Supporting information for

A short total synthesis of (+)-omaezakianol via an epoxide-opening cascade reaction

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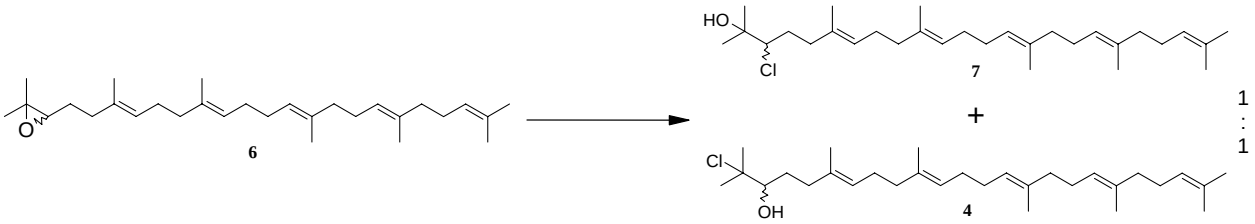
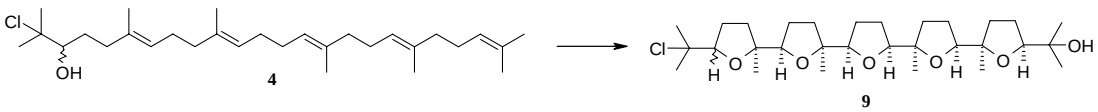
General information: ^{1}H NMR spectra were recorded in deuteriochloroform on Bruker 400/500 (400/500 MHz) spectrometers. ^{13}C NMR spectra were measured in deuteriochloroform on Bruker 400 (100 MHz) spectrometers. Chemical shifts were reported in parts per million (ppm) from tetramethylsilane with the solvent resonance as the internal standard ($CDCl_3$: 7.26 ppm for ^{1}H NMR, 77.0 ppm for ^{13}C NMR; CD_3OD: 3.31 ppm for ^{1}H NMR). Abbreviations for signal coupling are as follows: s = singlet, d = doublet; t = triplet, q = quartet, dd = doublet of doublets, m = multiplet. High-resolution mass spectrum (ES, positive) was determined on a Thermo LTQ FT Ultra Mass Spectrometer. Specific optical rotation was determined on an AP III/2w Polarimeter. Column chromatography was performed on Biotage® SP1 Flash Chromatography Purification System using a Biotage® SNAP KP-Sil cartridges (10g, 25g, 50g and 100g). All materials were purchased from commercial suppliers and used without further purification unless otherwise noted. Acetone was dried over activated 4 Å molecular sieves (activated in an oven at 100 °C for 10 h).



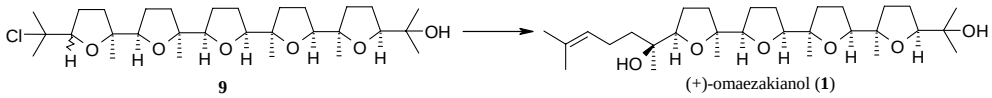
Chlorohydrin 4: To a solution of monoepoxide **6** (7.37 g, 17.2 mmol) in ether (100 mL) was added 1M HCl in ether (35 mL, 35 mmol). The mixture was stirred at room temperature for overnight. The reaction mixture was transferred to a separatory funnel, washed with saturated aqueous $NaHCO_3$, brine, dried

(Na_2SO_4), and concentrated *in vacuo*. The crude product was purified by chromatography on silica gel eluting with 5-10% EtOAc in hexanes to give compounds **4** (3.64 g, 46% yield) and **7** (3.58 g, 45% yield). Compound **4**: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 5.20-5.08 (m, 5 H), 3.48 (ddd, *J* = 10.4, 5.5, 1.9 Hz, 1H), 2.32-2.20 (m, 1H), 2.15-1.93 (m, 17H), 1.78-1.68 (m, 1H), 1.68 (d, *J* = 1.0 Hz, 3H), 1.61 (s, 3H), 1.60 (s, 12H), 1.59 (s, 3H), 1.55 (s, 3H), 1.50-1.38 (m, 1H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz) δ 135.1, 134.94, 134.88, 134.4, 131.2, 125.2, 124.4, 124.3, 78.51, 76.10, 39.76, 39.74, 39.69, 36.5, 29.8, 29.2, 28.3, 27.2, 26.8, 26.7, 26.6, 25.7, 17.7, 16.1, 16.01, 15.96 ppm. Compound **7**: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 5.25-5.05 (m, 5 H), 3.80 (dd, *J* = 11.3, 1.8 Hz, 1H), 2.36-2.26(m, 1H), 2.15-1.90 (m, 17H), 1.75-1.53 (m, 2H), 1.68 (d, *J* = 1.0 Hz, 3H), 1.60 (s, 15H), 1.30 (s, 3H), 1.28 (s, 3H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz) δ 135.1, 134.9, 133.2, 131.3, 125.8, 124.5, 124.4, 124.3, 73.7, 72.7, 39.76, 39.74, 39.67, 37.1, 31.4, 28.3, 26.8, 26.7, 26.6, 25.7, 25.1, 17.7, 16.1, 16.0, 15.9 ppm.



Pentacyclic compound 9: To a stirred solution of chlorohydrin **4** (0.709 g, 1.3 mmol) in MeCN-dimethoxymethane (DMM) (150 mL, 1:2, v/v) were added 100 mL of buffer (0.5 M solution of $Na_2B_4O_7{\cdot}10H_2O$ in 4×10^{-4} aqueous Na_2EDTA), n-Bu_4NHSO_4 (0.143 g, 0.42 mmol), and Shi catalyst **8** (1.18 g, 4.57 mmol). The mixture was then cooled in an ice bath, and a solution of Oxone® (8.13g, 13.2 mmol) in 60 mL 4×10^{-4} aqueous Na_2EDTA and a solution of K_2CO_3 (7.65 g, 55.4 mmol) in 60 mL water were added simultaneously via two syringe pumps over 1 h at 0°C. The mixture was stirred for additional 30 min at 0°C before it was diluted with H_2O (30 mL) and extracted with EtOAc (3 × 60 mL). The combined extracts were washed with brine, dried (Na_2SO_4), and concentrated *in vacuo*. The crude product was then dissolved in dry acetone (15 mL), and (1*R*)-10-camphorsulfonic acid (0.35 g, 1.5 mmol) was added. The solution was stirred at ambient temperature for 1 h. The reaction mixture was diluted with EtOAc (100 mL), washed with saturated aqueous $NaHCO_3$ (20 mL), brine (20 mL), dried (Na_2SO_4), and concentrated *in vacuo*. The crude product was purified by chromatography on silica gel eluting with 25-50% EtOAc in hexanes to give compound **9** as a 1:1 diastereomeric mixture (150 mg, 21% yield from **4**). ^{1}H NMR (CD_3OD, 400 MHz) δ 4.04-3.88 (m, 3H), 3.86-3.64 (m, 3H), 2.34-1.54 (m,

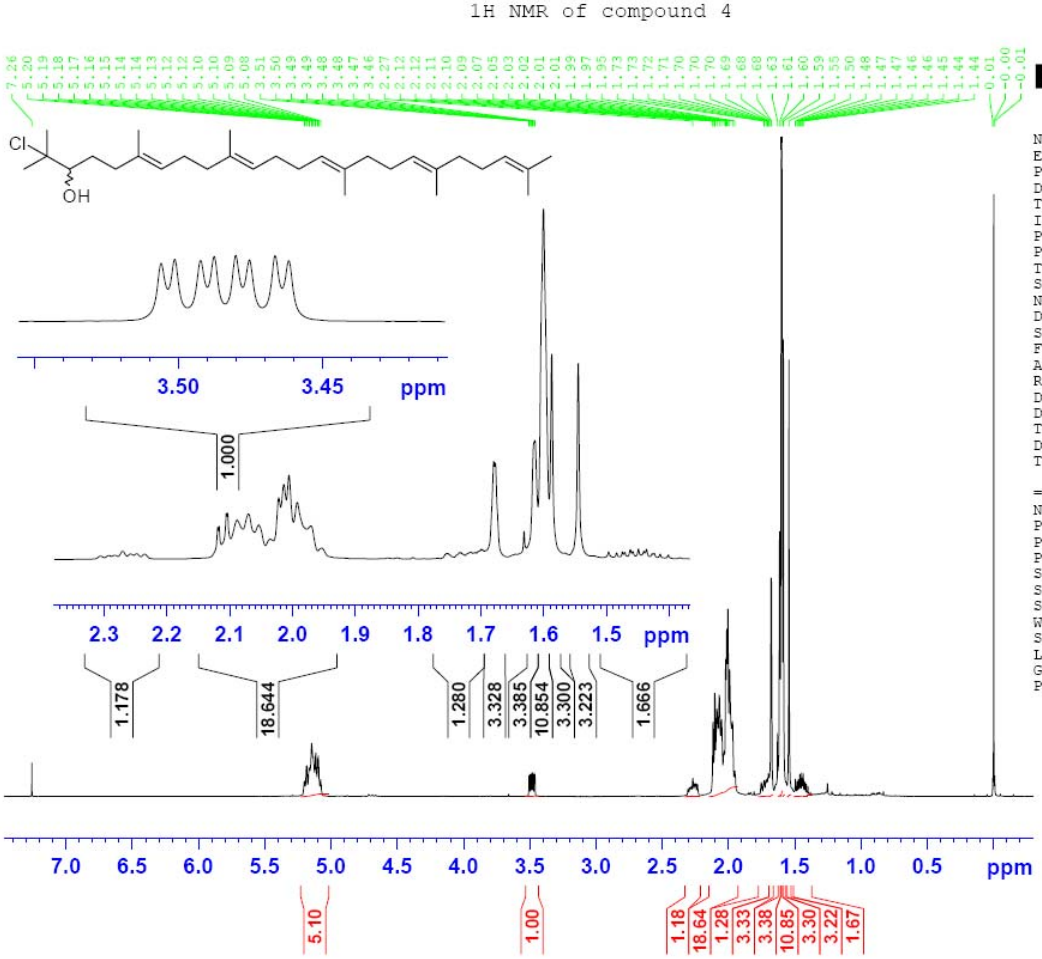
20H), 1.532 (s, 1.5H), 1.526 (s, 1.5H), 1.51 (s, 1.5H), 1.50 (s, 1.5H), 1.20-1.13 (multiple singlets, 15H), 1.08 (s, 3H) ppm.



9 (+)-omaezakianol (**1**)

(+)-omaezakianol (1): To a solution of **9** (0.15 g, 0.28 mmol) in Et_2O (4 mL) was added small pieces of Na (0.068 g, 2.96 mmol). The mixture was then heated at 60 °C in a sealed tube for 4 h. After cooling to room temperature, the excess Na was slowly quenched with 2-propanol (5 mL) and then water (5 mL). The mixture was then diluted with EtOAc (60 mL), washed with saturated aqueous $NaHCO_3$ (15 mL), brine (15 mL), dried (Na_2SO_4), and concentrated *in vacuo*. The crude product was purified by chromatography on silica gel eluting with 25-45% EtOAc in hexanes to give compound **1** (107 mg, 76% yield). $[\alpha]^{23}_D$ = +17.1 (c = 1.0, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 500 MHz) δ 5.09 (br t, *J* = 7.0 Hz, 1H), 4.01 (dd, *J* = 9.9, 5.9 Hz, 1H), 3.87 (t, *J* = 7.1 Hz, 1H), 3.83 (dd, *J* = 9.9, 6.2 Hz, 1H), 3.82 (dd, *J* = 7.1, 6.1 Hz, 1H), 3.75 (t, *J* = 7.4 Hz, 1H), 3.61 (br s, 1H), 3.16 (br s, 1H), 2.15-1.68 (m, 14H), 1.67 (s, 3H), 1.60 (s, 3H), 1.58-1.35 (m, 5H), 1.32 (ddd, *J* = 13.4, 12.0, 5.5 Hz, 1H), 1.22 (s, 3H), 1.21 (s, 3H), 1.15 (s, 3H), 1.14 (s, 3H), 1.13 (s, 3H), 1.05 (s, 3H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz) δ 131.4, 124.7, 85.5 (2C), 85.0, 84.8, 84.5, 84.2, 84.1, 83.6, 73.1, 71.7, 38.5, 35.9, 31.9, 31.0, 28.6, 28.1, 28.0, 26.51, 26.49, 26.2, 25.7, 25.2, 25.0, 24.8, 24.7, 22.4, 21.0, 17.6 ppm HRMS (ES, positive) $C_{30}H_{53}O_6$ $[M+H]^+$: calcd.: 509.3842; found: 509.3838.

1H NMR of compound 4



BRUKER

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NS	32
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SWH	8223.685 Hz
FIDRES	0.125483 Hz
AQ	3.9846387 sec
RG	20.2
DW	60.800 usec
DE	6.50 usec
TE	297.9 K
D1	2.00000000 sec
TD0	1
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NUC1	1H
P1	8.90 usec
PL1	-2.00 dB
PL1W	17.31766129 W
SFO1	400.3324722 MHz
SI	65536
SF	400.3300085 MHz
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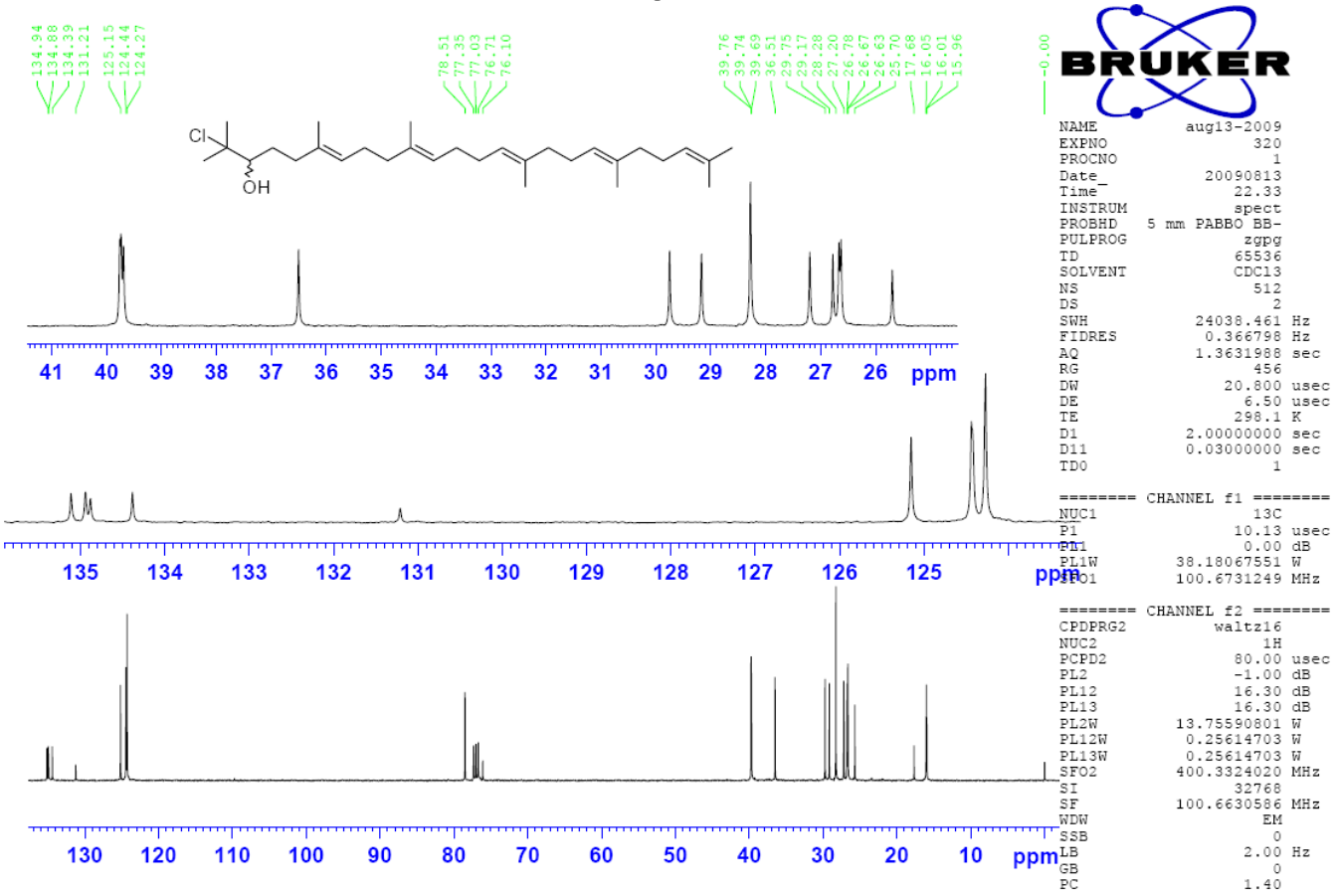
SSB	0
LB	0.30 Hz
GB	0
PC	1.00

13C NMR of compound 4



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DS	2
SWH	24038.461 Hz
FIDRES	0.366798 Hz
AQ	1.3631988 sec
RG	456
DW	20.800 usec
DE	6.50 usec
TE	298.1 K
D1	2.00000000 sec
D11	0.03000000 sec
TD0	1
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P1	10.13 usec
PL1	0.00 dB
PL1W	38.18067551 W
SFO1	100.6731249 MHz
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PCPD2	80.00 usec
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PL12	16.30 dB
PL13	16.30 dB
PL2W	13.75590801 W
PL12W	0.25614703 W
PL13W	0.25614703 W
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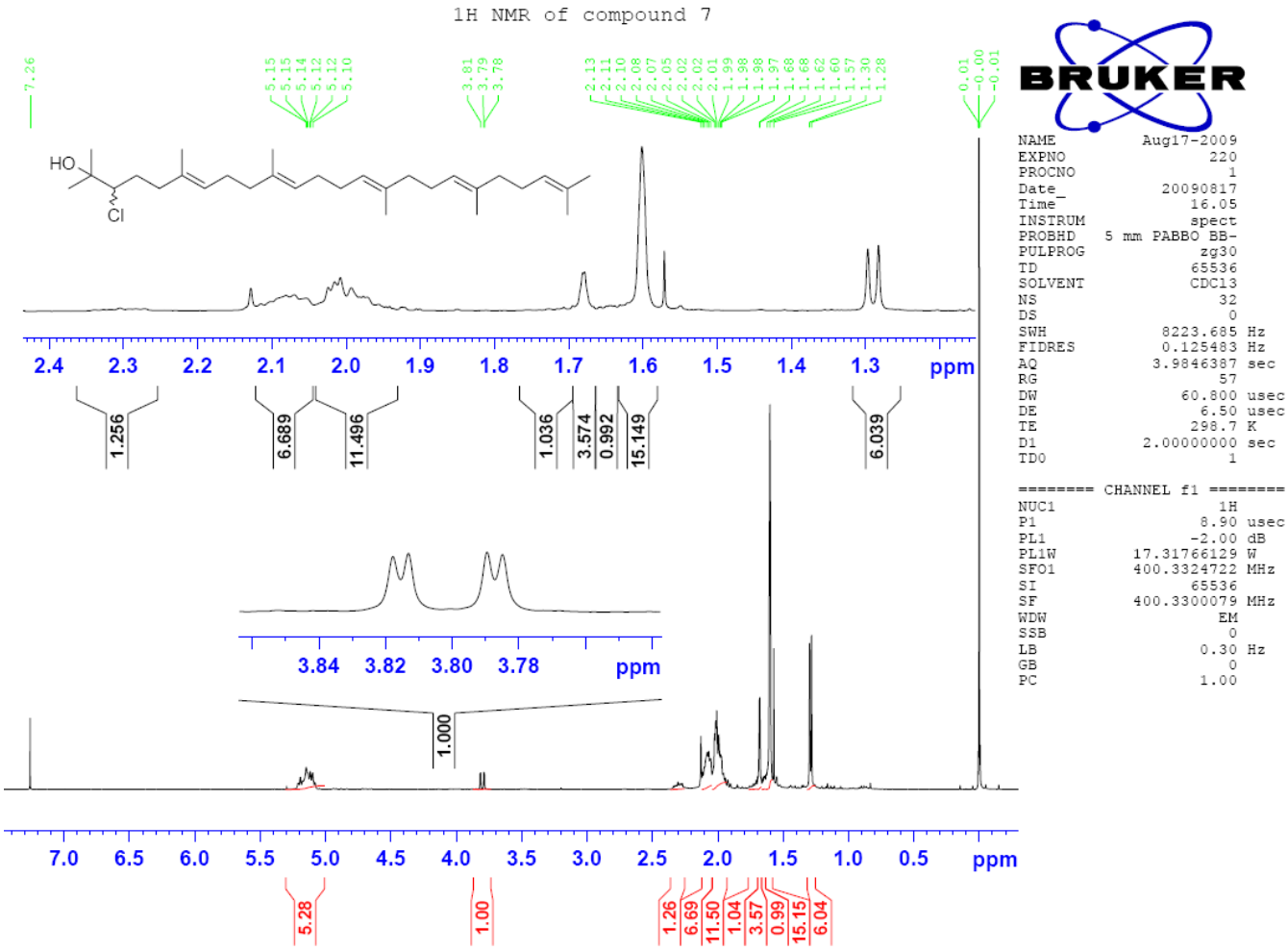
SI	32768
SF	100.6630586 MHz
WDW	EM
SSB	0
LB	2.00 Hz
GB	0
PC	1.40


1H NMR of compound 7
BRUKER
HO
Cl
NAME Aug17-2009
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PROCNO 1
Date_ 20090817
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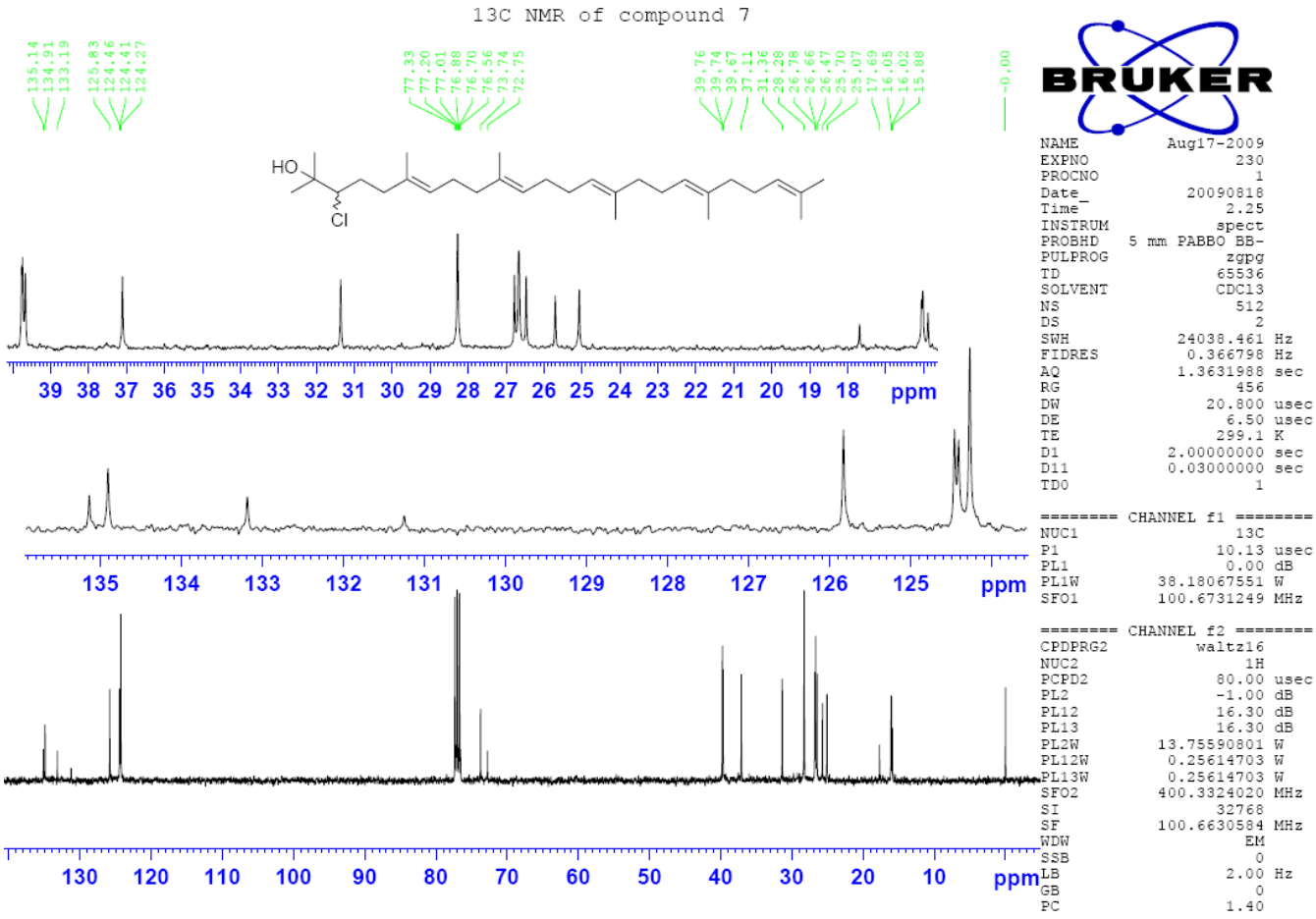
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 32
DS 0
SWH 8223.685 Hz
FIDRES 0.125483 Hz
AQ 3.9846387 sec
RG 57
DW 60.800 usec
DE 6.50 usec
TE 298.7 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 8.90 usec
PL1 -2.00 dB
PL1W 17.31766129 W
SFO1 400.3324722 MHz
SI 65536
SF 400.3300079 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
ppm



BRUKER

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SWH	24038.461 Hz
FIDRES	0.366798 Hz
AQ	1.3631988 sec
RG	456
DW	20.800 usec
DE	6.50 usec
TE	299.1 K
D1	2.00000000 sec
D11	0.03000000 sec
TD0	1
======== CHANNEL f1 ========	
NUC1	13C
P1	10.13 usec
PL1	0.00 dB
PL1W	38.18067551 W
SFO1	100.6731249 MHz
======== CHANNEL f2 ========	
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NUC2	1H
PCPD2	80.00 usec
PL2	-1.00 dB
PL12	16.30 dB
PL13	16.30 dB
PL2W	13.75590801 W
PL12W	0.25614703 W
PL13W	0.25614703 W
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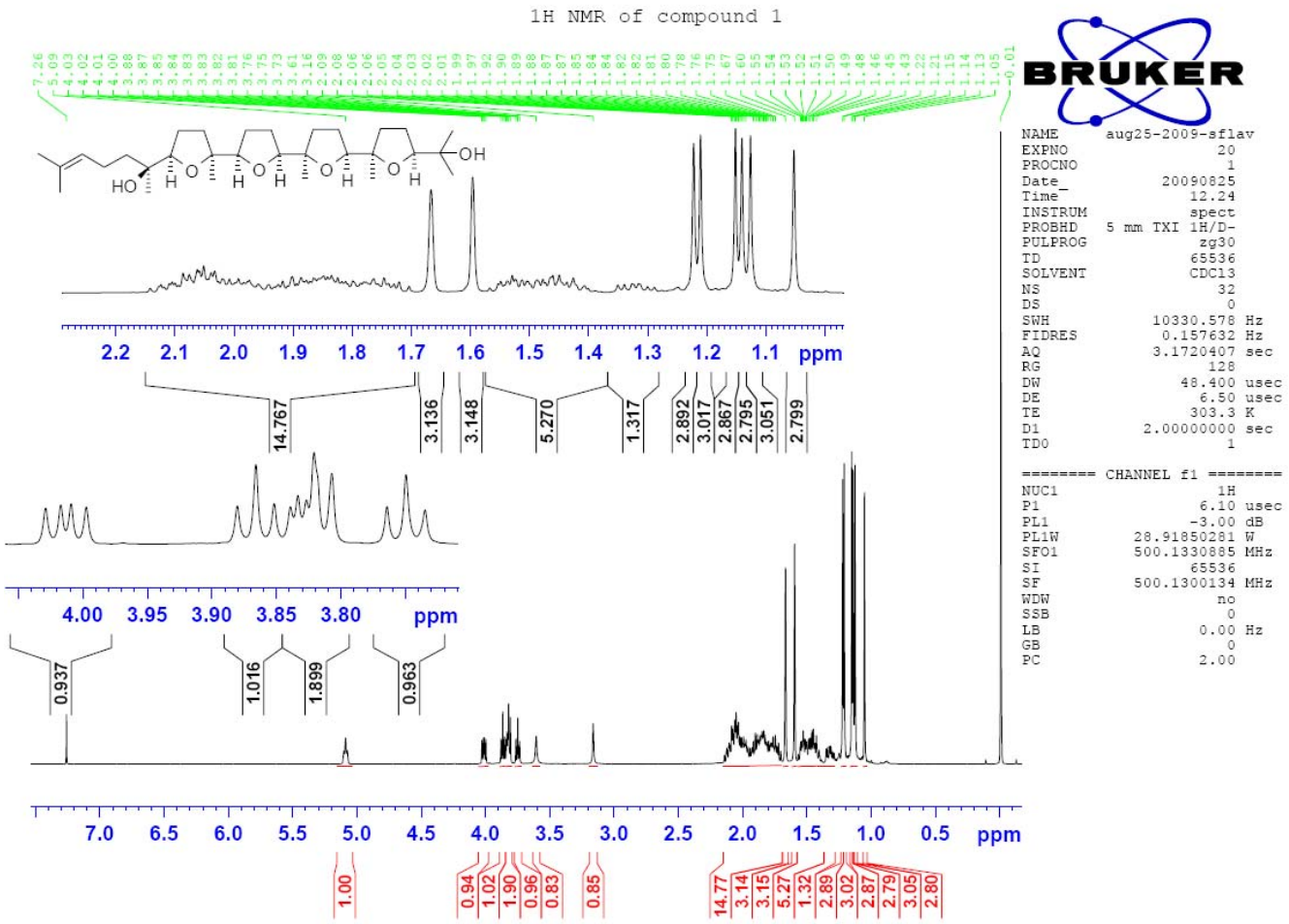
SI	32768
SF	100.6630584 MHz
WDW	EM
SSB	0
LB	2.00 Hz
GB	0
PC	1.40


1H NMR of compound 1
BRUKER
NAME aug25-2009-sflav
EXPNO 20
PROCNO 1
Date_ 20090825
Time 12.24
INSTRUM spect
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PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 32
DS 0
SWH 10330.578 Hz
FIDRES 0.157632 Hz
AQ 3.1720407 sec
RG 128
DW 48.400 usec
DE 6.50 usec
TE 303.3 K
D1 2.00000000 sec
TD0 1
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PL1 -3.00 dB
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SI 65536
SF 500.1300134 MHz
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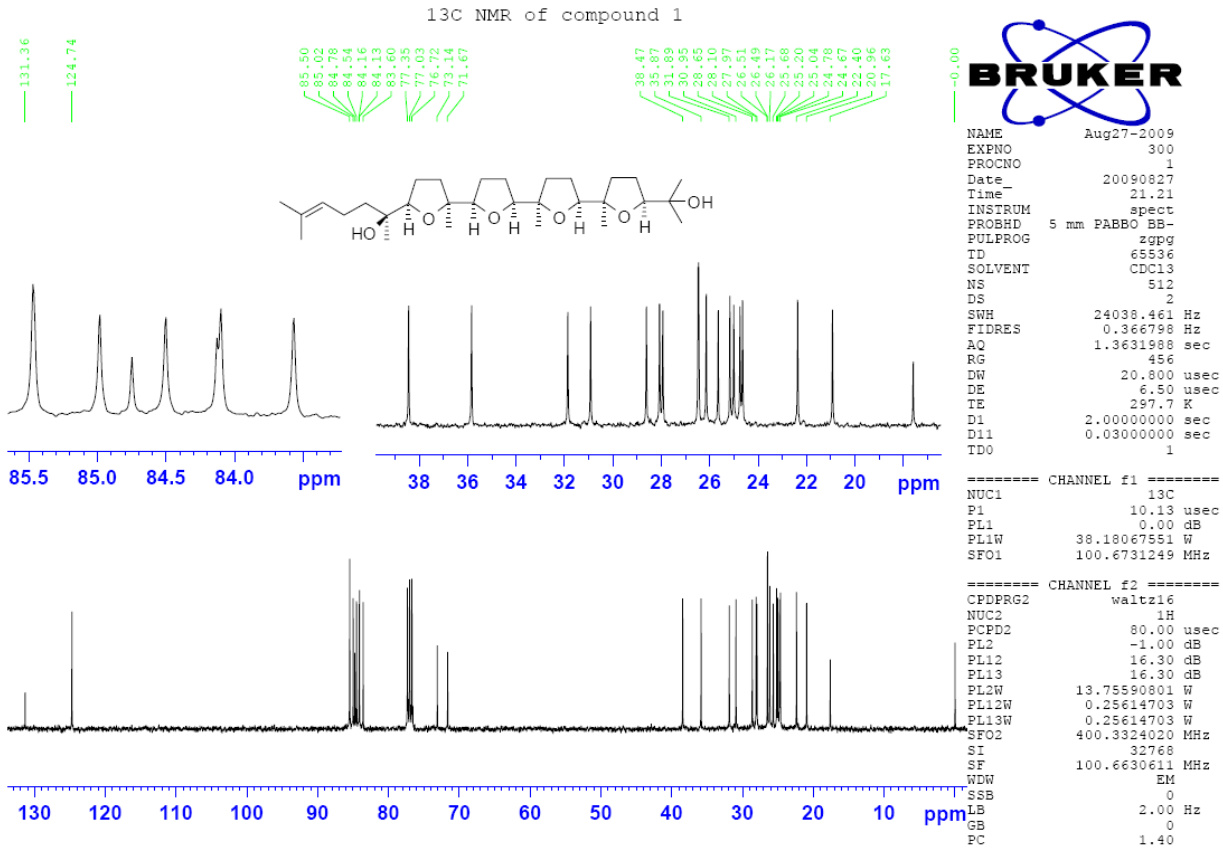
SSB 0
LB 0.00 Hz
GB 0
PC 2.00
HO
OH
ppm



BRUKER

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SOLVENT	CDCl3
NS	512
DS	2
SWH	24038.461 Hz
FIDRES	0.366798 Hz
AQ	1.3631988 sec
RG	456
DW	20.800 usec
DE	6.50 usec
TE	297.7 K
D1	2.00000000 sec
D11	0.03000000 sec
TD0	1
======== CHANNEL f1 ========	
NUC1	13C
P1	10.13 usec
PL1	0.00 dB
PL1W	38.18067551 W
SFO1	100.6731249 MHz
======== CHANNEL f2 ========	
CPDPRG2	waltz16
NUC2	1H
PCPD2	80.00 usec
PL2	-1.00 dB
PL12	16.30 dB
PL13	16.30 dB
PL2W	13.75590801 W
PL12W	0.25614703 W
PL13W	0.25614703 W
SFO2	400.3324020 MHz
SI	32768
SF	100.6630611 MHz
WDW	EM
SSB	0
LB	2.00 Hz
GB	0
PC	1.40