

Supporting Information for

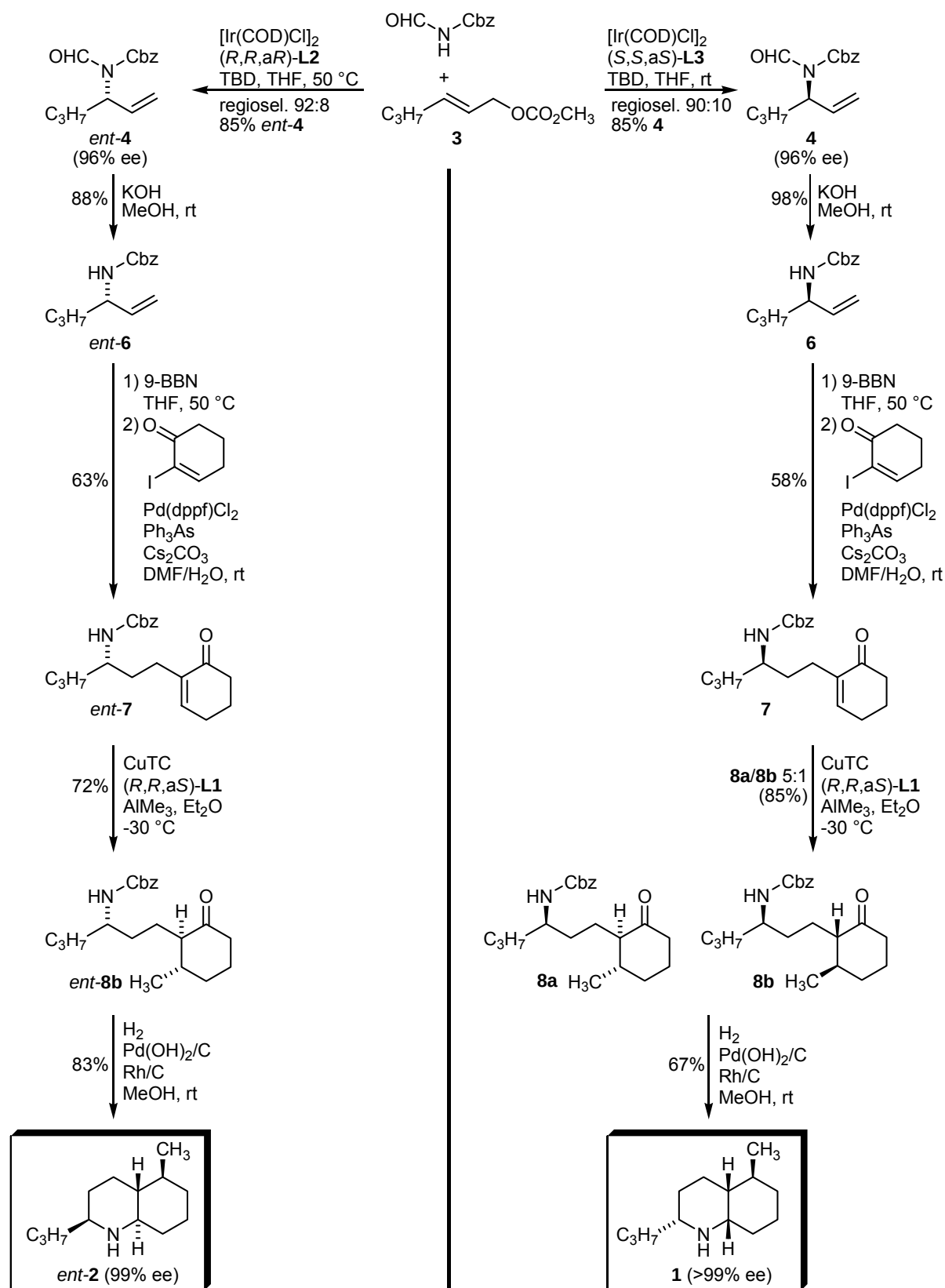
Enantioselective Syntheses of the Alkaloids *cis*-195A (Pumiliotoxin C) and *trans*-195A Based on Multiple Applications of Asymmetric Catalysis

Martin Gärtner, Jianping Qu, and Günter Helmchen*

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1. Summary of the Optimal Routes



2. Determination of Regioselectivity (cf. Table 1)

Current Data Parameters

NAME he_dh3r
EXPNO 10
PROCNO 1

F2 - Acquisition Parameters

Date 20090506
Time 9.04
INSTRUM spect
PROBHD 5 mm TBO 1H-BB
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 16
DS 0
SWH 2796.421 Hz
FIDRES 0.085340 Hz
AQ 5.8589683 sec
RG 645.1
DW 178.800 usec
DE 12.50 usec
TE 295.2 K
D1 1.00000000 sec
TD0 1

===== CHANNEL f1 =====

NUC1 1H
P1 12.60 usec
PL1 0.00 dB
SFO1 199.9209726 MHz

F2 - Processing parameters

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SF 199.9200077 MHz
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SSB 0
LB 0.10 Hz
GB 0
PC 1.00

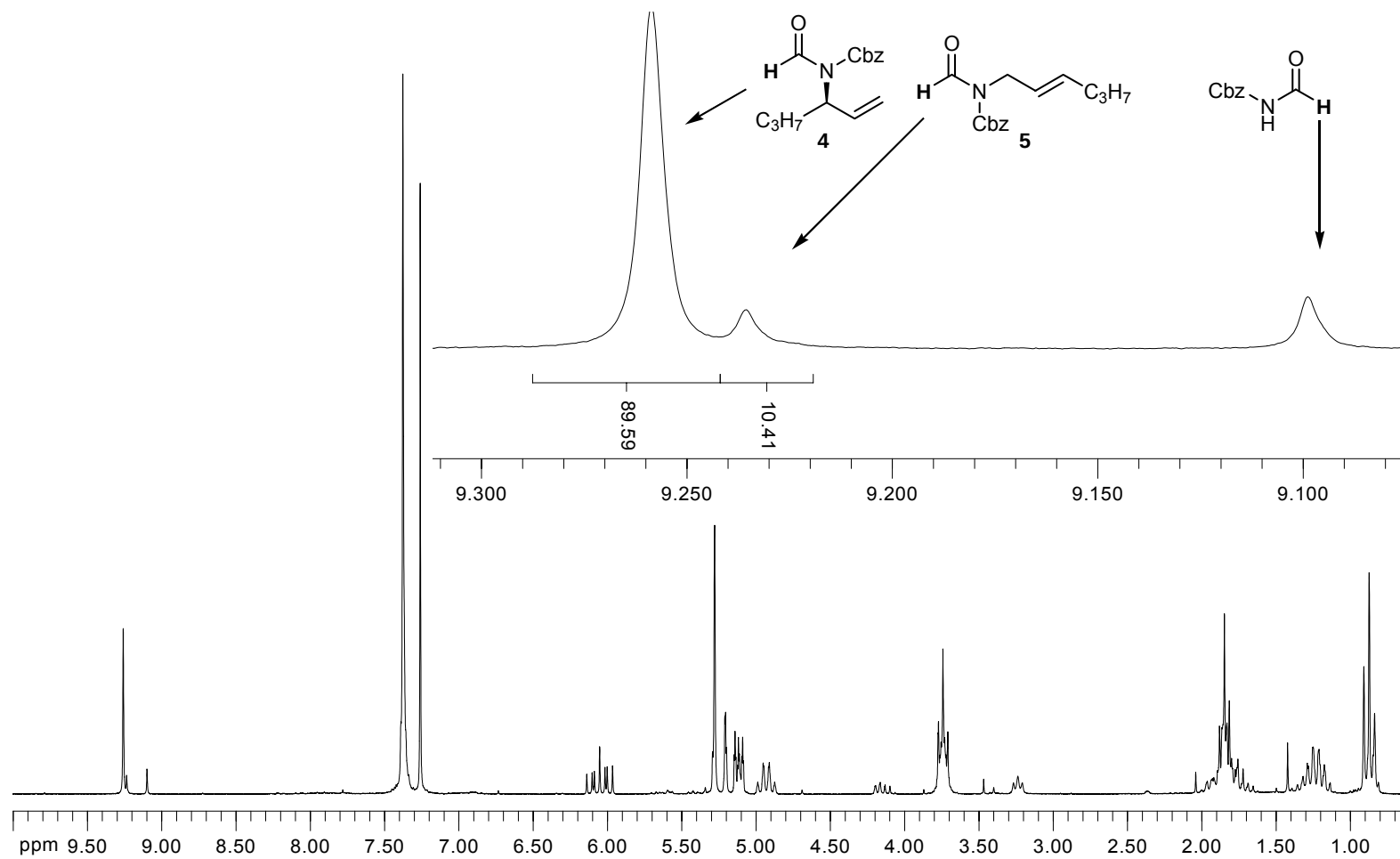


Figure 1: ^1H NMR of crude **4** (4/5 90:10).

3. Determination of Enantiomeric Excesses (cf. Tables 1, 2)

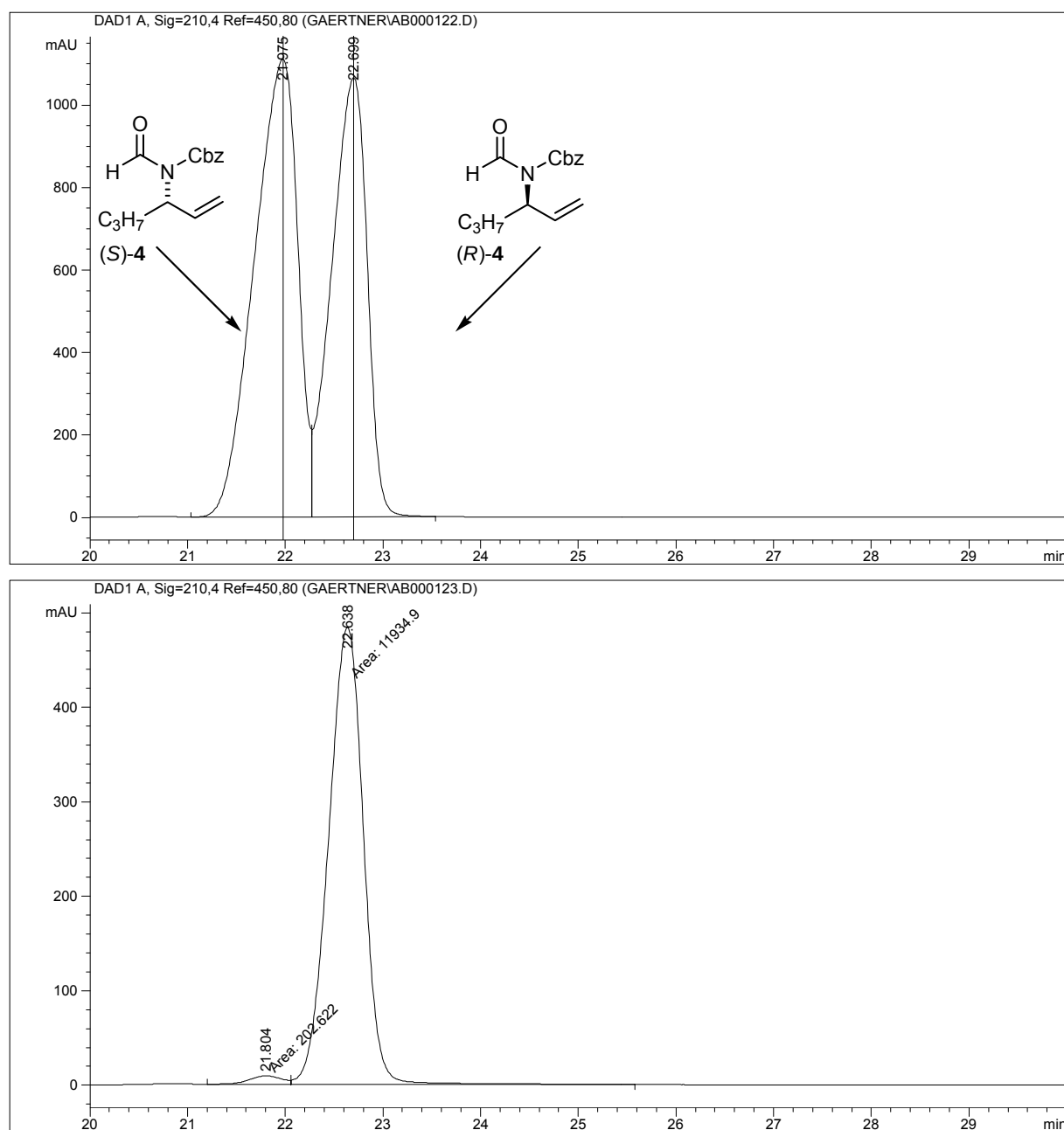


Figure 2: HPLC diagrams of racemic **4** (upper diagram) and enantioenriched (+)-(*R*)-**4** (lower diagram, 97% ee).

Instrument: HP 1100 Liquid Chromatograph

Column: Daicel Chiralcel OD-H (250 x 4.6 mm, 5 μ m) with guard cartridge OD-H (10 x 4 mm, 5 μ m).

Conditions: *n*-hexane/*i*PrOH 99.5:0.5, flow 0.5 mLmin⁻¹, 25 °C, λ = 210 nm.

Retention Times: $t_R((-)-(S)-4)$ = 22.0 min,
 $t_R((+)-(R)-4)$ = 22.7 min.

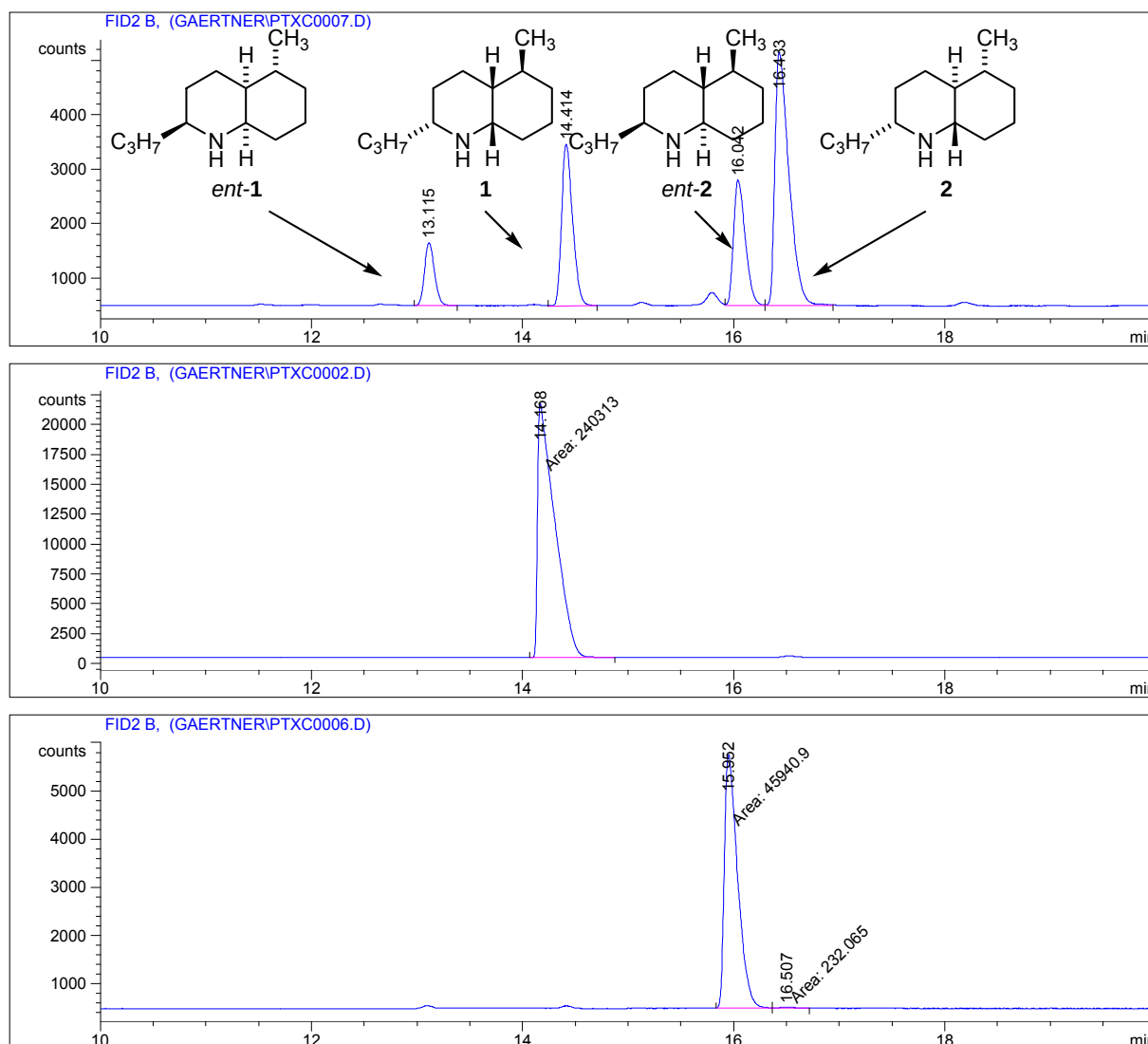


Figure 3: GC diagrams of racemic **1** and **2** (upper diagram), entioenriched **1** (middle diagram, >99% ee) and entioenriched **ent-2** (lower diagram, 99% ee).

Instrument: HP 5890 Gas Chromatograph

Column: Chrompack Permethyl- β -CD (WCOT fused silica, Cp-Cyclodextrin-B-236-M-19 (50 m x 0.25 mm)).

Conditions: isothermal 130 °C

Retention Times: $t_R((2S,4aS,5R,8aR)-(+)-\mathbf{1}) = 13.1$ min,
 $t_R((2R,4aR,5S,8aS)-(-)-\mathbf{1}) = 14.4$ min,
 $t_R((2S,4aR,5S,8aR)-(+)-\mathbf{2}) = 16.0$ min,
 $t_R((2R,4aS,5R,8aS)-(-)-\mathbf{2}) = 16.4$ min.

4. Determination of Diastereoselectivity (cf. Table 2)

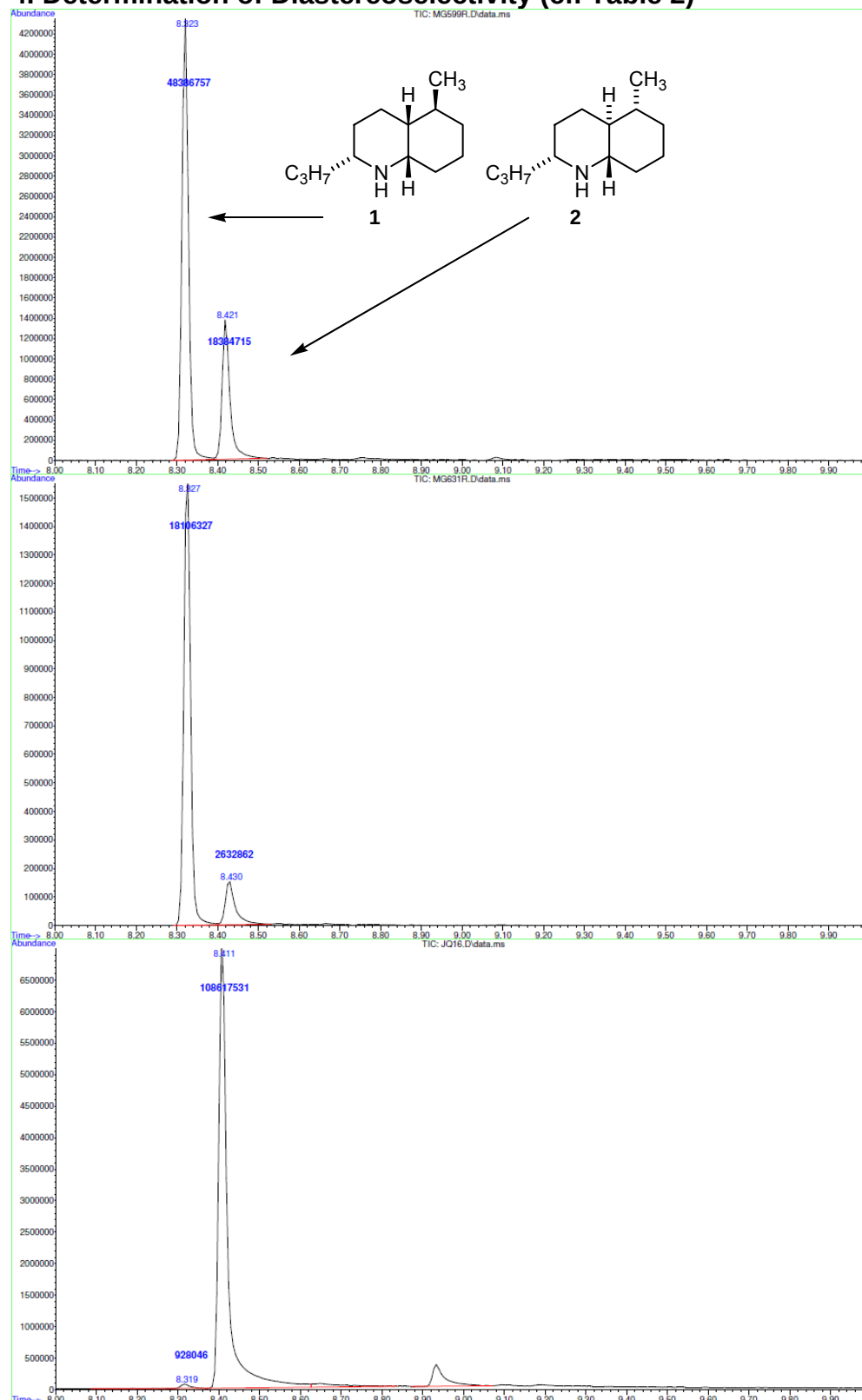
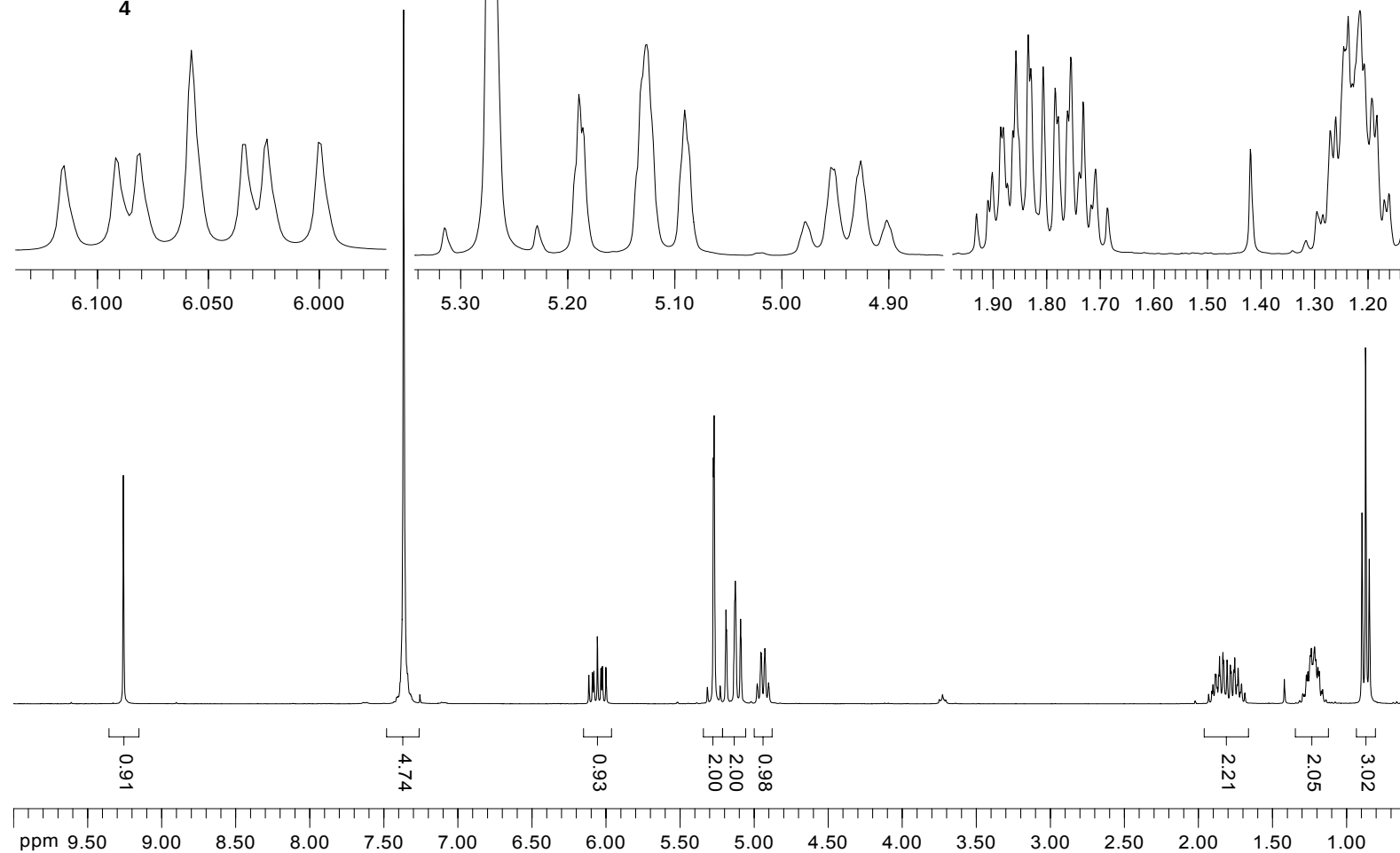
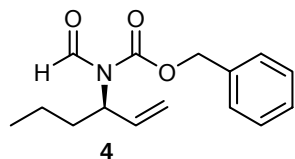


Figure 4: GC-MS chromatograms obtained after reductive amination.
 Upper diagram: Table 2, Entry 1, **1/2** 2:1;
 Middle diagram: Table 2, Entry 2, **1/2** >5:1;
 Lower diagram: Table 2, Entry 3, **1/2** <1:99.

5. ¹H and ¹³C NMR Spectra

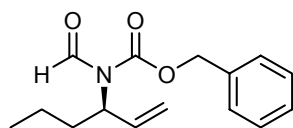


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PROCNO 1

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PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 16
DS 2
SWH 5995.204 Hz
FIDRES 0.182959 Hz
AQ 2.7329011 sec
RG 35.9
DW 83.400 usec
DE 6.00 usec
TE 300.0 K
D1 0.10000000 sec
TD0 2

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NUC1 1H
P1 11.50 usec
PL1 -2.20 dB
SFO1 300.1318008 MHz

F2 - Processing parameters
SI 16384
SF 300.1300000 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00



4

162.924

153.806

136.495

134.709

128.785

128.730

128.421

117.427

68.740

54.893

33.852

19.535

13.650

Current Data Parameters

NAME c090507ghdh.1V

EXPNO 3

PROCNO 1

F2 - Acquisition Parameters

Date 20090507

Time 7.33

INSTRUM spect

PROBHD 5 mm QNP 1H/13

PULPROG zgpg30

TD 65536

SOLVENT CDCl3

NS 224

DS 4

SWH 18832.393 Hz

FIDRES 0.287360 Hz

AQ 1.7400308 sec

RG 13004

DW 26.550 usec

DE 6.00 usec

TE 300.0 K

D1 1.0000000 sec

d11 0.0300000 sec

DELTA 0.89999998 sec

TD0 32

===== CHANNEL f1 =====

NUC1 13C

P1 11.60 usec

PL1 1.00 dB

SFO1 75.4764278 MHz

===== CHANNEL f2 =====

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NUC2 1H

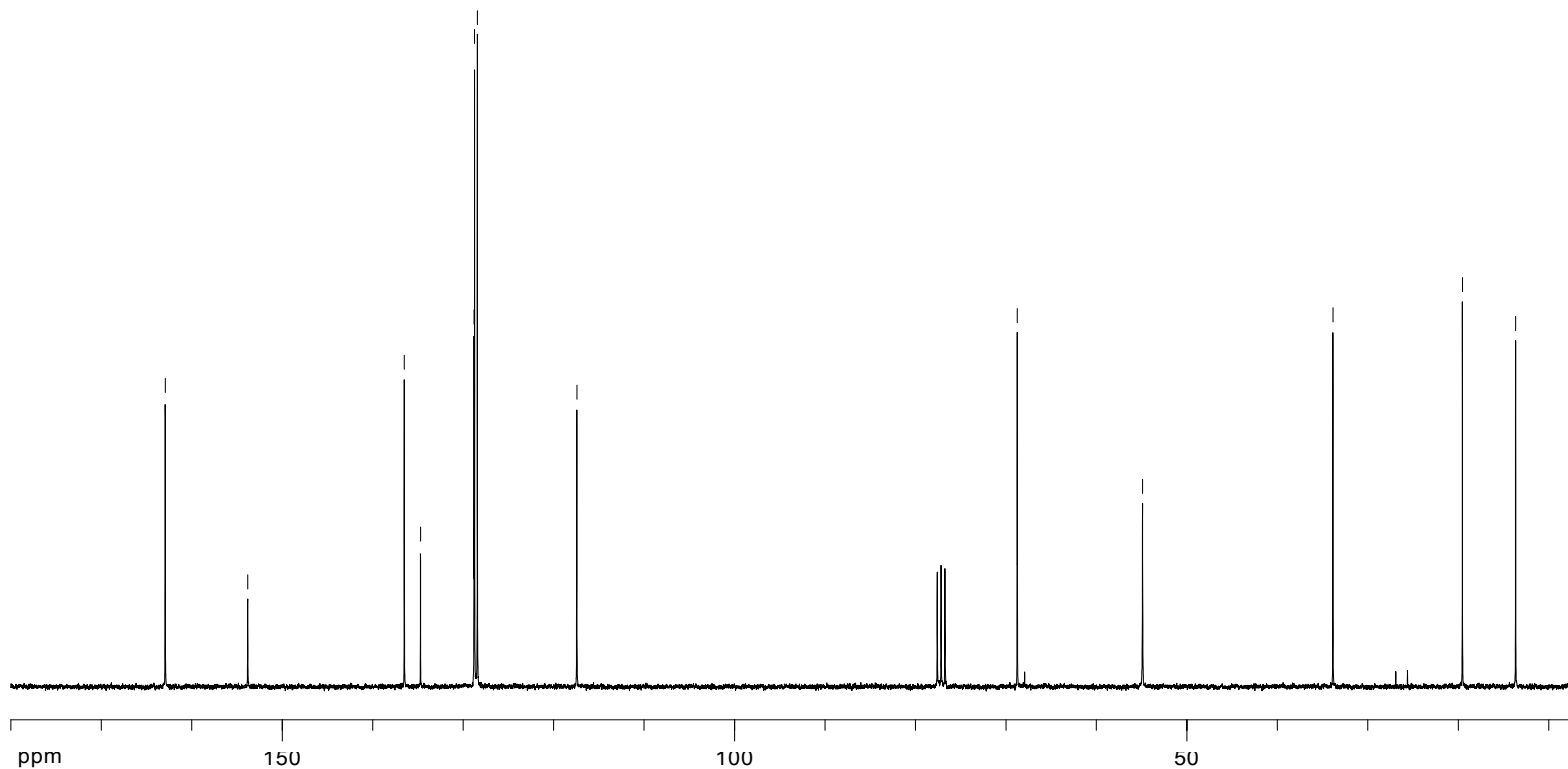
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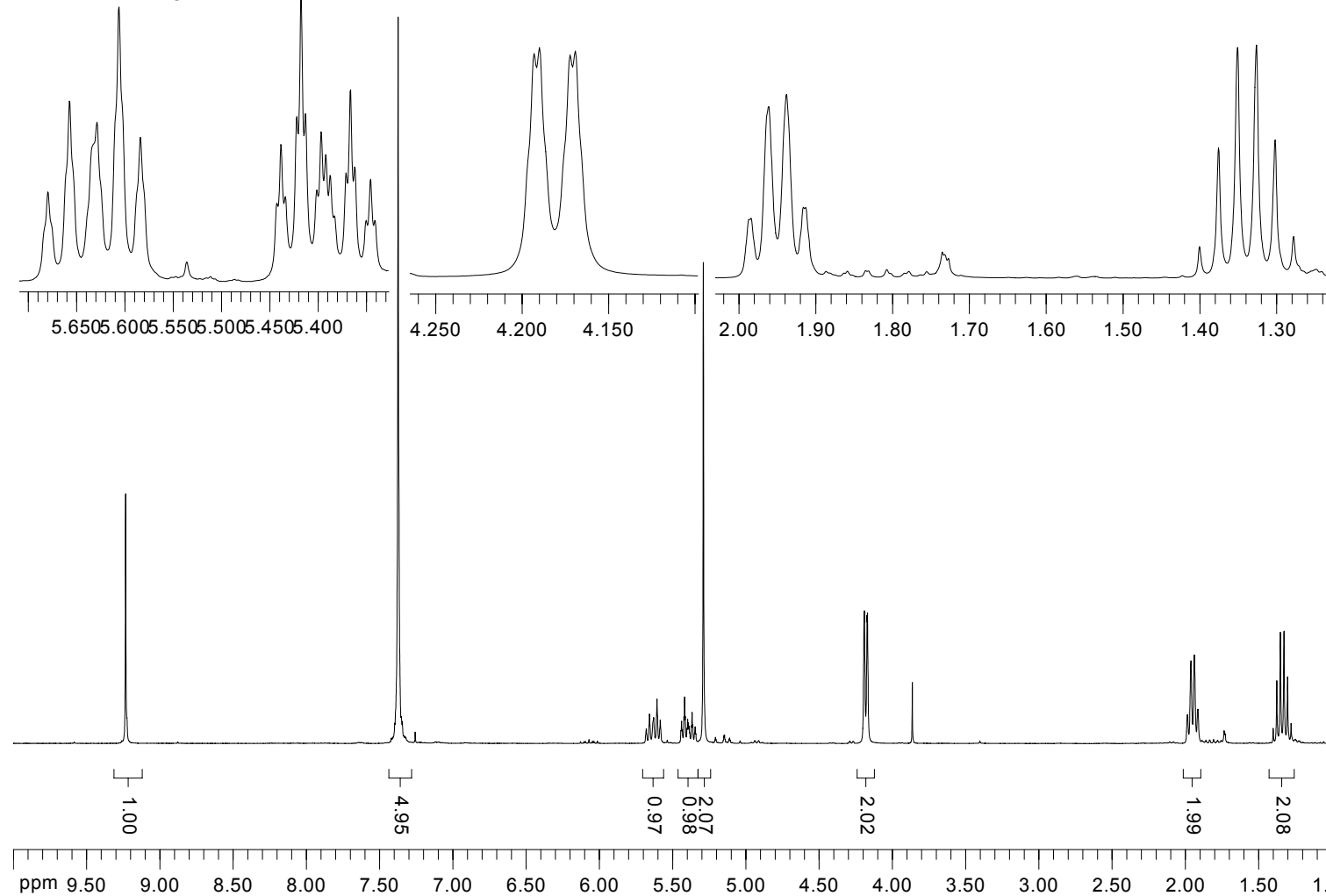
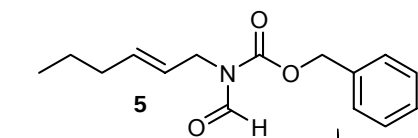
PL2 -2.20 dB

PL12 16.59 dB

PL13 20.59 dB

SFO2 300.1312005 MHz





Current Data Parameters

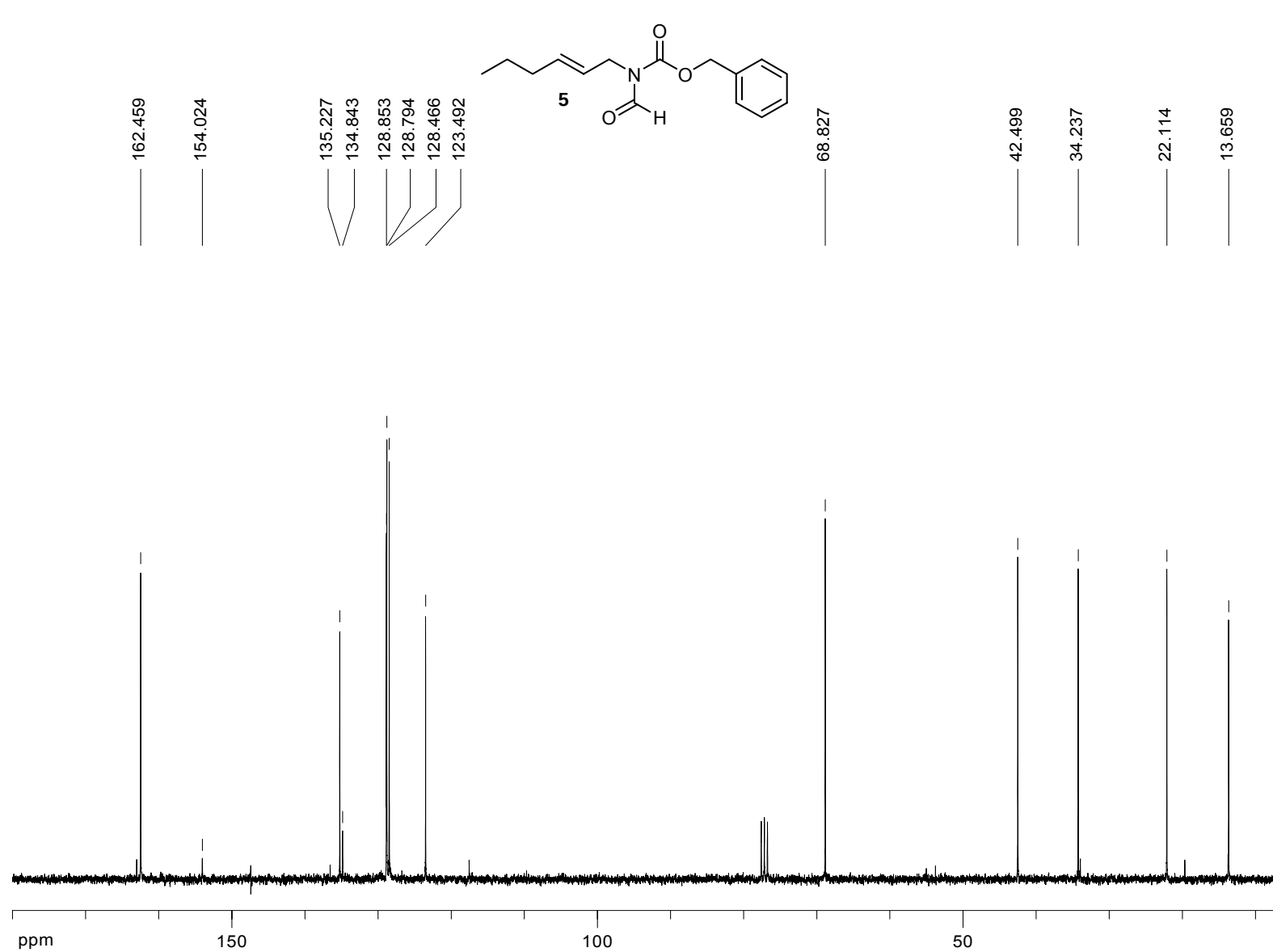
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PROCNO 1

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TD 16384
SOLVENT CDCl₃
NS 16
DS 2
SWH 5112.475 Hz
FIDRES 0.312041 Hz
AQ 1.6024052 sec
RG 40.3
DW 97.800 usec
DE 6.00 usec
TE 300.0 K
D1 2.00000000 sec
MCREST 0.00000000 sec
MCWRK 0.01500000 sec
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NUC1 1H
P1 10.00 usec
PL1 0.00 dB
SFO1 300.1321009 MHz

F2 - Processing parameters

SI 32768
SF 300.1300071 MHz
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LB 0.10 Hz
GB 0
PC 1.00



Current Data Parameters

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EXPNO 6
PROCNO 1

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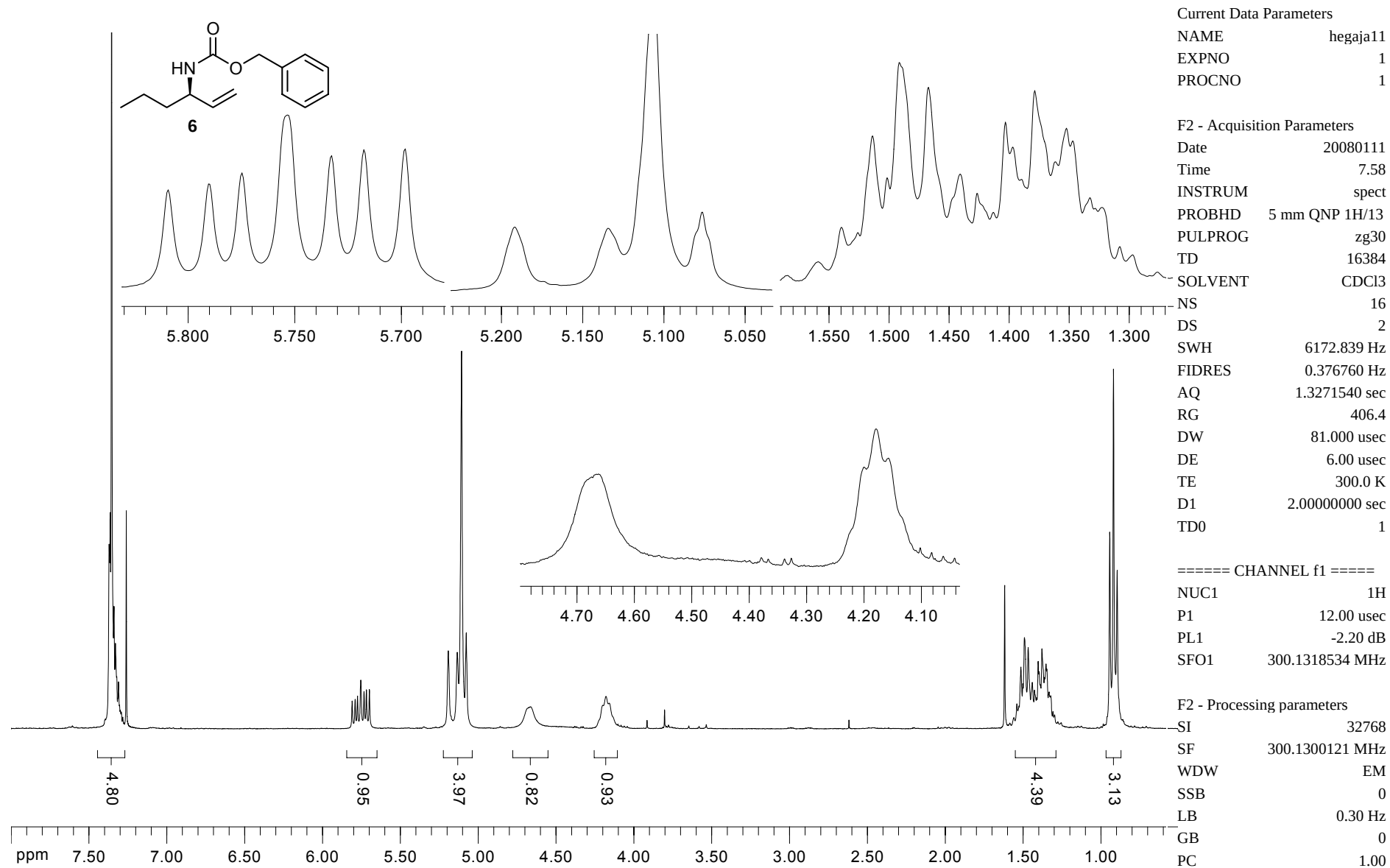
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PULPROG zgpg
TD 32768
SOLVENT CDCl3
NS 456
DS 4
SWH 21097.047 Hz
FIDRES 0.643831 Hz
AQ 0.7766516 sec
RG 9195.2
DW 23.700 usec
DE 6.00 usec
TE 300.0 K
D1 2.00000000 sec
d11 0.03000000 sec
DELTA 1.89999998 sec
MCWRK 0.01500000 sec

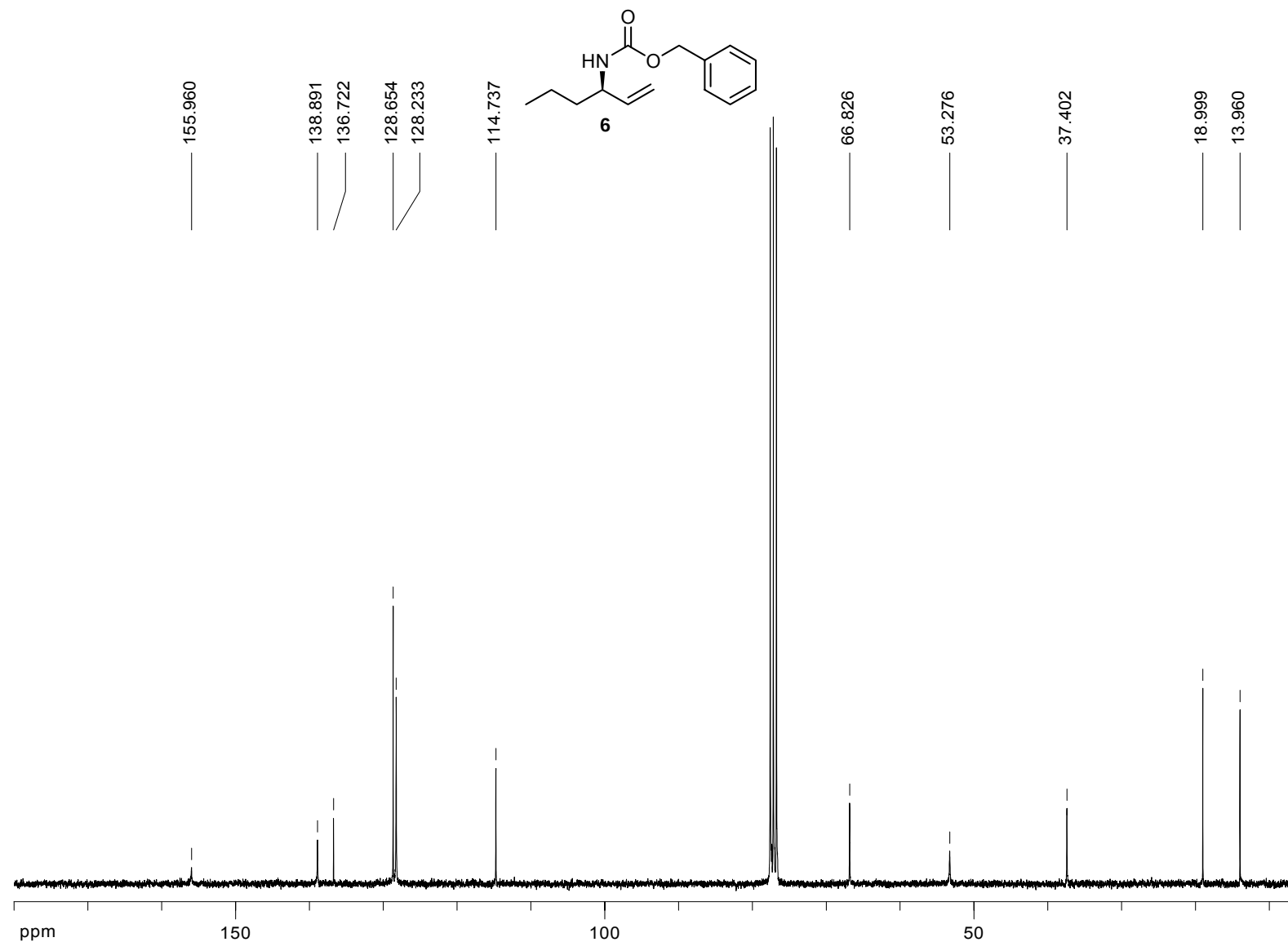
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NUC1 13C
P1 20.00 usec
PL1 0.00 dB
SFO1 75.4760204 MHz

===== CHANNEL f2 =====

CPDPRG2 waltz16
NUC2 1H
PCPD2 100.00 usec
PL2 0.00 dB
PL12 20.00 dB
PL13 120.00 dB
SFO2 300.1316507 MHz





Current Data Parameters

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EXPNO 2
PROCNO 1

F2 - Acquisition Parameters

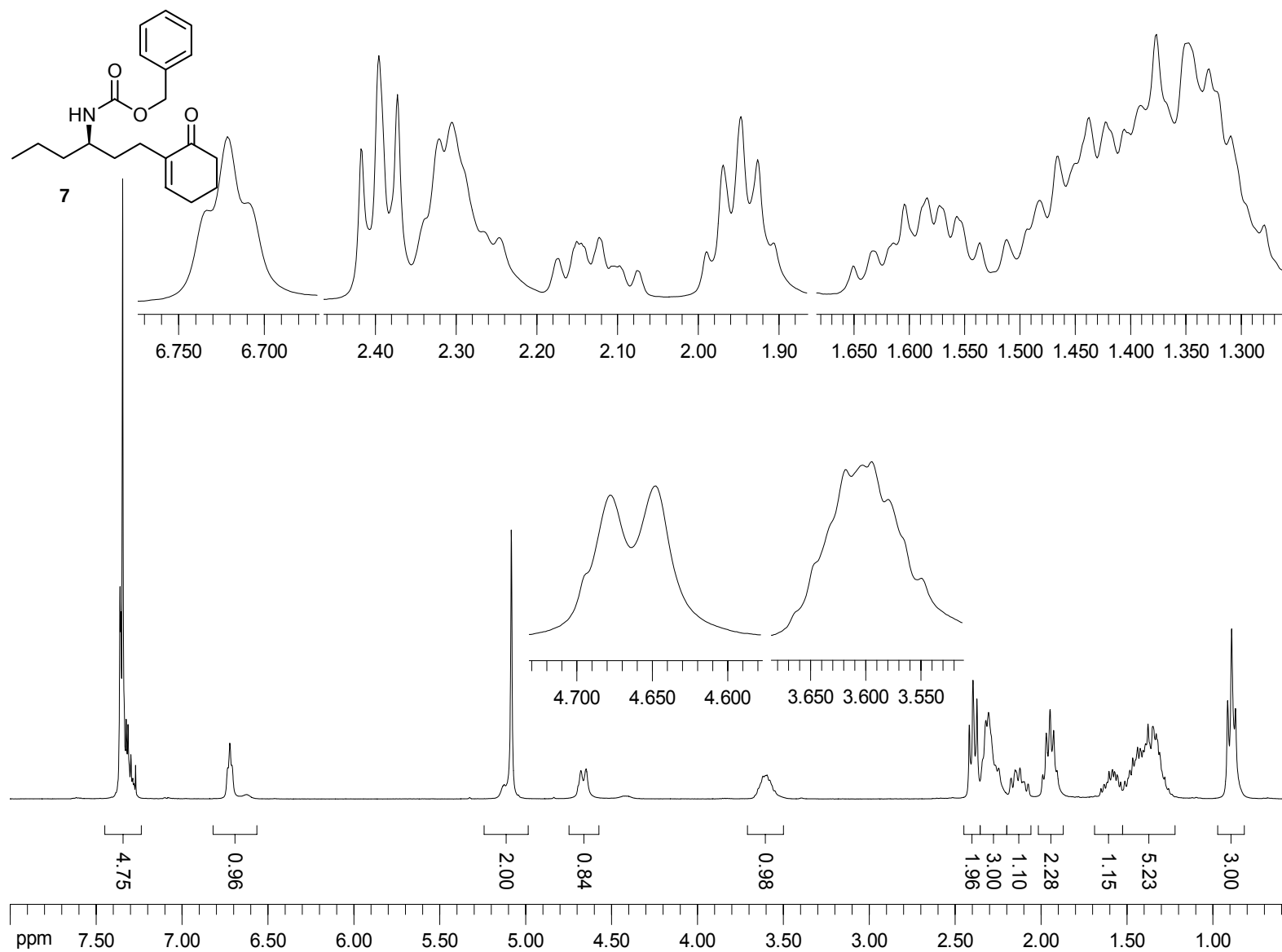
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TD 65536
SOLVENT CDCl3
NS 2880
DS 4
SWH 17985.611 Hz
FIDRES 0.274439 Hz
AQ 1.8219508 sec
RG 16384
DW 27.800 usec
DE 6.00 usec
TE 300.0 K
D1 2.00000000 sec
d11 0.03000000 sec
DELTA 1.89999998 sec
TD0 1

===== CHANNEL f1 =====

NUC1 13C
P1 12.00 usec
PL1 1.00 dB
SFO1 75.4752953 MHz

===== CHANNEL f2 =====

CPDPRG2 waltz16
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PCPD2 100.00 usec
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PL12 16.22 dB
PL13 17.00 dB
SFO2 300.1312005 MHz

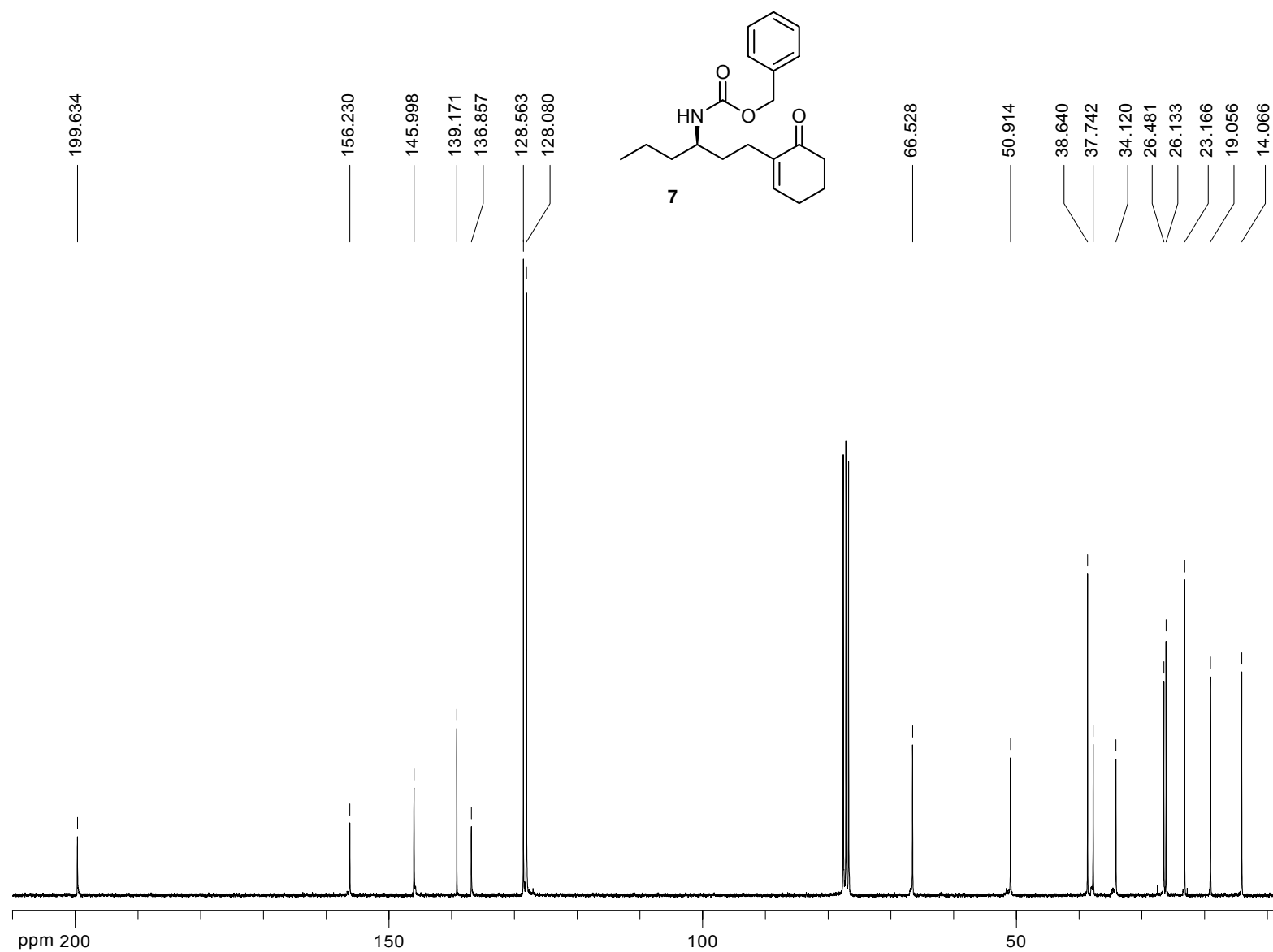


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 EXPNO 3
 PROCNO 1

F2 - Acquisition Parameters
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 PULPROG zg30
 TD 32768
 SOLVENT CDCl₃
 NS 16
 DS 2
 SWH 5995.204 Hz
 FIDRES 0.182959 Hz
 AQ 2.7329011 sec
 RG 181
 DW 83.400 usec
 DE 6.00 usec
 TE 300.0 K
 D1 0.10000000 sec
 TD0 2

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 NUC1 ¹H
 P1 11.50 usec
 PL1 -2.20 dB
 SFO1 300.1318008 MHz

F2 - Processing parameters
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 SF 300.1300030 MHz
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 SSB 0
 LB 0.30 Hz
 GB 0
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Current Data Parameters

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EXPNO 1
PROCNO 1

F2 - Acquisition Parameters

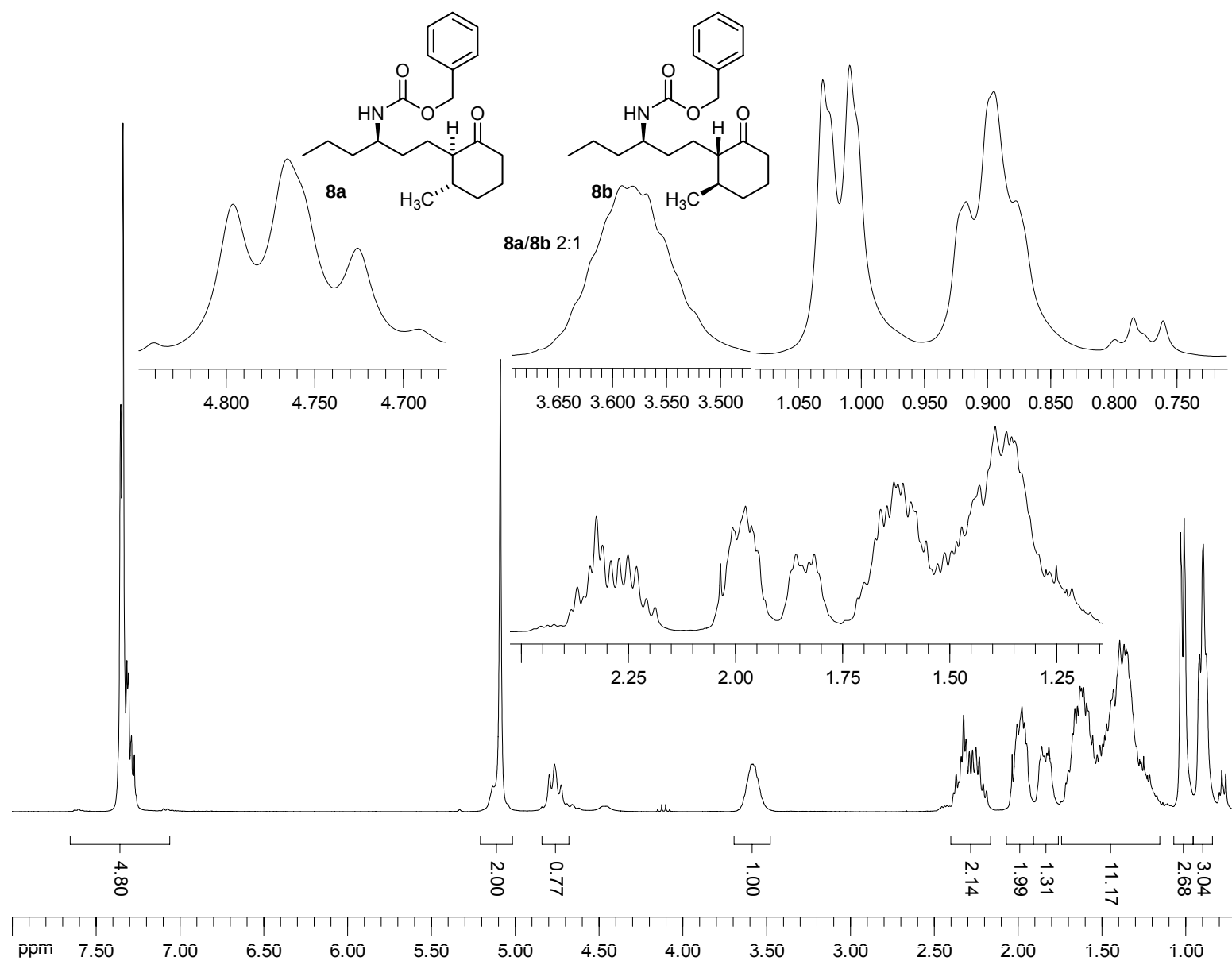
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SOLVENT CDCl3
NS 8000
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SWH 18832.393 Hz
FIDRES 0.287360 Hz
AQ 1.7400308 sec
RG 20642.5
DW 26.550 usec
DE 6.00 usec
TE 300.0 K
D1 1.00000000 sec
d11 0.03000000 sec
DELTA 0.89999998 sec
TD0 250

===== CHANNEL f1 =====

NUC1 13C
P1 11.60 usec
PL1 1.00 dB
SFO1 75.4764278 MHz

===== CHANNEL f2 =====

CPDPRG2 waltz65
NUC2 1H
PCPD2 100.00 usec
PL2 -2.20 dB
PL12 16.59 dB
PL13 20.59 dB
SFO2 300.1312005 MHz



Current Data Parameters

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EXPNO 2
PROCNO 1

F2 - Acquisition Parameters

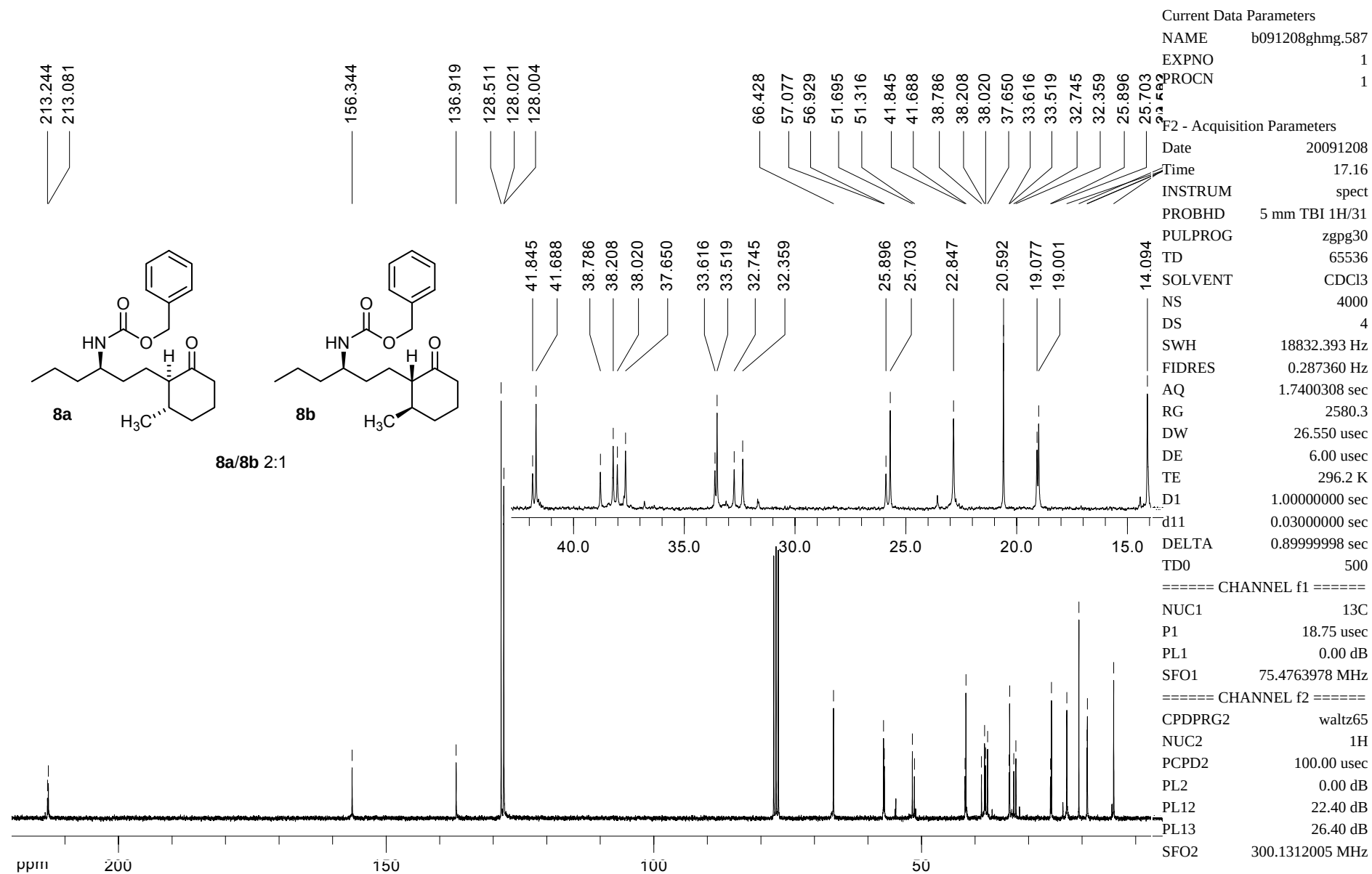
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TD 32768
SOLVENT CDCl₃
NS 40
DS 2
SWH 5995.204 Hz
FIDRES 0.182959 Hz
AQ 2.7329011 sec
RG 35.9
DW 83.400 usec
DE 6.00 usec
TE 296.2 K
D1 0.10000000 sec
TD0 5

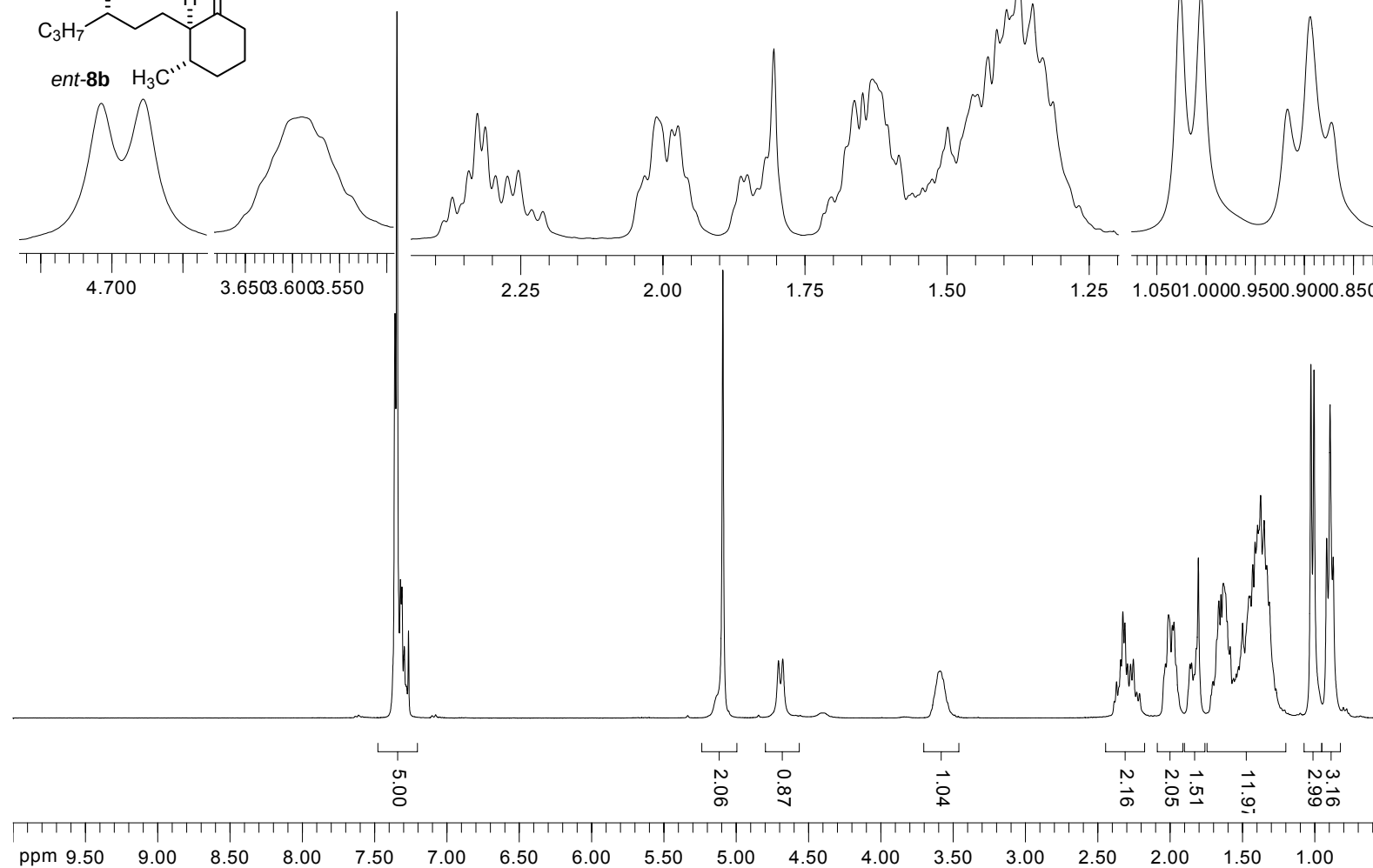
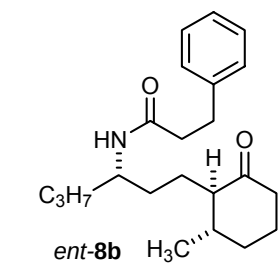
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P1 9.50 usec
PL1 0.00 dB
SFO1 300.1315007 MHz

F2 - Processing parameters

SI 32768
SF 300.1300028 MHz
WDW EM
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LB 0.30 Hz
GB 0
PC 1.00





Current Data Parameters

NAME b110927ghjq.Q-8a
EXPNO 2
PROCNO 1

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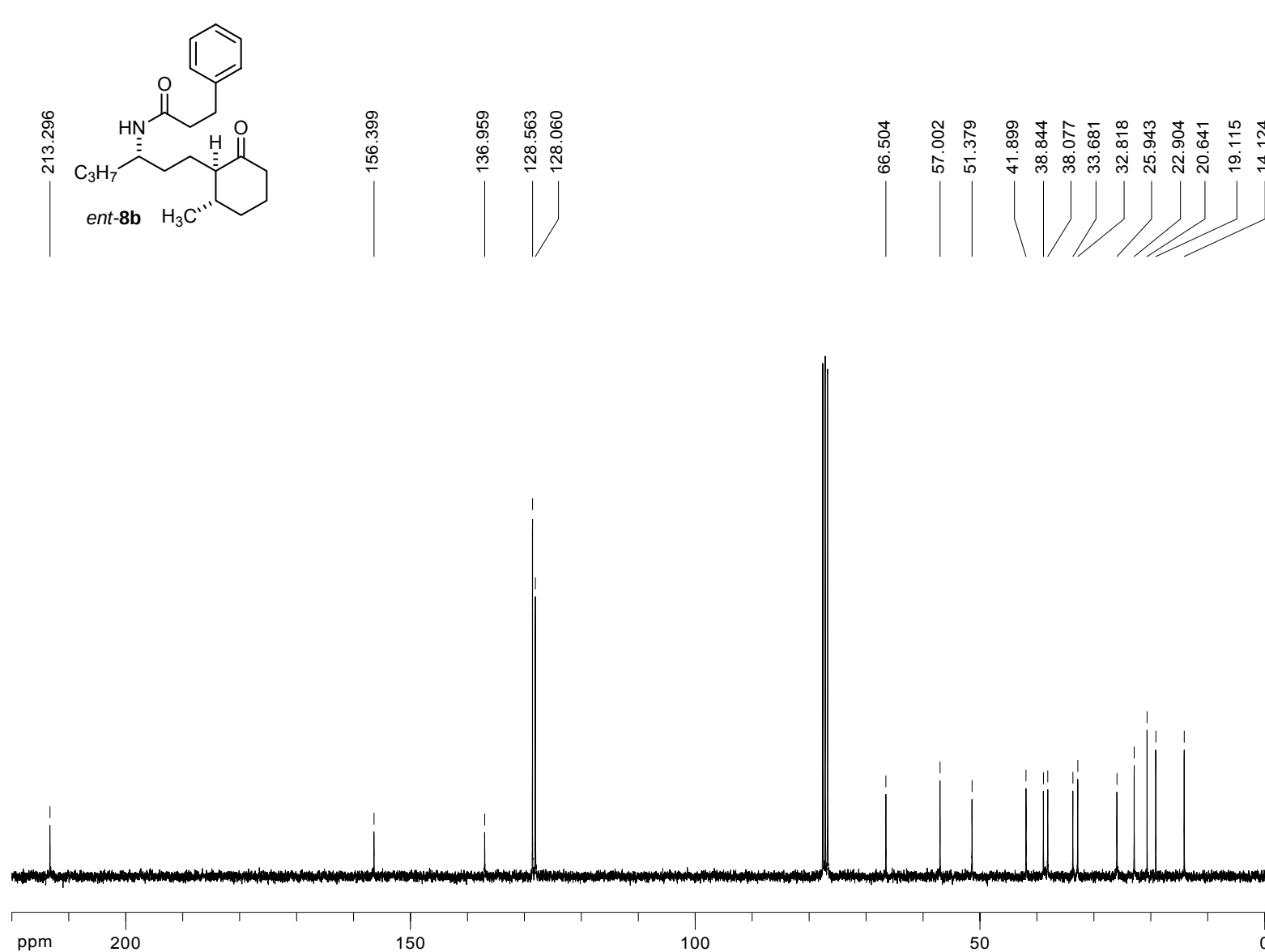
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SOLVENT CDCl3
NS 16
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SWH 8992.806 Hz
FIDRES 0.137219 Hz
AQ 3.6438515 sec
RG 90.5
DW 55.600 usec
DE 6.00 usec
TE 298.2 K
D1 0.10000000 sec
TD0 2

===== CHANNEL f1 =====

NUC1 1H
P1 9.50 usec
PL1 0.00 dB
SFO1 300.0815004 MHz

F2 - Processing parameters

SI 32768
SF 300.080068 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00



Current Data Parameters

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EXPNO 1
PROCNO 1

F2 - Acquisition Parameters

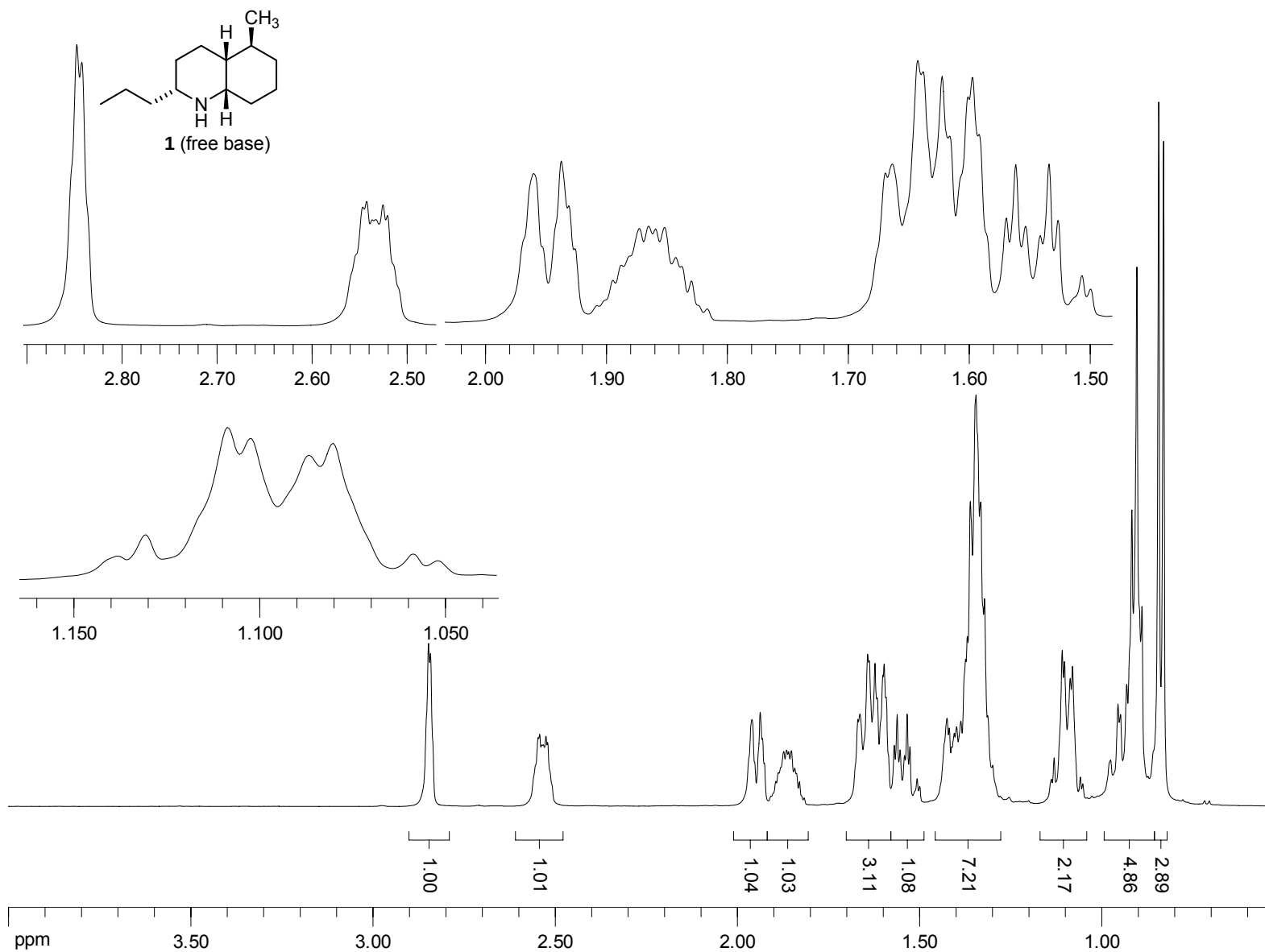
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SOLVENT CDCl3
NS 1200
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SWH 18832.393 Hz
FIDRES 0.287360 Hz
AQ 1.7400308 sec
RG 4096
DW 26.550 usec
DE 6.00 usec
TE 298.2 K
D1 1.00000000 sec
d11 0.03000000 sec
DELTA 0.89999998 sec
TD0 150

===== CHANNEL f1 =====

NUC1 13C
P1 18.75 usec
PL1 0.00 dB
SFO1 75.4638533 MHz

===== CHANNEL f2 =====

CPDPRG2 waltz65
NUC2 1H
PCPD2 100.00 usec
PL2 0.00 dB
PL12 22.40 dB
PL13 26.40 dB
SFO2 300.0812003 MHz



Current Data Parameters

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EXPNO 1
PROCNO 1

F2 - Acquisition Parameters

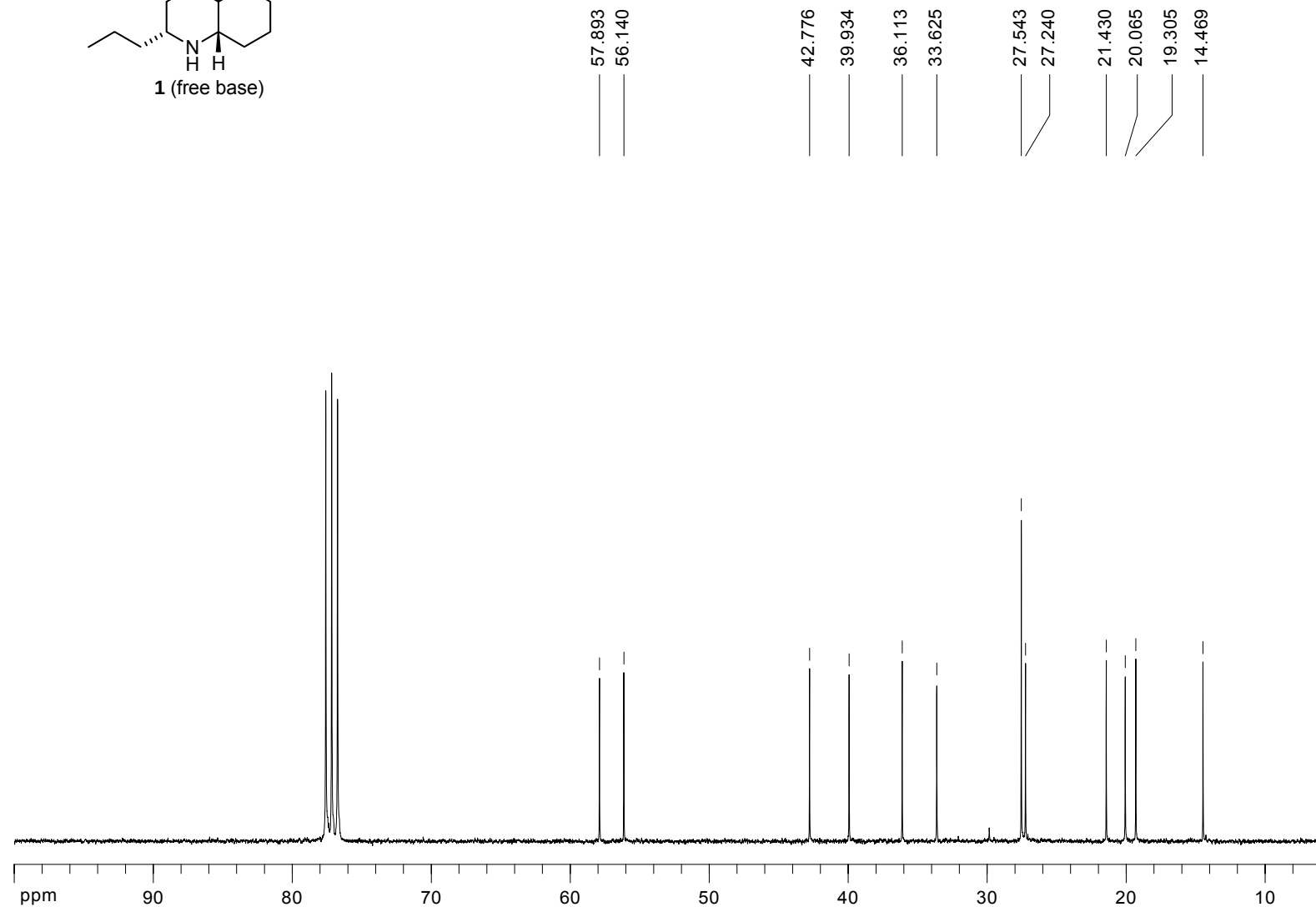
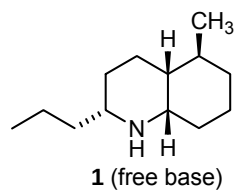
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PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 64
DS 2
SWH 8992.806 Hz
FIDRES 0.137219 Hz
AQ 3.6438515 sec
RG 40.3
DW 55.600 usec
DE 6.00 usec
TE 298.0 K
D1 0.10000000 sec
TD0 8

===== CHANNEL f1 =====

NUC1 1H
P1 11.00 usec
PL1 0.00 dB
SFO1 500.1325006 MHz

F2 - Processing parameters

SI 32768
SF 500.1300110 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00



57.893
56.140

42.776
39.934

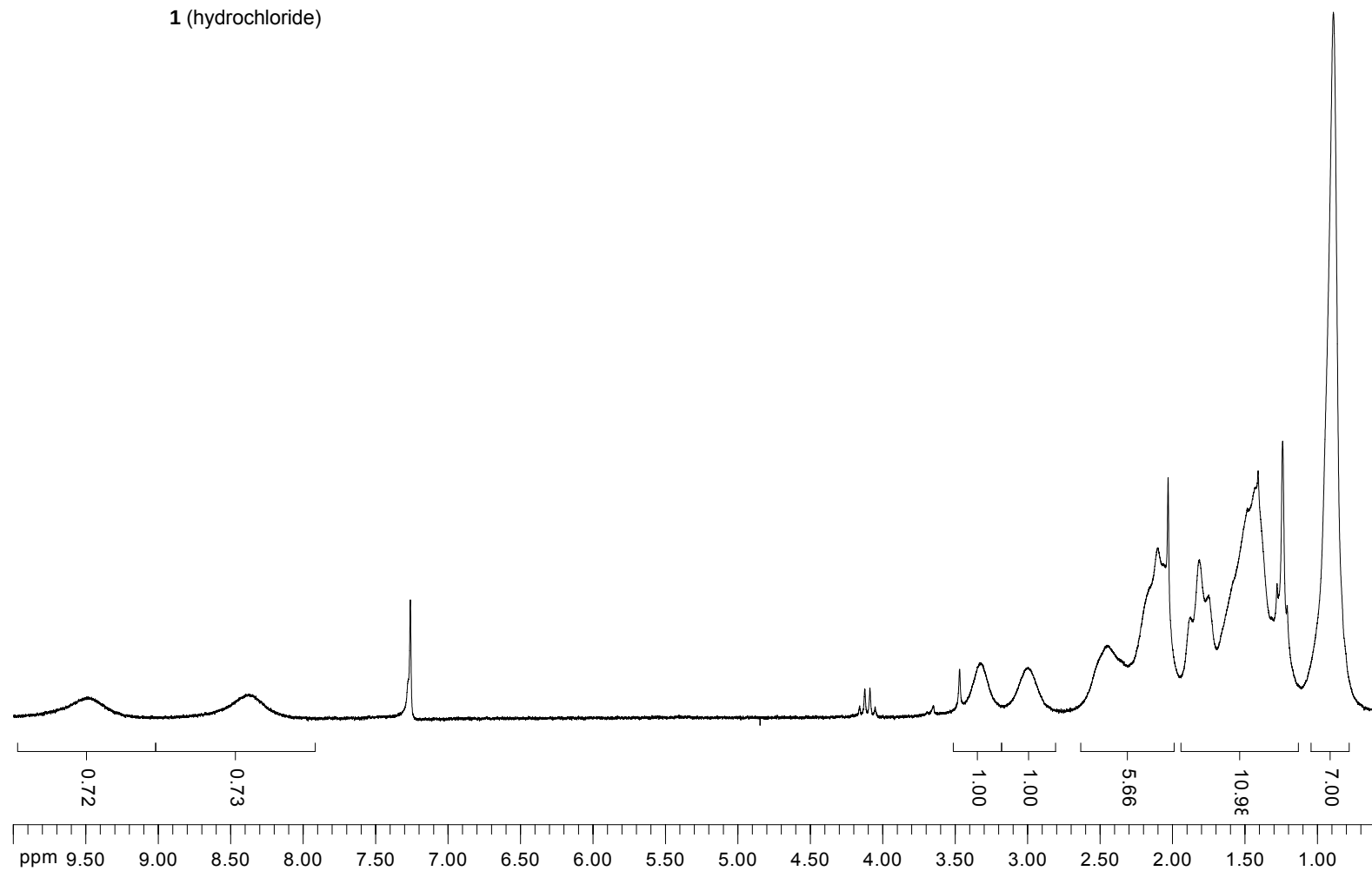
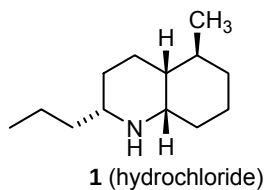
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27.240

21.430
20.065
19.305
14.469

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EXPNO 1
PROCNO 1

F2 - Acquisition Parameters
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Time 16.15
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PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 4800
DS 4
SWH 18832.393 Hz
FIDRES 0.287360 Hz
AQ 1.7400308 sec
RG 20642.5
DW 26.550 usec
DE 6.00 usec
TE 300.0 K
D1 1.00000000 sec
d11 0.03000000 sec
DELTA 0.89999998 sec
TD0 150
===== CHANNEL f1 =====
NUC1 13C
P1 11.60 usec
PL1 1.00 dB
SFO1 75.4764278 MHz
===== CHANNEL f2 =====
CPDPRG2 waltz65
NUC2 1H
PCPD2 100.00 usec
PL2 -2.20 dB
PL12 16.59 dB
PL13 20.59 dB
SFO2 300.1312005 MHz

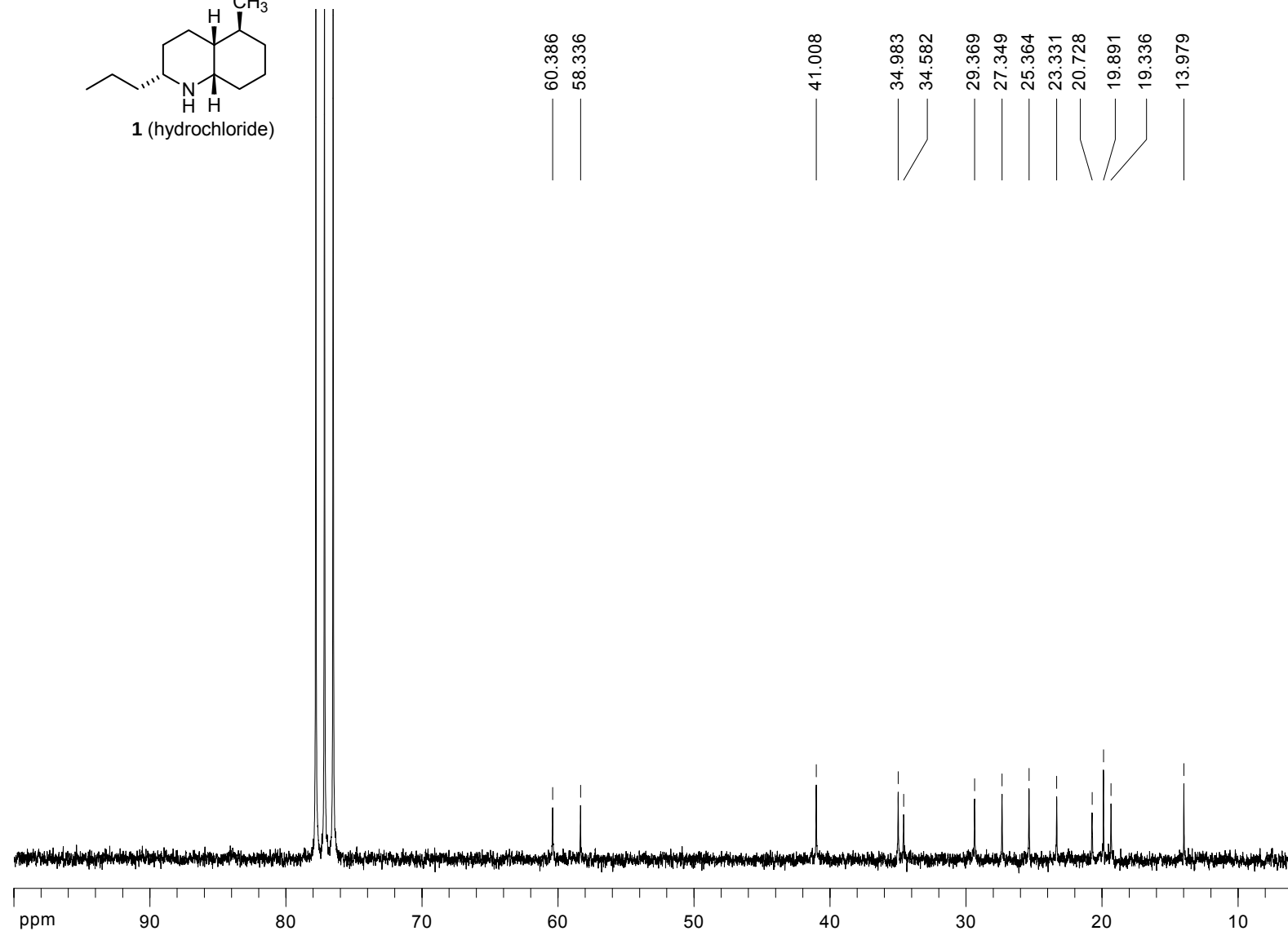
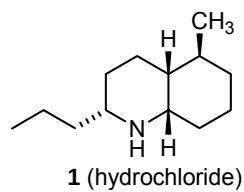


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 Time 17.50
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 PROBHD 5 mm TBO BB-1H
 PULPROG zg30
 TD 32768
 SOLVENT CDCl3
 NS 16
 DS 0
 SWH 2796.421 Hz
 FIDRES 0.085340 Hz
 AQ 5.8589683 sec
 RG 645.1
 DW 178.800 usec
 DE 12.50 usec
 TE 295.2 K
 D1 1.00000000 sec
 TD0 1

===== CHANNEL f1 =====
 NUC1 1H
 P1 12.60 usec
 PL1 0.00 dB
 SFO1 199.9209726 MHz

F2 - Processing parameters
 SI 32768
 SF 199.9200077 MHz
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 GB 0
 PC 1.00



Current Data Parameters

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EXPNO 11
PROCNO 1

F2 - Acquisition Parameters

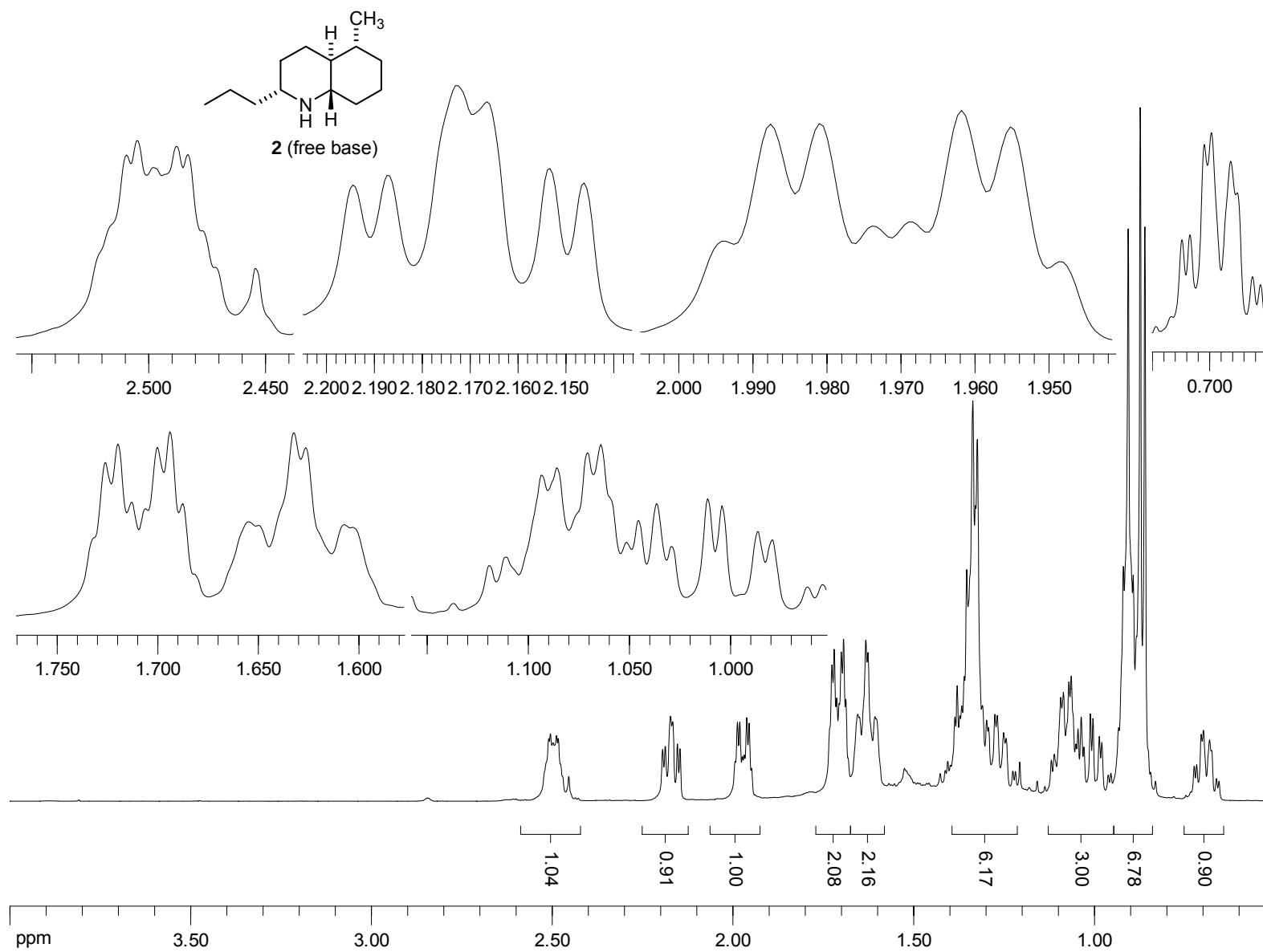
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SOLVENT CDCl3
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SWH 16129.032 Hz
FIDRES 0.246110 Hz
AQ 2.0316660 sec
RG 181
DW 31.000 usec
DE 15.50 usec
TE 295.2 K
D1 1.29999995 sec
d11 0.03000000 sec
DELTA 1.19999993 sec
TD0 1

===== CHANNEL f1 =====

NUC1 13C
P1 6.50 usec
PL1 -3.00 dB
SFO1 50.2764591 MHz

===== CHANNEL f2 =====

CPDPRG2 waltz16
NUC2 1H
PCPD2 110.00 usec
PL2 0.00 dB
PL12 22.00 dB
PL13 30.00 dB
SFO2 199.9211995 MHz

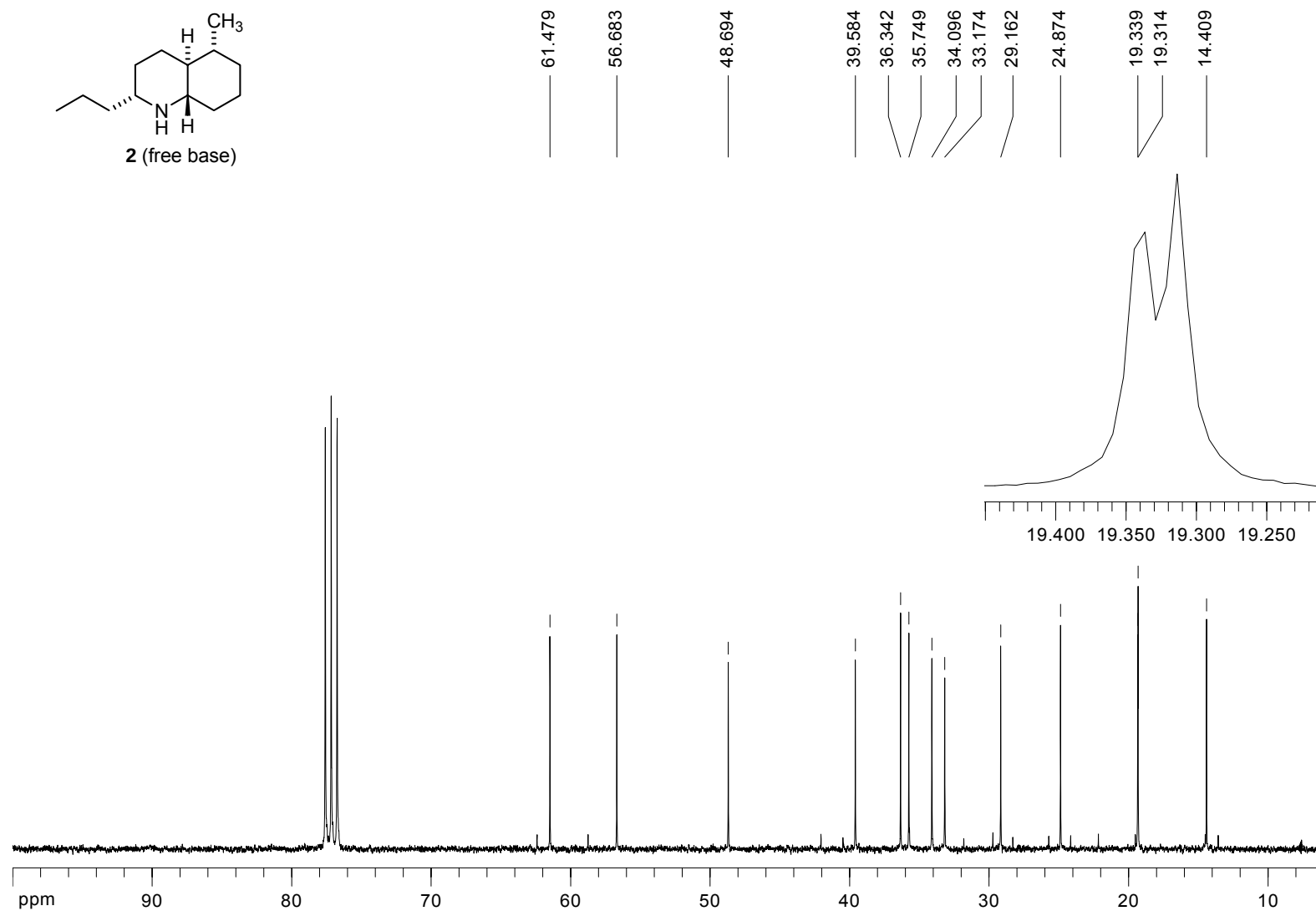
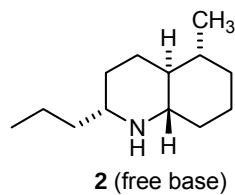


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 PULPROG zg30
 TD 65536
 SOLVENT CDCl3
 NS 64
 DS 2
 SWH 8992.806 Hz
 FIDRES 0.137219 Hz
 AQ 3.6438515 sec
 RG 90.5
 DW 55.600 usec
 DE 6.00 usec
 TE 298.1 K
 D1 0.10000000 sec
 TD0 8

===== CHANNEL f1 =====
 NUC1 1H
 P1 11.00 usec
 PL1 0.00 dB
 SFO1 500.1325006 MHz

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 SF 500.1300114 MHz
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 SSB 0
 LB 0.30 Hz
 GB 0
 PC 1.00



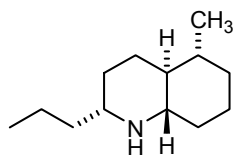
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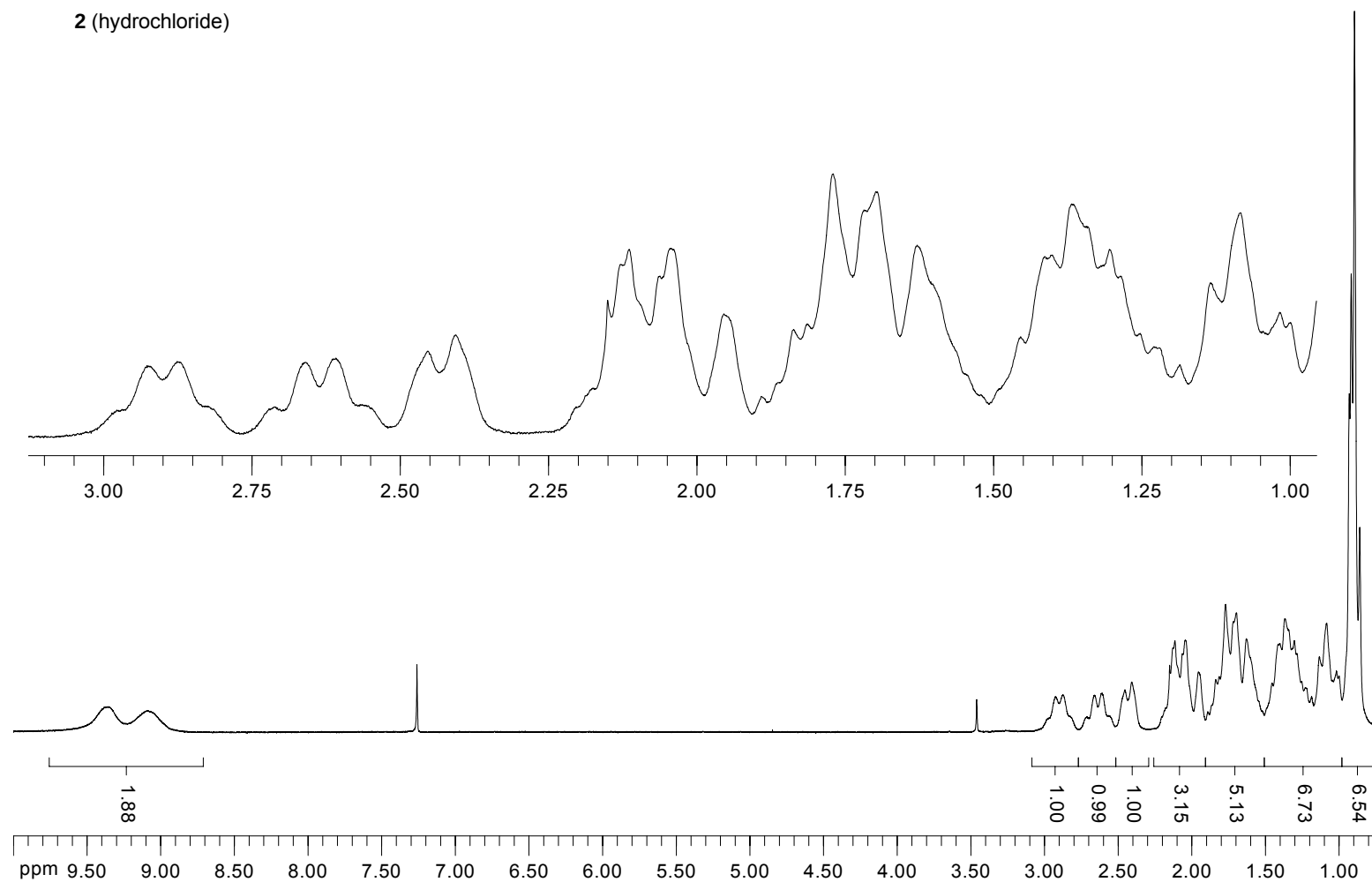
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TD 65536
SOLVENT CDCl3
NS 1537
DS 4
SWH 18832.393 Hz
FIDRES 0.287360 Hz
AQ 1.7400308 sec
RG 13004
DW 26.550 usec
DE 6.00 usec
TE 300.0 K
D1 1.00000000 sec
d11 0.03000000 sec
DELTA 0.89999998 sec
TD0 512

===== CHANNEL f1 =====
NUC1 13C
P1 11.60 usec
PL1 1.00 dB
SFO1 75.4764278 MHz
===== CHANNEL f2 =====
CPDPRG2 waltz65
NUC2 1H
PCPD2 100.00 usec
PL2 -2.20 dB
PL12 16.59 dB
PL13 20.59 dB
SFO2 300.1312005 MHz



2 (hydrochloride)



Current Data Parameters

NAME he_mg599bHCl
EXPNO 10
PROCNO 1

F2 - Acquisition Parameters

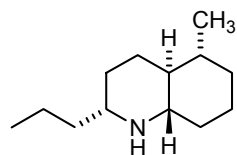
Date 20100212
Time 16.39
INSTRUM spect
PROBHD 5 mm TBO BB-1H
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 16
DS 0
SWH 2796.421 Hz
FIDRES 0.085340 Hz
AQ 5.8589683 sec
RG 322.5
DW 178.800 usec
DE 12.50 usec
TE 296.2 K
D1 1.00000000 sec
TD0 1

===== CHANNEL f1 =====

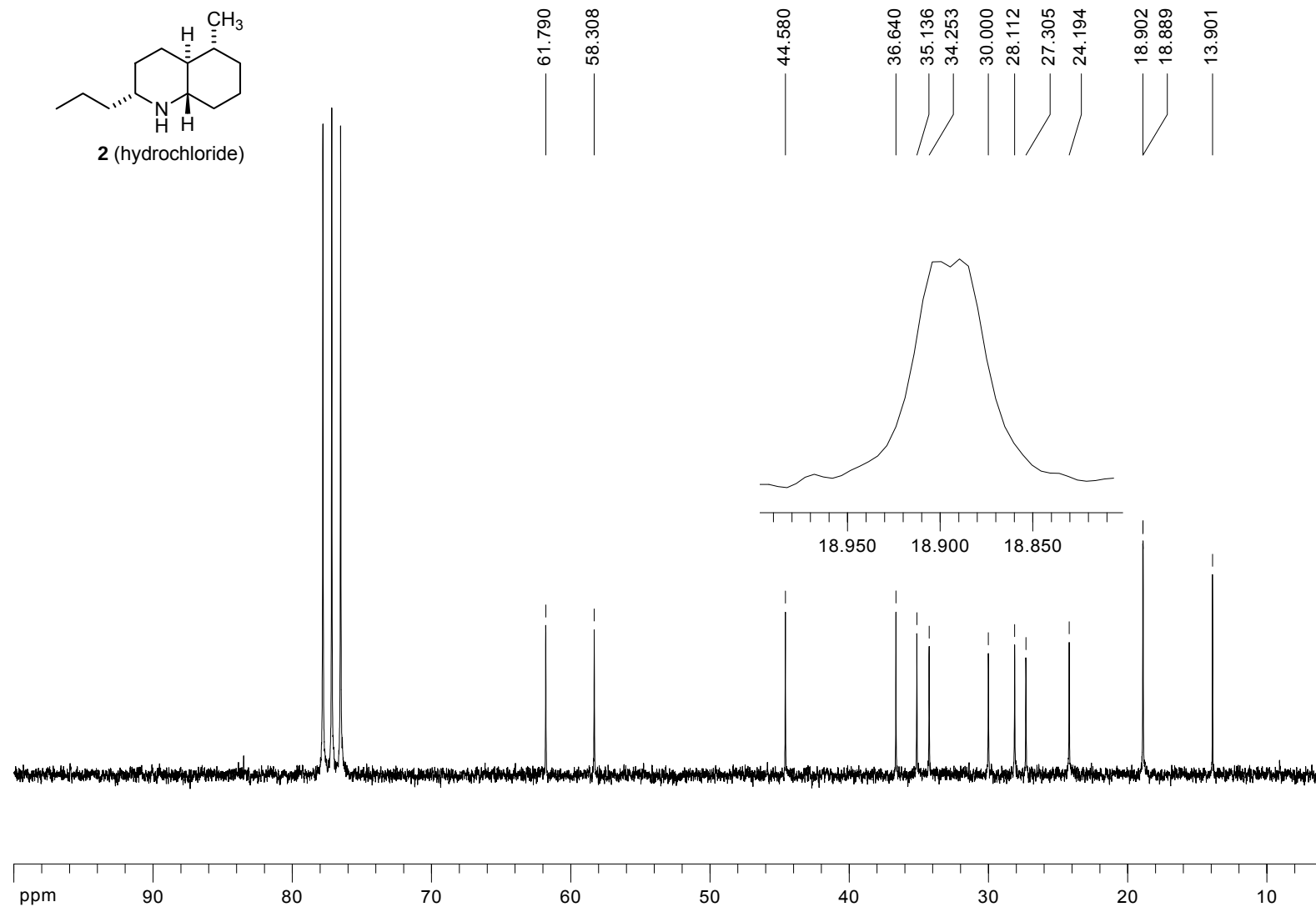
NUC1 1H
P1 12.60 usec
PL1 0.00 dB
SFO1 199.9209726 MHz

F2 - Processing parameters

SI 32768
SF 199.9200078 MHz
WDW EM
SSB 0
LB 0.10 Hz
GB 0
PC 1.00



2 (hydrochloride)



Current Data Parameters

NAME he_mg599bHCl
EXPNO 11
PROCN 1

F2 - Acquisition Parameters

Date 20100212
Time 20.03
INSTRUM spect
PROBHD 5 mm TBO 1H-BB
PULPROG zgpg30
TD 65536
SOLVENT CDCl₃
NS 1024
DS 0
SWH 16129.032 Hz
FIDRES 0.246110 Hz
AQ 2.0316660 sec
RG 8192
DW 31.000 usec
DE 15.50 usec
TE 296.2 K
D1 1.29999995 sec
d11 0.03000000 sec
DELTA 1.19999993 sec
TD0 1
===== CHANNEL f1 =====
NUC1 ¹³C
P1 6.50 usec
PL1 -3.00 dB
SFO1 50.2764591 MHz
===== CHANNEL f2 =====
CPDPRG2 waltz16
NUC2 ¹H
PCPD2 110.00 usec
PL2 0.00 dB
PL12 22.00 dB
PL13 30.00 dB
SFO2 199.9211995 MHz