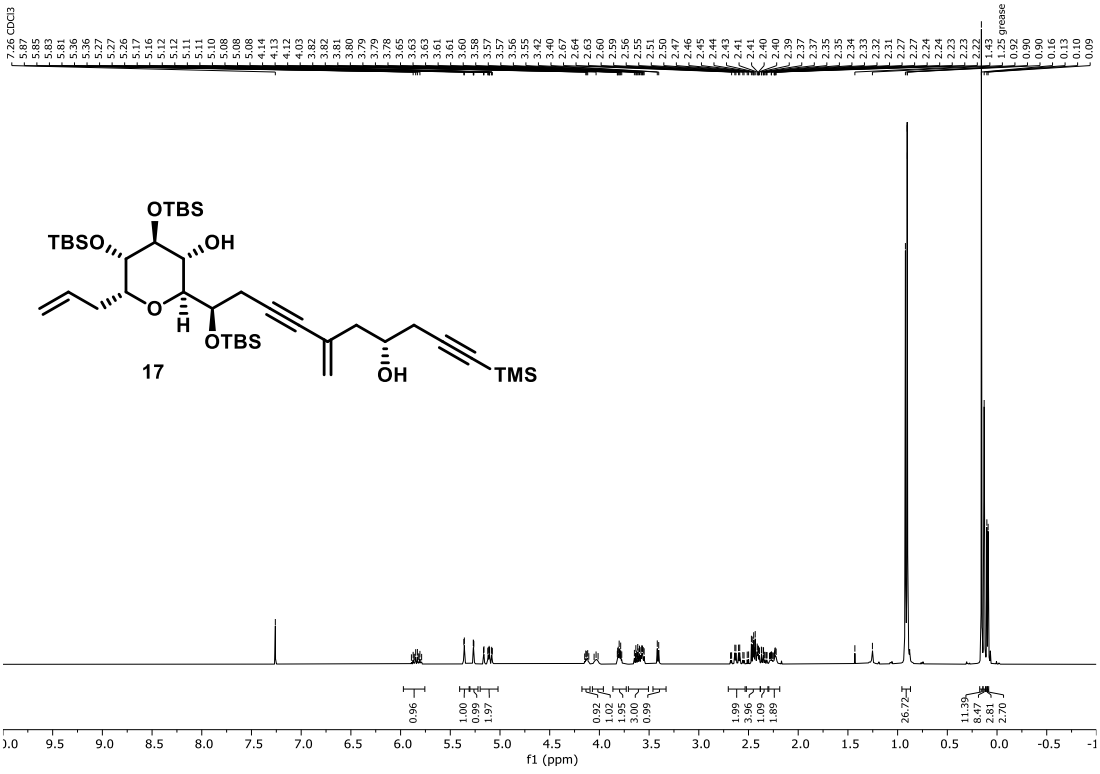
OH
TBSO
OH
SiMe3
S5
f1 (ppm)


f1 (ppm)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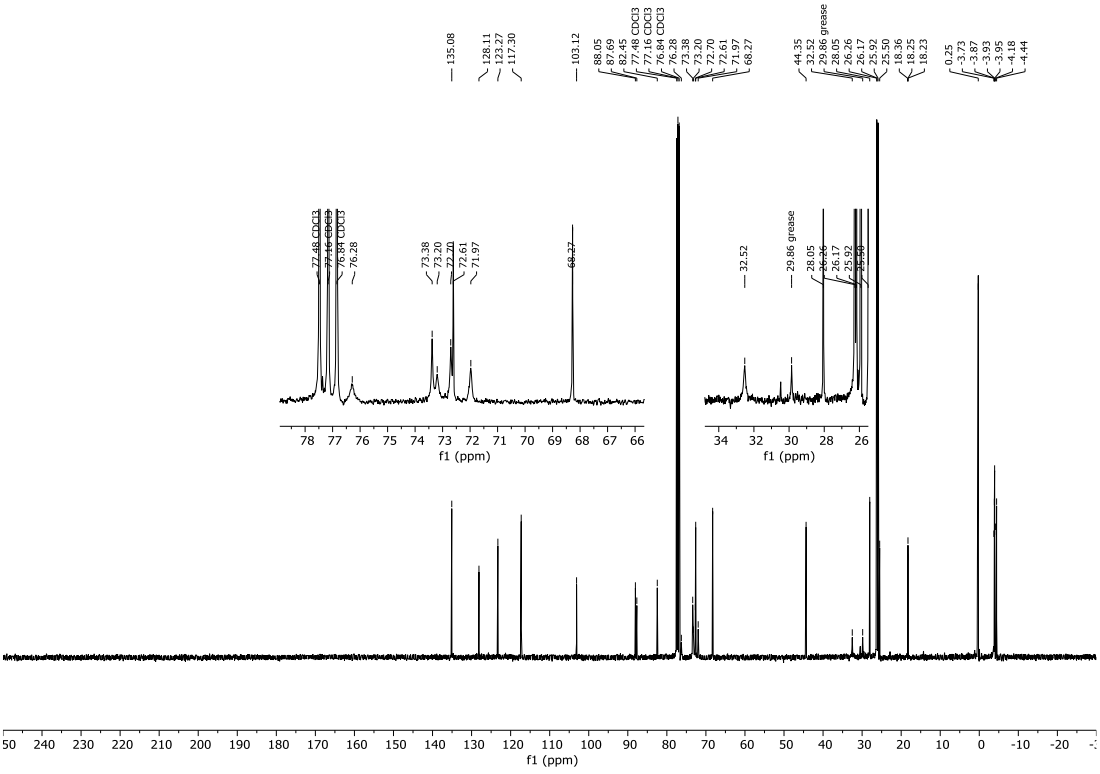
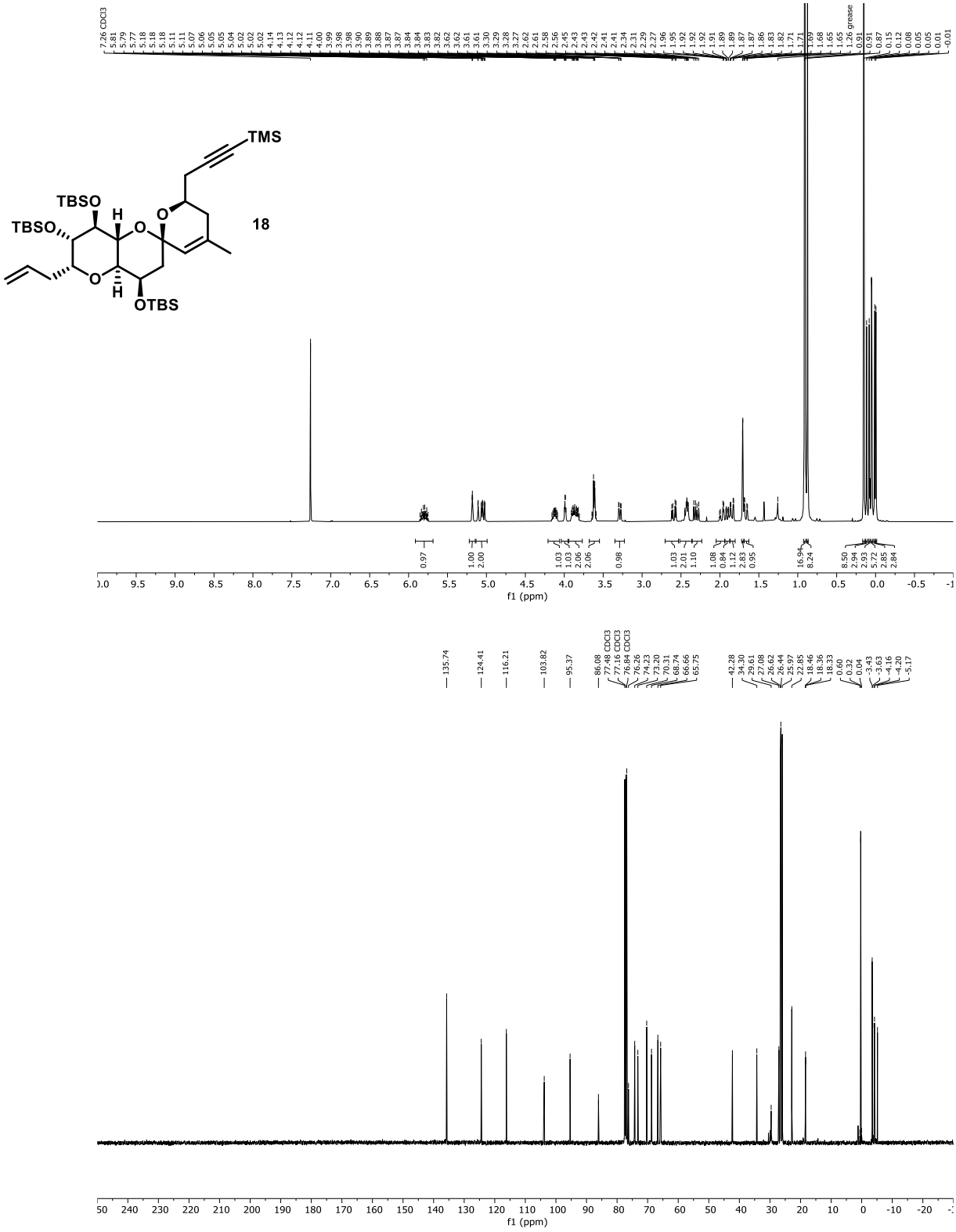
OH
O
H
OTBS
17
OH
TMS
f1 (ppm)


f1 (ppm)
f1 (ppm)
f1 (ppm)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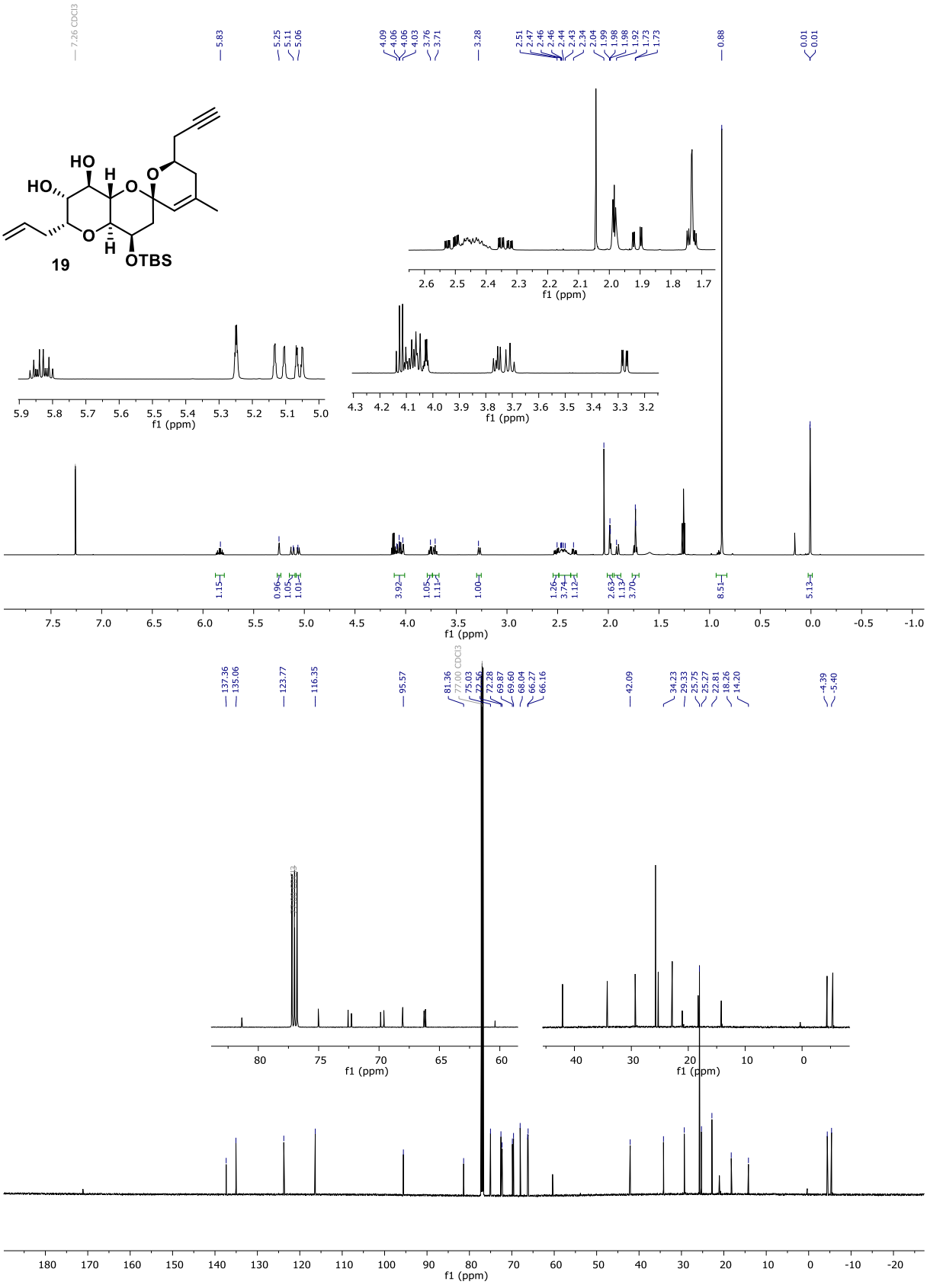
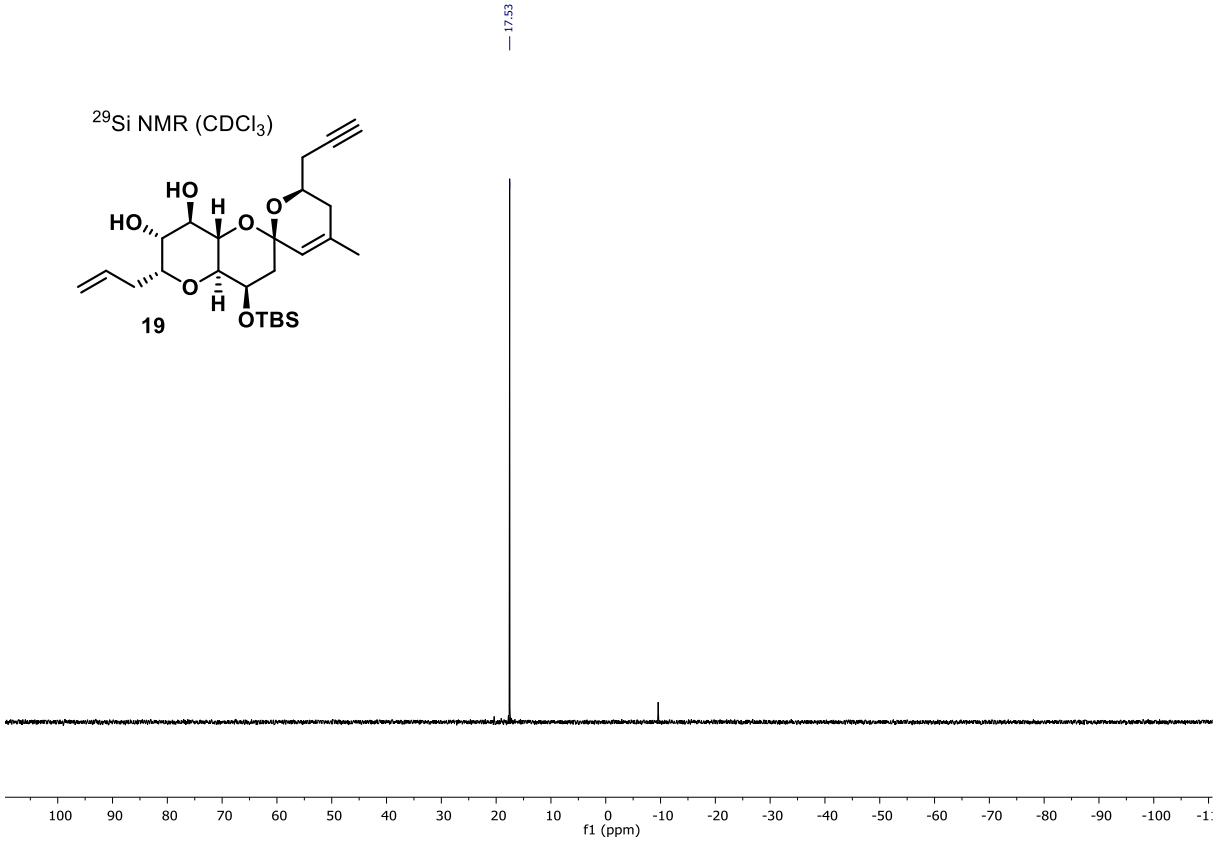
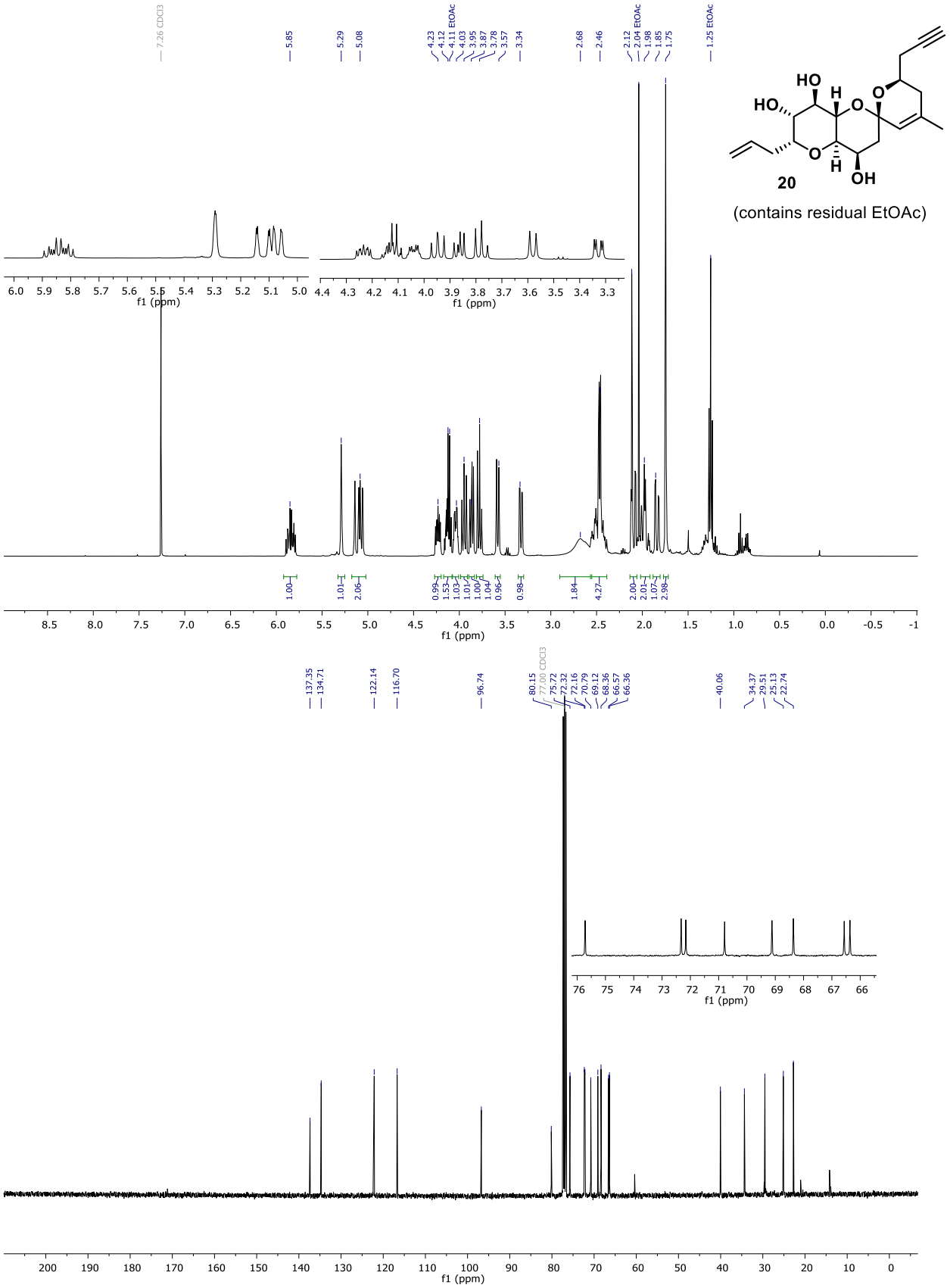
TBSO
TBSO
H
O
O
O
H
OTBS
18
f1 (ppm)
f1 (ppm)


HO
HO
H
O
O
H
OTBS
19
f1 (ppm)


17.53
^{29}Si NMR ($CDCl_3$)
HO
HO
H
O
O
O
H
OTBS
19
100
90
80
70
60
50
40
30
20
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
f1 (ppm)


7.26 CDCl3
5.85
5.29
5.08
4.23
4.12
4.11 EtOAc
4.03
3.95
3.87
3.78
3.57
3.34
2.68
2.46
2.12
2.04 EtOAc
1.98
1.85
1.75
1.25 EtOAc
HO
HO
H
O
O
O
H
OH
20
(contains residual EtOAc)
f1 (ppm)
137.35
134.71
122.14
116.70
96.74
80.15
77.00 CDCl3
75.72
72.32
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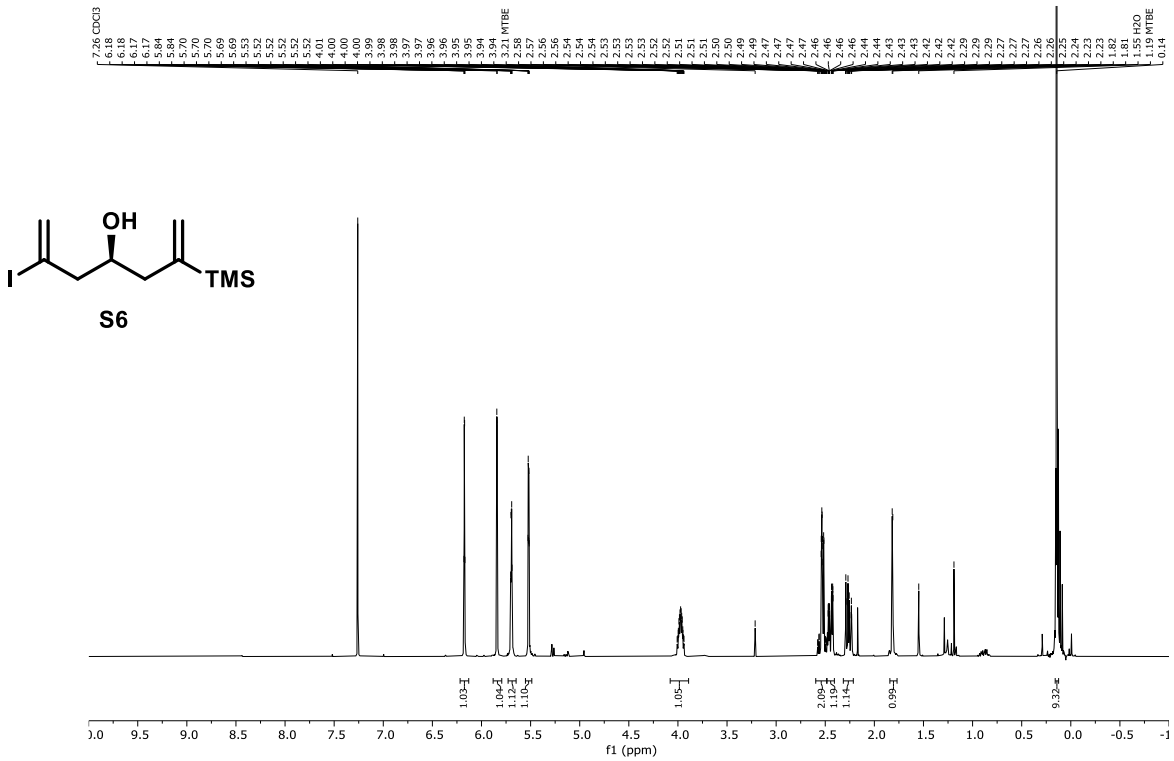
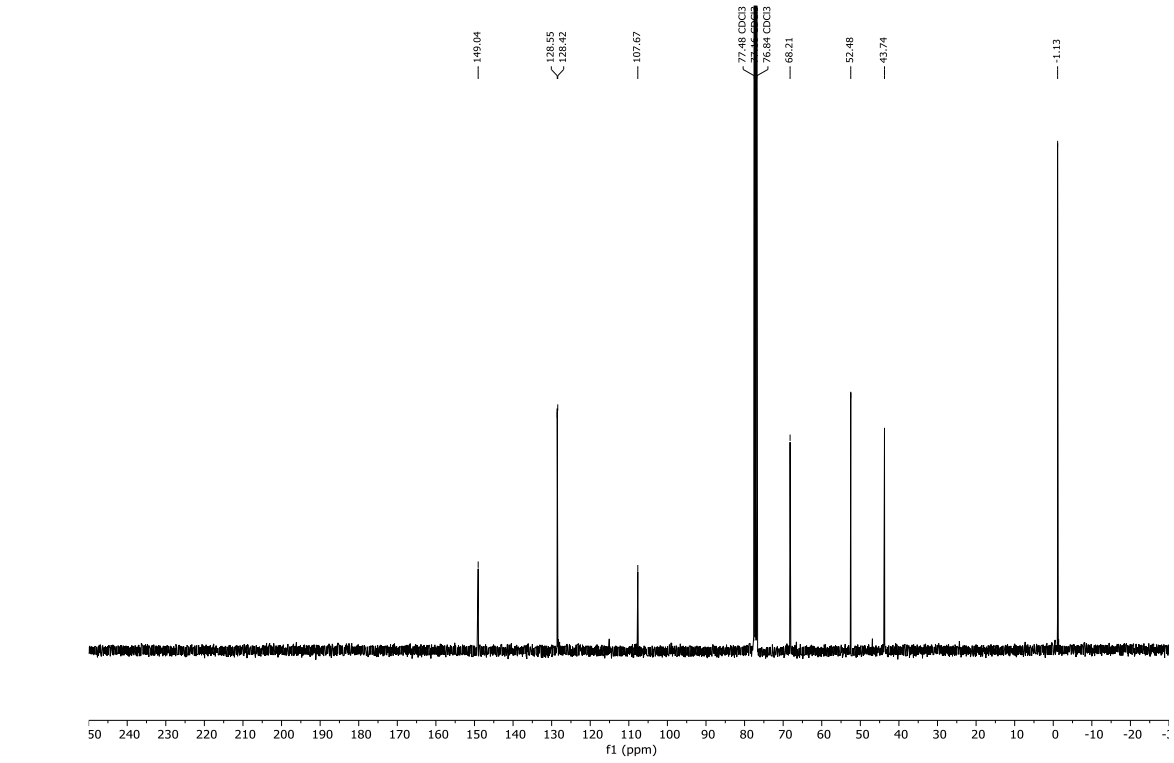
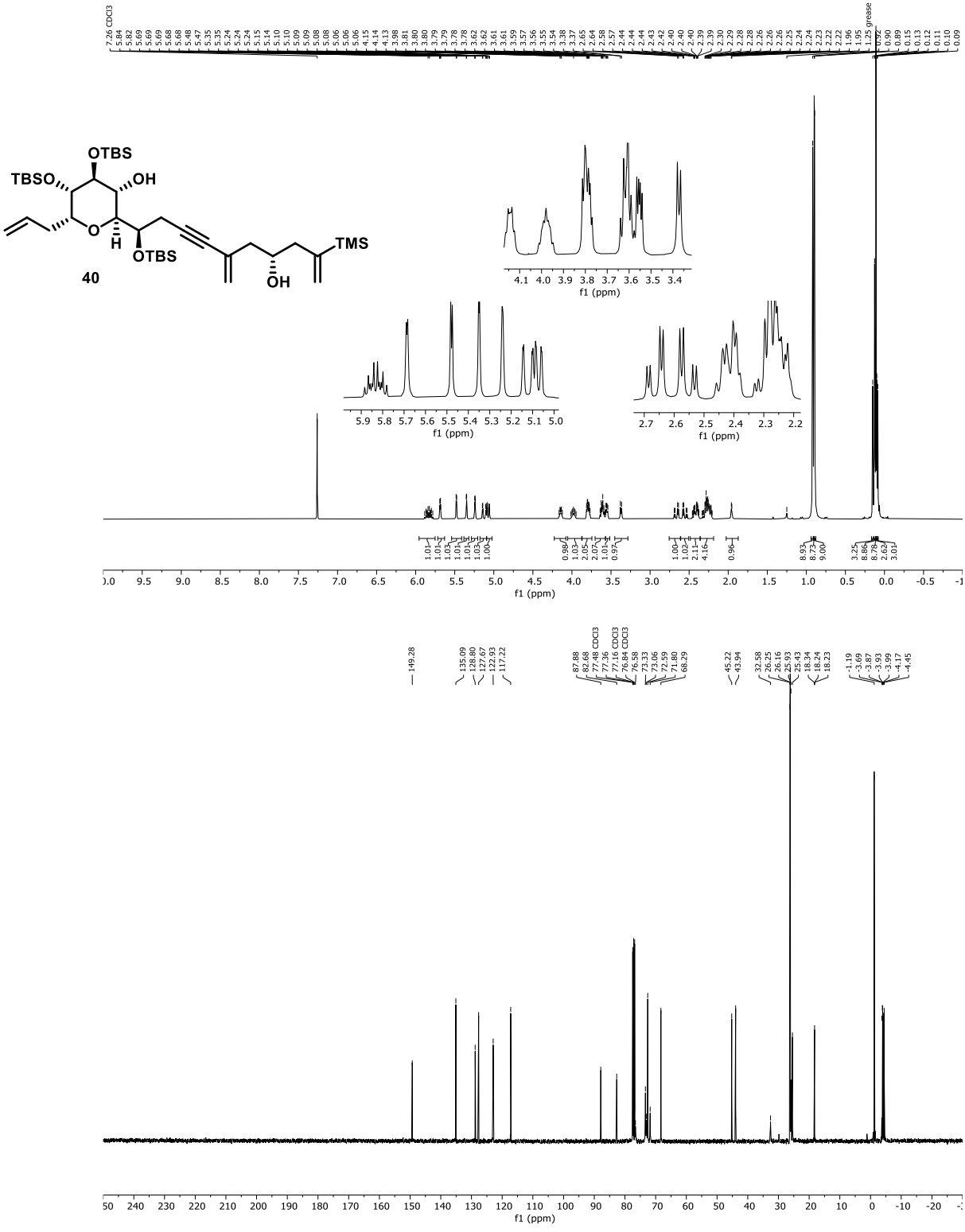
66.36
40.06
34.37
29.51
25.13
22.74


OH
I
TMS
S6
f1 (ppm)


149.04
128.55
128.42
107.67
77.48 CDCl3
76.84 CDCl3
68.21
52.48
43.74
-1.13
f1 (ppm)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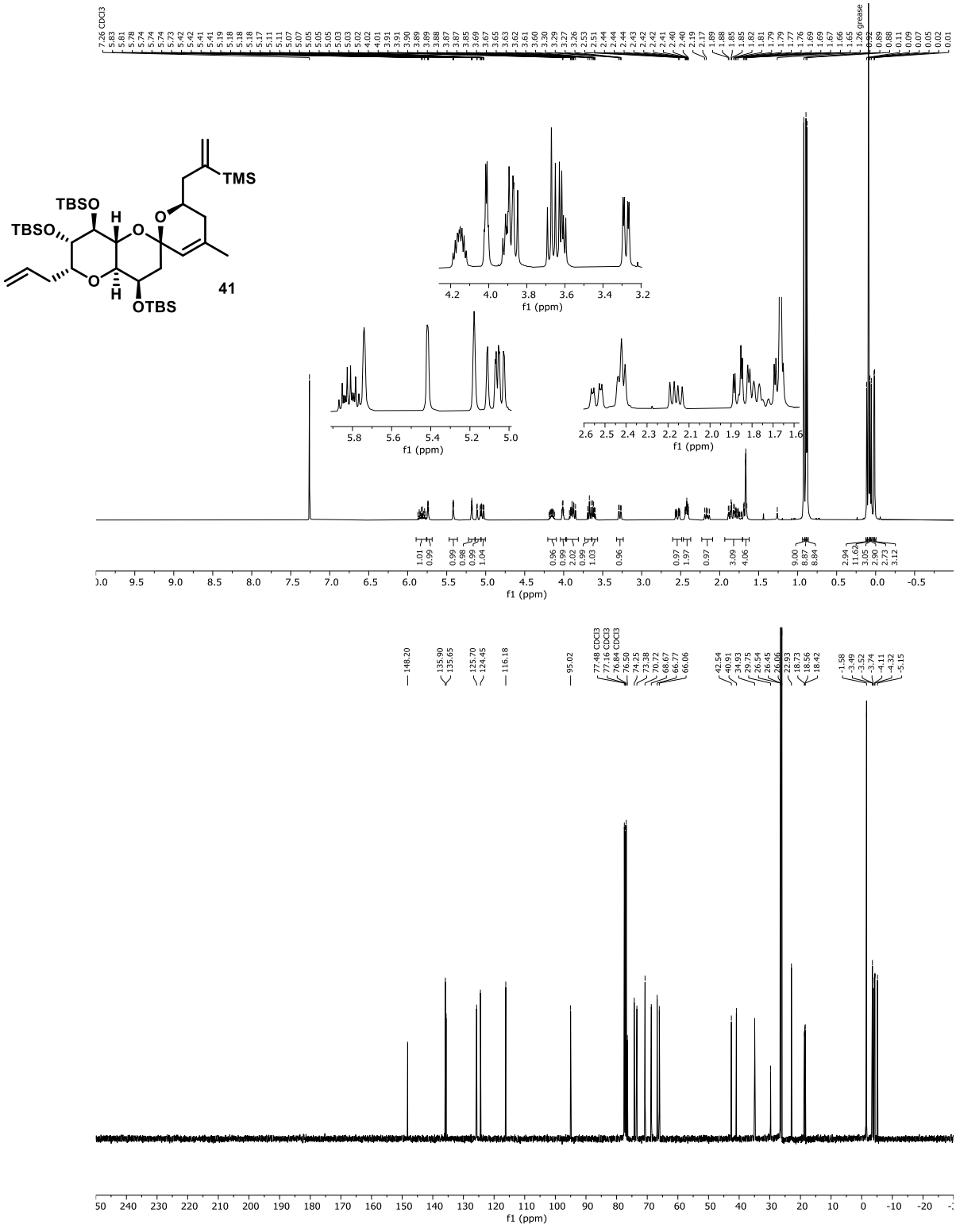
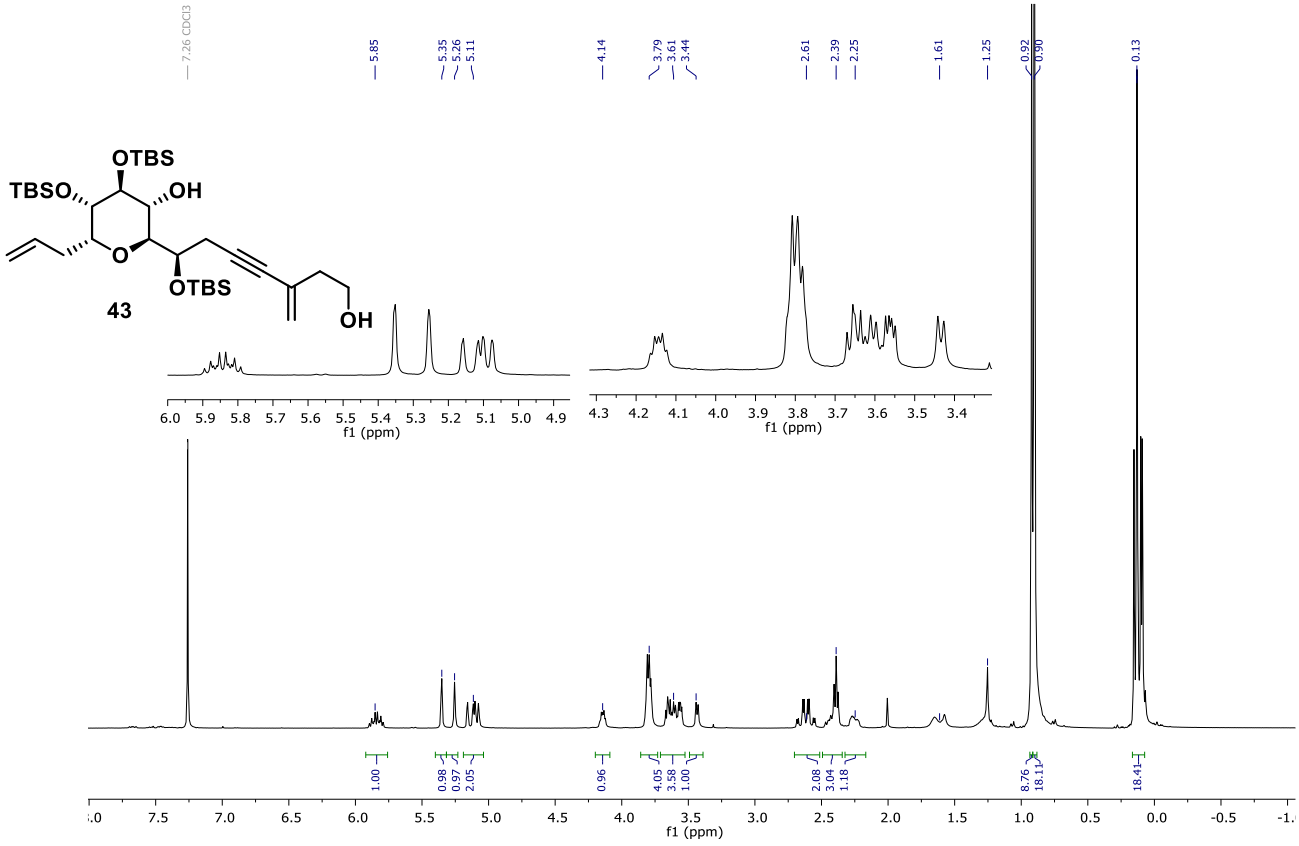
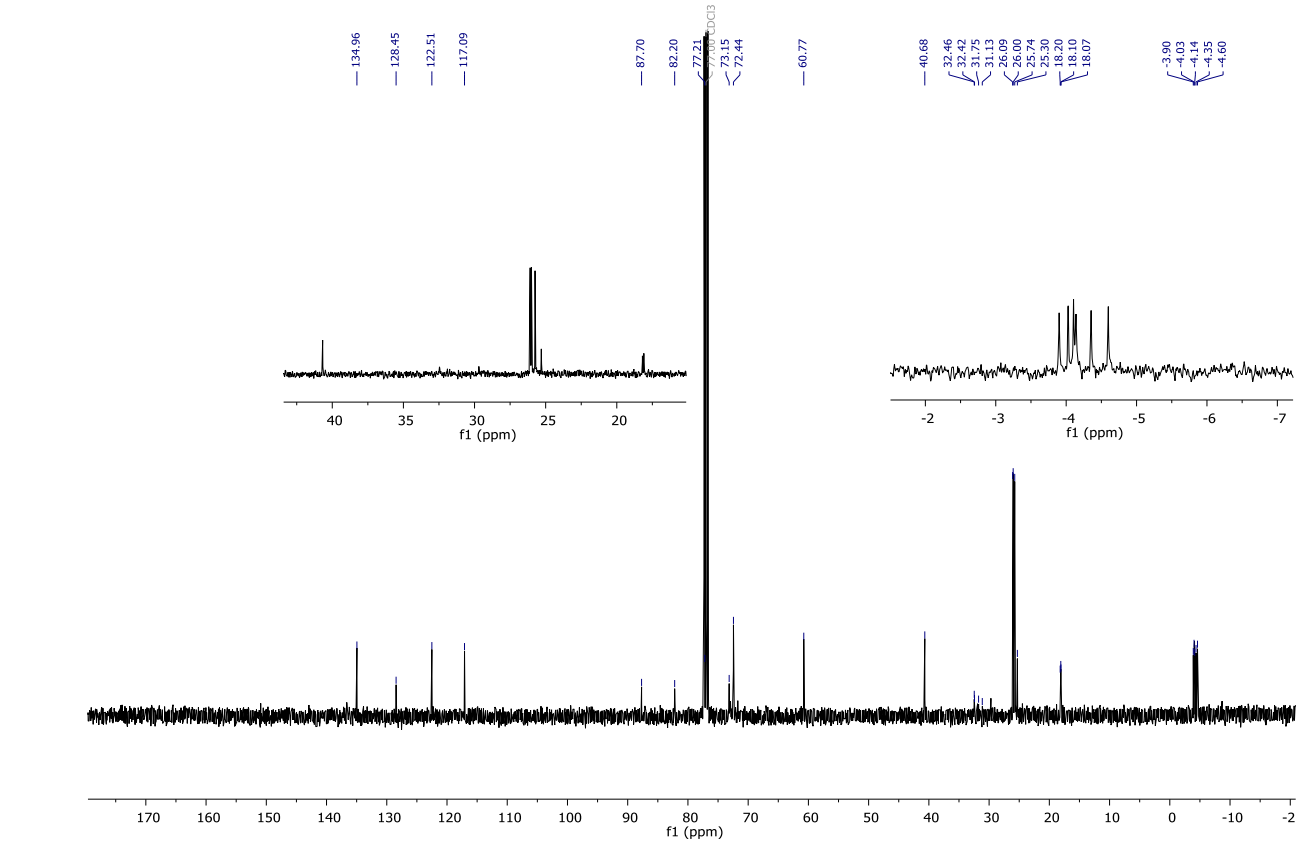
OH
H
O
OTBS
TMS
OH
40
f1 (ppm)


TMS
TBSO
TBSO
H
O
O
O
H
OTBS
41
f1 (ppm)


OTBS
TBSO
OH
O
OTBS
OH
43
7.26 CDCl3
5.85
5.35
5.26
5.11
4.14
3.79
3.61
3.44
2.61
2.39
2.25
1.61
1.25
0.92
0.90
0.13
1.00
0.98
0.97
2.05
0.96
4.05
3.58
1.00
2.08
3.04
1.18
8.76
18.11
18.41
f1 (ppm)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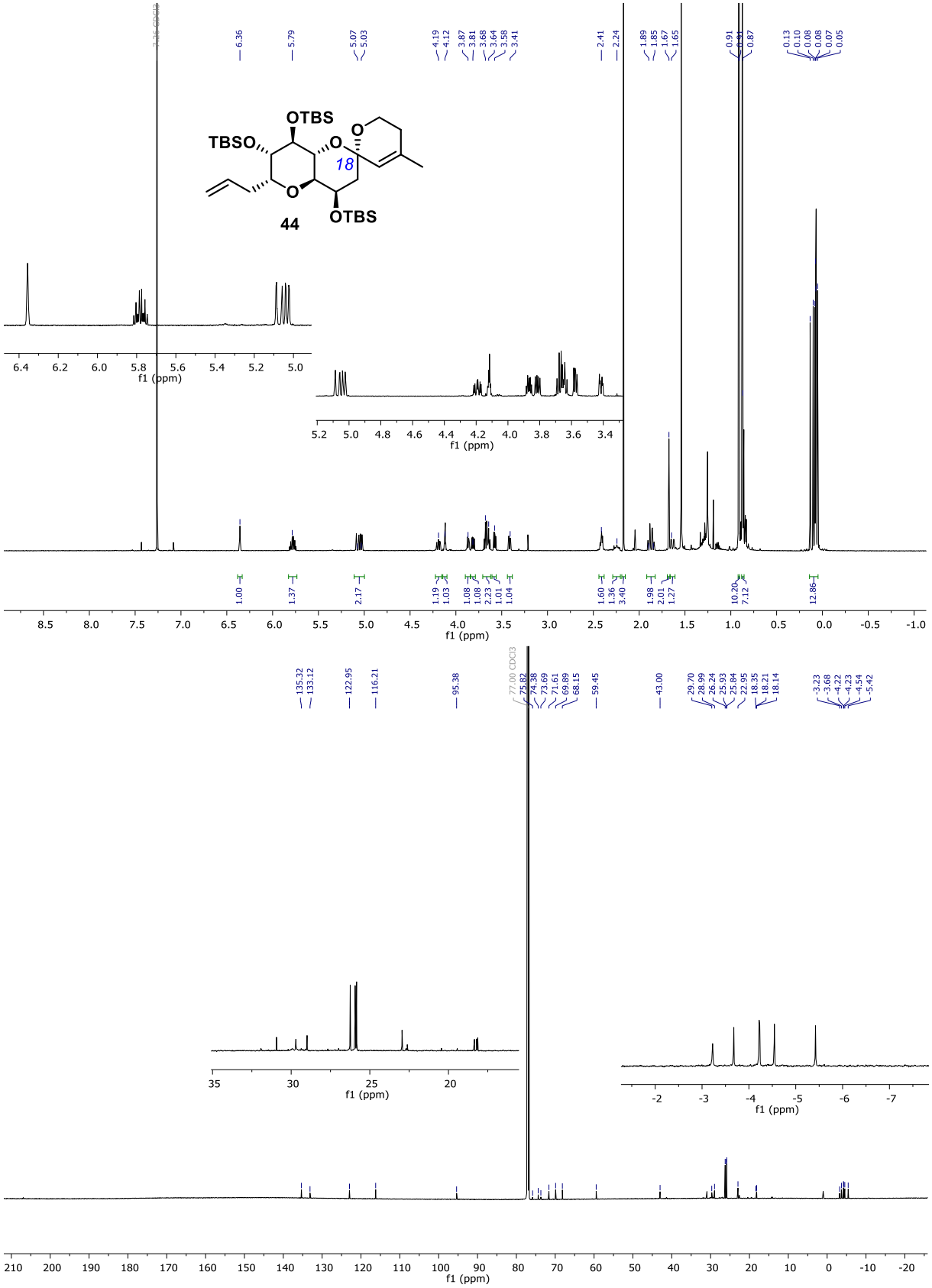
122.51
117.09
87.70
82.20
77.21
CDCl3
73.15
72.44
60.77
40.68
32.46
32.42
31.75
31.13
26.09
26.00
25.74
25.30
18.20
18.10
18.07
-3.90
-4.03
-4.14
-4.35
-4.60
f1 (ppm)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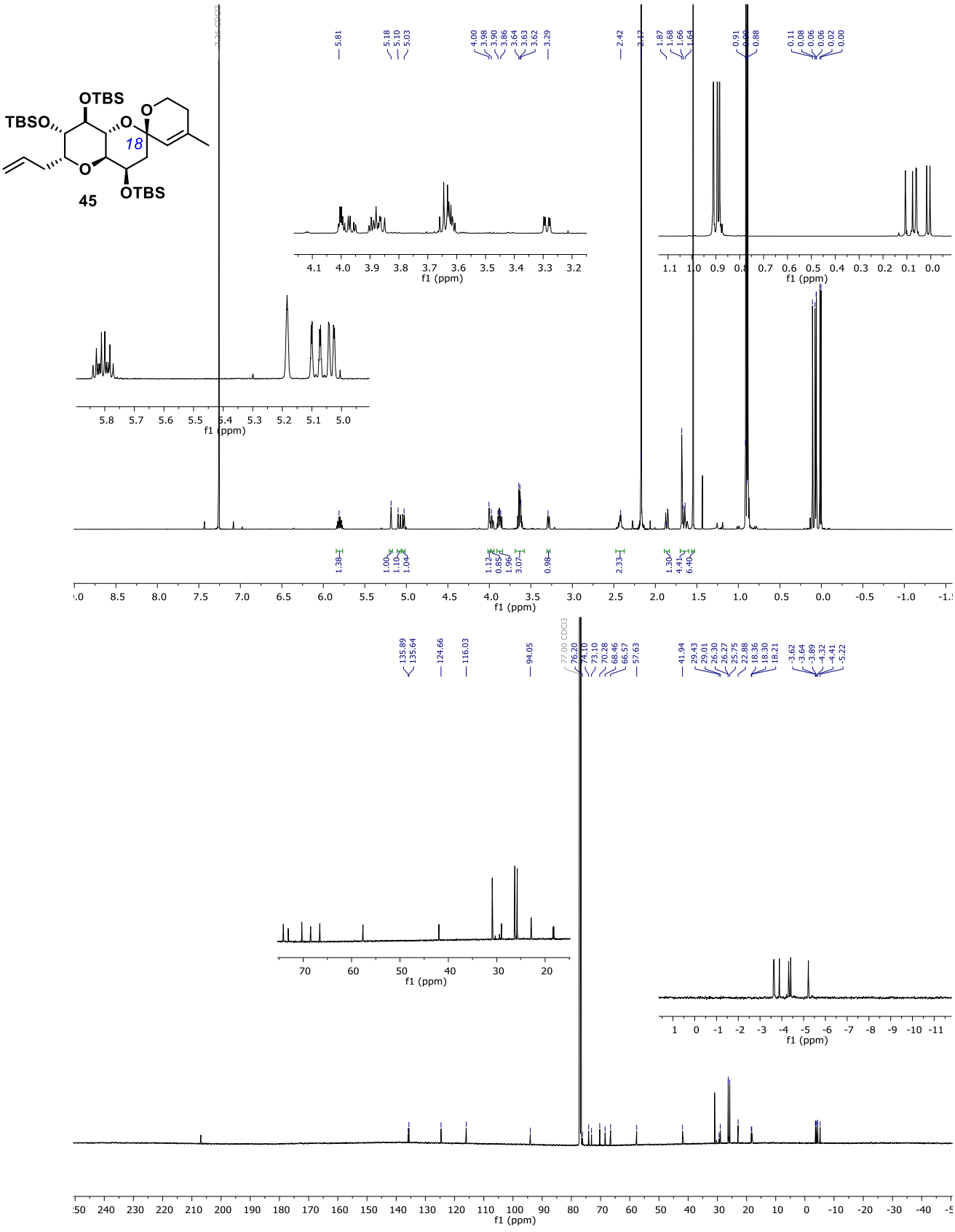
TBSO
O
O
18
O
OTBS
44
f1 (ppm)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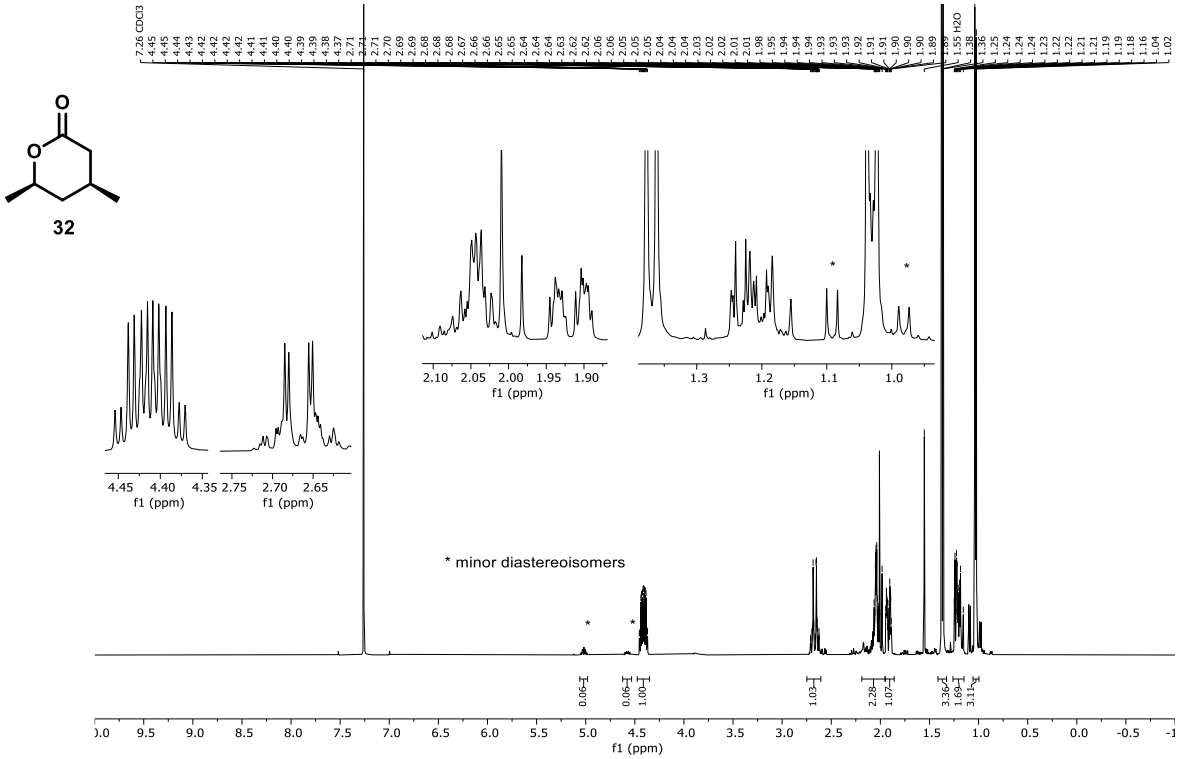
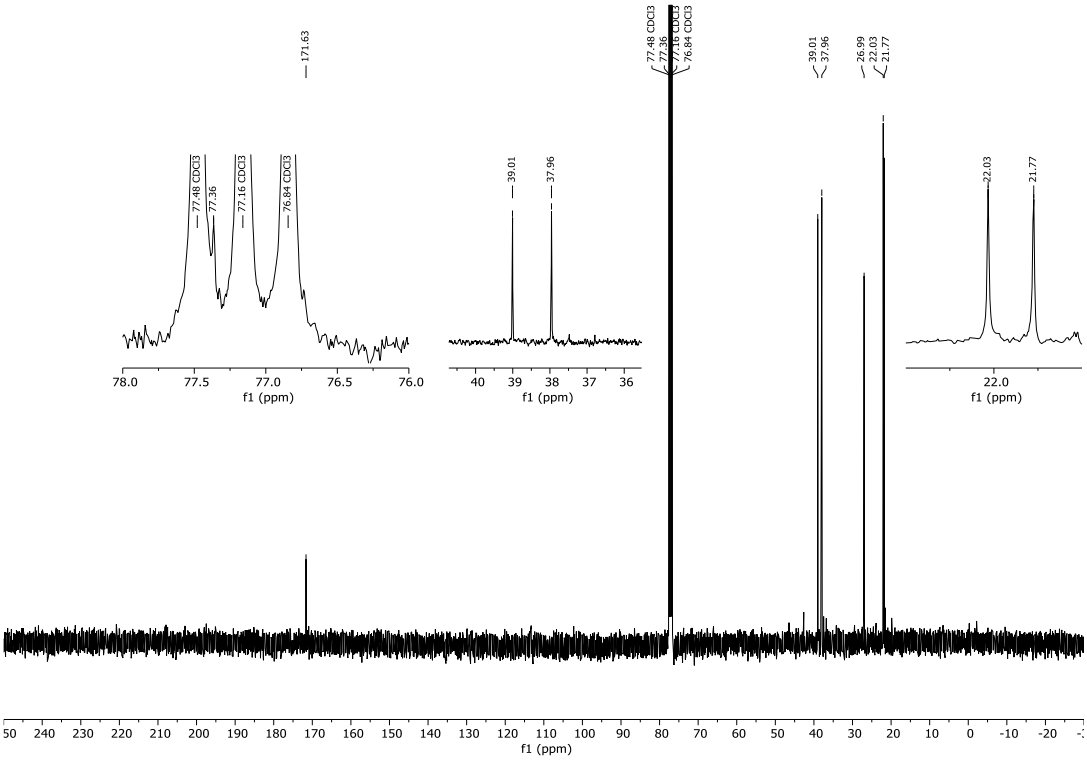
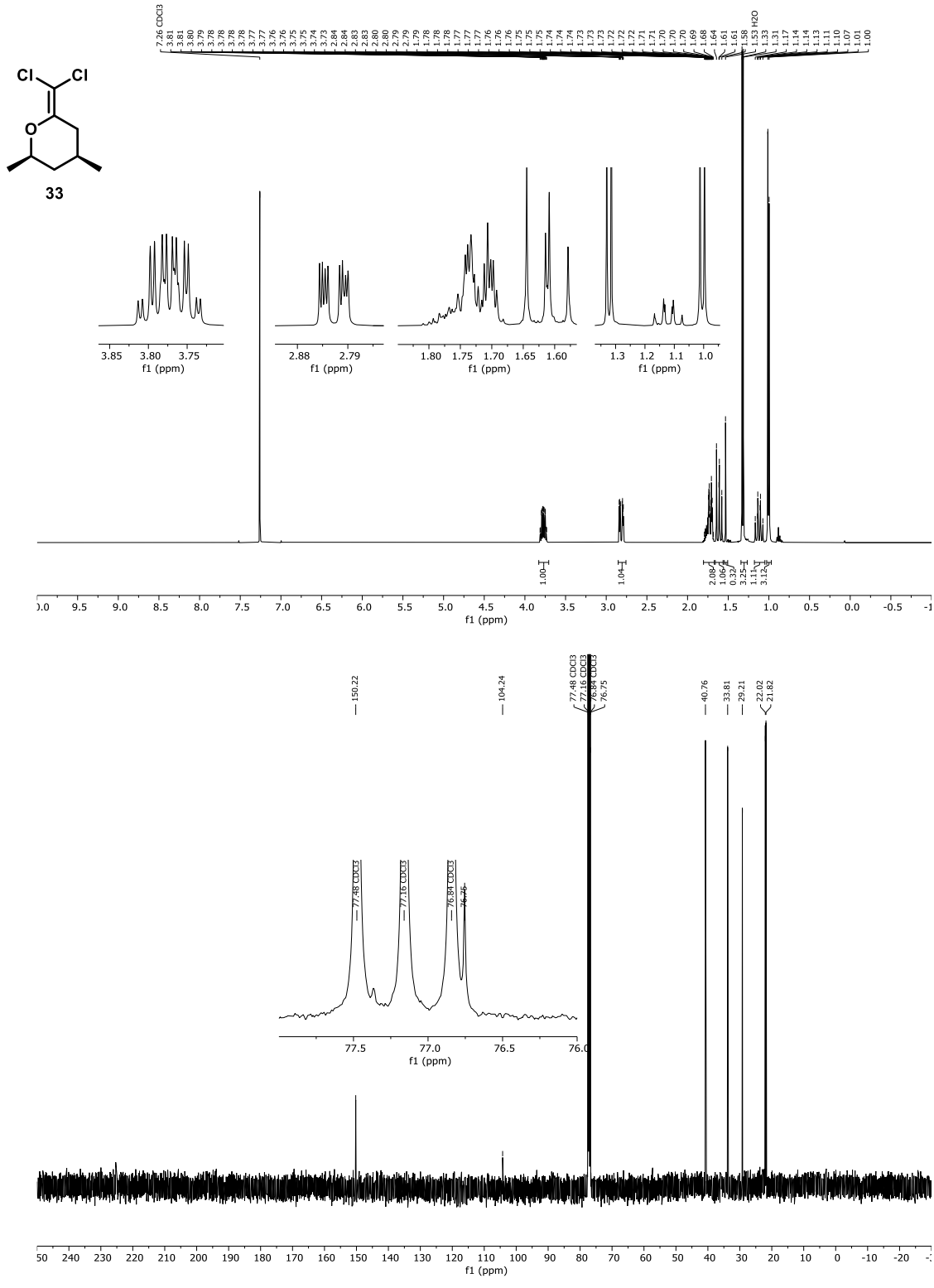
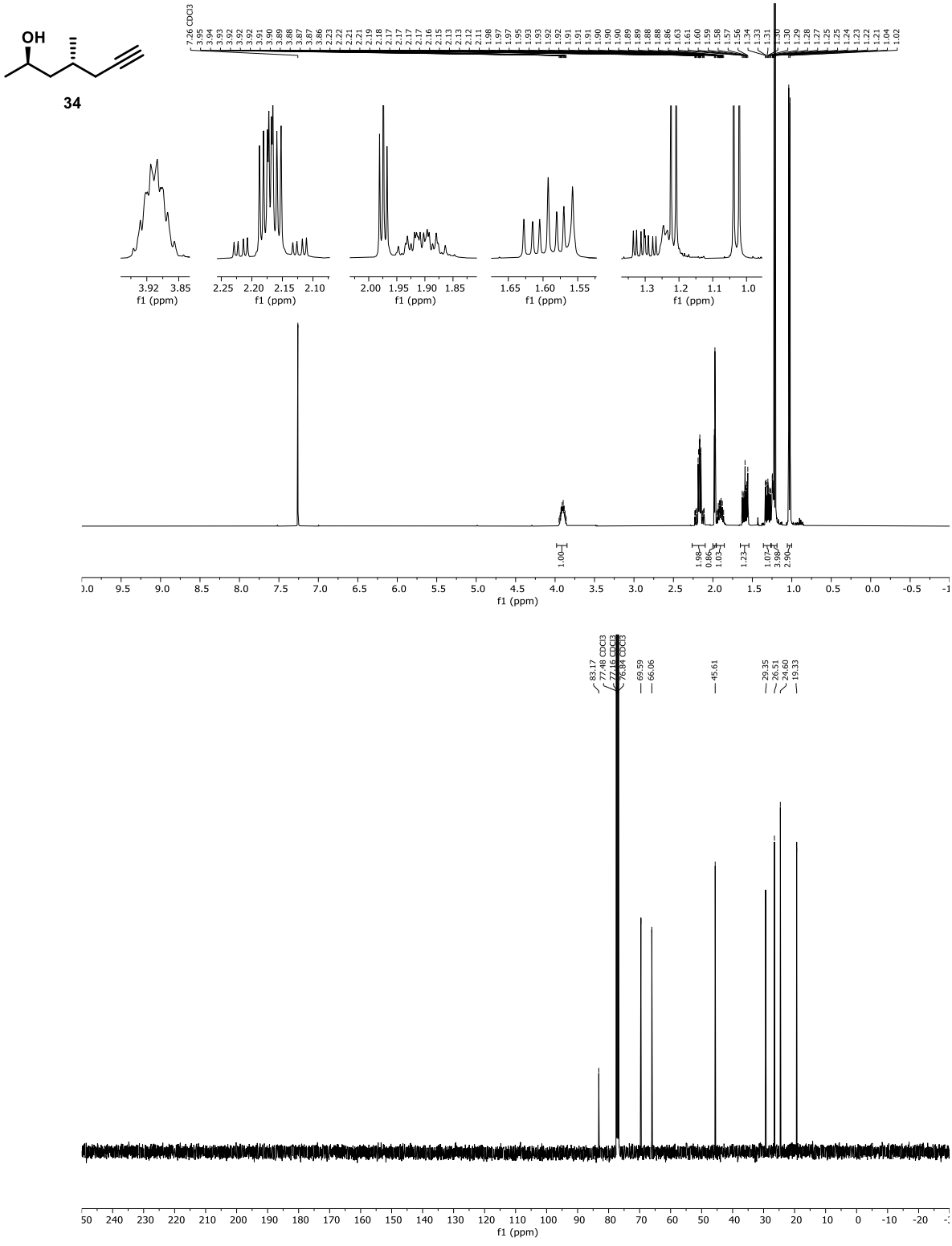
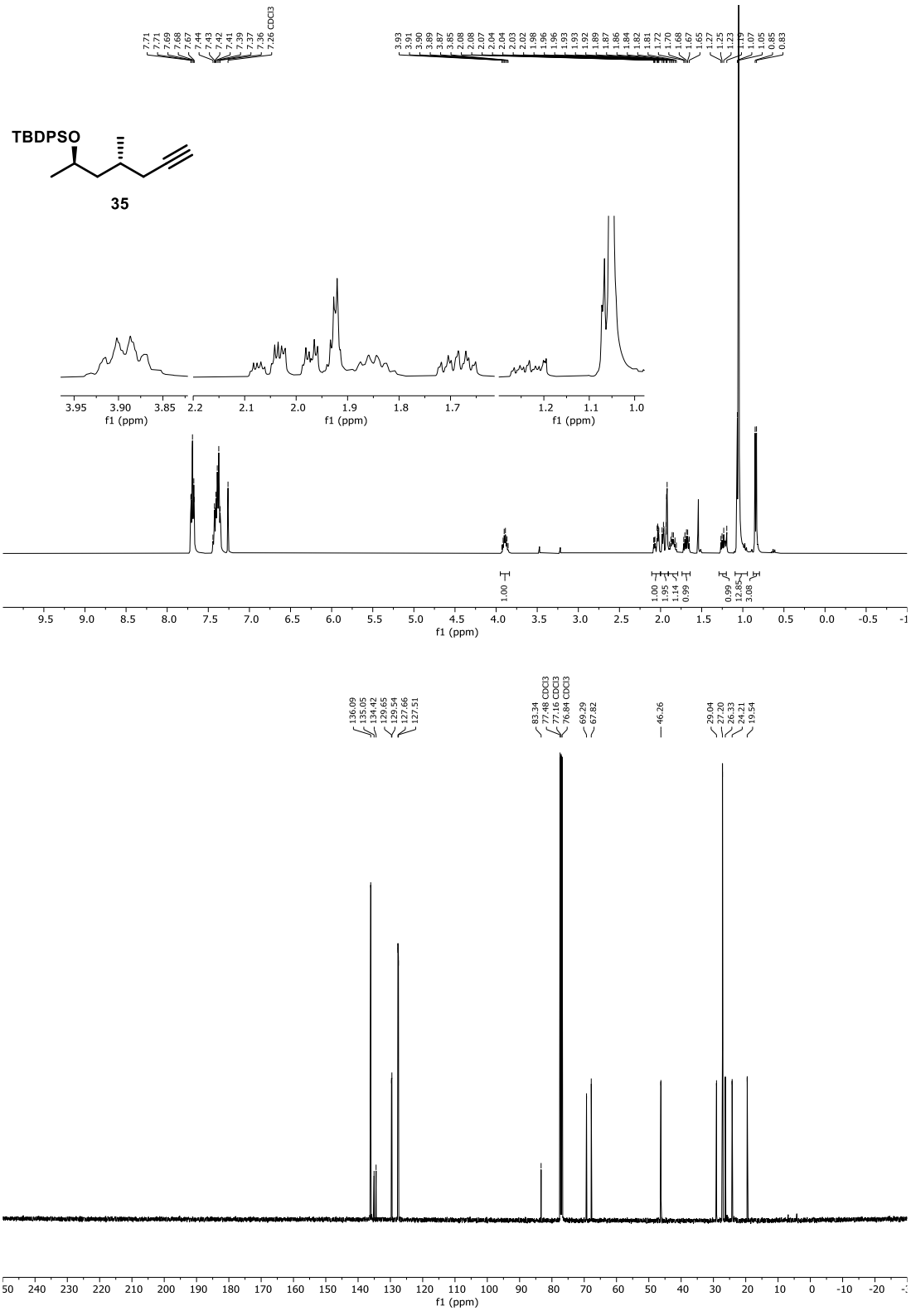
TBSO
O
O
O
18
O
OTBS
45
f1 (ppm)

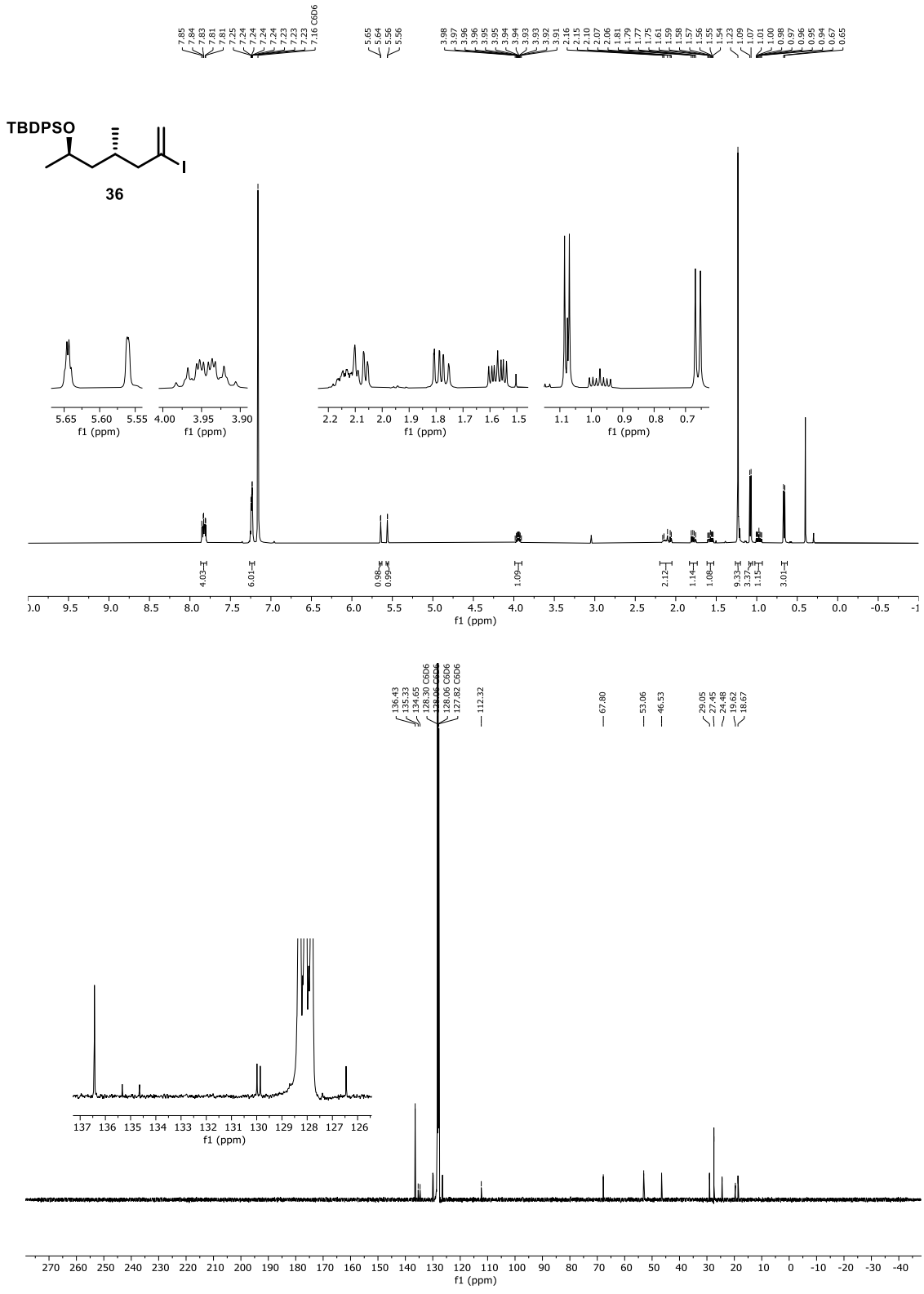

32
* minor diastereoisomers
f1 (ppm)

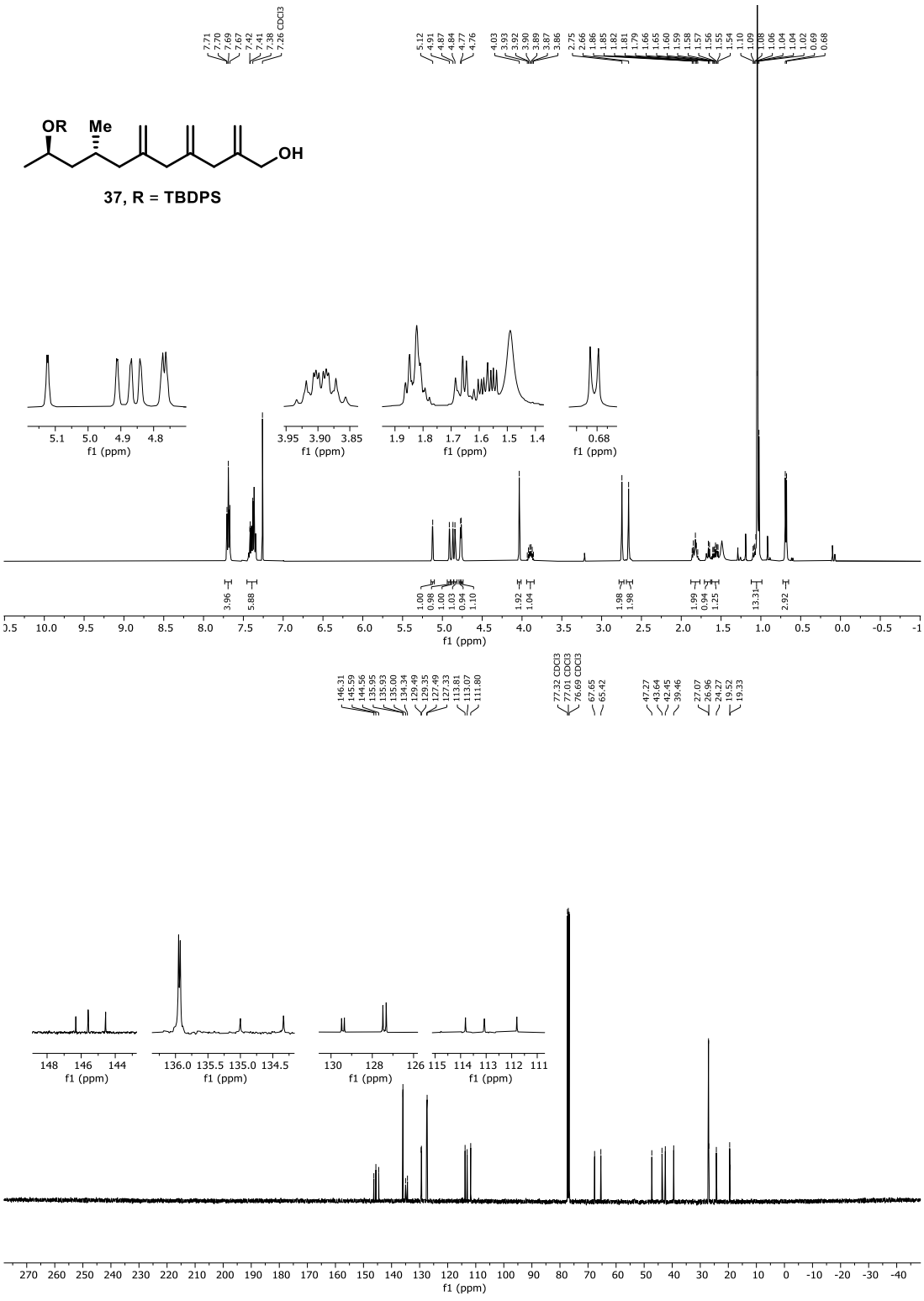

171.63
77.48 CDCl3
77.36
77.16 CDCl3
76.84 CDCl3
39.01
37.96
26.99
22.03
21.77
f1 (ppm)

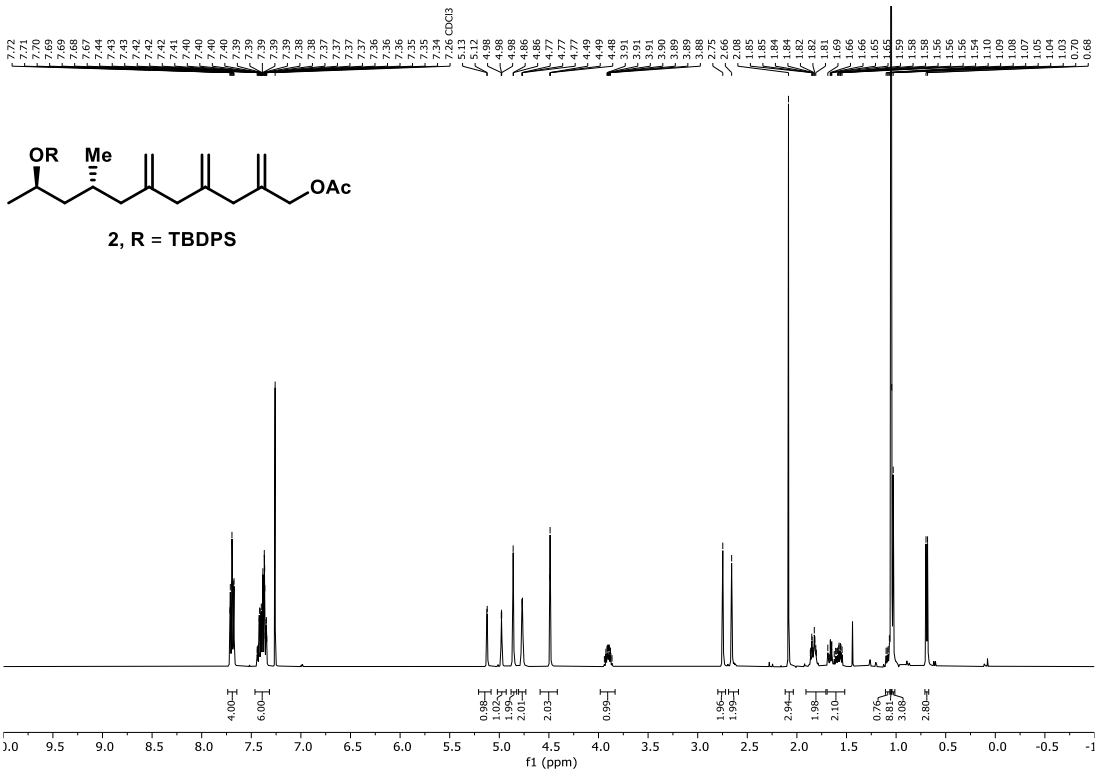

Cl
Cl
O
33
7.26 CDCl3
3.81
3.80
3.79
3.78
3.77
3.76
3.75
3.74
3.73
2.84
2.83
2.82
2.80
2.79
1.79
1.78
1.77
1.76
1.75
1.74
1.73
1.72
1.71
1.70
1.69
1.68
1.64
1.61
1.58
1.53 H2O
1.33
1.31
1.17
1.14
1.13
1.11
1.10
1.07
1.01
1.00
f1 (ppm)
1.00
1.04
2.08
1.06
0.32
3.25
1.11
3.12
150.22
104.24
77.48 CDCl3
77.16 CDCl3
76.84 CDCl3
76.75
40.76
33.81
29.21
22.02
21.82

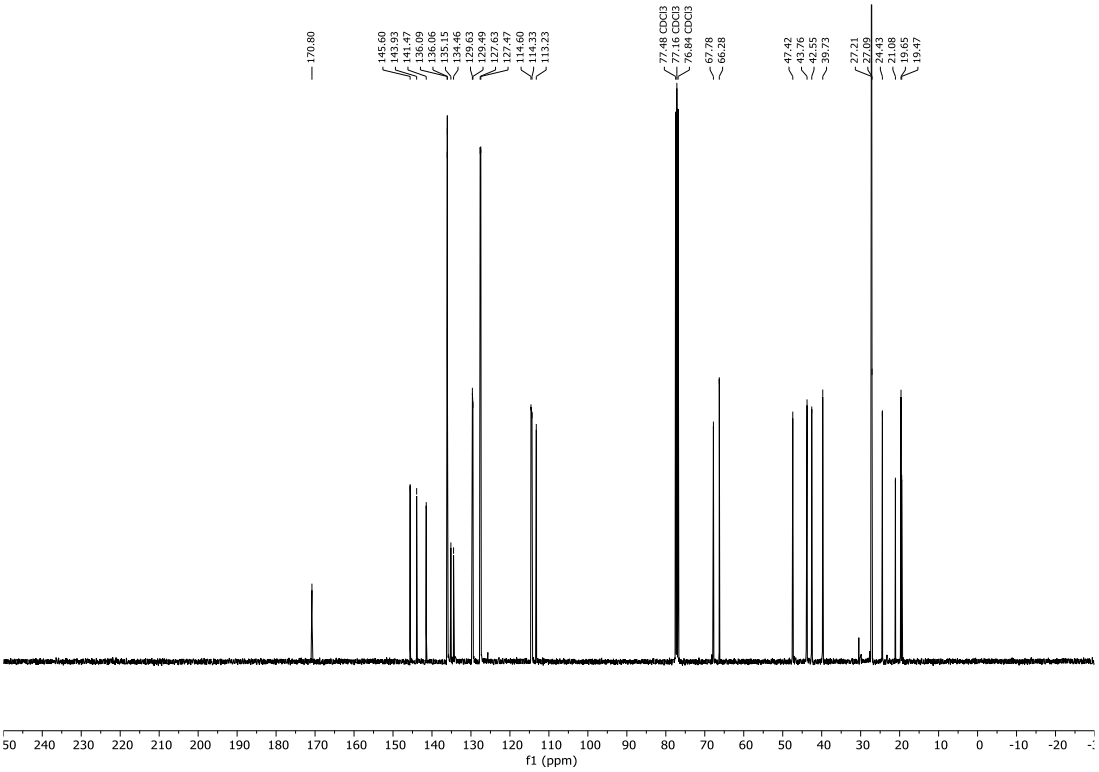

OH
34
7.26 CDCl3
f1 (ppm)
1.00
1.98
0.86
1.03
1.23
1.07
3.98
2.90
83.17
77.48 CDCl3
77.16 CDCl3
76.84 CDCl3
69.59
66.06
45.61
29.35
26.51
24.60
19.33

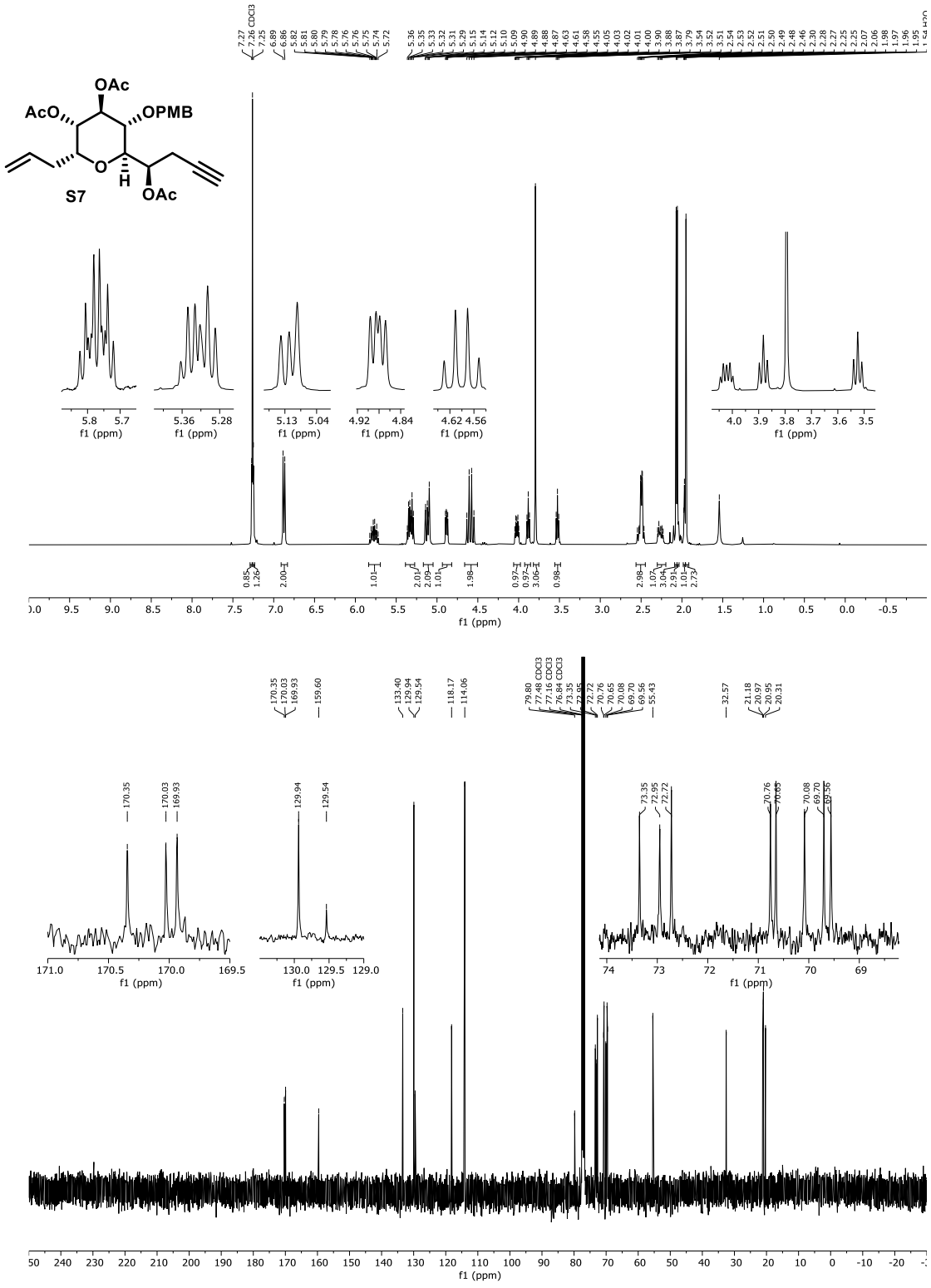

TBDPSO
35
f1 (ppm)

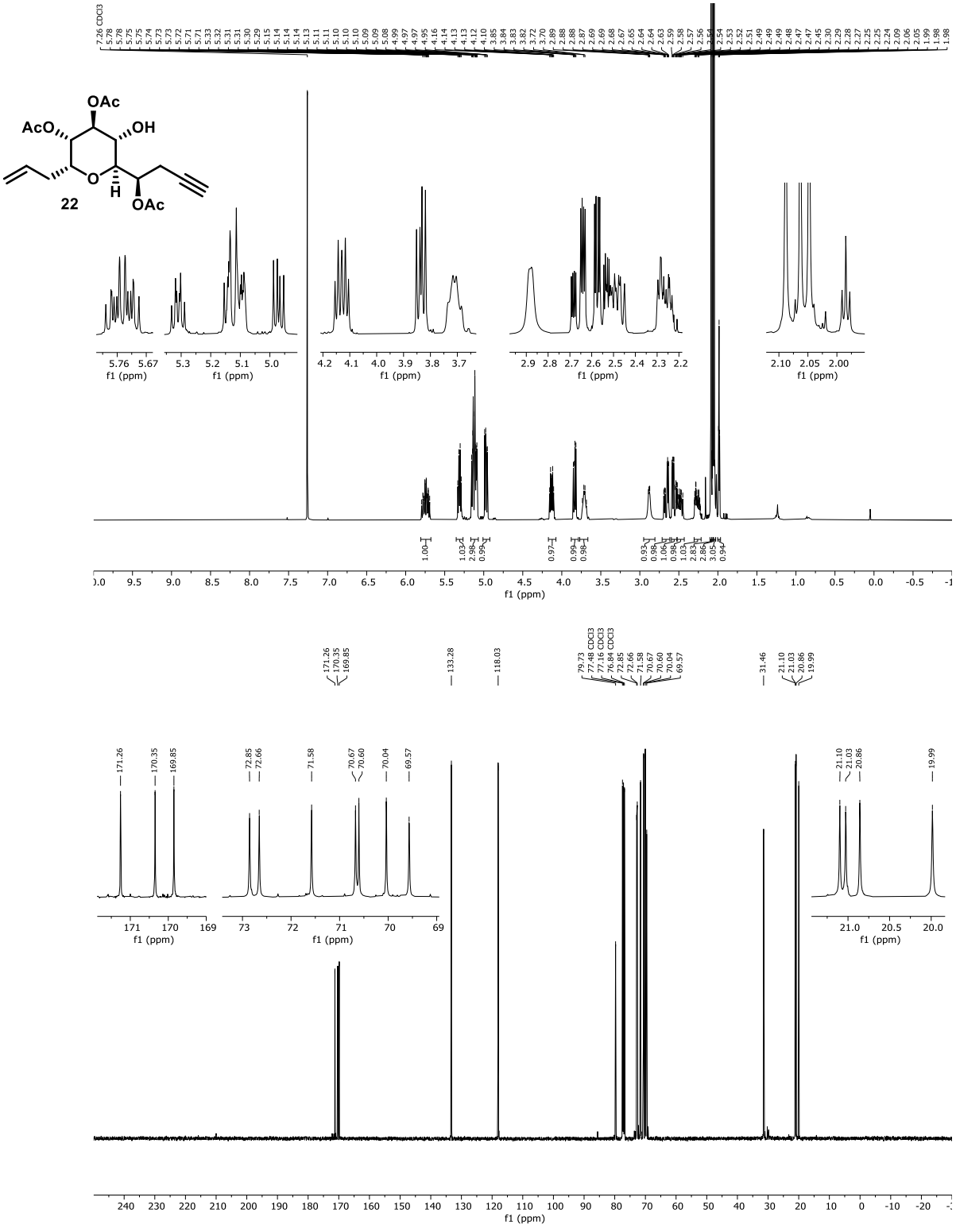

TBDPSO
36
f1 (ppm)

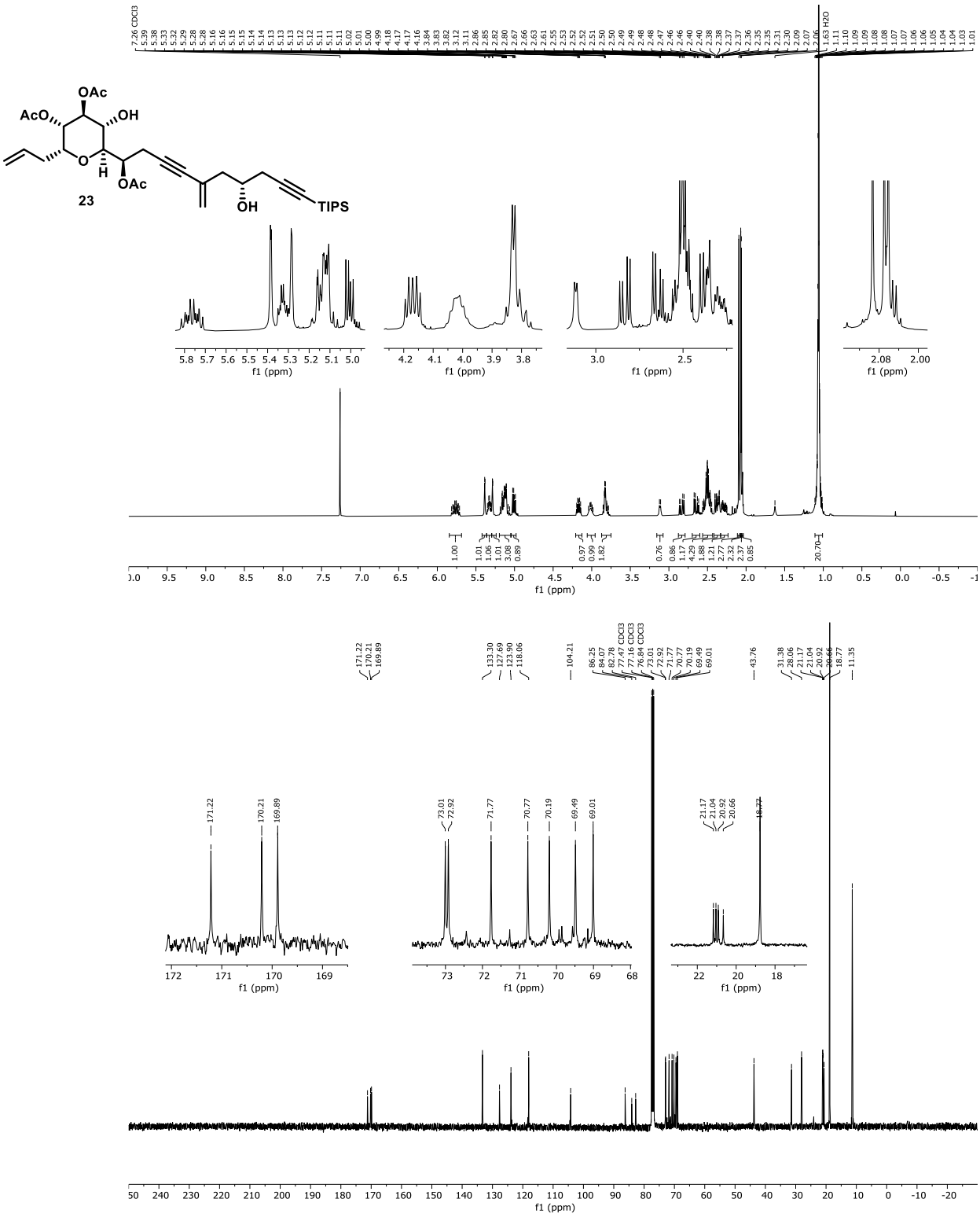

OR
Me
OH
37, R = TBDPS
f1 (ppm)

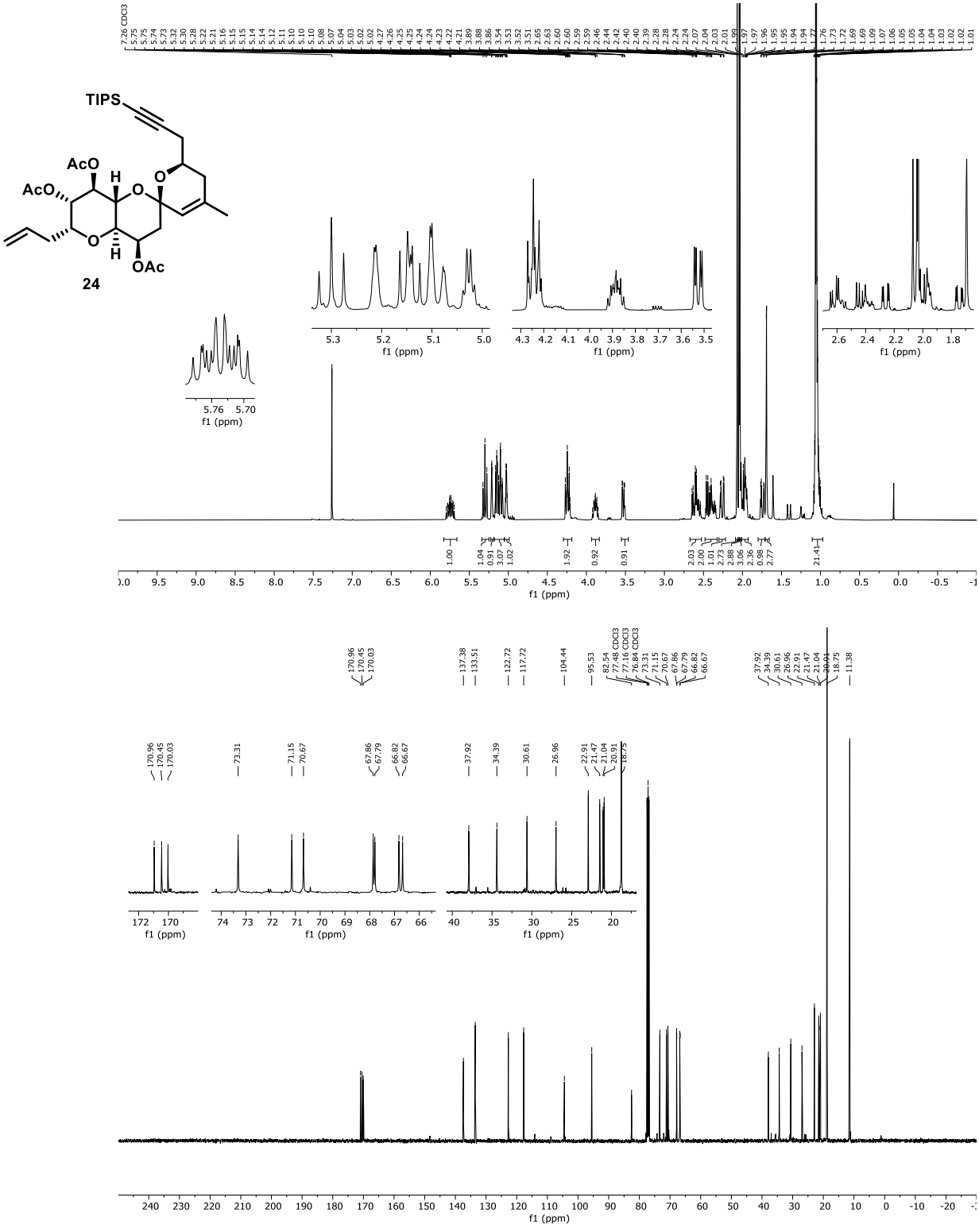

OR
Me
OAc
2, R = TBDPS
f1 (ppm)

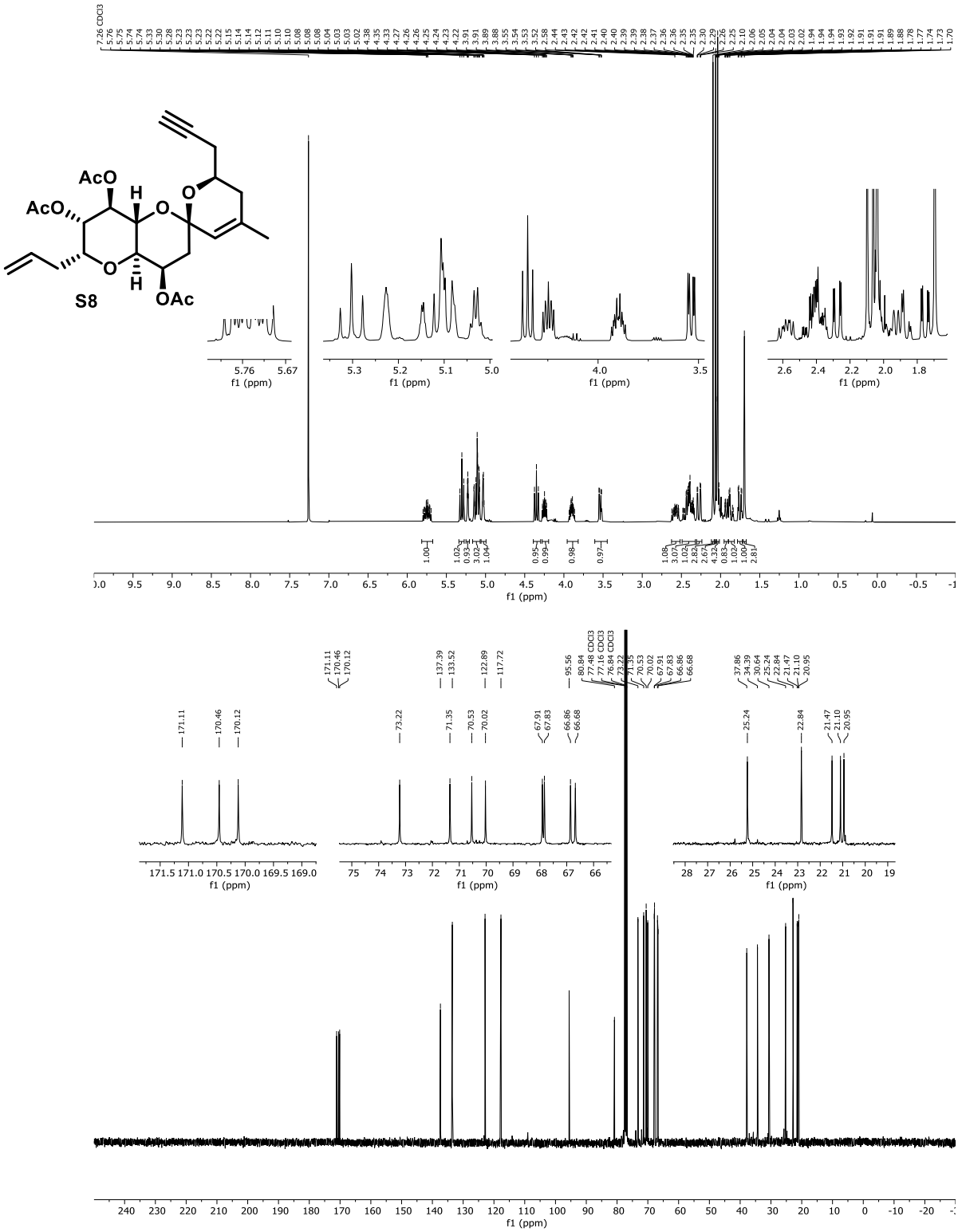

f1 (ppm)

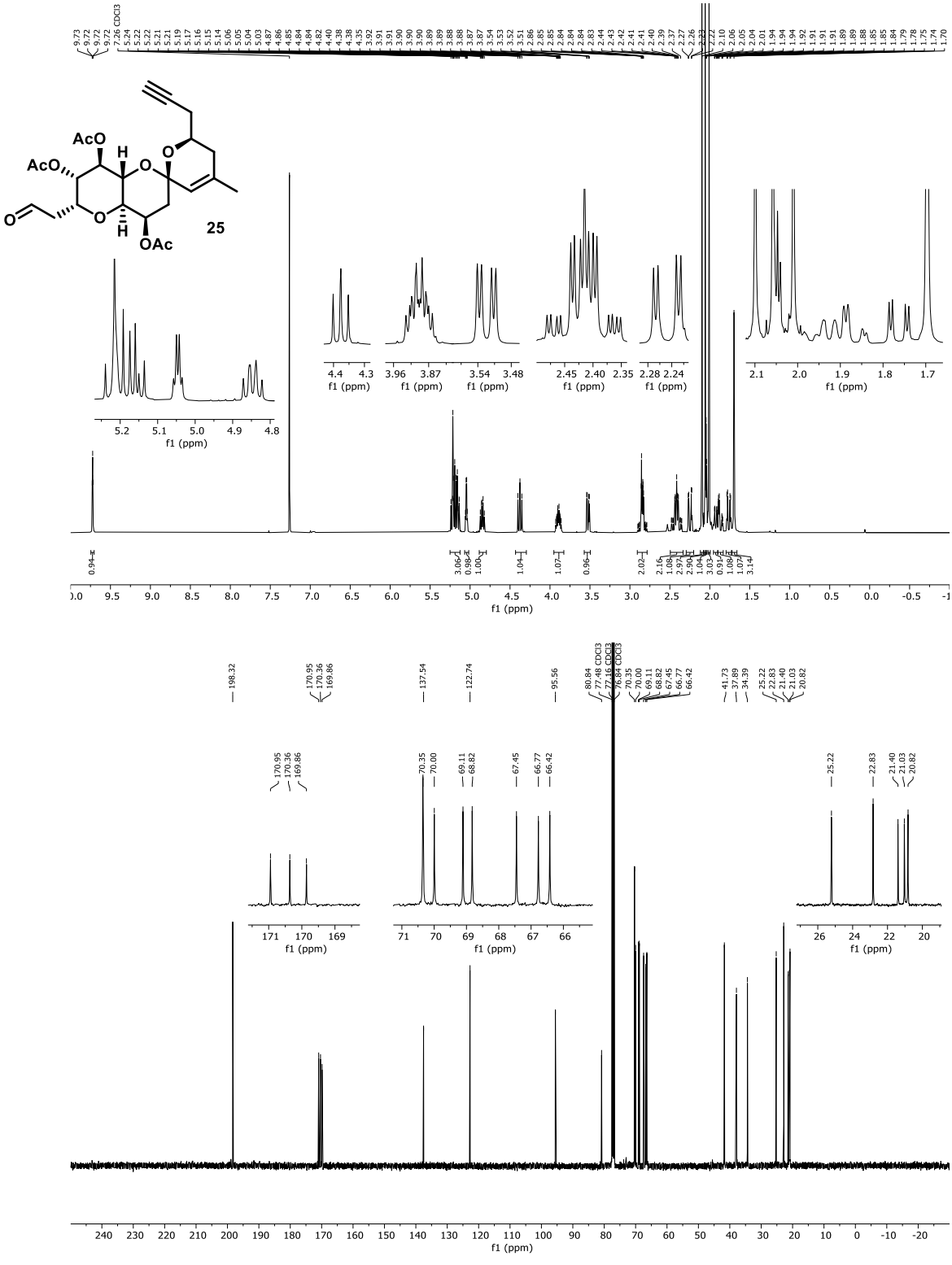

OAc
AcO
OPMB
O
H
OAc
S7
f1 (ppm)

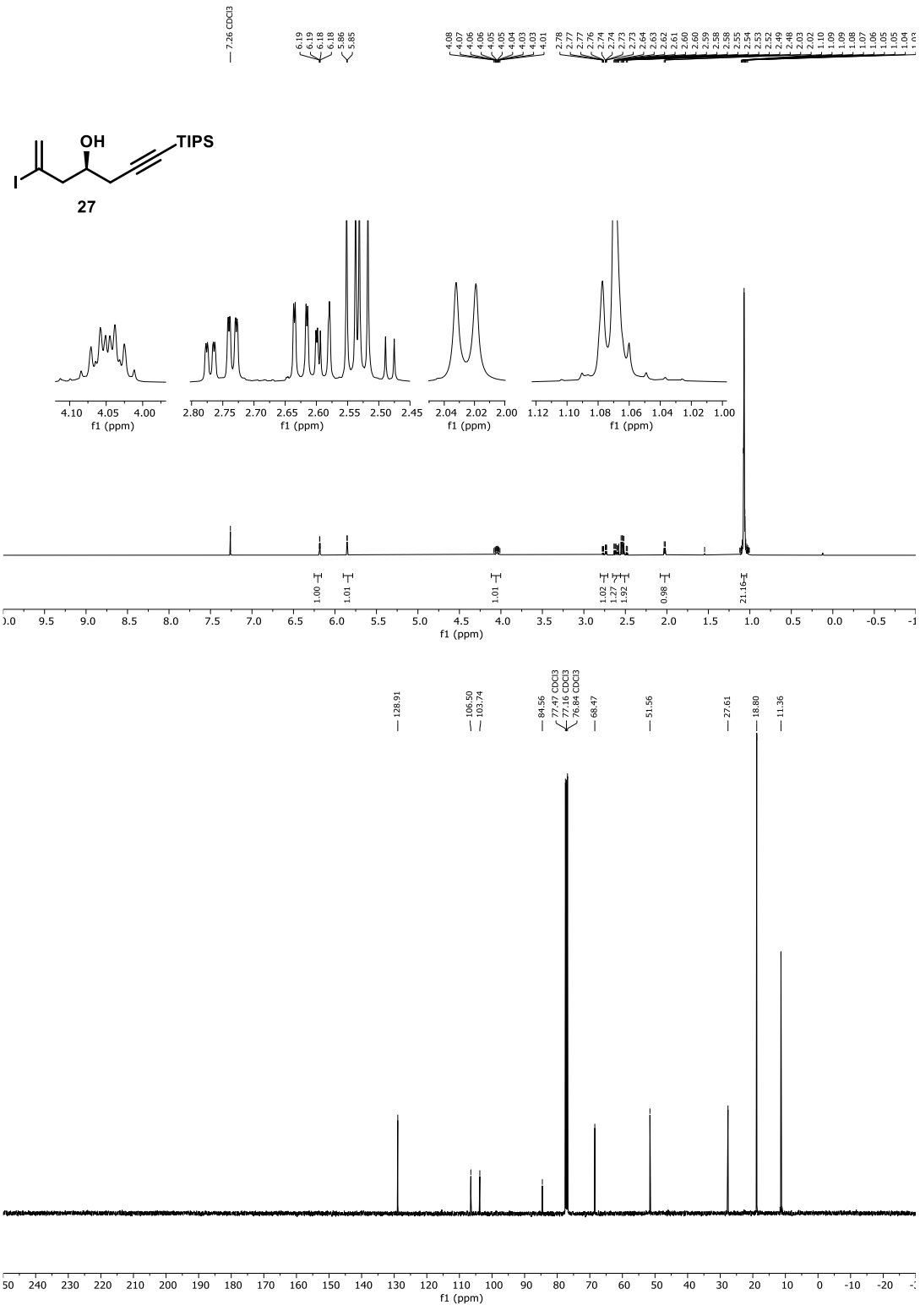

OAc
AcO
OH
O
H
OAc
22
f1 (ppm)

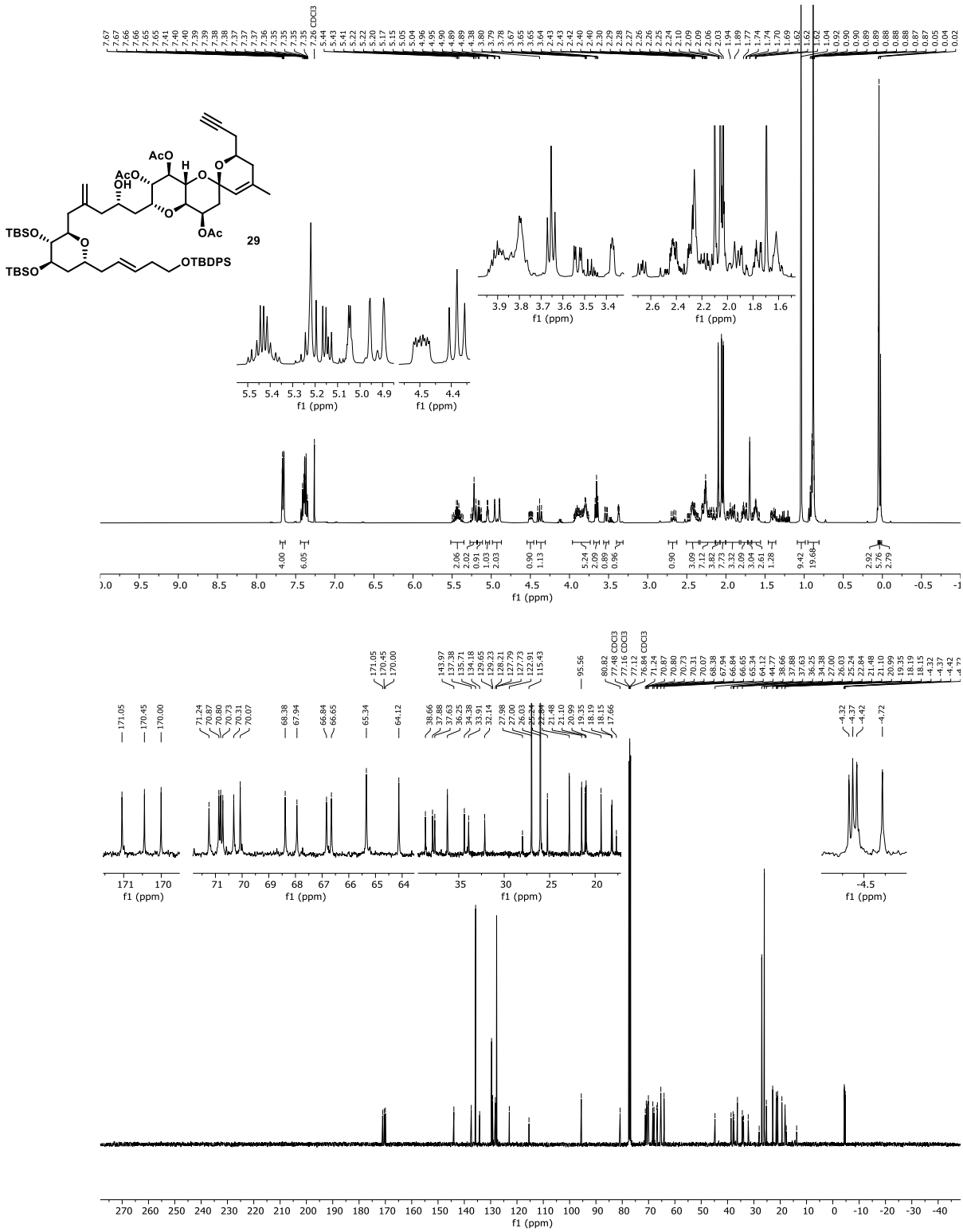

OAc
AcO
OH
O
H
OAc
23
OH
TIPS
f1 (ppm)

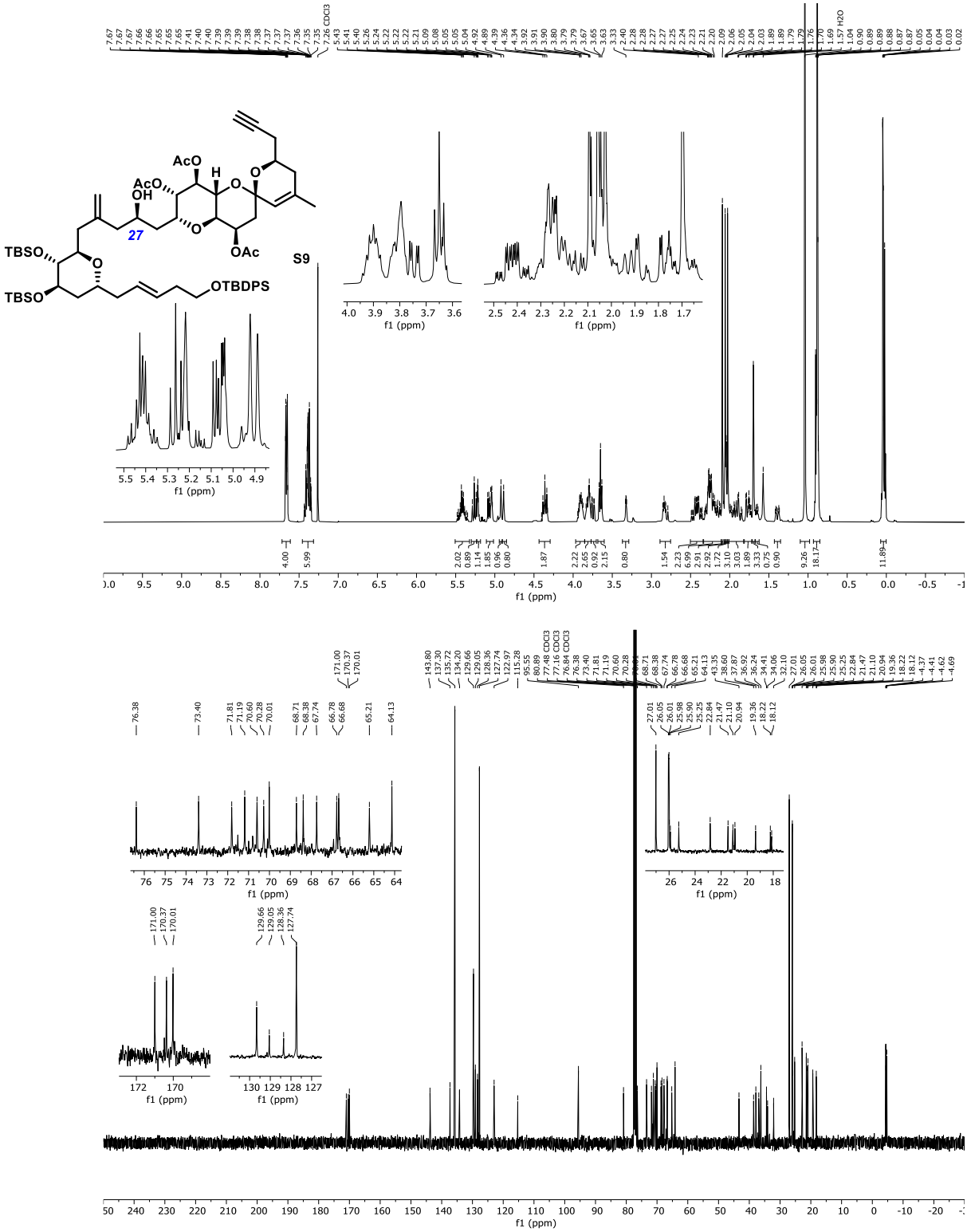

TIPS
AcO
AcO
H
O
O
O
H
OAc
24
f1 (ppm)

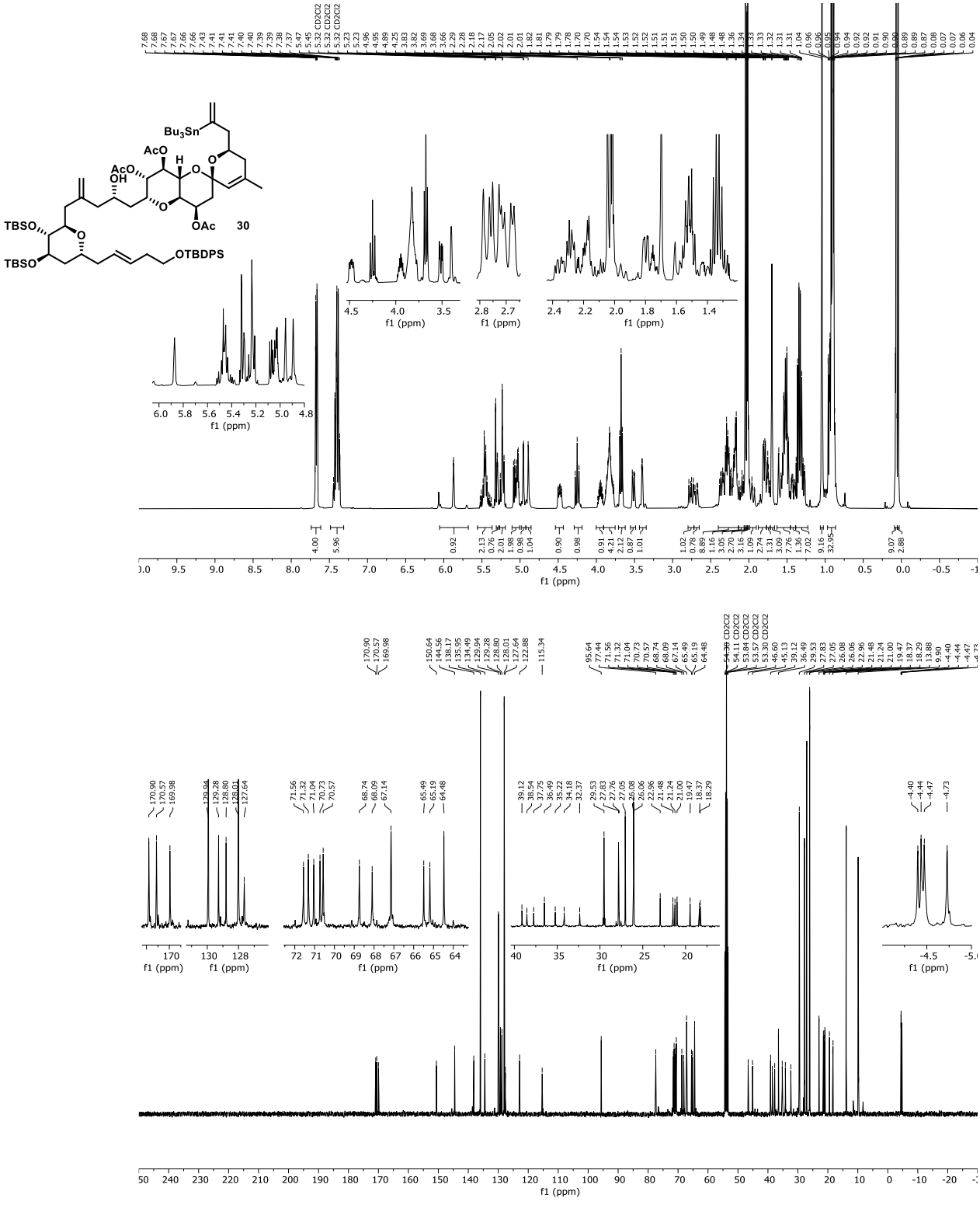

AcO
AcO
H
O
O
O
H
OAc
S8
f1 (ppm)

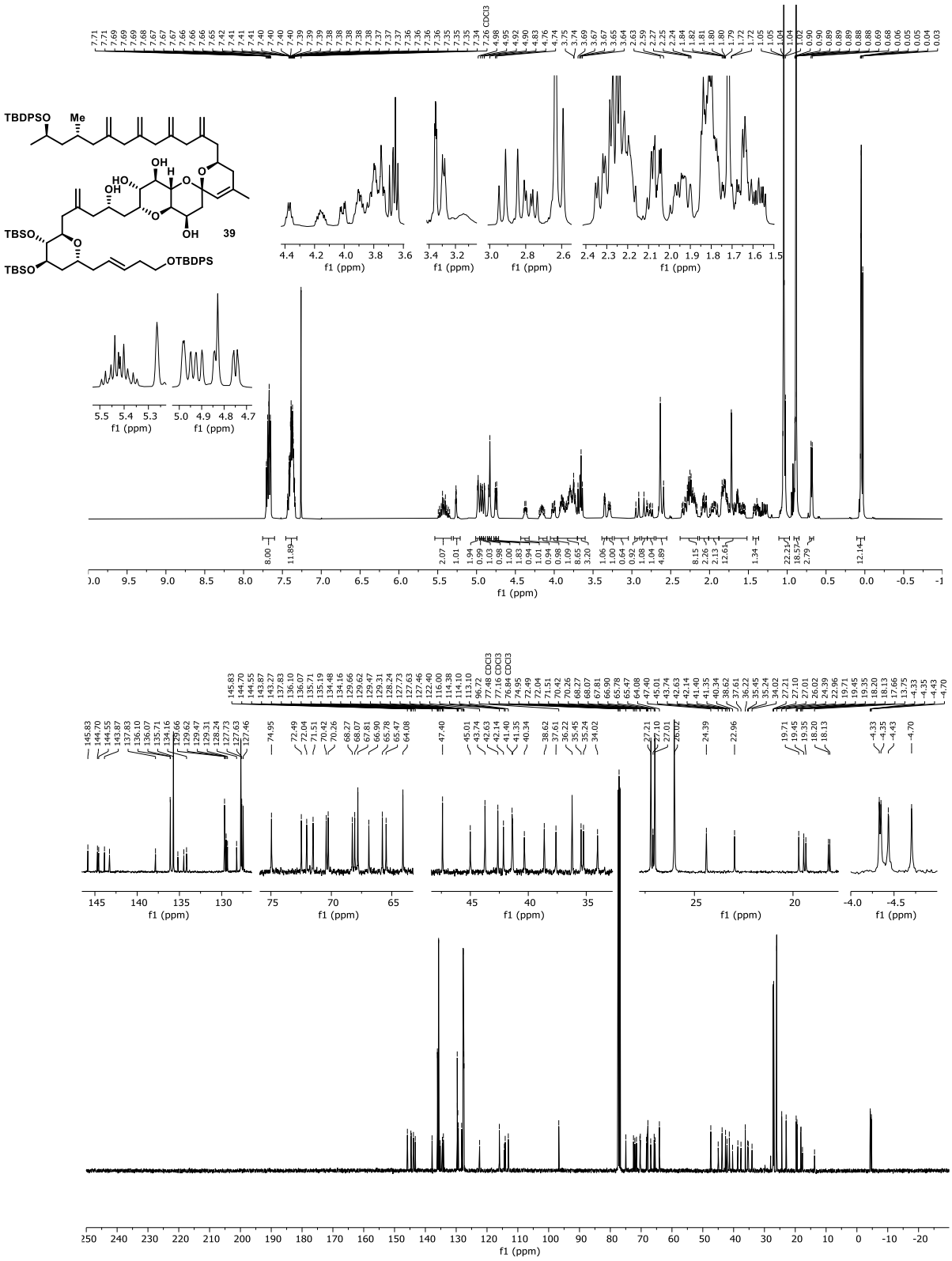

AcO
AcO
H
O
O
O
H
OAc
25
f1 (ppm)

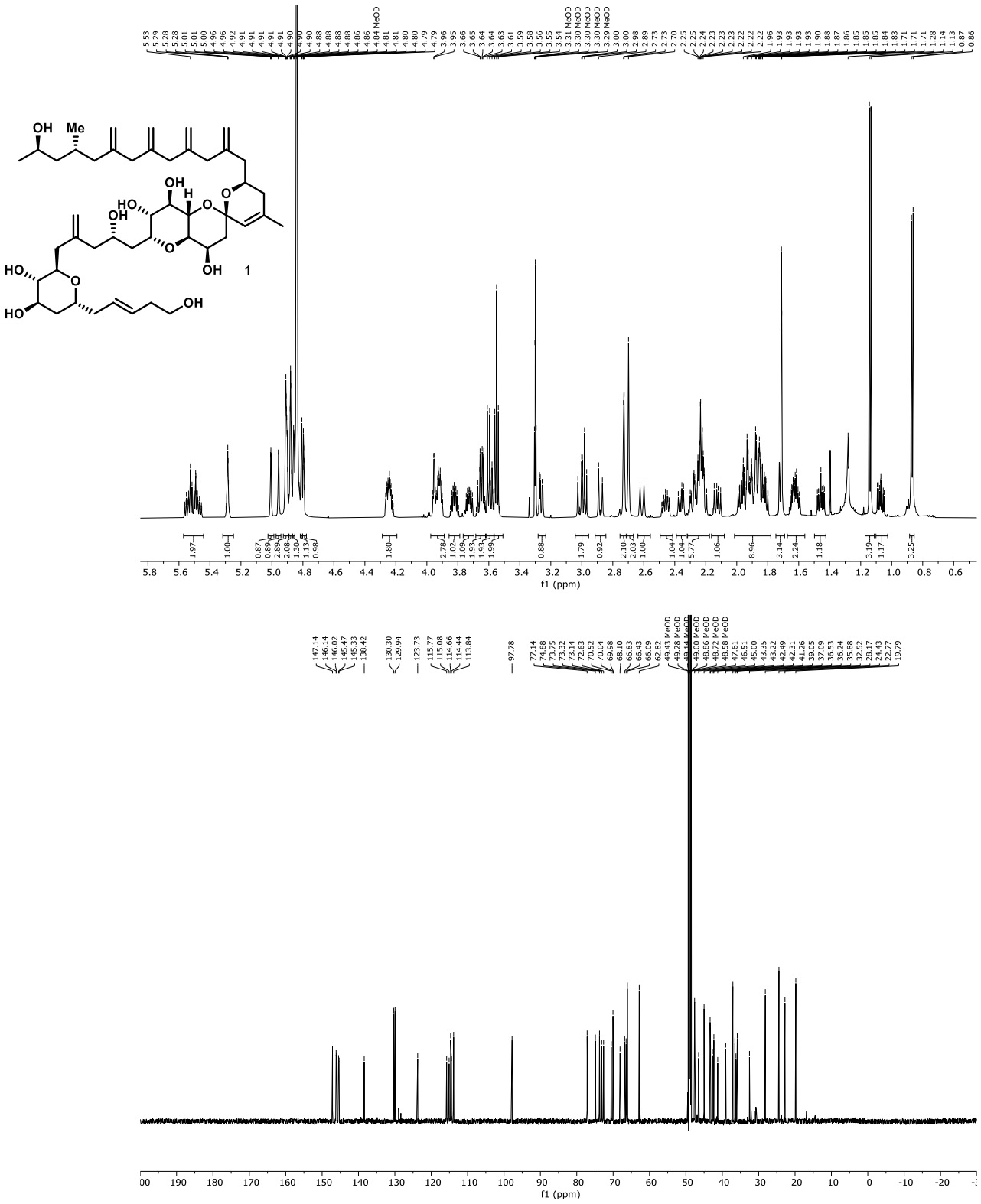

OH
TIPS
I
27
7.26 CDCl3
6.19
6.19
6.18
6.18
5.86
5.85
4.08
4.07
4.06
4.06
4.05
4.05
4.04
4.03
4.03
4.01
2.78
2.77
2.77
2.76
2.74
2.74
2.73
2.73
2.64
2.63
2.62
2.61
2.60
2.60
2.59
2.58
2.58
2.55
2.54
2.53
2.52
2.49
2.48
2.03
2.02
1.10
1.09
1.09
1.08
1.07
1.06
1.05
1.05
1.04
4.10 4.05 4.00
f1 (ppm)
2.80 2.75 2.70 2.65 2.60 2.55 2.50 2.45
f1 (ppm)
2.04 2.02 2.00
f1 (ppm)
1.12 1.10 1.08 1.06 1.04 1.02 1.00
f1 (ppm)
1.00
1.01
1.01
1.02
1.27
1.92
0.98
21.16
f1 (ppm)
128.91
106.50
103.74
84.56
77.47 CDCl3
77.16 CDCl3
76.84 CDCl3
68.47
51.56
27.61
18.80
11.36
f1 (ppm)


AcO
AcO
OH
H
O
O
O
O
OAc
TBSO
O
TBSO
OTBDPS
29
f1 (ppm)


AcO
AcO
OH
H
O
O
O
OAc
TBSO
O
TBSO
OTBDPS
27
S9
f1 (ppm)


Bu3Sn
AcO
AcO
OH
H
O
O
O
O
OAc
30
TBSO
TBSO
O
OTBDPS
f1 (ppm)


TBDPSO
Me
OH
H
HO
OH
O
O
O
OH
39
TBSO
O
TBSO
OTBDPS
CDCl3
f1 (ppm)


OH
Me
OH
H
HO
O
OH
HO
O
OH
1
HO
O
HO
OH
f1 (ppm)
f1 (ppm)

References

1. Hess, S. N.; Mo, X.; Wirtz, C.; Fürstner, A., Total Synthesis of Limaol. *J. Am. Chem. Soc.* **2021,** *143* (6), 2464-2469.
2. Brooks, J. L.; Frontier, A. J., Cyclization Cascades Initiated by 1,6-Conjugate Addition. *J. Am. Chem. Soc.* **2012,** *134* (40), 16551-16553.
3. Lin, Y.-S.; Li, G.-D.; Mao, S.-P.; Chai, J.-D., Long-Range Corrected Hybrid Density Functionals with Improved Dispersion Corrections. *J. Chem. Theory Comput.* **2013,** *9* (1), 263-272.
4. Weigend, F.; Ahlrichs, R., Balanced Basis Sets of Split Valence, Triple Zeta Valence and Quadruple Zeta Valence Quality for H to Rn: Design and Assessment of Accuracy. *Phys. Chem. Chem. Phys.* **2005,** *7*, 3297.
5. Weigend, F., Accurate Coulomb-fitting basis sets for H to Rn. *Physical Chemistry Chemical Physics* **2006,** *8* (9), 1057-1065.
6. Nieto-Oberhuber, C.; López, S.; Echavarren, A. M., Intramolecular [4 + 2] Cycloadditions of 1,3-Enynes or Arylalkynes with Alkenes with Highly Reactive Cationic Phosphine Au(I) Complexes. *J. Am. Chem. Soc.* **2005,** *127* (17), 6178-6179.
7. Fehr, M. J.; Consiglio, G.; Scalone, M.; Schmid, R., Asymmetric Hydrogenation of Substituted 2-Pyrones. *J. Org. Chem.* **1999,** *64* (16), 5768-5776.
8. Fehr, M. J.; Consiglio, G.; Scalone, M.; Schmid, R., Stereochemical aspects of the enantioselective hydrogenation of 2-pyrones. *New Journal of Chemistry* **1998,** *22* (12), 1499-1504.
9. Feiken, N.; Pregosin, P. S.; Trabesinger, G.; Scalone, M., (6,6'-Dimethoxybiphenyl-2,2'-diyl)bis(diphenylphosphine) (MeO-BIPHEP) as a Six-Electron Donor in $[Ru(\eta^5\text{-}C_8H_{11})(MeO\text{-}BIPHEP)]^+$ Cations. Coordination of a Biaryl Double Bond, As Shown by ^{13}C NMR and X-ray Crystallography. *Organometallics* **1997,** *16* (4), 537-543.
10. Yadav, J. S.; Prahlad, V.; Chander, M. C., A new reaction for the preparation of acetylenic alcohols from lactones. *J. Chem. Soc., Chem. Commun.* **1993,** (2), 137-138.
11. Corey, E. J.; Imwinkelried, R.; Pikul, S.; Xiang, Y. B., Practical enantioselective Diels-Alder and aldol reactions using a new chiral controller system. *J. Am. Chem. Soc.* **1989,** *111* (14), 5493-5495.
12. Hoye, T. R.; Jeffrey, C. S.; Shao, F., Mosher ester analysis for the determination of absolute configuration of stereogenic (chiral) carbinol carbons. *Nat. Protoc.* **2007,** *2*, 2451.
13. Yang, A. R.; Lee, S.; Yoo, Y. D.; Kim, H. S.; Jeong, E. J.; Rho, J. R., Limaol: A Polyketide from the Benthic Marine Dinoflagellate Prorocentrum lima. *J. Nat. Prod.* **2017,** *80*, 1688-1692.