



Supporting Information for

Formal Total Synthesis of Actinoranone and Asymmetric Synthesis of Labda-7,13-(*E*)-dien-15-ol

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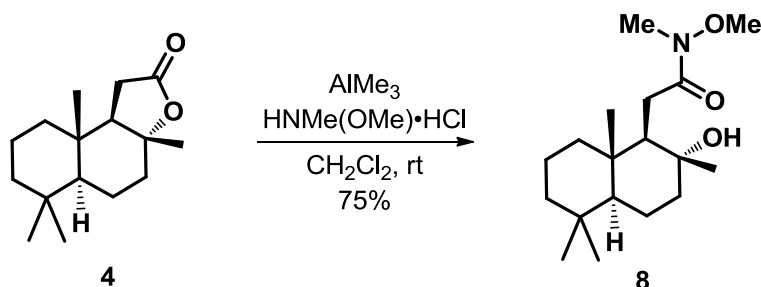
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I. General Information.

Starting materials and reagents were obtained from commercial sources and used as received unless otherwise specified. Dichloromethane, triethylamine and pyridine were treated with calcium hydride and distilled before use. Tetrahydrofuran and diethylether were treated with metallic sodium and benzophenone and distilled before use. Anhydrous *N,N*-dimethylformamide, dimethylsulfoxide and diglyme were obtained from Aldrich. Anhydrous methanol, isopropyl alcohol, acetonitrile and toluene were dried over molecular sieves 3A (10% w/v) for more than one week before use. Anhydrous reactions were carried out with continuous stirring under atmosphere of dry nitrogen or argon. Progress of the reactions was monitored by thin-layer chromatography (TLC) analysis (Merck, silica gel 60 F254 on aluminum plates), unless otherwise stated. Flash chromatography purifications were performed with silica gel 60, 220-440 mesh, Sigma-Aldrich. ^1H NMR and ^{13}C NMR were recorded on Bruker 250, the chemical shifts (δ) were reported in parts per million (ppm) relative to deuterated solvent as the internal standard (CDCl_3 : 7.26 ppm for ^1H NMR and 77.0 ppm for ^{13}C NMR), coupling constants (J) are in hertz (Hz). The following abbreviations were used to designate chemical shift multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, quint = quintet, m = multiplet, br. = broad signal. NMR spectra were processed using ACD/NMR Processor Academic Edition version 12.01. High resolution mass spectra (HRMS) were recorded on a Waters Xevo Q-ToF apparatus operating in electrospray mode (ES). Infrared spectra with Fourier transform (FTIR) were recorded on a Thermo Scientific Nicolet iS5, the principal absorptions are listed in cm^{-1} . Optical rotation were measured at 25 °C in a Perkin–Elmer 341 polarimeter, with sodium lamp, the measure is described as follow $[\alpha]_{\text{D}}^{\text{T}}$ (c (g/100 mL), solvent). GC/MS analyses were carried out on an Agilent 9870A gas chromatography with quadrupole mass analyzer (GC-MS) equipped with a split/splitless injector; the column set for all runs consisted of a 30 m \times 0.250 mm HP-5MS column; the oven temperature was increased from 60 to 180 °C at the rate of 20 °C/min and was then further increased to 280 °C at 30 °C/min; the injector and MS transfer lines were at 280 and 230 °C, respectively, and the MS ionization source was maintained at 230 °C using 70 eV; the spectrometer was operated with a mass scan range of 30-400 m/z , resulting in an acquisition rate of 25 spectra/s; the data acquisitions were processed via the GC-MS 5975C data analysis. X-Ray analysis was performed on a Bruker Apex CCD Detector Diffractometer, the data were refined using the software Olex2 v 1.2, and the 3D structure was generated with the software Mercury 3.8. IUPAC names of the compounds were generated using ChemBioDraw Ultra 13.0.

II. Experimental procedures and spectral data.

2-((1*R*,2*R*,4*aS*,8*aS*)-2-hydroxy-2,5,5,8*a*-tetramethyldecahydronaphthalen-1-yl)-*N*-methoxy-*N*-methylacetamide (**8**).



Me₃Al (1 M in heptane, 8.0 mL, 8.0 mmol, 2 equiv) was added to a suspension of MeONHMe·HCl (756 mg, 7.7 mmol, 1 equiv) in dry CH₂Cl₂ (20 mL) at 0 °C (**CAUTION!** *gas evolution*). After addition, the cooling bath was removed and the mixture was kept under magnetic stirring at room temperature for 2 h. Next, a solution of (+)-sclareolide (**4**, 97%, 1000 mg, 3.88 mmol, 1 equiv) in dry CH₂Cl₂ (10 mL) was added to the reaction, and the stirring continued for 18 h at room temperature. After cooling to 0 °C, an aqueous solution of HCl (1 M, 30 mL) was slowly added (**CAUTION!** *gas evolution*). The organic phase was separated and the aqueous phase was extracted with CH₂Cl₂ (2 x 25 mL). The organic phases were combined, dried over anhydrous Na₂SO₄ and concentrated under reduced pressure. The residue was purified by flash chromatography (SiO₂, hexanes/EtOAc 50:50 to 30:70) to furnish amide **8** (908 mg, 2.9 mmol) as a white solid in 75% yield.

TLC (SiO₂): R_f = 0.30 (hexanes/EtOAc 50:50);

M.p.: 102-106 °C;

[α]_D²⁵ = +37 (*c* 1.0, CHCl₃), [α]_{D,lit} = +39.3 (*c* 0.98, CHCl₃);¹

¹H NMR (250 MHz, CDCl₃): δ 0.78 (s, 3H), 0.81 (s, 3H), 0.86 (s, 3H), 1.14 (s, 3H), 0.89-1.73 (m, 10H), 1.86-2.03 (m, 2H), 2.37-2.63 (m, 3H), 3.17 (s, 3H), 3.71 (s, 3H);

¹³C NMR (62.9 MHz, CDCl₃): δ 15.7 (CH₃), 18.4 (CH₂), 20.5 (CH₂), 21.3 (CH₃), 23.2 (CH₃), 26.8 (CH₂), 33.1 (C), 33.2 (2CH₃), 38.5 (C), 39.2 (CH₂), 41.7 (CH₂), 44.4 (CH₂), 55.8 (CH), 56.1 (CH), 61.1 (CH₃), 72.7 (C), 176.0 (C).

¹ Kumar, C. N. S. S. P.; Chein, R.-J. *Org. Lett.* **2014**, *16*, 2990-2992.

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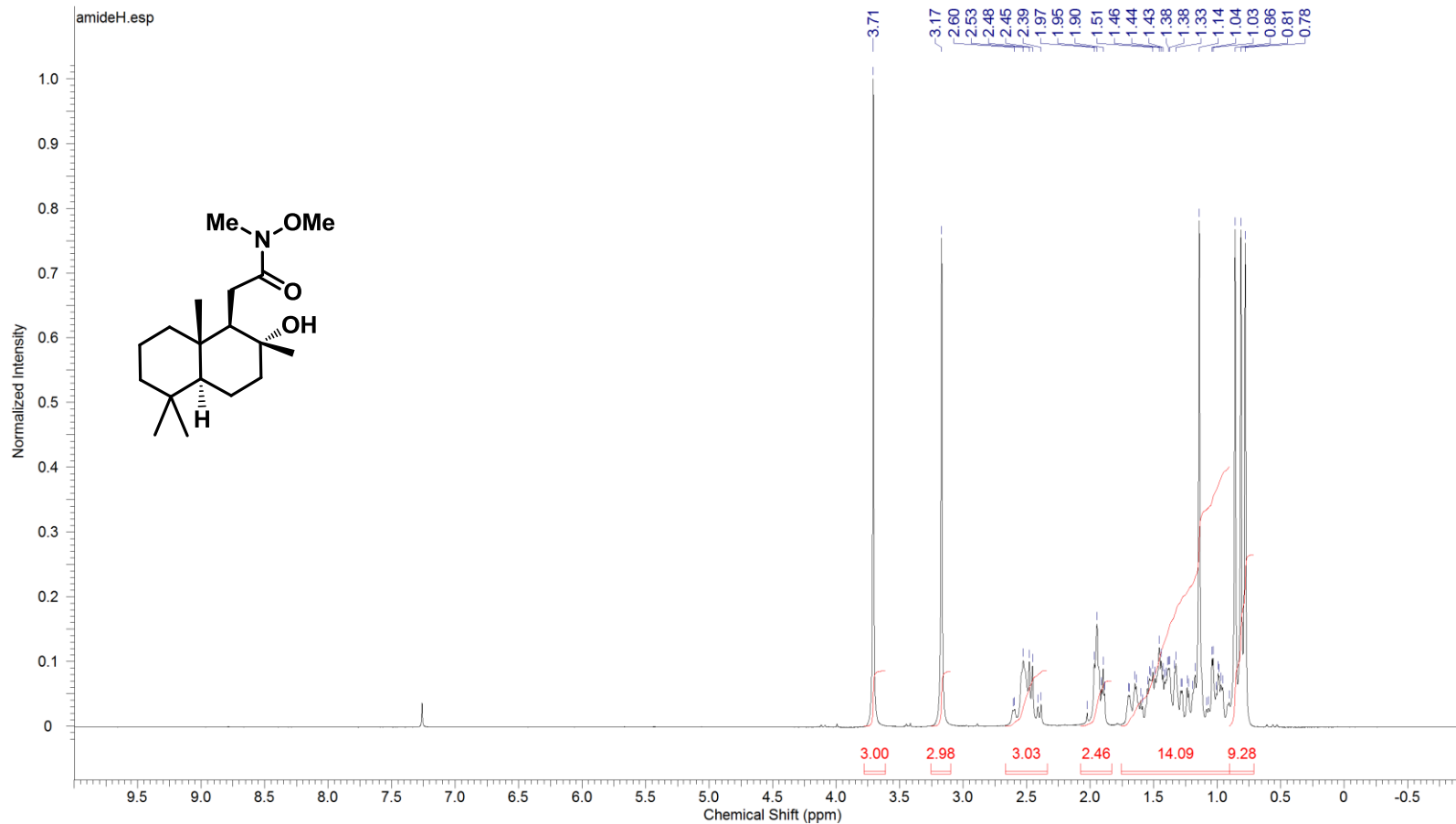


Figure S1. ^1H NMR spectrum (CDCl_3 , 250 MHz) of compound **8**.

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Spectrum Type	STANDARD	Sweep Width (Hz)	15059.78	Temperature (degree C)	25.160		

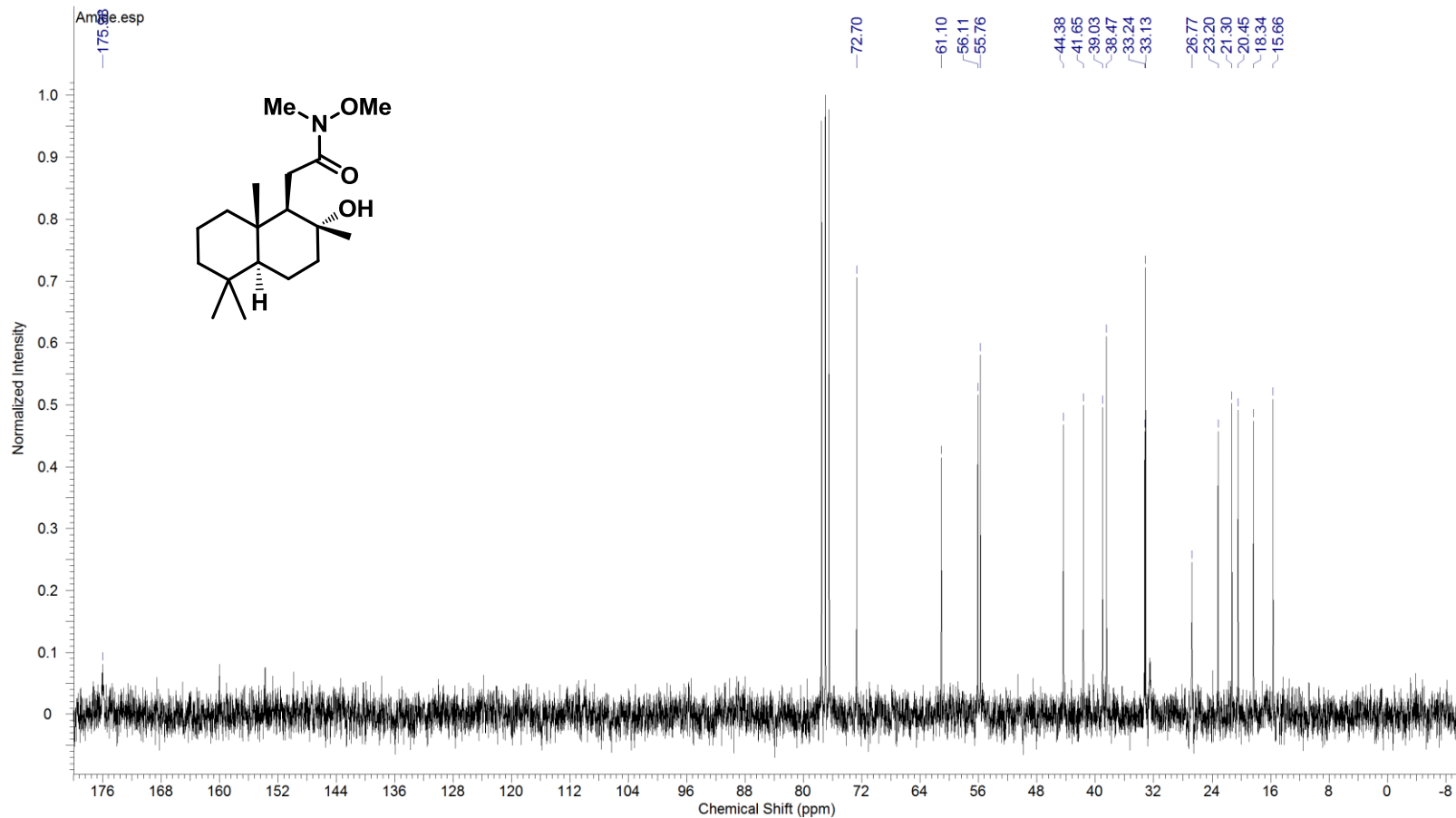


Figure S2. ¹³C NMR spectrum (CDCl₃, 62.9 MHz) of compound **8**.

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Owner	root	Points Count	32768	Pulse Sequence	dept135	Receiver Gain	16384.00	SW(cyclical) (Hz)	15060.24
Solvent	CHLOROFORM-d			Spectrum Offset (Hz)	6289.0518	Spectrum Type	DEPT135	Sweep Width (Hz)	15059.78
Temperature (degree C)	25.160								

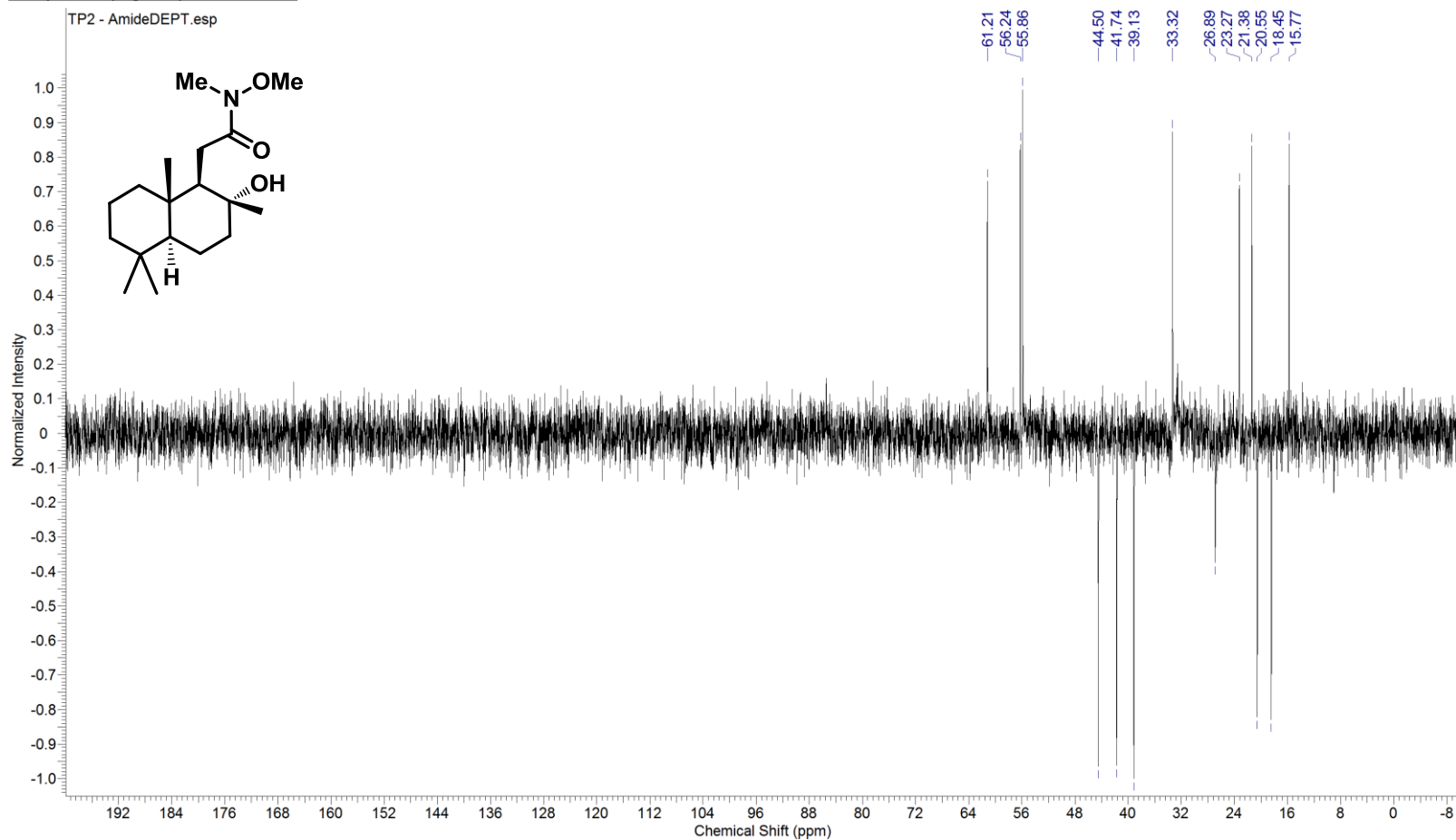
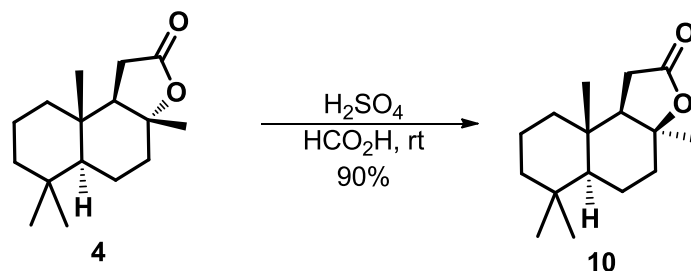


Figure S3. DEPT 135 NMR spectrum (CDCl_3 , 62.9 MHz) of compound **8**.

(3a*S*,5a*S*,9a*S*,9b*R*)-3a,6,6,9a-tetramethyldecahydronaphtho[2,1-*b*]furan-2(3a*H*)-one (**10**).



Solid (+)-sclareolide (**4**, 97%, 2.58 g, 10.0 mmol, 1 equiv) was added to a solution of sulfuric acid (95%, 1.68 mL, 30.0 mmol, 3 equiv) in formic acid (98%, 42 mL) at room temperature. After 4 h, the mixture was diluted with cold H_2O (100 mL) and extracted with Et_2O (2 x 100 mL). The combined organic phases were washed with saturated aqueous solution of NaHCO_3 (30 mL), brine (30 mL), dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The residue was purified by flash chromatography (SiO_2 , hexanes/ EtOAc 85:15) to furnish lactone **10** (2253 mg, 9.0 mmol) as a white solid in 90% yield.

Note: The high purity of formic acid (>97%) was essential for full conversion. The use of formic acid of 85% purity led to incomplete conversion even with prolonged reaction time.

TLC (SiO_2): $R_f = 0.70$ (hexanes/ EtOAc 50:50);

M.p.: 87-89 °C;

$[\alpha]_{\text{D}}^{25} = -27$ (c 1.0, CHCl_3), $[\alpha]_{\text{D, lit}} = -31.7$ (c 0.4, CHCl_3);²

^1H NMR (250 MHz, CDCl_3): δ 0.78 (s, 3H), 0.82 (s, 6H), 0.75-0.87 (m, 2H), 1.01-1.15 (m, 1H), 1.23 (s, 3H), 1.26-1.61 (m, 7H), 1.69 (d, $J = 7.7$ Hz, 1H), 2.14-2.26 (m, 1H), 2.27 (d, $J = 18.0$ Hz, 1H), 2.64 (dd, $J = 17.9, 7.9$ Hz, 1H);

^{13}C NMR (62.9 MHz, CDCl_3): δ 14.3 (CH_3), 17.8 (CH_2), 18.0 (CH_2), 21.9 (CH_3), 29.7 (CH_3), 32.1 (CH_2), 32.6 (C), 33.3 (CH_3), 34.8 (CH_2), 35.7 (C), 40.5 (CH_2), 41.4 (CH_2), 51.2 (CH), 54.4 (CH), 85.3 (C), 177.4 (C).

² Quideau, S.; Lebon, M.; Lamidey, A.-M. *Org. Lett.* **2002**, *4*, 3975-3978.

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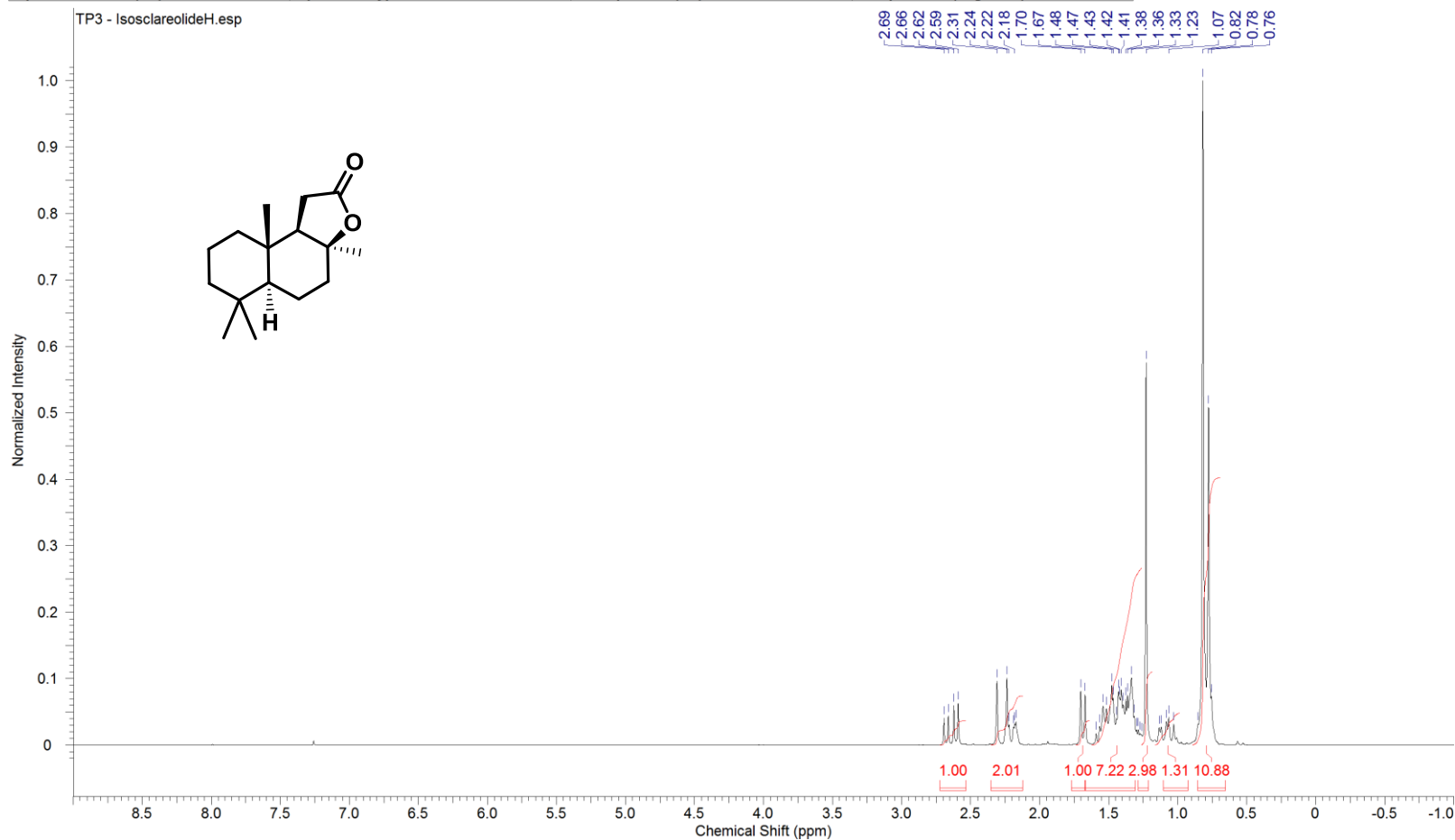


Figure S4. ^1H NMR spectrum (CDCl_3 , 250 MHz) of compound **10**.

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Solvent	CHLOROFORM-d			Spectrum Offset (Hz)	6277.1221	Spectrum Type	STANDARD
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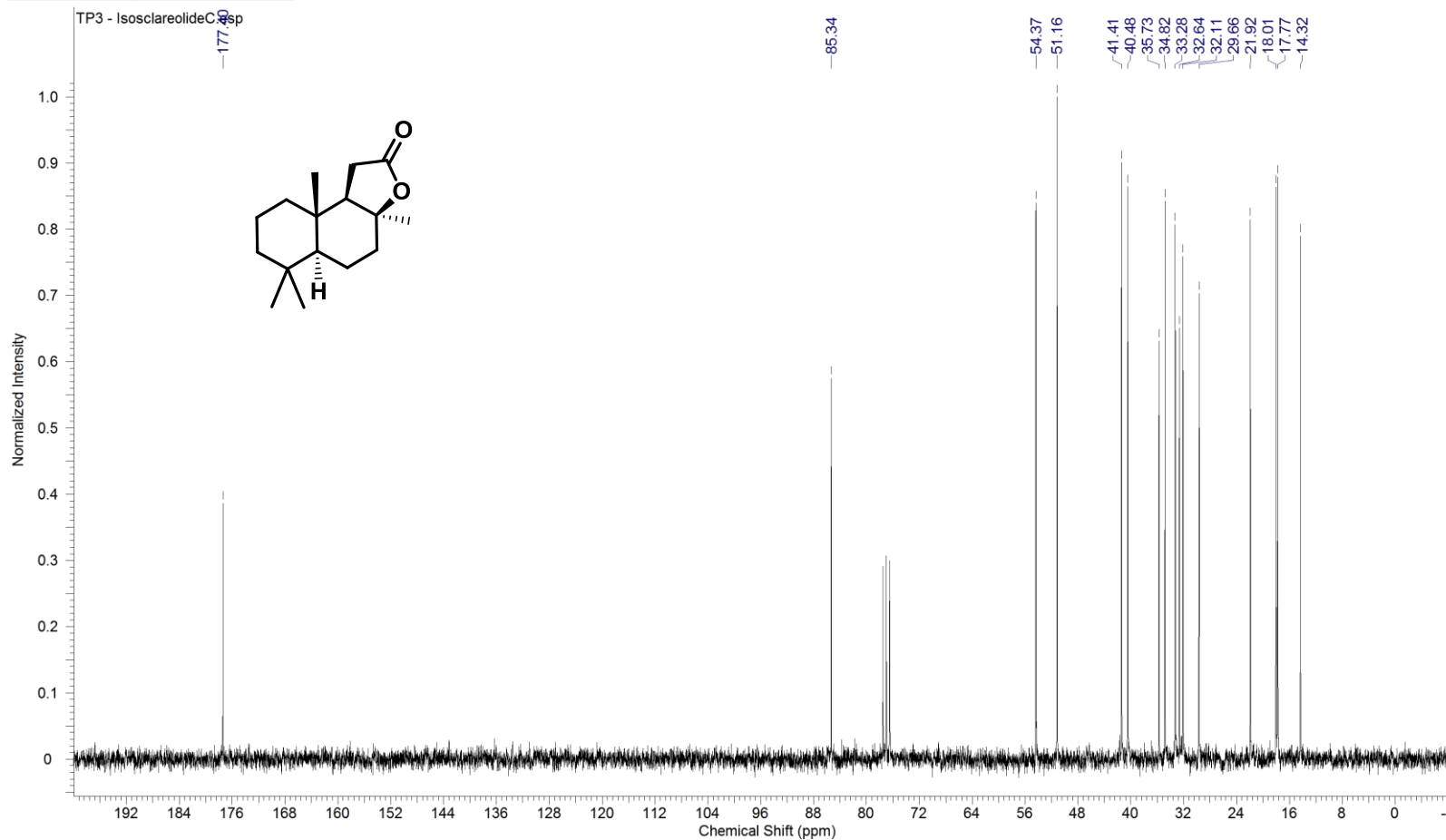


Figure S5. ^{13}C NMR spectrum (CDCl_3 , 62.9 MHz) of compound **10**.

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Owner	root	Points Count	32768	Pulse Sequence	dept135	Receiver Gain	16384.00
Solvent	CHLOROFORM-d			Spectrum Offset (Hz)	6289.0518	Spectrum Type	DEPT135
Temperature (degree C)	25.160					SW(cyclical) (Hz)	15060.24
						Sweep Width (Hz)	15059.78

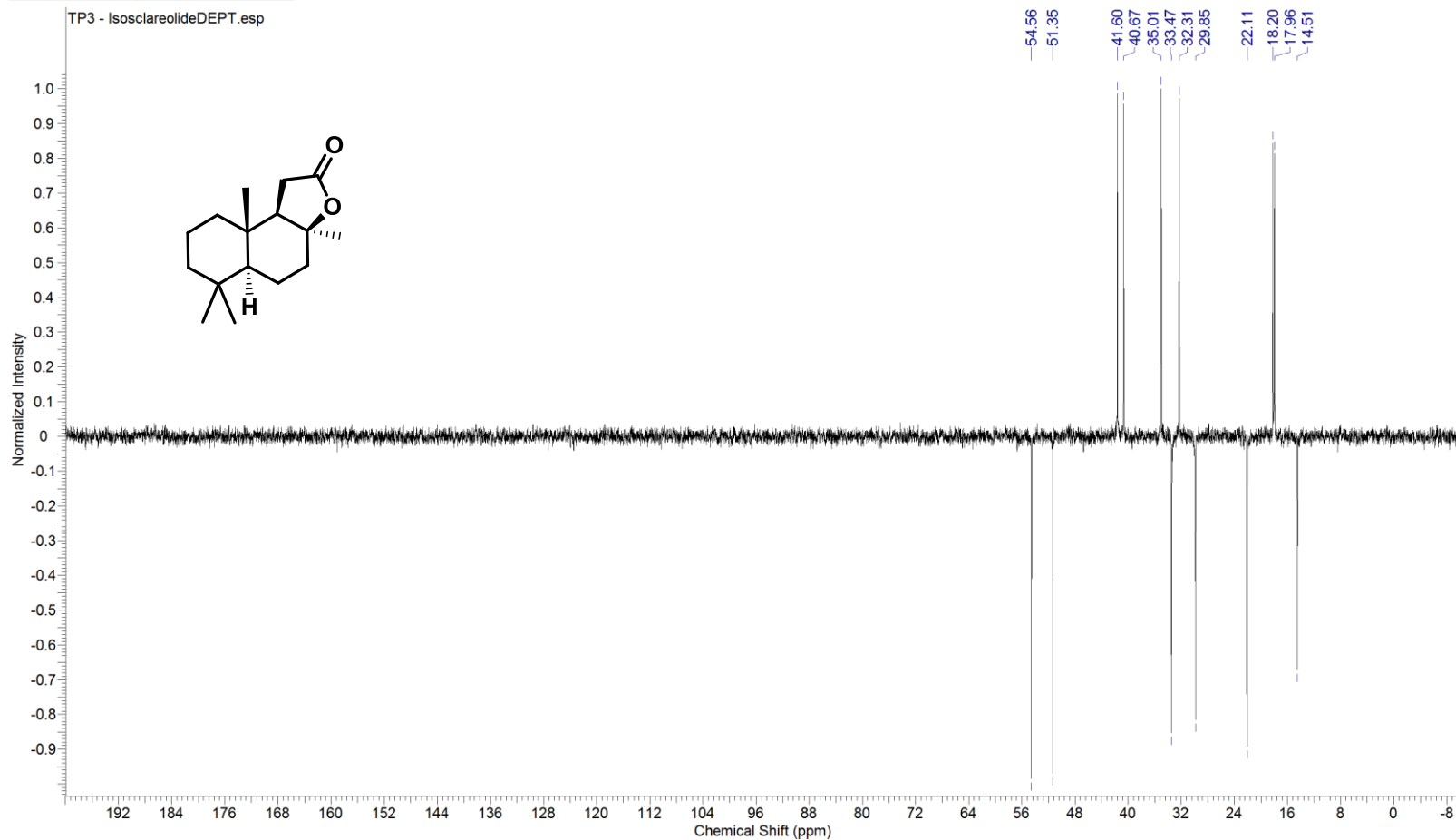
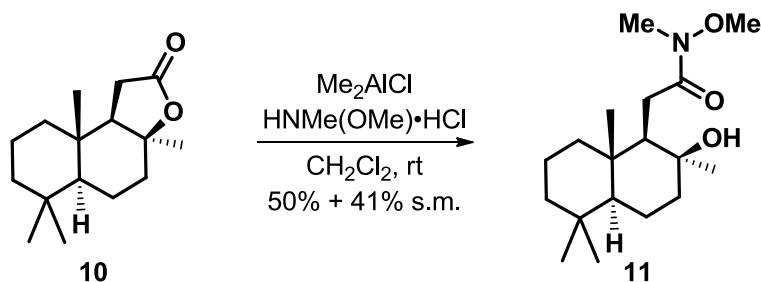


Figure S6. DEPT 135 NMR spectrum (CDCl_3 , 62.9 MHz) of compound **10**.

2-((1*R*,2*S*,4*aS*,8*aS*)-2-hydroxy-2,5,5,8*a*-tetramethyldecahydronaphthalen-1-yl)-*N*-methoxy-*N*-methylacetamide (**11**).



Me_2AlCl (0.9 M in heptane, 8.0 mL, 7.2 mmol, 3 equiv) was added to a suspension of MeONHMe·HCl (702 mg, 7.2 mmol, 1 equiv) in dry CH_2Cl_2 (20 mL) at 0 °C (**CAUTION!** *gas evolution*). After addition, the cooling bath was removed and the mixture was kept under magnetic stirring at room temperature for 2 h. Next, a solution of isosclareolide (**10**, 619 mg, 2.4 mmol, 1 equiv) in dry CH_2Cl_2 (20 mL) was added to the reaction, and the stirring continued at room temperature for 18 h. After cooling to 0 °C, an aqueous solution of HCl (1 M, 50 mL) was slowly added (**CAUTION!** *gas evolution*). The organic phase was separated and the aqueous phase was extracted with CH_2Cl_2 (2 x 50 mL). The organic phases were combined, dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The residue was purified by flash chromatography (SiO_2 , hexanes/EtOAc 85:15 to 30:70) to furnish amide **11** (375 mg, 1.2 mmol) as a white solid in 50% yield (85% yield based on the recovery of starting material), along recovered isosclareolide (**10**, 254 mg, 1.0 mmol) as a white solid in 41% yield.

Note: Use of Me_3Al led to little conversion (<5%) and the use of Me_2AlCl for prolonged reaction time at room temperature or use of refluxing conditions did not improve the yield.

TLC (SiO_2): R_f = 0.30 (hexanes/EtOAc 50:50);

M.p.: 140-144 °C;

$[\alpha]_D^{25}$ = +24 (*c* 1.0, CHCl_3);

IR (ATR, cm^{-1}): 3450, 2919, 2850, 1644, 1459, 1418, 1387, 1172, 1125, 1001, 915, 899;

^1H NMR (250 MHz, CDCl_3): δ 0.78 (s, 3H), 0.83 (s, 3H), 0.93 (s, 3H), 1.00 (s, 3H), 0.87-1.07 (m, 2H), 1.08-1.76 (m, 10H), 1.81-1.89 (m, 1H), 2.28 (dd, J = 18.0, 2.7 Hz, 1H), 2.70 (dd, J = 18.0, 5.8 Hz, 1H), 3.13 (s, 3H), 3.67 (s, 3H);

^{13}C NMR (62.9 MHz, CDCl_3): δ 15.6 (CH_3), 18.1 (CH_2), 18.2 (CH_2), 21.5 (CH_3), 26.8 (CH_2), 30.4 (CH_3), 32.7 (CH_3), 33.1 (C), 33.3 (CH_3), 38.0 (C), 38.7 (CH_2), 41.7 (CH_2), 42.3 (CH_2), 52.2 (CH), 55.3 (CH), 61.1 (CH_3), 72.7 (C), 175.3 (C);

HRMS (ESI +): m/z calculated for $\text{C}_{18}\text{H}_{33}\text{O}_3\text{NNa}^+$ [$\text{M}+\text{Na}$] $^+$ 334.2353, found 334.2367.

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Solvent	CHLOROFORM-d			Spectrum Offset (Hz)	1544.6561	Spectrum Type	STANDARD
Temperature (degree C)	25.160					SW(cyclical) (Hz)	5175.98
						Sweep Width (Hz)	5175.83

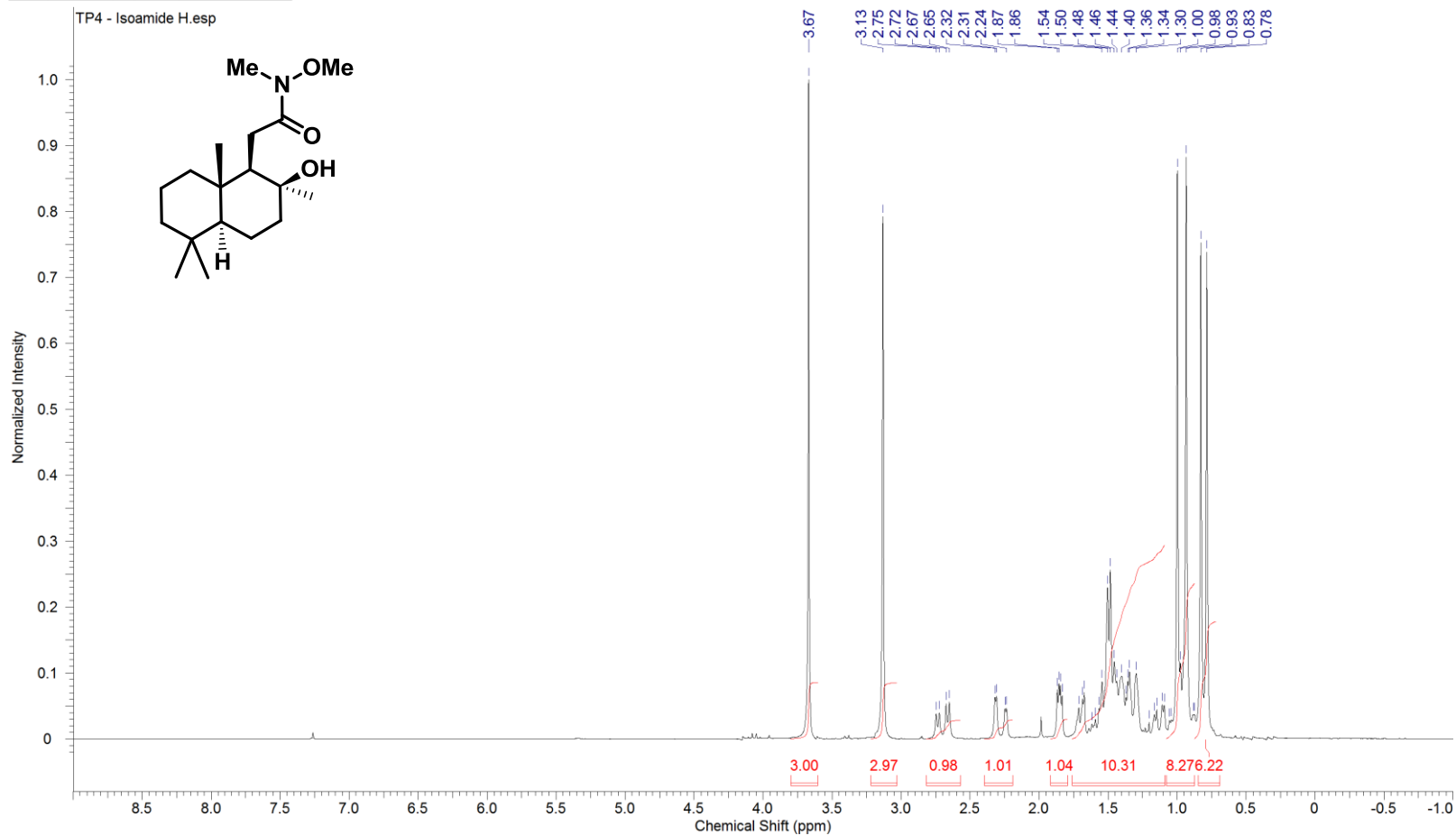


Figure S7. ^1H NMR spectrum (CDCl_3 , 250 MHz) of compound **11**.

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Owner	root	Points Count	32768	Pulse Sequence	zgpg30	Receiver Gain	456.10
Solvent	CHLOROFORM-d			Spectrum Offset (Hz)	6284.4756	Spectrum Type	STANDARD
Temperature (degree C)	25.260					SW(cyclical) (Hz)	15060.24
						Sweep Width (Hz)	15059.78

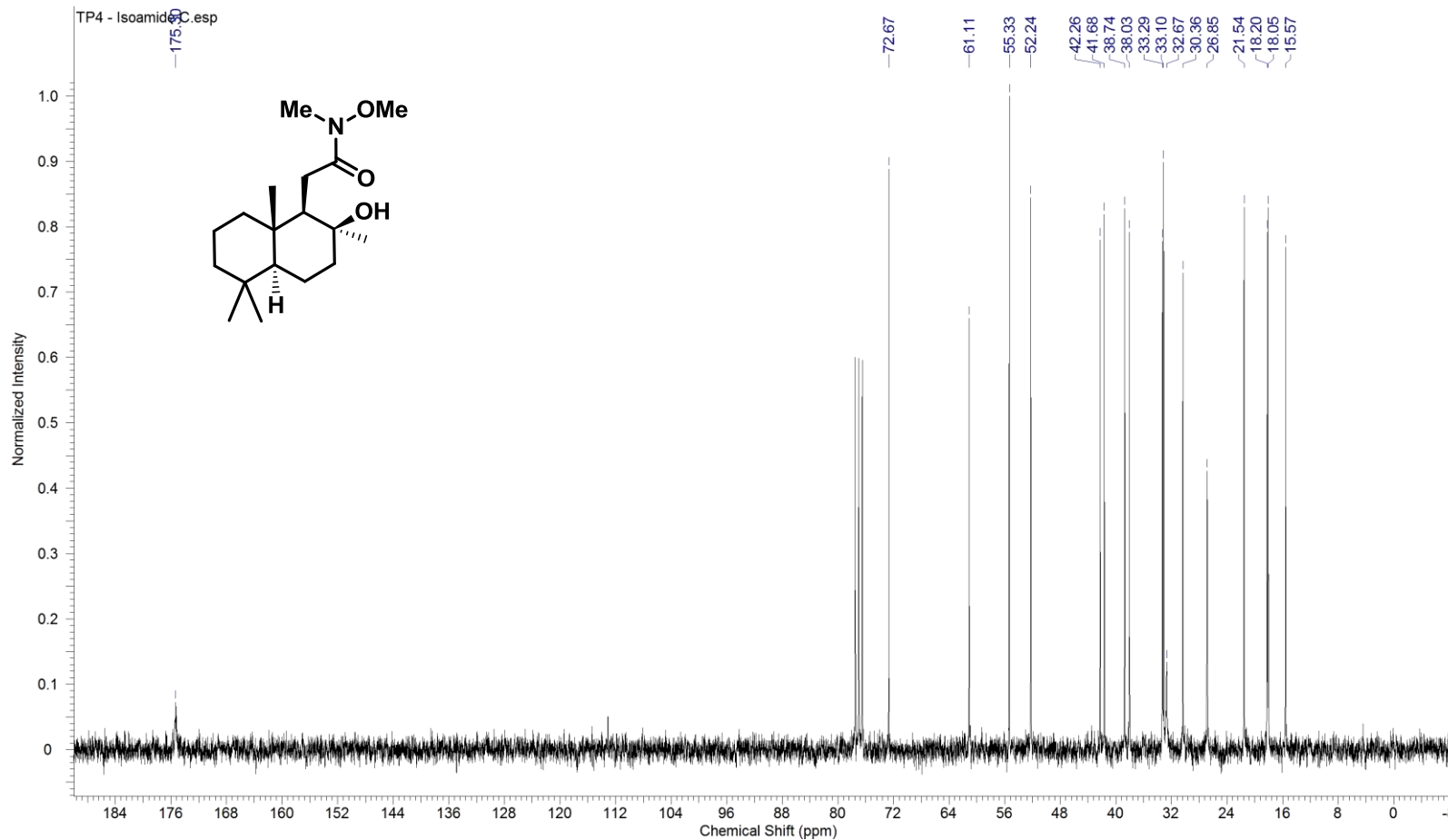


Figure S8. ^{13}C NMR spectrum (CDCl_3 , 62.9 MHz) of compound **11**.

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Owner	root	Points Count	32768	Pulse Sequence	dept135	Receiver Gain	1824.60
Solvent	CHLOROFORM-d			Spectrum Offset (Hz)	6289.0518	Spectrum Type	DEPT135
Temperature (degree C)	25.160					SW(cyclical) (Hz)	15060.24
						Sweep Width (Hz)	15059.78

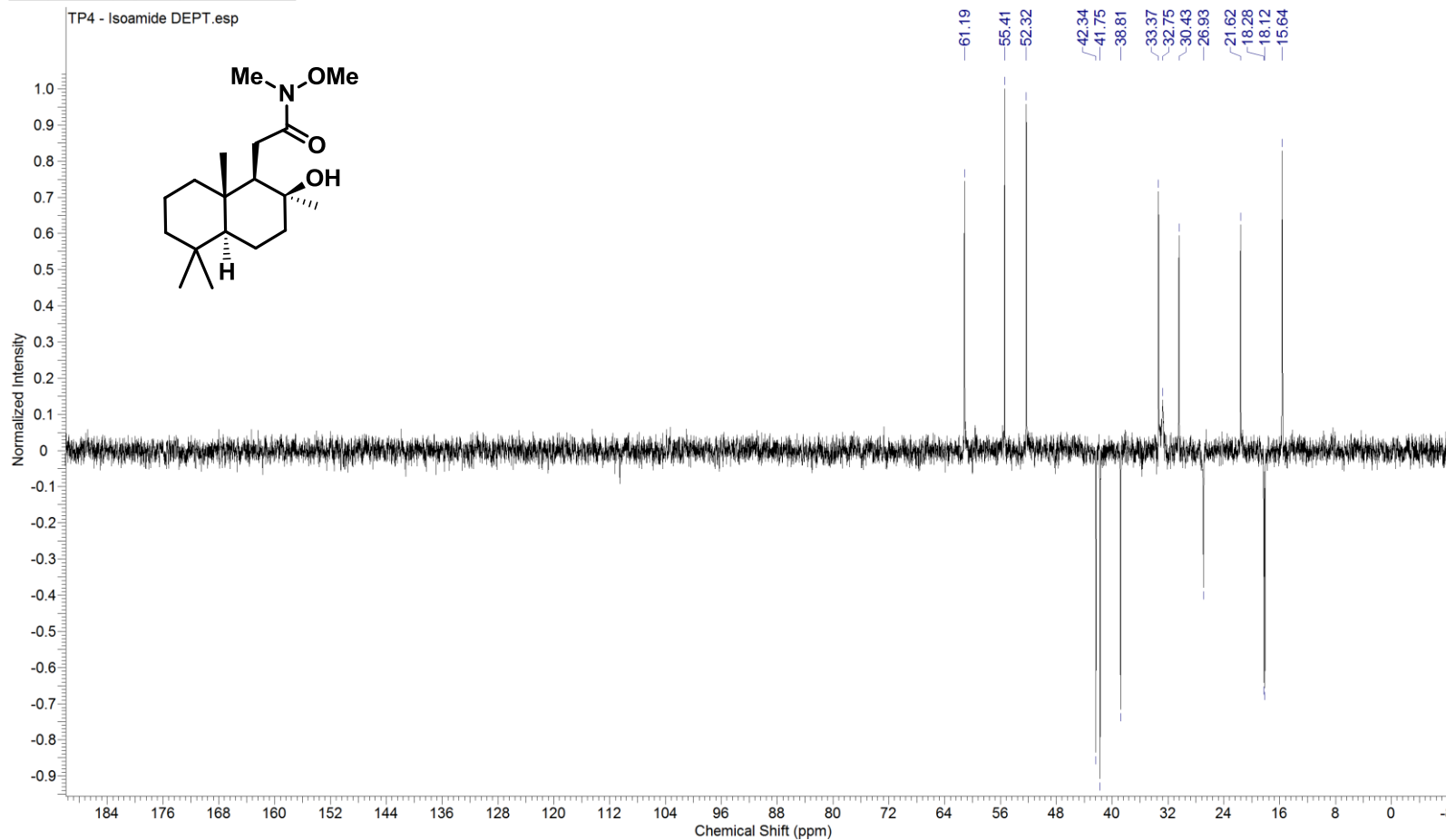
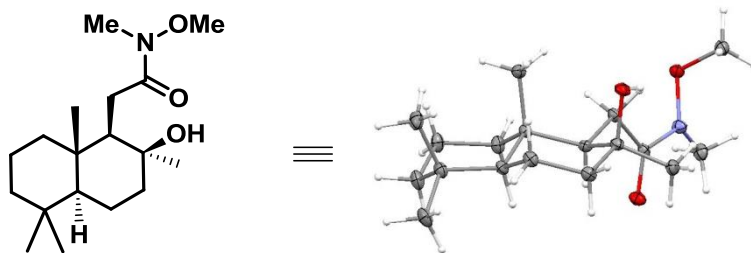


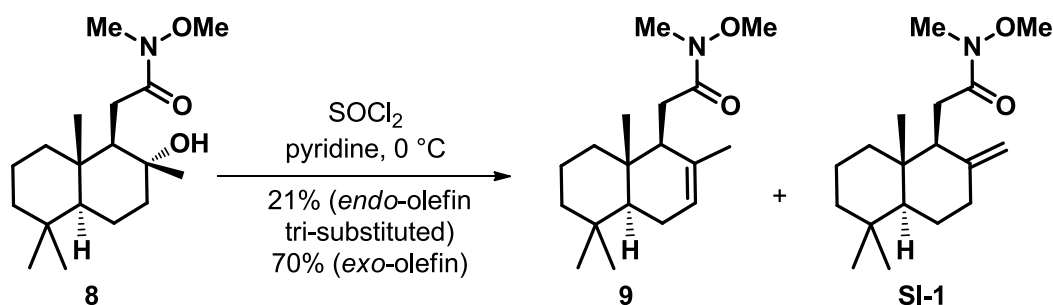
Figure S9. DEPT 135 NMR spectrum (CDCl_3 , 62.9 MHz) of compound **11**.

X-Ray crystal structure of compound 11 (CCDC1543718)



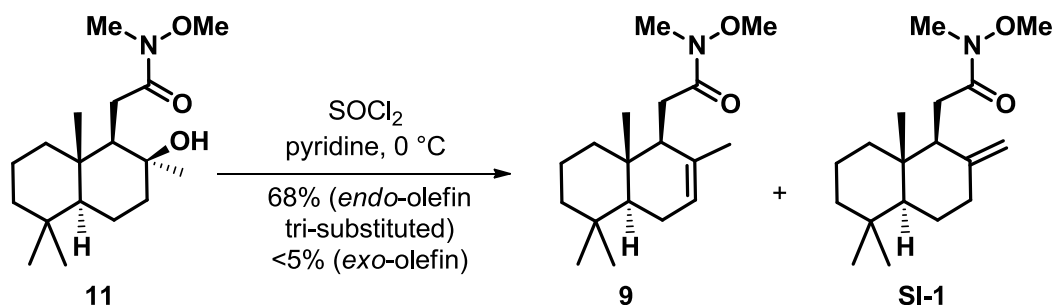
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Formula weight	311.47
Temperature/K	150.0
Crystal system	monoclinic
Space group	P2 ₁
a/Å	10.7535(5)
b/Å	6.9720(3)
c/Å	12.6570(6)
α/°	90
β/°	110.710(2)
γ/°	90
Volume/Å ³	887.62(7)
Z	2
ρ _{calc} /cm ³	1.1653
μ/mm ⁻¹	0.614
F(000)	345.0
Crystal size/mm ³	0.253 × 0.048 × 0.044
Radiation	Cu K _α (λ = 1.54184)
2θ range for data collection/°	7.46 to 135.98
Index ranges	-12 ≤ h ≤ 12, -7 ≤ k ≤ 8, -14 ≤ l ≤ 11
Reflections collected	6361
Independent reflections	2757 [R _{int} = 0.0329, R _{sigma} = 0.0378]
Data/restraints/parameters	2757/0/205
Goodness-of-fit on F ²	0.908
Final R indexes [I ≥ 2σ (I)]	R ₁ = 0.0341, wR ₂ = 0.1014
Final R indexes [all data]	R ₁ = 0.0349, wR ₂ = 0.1034
Largest diff. peak/hole / e Å ⁻³	0.22/-0.21
Flack parameter	0.15(17)

***N*-methoxy-*N*-methyl-2-((1*S*,4*aS*,8*aS*)-2,5,5,8*a*-tetramethyl-1,4,4*a*,5,6,7,8,8*a*-octahydronaphthalen-1-yl)acetamide (9) and *N*-methoxy-*N*-methyl-2-((1*S*,4*aS*,8*aS*)-5,5,8*a*-trimethyl-2-methylenedecahydronaphthalen-1-yl)acetamide (SI-1).**



SOCl_2 (1.16 mL, 16 mmol, 10 equiv) was added to dry pyridine (7.5 mL) at 0°C (**CAUTION! exothermic process**), this solution was stirred for 5 min, then was transferred to a solution of alcohol **8** (498 mg, 1.60 mmol, 1 equiv) in dry pyridine (7.5 mL) at 0°C . After 30 min, H_2O (30 mL) was slowly added. The mixture was extracted with CH_2Cl_2 (2 x 30 mL), the organic phases were combined, dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The residue was purified by flash chromatography (SiO_2 , hexanes/EtOAc 85:15) to furnish *endo*-olefin **9** (100 mg, 0.34 mmol) as a colorless oil in 21% yield, along *exo*-olefin **SI-1** (330 mg, 1.12 mmol) as a white solid in 70% yield.

Note: Attempts to isomerize the *exo*-olefin **SI-1** into the *endo*-olefin **9** as described by de la Torre and coworkers³ led to poor results, obtaining at the best run 20% of the desired product as an inseparable mixture with isosclareolide (**10**).



The experimental procedure was conducted as reported for its epimer (see above) to furnish the *endo*-olefin **9** (319 mg, 1.09 mmol) as a colorless oil in 68% yield, and trace amounts (less than 5% yield) of the *exo*-olefin **SI-1**.

Data for *endo*-olefin **9**:

TLC (SiO_2): $R_f = 0.26$ (hexanes/EtOAc 85:15);

$[\alpha]_D^{25} = +21$ (c 1.0, CHCl_3), $[\alpha]_{D,\text{lit}} = +15.2$ (c 0.25, CHCl_3);³

³ de la Torre, M. C.; García, I.; Sierra, M. A. *J. Nat. Prod.* **2002**, *65*, 661-668.

¹H NMR (250 MHz, CDCl₃): δ 0.79 (s, 3H), 0.85 (s, 3H), 0.87 (s, 3H), 1.52 (s, 3H), 1.00-2.06 (m, 9H), 2.28 (dd, *J* = 16.7, 2.5 Hz, 1H), 2.46 (dd, *J* = 16.7, 9.2 Hz, 1H), 2.61-2.72 (m, 1H), 3.17 (s, 3H), 3.68 (s, 3H), 5.40 (br. s, 1H);

¹³C NMR (62.9 MHz, CDCl₃): δ 14.0 (CH₃), 18.5 (CH₂), 21.1 (CH₃), 21.6 (CH₃), 23.5 (CH₂), 28.9 (CH₂), 32.6 (CH₃), 32.7 (C), 32.9 (CH₃), 35.7 (C), 38.7 (CH₂), 41.9 (CH₂), 48.8 (CH), 49.5 (CH), 60.9 (CH₃), 121.9 (CH), 134.0 (C), 175.2 (C).

Data for *exo*-olefin SI-1:

TLC (SiO₂): R_f = 0.19 (hexanes/EtOAc 85:15);

M.p.: 82-85 °C (lit.: 84-86 °C);

[α]_D²⁵ = −29 (*c* 1.0, CHCl₃), [α]_{D,lit} = −30.9 (*c* 0.99, CHCl₃);¹

¹H NMR (250 MHz, CDCl₃): δ 0.64 (s, 3H), 0.72 (s, 3H), 0.79 (s, 3H), 0.98-1.70 (m, 9H), 1.93-2.11 (m, 1H), 2.21-2.34 (m, 2H), 2.39 (d, *J* = 10.3 Hz, 1H), 2.59 (dd, *J* = 15.5, 9.8 Hz, 1H), 3.05 (s, 3H), 3.62 (s, 3H), 4.34 (s, 1H), 4.62 (s, 1H);

¹³C NMR (62.9 MHz, CDCl₃): δ 14.4 (CH₃), 18.9 (CH₂), 21.4 (CH₃), 23.7 (CH₂), 26.8 (CH₂), 32.1 (CH₃), 33.1 (C), 33.2 (CH₃), 37.2 (CH₂), 38.47 (CH₂), 38.53 (C), 41.7 (CH₂), 51.2 (CH), 54.7 (CH), 60.9 (CH₃), 105.5 (CH₂), 149.2 (C), 174.2 (C).

Acquisition Time (sec)	3.1654	Comment	LN412A	Date	19 Jan 2017 17:03:28		
Date Stamp	19 Jan 2017 17:03:28			File Name	C:\Users\Luiz\Desktop\Luiz\PhD\NMR\jan17\jan19\ftH1\1\1\PDATA\1\1r		
Frequency (MHz)	250.13	Nucleus	1H	Number of Transients	9	Origin	spect
Owner	root	Points Count	32768	Pulse Sequence	zg30	Receiver Gain	161.30
Solvent	CHLOROFORM-d			Spectrum Offset (Hz)	1544.4923	Spectrum Type	STANDARD
Temperature (degree C)	25.160					SW(cyclical) (Hz)	5175.98
						Sweep Width (Hz)	5175.83

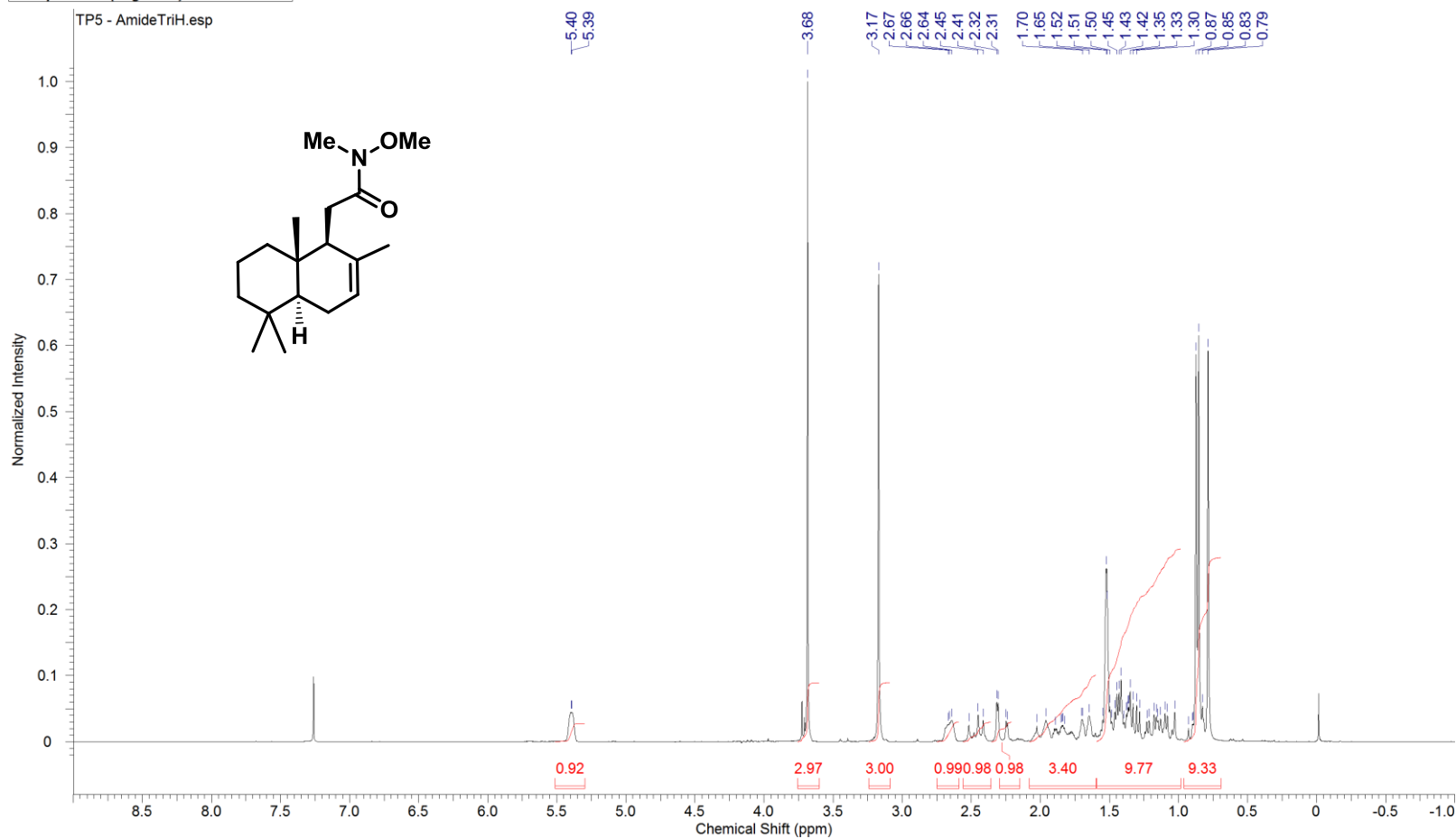


Figure S10. ^1H NMR spectrum (CDCl_3 , 250 MHz) of compound **9**.

Acquisition Time (sec)	1.0879	Comment	LN412B	Date	20 Jan 2017 10:37:20		
Date Stamp	20 Jan 2017 10:37:20			File Name	C:\Users\Luiz\Desktop\Luiz\PhD\NMR\jan17\jan20\ftH1\2\PDATA\1\1r		
Frequency (MHz)	62.90	Nucleus	13C	Number of Transients	35	Origin	spect
Owner	root	Points Count	32768	Pulse Sequence	zgpg30	Receiver Gain	812.70
Solvent	CHLOROFORM-d			Spectrum Offset (Hz)	6279.4194	Spectrum Type	STANDARD
Temperature (degree C)	25.260					SW(cyclical) (Hz)	15060.24
						Sweep Width (Hz)	15059.78

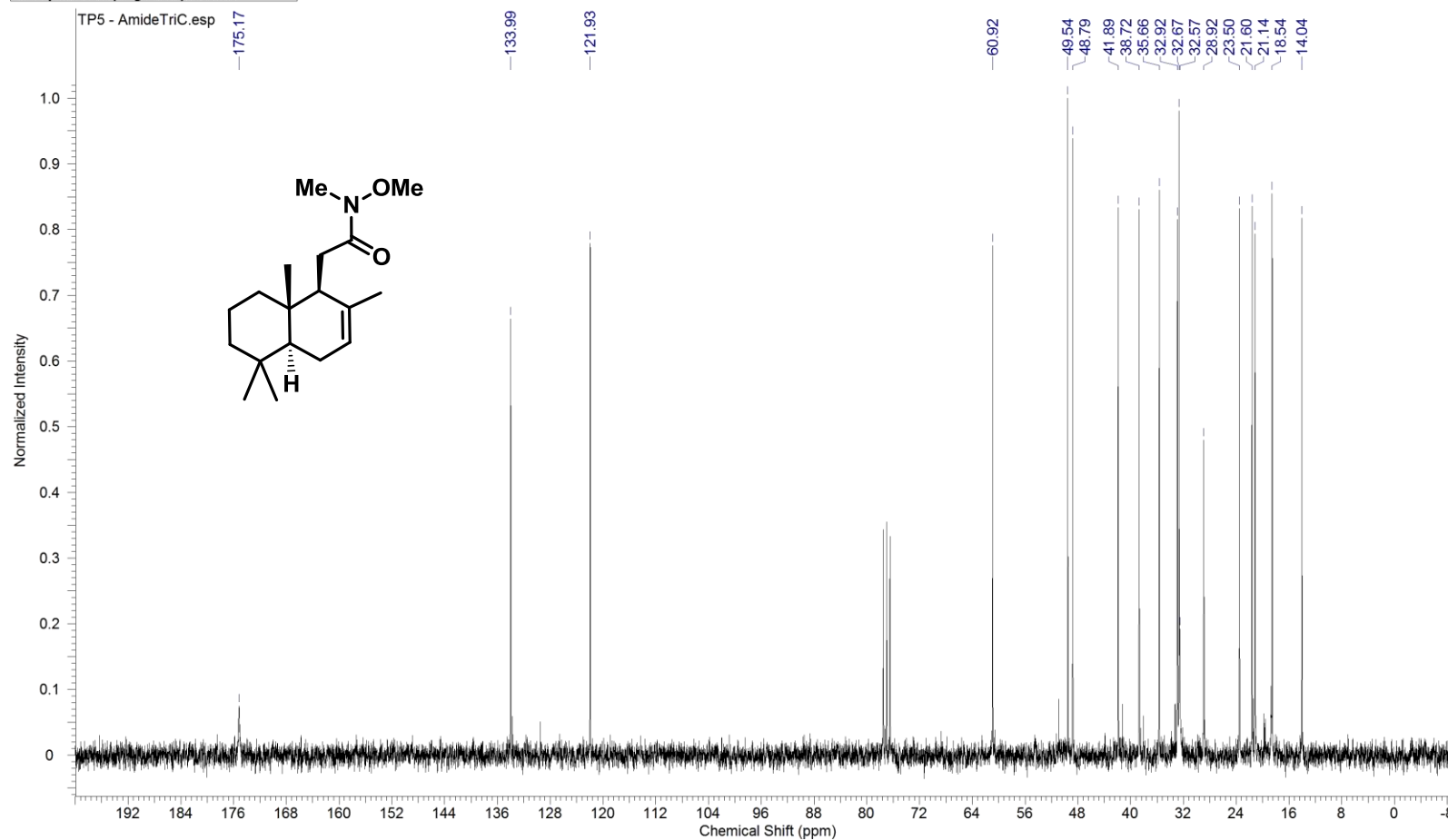


Figure S11. ^{13}C NMR spectrum (CDCl_3 , 62.9 MHz) of compound **9**.

Acquisition Time (sec)	0.5439	Comment	LN412A	Date	19 Jan 2017 17:05:36		
Date Stamp	19 Jan 2017 17:05:36			File Name	C:\Users\Luiz\Desktop\Luiz\PhD\NMR\jan17\jan19\ftH1\2\PDATA\1\1r		
Frequency (MHz)	62.90	Nucleus	13C	Number of Transients	40	Origin	spect
Owner	root	Points Count	32768	Pulse Sequence	dept135	Receiver Gain	2048.00
Solvent	CHLOROFORM-d			Spectrum Offset (Hz)	6275.6401	Spectrum Type	DEPT135
Temperature (degree C)	25.160					SW(cyclical) (Hz)	15060.24
						Sweep Width (Hz)	15059.78

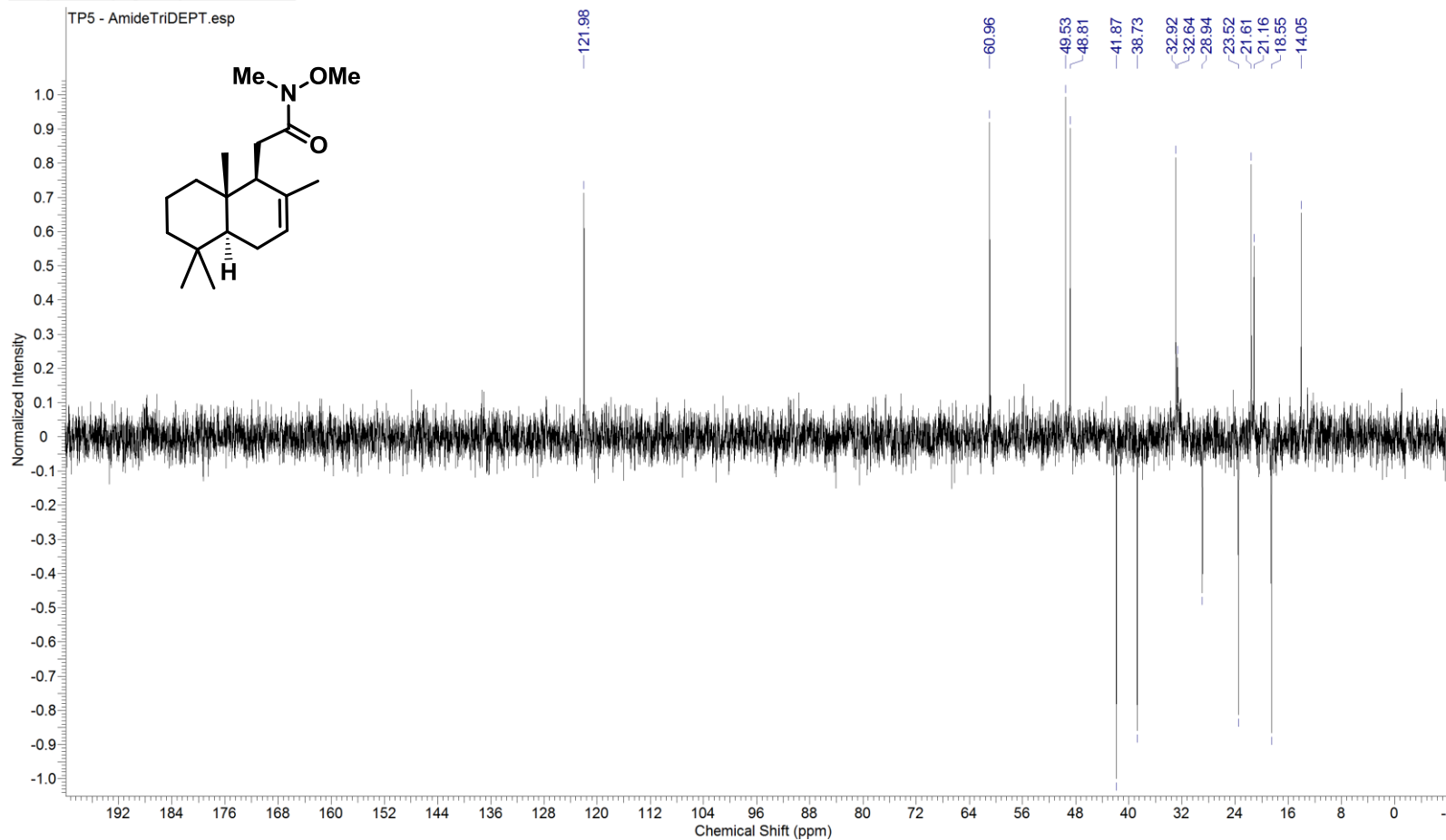


Figure S12. DEPT 135 NMR spectrum (CDCl_3 , 62.9 MHz) of compound **9**.

Acquisition Time (sec)	3.1654	Comment	LN64B-D	Date	07 Nov 2015 18:16:00
Date Stamp	07 Nov 2015 18:16:00				
File Name	\\nmrsparc.iqm.unicamp.br\spectros\bruker250\2015\nov15\data\Julio Pastre\nmr\nov07\ftH3\1\PDATA\1\1r				
Frequency (MHz)	250.13	Nucleus	¹ H	Number of Transients	9
Original Points Count	16384	Owner	root	Points Count	32768
Receiver Gain	45.30	SW(cyclical) (Hz)	5175.98	Solvent	CHLOROFORM-d
Spectrum Offset (Hz)	1544.6561	Spectrum Type	STANDARD	Sweep Width (Hz)	5175.83
				Temperature (degree C)	25.660

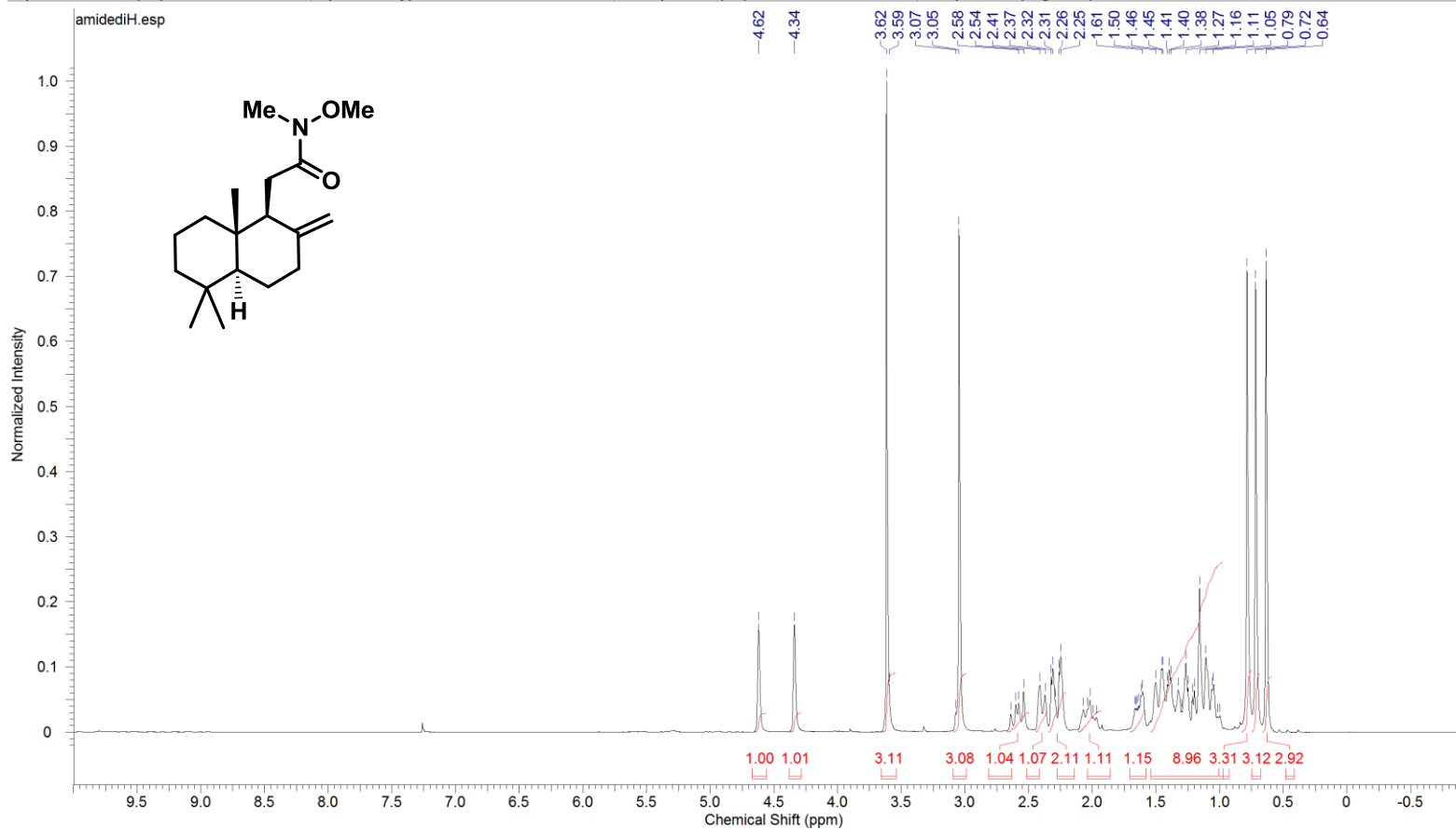


Figure S13. ¹H NMR spectrum (CDCl₃, 250 MHz) of compound SI-1.

Acquisition Time (sec)	1.0879	Comment	LN64B-D	Date	07 Nov 2015 18:20:16			
Date Stamp	07 Nov 2015 18:20:16							
File Name	\\nmrparc.lqm.unicamp.br\spectros\bruker250\2015\nov15\data\Julio Pastre\nmr\nov07\ftH3\3\PDATA\1\1r				Frequency (MHz)	62.90		
Nucleus	13C	Number of Transients	33	Origin	spect	Original Points Count	16384	
Owner	root	Points Count	32768	Pulse Sequence	zgpg30	Receiver Gain	512.00	
SW(cyclical) (Hz)	15060.24	Solvent	CHLOROFORM-d	Temperature (degree C) 25.560			Spectrum Offset (Hz)	6272.5254
Spectrum Type	STANDARD	Sweep Width (Hz)	15059.78					

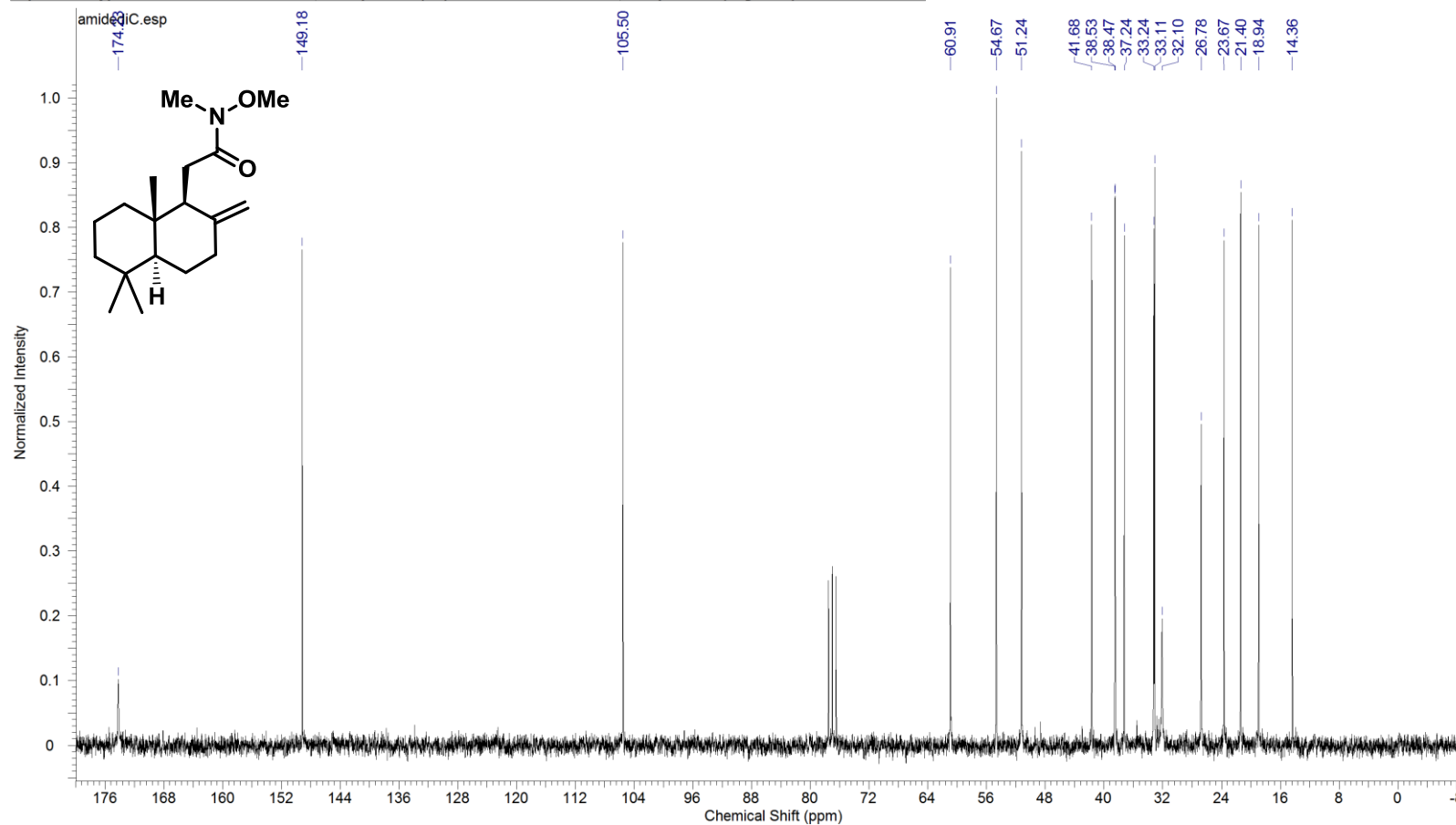


Figure S14. ¹³C NMR spectrum (CDCl₃, 62.9 MHz) of compound **SI-1**.

Acquisition Time (sec)	0.5439	Comment	LN64B-D	Date	07 Nov 2015 18:18:08		
Date Stamp	07 Nov 2015 18:18:08			File Name	C:\Users\Luiz\AppData\Local\Temp\Rar\Ra0.953\nov07\ftH3\2\PDATA\1\1r		
Frequency (MHz)	62.90	Nucleus	13C	Number of Transients	13	Origin	spect
Owner	root	Points Count	32768	Pulse Sequence	dept135	Receiver Gain	812.70
Solvent	CHLOROFORM-d			Spectrum Offset (Hz)	6289.0518	Spectrum Type	DEPT135
Temperature (degree C)	25.460					SW(cyclical) (Hz)	15060.24
						Sweep Width (Hz)	15059.78

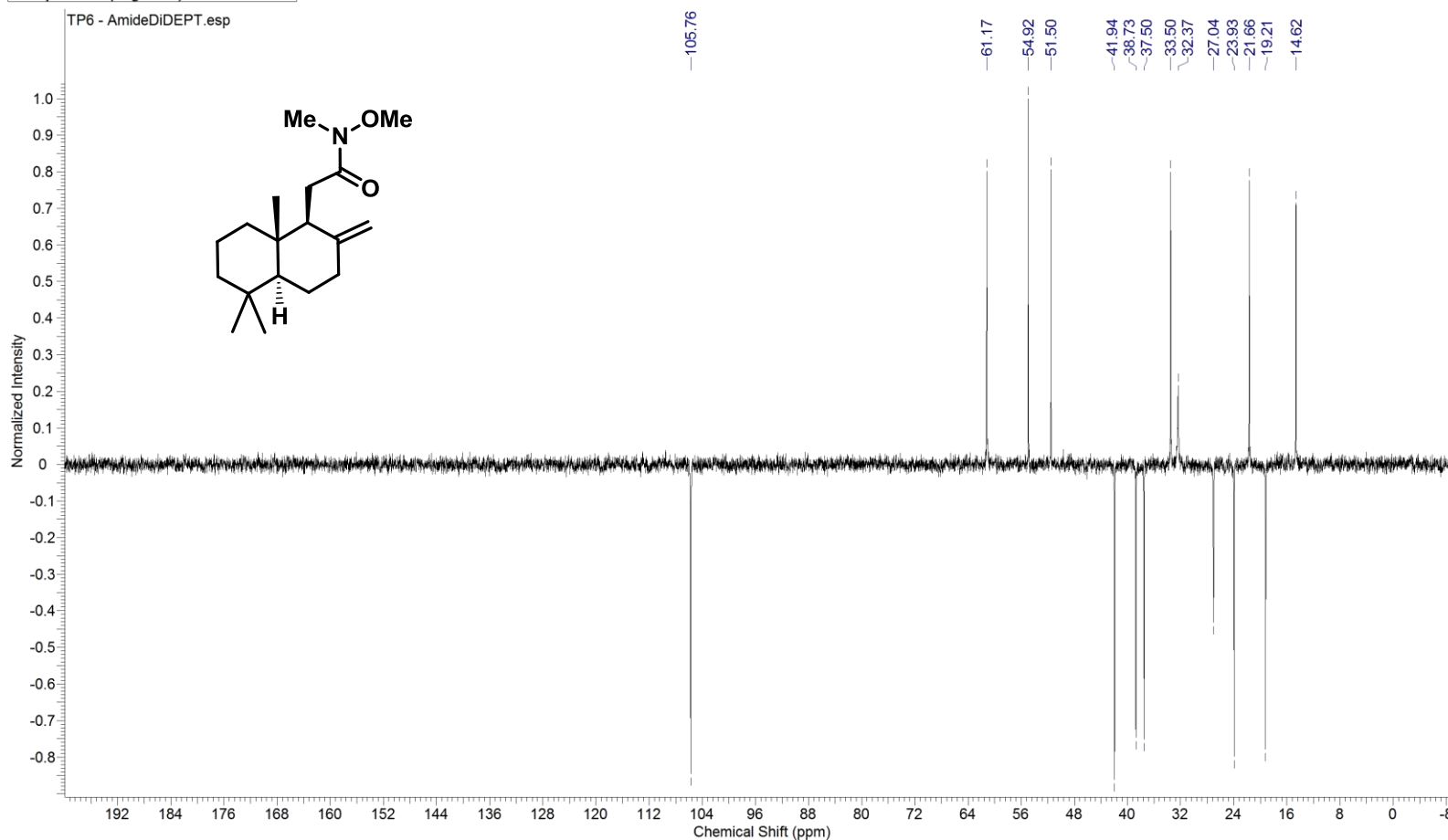
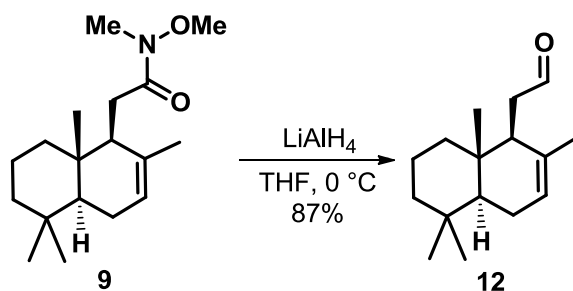


Figure S15. DEPT 135 NMR spectrum (CDCl_3 , 62.9 MHz) of compound **SI-1**.

2-((1*S*,4*aS*,8*aS*)-2,5,5,8*a*-tetramethyl-1,4,4*a*,5,6,7,8,8*a*-octahydronaphthalen-1-yl)acetaldehyde (**12**).



Solid LiAlH₄ (361 mg, 9.5 mmol, 5 equiv) was added to a solution of amide **9** (558 mg, 1.90 mmol, 1 equiv) in dry THF (38 mL) at 0 °C. After 2 h at the same temperature, an aqueous solution of HCl (1 M, 40 mL) was slowly added (*CAUTION! gas evolution*). The mixture was extracted with EtOAc (80 mL), the organic phase was dried over anhydrous MgSO₄ and concentrated under reduced pressure. The residue was purified by flash chromatography (SiO₂, hexanes/EtOAc 95:5) to furnish aldehyde **12** (388 mg, 1.65 mmol) as a colorless oil in 87% yield.

TLC (SiO₂): R_f = 0.32 (hexanes/EtOAc 95:5);

[α]_D²⁵ = −15 (*c* 1.0, CHCl₃), [α]_{D, lit} = −29.2 (*c* 0.161, CHCl₃);⁴

¹H NMR (250 MHz, CDCl₃): δ 0.77 (s, 3H), 0.87 (s, 3H), 0.88 (s, 3H), 1.51 (s, 3H), 1.00-2.06 (m, 9H), 2.37-2.59 (m, 3H), 5.46 (br. s, 1H), 9.84 (t, *J* = 1.6 Hz, 1H);

¹³C NMR (62.9 MHz, CDCl₃): δ 14.2 (CH₃), 18.7 (CH₂), 21.8 (CH₃), 22.5 (CH₃), 23.6 (CH₂), 32.9 (C), 33.1 (CH₃), 36.0 (C), 39.5 (CH₂), 42.0 (CH₂), 42.3 (CH₂), 48.5 (CH), 49.8 (CH), 123.4 (CH), 132.9 (C), 203.5 (CH).

⁴ de la Torre, M. C.; García, I.; Sierra, M. A. *Tetrahedron Lett.* **2002**, 43, 6351-6353.

Acquisition Time (sec)	3.1654	Comment	LN170	Date	22 Mar 2016 17:01:04
Date Stamp	22 Mar 2016 17:01:04				
File Name	\\nmrparc.lqm.unicamp.br\spectros\bruker250\2016\mar16\data\Julio Pastre\nmr\mar22\ftH1\1\PDATA\1\1r				
Frequency (MHz)	250.13	Nucleus	1H	Number of Transients	17
Original Points Count	16384	Owner	root	Points Count	32768
Receiver Gain	287.40	SW(cyclical) (Hz)	5175.98	Solvent	CHLOROFORM-d
Spectrum Offset (Hz)	1544.6561	Spectrum Type	STANDARD	Sweep Width (Hz)	5175.83
				Temperature (degree C)	23.360

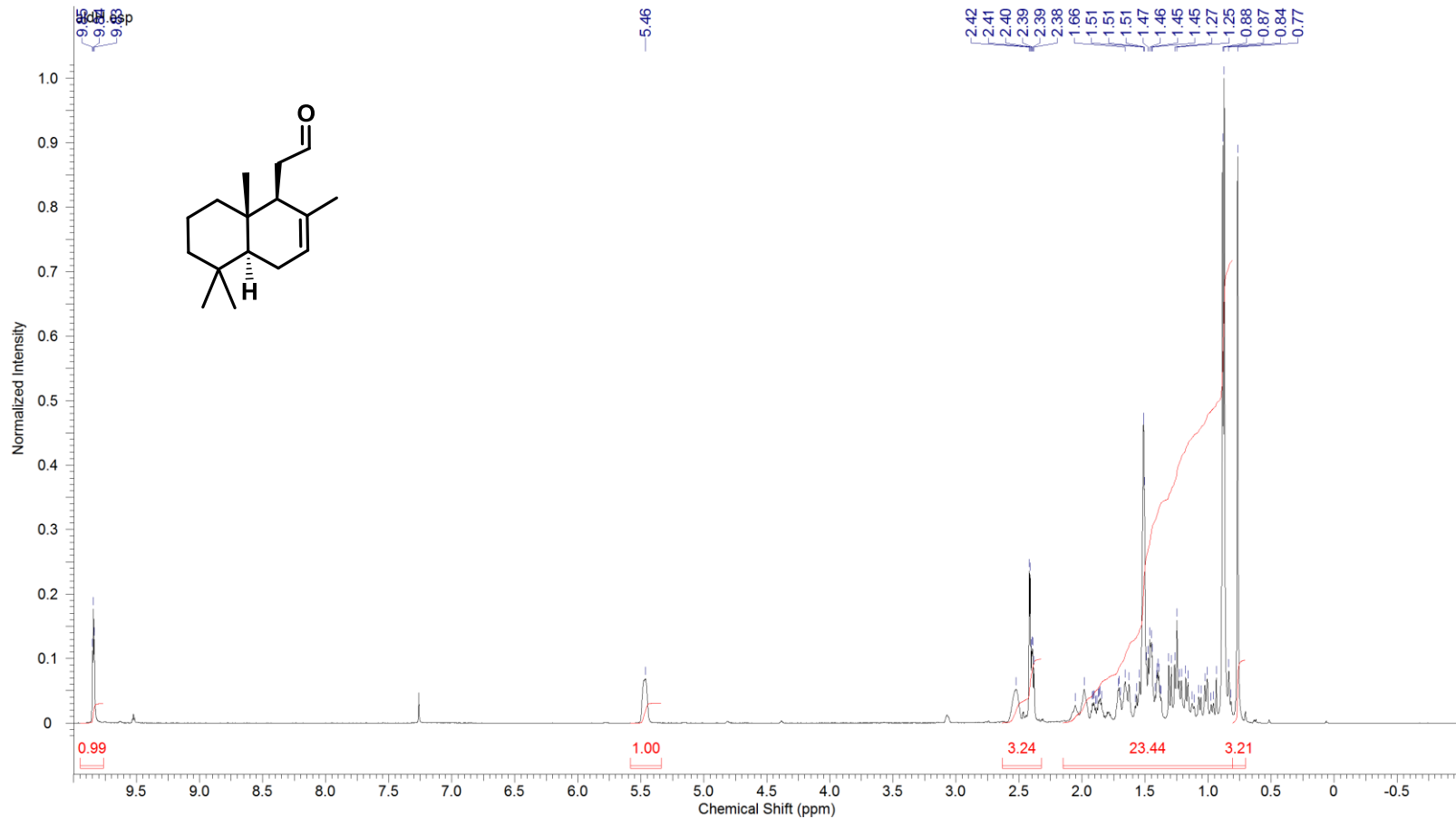


Figure S16. ^1H NMR spectrum (CDCl_3 , 250 MHz) of compound **12**.

Acquisition Time (sec)	1.0879	Comment	LN170	Date	22 Mar 2016 17:05:20			
Date Stamp	22 Mar 2016 17:05:20							
File Name	\\nmrparc.iqm.unicamp.br\spectros\bruker250\2016\mar16\data\Julio Pastre\nmr\mar22\ftH1\3\PDATA\1\1r				Frequency (MHz)	62.90		
Nucleus	¹³ C	Number of Transients	45	Origin	spect	Original Points Count	16384	
Owner	root	Points Count	32768	Pulse Sequence	zgpg30	Receiver Gain	645.10	
SW(cyclical) (Hz)	15060.24	Solvent	CHLOROFORM-d				Spectrum Offset (Hz)	6289.0518
Spectrum Type	STANDARD	Sweep Width (Hz)	15059.78	Temperature (degree C)	23.560			

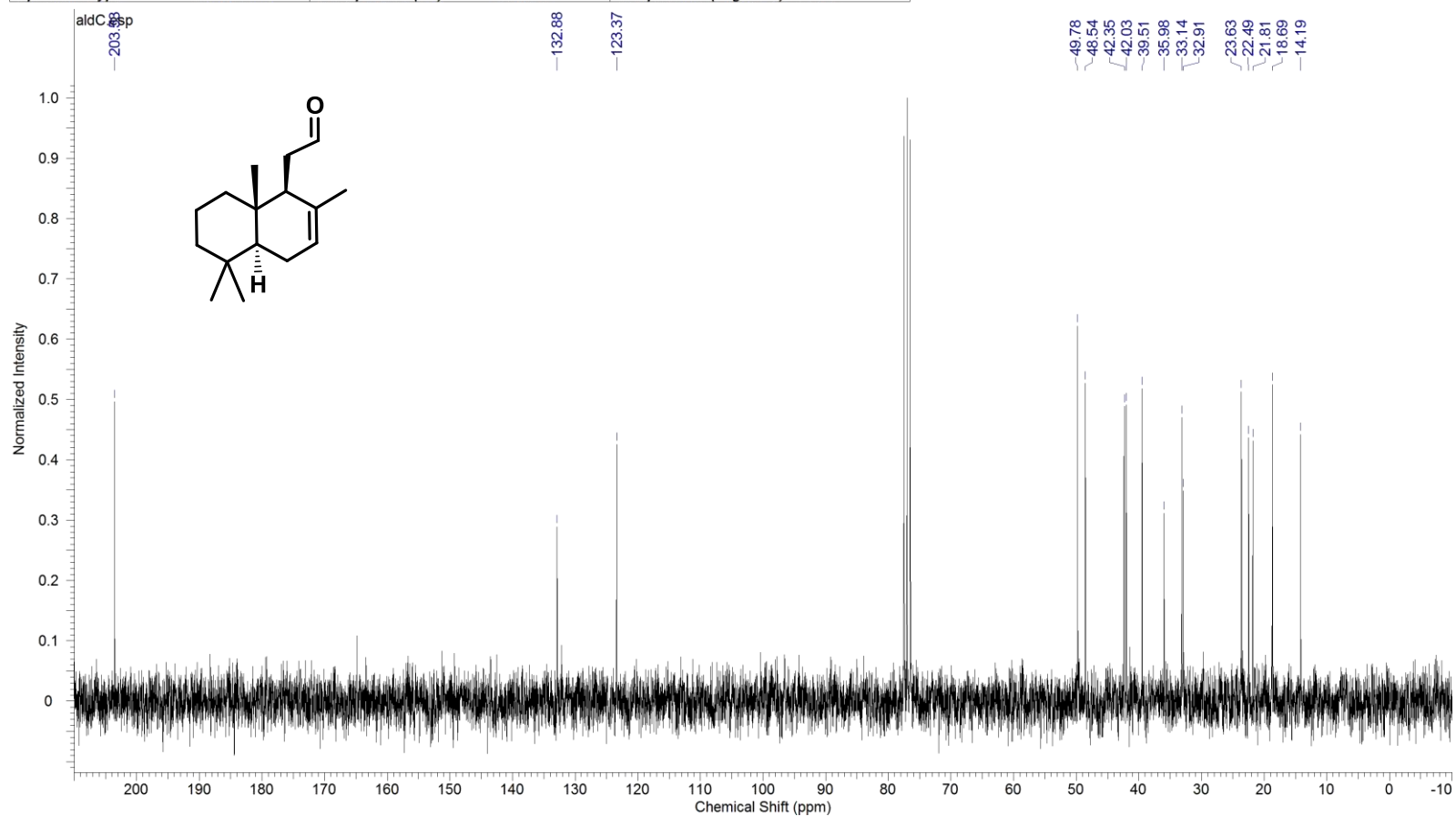


Figure S17. ¹³C NMR spectrum (CDCl₃, 62.9 MHz) of compound **12**.

Acquisition Time (sec)	0.5439	Comment	LN170	Date	22 Mar 2016 17:03:12		
Date Stamp	22 Mar 2016 17:03:12			File Name	C:\Users\Luiz\Desktop\Luiz\PhD\NMR\mar16\mar22\ftH1\2\PDATA\1\1r		
Frequency (MHz)	62.90	Nucleus	¹³ C	Number of Transients	32	Origin	spect
Owner	root	Points Count	32768	Pulse Sequence	dept135	Receiver Gain	2048.00
Solvent	CHLOROFORM-d			Spectrum Offset (Hz)	6289.0518	Spectrum Type	DEPT135
Temperature (degree C)	23.360					SW(cyclical) (Hz)	15060.24
						Sweep Width (Hz)	15059.78

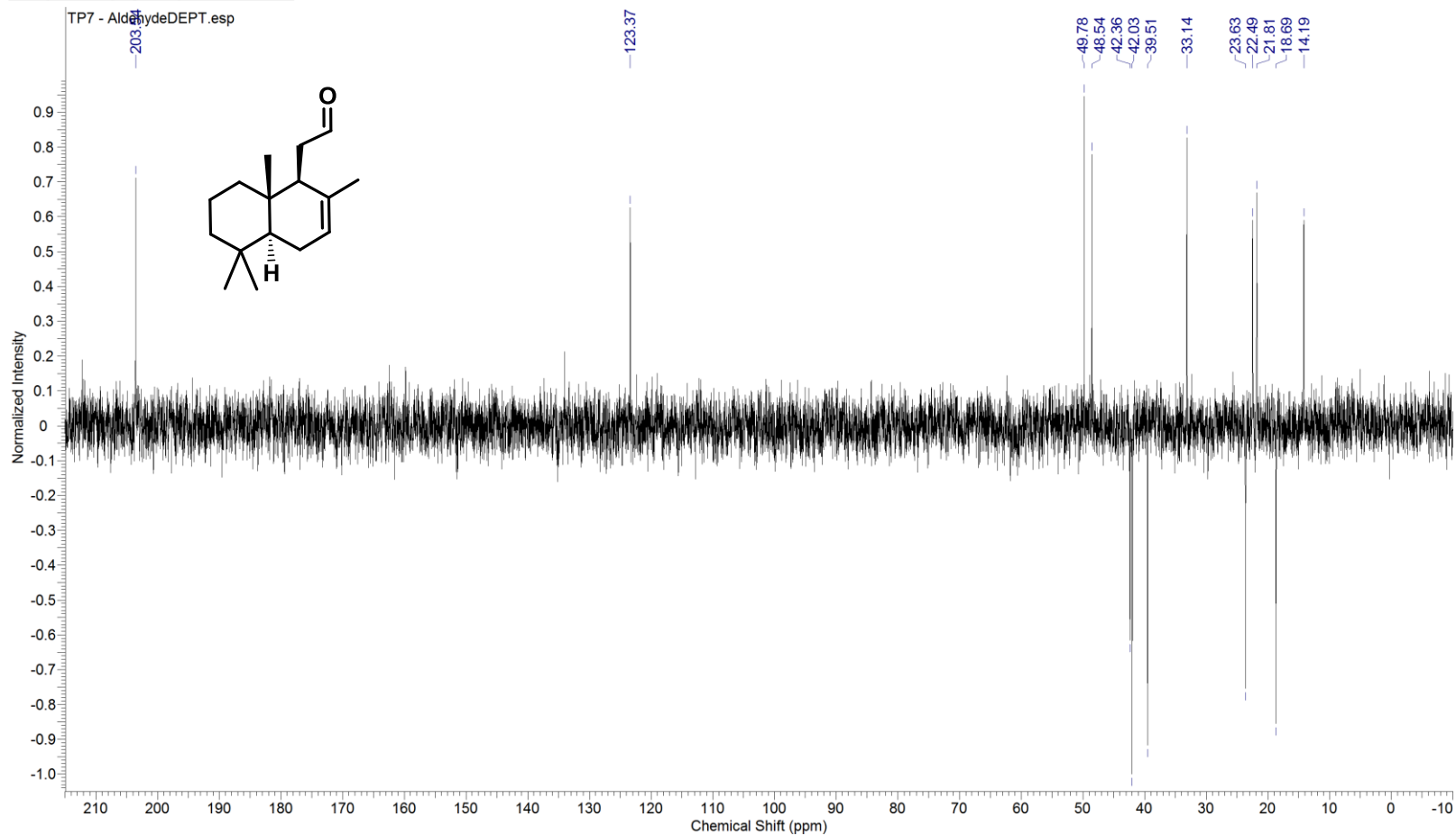
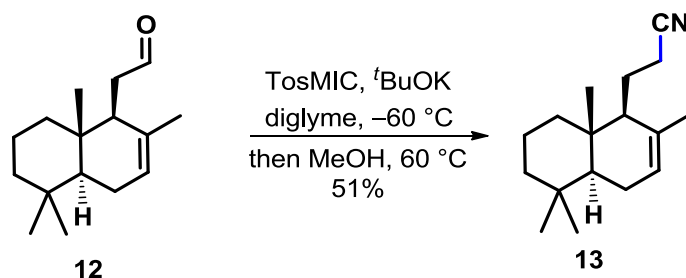


Figure S18. DEPT 135 NMR spectrum (CDCl_3 , 62.9 MHz) of compound **12**.

3-((1*S*,4*aS*,8*aS*)-2,5,5,8*a*-tetramethyl-1,4,4*a*,5,6,7,8,8*a*-octahydronaphthalen-1-yl)propanenitrile (**13**).



TosMIC (83.7 mg, 0.42 mmol, 2 equiv) in dry diglyme (2 mL) was added dropwise to a mixture of *t*-BuOK (74.4 mg, 0.63 mmol, 3 equiv) in diglyme (1 mL) at $-60\text{ }^{\circ}\text{C}$, and the resulting mixture was stirred for 10 min. A solution of aldehyde **12** (49.2 mg, 0.21 mmol, 1 equiv) in diglyme (2 mL) was added dropwise to the reaction at $-60\text{ }^{\circ}\text{C}$, the medium was stirred at this temperature for 1 h, and for 30 min at room temperature. Next, dry MeOH (2.5 mL) was added, and the reaction was stirred at $60\text{ }^{\circ}\text{C}$ for 1 h. After that, the volatiles were removed under reduced pressure, and the residue was diluted with a saturated solution of NH_4Cl and the mixture was extracted with EtOAc (2 x 15 mL). The organic layers were combined, dried over anhydrous Na_2SO_4 , and concentrated under reduced pressure. The residue was subjected to flash chromatography (SiO_2 , hexanes/EtOAc 95:5 to 90:10) to give the nitrile **13** (26.5 mg, 0.108 mmol) as a colorless oil in 51% yield.

TLC (SiO_2): $R_f = 0.31$ (hexanes/EtOAc 95:5);

$[\alpha]_D^{25} = -1$ (*c* 1.0, CHCl_3);

IR (ATR, cm^{-1}): 2923, 2848, 2245, 1457, 1388, 1168, 1051, 805;

^1H NMR (250 MHz, CDCl_3): δ 0.76 (s, 3H), 0.86 (s, 3H), 0.88 (s, 3H), 0.80-1.30 (m, 3H), 1.67 (s, 3H), 1.36-2.08 (m, 9H), 2.25-2.43 (m, 1H), 2.44-2.60 (m, 1H), 5.46 (br. s, 1H);

^{13}C NMR (62.9 MHz, CDCl_3): δ 13.6 (CH_3), 18.6 (CH_2), 18.9 (CH_2), 21.8 (CH_3), 22.0 (CH_3), 23.1 (CH_2), 23.7 (CH_2), 32.9 (C), 33.1 (CH_3), 36.6 (C), 39.0 (CH_2), 42.0 (CH_2), 49.8 (CH), 53.8 (CH), 119.9 (C), 123.9 (CH), 132.9 (C);

HRMS (ESI $+$): m/z calculated for $\text{C}_{17}\text{H}_{27}\text{NNa}^+$ [$\text{M}+\text{Na}$] $^+$ 268.2036, found 268.2031.

Acquisition Time (sec)	3.1654	Comment	LN212	Date	18 Jul 2016 16:31:12		
Date Stamp	18 Jul 2016 16:31:12			File Name	C:\Users\Luiz\Desktop\Luiz\PhD\NMR\jul16\jul18\ftH1\1\1\PDATA\1\1r		
Frequency (MHz)	250.13	Nucleus	1H	Number of Transients	17	Origin	spect
Owner	root	Points Count	32768	Pulse Sequence	zg30	Receiver Gain	362.00
Solvent	CHLOROFORM-d			Spectrum Offset (Hz)	1544.9661	Spectrum Type	STANDARD
Temperature (degree C)	25.160					SW(cyclical) (Hz)	5175.98
						Sweep Width (Hz)	5175.83

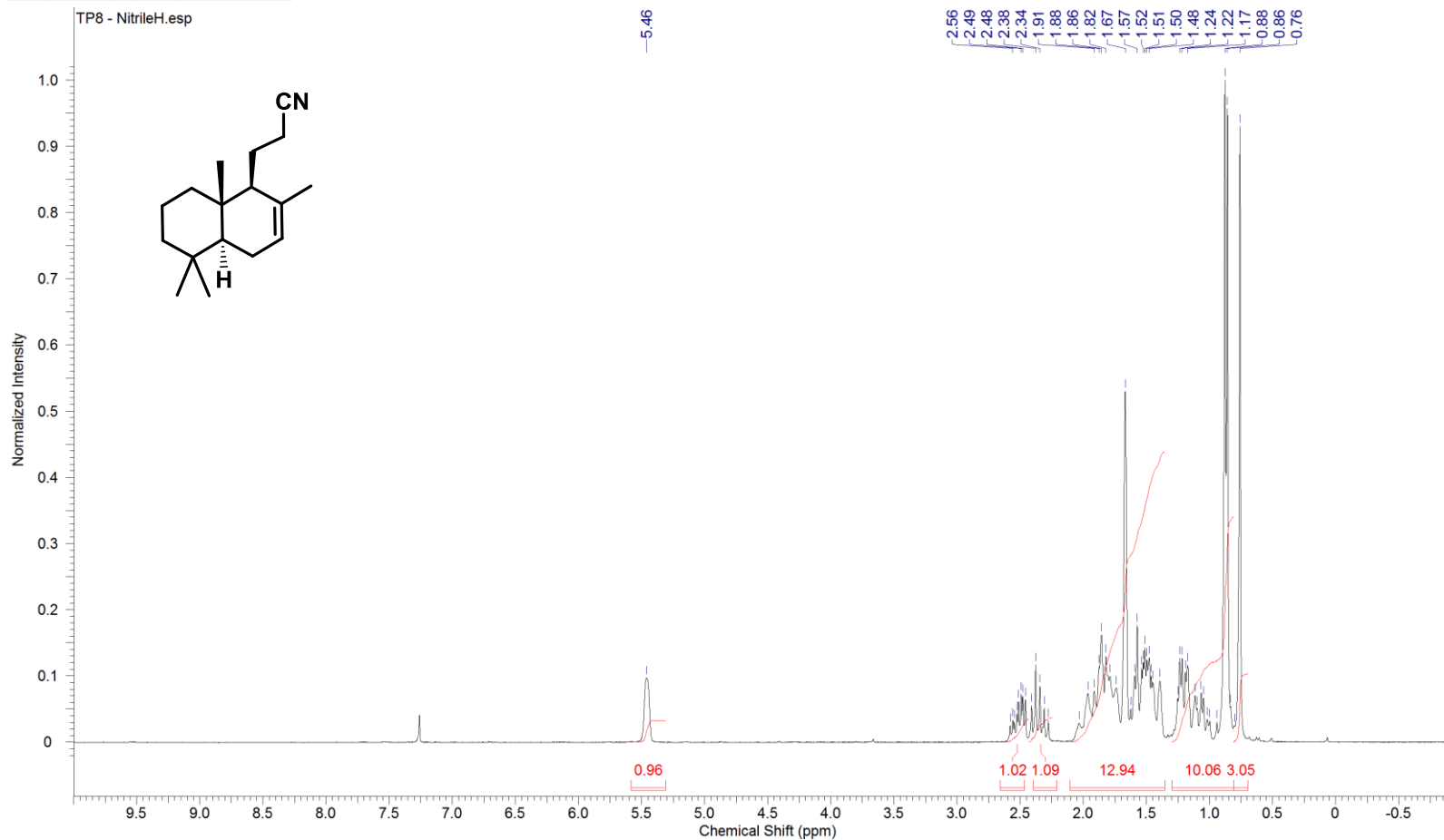


Figure S19. ^1H NMR spectrum (CDCl_3 , 250 MHz) of compound **13**.

Acquisition Time (sec)	1.0879	Comment	LN212	Date	18 Jul 2016 16:33:20		
Date Stamp	18 Jul 2016 16:33:20			File Name	C:\Users\Luiz\Desktop\Luiz\PhD\NMR\jul16\jul18\ftH1\2\PDATA\1\1r		
Frequency (MHz)	62.90	Nucleus	13C	Number of Transients	97	Origin	spect
Owner	root	Points Count	32768	Pulse Sequence	zgpg30	Receiver Gain	724.10
Solvent	CHLOROFORM-d			Spectrum Offset (Hz)	6288.6118	Spectrum Type	STANDARD
Temperature (degree C)	25.160					SW(cyclical) (Hz)	15060.24
						Sweep Width (Hz)	15059.78

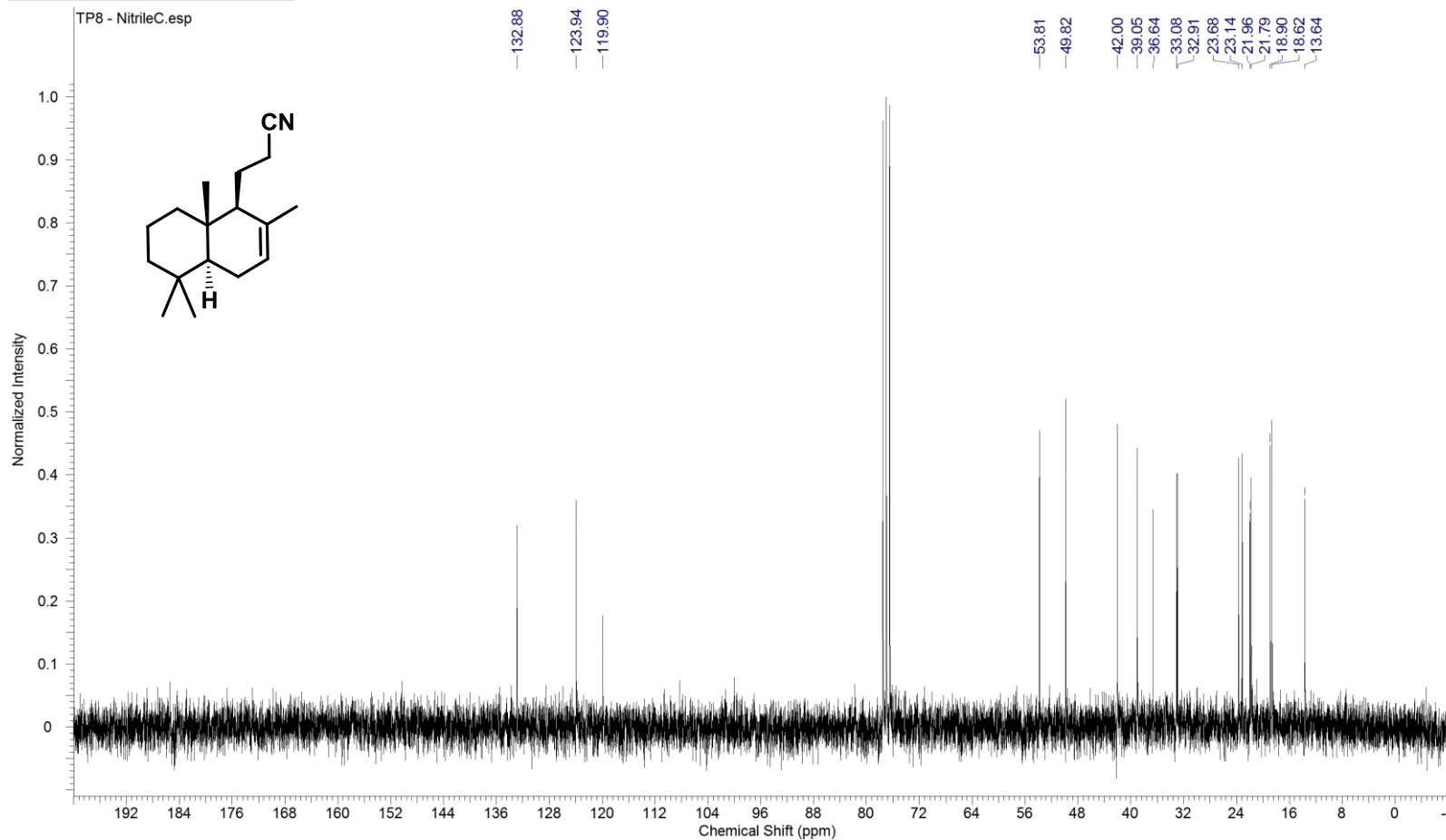


Figure S20. ^{13}C NMR spectrum (CDCl_3 , 62.9 MHz) of compound **13**.

Acquisition Time (sec)	0.5439	Comment	LN212	Date	19 Jul 2016 08:24:48		
Date Stamp	19 Jul 2016 08:24:48			File Name	C:\Users\Luiz\Desktop\Luiz\PhD\NMR\jul16\jul19\ftH1\2\PDATA\1\1r		
Frequency (MHz)	62.90	Nucleus	13C	Number of Transients	56	Origin	spect
Owner	root	Points Count	32768	Pulse Sequence	dept135	Receiver Gain	16384.00
Solvent	CHLOROFORM-d			Spectrum Offset (Hz)	6289.0518	Spectrum Type	DEPT135
Temperature (degree C)	25.160					Sweep Width (Hz)	15059.78

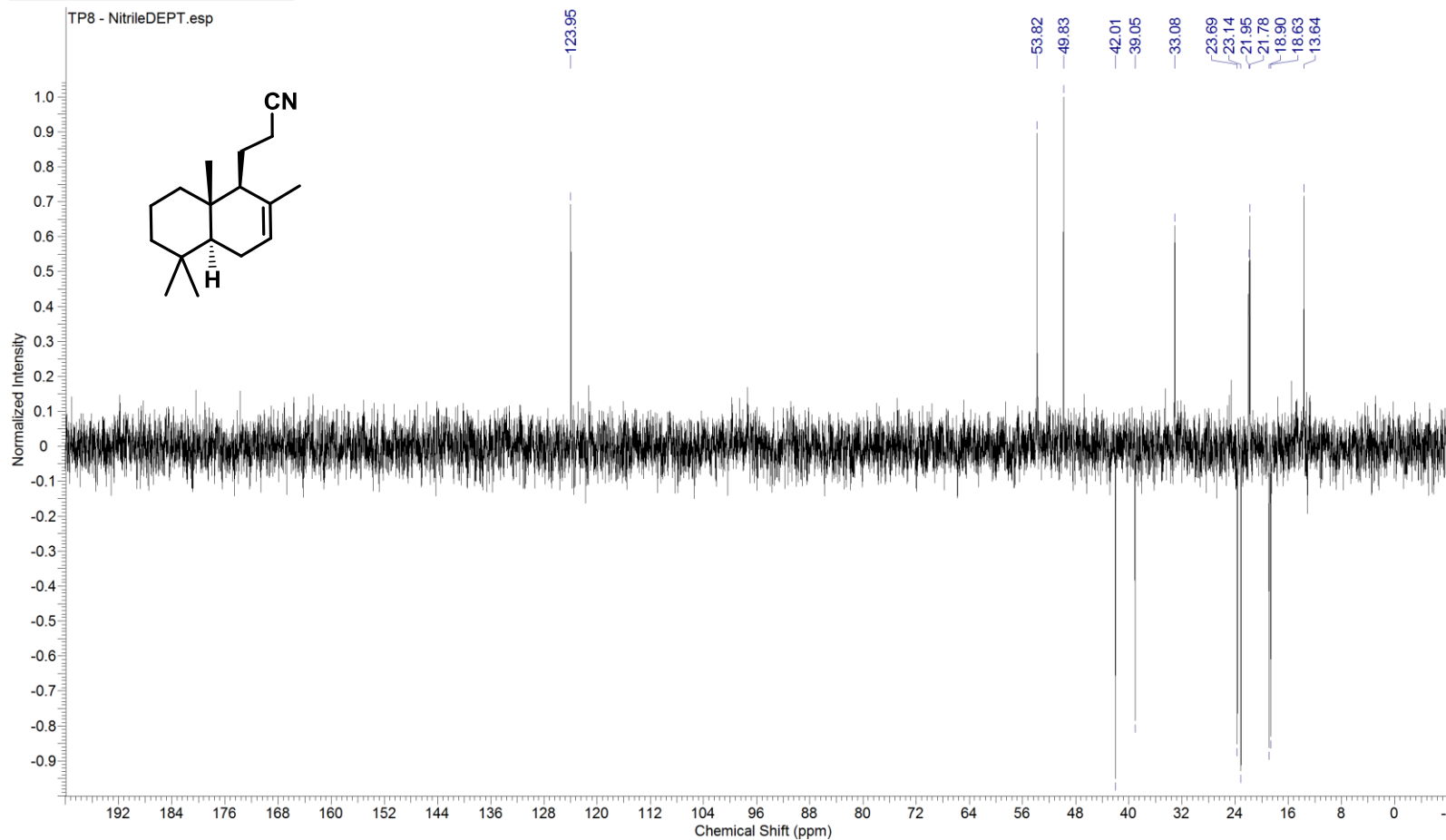
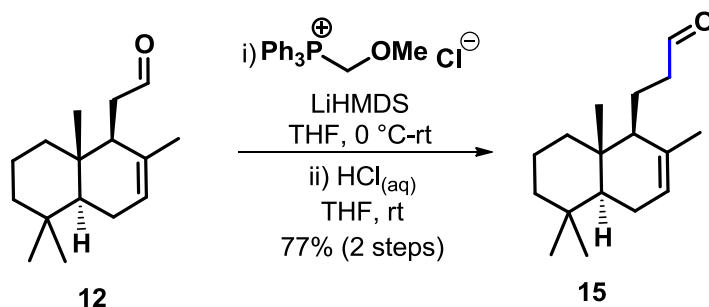


Figure S21. DEPT 135 NMR spectrum (CDCl_3 , 62.9 MHz) of compound **13**.

3-((1*S*,4*aS*,8*aS*)-2,5,5,8*a*-tetramethyl-1,4,4*a*,5,6,7,8,8*a*-octahydronaphthalen-1-yl)propanal (15**).**



To a suspension of (methoxymethyl)triphenylphosphonium chloride (163 mg, 0.46 mmol, 2 equiv) in dry THF (2 mL) was added a solution of LiHMDS (1 M in THF, 345 μL , 0.345 mmol, 1.5 equiv) at 0 ° and the reaction was stirred at this temperature for 30 min. After this period, the brownish mixture was transferred *via* cannula to a flask containing a solution of aldehyde **12** (53.9 mg, 0.230 mmol, 1 equiv) in dry THF (2 mL) at 0 °C, and the resulting mixture was stirred for 30 min at 0 °C and 4 h at room temperature. Next, the reaction was quenched by addition of saturated aqueous solution of NH_4Cl (10 mL), and was extracted with EtOAc (10 mL). The organic phase was washed with brine (5 mL), dried over anhydrous MgSO_4 and concentrated under reduced pressure. The residue obtained was subjected to flash chromatography (SiO_2 , hexanes/EtOAc 95:5) to afford a mixture of (*E*) and (*Z*)-enol ethers, which were immediately used in the next reaction.

TLC (SiO_2): $R_f = 0.45$ (hexanes:EtOAc 95:5).

The mixture of (*E*) and (*Z*)-enol ethers obtained above was diluted in THF (2 mL) and a solution of HCl (6 M in H_2O , 0.4 mL, 2.4 mmol, 10 equiv) was added dropwise at 0 °C. The mixture was stirred at room temperature for 2 h, and was diluted with H_2O (8 mL), followed by an extraction with EtOAc (8 mL). The organic phase was washed with brine (5 mL), dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The residue was subjected to flash chromatography (SiO_2 , hexanes/EtOAc 95:5) to give aldehyde **15** (44.0 mg, 0.177 mmol) as a colorless oil in 77% yield.

TLC (SiO_2): $R_f = 0.30$ (hexanes/EtOAc 95:5);

$[\alpha]_D^{25} = +21$ (c 1.0, CHCl_3);

IR (ATR, cm^{-1}): 2923, 2846, 1726, 1457, 1387, 1050, 983;

^1H NMR (250 MHz, CDCl_3): δ 0.79 (s, 3H), 0.85 (s, 3H), 0.88 (s, 3H), 0.81-1.04 (m, 1H), 1.15 (dd, $J = 11.8, 5.0$ Hz, 2H), 1.66 (s, 3H), 1.36-1.71 (m, 5H), 1.79-2.03 (m, 4H), 2.43 (dddd, $J = 17.4, 8.8, 6.5, 1.9$ Hz, 1H), 2.65 (dddd, $J = 17.2, 9.9, 5.5, 1.6$ Hz, 1H), 5.42 (br. s, 1H), 9.76 (t, $J = 1.7$ Hz, 1H);

^{13}C NMR (62.9 MHz, CDCl_3): δ 13.6 (CH_3), 18.7 (CH_2), 19.1 (CH_2), 21.8 (CH_3), 22.1 (CH_3), 23.7 (CH_2), 32.9 (C), 33.1 (CH_3), 36.9 (C), 39.4 (CH_2), 42.2 (CH_2), 46.0 (CH_2), 50.0 (CH), 54.3 (CH), 123.2 (CH), 134.1 (C), 202.4 (CH);

HRMS (ESI +): m/z calculated for $\text{C}_{17}\text{H}_{28}\text{ONa}^+$ $[\text{M}+\text{Na}]^+$ 271.2032, found 271.2013.

Acquisition Time (sec)	1.0879	Comment	LN227	Date	02 Aug 2016 16:09:52		
Date Stamp	02 Aug 2016 16:09:52			File Name	C:\Users\Luiz\Desktop\Luiz\PhD\NMR\ago16\ago02\ftH3\2\PDATA\1\1r		
Frequency (MHz)	62.90	Nucleus	13C	Number of Transients	27	Origin	spect
Owner	root	Points Count	32768	Pulse Sequence	zgpg30	Receiver Gain	362.00
Solvent	CHLOROFORM-d			Spectrum Offset (Hz)	6289.0518	Spectrum Type	STANDARD
Temperature (degree C)	25.260					SW(cyclical) (Hz)	15060.24
						Sweep Width (Hz)	15059.78

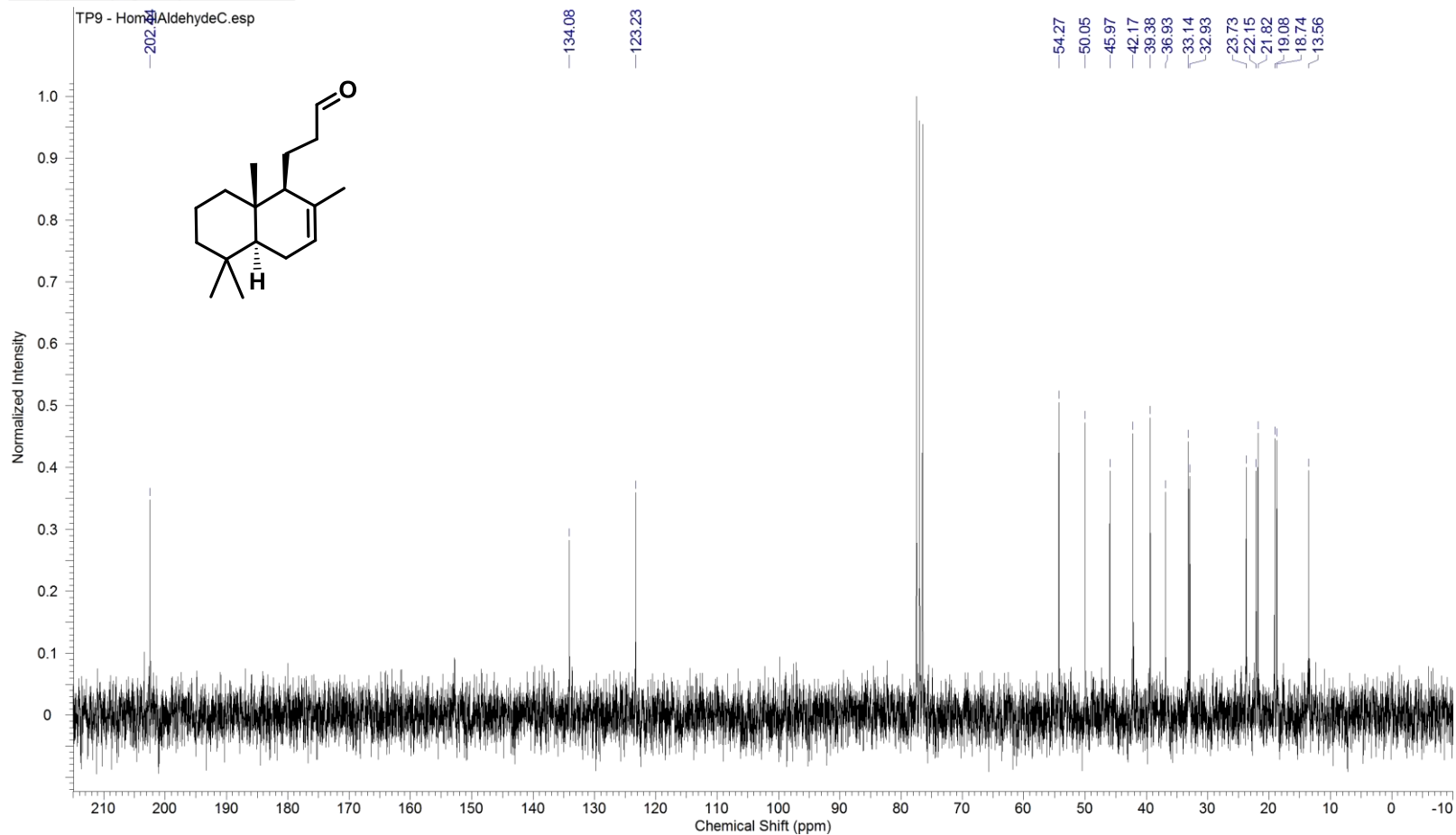


Figure S23. ^{13}C NMR spectrum (CDCl_3 , 62.9 MHz) of compound **15**.

Acquisition Time (sec)	0.5439	Comment	LN227	Date	02 Aug 2016 16:07:44		
Date Stamp	02 Aug 2016 16:07:44			File Name	C:\Users\Luiz\Desktop\Luiz\PhD\NMR\ago16\ago02\ftH3\3\PDATA\1\1r		
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Owner	root	Points Count	32768	Pulse Sequence	dept135	Receiver Gain	2580.30
Solvent	CHLOROFORM-d			Spectrum Offset (Hz)	6289.0518	Spectrum Type	DEPT135
Temperature (degree C)	25.160					SW(cyclical) (Hz)	15060.24
						Sweep Width (Hz)	15059.78

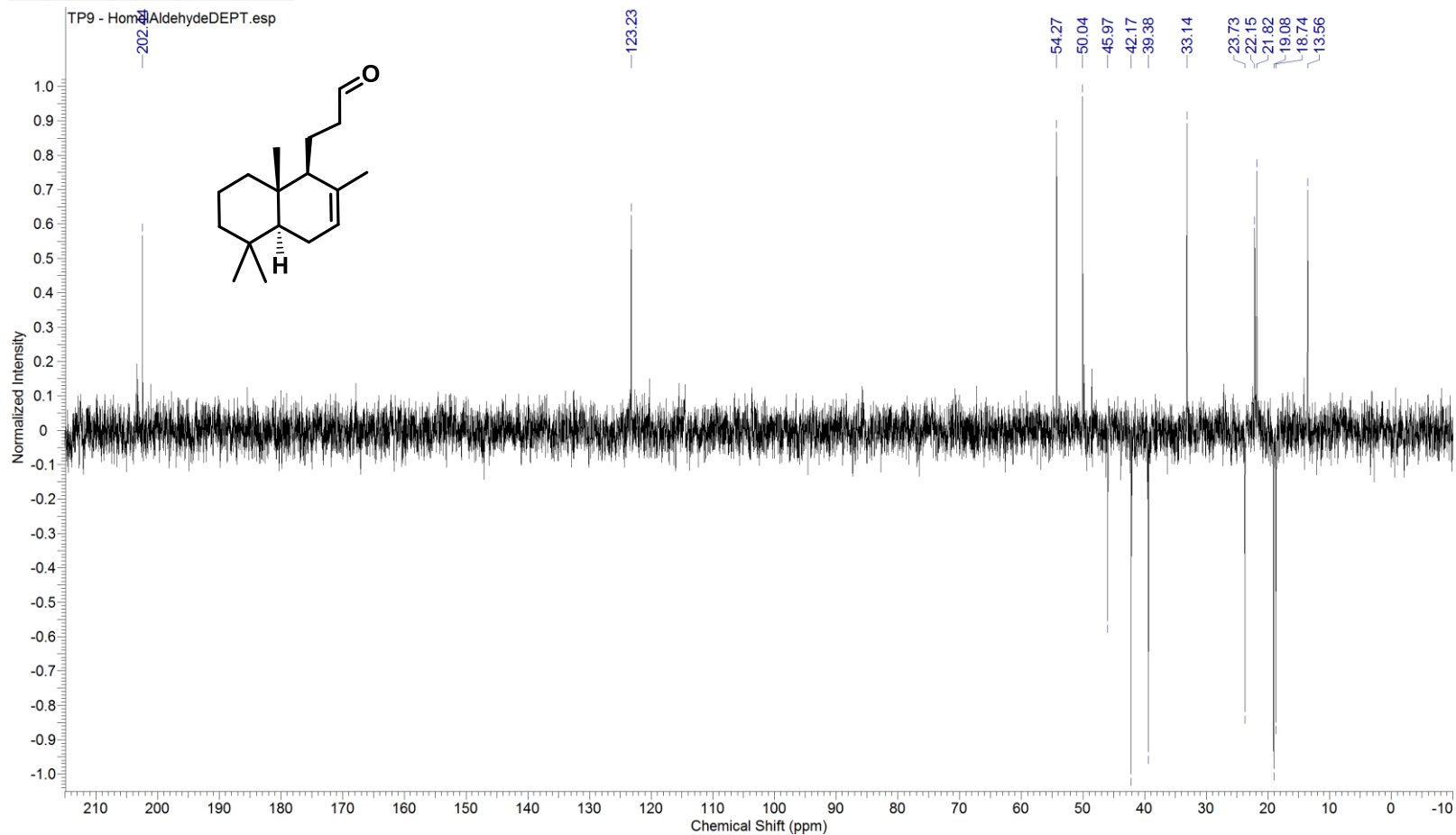
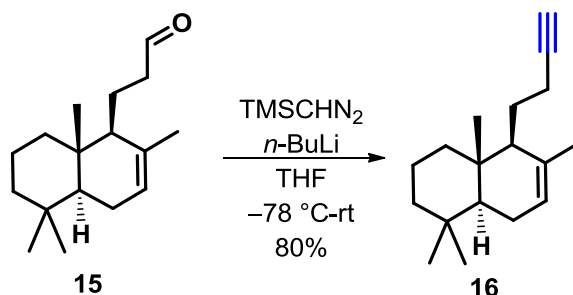


Figure S24. DEPT 135 NMR spectrum (CDCl_3 , 62.9 MHz) of compound **15**.

(4a*S*,5*S*,8a*S*)-5-(but-3-yn-1-yl)-1,1,4a,6-tetramethyl-1,2,3,4,4a,5,8,8a-octahydronaphthalene (**16**).



TMSCHN₂ solution (2 M in hexanes, 0.76 mL, 1.52 mmol, 4 equiv) was added to THF (5 mL), the resulting mixture was cooled to $-78\text{ }^\circ\text{C}$, then a solution of *n*-BuLi (2.5 M in hexanes, 0.46 mL, 1.15 mmol, 3 equiv) was added dropwisely and the reaction was stirred at the same temperature for 30 min. Next, a solution of aldehyde **15** (94.4 mg, 0.38 mmol, 1 equiv) in THF (3 mL) was added to the reaction and the resulting mixture was stirred at $-78\text{ }^\circ\text{C}$ for 1 h, and then at room temperature for 1 h. The reaction was quenched by addition of saturated aqueous solution of NH₄Cl (10 mL), followed by the extraction with Et₂O (2 x 10 mL). The combined organic extracts were dried over anhydrous MgSO₄ and concentrated under reduced pressure. The residue was subjected to flash chromatography (SiO₂, hexanes) to afford the alkyne **16** (74.4 mg, 0.30 mmol) as a colorless oil in 80% yield.

TLC (SiO₂): R_f = 0.72 (hexanes);

[α]_D²⁵ = +12 (*c* 1.0, CHCl₃);

IR (ATR, cm⁻¹): 3312, 2923, 2847, 2118, 1457, 1387, 1050, 983;

¹H NMR (250 MHz, CDCl₃): δ 0.76 (s, 3H), 0.86 (s, 3H), 0.88 (s, 3H), 0.80-1.29 (m, 4H), 1.96 (t, *J* = 2.6 Hz, 1H), 1.35-2.06 (m, 11H), 2.10-2.27 (m, 1H), 2.37 (dddd, *J* = 16.8, 9.0, 5.0, 2.5 Hz, 1H), 5.40 (br. s, 1H);

¹³C NMR (62.9 MHz, CDCl₃): δ 13.6 (CH₃), 18.7 (CH₂), 20.3 (CH₂), 21.8 (CH₃), 22.1 (CH₃), 23.8 (CH₂), 26.2 (CH₂), 32.9 (C), 33.1 (CH₃), 36.6 (C), 39.1 (CH₂), 42.2 (CH₂), 50.0 (CH), 53.7 (CH), 68.3 (CH), 84.8 (C), 122.8 (CH), 134.5 (C);

GC/MS (EI): *m/z* calculated for C₁₇H₂₅ [M-CH₃]⁺ 229, found: 229.

Acquisition Time (sec)	3.1654	Comment	LN378	Date	09 Dec 2016 16:42:08		
Date Stamp	09 Dec 2016 16:42:08			File Name	C:\Users\Luiz\Desktop\Luiz\PhD\NMR\dez16\dez09\ftH2\1\PDATA\1\1r		
Frequency (MHz)	250.13	Nucleus	1H	Number of Transients	17	Origin	spect
Owner	root	Points Count	32768	Pulse Sequence	zg30	Receiver Gain	362.00
Solvent	CHLOROFORM-d			Spectrum Offset (Hz)	1544.6561	Spectrum Type	STANDARD
Temperature (degree C)	25.160					SW(cyclical) (Hz)	5175.98
						Sweep Width (Hz)	5175.83

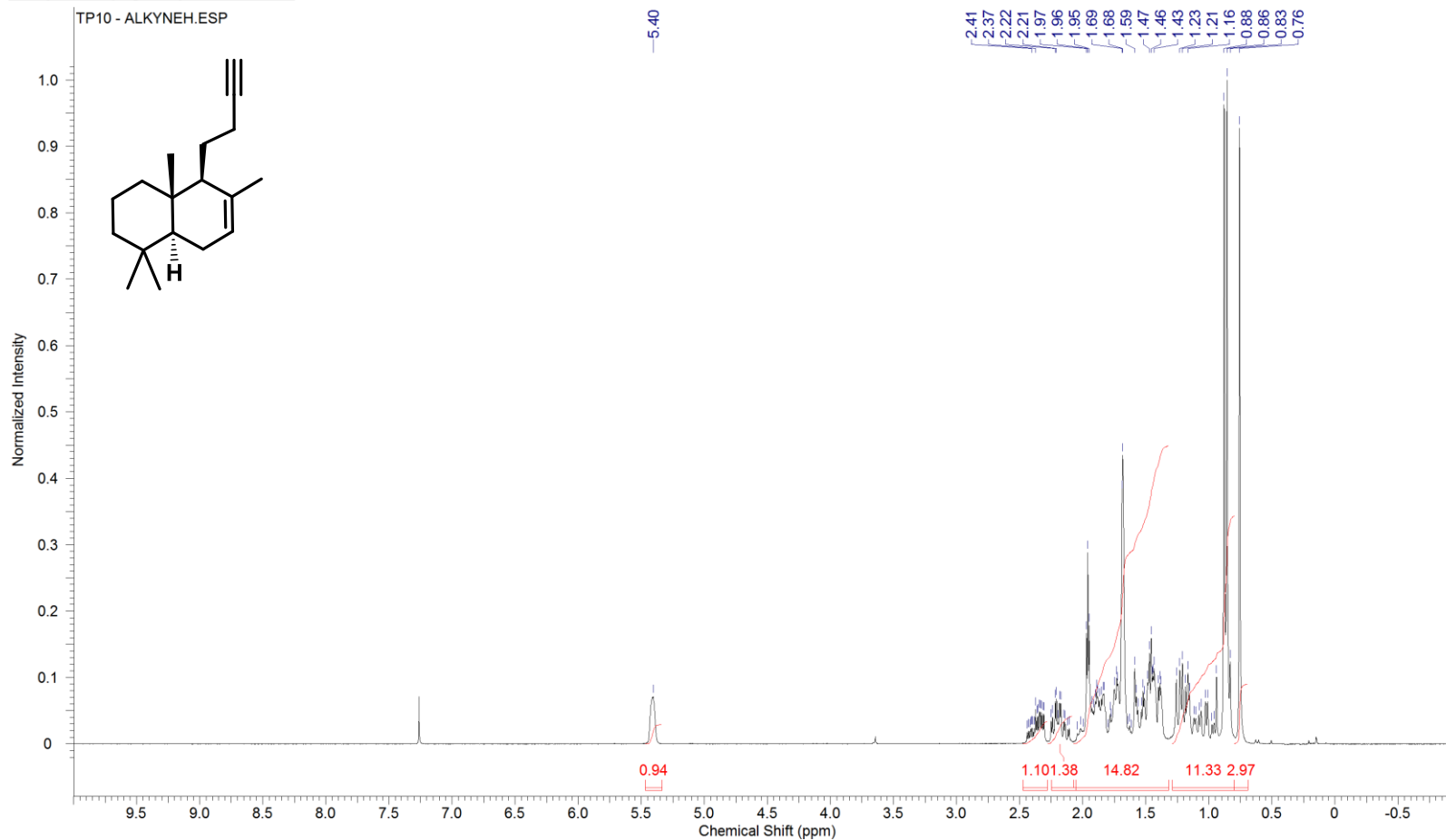


Figure S25. ^1H NMR spectrum (CDCl_3 , 250 MHz) of compound **16**.

Acquisition Time (sec)	1.0879	Comment	LN378	Date	09 Dec 2016 16:46:24		
Date Stamp	09 Dec 2016 16:46:24			File Name	C:\Users\Luiz\Desktop\Luiz\PhD\NMR\dez16\dez09\ftH2\2\PDATA\1\1r		
Frequency (MHz)	62.90	Nucleus	13C	Number of Transients	120	Origin	spect
Owner	root	Points Count	32768	Pulse Sequence	zgpg30	Receiver Gain	645.10
Solvent	CHLOROFORM-d			Spectrum Offset (Hz)	6289.0518	Spectrum Type	STANDARD
Temperature (degree C)	25.160					SW(cyclical) (Hz)	15060.24
						Sweep Width (Hz)	15059.78

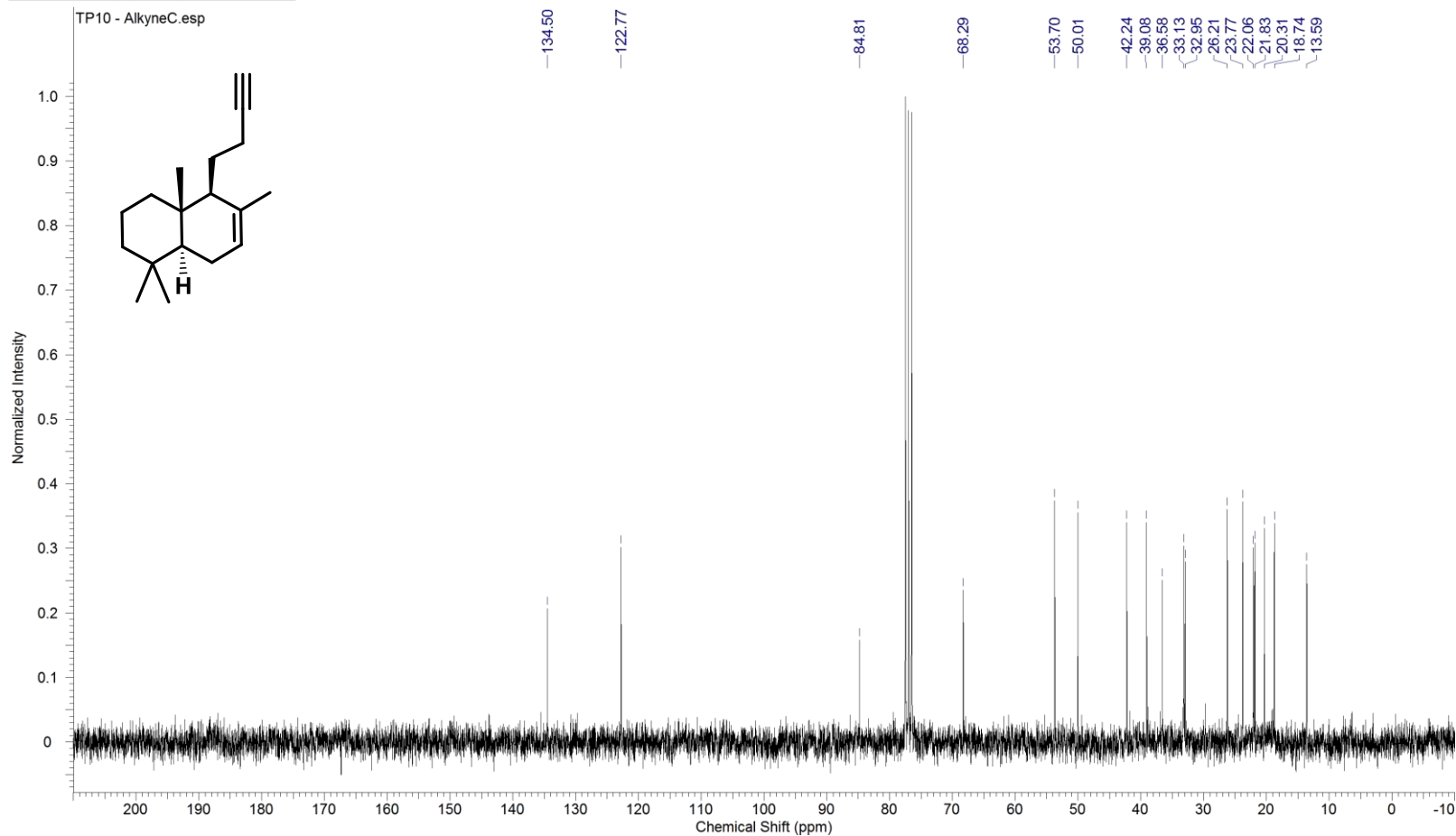


Figure S26. ^{13}C NMR spectrum (CDCl_3 , 62.9 MHz) of compound **16**.

Acquisition Time (sec)	0.5439	Comment	LN378	Date	09 Dec 2016 16:52:48		
Date Stamp	09 Dec 2016 16:52:48			File Name	C:\Users\Luiz\Desktop\Luiz\PhD\NMR\dez16\dez09\ftH2\3\PDATA\1\1r		
Frequency (MHz)	62.90	Nucleus	13C	Number of Transients	163	Origin	spect
Owner	root	Points Count	32768	Pulse Sequence	dept135	Receiver Gain	16384.00
Solvent	CHLOROFORM-d			Spectrum Offset (Hz)	6289.0518	Spectrum Type	DEPT135
Temperature (degree C)	25.160					SW(cyclical) (Hz)	15060.24
						Sweep Width (Hz)	15059.78

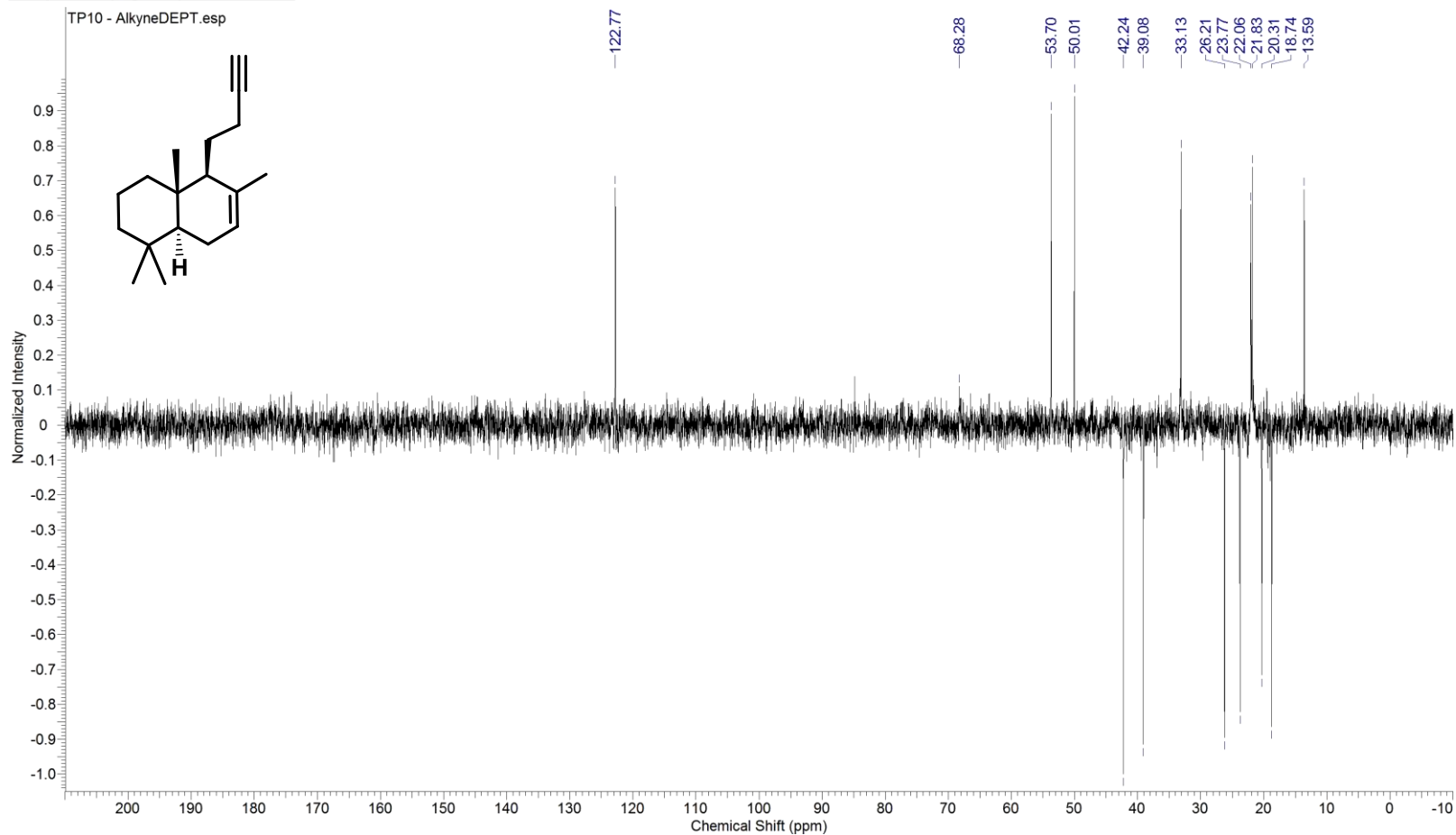
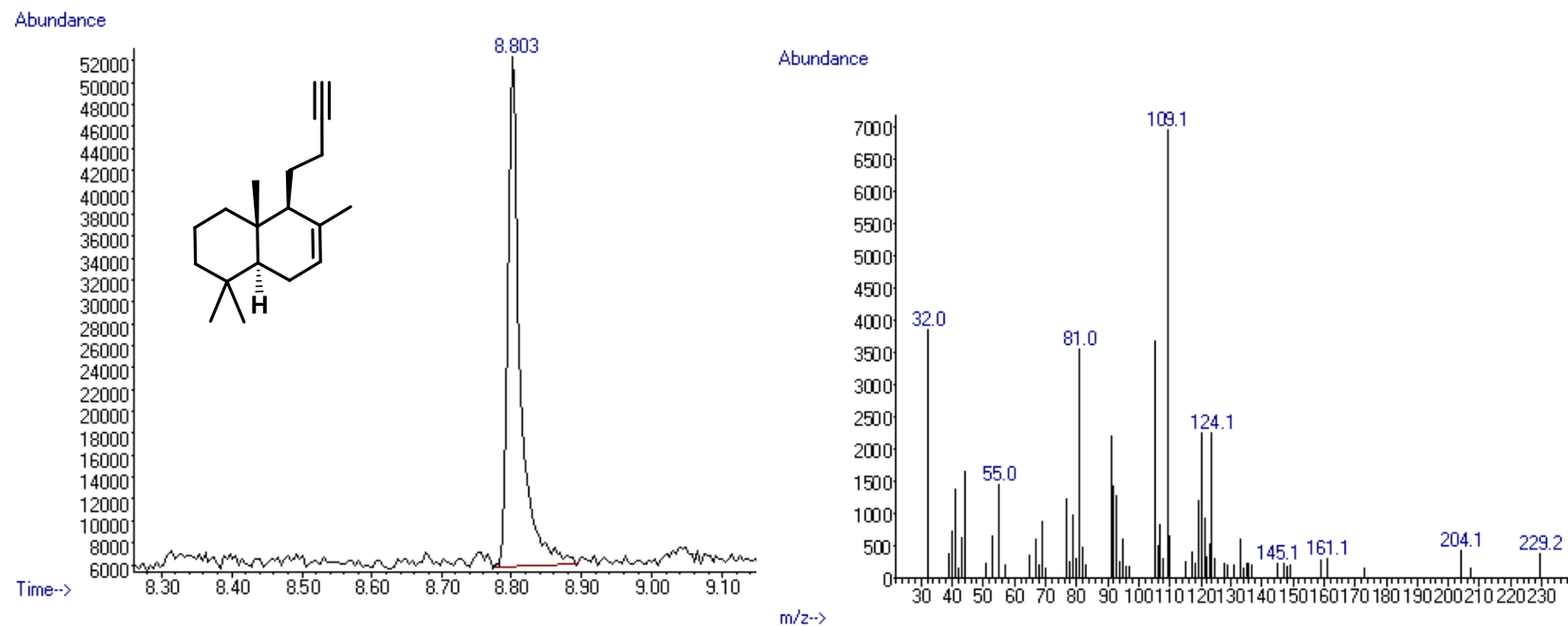


Figure S27. DEPT 135 NMR spectrum (CDCl_3 , 62.9 MHz) of compound **16**.

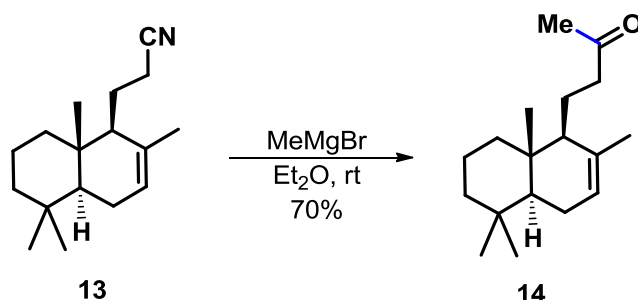


$t_R = 8.803 \text{ min}$, $[M-CH_3]^+ = 229$

Figure S28. GC/MS analysis of compound 16.

4-((1*S*,4*aS*,8*aS*)-2,5,5,8*a*-tetramethyl-1,4,4*a*,5,6,7,8,8*a*-octahydronaphthalen-1-yl)butan-2-one (14**).**

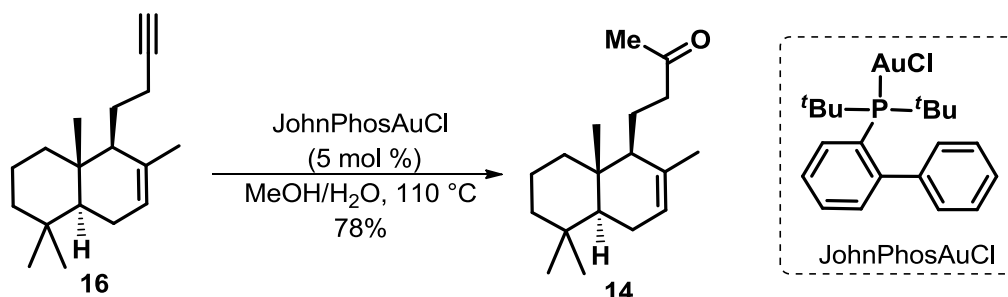
Procedure A:



MeMgBr solution (3 M in Et₂O, 1.6 mL, 4.8 mmol, 3 equiv) was added dropwise to a solution of nitrile **13** (393 mg, 1.6 mmol, 1 equiv) in dry Et₂O (15 mL) at 0 °C, the reaction was warmed to room temperature and was stirred for 16 h. The reaction was quenched by addition of saturated aqueous solution of NH₄Cl (10 mL), followed by extraction with EtOAc (2 x 20 mL). The combined organic extracts were dried over anhydrous MgSO₄ and concentrated under reduced pressure. The residue was subjected to flash chromatography (SiO₂, hexanes/EtOAc 90:10) to give the ketone **14** (295 mg, 1.1 mmol) as a colorless oil in 70% yield.

Note: Nitrile **13** and ketone **14** presented similar R_f using TLC with SiO₂ and different eluents, the progress of reaction was monitored by GC/MS analysis.

Procedure B:



A pressure tube was charged with alkyne **16** (16.0 mg, 64 μmol, 1 equiv), methanol (2 mL) and H₂O (1 mL) were added followed by JohnPhosAuCl (1.7 mg, 3.2 μmol, 5 mol %), the pressure tube was sealed and heated at 110 °C for 90 min. The mixture was cooled to room temperature, then methanol was removed under reduced pressure. The remaining residue was extracted with CH₂Cl₂ (2 x 5 mL), the combined organic phases were dried over anhydrous Na₂SO₄ and concentrated under reduced pressure. The residue was subjected to flash chromatography (SiO₂, hexanes/EtOAc 95:5 to 90:10) to give ketone **14** (13.1 mg, 50 μmol) as a colorless oil in 78% yield.

TLC (SiO₂): R_f = 0.40 (hexanes/EtOAc 90:10);

[α]_D²⁵ = +20 (c 1.0, CHCl₃);

IR (ATR, cm⁻¹): 2924, 2851, 1717, 1662, 1463, 1365, 1331, 1162;

¹H NMR (250 MHz, CDCl₃): δ 0.77 (s, 3H), 0.85 (s, 3H), 0.88 (s, 3H), 0.81-1.24 (m, 4H), 1.66 (s, 3H), 1.33-1.71 (m, 4H), 1.72-2.05 (m, 4H), 2.14 (s, 3H), 2.41 (ddd, *J* = 16.1, 9.9, 6.0 Hz, 1H), 2.64 (ddd, *J* = 16.7, 10.7, 5.3 Hz, 1H), 5.41 (br. s, 1H);

¹³C NMR (62.9 MHz, CDCl₃): δ 13.6 (CH₃), 18.7 (CH₂), 20.9 (CH₂), 21.8 (CH₃), 22.1 (CH₃), 23.7 (CH₂), 29.9 (CH₂), 32.9 (C), 33.2 (CH₃), 36.9 (C), 39.3 (CH₂), 42.2 (CH₂), 45.9 (CH₂), 50.1 (CH), 54.3 (CH), 123.0 (CH), 134.4 (C), 208.8 (C);

HRMS (ESI +): *m/z* calculated for C₁₈H₃₀ONa⁺ [M+Na]⁺ 285.2189, found 285.2200.

Acquisition Time (sec)	3.1654	Comment	LN499	Date	20 Mar 2017 08:31:12		
Date Stamp	20 Mar 2017 08:31:12			File Name	C:\Users\Luiz\Desktop\Luiz\PhD\NMR\mar17\mar20\ftH1\1\PDATA\1\1r		
Frequency (MHz)	250.13	Nucleus	1H	Number of Transients	9	Origin	spect
Owner	root	Points Count	32768	Pulse Sequence	zg30	Receiver Gain	574.70
Solvent	CHLOROFORM-d			Spectrum Offset (Hz)	1544.6561	Spectrum Type	STANDARD
Temperature (degree C)	25.160					SW(cyclical) (Hz)	5175.98
						Sweep Width (Hz)	5175.83

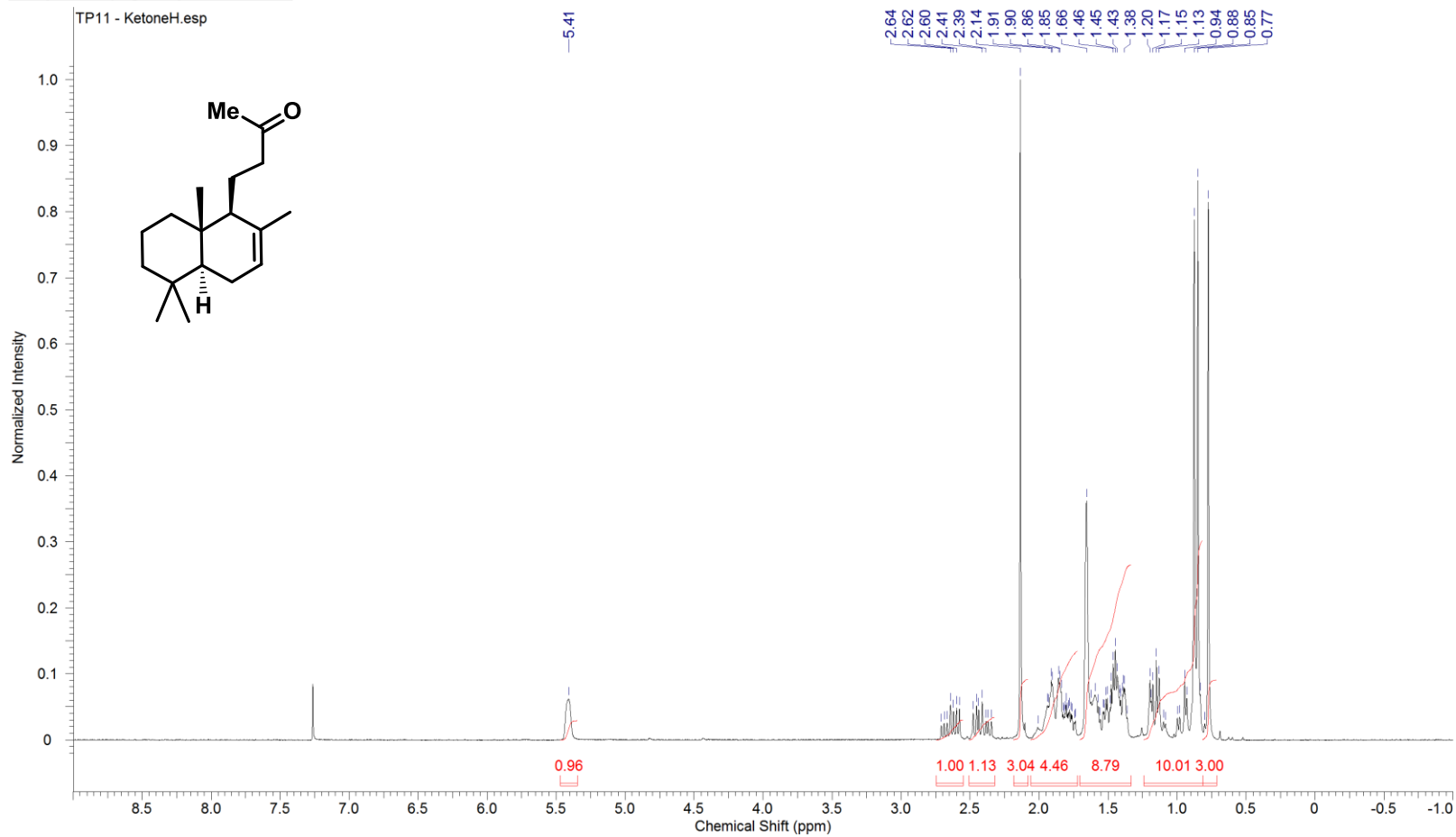


Figure S29. ^1H NMR spectrum (CDCl_3 , 250 MHz) of compound **14**.

Acquisition Time (sec)	1.0879	Comment	LN232-I	Date	03 Aug 2016 13:12:48		
Date Stamp	03 Aug 2016 13:12:48			File Name	C:\Users\Luiz\Desktop\Luiz\PhD\NMR\ago16\ago03\ftH2\3\PDATA\1\1r		
Frequency (MHz)	62.90	Nucleus	13C	Number of Transients	70	Origin	spect
Owner	root	Points Count	32768	Pulse Sequence	zgpg30	Receiver Gain	512.00
Solvent	CHLOROFORM-d			Spectrum Offset (Hz)	6289.0518	Spectrum Type	STANDARD
Temperature (degree C)	25.160					SW(cyclical) (Hz)	15060.24
						Sweep Width (Hz)	15059.78

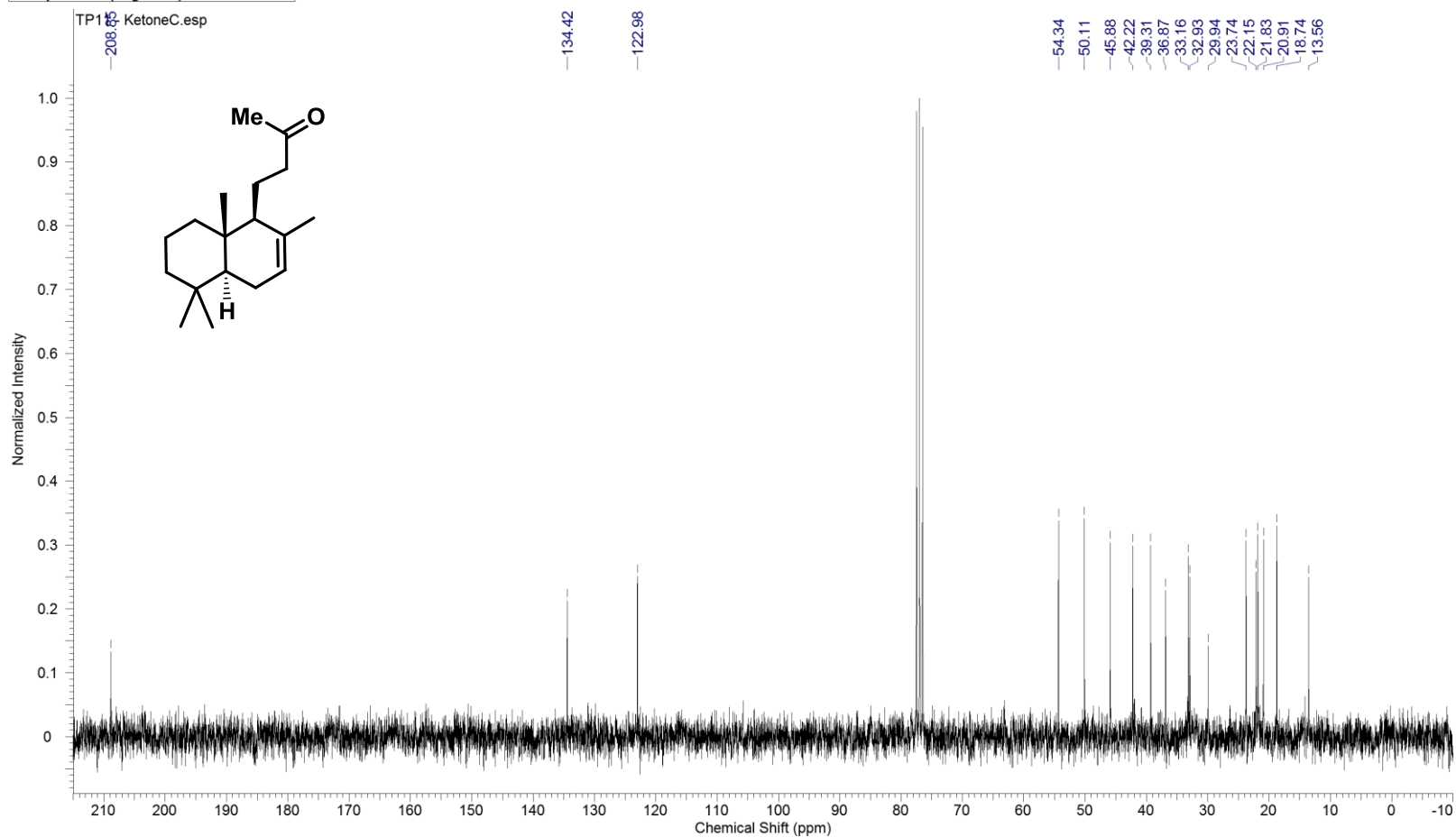


Figure S30. ^{13}C NMR spectrum (CDCl_3 , 62.9 MHz) of compound **14**.

Acquisition Time (sec)	0.5439	Comment	LN246	Date	22 Aug 2016 19:26:08		
Date Stamp	22 Aug 2016 19:26:08			File Name	C:\Users\Luiz\Desktop\Luiz\PhD\NMR\ago16\ago22\ftH1\2\PDATA\1\1r		
Frequency (MHz)	62.90	Nucleus	13C	Number of Transients	166	Origin	spect
Owner	root	Points Count	32768	Pulse Sequence	dept135	Receiver Gain	2580.30
Solvent	CHLOROFORM-d			Spectrum Offset (Hz)	6289.0518	Spectrum Type	DEPT135
Temperature (degree C)	25.160					SW(cyclical) (Hz)	15060.24
						Sweep Width (Hz)	15059.78

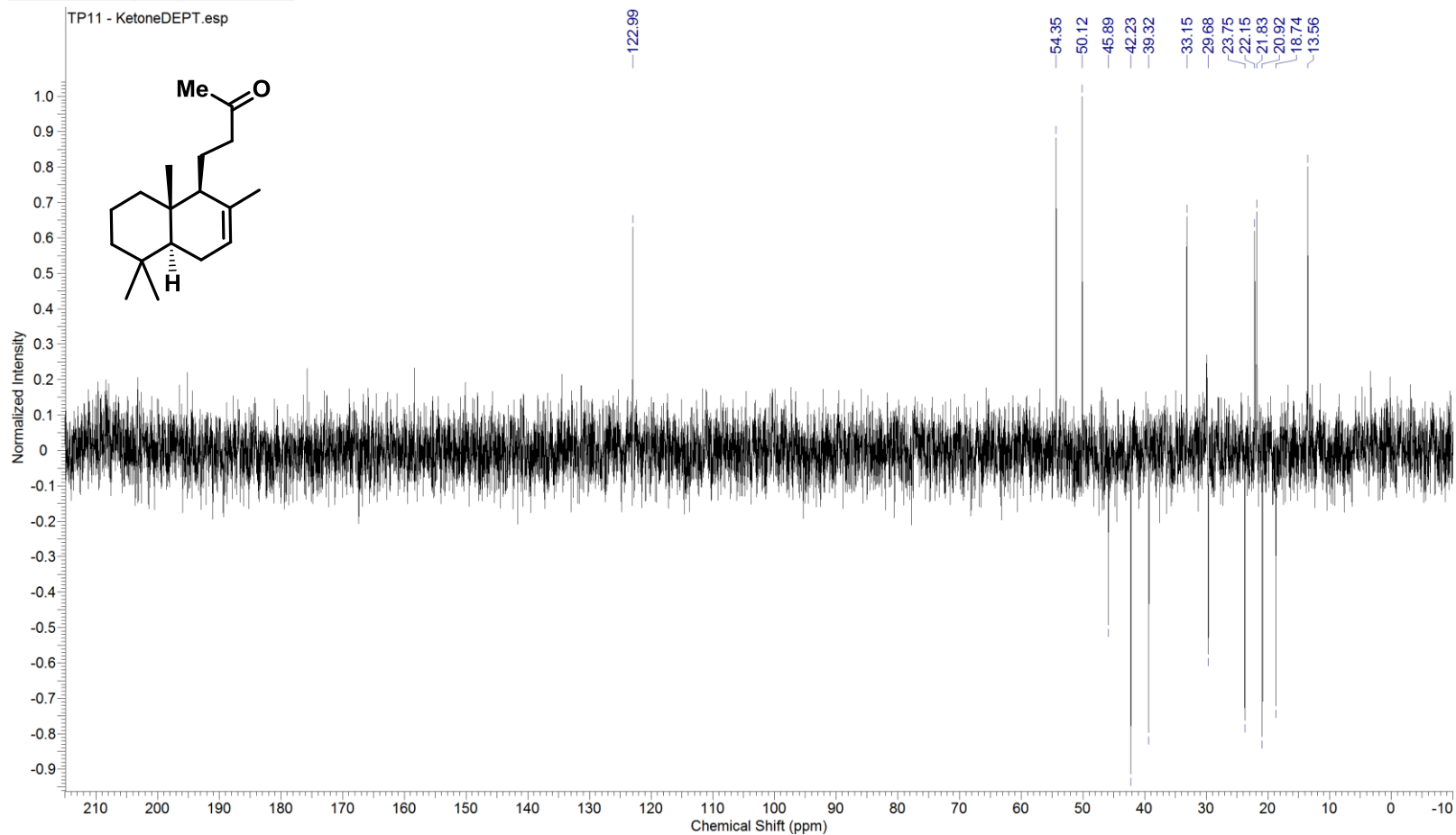
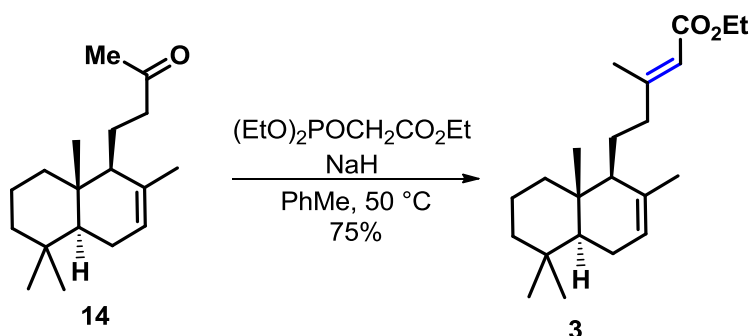


Figure S31. DEPT 135 NMR spectrum (CDCl₃, 62.9 MHz) of compound **14**.

(E)-ethyl 3-methyl-5-((1*S*,4*aS*,8*aS*)-2,5,5,8*a*-tetramethyl-1,4,4*a*,5,6,7,8,8*a*-octahydronaphthalen-1-yl)pent-2-enoate (3**).**



Triethyl phosphonoacetate (583 μL , 2.85 mmol, 3 equiv) was added to a solution of ketone **14** (249 mg, 0.95 mmol, 1 equiv) in dry toluene (9.5 mL) at room temperature. Next, sodium hydride (60% w/w in mineral oil, 110 mg, 2.75 mmol, 2.9 equiv) was added to the mixture, which was then stirred for 10 min at room temperature and for 14 h at 50 $^\circ\text{C}$. After cooling to room temperature, the reaction was quenched by the addition of brine (20 mL) and EtOAc (20 mL) was added to the mixture. The organic phase was separated, dried over anhydrous MgSO_4 and concentrated under reduced pressure. The residue was subjected to flash chromatography (SiO_2 , hexanes/EtOAc 97:3) to give the ester **3** (236 mg, 0.71 mmol) as a colorless oil in 75% yield.

Note: The minor (*Z*)-isomer was detected by GC/MS analysis of the crude (ca. 5.5% of the product) and was separated from the (*E*)-isomer during the chromatographic separation.

TLC (SiO_2): R_f = 0.48 (hexanes/EtOAc 95:5);

$[\alpha]_D^{25}$ = +27 (*c* 1.0, CHCl_3);

IR (ATR, cm^{-1}): 2923, 1716, 1648, 1457, 1386, 1221, 1143, 1040, 861;

^1H NMR (250 MHz, CDCl_3): δ 0.75 (s, 3H), 0.85 (s, 3H), 0.87 (s, 3H), 1.27 (t, J = 7.1 Hz, 3H), 1.69 (s, 3H), 0.79-1.74 (m, 9H), 2.16 (d, J = 1.3 Hz, 3H), 1.74-2.22 (m, 4H), 2.26-2.43 (m, 1H), 4.15 (q, J = 7.2 Hz, 2H), 5.40 (br. s, 1H), 5.66 (q, J = 1.0 Hz, 1H);

^{13}C NMR (62.9 MHz, CDCl_3): δ 13.5 (CH_3), 14.3 (CH_3), 18.7 (CH_2), 18.9 (CH_3), 21.8 (CH_3), 22.1 (CH_3), 23.8 (CH_2), 25.3 (CH_2), 32.9 (C), 33.1 (CH_3), 36.8 (C), 39.1 (CH_2), 42.2 (CH_2), 43.4 (CH_2), 50.1 (CH), 54.4 (CH), 59.4 (CH_2), 115.5 (CH), 122.7 (CH), 134.7 (C), 160.3 (C), 166.8 (C);

HRMS (ESI +): m/z calculated for $\text{C}_{22}\text{H}_{36}\text{O}_2\text{Na}^+$ $[\text{M}+\text{Na}]^+$ 355.2608, found 355.2613.

Acquisition Time (sec)	3.1654	Comment	LN385	Date	14 Dec 2016 14:29:52		
Date Stamp	14 Dec 2016 14:29:52			File Name	C:\Users\Luiz\Desktop\Luiz\PhD\NMR\dez16\dez14\ftH1\1\PDATA\1\1r		
Frequency (MHz)	250.13	Nucleus	1H	Number of Transients	17	Origin	spect
Owner	root	Points Count	32768	Pulse Sequence	zg30	Receiver Gain	256.00
Solvent	CHLOROFORM-d			Spectrum Offset (Hz)	1544.6561	Spectrum Type	STANDARD
Temperature (degree C)	25.160					SW(cyclical) (Hz)	5175.98
						Sweep Width (Hz)	5175.83

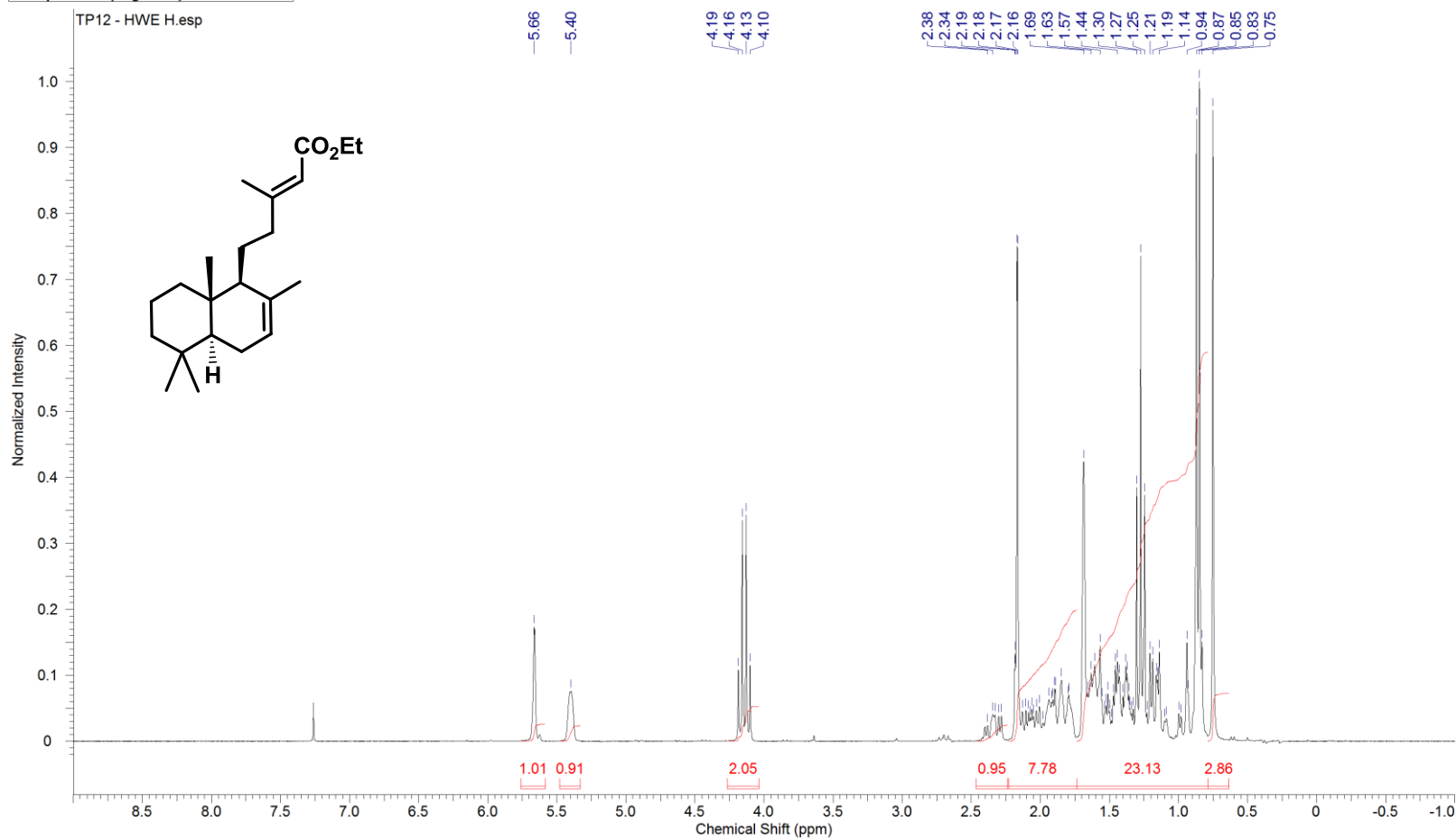


Figure S32. ¹H NMR spectrum (CDCl₃, 250 MHz) of compound **3**.

Acquisition Time (sec)	1.0879	Comment	LN385	Date	14 Dec 2016 14:40:32		
Date Stamp	14 Dec 2016 14:40:32			File Name	C:\Users\Luiz\Desktop\Luiz\PhD\NMR\dez16\dez14\ftH1\3\PDATA\1\1r		
Frequency (MHz)	62.90	Nucleus	13C	Number of Transients	121	Origin	spect
Owner	root	Points Count	32768	Pulse Sequence	zgpg30	Receiver Gain	456.10
Solvent	CHLOROFORM-d			Spectrum Offset (Hz)	6289.0518	Spectrum Type	STANDARD
Temperature (degree C)	25.160					SW(cyclical) (Hz)	15060.24
						Sweep Width (Hz)	15059.78

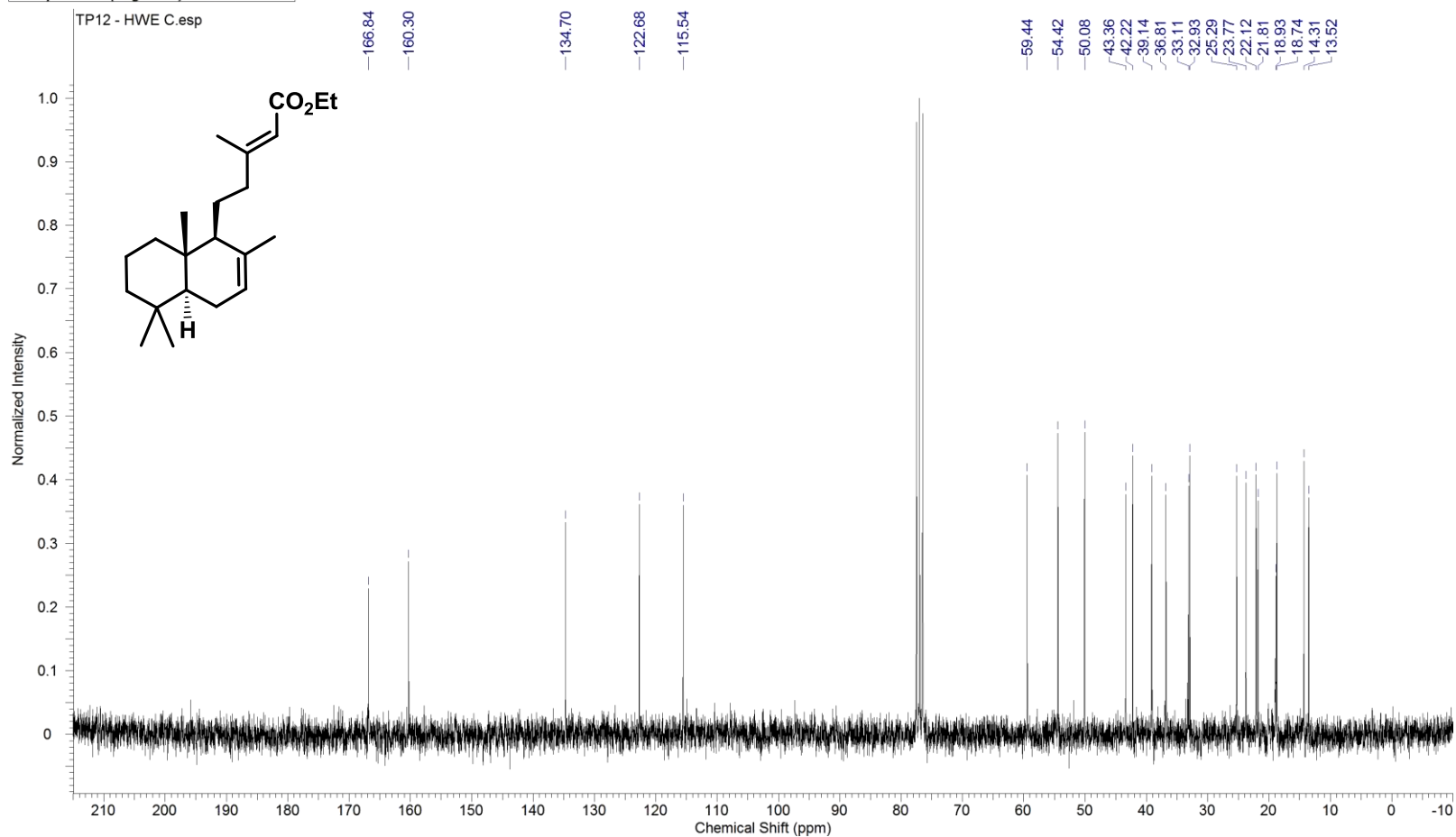


Figure S33. ^{13}C NMR spectrum (CDCl_3 , 62.9 MHz) of compound **3**.

Acquisition Time (sec)	0.5439	Comment	LN385	Date	14 Dec 2016 14:34:08		
Date Stamp	14 Dec 2016 14:34:08			File Name	C:\Users\Luiz\Desktop\Luiz\PhD\NMR\dez16\dez14\ftH1\2\PDATA\1\1r		
Frequency (MHz)	62.90	Nucleus	¹³ C	Number of Transients	104	Origin	spect
Owner	root	Points Count	32768	Pulse Sequence	dept135	Receiver Gain	912.30
Solvent	CHLOROFORM-d			Spectrum Offset (Hz)	6289.0518	Spectrum Type	DEPT135
Temperature (degree C)	25.160					SW(cyclical) (Hz)	15060.24
						Sweep Width (Hz)	15059.78

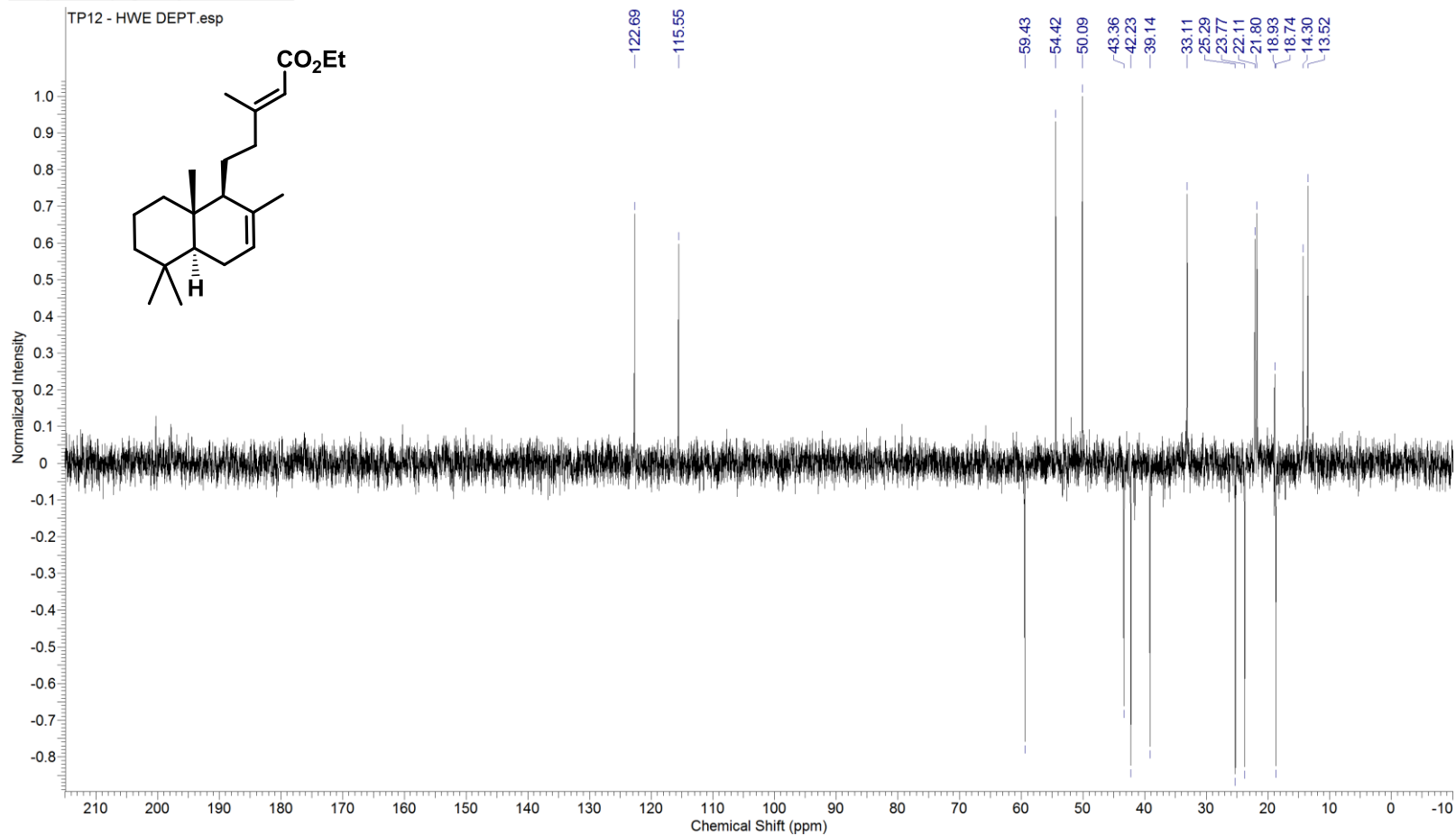
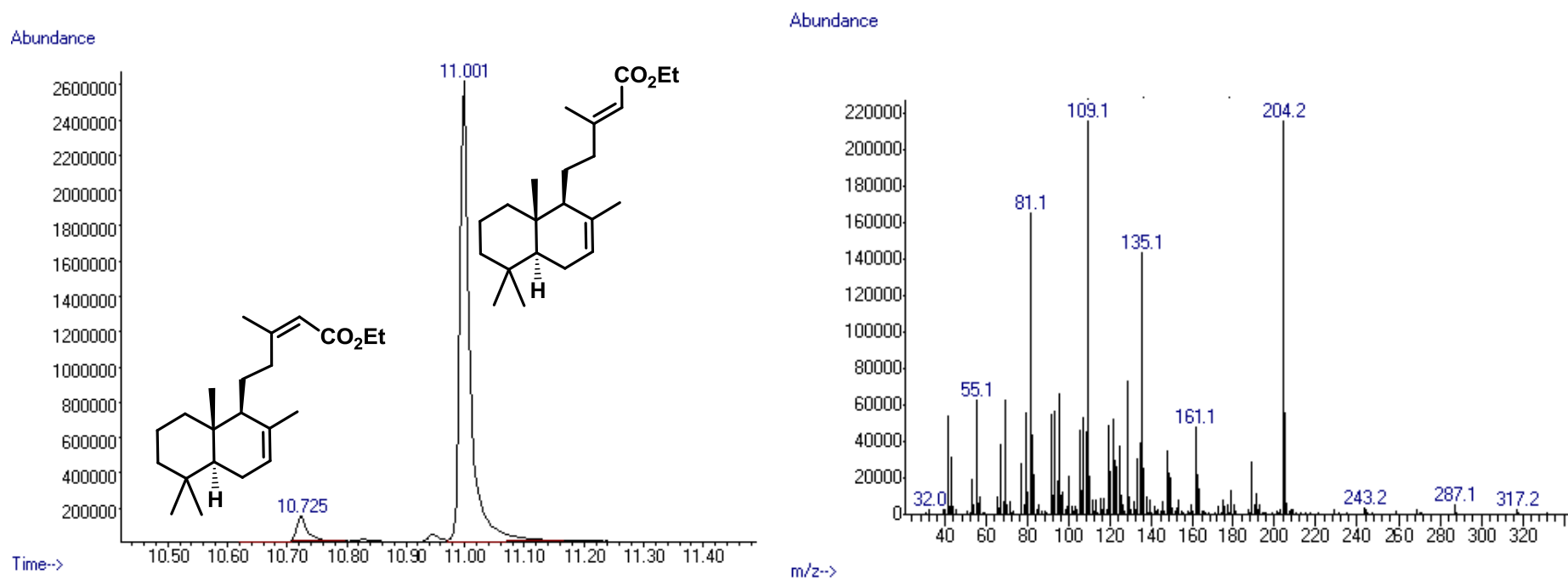


Figure S34. DEPT 135 NMR spectrum (CDCl_3 , 62.9 MHz) of compound **3**.

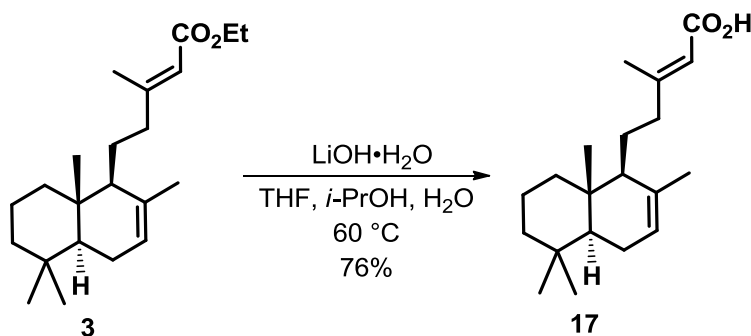


t_R (Z-isomer) = 10.725 min, $[M-CH_3]^+ = 317.2$, area: 5.5%

t_R (E-isomer) = 11.001 min, $[M-CH_3]^+ = 317.2$, area: 94.5%

Figure S35. GC/MS analysis of compound **3** before the chromatographic separation.

(*E*)-3-methyl-5-((1*S*,4*aS*,8*aS*)-2,5,5,8*a*-tetramethyl-1,4,4*a*,5,6,7,8,8*a*-octahydronaphthalen-1-yl)pent-2-enoic acid (17**).**



Solid LiOH·H₂O (298 mg, 12.2 mmol, 20 equiv) was added to a solution of ester **3** (203 mg, 0.610 mmol, 1 equiv) in a mixture of THF, *i*-PrOH and H₂O (21 mL, 1:1:1). The reaction was stirred at 60 °C for 20 h, then the volatiles were removed under reduced pressure. To the remaining residue, EtOAc (30 mL) and HCl solution (1 M, 30 mL) were added. The organic phase was separated, washed with brine (20 mL), dried over anhydrous MgSO₄ and concentrated under reduced pressure. The residue was subjected to flash chromatography (SiO₂, hexanes/EtOAc 85:15) to give the carboxylic acid **17** (141 mg, 0.463 mmol) as a white solid in 76% yield.

TLC (SiO₂): R_f = 0.46 (hexanes/EtOAc 75:25);

[α]_D²⁵ = +34 (*c* 1.0, CHCl₃);

IR (ATR, cm⁻¹): 3441 (broad), 2946 (broad), 2924, 2849, 1693, 1639, 1437, 1257, 1173, 867;

¹H NMR (250 MHz, CDCl₃): δ 0.76 (s, 3H), 0.86 (s, 3H), 0.88 (s, 3H), 0.80-1.03 (m, 2H), 1.08-1.73 (m, 7H), 1.70 (s, 3H), 2.19 (d, *J* = 1.1 Hz, 3H), 1.75-2.25 (m, 4H), 2.30-2.46 (m, 1H), 5.41 (br. s, 1H), 5.70 (q, *J* = 0.8 Hz, 1H), 11.46 (br. s, 1H);

¹³C NMR (62.9 MHz, CDCl₃): δ 13.5 (CH₃), 18.7 (CH₂), 19.3 (CH₃), 21.8 (CH₃), 22.1 (CH₃), 23.8 (CH₂), 25.3 (CH₂), 32.9 (C), 33.1 (CH₃), 36.8 (C), 39.2 (CH₂), 42.2 (CH₂), 43.6 (CH₂), 50.1 (CH), 54.4 (CH), 115.1 (CH), 122.8 (CH), 134.6 (C), 163.6 (C), 172.2 (C);

HRMS (ESI +): *m/z* calculated for C₂₀H₃₂O₂Na⁺ [M+Na]⁺ 327.2295, found 327.2286.

Acquisition Time (sec)	3.1654	Comment	LN504	Date	29 Mar 2017 16:50:24		
Date Stamp	29 Mar 2017 16:50:24			File Name	C:\Users\Luiz\Desktop\Luiz\PhD\NMR\17-3-mar\mar29\ftH4\1\PDATA\1\1r		
Frequency (MHz)	250.13	Nucleus	1H	Number of Transients	9	Origin	spect
Owner	root	Points Count	32768	Pulse Sequence	zg30	Receiver Gain	322.50
Solvent	CHLOROFORM-d			Spectrum Offset (Hz)	1544.6561	Spectrum Type	STANDARD
Temperature (degree C)	25.160					SW(cyclical) (Hz)	5175.98
						Sweep Width (Hz)	5175.83

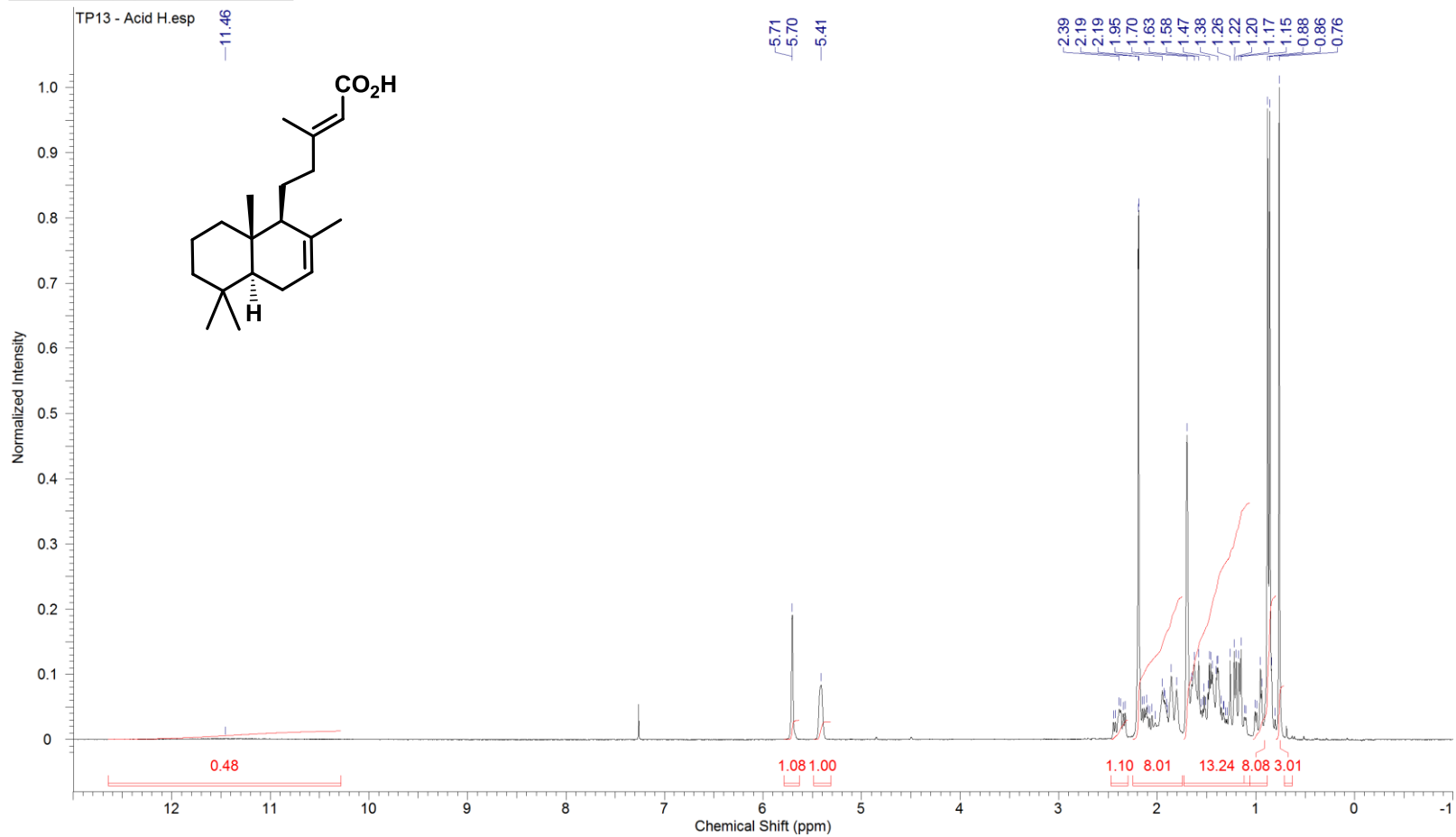


Figure S36. ¹H NMR spectrum (CDCl₃, 250 MHz) of compound **17**.

Acquisition Time (sec)	1.0879	Comment	LN504	Date	29 Mar 2017 16:54:40		
Date Stamp	29 Mar 2017 16:54:40			File Name	C:\Users\Luiz\Desktop\Luiz\PhD\NMR\17-3-mar\mar29\ftH4\2\PDATA\1\1r		
Frequency (MHz)	62.90	Nucleus	¹³ C	Number of Transients	100	Origin	spect
Owner	root	Points Count	32768	Pulse Sequence	zgpg30	Receiver Gain	912.30
Solvent	CHLOROFORM-d			Spectrum Offset (Hz)	6289.0518	Spectrum Type	STANDARD
Temperature (degree C)	25.160					SW(cyclical) (Hz)	15060.24
						Sweep Width (Hz)	15059.78

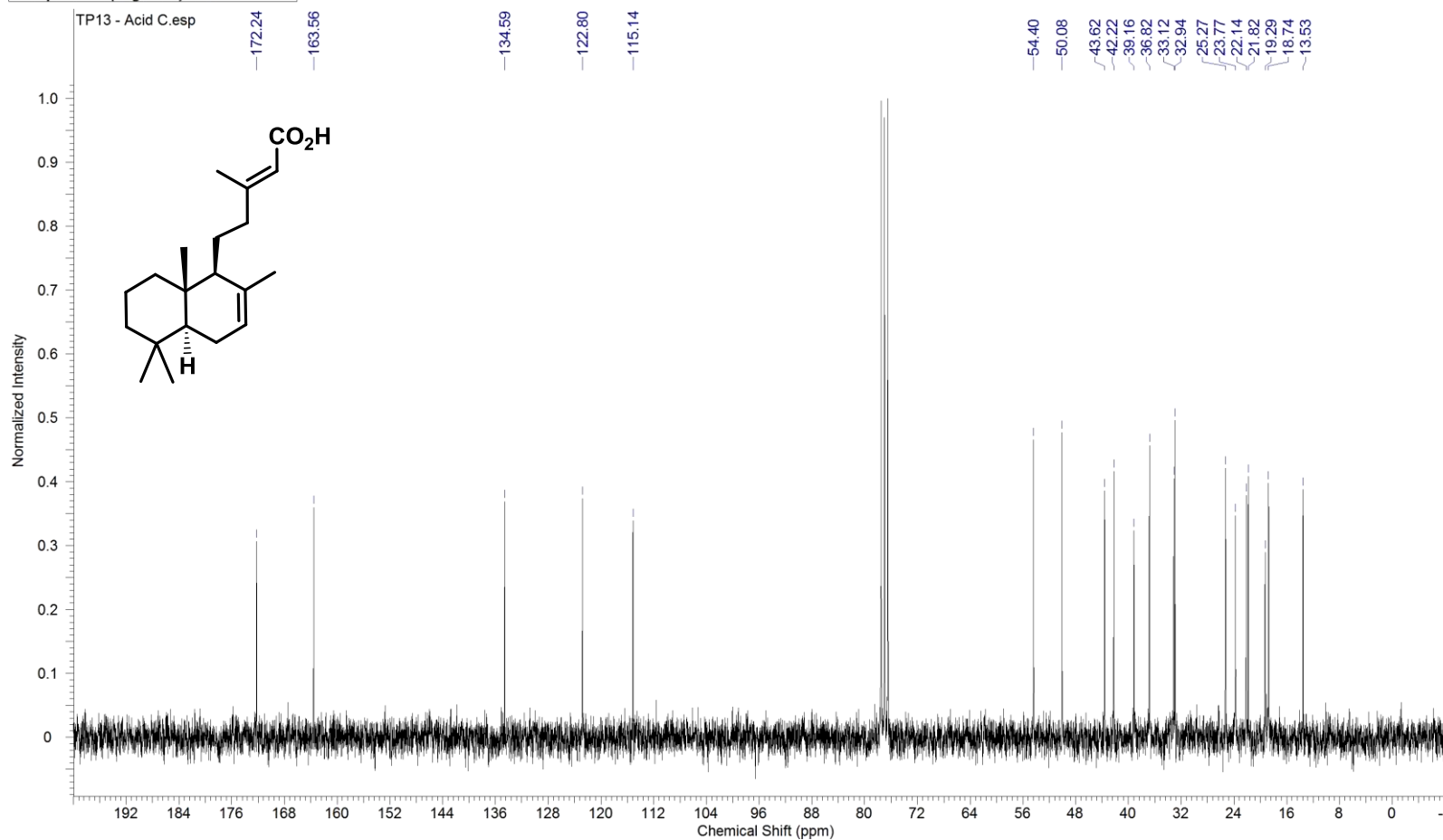


Figure S37. ¹³C NMR spectrum (CDCl₃, 62.9 MHz) of compound **17**.

Acquisition Time (sec)	0.5439	Comment	LN386	Date	19 Dec 2016 12:30:24		
Date Stamp	19 Dec 2016 12:30:24			File Name	C:\Users\Luiz\Desktop\Luiz\PhD\NMR\16-12-dez\dez19\ftH1\2\PDATA\1\1r		
Frequency (MHz)	62.90	Nucleus	13C	Number of Transients	137	Origin	spect
Owner	root	Points Count	32768	Pulse Sequence	dept135	Receiver Gain	16384.00
Solvent	CHLOROFORM-d			Spectrum Offset (Hz)	6289.0518	Spectrum Type	DEPT135
Temperature (degree C)	22.460					SW(cyclical) (Hz)	15060.24
						Sweep Width (Hz)	15059.78

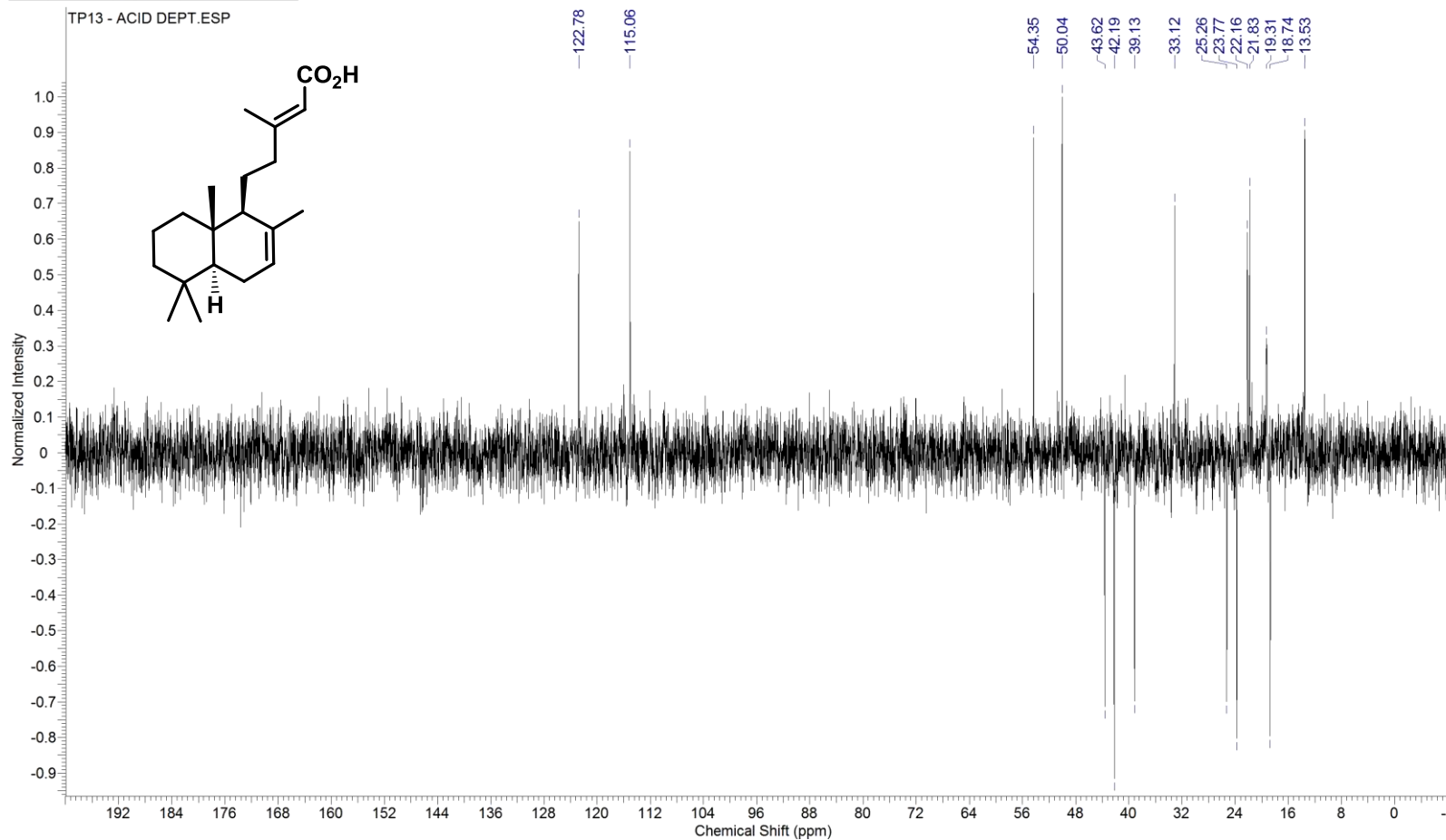
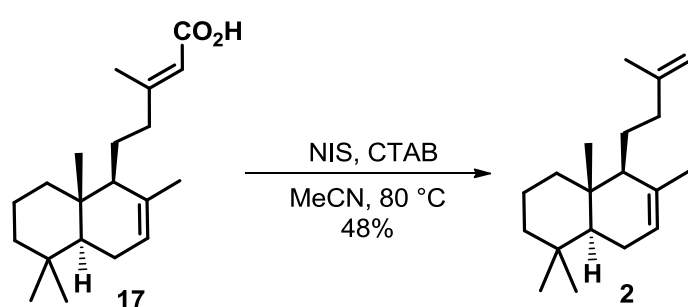


Figure S38. DEPT 135 NMR spectrum (CDCl₃, 62.9 MHz) of compound **17**.

(4a*S*,5*S*,8a*S*)-5-((*E*)-4-iodo-3-methylbut-3-en-1-yl)-1,1,4a,6-tetramethyl-1,2,3,4,4a,5,8,8a-octahydronaphthalene (**2**).



A flask was charged with carboxylic acid **17** (93.2 mg, 0.306 mmol, 1 equiv) and CTAB (113 mg, 0.306 mmol, 1 equiv), the flask was purged with nitrogen, and dry acetonitrile (7 mL) was added followed by NIS (138 mg, 0.612 mmol, 2 equiv). The reaction mixture was heated at 80 °C for 1 h and, after cooling to room temperature, solvent was partially removed under reduced pressure to ~1 mL of crude reaction mixture. This residue was subjected to flash chromatography (SiO₂, hexanes) to give the iodide **2** (56.5 mg, 0.146 mmol) as a colorless oil in 48% yield.

TLC (SiO₂): R_f = 0.90 (hexanes);

[α]_D²⁵ = +35 (*c* 1.0, CHCl₃), [α]_{D,lit}²⁰ = +33 (*c* 0.8, CHCl₃);⁵

¹H NMR (250 MHz, CDCl₃): δ 0.75 (s, 3H), 0.86 (s, 3H), 0.88 (s, 3H), 0.80-1.02 (m, 2H) 1.07-1.64 (m, 10H), 1.68 (s, 3H), 1.85 (d, *J* = 0.8 Hz, 3H), 1.75-2.06 (m, 3H), 2.16 (ddd, *J* = 14.1, 10.3, 6.3 Hz, 1H), 2.40 (ddd, *J* = 14.4, 11.4, 4.6 Hz, 1H), 5.40 (br. s, 1H), 5.90 (q, *J* = 0.8 Hz, 1H);

¹³C NMR (62.9 MHz, CDCl₃): δ 13.6 (CH₃), 18.8 (CH₂), 21.8 (CH₃), 22.2 (CH₃), 23.8 (CH₂), 24.0 (CH₃), 25.6 (CH₃), 32.9 (C), 33.1 (CH₃), 36.8 (C), 39.2 (CH₂), 42.0 (CH₂), 42.3 (CH₂), 50.1 (CH), 54.3 (CH), 74.9 (CH), 122.6 (CH), 134.8 (C), 148.5 (C).

⁵ Guo, Y.-a.; Zhao, M.; Xu, Z.; Ye, T. *Chem. Eur. J.* **2017**, *23*, 3572-3576.

Acquisition Time (sec)	3.1654	Comment	LN513	Date	01 Apr 2017 17:11:44		
Date Stamp	01 Apr 2017 17:11:44			File Name	C:\Users\Luiz\Desktop\Luiz\PhD\NMR\17-4-abr\abr01\ftH2\1\PDATA\1\1r		
Frequency (MHz)	250.13	Nucleus	1H	Number of Transients	17	Origin	spect
Owner	root	Points Count	32768	Pulse Sequence	zg30	Receiver Gain	287.40
Solvent	CHLOROFORM-d			Spectrum Offset (Hz)	1544.6561	Spectrum Type	STANDARD
Temperature (degree C)	25.160					SW(cyclical) (Hz)	5175.98
						Sweep Width (Hz)	5175.83

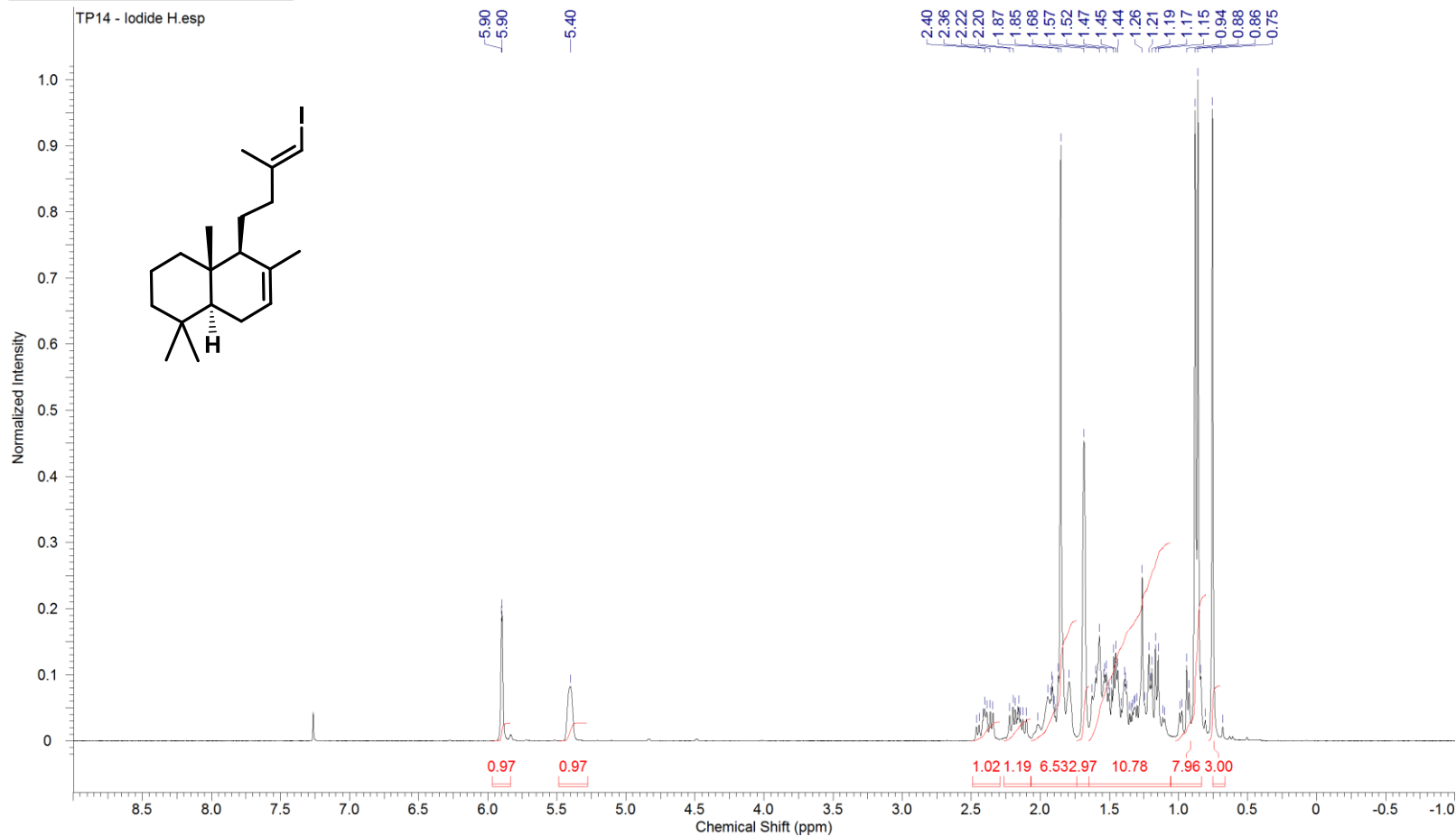


Figure S39. ^1H NMR spectrum (CDCl_3 , 250 MHz) of compound **2**.

Acquisition Time (sec)	1.0879	Comment	LN513	Date	01 Apr 2017 17:20:16		
Date Stamp	01 Apr 2017 17:20:16			File Name	C:\Users\Luiz\Desktop\Luiz\PhD\NMR\17-4-abr\abr01\ftH2\3\IPDATA\1\1r		
Frequency (MHz)	62.90	Nucleus	13C	Number of Transients	64	Origin	spect
Owner	root	Points Count	32768	Pulse Sequence	zgpg30	Receiver Gain	1824.60
Solvent	CHLOROFORM-d			Spectrum Offset (Hz)	6289.0518	Spectrum Type	STANDARD
Temperature (degree C)	25.160					SW(cyclical) (Hz)	15060.24
						Sweep Width (Hz)	15059.78

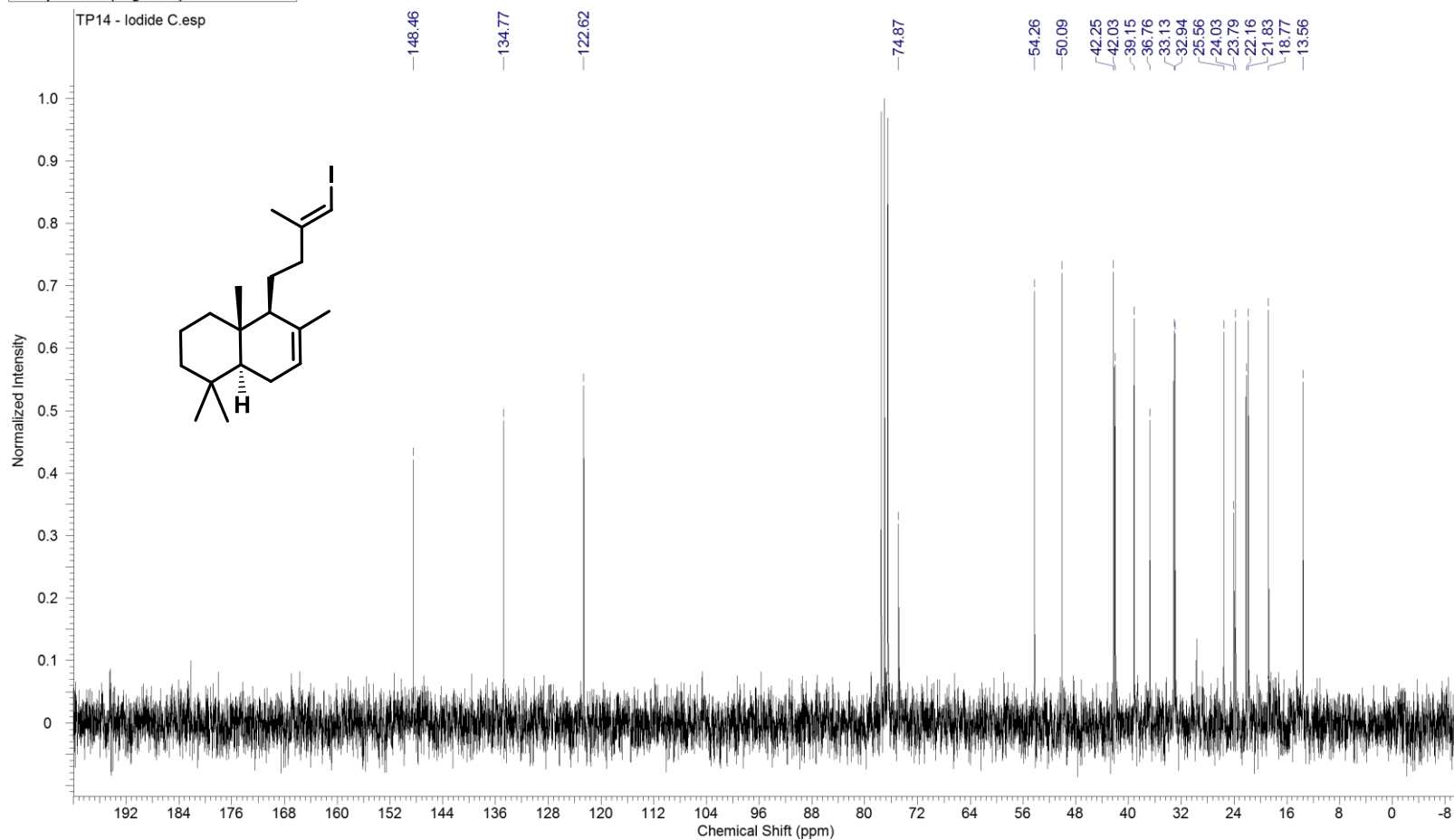


Figure S40. ^{13}C NMR spectrum (CDCl_3 , 62.9 MHz) of compound **2**.

Acquisition Time (sec)	0.5439	Comment	LN513	Date	01 Apr 2017 17:13:52		
Date Stamp	01 Apr 2017 17:13:52			File Name	C:\Users\Luiz\Desktop\Luiz\PhD\NMR\17-4-abr\abr01\ftH2\2\PDATA\1\1r		
Frequency (MHz)	62.90	Nucleus	13C	Number of Transients	100	Origin	spect
Owner	root	Points Count	32768	Pulse Sequence	dept135	Receiver Gain	1625.50
Solvent	CHLOROFORM-d			Spectrum Offset (Hz)	6289.0518	Spectrum Type	DEPT135
Temperature (degree C)	25.160					SW(cyclical) (Hz)	15060.24
						Sweep Width (Hz)	15059.78

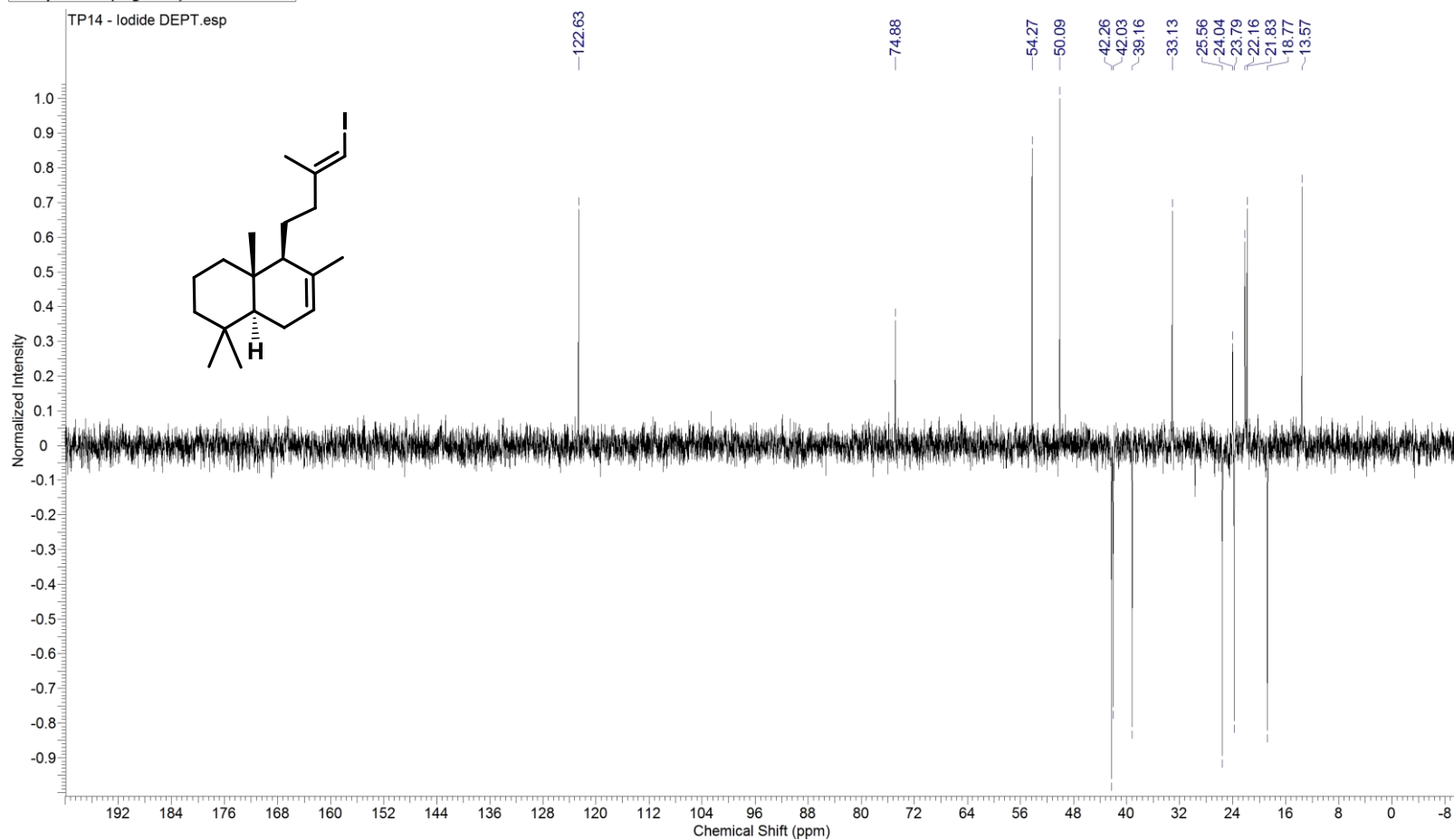
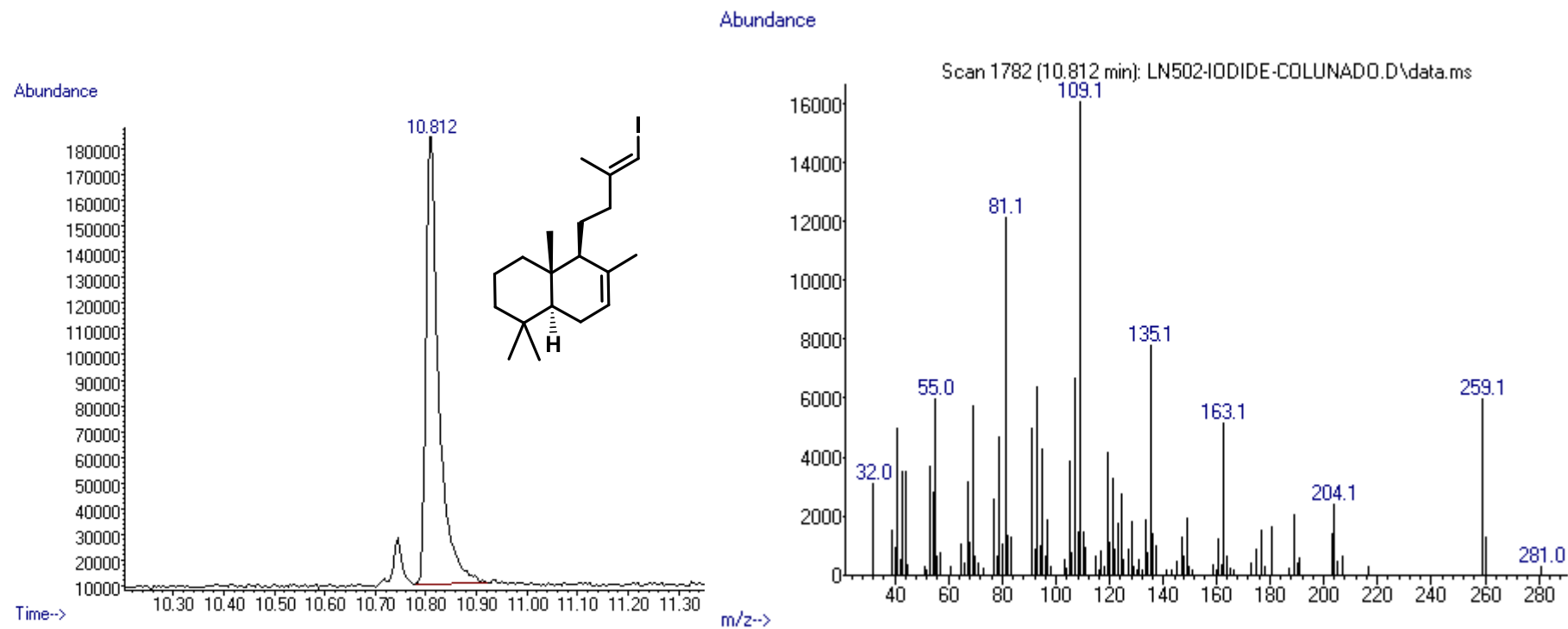


Figure S41. DEPT 135 NMR spectrum (CDCl_3 , 62.9 MHz) of compound **2**.



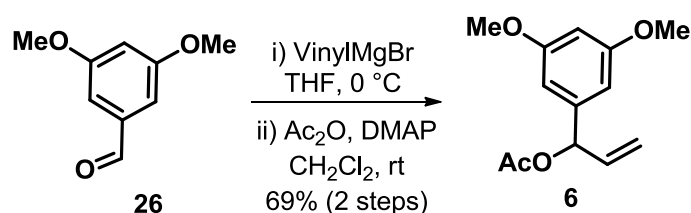
$t_R = 10.812 \text{ min}$, $[M-I]^+ = 259.1$

Figure S42. GC/MS analysis of compound **2**.

Table 1. Comparison between ^{13}C NMR spectra of compound **2** and reported by Xu and Ye⁵

Pastre (this work)	Xu and Ye⁵	$\Delta\delta$
13.6	13.6	0.0
18.8	18.8	0.0
21.8	21.9	-0.1
22.2	22.2	0.0
23.8	23.8	0.0
24.0	24.1	0.0
25.6	25.6	0.0
32.9	33.0	-0.1
33.1	33.1	0.0
36.8	36.8	0.0
39.2	39.2	0.0
42.0	42.0	0.0
42.3	42.3	0.0
50.1	50.1	0.0
54.3	54.2	+0.1
74.9	74.9	0.0
122.6	122.6	0.0
134.8	134.8	0.0
148.5	148.5	0.0

1-(3,5-dimethoxyphenyl)allyl acetate (6).



VinylMgBr (1 M in THF, 7.2 mL, 7.2 mmol, 2 equiv) was added dropwise to a solution of aldehyde **26** (610 mg, 3.6 mmol, 1 equiv) in THF (30 mL) at 0 °C. The reaction was stirred for 30 min at the same temperature and was then quenched by addition of saturated aqueous solution of NH₄Cl (50 mL). The mixture was extracted with EtOAc (2 x 50 mL), the organic phases were combined, dried over anhydrous MgSO₄ and concentrated under reduced pressure. The residue was subjected to flash chromatography (SiO₂, hexanes/EtOAc 90:10 to 60:40) to give the allylic alcohol intermediate along with minor impurities (550 mg, 2.83 mmol), this material was used in the next reaction.

The allylic alcohol was diluted in dry CH₂Cl₂ (20 mL) and to this mixture were added Et₃N (0.79 mL, 5.6 mmol, 2 equiv), DMAP (17 mg, 0.14 mmol, 5 mol %) and Ac₂O (0.40 mL, 4.2 mmol, 1.5 equiv) at room temperature, and the reaction mixture was stirred for 1 h. The reaction was quenched by the addition of brine (20 mL) and was extracted with CH₂Cl₂ (2 x 20 mL). The organic phases were combined, dried over anhydrous Na₂SO₄ and concentrated under reduced pressure. The residue was subjected to flash chromatography (SiO₂, hexanes/EtOAc 90:10) to give the acetate **6** (587 mg, 2.48 mmol) as a colorless oil in 69% overall yield (for 2 steps).

TLC (SiO₂): R_f = 0.39 (hexanes/EtOAc 90:10);

IR (ATR, cm⁻¹): 2955, 2941, 2909, 2840, 1737, 1598, 1460, 1372, 1229, 1206, 1067, 933, 750;

¹H NMR (250 MHz, CDCl₃): δ 2.06 (s, 3H), 3.71 (s, 6H), 5.18 (dt, *J* = 10.3, 1.1 Hz, 1H), 5.27 (dt, *J* = 17.2, 1.1 Hz, 1H), 5.95 (ddd, *J* = 17.0, 10.4, 6.0 Hz, 1H), 6.17 (d, *J* = 6.0 Hz, 1H), 6.37 (t, *J* = 2.3 Hz, 1H), 6.50 (d, *J* = 2.2 Hz, 2H);

¹³C NMR (62.9 MHz, CDCl₃): δ 20.9 (CH₃), 55.1 (2CH₃), 76.0 (CH), 99.8 (CH), 105.0 (2CH), 116.7 (CH₂), 136.2 (CH), 141.3 (C), 160.9 (2C), 169.6 (C);

HRMS (ESI +): *m/z* calculated for C₁₃H₁₆O₄Na⁺ [M+Na]⁺ 259.0941, found 259.0949.

Acquisition Time (sec)	3.1654	Comment	LN482	Date	06 Mar 2017 11:43:12				
Date Stamp	06 Mar 2017 11:43:12			File Name	C:\Users\Luiz\Desktop\Luiz\PhD\NMR\17-3-mar\mar07\ftH1\1\PDATA\1\1r				
Frequency (MHz)	250.13	Nucleus	1H	Number of Transients	9	Origin	spect	Original Points Count	16384
Owner	root	Points Count	32768	Pulse Sequence	zg30	Receiver Gain	50.80	SW(cyclical) (Hz)	5175.98
Solvent	CHLOROFORM-d			Spectrum Offset (Hz)	1544.6561	Spectrum Type	STANDARD	Sweep Width (Hz)	5175.83
Temperature (degree C)	25.160								

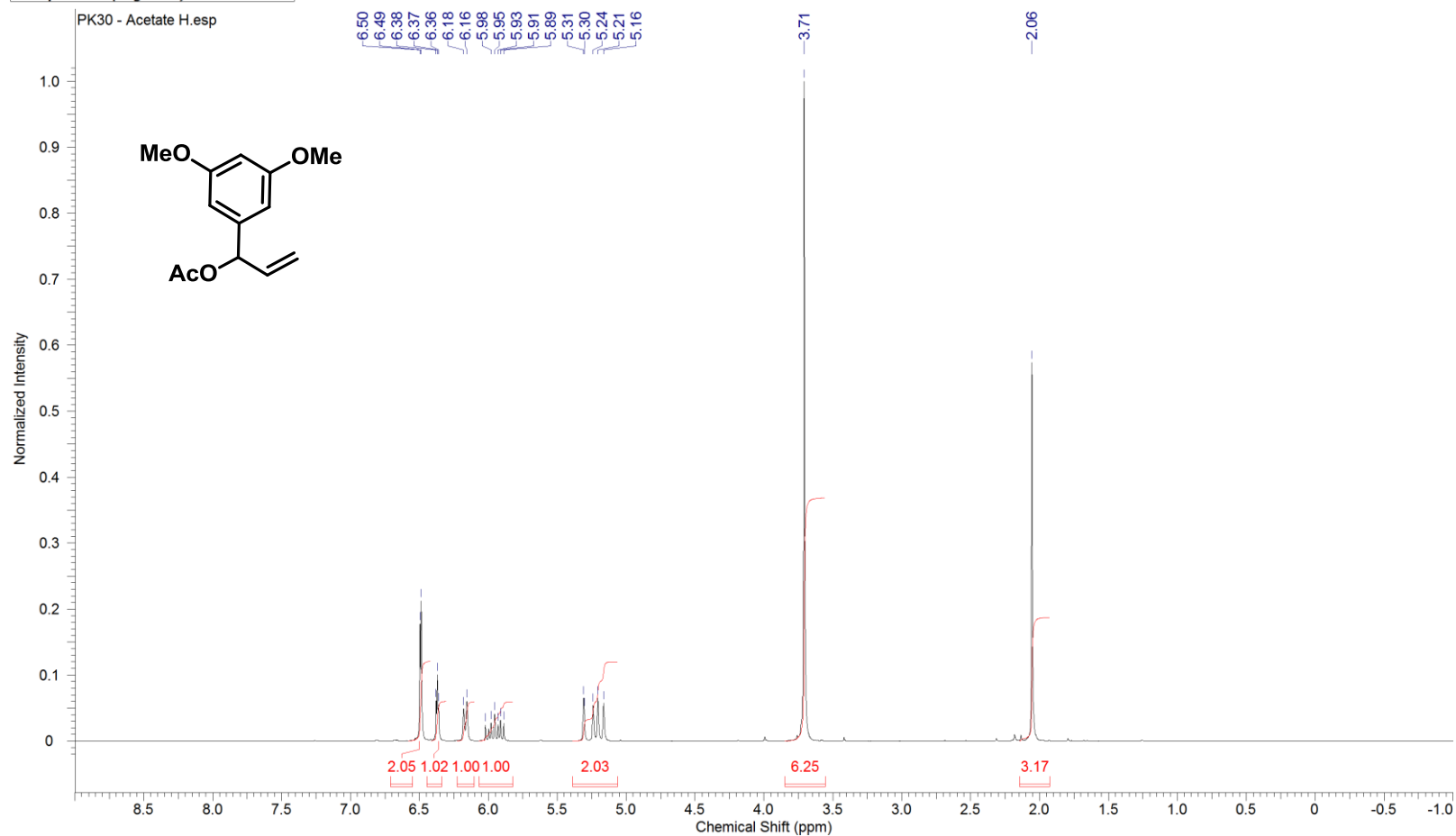


Figure S43. ^1H NMR spectrum (CDCl_3 , 250 MHz) of compound **6**.

Acquisition Time (sec)	1.0879	Comment	LN482	Date	06 Mar 2017 11:47:28		
Date Stamp	06 Mar 2017 11:47:28			File Name	C:\Users\Luiz\Desktop\Luiz\PhD\NMR\17-3-mar\mar07\ftH1\2\PDATA\11r		
Frequency (MHz)	62.90	Nucleus	13C	Number of Transients	13	Origin	spect
Owner	root	Points Count	32768	Pulse Sequence	zgpg30	Receiver Gain	512.00
Solvent	CHLOROFORM-d			Spectrum Offset (Hz)	6289.0518	Spectrum Type	STANDARD
Temperature (degree C)	25.160					SW(cyclical) (Hz)	15060.24
						Sweep Width (Hz)	15059.78

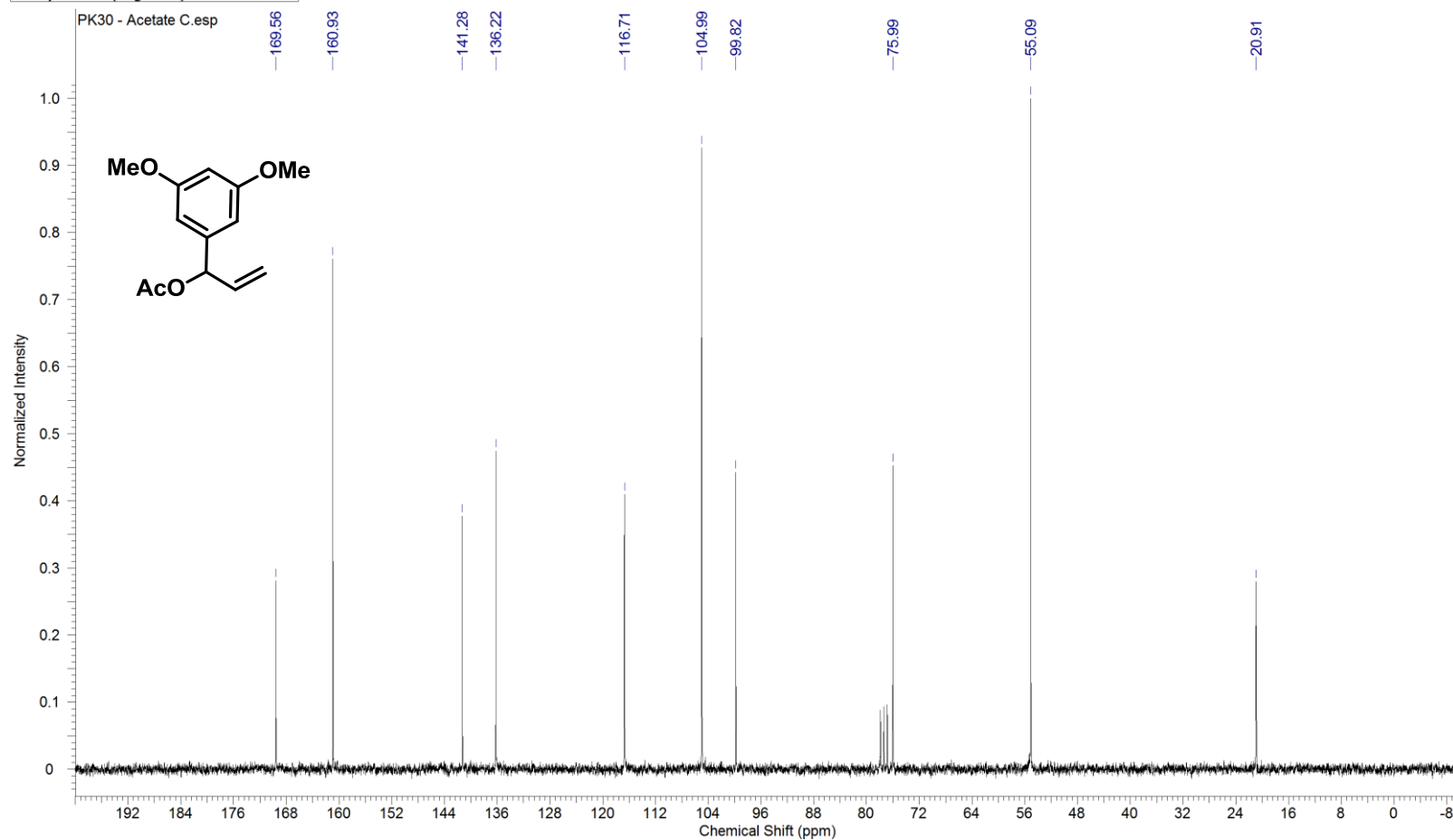


Figure S44. ¹³C NMR spectrum (CDCl₃, 62.9 MHz) of compound **6**.

Acquisition Time (sec)	0.5439	Comment	LN482	Date	06 Mar 2017 11:47:28		
Date Stamp	06 Mar 2017 11:47:28			File Name	C:\Users\Luiz\Desktop\Luiz\PhD\NMR\17-3-mar\mar07\ftH1\3\PDATA\1\1r		
Frequency (MHz)	62.90	Nucleus	13C	Number of Transients	11	Origin	spect
Owner	root	Points Count	32768	Pulse Sequence	dept135	Receiver Gain	1625.50
Solvent	CHLOROFORM-d			Spectrum Offset (Hz)	6289.0518	Spectrum Type	DEPT135
Temperature (degree C)	25.160					SW(cyclical) (Hz)	15060.24
						Sweep Width (Hz)	15059.78

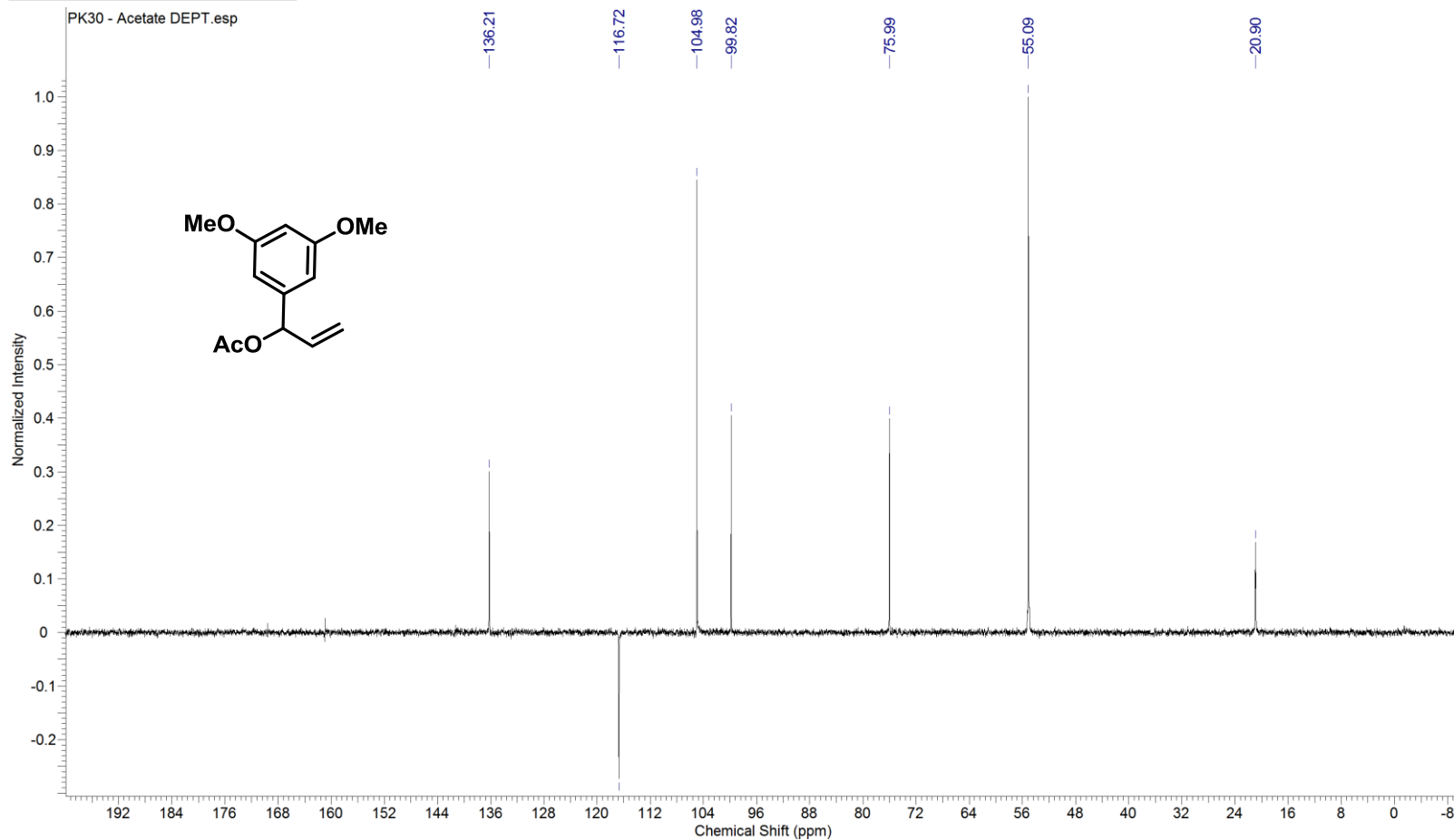
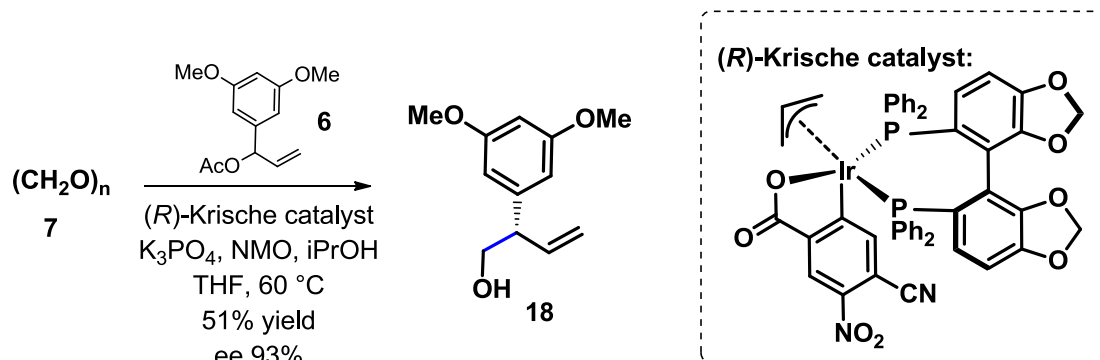


Figure S45. DEPT 135 NMR spectrum (CDCl_3 , 62.9 MHz) of compound **6**.

(S)-2-(3,5-dimethoxyphenyl)but-3-en-1-ol (18).



A pressure tube was charged with paraformaldehyde (**7**, 12.6 mg, 0.42 mmol of CH_2O units, 1 equiv), K_3PO_4 (45.5 mg, 0.21 mmol, 0.5 equiv), (R)-Krische catalyst⁶ (21.7 mg, 0.021 mmol, 5 mol %), NMO (39.4 mg, 0.34 mmol, 0.8 equiv) and allylic acetate **6** (149 mg, 0.63 mmol, 1.5 equiv). The tube was purged with argon, and dry THF (1.0 mL) was added followed by dry isopropyl alcohol (64.3 μL , 0.84 mmol, 2 equiv), the pressure tube was sealed and heated at 60 °C for 36 h. After this period, the mixture was cooled to room temperature, the volatiles were removed under reduced pressure, and the residue was subjected to flash chromatography (SiO_2 , hexanes/EtOAc 90:10 to 75:25) to give alcohol **18** (45 mg, 0.216 mmol) as a colorless oil in 51% yield.

TLC (SiO_2): R_f = 0.23 (hexanes/EtOAc 75:25);

ee = 93% (determined by ^{19}F NMR of Mosher ester derivatives);

$[\alpha]_D^{25}$ = +28 (c 1.0, CHCl_3);

IR (ATR, cm^{-1}): 3393 (broad), 3003, 2395, 2831, 1602, 1466, 1434, 1208, 1153, 1067, 917, 840;

^1H NMR (250 MHz, CDCl_3): δ 1.59 (br. s, 1H), 3.46 (q, J = 7.1 Hz, 1H), 3.78 (s, 6H), 3.76-3.87 (m, 2H), 5.14-5.27 (m, 2H), 5.89-6.07 (m, 1H), 6.36 (t, J = 2.1 Hz, 1H), 6.39 (d, J = 2.2 Hz, 2H);

^{13}C NMR (62.9 MHz, CDCl_3): δ 52.7 (CH), 55.3 (2 CH_3), 65.9 (CH_2), 98.6 (CH), 106.1 (2CH), 117.1 (CH_2), 137.9 (CH), 143.0 (C), 161.0 (2C);

HRMS (ESI +): m/z calculated for $\text{C}_{12}\text{H}_{16}\text{O}_3\text{Na}^+$ $[\text{M}+\text{Na}]^+$ 231.0992, found 231.0994.

⁶ The catalyst was synthesized, with similar results, according to the procedure described in: Garza, V. J.; Krische, M. J. *J. Am. Chem. Soc.* **2016**, *138*, 3655-3658.

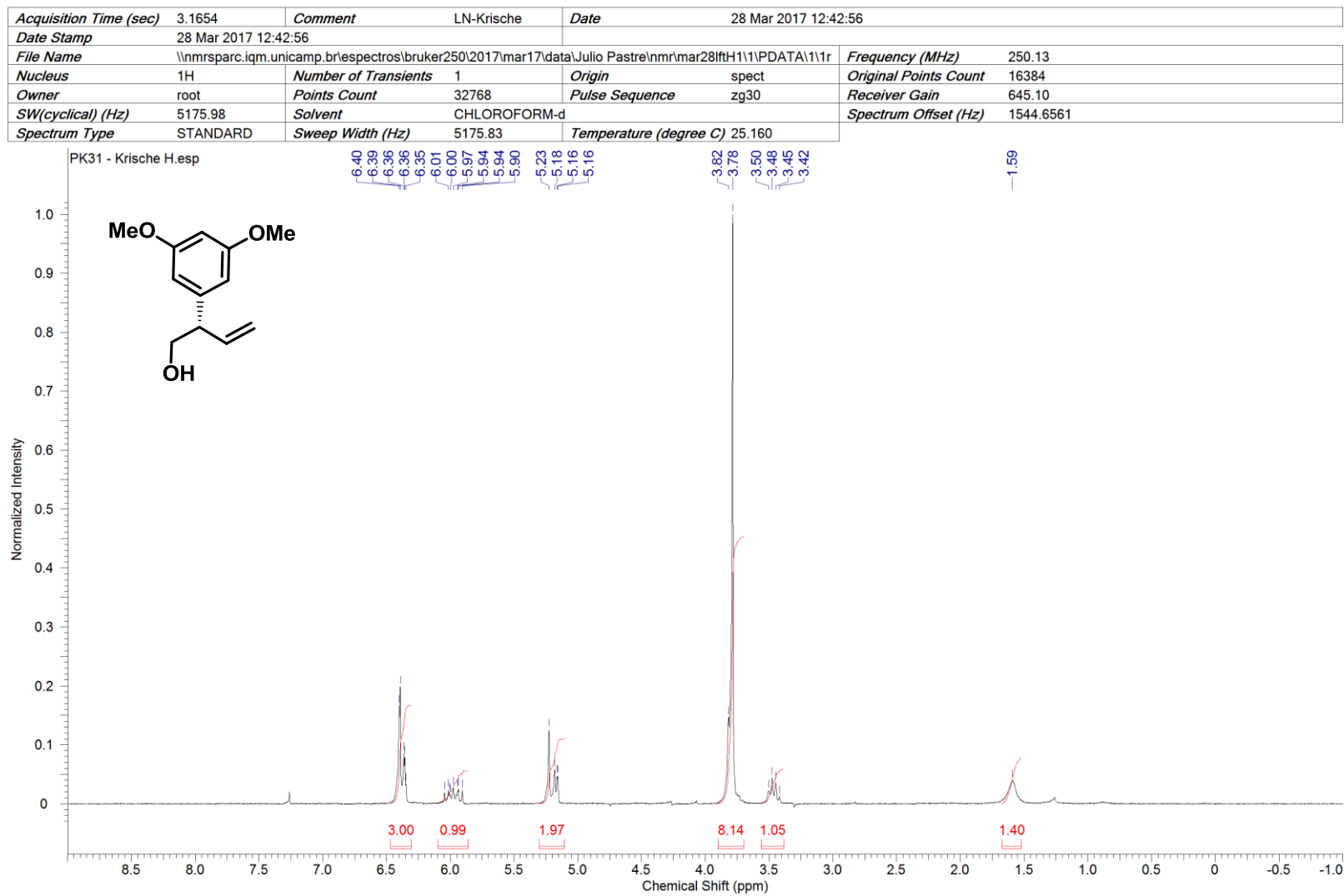


Figure S46. ¹H NMR spectrum (CDCl₃, 250 MHz) of compound **18**.

Acquisition Time (sec)	1.0879	Comment	LN-Krische	Date	28 Mar 2017 12:42:56			
Date Stamp	28 Mar 2017 12:42:56							
File Name	\\nmrparc.lqm.unicamp.br\spectros\bruker250\2017\mar17\data\Julio Pastre\nmr\mar28\ftH1\2\PDATA\1\1r				Frequency (MHz)	62.90		
Nucleus	¹³ C	Number of Transients	100	Origin	spect	Original Points Count	16384	
Owner	root	Points Count	32768	Pulse Sequence	zgpg30	Receiver Gain	724.10	
SW(cyclical) (Hz)	15060.24	Solvent	CHLOROFORM-d				Spectrum Offset (Hz)	6289.0518
Spectrum Type	STANDARD	Sweep Width (Hz)	15059.78	Temperature (degree C)	25.160			

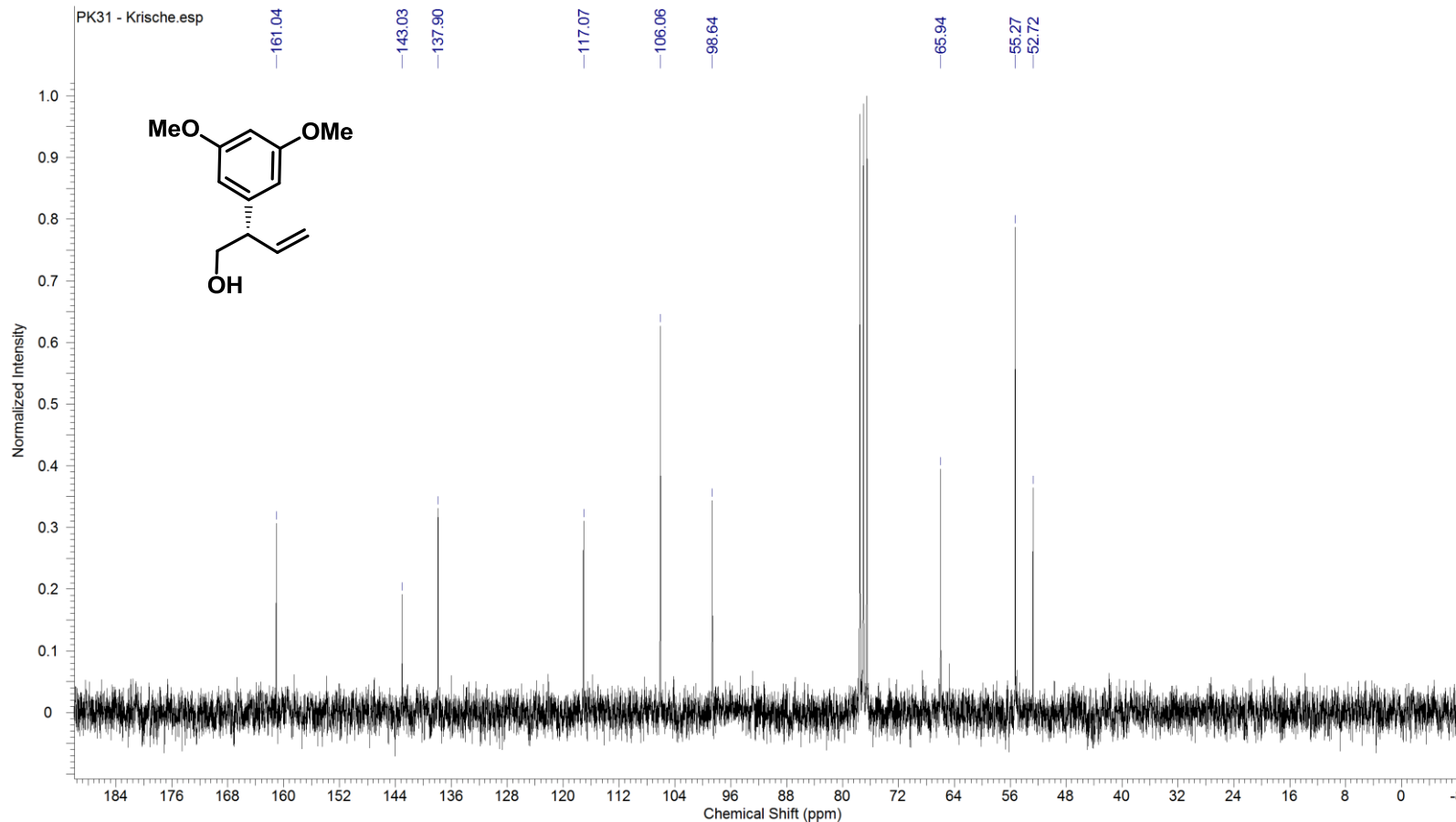


Figure S47. ¹³C NMR spectrum (CDCl₃, 62.9 MHz) of compound **18**.

Acquisition Time (sec)	0.5439	Comment	LN-Krische	Date	28 Mar 2017 12:49:20		
Date Stamp	28 Mar 2017 12:49:20						
File Name	\\nmrparc.lqm.unicamp.br\spectros\bruker250\2017\mar17\data\Julio Pastre\nmr\mar28\ftH1\3\PDATA\1\1r				Frequency (MHz)	62.90	
Nucleus	¹³ C	Number of Transients	64	Origin	spect	Original Points Count	8192
Owner	root	Points Count	32768	Pulse Sequence	dept135	Receiver Gain	1290.20
SW(cyclical) (Hz)	15060.24	Solvent	CHLOROFORM-d			Spectrum Offset (Hz)	6289.0518
Spectrum Type	DEPT135	Sweep Width (Hz)	15059.78	Temperature (degree C)	25.160		

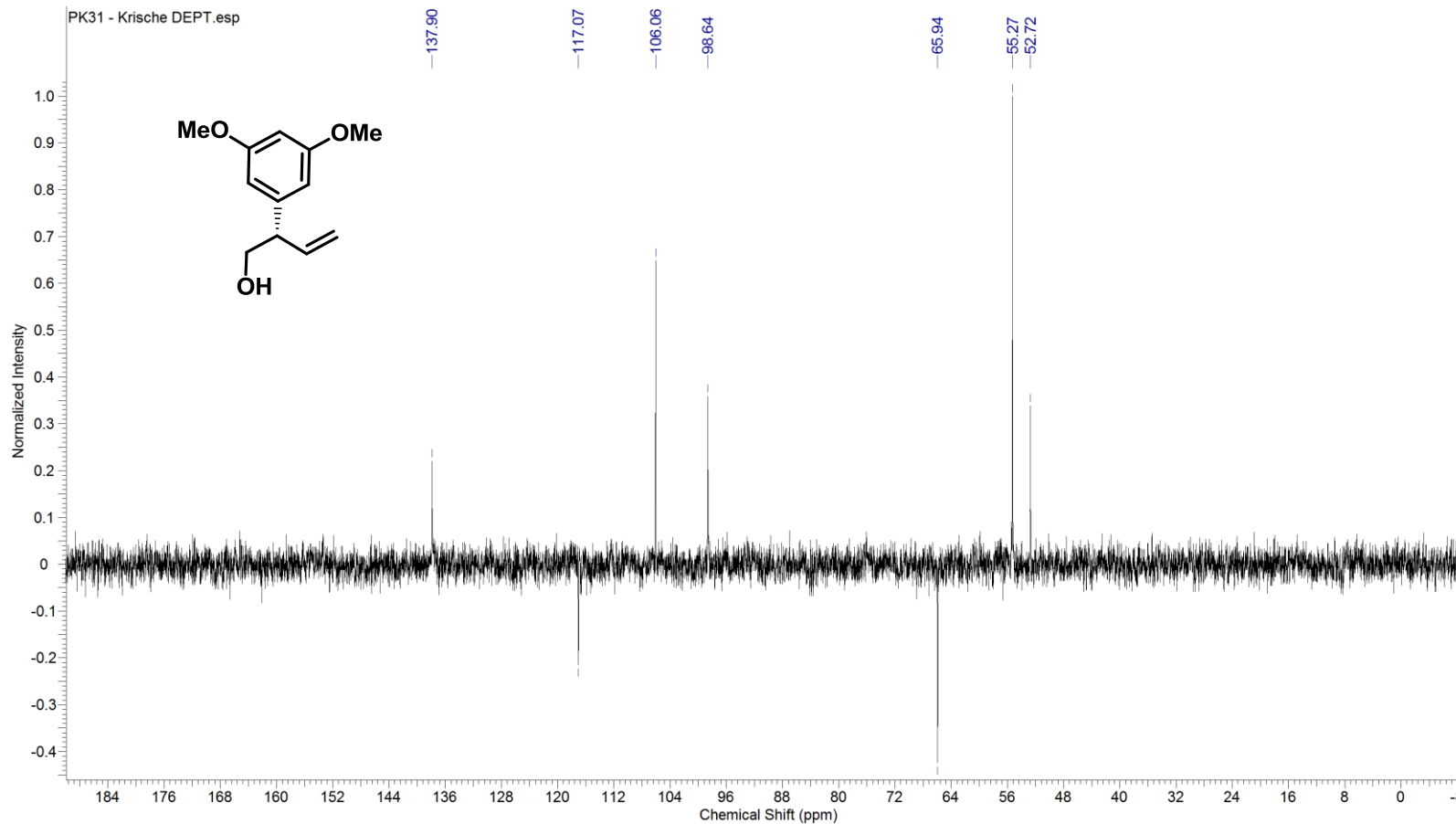


Figure S48. DEPT 135 NMR spectrum (CDCl_3 , 62.9 MHz) of compound **18**.

Acquisition Time (sec)	1.1600	Comment	Mosher-chr	Date	31 Mar 2017 16:26:56
Date Stamp	31 Mar 2017 16:26:56			File Name	C:\Users\Luiz\Desktop\Luiz\PhD\NMR\17-3-mar\mar31\ftH2\2\pdata\1\1r
Frequency (MHz)	235.36	Nucleus	19F	Number of Transients	33
Original Points Count	65536	Owner	psm	Points Count	65536
Receiver Gain	645.10	SW(cyclical) (Hz)	56497.18	Solvent	CHLOROFORM-d
Spectrum Offset (Hz)	-23536.0215	Spectrum Type	STANDARD	Sweep Width (Hz)	56496.31
				Temperature (degree C)	25.160

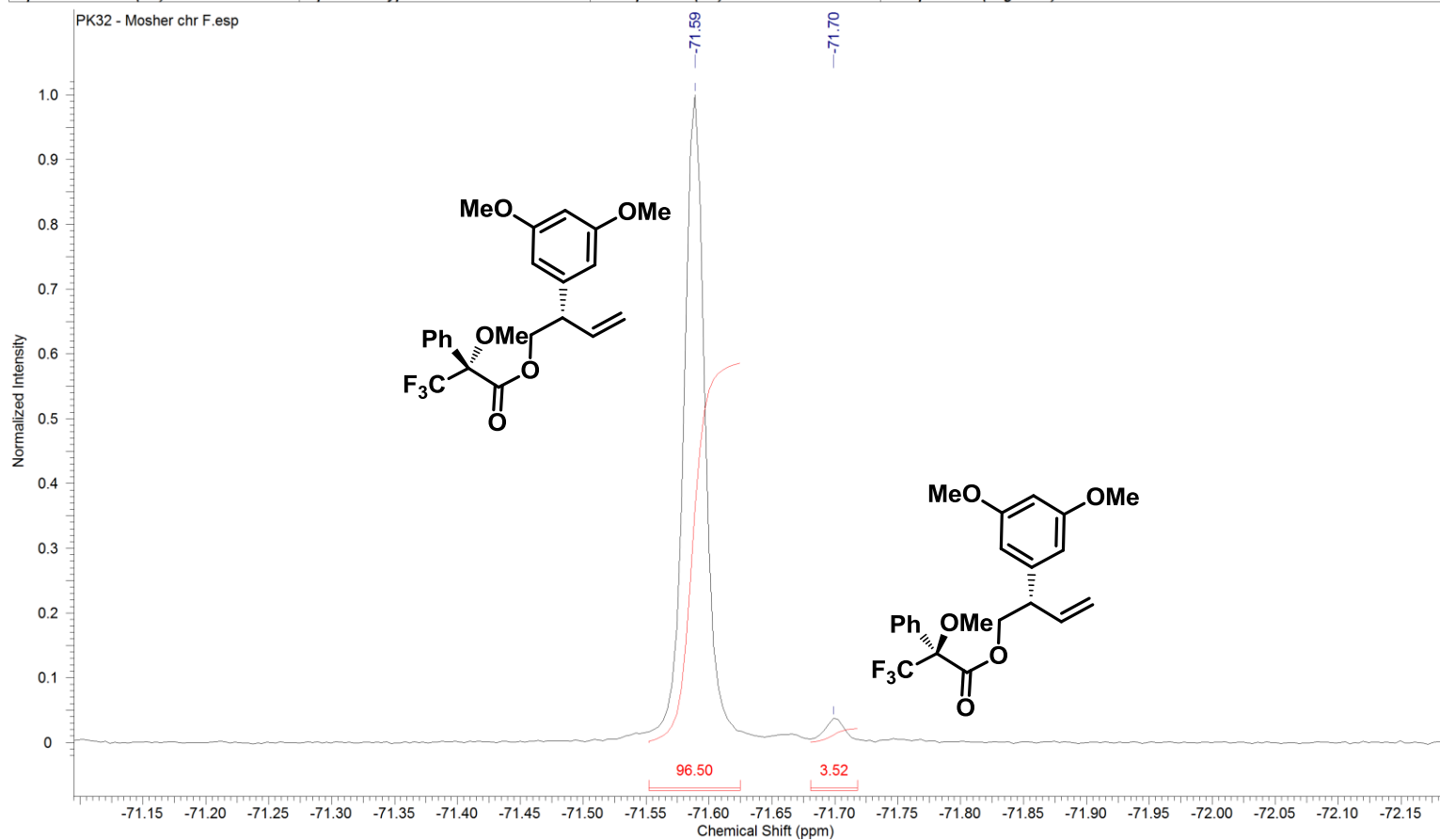
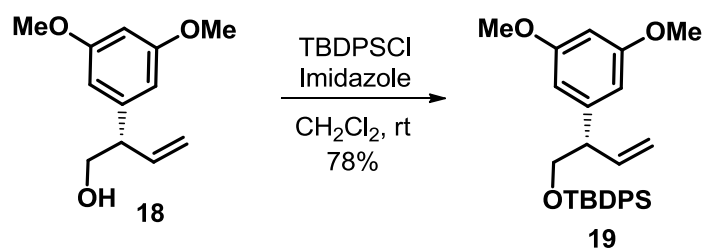


Figure S50. ^{19}F NMR spectrum (CDCl_3 , 235 MHz) of Mosher's esters prepared with (S)-Mosher acyl chloride.

(S)-tert-butyl((2-(3,5-dimethoxyphenyl)but-3-en-1-yl)oxy)diphenylsilane (19).



Imidazole (27 mg, 0.40 mmol, 2 equiv) and TBDPSCI (80 μ L, 0.30 mmol, 1.5 equiv) were added to a solution of alcohol **18** (41.7 mg, 0.20 mmol, 1 equiv) in CH_2Cl_2 (10 mL) at room temperature. After stirring the reaction for 18 h, H_2O (15 mL) was added, and the mixture was extracted with CH_2Cl_2 (20 mL). The combined organic phase was dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The residue was purified by flash chromatography (SiO_2 , hexanes/EtOAc 90:10) to give the silyl ether **19** (70 mg, 0.16 mmol) as a colorless oil in 78% yield.

TLC (SiO_2): R_f = 0.40 (hexanes/EtOAc 90:10);

$[\alpha]_D^{25}$ = +10 (c 1.0, CHCl_3);

IR (ATR, cm^{-1}): 3073, 2955, 2933, 2859, 1598, 1463, 1430, 1206, 1156, 1113, 1070, 1000, 828, 705, 616;

^1H NMR (250 MHz, CDCl_3): δ 1.07 (s, 9H), 3.50 (q, J = 7.0 Hz, 1H), 3.78 (s, 6H), 3.84–4.00 (m, 2H), 5.13–5.24 (m, 2H), 6.10 (ddd, J = 16.4, 11.2, 7.4 Hz, 1H), 6.39 (s, 3H), 7.33–7.50 (m, 6H), 7.58–7.69 (m, 4H);

^{13}C NMR (62.9 MHz, CDCl_3): δ 19.3 (C), 29.9 (3 CH_3), 52.5 (CH), 55.2 (2 CH_3), 67.6 (CH_2), 98.6 (CH), 106.4 (2CH), 116.2 (CH_2), 127.6 (4CH), 129.6 (2CH), 133.7 (C), 133.8 (C), 135.66 (2CH), 135.70 (2CH), 138.6 (CH), 144.2 (C), 160.7 (2C);

HRMS (ESI +): m/z calculated for $\text{C}_{28}\text{H}_{34}\text{O}_3\text{SiNa}^+$ $[\text{M}+\text{Na}]^+$ 469.2169, found 469.2158.

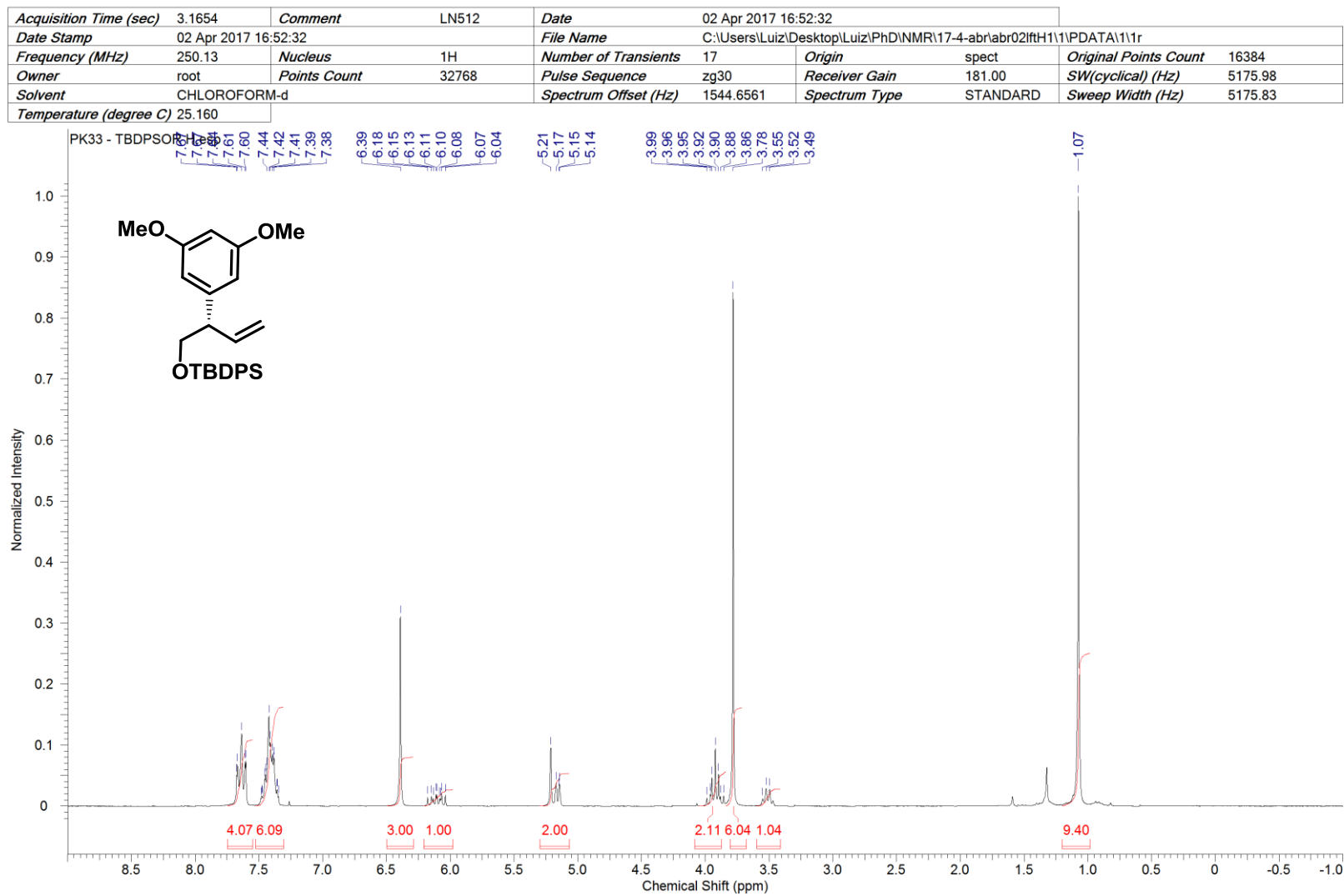


Figure S51. ^1H NMR spectrum (CDCl_3 , 250 MHz) of compound **19**.

Acquisition Time (sec)	1.0879	Comment	LN512	Date	02 Apr 2017 16:54:40		
Date Stamp	02 Apr 2017 16:54:40			File Name	C:\Users\Luiz\Desktop\Luiz\PhD\NMR\17-4-abr\abr02\ftH1\2\PDATA\1\1r		
Frequency (MHz)	62.90	Nucleus	13C	Number of Transients	30	Origin	spect
Owner	root	Points Count	32768	Pulse Sequence	zgpg30	Receiver Gain	645.10
Solvent	CHLOROFORM-d			Spectrum Offset (Hz)	6289.0518	Spectrum Type	STANDARD
Temperature (degree C)	25.160					SW(cyclical) (Hz)	15060.24
						Sweep Width (Hz)	15059.78

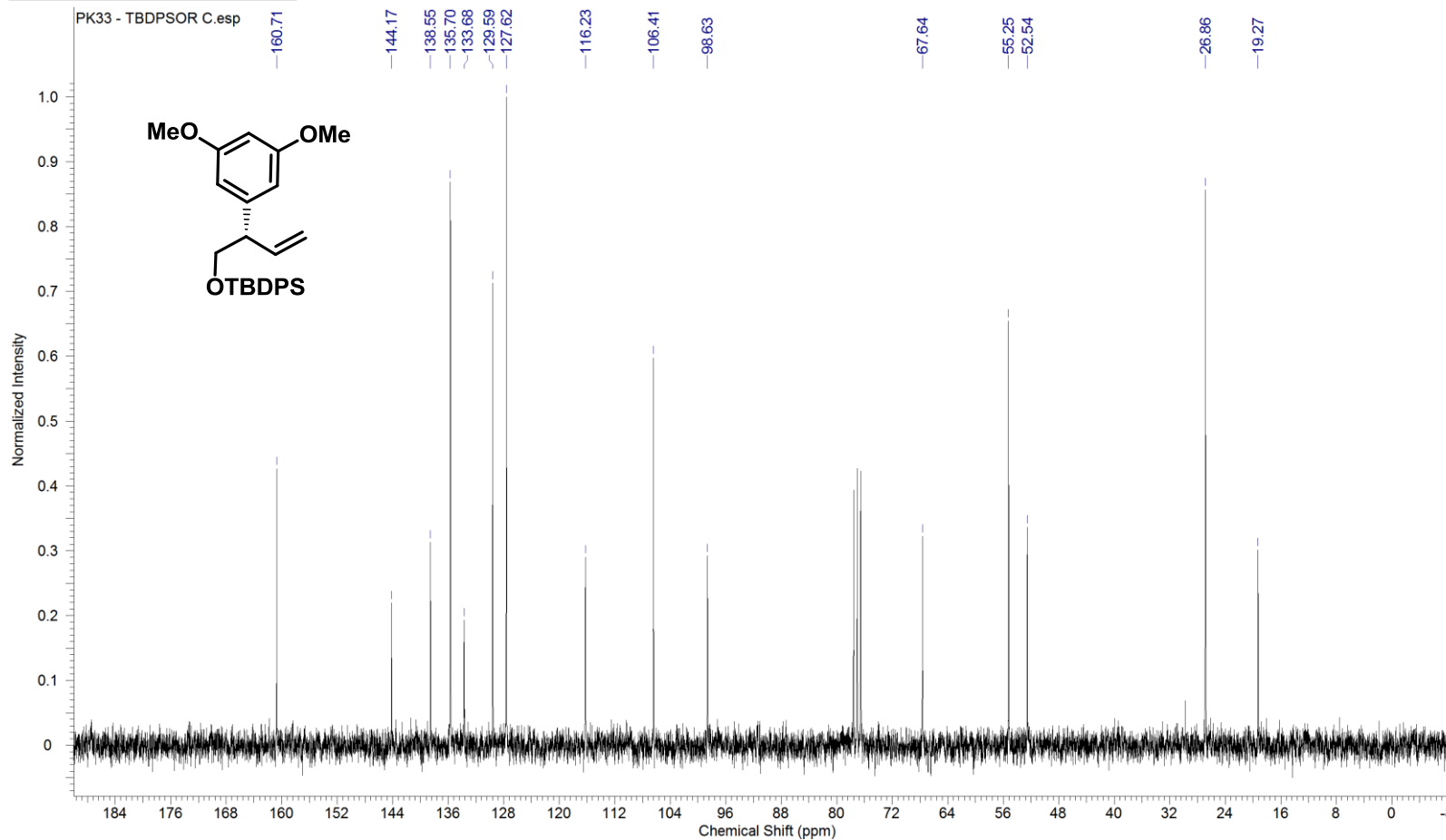


Figure S52. ^{13}C NMR spectrum (CDCl_3 , 62.9 MHz) of compound **19**.

Acquisition Time (sec)	0.5439	Comment	LN512	Date	02 Apr 2017 16:58:56				
Date Stamp	02 Apr 2017 16:58:56			File Name	C:\Users\Luiz\Desktop\Luiz\PhD\NMR\17-4-abr\abr02\ftH1\3\PDATA\1\1r				
Frequency (MHz)	62.90	Nucleus	13C	Number of Transients	14	Origin	spect	Original Points Count	8192
Owner	root	Points Count	32768	Pulse Sequence	dept135	Receiver Gain	812.70	SW(cyclical) (Hz)	15060.24
Solvent	CHLOROFORM-d			Spectrum Offset (Hz)	6289.0518	Spectrum Type	DEPT135	Sweep Width (Hz)	15059.78
Temperature (degree C)	25.160								

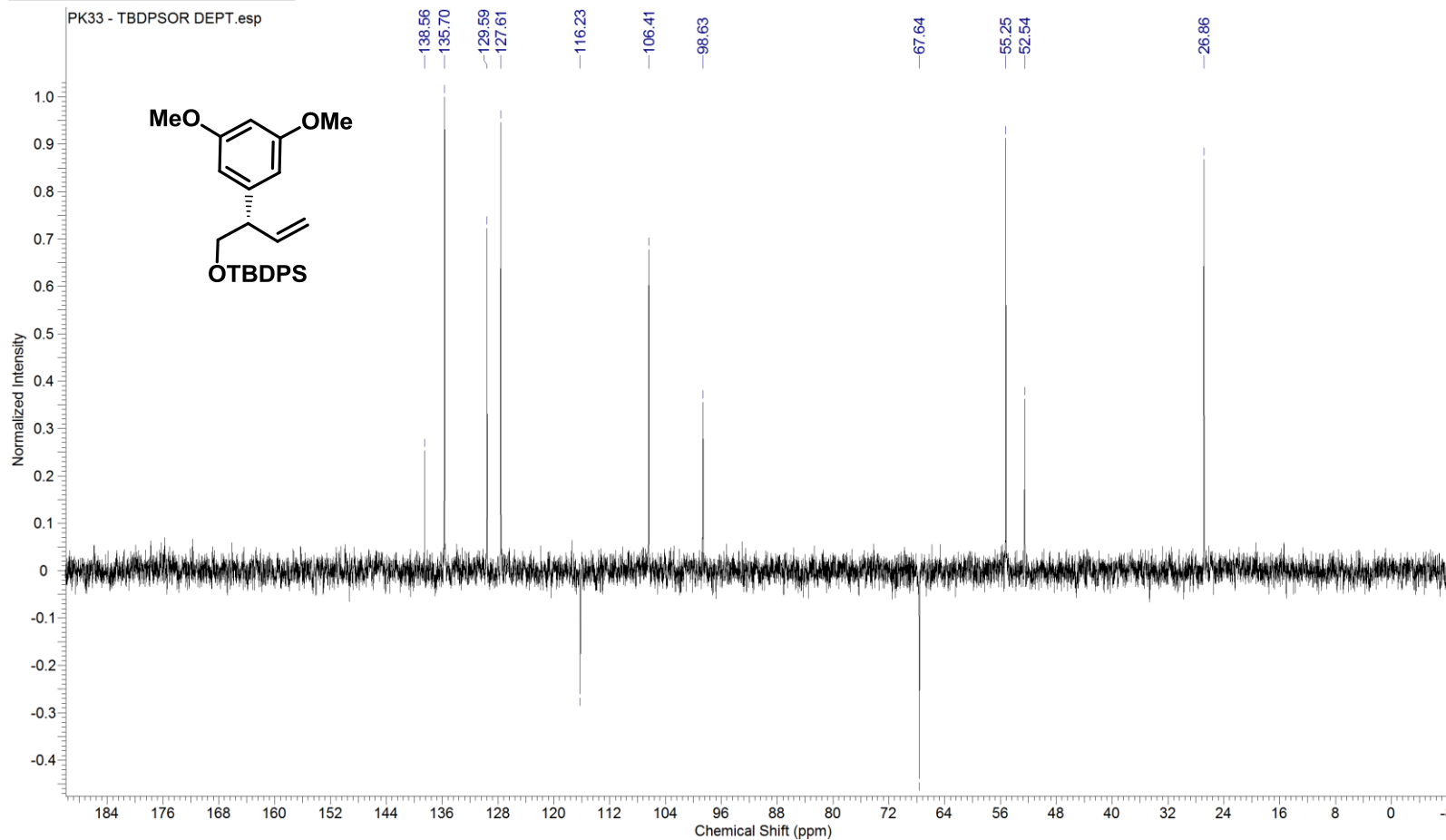
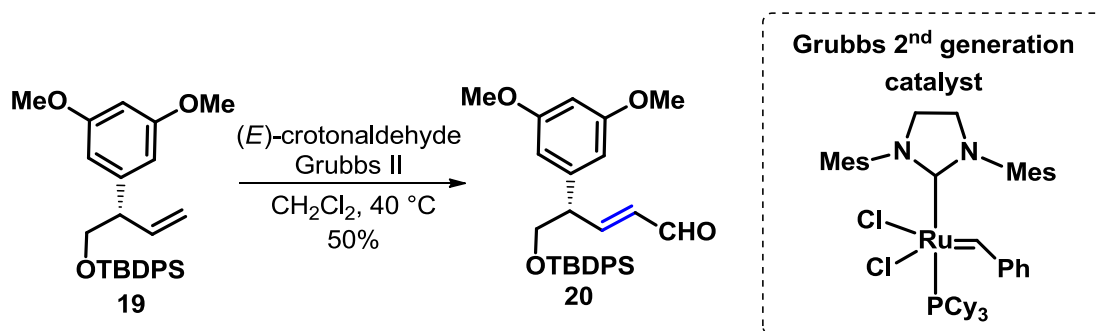


Figure S53. DEPT 135 NMR spectrum (CDCl_3 , 62.9 MHz) of compound **19**.

(*S,E*)-5-((*tert*-butyldiphenylsilyl)oxy)-4-(3,5-dimethoxyphenyl)pent-2-enal (20**).**



Freshly distilled (*E*)-crotonaldehyde (60 μL , 0.65 mmol, 5 equiv) was added to a solution of alkene **19** (58 mg, 0.13 mmol, 1 equiv) in CH_2Cl_2 (1.3 mL). Next, 2nd generation Grubbs' catalyst (11 mg, 13 μmol , 10 mol %) was added and the mixture was stirred at 40°C for 18 h. The reaction contents were directly subjected to flash chromatography (SiO_2 , hexanes/EtOAc 90:10) to give enal **20** (31 mg, 65 μmol) as a colorless oil in 50% yield.

TLC (SiO_2): $R_f = 0.20$ (hexanes/EtOAc 90:10);

$[\alpha]_D^{25} = +10$ (c 1.0, CHCl_3);

IR (ATR, cm^{-1}): 2954, 2929, 2857, 1693, 1598, 1460, 1430, 1206, 1156, 1115, 826, 745, 704;

^1H NMR (250 MHz, CDCl_3): δ 1.04 (s, 9H), 3.67 (q, $J = 6.9$ Hz, 1H), 3.74 (s, 6H), 3.92-3.99 (m, 2H), 6.17 (ddd, $J = 15.8, 7.9, 1.3$ Hz, 1H), 6.26 (d, $J = 2.2$ Hz, 2H), 6.36 (t, $J = 2.2$ Hz, 1H), 6.99 (dd, $J = 15.8, 6.9$ Hz, 1H), 7.32-7.48 (m, 6H), 7.54-7.63 (m, 4H), 9.52 (d, $J = 7.7$ Hz, 1H);

^{13}C NMR (62.9 MHz, CDCl_3): δ 19.2 (C), 26.8 (3 CH_3), 51.4 (CH), 55.3 (2 CH_3), 66.6 (CH_2), 99.0 (CH), 106.4 (2CH), 127.7 (4CH), 129.8 (2CH), 133.2 (2C), 133.6 (CH), 135.58 (2CH), 135.61 (2CH), 141.1 (C), 157.6 (CH), 161.0 (2C), 193.9 (CH);

HRMS (ESI +): m/z calculated for $\text{C}_{29}\text{H}_{34}\text{O}_4\text{SiNa}^+$ $[\text{M}+\text{Na}]^+$ 497.2119, found 497.2117.

Acquisition Time (sec)	1.0879	Comment	LN518	Date	08 Apr 2017 14:12:32		
Date Stamp	08 Apr 2017 14:12:32			File Name	C:\Users\Luiz\Desktop\Luiz\PhD\NMR\17-4-abr\abr08\ftH1\2\IPDATA\1\1r		
Frequency (MHz)	62.90	Nucleus	13C	Number of Transients	274	Origin	spect
Owner	root	Points Count	32768	Pulse Sequence	zgpg30	Receiver Gain	574.70
Solvent	CHLOROFORM-d			Spectrum Offset (Hz)	6289.0518	Spectrum Type	STANDARD
Temperature (degree C)	25.260					SW(cyclical) (Hz)	15060.24
						Sweep Width (Hz)	15059.78

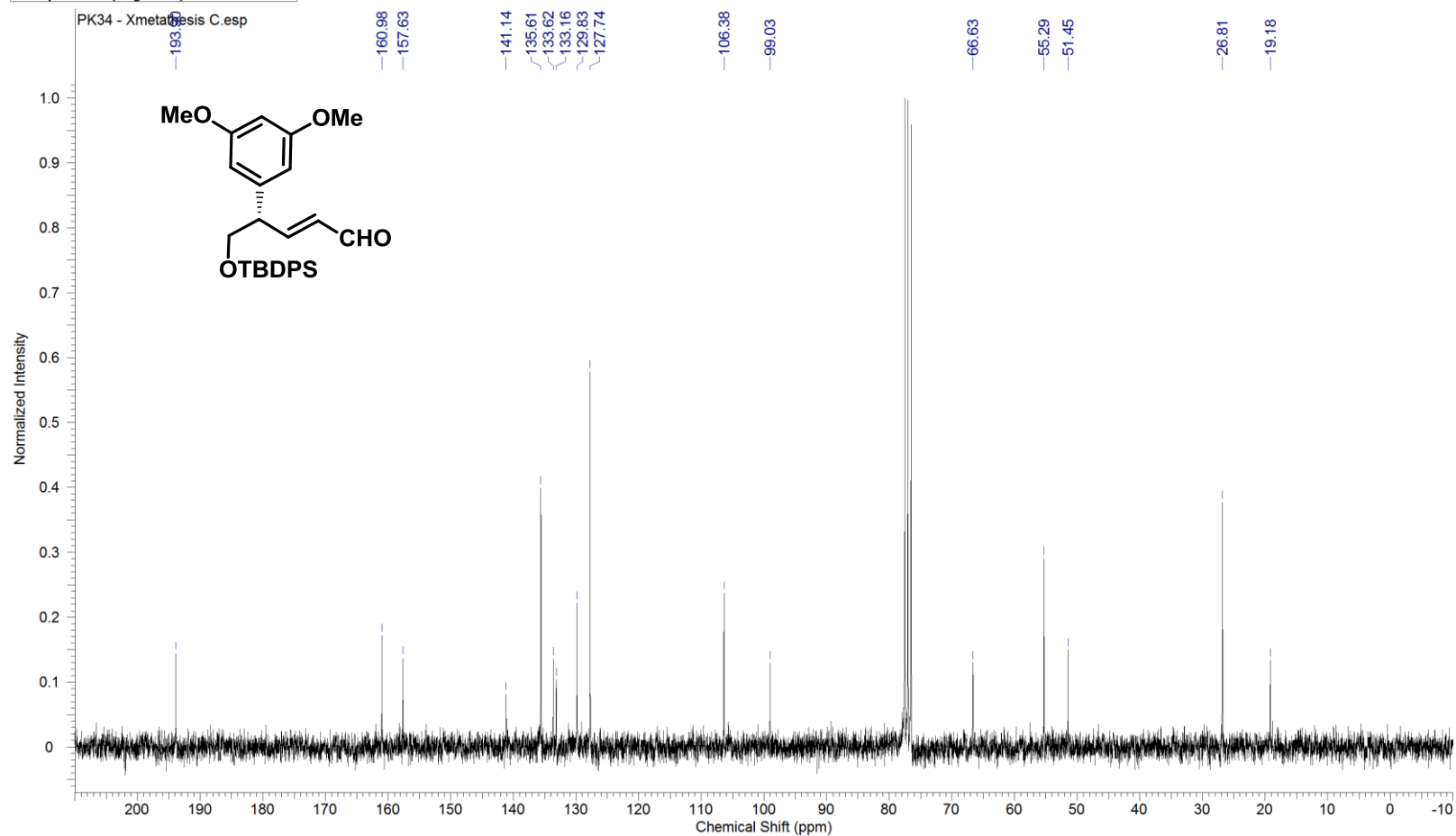


Figure S55. ^{13}C NMR spectrum (CDCl_3 , 62.9 MHz) of compound **20**.

Acquisition Time (sec)	0.5439	Comment	LN518	Date	08 Apr 2017 14:27:28			
Date Stamp	08 Apr 2017 14:27:28							
File Name	\\nmrparc.lqm.unicamp.br\spectros\bruker250\2017\abr17\data\Julio Pastre\nmr\abr08\ftH1\3\PDATA\1\1r				Frequency (MHz)	62.90		
Nucleus	¹³ C	Number of Transients	170	Origin	spect	Original Points Count	8192	
Owner	root	Points Count	32768	Pulse Sequence	dept135	Receiver Gain	4597.60	
SW(cyclical) (Hz)	15060.24	Solvent	CHLOROFORM-d				Spectrum Offset (Hz)	6289.0518
Spectrum Type	DEPT135	Sweep Width (Hz)	15059.78				Temperature (degree C)	25.160

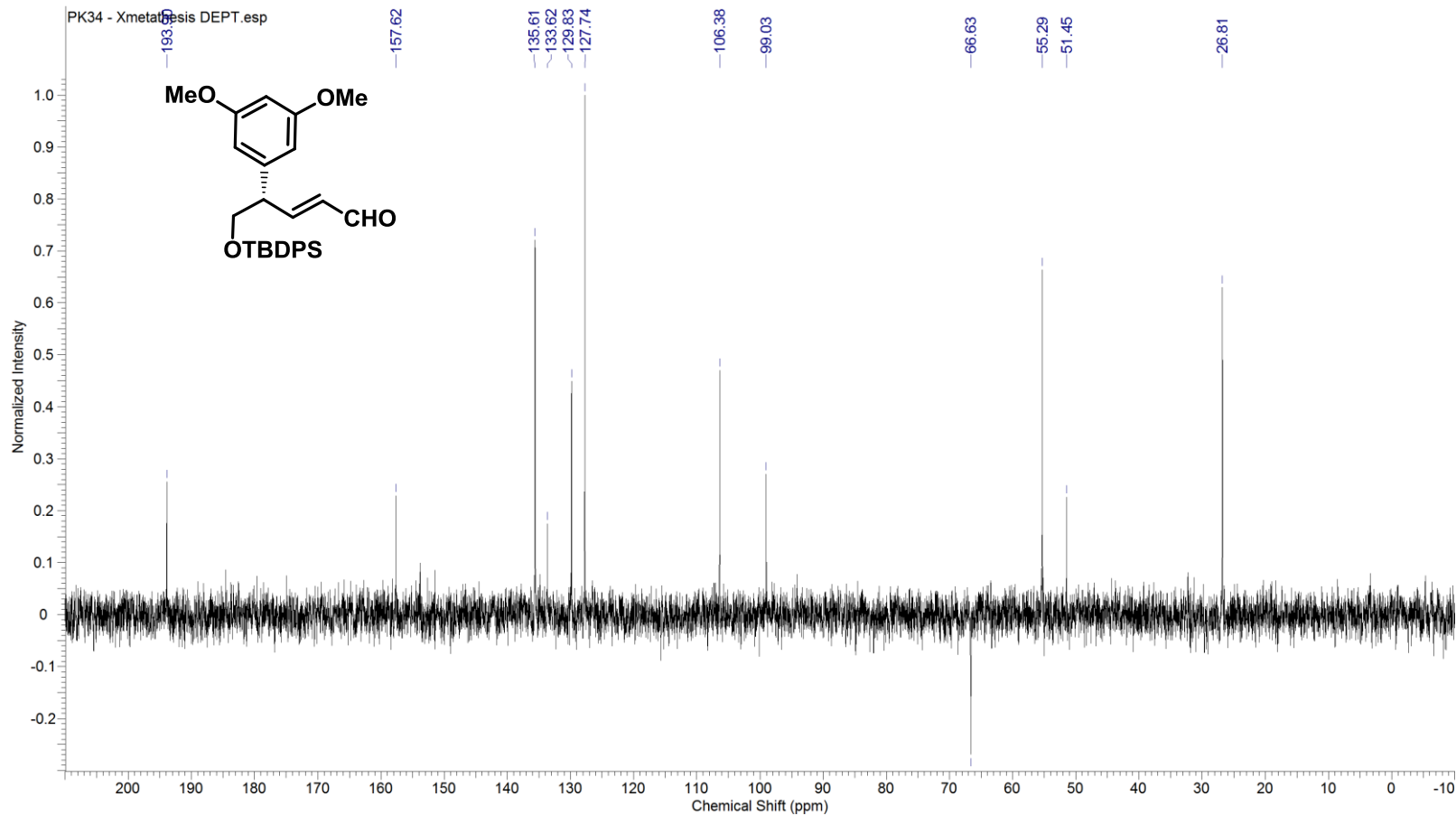
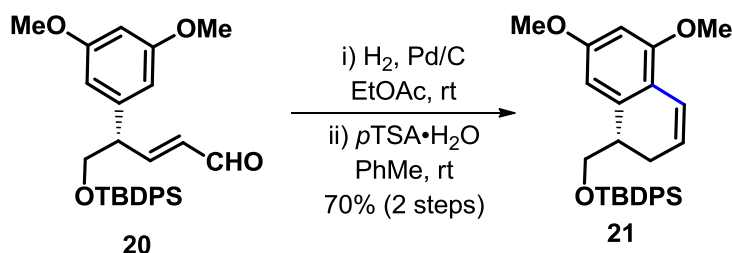


Figure S56. DEPT 135 NMR spectrum (CDCl_3 , 62.9 MHz) of compound **20**.

(*S*)-tert-butyl((5,7-dimethoxy-1,2-dihydronaphthalen-1-yl)methoxy)diphenylsilane (**21**).



Pd/C (5% w/w, 5.6 mg, 2.6 μmol , 5 mol %) was added to a solution of enal **20** (25.2 mg, 53.0 μmol , 1 equiv) in EtOAc (5 mL) at room temperature. This mixture was purged with H_2 and was stirred for 2 h. Next, the reaction contents were directly filtered through a plug of silica using EtOAc as eluent to furnish the saturated aldehyde, which was used in the next step without further purification.

TLC (SiO_2): $R_f = 0.60$ (hexanes/EtOAc 75:25).

The saturated aldehyde obtained above was diluted in dry toluene (2.5 mL), and $p\text{TSA}\cdot\text{H}_2\text{O}$ (9.2 mg, 53 μmol , 1 equiv) was added to the reaction at room temperature. The mixture was stirred for 1 h, then saturated aqueous solution of NaHCO_3 (5 mL) and EtOAc (15 mL) were added. The organic phase was separated, washed with brine (5 mL), dried over anhydrous Na_2SO_4 , and concentrated under reduced pressure. The residue was subjected to flash chromatography (SiO_2 , hexanes/EtOAc 95: 5 to 90:10) to give the bicycle **21** (17.0 mg, 37.1 μmol) as a colorless oil in 70% yield.

TLC (SiO_2): $R_f = 0.40$ (hexanes/EtOAc 90:10);

$[\alpha]_D^{25} = +5$ (c 1.0, CHCl_3);

IR (ATR, cm^{-1}): 2955, 2926, 2857, 1726, 1605, 1579, 1465, 1428, 1270, 1151, 1087, 830, 704, 616;

^1H NMR (250 MHz, CDCl_3): δ 1.10 (s, 9H), 2.35-2.69 (m, 2H), 2.83-2.97 (m, 1H), 3.75 (s, 3H), 3.57-3.77 (m, 2H), 3.80 (s, 3H), 5.64-5.75 (m, 1H), 6.21 (d, $J = 2.0$ Hz, 1H), 6.31 (d, $J = 2.0$ Hz, 1H), 6.68 (dd, $J = 9.8, 2.7$ Hz, 1H), 7.32-7.48 (m, 6H), 7.59-7.70 (4H);

^{13}C NMR (62.9 MHz, CDCl_3): δ 19.3 (C), 24.4 (CH_2), 26.9 (3CH_3), 40.8 (CH), 55.3 (CH_3), 55.5 (CH_3), 67.1 (CH_2), 96.9 (CH), 105.5 (CH), 116.1 (C), 120.5 (CH), 122.5 (CH), 127.6 (4CH), 129.5 (2CH), 133.8 (C), 133.9 (C), 135.7 (4CH), 138.1 (C), 155.8 (C), 159.3 (C);

HRMS (ESI +): m/z calculated for $\text{C}_{29}\text{H}_{34}\text{O}_3\text{SiNa}^+$ $[\text{M}+\text{Na}]^+$ 481.2169, found 481.2153.

Acquisition Time (sec)	1.0879	Comment	LN454	Date	16 Feb 2017 17:14:08		
Date Stamp	16 Feb 2017 17:14:08			File Name	C:\Users\Luiz\Desktop\Luiz\PhD\NMR\17-2-fev\16ftH3\2\PDATA\1\1r		
Frequency (MHz)	62.90	Nucleus	13C	Number of Transients	54	Origin	spect
Owner	root	Points Count	32768	Pulse Sequence	zgpg30	Receiver Gain	574.70
Solvent	CHLOROFORM-d			Spectrum Offset (Hz)	6289.0518	Spectrum Type	STANDARD
Temperature (degree C)	25.160					SW(cyclical) (Hz)	15060.24
						Sweep Width (Hz)	15059.78

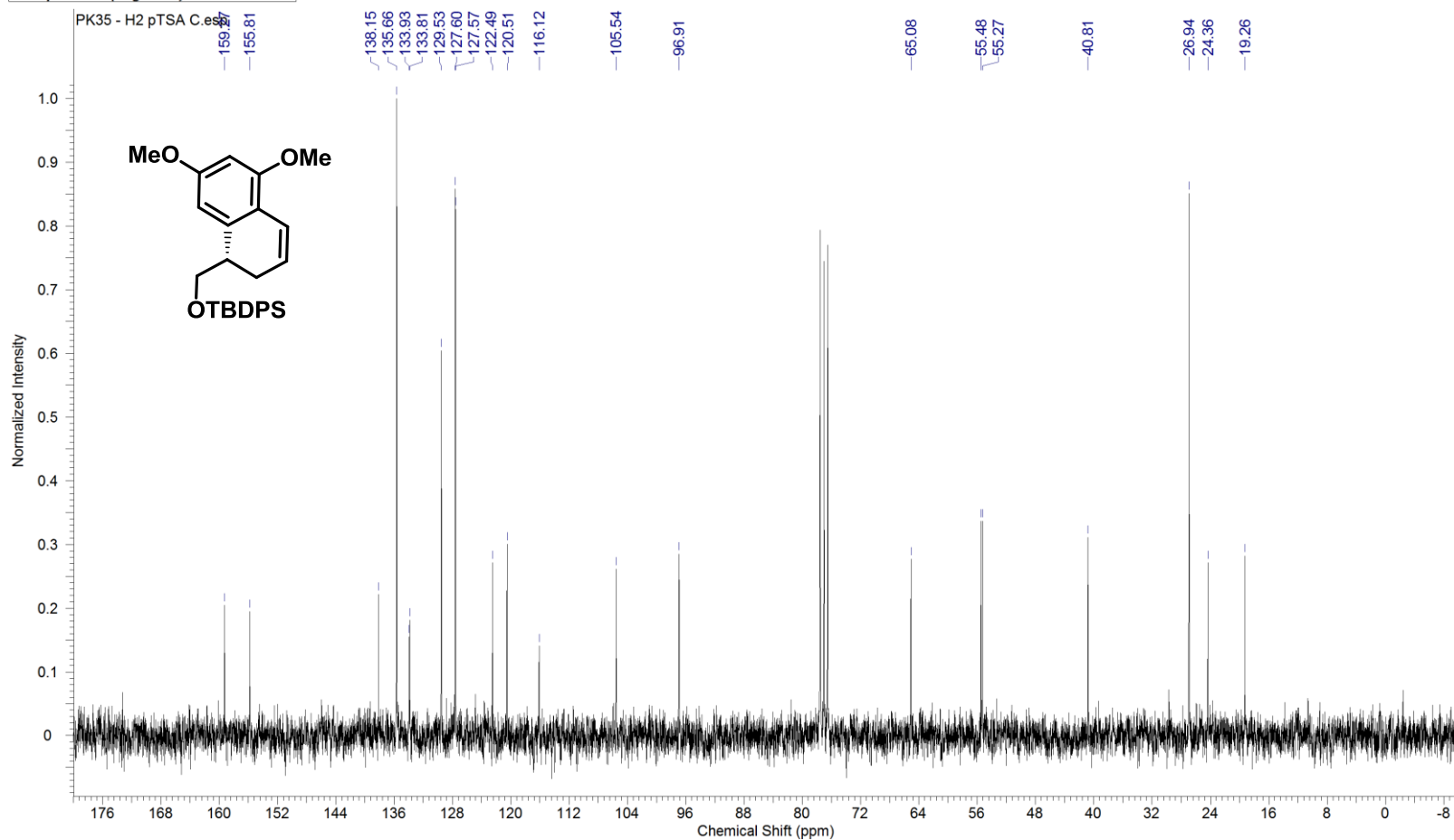


Figure S58. ^{13}C NMR spectrum (CDCl_3 , 62.9 MHz) of compound **21**.

Acquisition Time (sec)	0.5439	Comment	LN454	Date	16 Feb 2017 17:16:16	
Date Stamp	16 Feb 2017 17:16:16			File Name	C:\Users\Luiz\Desktop\Luiz\PhD\NMR\17-2-fev\fev16\ftH3\3\PDATA\1\1r	
Frequency (MHz)	62.90	Nucleus	13C	Number of Transients	23	Origin spect
Owner	root	Points Count	32768	Pulse Sequence	dept135	Receiver Gain 1290.20
Solvent	CHLOROFORM-d			Spectrum Offset (Hz)	6289.0518	Spectrum Type DEPT135
Temperature (degree C)	25.160					SW(cyclical) (Hz) 15060.24
						Sweep Width (Hz) 15059.78

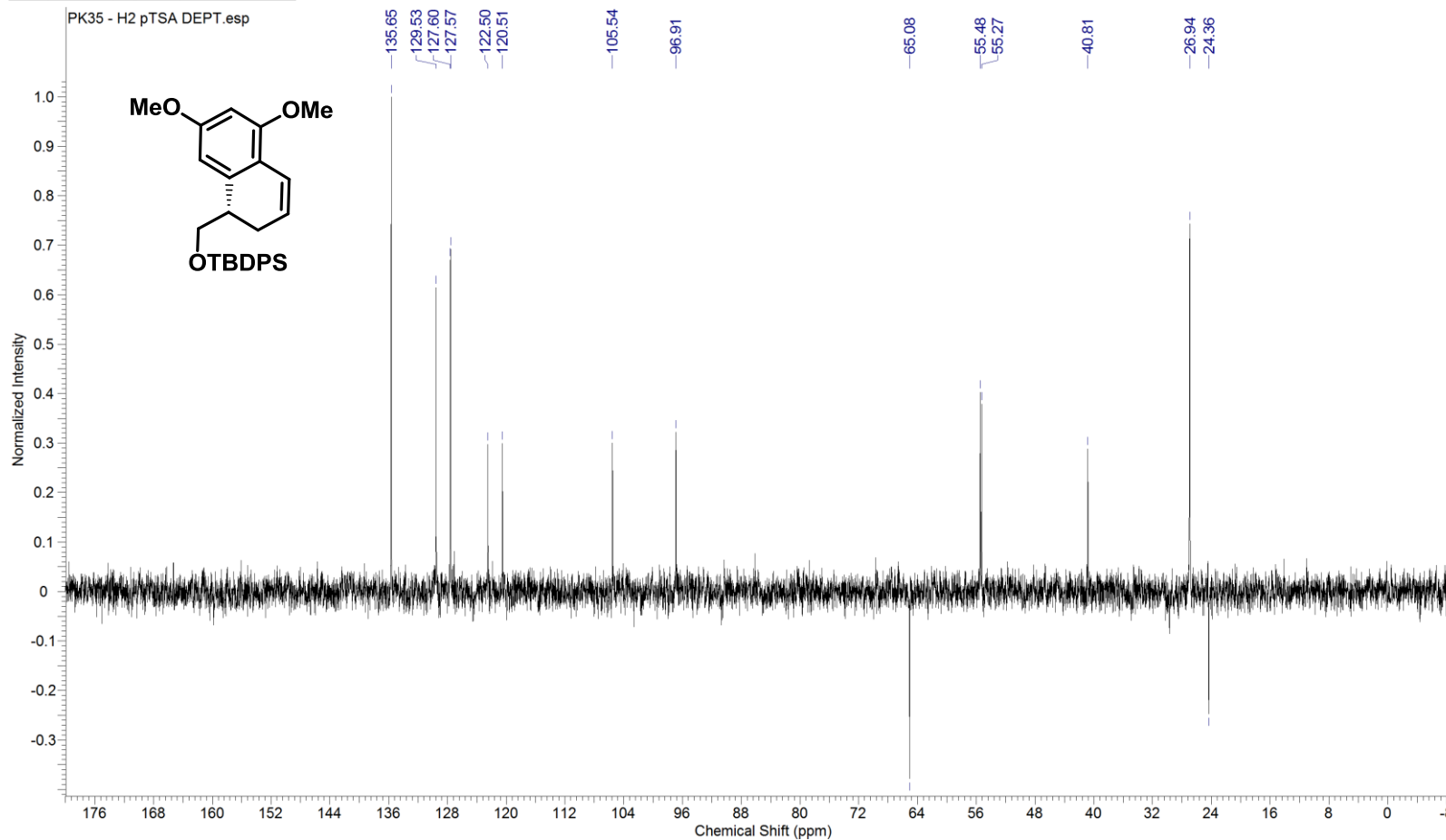
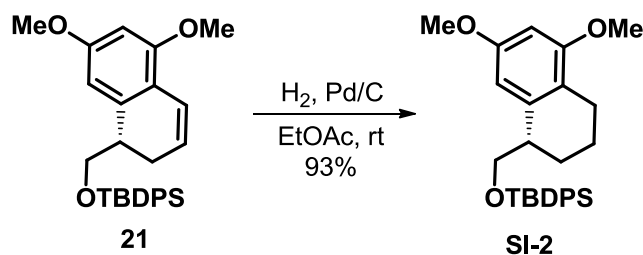


Figure S59. DEPT 135 NMR spectrum (CDCl_3 , 62.9 MHz) of compound **21**.

(*S*)-tert-butyl((5,7-dimethoxy-1,2,3,4-tetrahydronaphthalen-1-yl)methoxy)diphenylsilane (**SI-2**).



Pd/C (5% w/w, 72 mg, 34 μ mol, 5 mol %) was added to a solution of alkene **21** (312 mg, 0.68 mmol, 1 equiv) in EtOAc (34 mL) at room temperature. This mixture was purged with H₂ and was stirred for 14 h. Next, the solvent was removed under reduced pressure, and the residue was subjected to flash chromatography (SiO₂, hexanes:EtOAc, 90:10) to afford the tetraline **SI-2** (290 mg, 0.63 mmol) as a colorless oil in 93% yield.

TLC (SiO₂): R_f = 0.44 (hexanes/EtOAc 90:10);

[α]_D²⁵ = -20 (*c* 1.0, CHCl₃);

IR (ATR, cm⁻¹): 2933, 2859, 1609, 1594, 1465, 1430, 1203, 1147, 1115, 1087, 826, 705;

¹H NMR (250 MHz, CDCl₃): δ 1.11 (s, 9H), 1.62-1.85 (m, 3H), 2.01-2.18 (m, 1H), 2.36-2.53 (m, 1H), 2.62 (dt, *J* = 17.4, 4.9 Hz, 1H), 2.87-3.01 (m, 1H), 3.69 (s, 3H), 3.78 (s, 3H), 3.70-3.89 (m, 2H), 6.16 (d, *J* = 2.2 Hz, 1H), 6.29 (d, *J* = 2.2 Hz, 1H), 7.33-7.48 (m, 6H), 7.63-7.76 (4H);

¹³C NMR (62.9 MHz, CDCl₃): δ 18.5 (CH₂), 19.3 (C), 22.6 (CH₂), 24.3 (CH₂), 26.9 (3CH₃), 41.0 (CH), 55.2 (2CH₃), 67.9 (CH₂), 96.2 (CH), 104.7 (CH), 119.2 (C), 127.6 (4CH), 129.6 (2CH), 133.8 (C), 134.0 (C), 135.65 (2CH), 135.69 (2CH), 138.9 (C), 158.0 (2C);

HRMS (ESI +): *m/z* calculated for C₂₉H₃₆O₃SiNa⁺ [M+Na]⁺ 483.2326, found 483.2321.

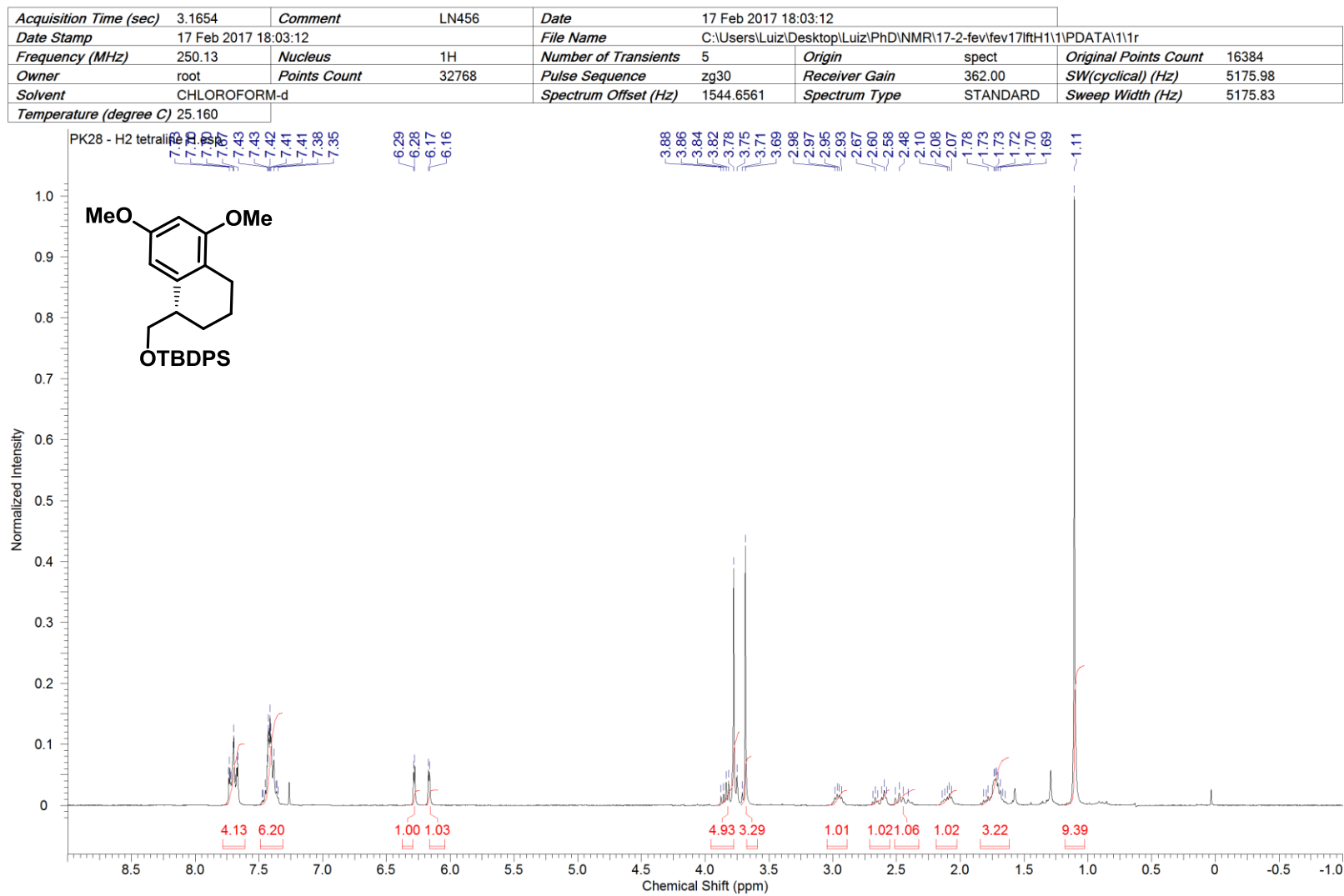


Figure S60. ^1H NMR spectrum (CDCl_3 , 250 MHz) of compound **SI-2**.

Acquisition Time (sec)	1.0879	Comment	LN456	Date	17 Feb 2017 18:05:20		
Date Stamp	17 Feb 2017 18:05:20			File Name	C:\Users\Luiz\Desktop\Luiz\PhD\NMR\17-2-fev\171ft\12\PDATA\1\1r		
Frequency (MHz)	62.90	Nucleus	13C	Number of Transients	64	Origin	spect
Owner	root	Points Count	32768	Pulse Sequence	zgpg30	Receiver Gain	645.10
Solvent	CHLOROFORM-d			Spectrum Offset (Hz)	6289.0518	Spectrum Type	STANDARD
Temperature (degree C)	25.160					SW(cyclical) (Hz)	15060.24
						Sweep Width (Hz)	15059.78

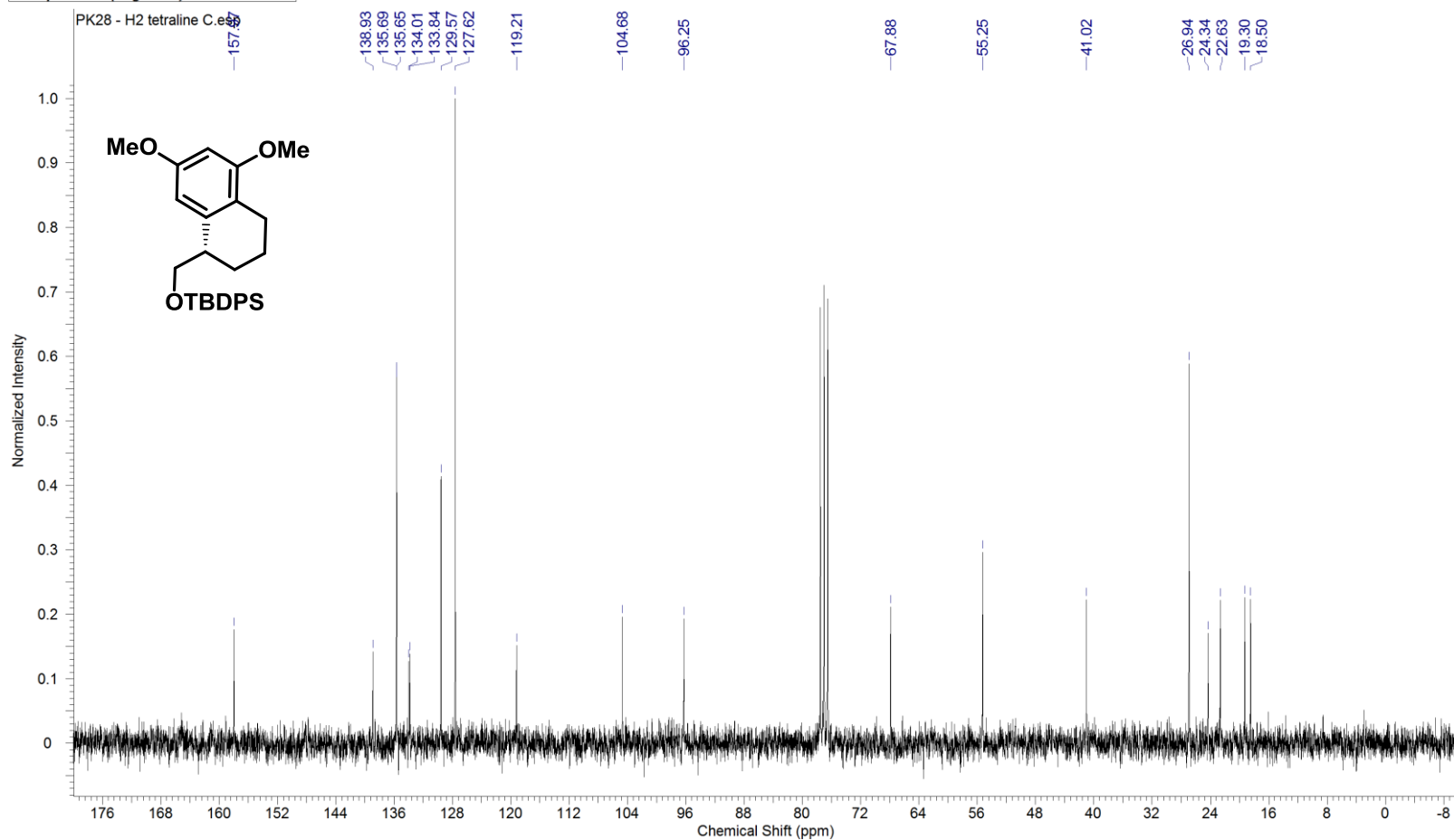


Figure S61. ^{13}C NMR spectrum (CDCl_3 , 62.9 MHz) of compound **SI-2**.

Acquisition Time (sec)	0.5439	Comment	LN456	Date	17 Feb 2017 18:09:36		
Date Stamp	17 Feb 2017 18:09:36			File Name	C:\Users\Luiz\Desktop\Luiz\PhD\NMR\17-2-fev\fev17\ftH1\3\PDATA\11r		
Frequency (MHz)	62.90	Nucleus	13C	Number of Transients	28	Origin	spect
Owner	root	Points Count	32768	Pulse Sequence	dept135	Receiver Gain	1448.20
Solvent	CHLOROFORM-d			Spectrum Offset (Hz)	6289.0518	Spectrum Type	DEPT135
Temperature (degree C)	25.160					SW(cyclical) (Hz)	15060.24
						Sweep Width (Hz)	15059.78

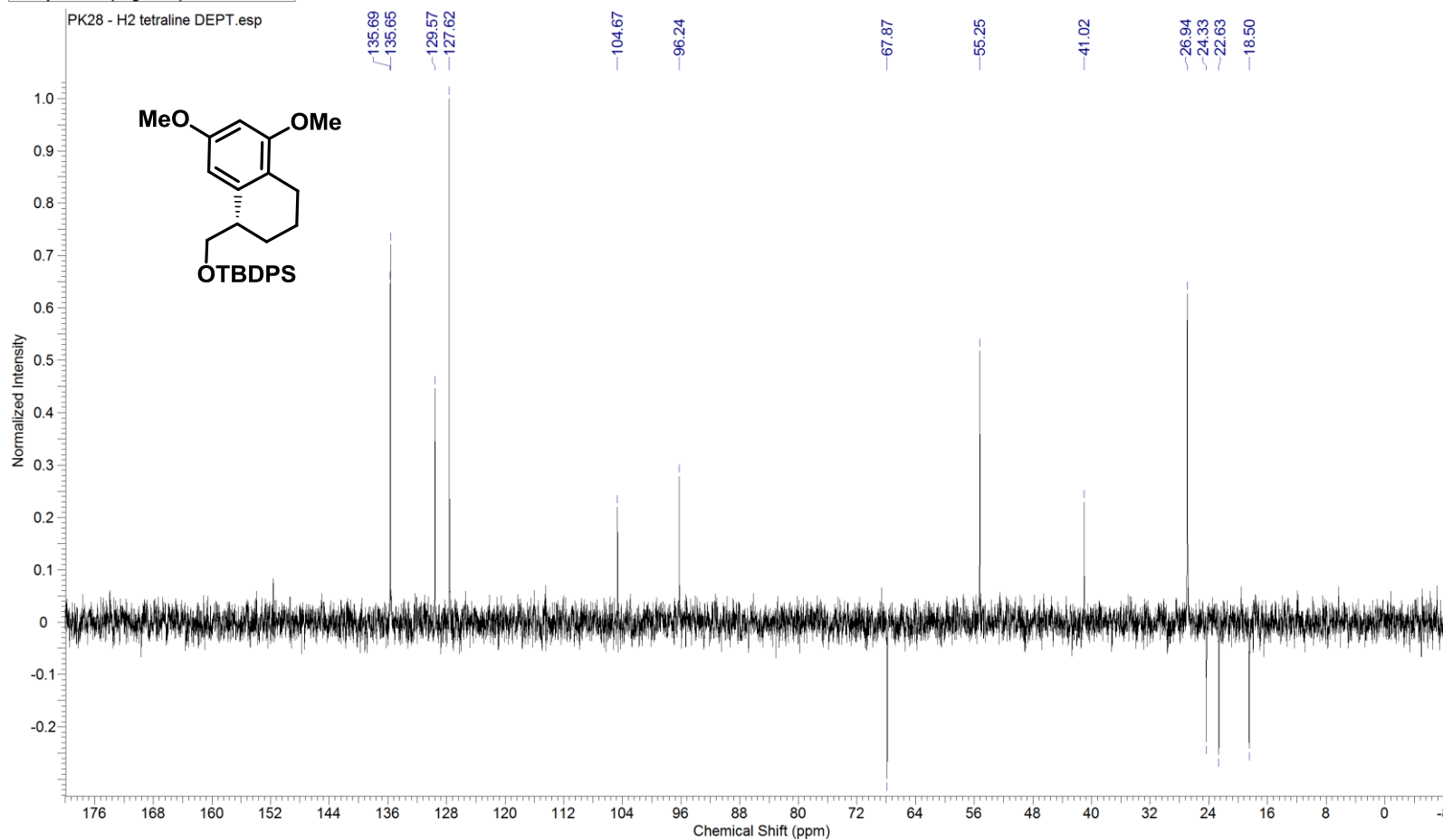
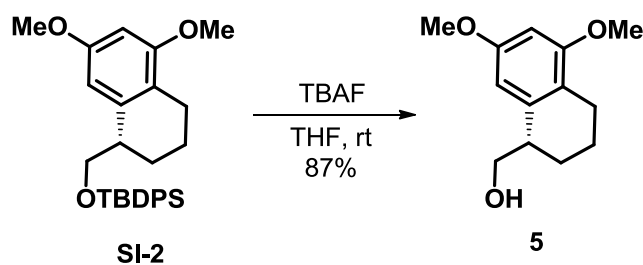


Figure S62. DEPT 135 NMR spectrum (CDCl_3 , 62.9 MHz) of compound **SI-2**.

(S)-(5,7-dimethoxy-1,2,3,4-tetrahydronaphthalen-1-yl)methanol (5**).**



TBAF solution (1 M in THF, 1.4 mL, 1.4 mmol, 2 equiv) was added to a mixture of silyl ether **SI-2** (322 mg, 0.70 mmol, 1 equiv) in dry THF (14 mL) at room temperature. This mixture was stirred for 2 h, then was quenched by addition of saturated aqueous solution of NH_4Cl (30 mL). The mixture was extracted with EtOAc (2 x 30 mL). The organic phases were combined, dried over anhydrous MgSO_4 , and concentrated under reduced pressure. The residue was subjected to flash chromatography (SiO_2 , hexanes/EtOAc 85:15 to 75:25) to furnish alcohol **5** (135 mg, 0.61 mmol) as a colorless oil in 87% yield.

TLC (SiO_2): $R_f = 0.27$ (hexanes/EtOAc 75:25);

$[\alpha]_{\text{D}}^{25} = -2$ (c 1.0, CHCl_3), for *ent*-**5** $[\alpha]_{\text{D},\text{lit}}^{20} = +3.5$ (c 1.0, CHCl_3);⁶

^1H NMR (250 MHz, CDCl_3): δ 1.59 (br. s, 1H), 1.68-1.98 (m, 4H), 2.42-2.70 (m, 2H), 2.93 (quint, $J = 5.3$ Hz, 1H), 3.79 (s, 6H), 3.77-3.84 (m, 2H), 6.32 (d, $J = 2.2$ Hz, 1H), 6.39 (d, $J = 2.2$ Hz, 1H);

^{13}C NMR (62.9 MHz, CDCl_3): δ 19.1 (CH_2), 22.6 (CH_2), 24.9 (CH_2), 40.8 (CH), 55.3 (2CH_3), 67.0 (CH_2), 96.2 (CH), 104.2 (CH), 119.4 (C), 138.4 (C), 158.3 (2C).

Acquisition Time (sec)	1.0879	Comment	LN493	Date	14 Mar 2017 16:46:08				
Date Stamp	14 Mar 2017 16:46:08			File Name	C:\Users\Luiz\Desktop\Luiz\PhD\NMR\17-3-mar\mar14\ftH1\2\pdata\11r				
Frequency (MHz)	62.90	Nucleus	13C	Number of Transients	100	Origin	spect	Original Points Count	16384
Owner	root	Points Count	32768	Pulse Sequence	zgpg30	Receiver Gain	812.70	SW(cyclical) (Hz)	15060.24
Solvent	CHLOROFORM-d			Spectrum Offset (Hz)	6289.0518	Spectrum Type	STANDARD	Sweep Width (Hz)	15059.78
Temperature (degree C)	25.260								

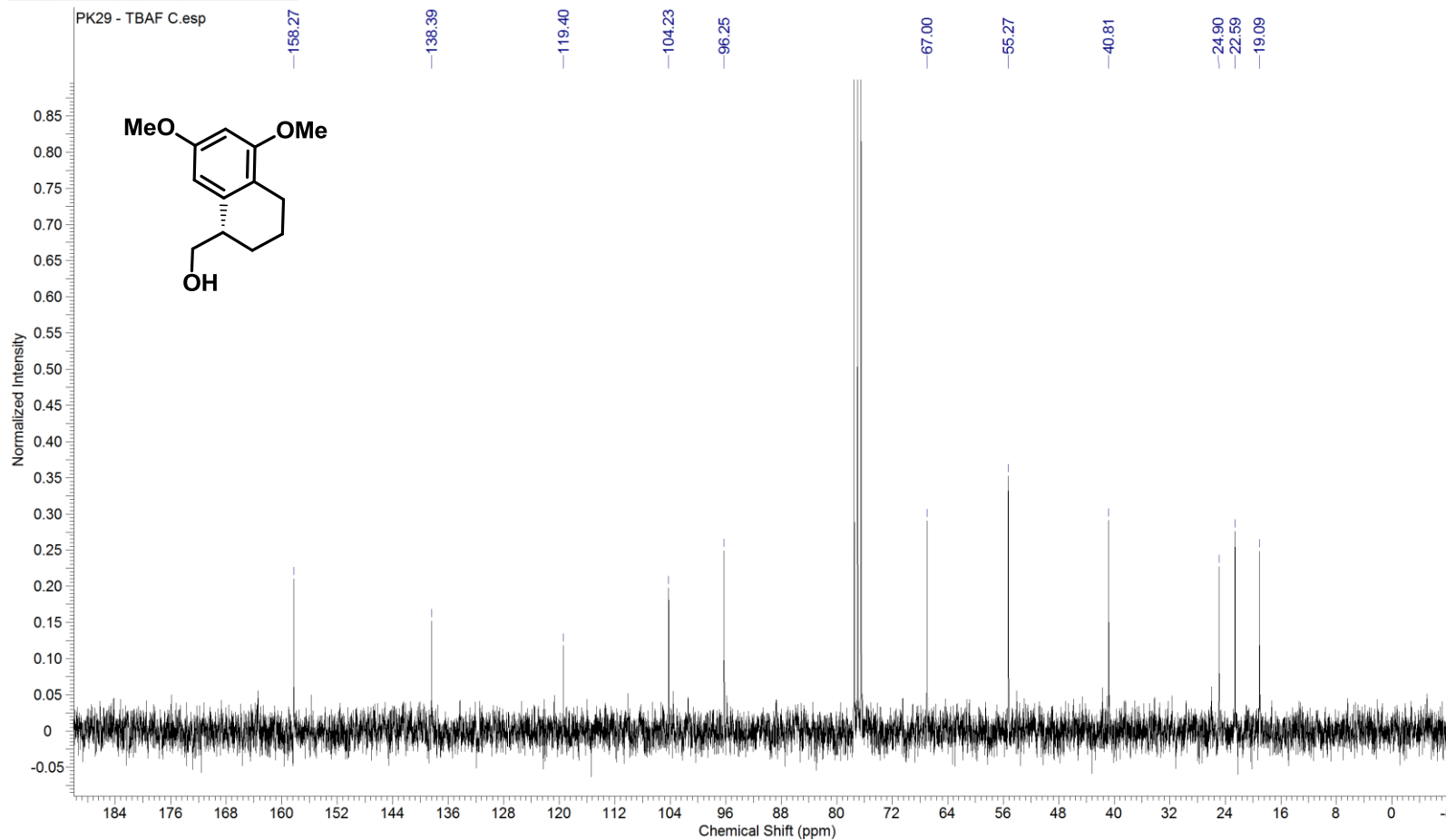


Figure S64. ^{13}C NMR spectrum (CDCl_3 , 62.9 MHz) of compound **5**.

Acquisition Time (sec)	0.5439	Comment	LN493	Date	14 Mar 2017 16:50:24		
Date Stamp	14 Mar 2017 16:50:24			File Name	C:\Users\Luiz\Desktop\Luiz\PhD\NMR\17-3-mar\mar14\ftH1\3\PDATA\1\1r		
Frequency (MHz)	62.90	Nucleus	13C	Number of Transients	50	Origin	spect
Owner	root	Points Count	32768	Pulse Sequence	dept135	Receiver Gain	1448.20
Solvent	CHLOROFORM-d			Spectrum Offset (Hz)	6289.0518	Spectrum Type	DEPT135
Temperature (degree C)	25.160					SW(cyclical) (Hz)	15060.24
						Sweep Width (Hz)	15059.78

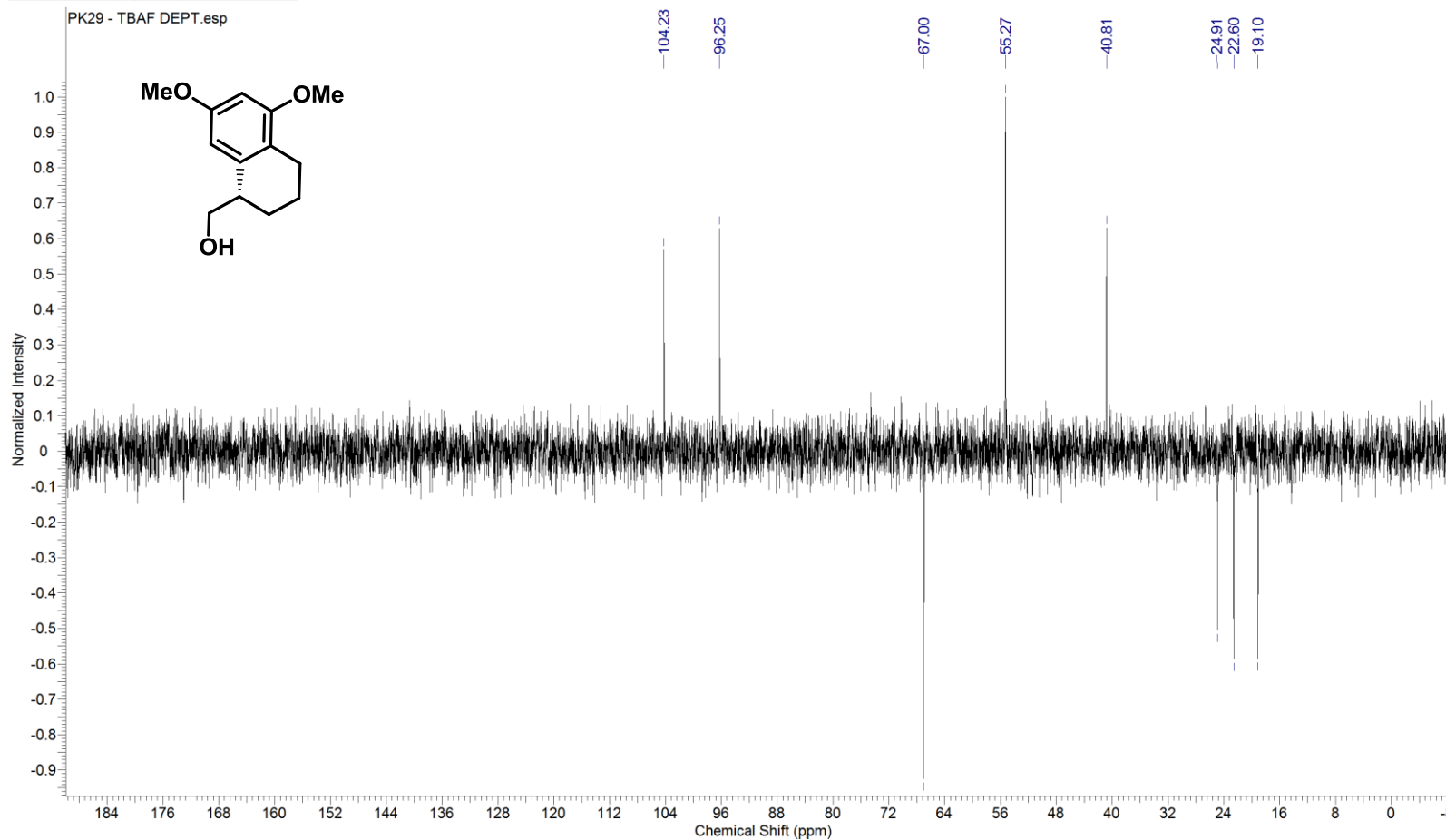
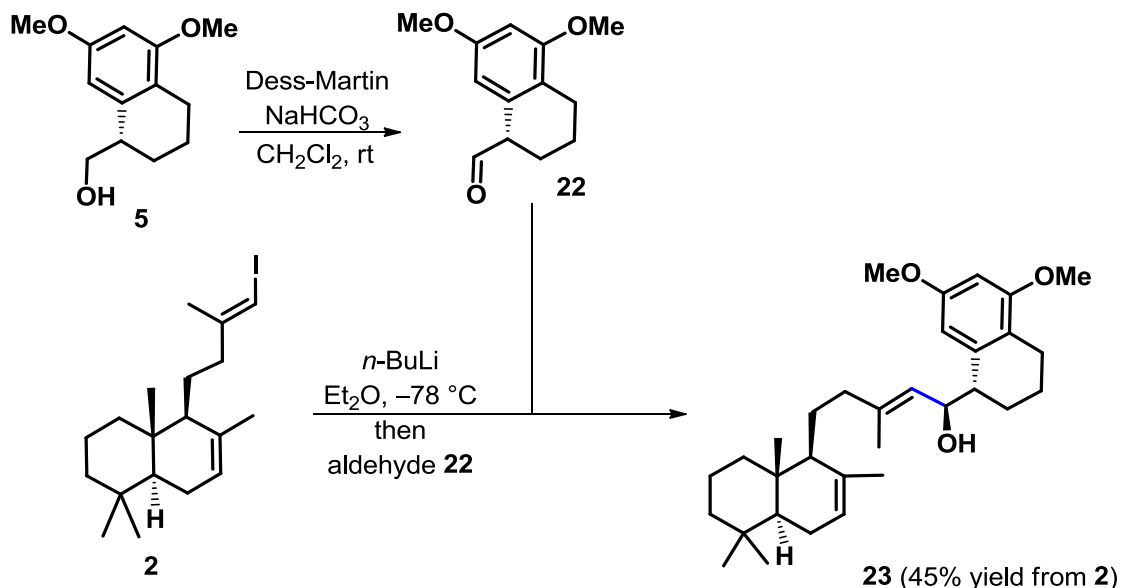


Figure S65. DEPT 135 NMR spectrum (CDCl_3 , 62.9 MHz) of compound **5**.

Table 2. Comparison between ^{13}C NMR spectra of compound **5** and reported by Xu and Ye⁵

Pastre (this work)	Xu and Ye⁵	$\Delta\delta$
19.1	19.1	0.0
22.6	22.6	0.0
24.9	25.0	−0.1
40.8	40.9	−0.1
55.3 (2CH₃)	55.3 (2CH ₃)	0.0
67.0	67.0	0.0
96.2	96.3	−0.1
104.2	104.3	−0.1
119.4	119.4	0.0
138.4	138.4	0.0
158.3 (2C)	158.3 (2C)	0.0

(*S,E*)-1-((*S*)-5,7-dimethoxy-1,2,3,4-tetrahydronaphthalen-1-yl)-3-methyl-5-((1*S*,4*aS*,8*aS*)-2,5,5,8*a*-tetramethyl-1,4,4*a*,5,6,7,8,8*a*-octahydronaphthalen-1-yl)pent-2-en-1-ol (**23**).



Solid NaHCO_3 (23.0 mg, 0.27 mmol, 2.2 equiv) and Dess-Martin periodinane (79.1 mg, 0.19 mmol, 1.5 equiv) were added to a solution of alcohol **5** (41.4 mg, 0.19 mmol, 1.5 equiv) in dry CH_2Cl_2 (5 mL) at room temperature. This mixture was stirred for 1 h, then the solvent was removed under reduced pressure, and the aldehyde was purified by flash chromatography (SiO_2 , hexanes/ EtOAc 90:10) to furnish aldehyde **22**, which was immediately used in the next step.

TLC (SiO_2): R_f = 0.60 (hexanes/ EtOAc 75:25);

$n\text{-BuLi}$ solution (2.14 M in hexanes, 118 μL , 0.25 mmol, 2 equiv) was added dropwisely to a solution of iodide **2** (48.0 mg, 0.12 mmol, 1 equiv) in Et_2O (2 mL) at -78°C , the resulting mixture was stirred for 1 h at the same temperature. Next, a solution of the freshly prepared aldehyde **22** in dry Et_2O (2 mL) was added dropwisely to the vinyl lithium solution, the reaction was stirred for 1 h at -78°C , and 16 h at -60°C (cryostat bath). The reaction was quenched by addition of NH_4Cl saturated solution (10 mL), and was extracted with EtOAc (2 x 10 mL). The combined organic phases were dried over anhydrous MgSO_4 , and concentrated under reduced pressure. The residue was subjected to flash chromatography (SiO_2 , hexanes/ EtOAc 90:10) to furnish alcohol **23** (27.0 mg, 56 μmol) as a colorless oil in 45% yield.

Note: Analysis of a crude sample showed dr = 3:1, after chromatography the alcohol **23** was obtained as a single isomer in 45% yield. Substitution of $n\text{-BuLi}$ by $t\text{-BuLi}$ led to 25% yield of alcohol **23** and the same dr = 3:1 (crude sample). The analyses were performed with CHCl_3 or CDCl_3 treated with anhydrous K_2CO_3 to remove residual acidity, in order to prevent decomposition. $n\text{-BuLi}$ and $t\text{-BuLi}$ were recently titrated using cyclohexanol (75 mg, 0.75 mmol) diluted in dry THF (5 mL), with 2,2'-bipyridine (bipy) as indicator.

TLC (SiO_2): R_f = 0.21 (hexanes/ EtOAc 90:10);

$[\alpha]_{\text{D}}^{25} = +16$ (c 1.0, CHCl_3), $[\alpha]_{\text{D, lit}}^{20} = +19.2$ (c 1.6, CHCl_3);⁶

^1H NMR (250 MHz, CDCl_3): δ 0.76 (s, 3H), 0.86 (s, 3H), 0.88 (s, 3H), 0.79-1.04 (m, 1H), 1.58 (d, $J = 1.1$ Hz, 3H), 1.69 (s, 3H), 1.05-1.73 (m, 11H), 1.73-2.07 (m, 6H), 2.21 (td, $J = 12.8, 4.5$ Hz, 1H), 2.43-2.71 (m, 2H), 2.86 (q, $J = 5.6$ Hz, 1H), 3.78 (s, 3H), 3.79 (s, 3H), 4.76 (dd, $J = 8.2, 4.9$ Hz, 1H), 5.30 (dq, $J = 8.2, 0.9$ Hz, 1H), 5.39 (br. s, 1H), 6.32 (d, $J = 2.4$ Hz, 1H), 6.48 (d, $J = 2.4$ Hz, 1H);

^{13}C NMR (62.9 MHz, CDCl_3): δ 13.5 (CH_3), 16.8 (CH_3), 18.8 (CH_2), 20.2 (CH_2), 21.8 (CH_3), 22.2 (CH_3), 22.6 (CH_2), 23.4 (CH_2), 23.8 (CH_2), 25.6 (CH_2), 33.0 (C), 33.1 (CH_3), 36.8 (C), 39.2 (CH_2), 42.3 (2CH_2), 44.2 (CH), 50.2 (CH), 54.6 (CH), 55.3 (2CH_3), 71.6 (CH), 96.0 (CH), 104.6 (CH), 120.3 (C), 122.3 (CH), 125.8 (CH), 135.3 (C), 138.5 (C), 138.9 (C), 158.1 (2C).

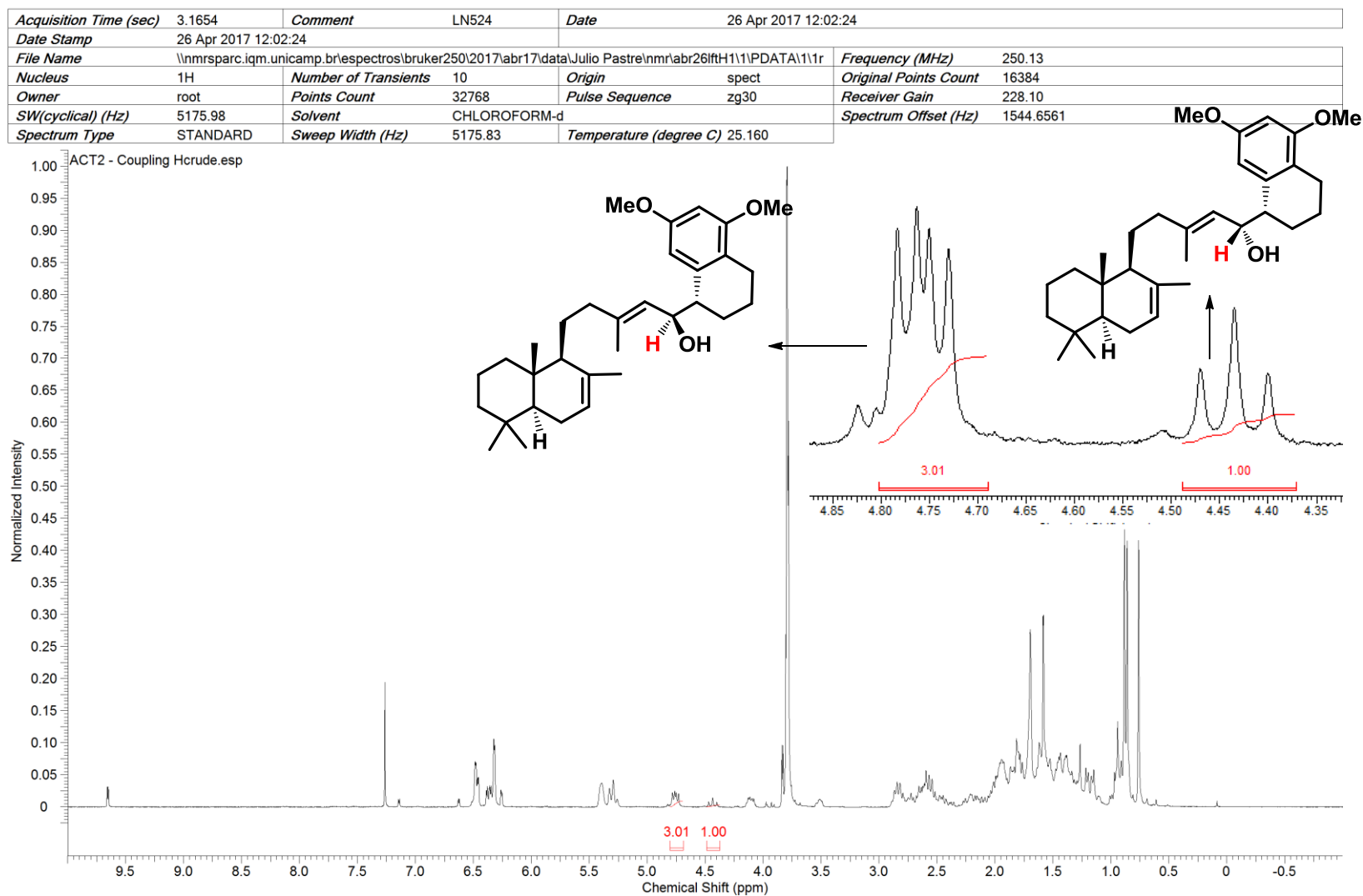


Figure S66. ^1H NMR spectrum (CDCl_3 , 250 MHz) of crude mixture (**dr** = 3:1).

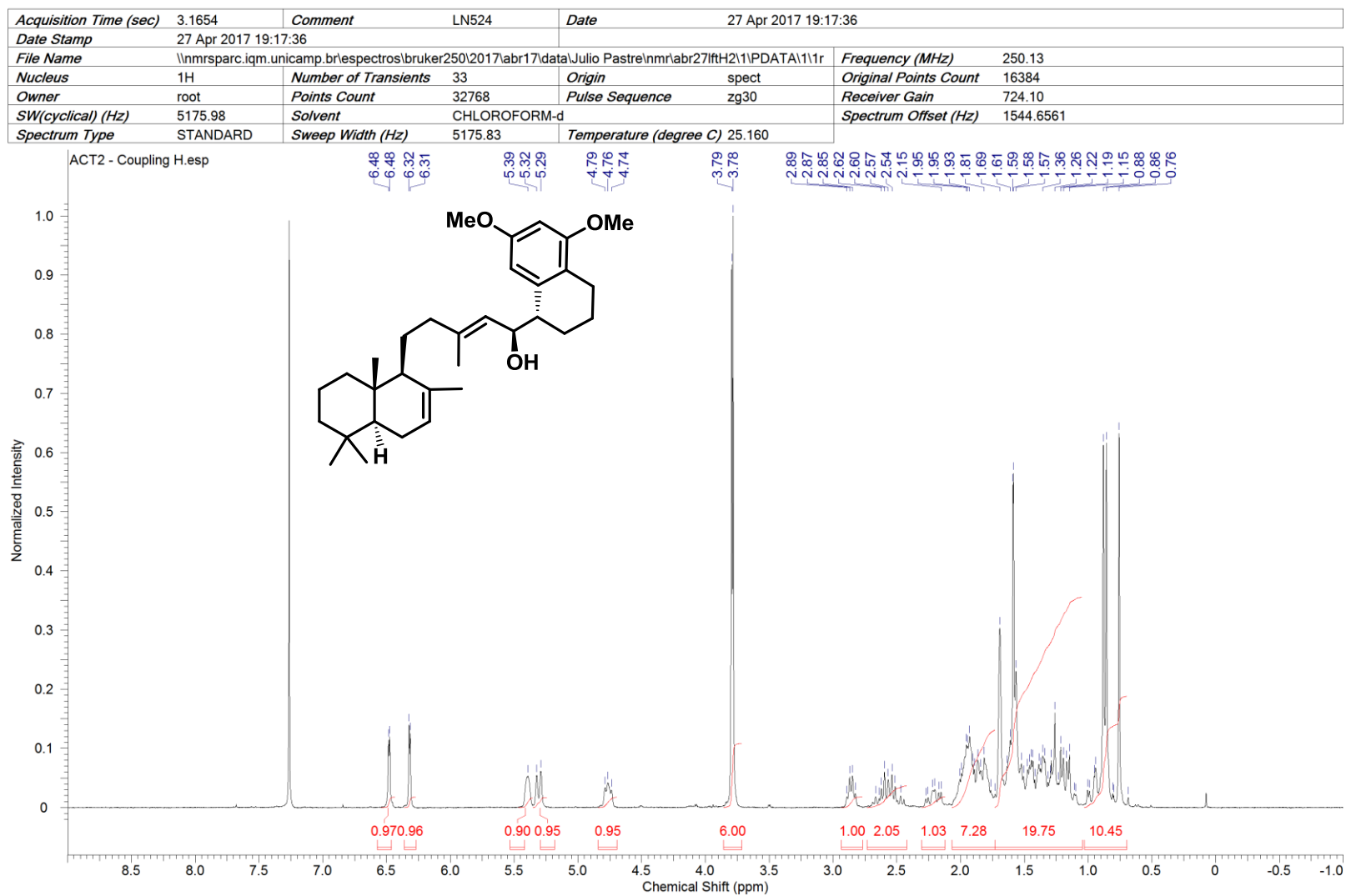


Figure S67. ^1H NMR spectrum (CDCl_3 , 250 MHz) of compound **23**.

Acquisition Time (sec)	1.0879	Comment	LN524	Date	27 Apr 2017 19:43:12		
Date Stamp	27 Apr 2017 19:43:12						
File Name	\\nmrsparc.iqm.unicamp.br\spectros\bruker250\2017\abr17\data\Julio Pastre\nmr\abr27\ftH2\3\PDATA\1\1r			Frequency (MHz)	62.90		
Nucleus	13C	Number of Transients	1002	Origin	spect	Original Points Count	16384
Owner	root	Points Count	32768	Pulse Sequence	zgpg30	Receiver Gain	574.70
SW(cyclical) (Hz)	15060.24	Solvent	CHLOROFORM-d	Spectrum Offset (Hz)			6289.9907
Spectrum Type	STANDARD	Sweep Width (Hz)	15059.78	Temperature (degree C)	25.160		

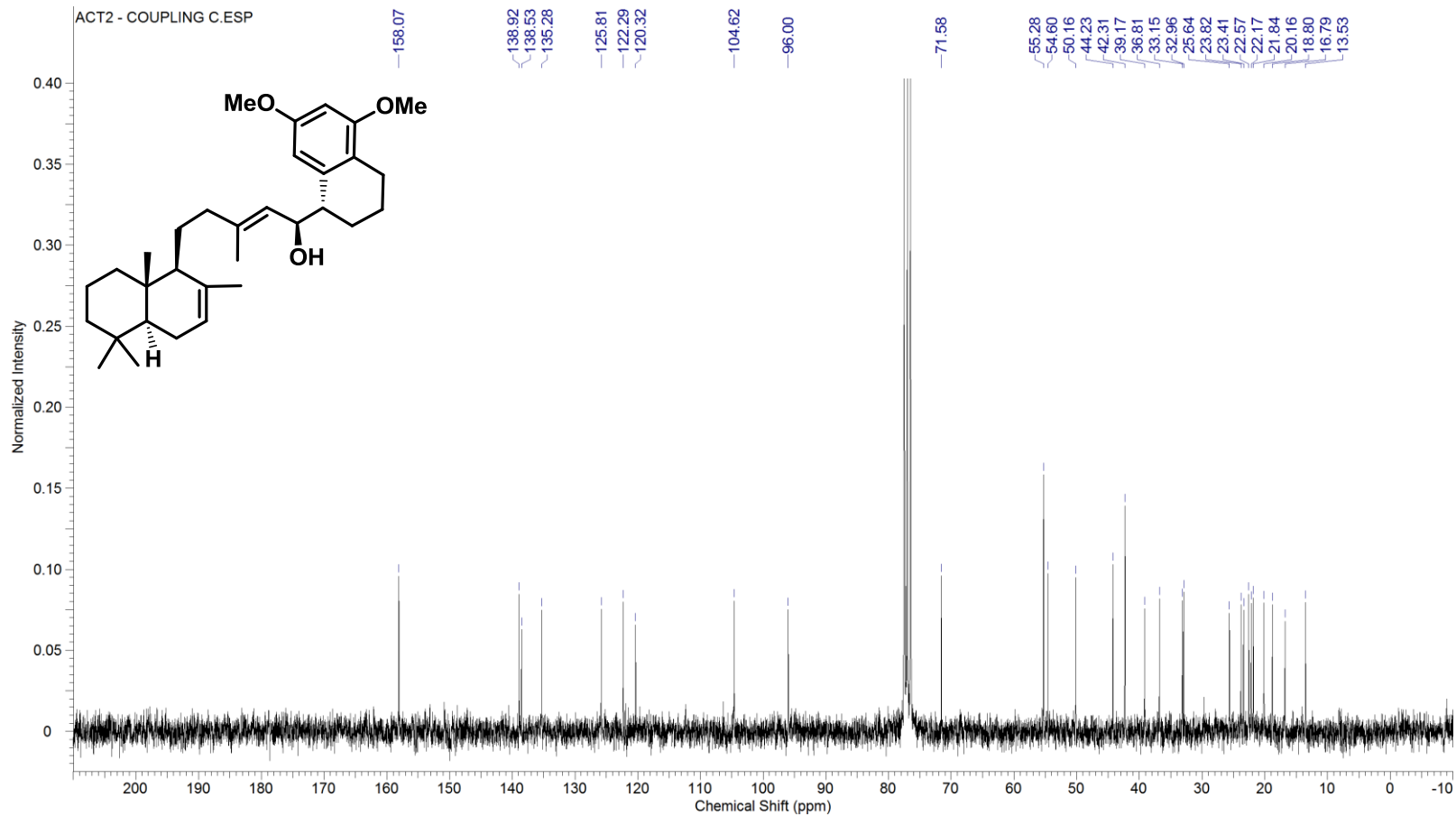


Figure S68. ¹³C NMR spectrum (CDCl₃, 62.9 MHz) of compound **23**.

Acquisition Time (sec)	0.5439	Comment	LN524	Date	27 Apr 2017 19:26:08		
Date Stamp	27 Apr 2017 19:26:08						
File Name	\\nmrparc.lqm.unicamp.br\spectros\bruker250\2017\abr17\data\Julio Pastre\nmr\abr27\ftH2\2\PDATA\1\1r				Frequency (MHz)	62.90	
Nucleus	13C	Number of Transients	444	Origin	spect	Original Points Count	8192
Owner	root	Points Count	32768	Pulse Sequence	dept135	Receiver Gain	16384.00
SW(cyclical) (Hz)	15060.24	Solvent	CHLOROFORM-d	Spectrum Offset (Hz)			6289.0518
Spectrum Type	DEPT135	Sweep Width (Hz)	15059.78	Temperature (degree C)	25.160		

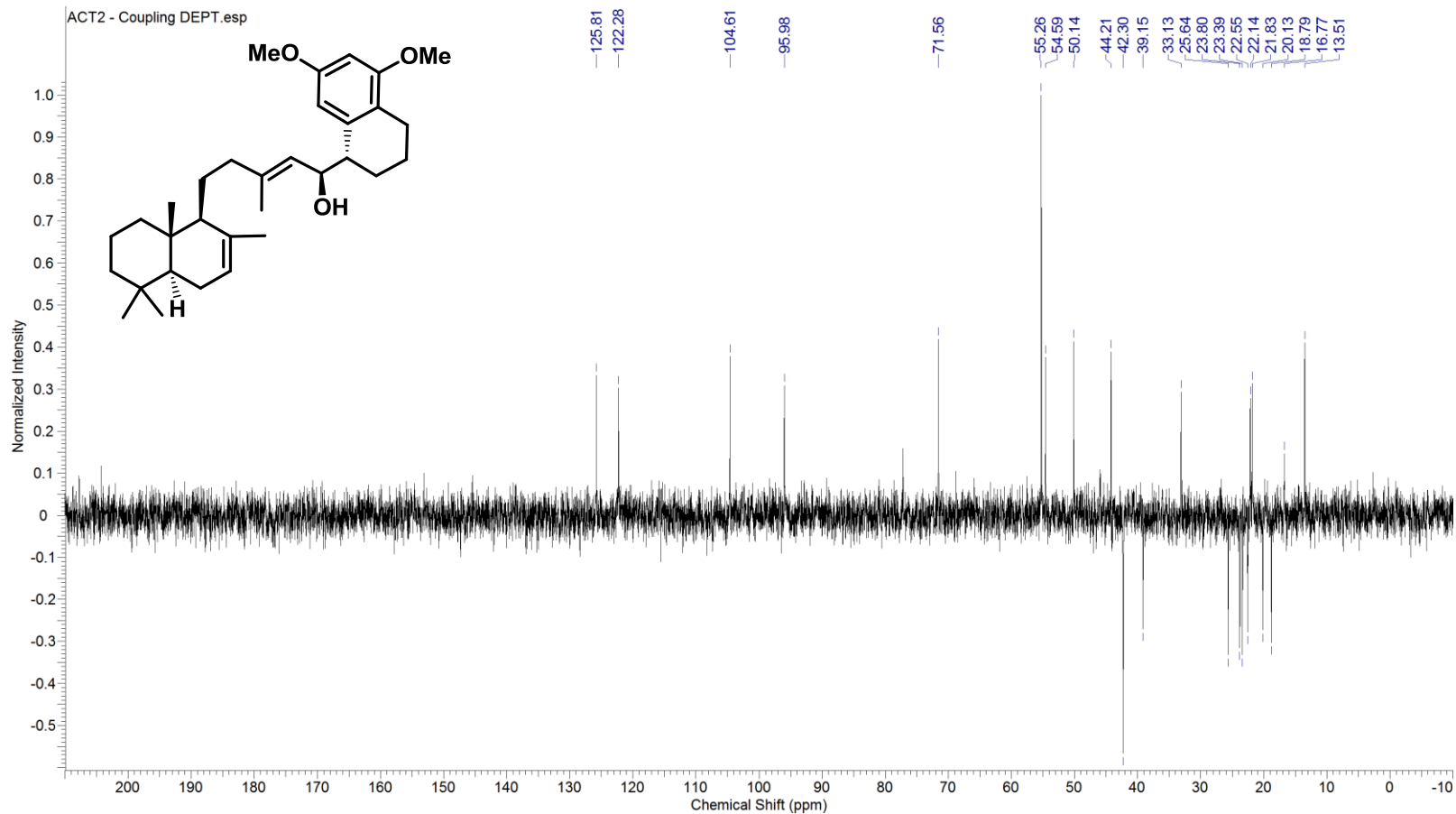


Figure S69. DEPT 135 NMR spectrum (CDCl₃, 62.9 MHz) of compound **23**.

Table 3. Comparison between ^{13}C NMR spectra of compound **23** and reported by Xu and Ye⁵

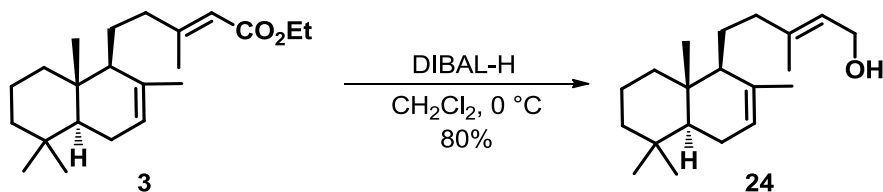
Pastre (this work)	Xu and Ye ⁵	$\Delta\delta$
13.5	13.5	0.0
16.8	16.8	0.0
18.8	18.8	0.0
20.2	20.1	+0.1
21.8	21.8	0.0
22.2	22.1	+0.1
22.6	22.6	0.0
23.4	23.5	-0.1
23.8	23.8	0.0
25.6	25.6	0.0
33.0	33.0	0.0
33.1	33.1	0.0
36.8	36.8	0.0
39.2	39.2	0.0
42.3	42.3	0.0
42.3	42.4	-0.1
44.2	44.3	-0.1
50.2	50.2	0.0
54.6	54.7	-0.1
55.3 (2CH ₃)	55.3 (2CH ₃)	0.0
-	67.9*	-
71.6	71.6	0.0
96.0	96.1	-0.1
104.6	104.8	-0.2
120.3	120.3	0.0
122.3	122.3	0.0
125.8	125.9	-0.1
135.3	135.3	0.0
138.5	138.6	-0.1
138.9	138.9	0.0
158.1 (2C)	158.1 (2C)	0.0

*Misassigned signal, probably referent to THF as impurity. Signal at 25.6 ppm is common to THF and **23**. Such impurity can also be seen in the ^1H NMR spectrum.⁵

^{13}C NMR of THF in CDCl_3 : 25.62 (CH_2) and 67.97 (CH_2O)⁷

⁷ Gottlieb, H. E.; Kotlyar, V.; Nudelman, A. *J. Org. Chem.* **1997**, 62, 7512-7515.

(*E*)-3-methyl-5-((1*S*,4*aS*,8*aS*)-2,5,5,8*a*-tetramethyl-1,4,4*a*,5,6,7,8,8*a*-octahydronaphthalen-1-yl)pent-2-en-1-ol (24**).**



A freshly prepared solution of DIBAL-H (1.0 M in CH₂Cl₂, 215 μ L, 215 μ mol, 5 equiv) was added to a solution of ester **3** (14.3 mg, 43 μ mol, 1 equiv) in dry CH₂Cl₂ (2 mL) at 0 $^\circ$ C. After stirring the reaction for 1 h at 0 $^\circ$ C, Et₂O (10 mL) and saturated aqueous solution of Rochelle's salt were added, and the reaction was vigorously stirred for 30 min at 0 $^\circ$ C and 1 h at room temperature. After separation of phases, the aqueous layer was extracted with Et₂O (10 mL). The organic phases were combined, dried over anhydrous MgSO₄ and concentrated under reduced pressure. The residue was subjected to flash chromatography (SiO₂, hexanes/EtOAc 97:3 to 90:10) to afford the alcohol **24** (10 mg, 34 μ mol) as a colorless oil in 80% yield.

TLC (SiO₂): R_f = 0.27 (hexanes/EtOAc 90:10);

$[\alpha]_{\text{D}}^{25} = +5$ (*c* 0.5, CHCl₃), $[\alpha]_{\text{D, lit}}^{25} = +12$ (*c* 0.690, CHCl₃);⁸

¹H NMR (250 MHz, CDCl₃): δ 0.76 (s, 3H), 0.86 (s, 3H), 0.88 (s, 3H), 0.80-1.04 (m, 2H), 1.56 (s, 3H), 1.69 (s, 3H), 1.05-2.09 (m, 12H), 2.13-2.31 (m, 1H), 4.09-4.20 (m, 2H), 5.33-5.47 (m, 2H);

¹³C NMR (62.9 MHz, CDCl₃): δ 13.5 (CH₃), 16.4 (CH₃), 18.8 (CH₂), 21.8 (CH₃), 22.2 (CH₃), 23.8 (CH₂), 25.6 (CH₂), 32.9 (C), 33.1 (CH₃), 36.8 (C), 39.1 (CH₂), 42.0 (CH₂), 42.3 (CH₂), 50.1 (CH), 54.4 (CH), 59.4 (CH₂), 122.3 (CH), 123.3 (CH), 135.2 (C), 140.4 (C).

⁸ Suzuki, H.; Noma, M.; Kawashima, N. *Phytochemistry*, **1983**, 22, 1294-1295.

Acquisition Time (sec)	3.1654	Comment	LN256A	Date	31 Aug 2016 09:03:12			
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Nucleus	1H	Number of Transients	43	Origin	spect	Original Points Count	16384	
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SW(cyclical) (Hz)	5175.98	Solvent	CHLOROFORM-d	Temperature (degree C) 25.160			Spectrum Offset (Hz)	1544.6561
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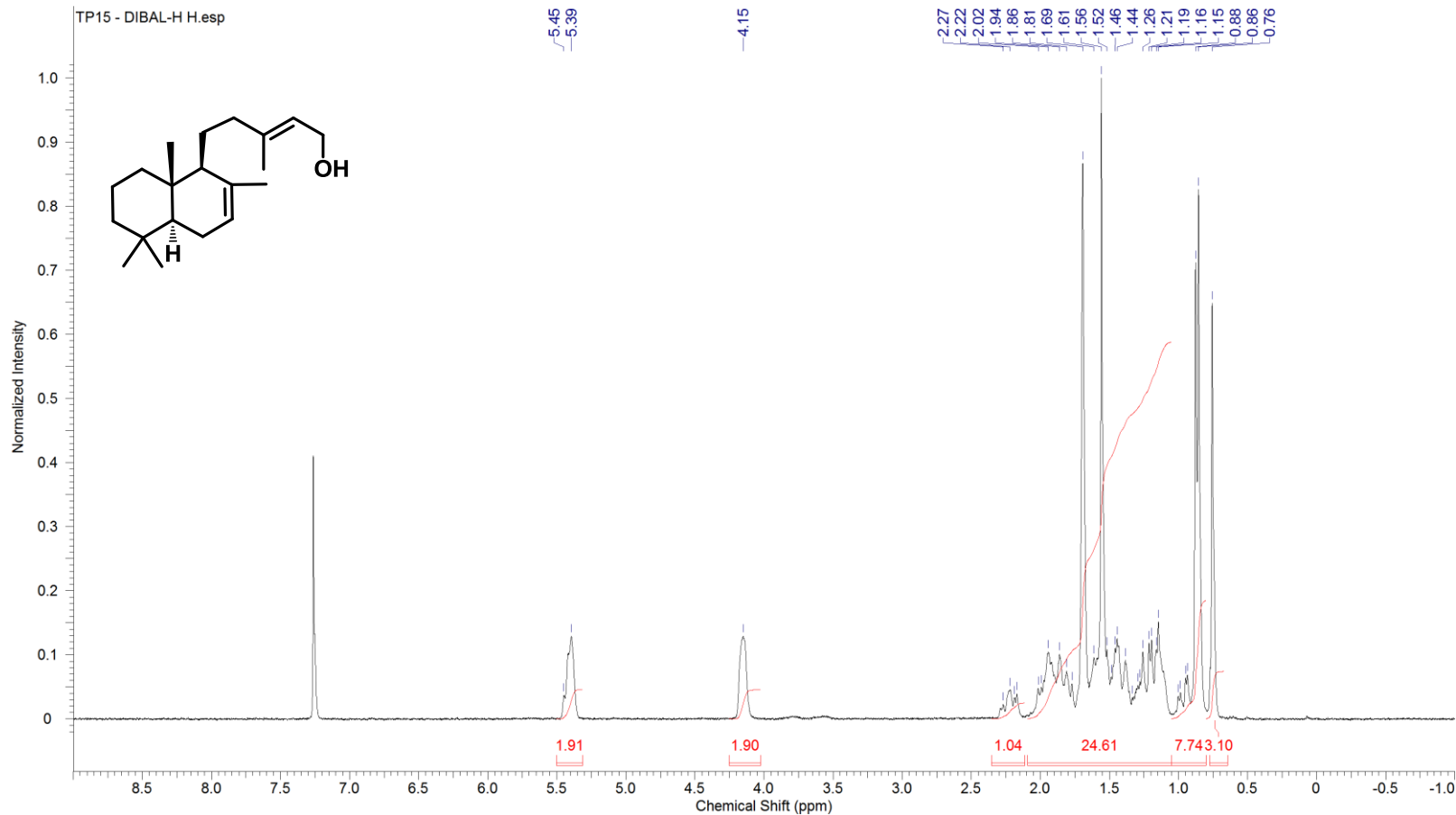


Figure S70. ¹H NMR spectrum (CDCl₃, 250 MHz) of compound **24**.

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Date Stamp	01 Sep 2016 07:05:52						
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Nucleus	¹³ C	Number of Transients	10240	Origin	spect	Original Points Count	16384
Owner	root	Points Count	32768	Pulse Sequence	zgpg30	Receiver Gain	574.70
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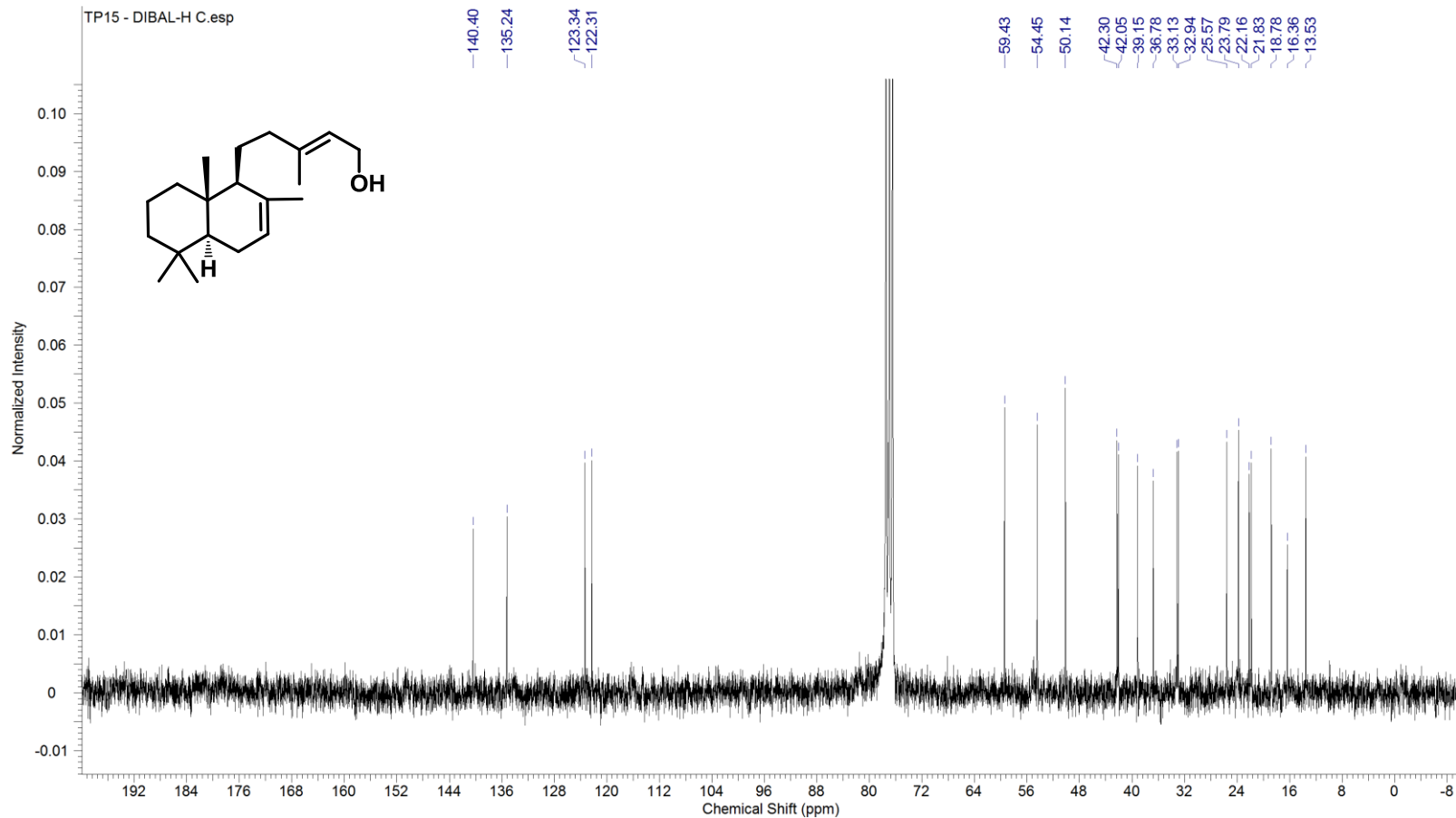


Figure S71. ¹³C NMR spectrum (CDCl₃, 62.9 MHz) of compound **24**.

Acquisition Time (sec)	0.5439	Comment	LN256	Date	31 Aug 2016 21:57:36	
Date Stamp	31 Aug 2016 21:57:36			File Name	C:\Users\Luiz\Desktop\Luiz\PhD\NMR\ago16\ago31ftH6\2\PDATA\1\1r	
Frequency (MHz)	62.90	Nucleus	¹³ C	Number of Transients	1024	Origin spect
Owner	root	Points Count	32768	Pulse Sequence	dept135	Receiver Gain 724.10
Solvent	CHLOROFORM-d			Spectrum Offset (Hz)	6289.0518	Spectrum Type DEPT135
Temperature (degree C)	25.160					SW(cyclical) (Hz) 15060.24
						Sweep Width (Hz) 15059.78

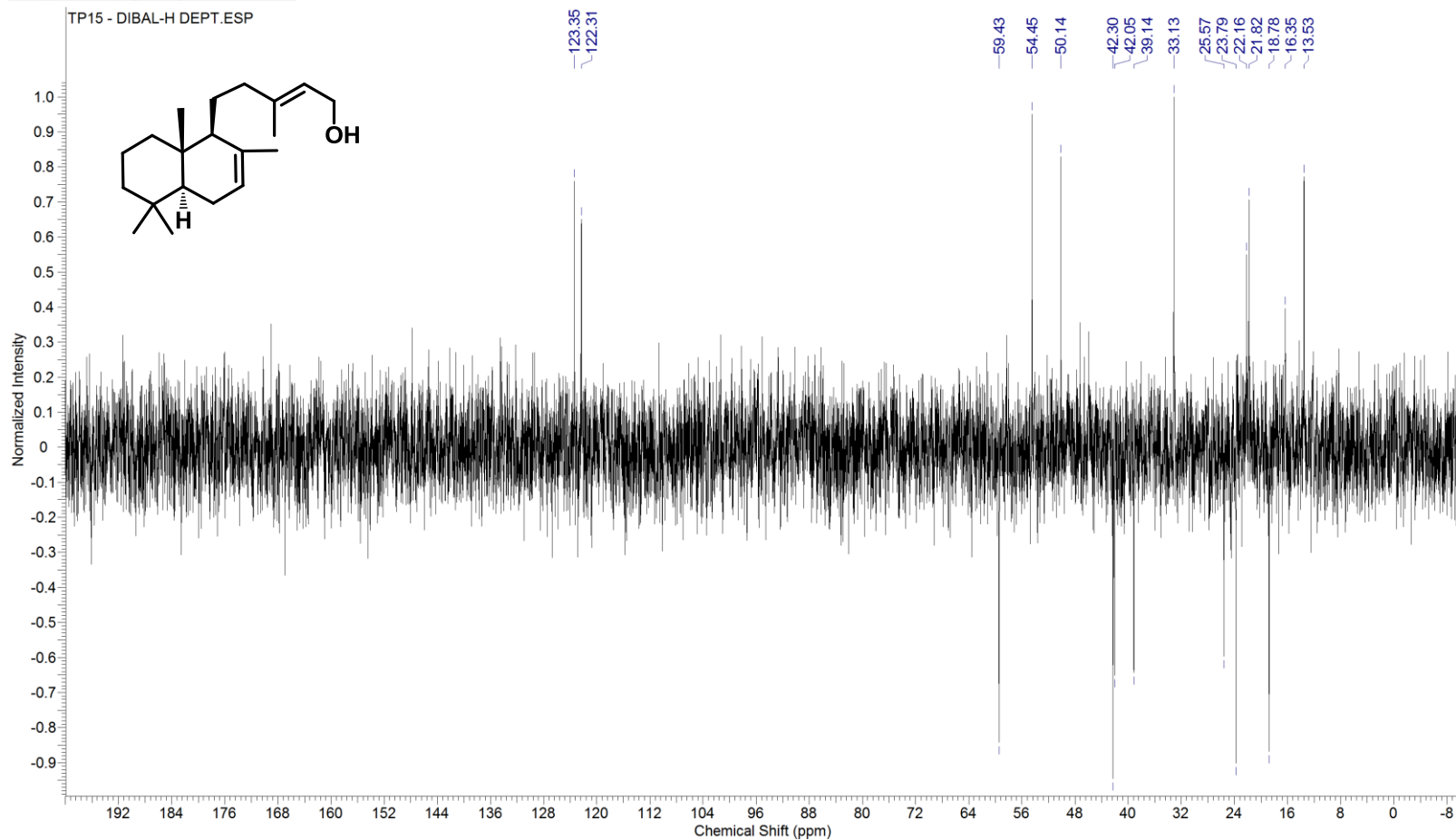


Figure S72. DEPT 135 NMR spectrum (CDCl₃, 62.9 MHz) of compound **24**.

Table 4. Comparison between ^{13}C NMR spectra of compound $\lambda^7,13\text{-(E)}$ -dien-15-ol (**24**) and reported by Kawashima and co-workers⁸

Pastre (this work)	Kawashima ⁸	$\Delta\delta$
13.5	13.5	0.0
16.4	16.3	+0.1
18.8	18.8	-0.1
21.8	21.9	0.0
22.2	22.2	0.0
23.8	23.8	0.0
25.6	25.6	0.0
32.9	32.9	0.0
33.1	33.2	-0.1
36.8	36.7	+0.1
39.1	39.2	-0.1
42.0	42.2	-0.2
42.3	42.3	0.0
50.1	50.1	0.0
54.4	54.5	-0.1
59.4	59.0	+0.4
122.3	122.3	0.0
123.3	123.7	-0.4
135.2	135.1	-0.1
140.4	139.6	-0.8