SUPPORTING INFORMATION

Isolation of a High Affinity Cannabinoid for Human CB1 Receptor from a Medicinal Cannabis Variety: Δ⁹-Tetrahydrocannabutol, the Butyl Homologue of Δ⁹-Tetrahydrocannabinol

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TABLE OF CONTENT

HRMS spectra of carboxylated and neutral cannabinoids

Figure S1. HRMS spectra of CBDA, CBDBA and CBDVA in negative ionization mode. A putative structure is given for each fragment. Dotted red lines indicate correspondence of fragments between pentyl (*m/z*), butyl (*m/z*-CH_3) and propyl (*m/z*-C_2H_5) forms.

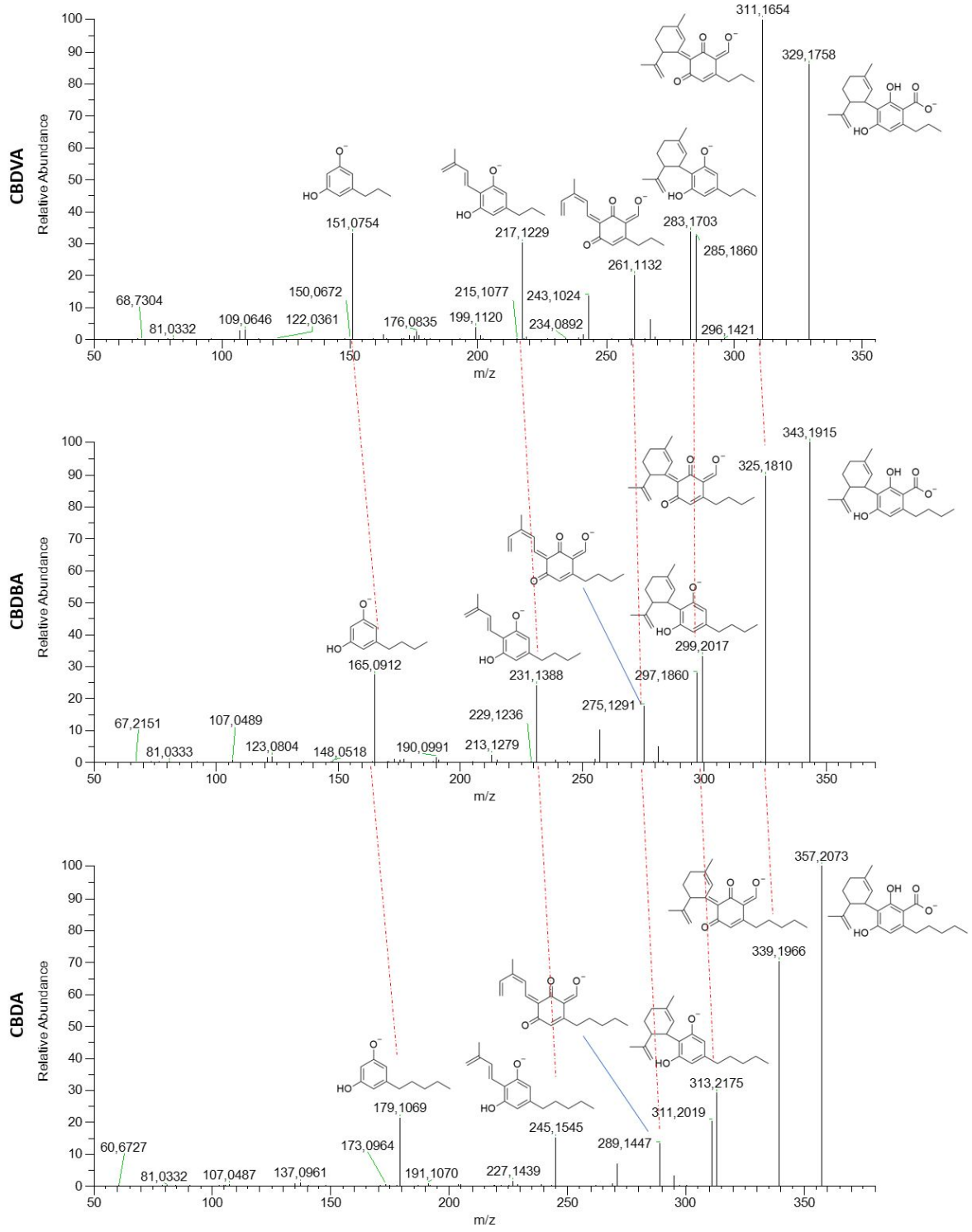


Figure S2. HRMS spectra of THCA, THCBA and THCVA in negative ionization mode. A putative structure is given for each fragment. Dotted red lines indicate correspondence of fragments between pentyl (*m/z*), butyl (*m/z*-CH_3) and propyl (*m/z*-C_2H_5) forms.

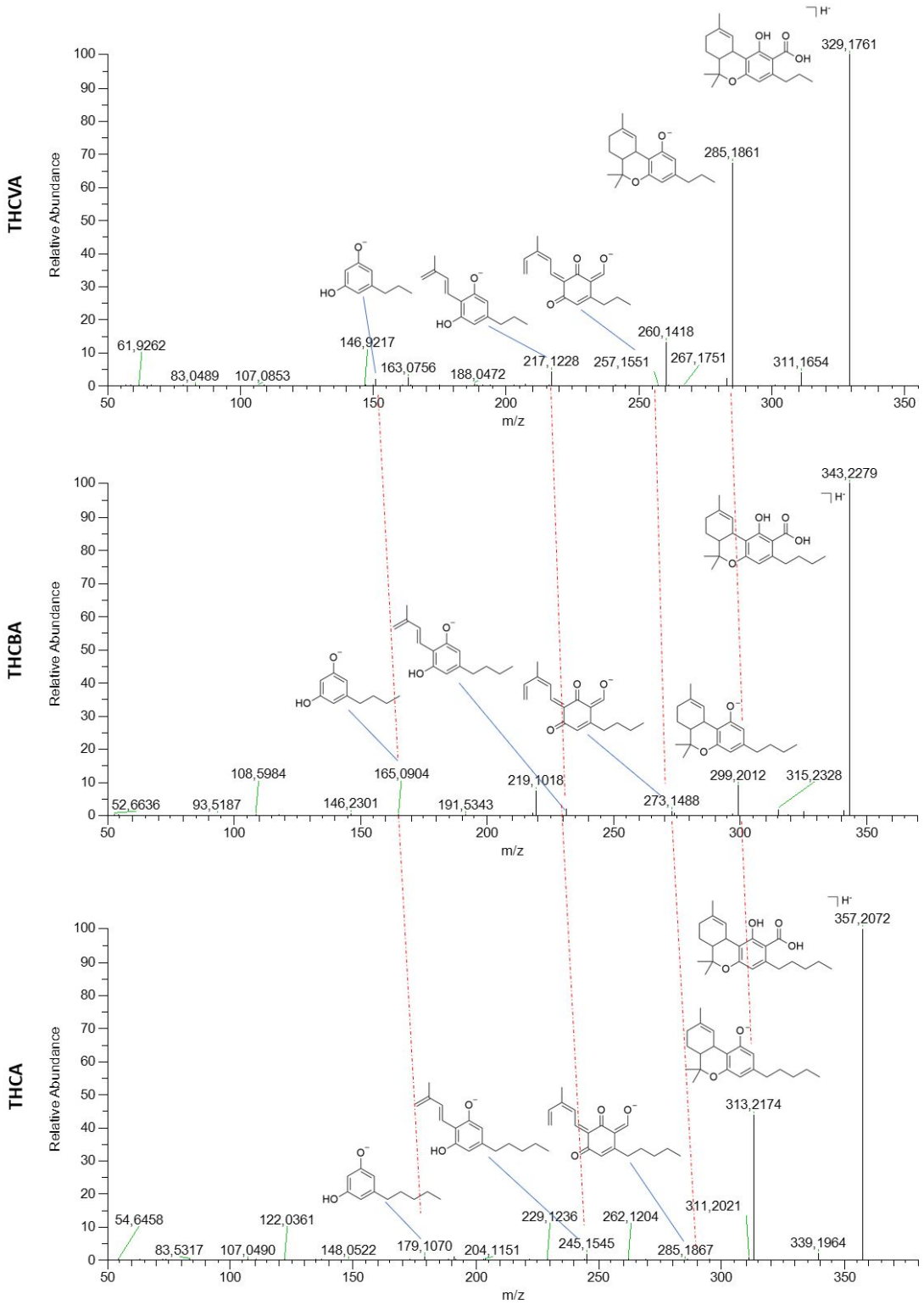


Figure S3. HRMS spectra of CBDA, CBDBA and CBDVA in positive ionization mode. A putative structure is given for each fragment. Dotted red lines indicate correspondence of fragments between pentyl (*m/z*), butyl (*m/z*-CH_3) and propyl (*m/z*-C_2H_5) forms.

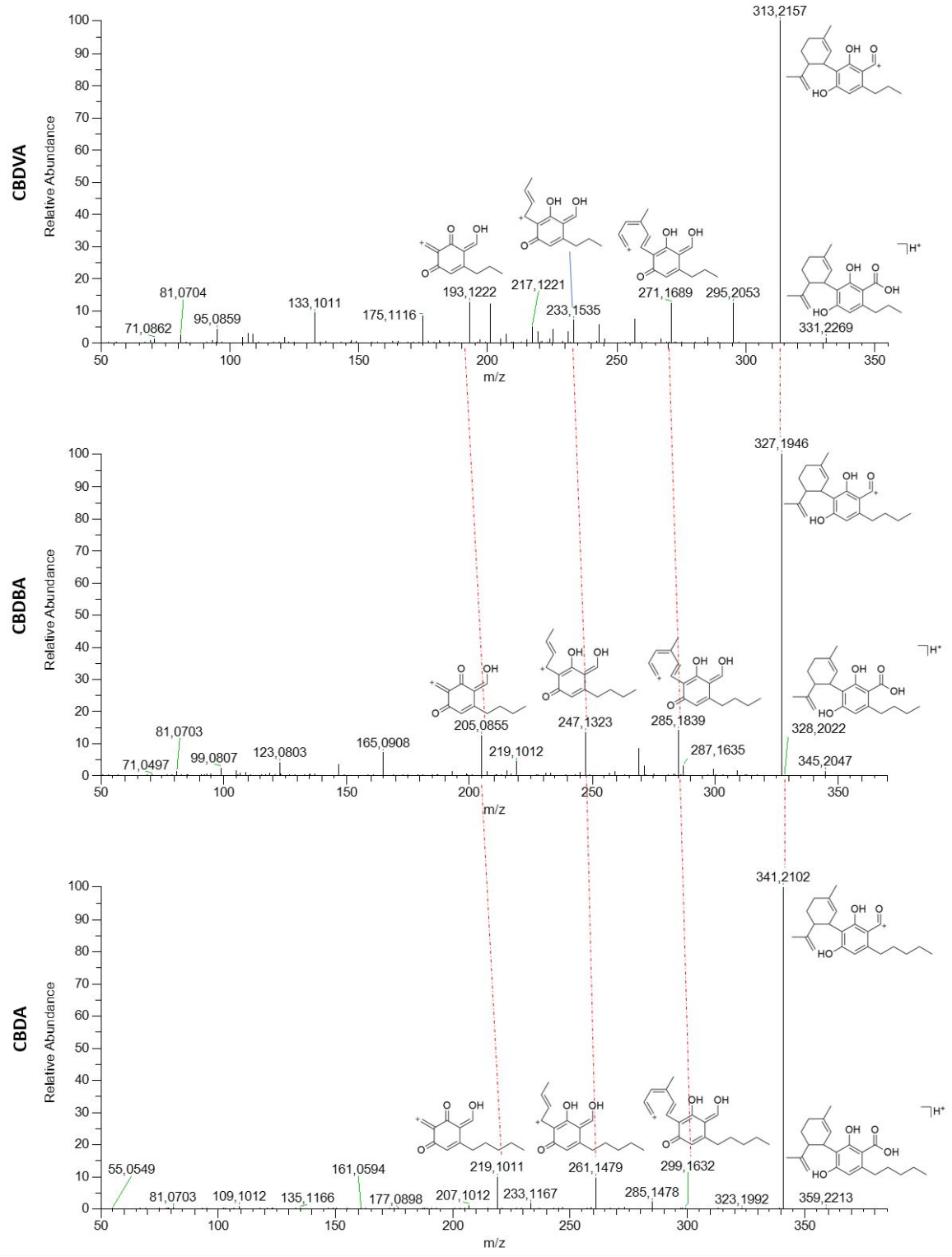


Figure S4. HRMS spectra of THCA, THCBA and THCVA in positive ionization mode. A putative structure is given for each fragment. Dotted red lines indicate correspondence of fragments between pentyl (*m/z*), butyl (*m/z*-CH_3) and propyl (*m/z*-C_2H_5) forms.

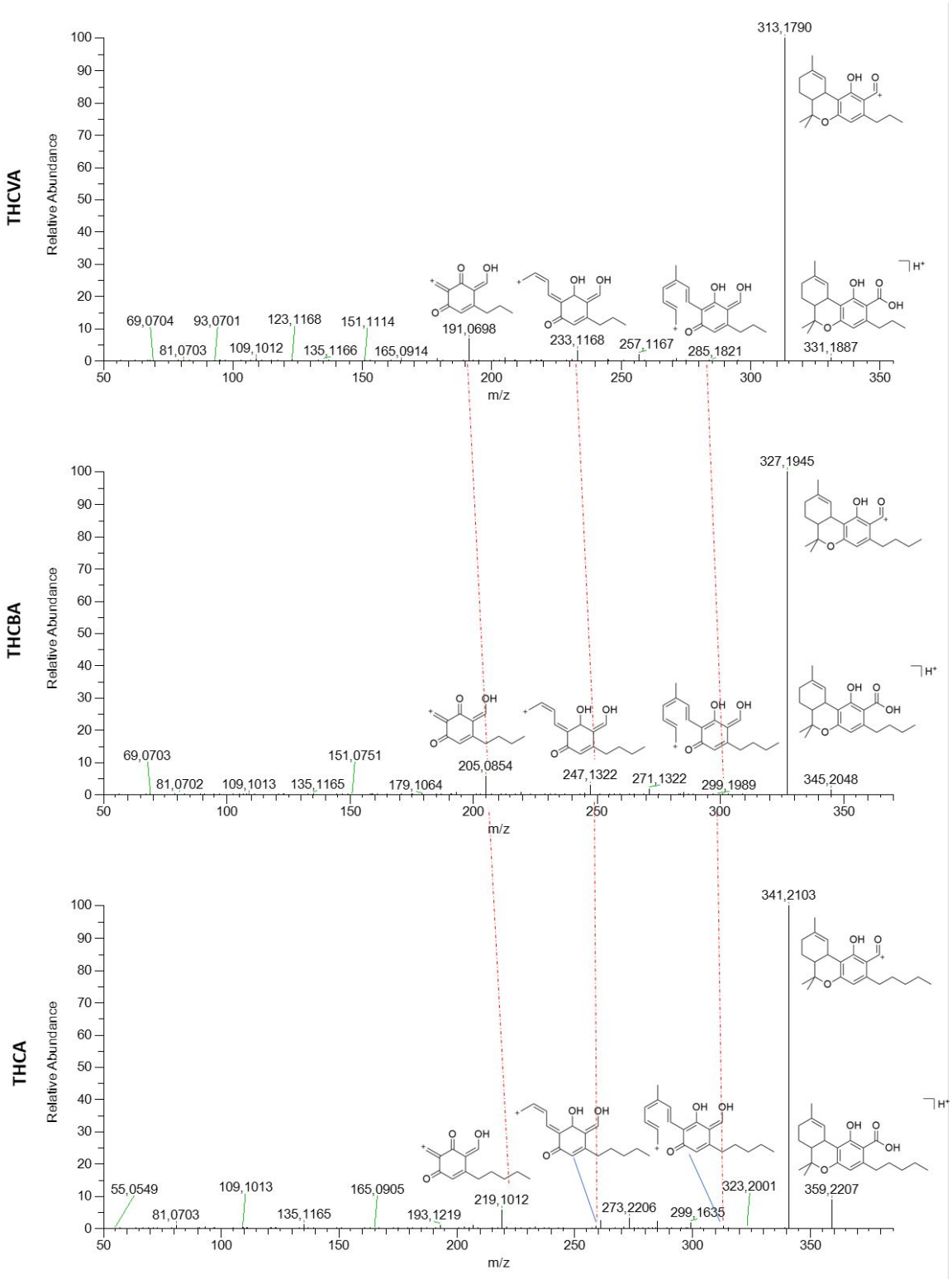


Figure S5. Comparison of CBDB (top) and Δ^9-THCB (bottom) HRMS spectrum in negative ionization mode. A putative structure is given for each fragment.

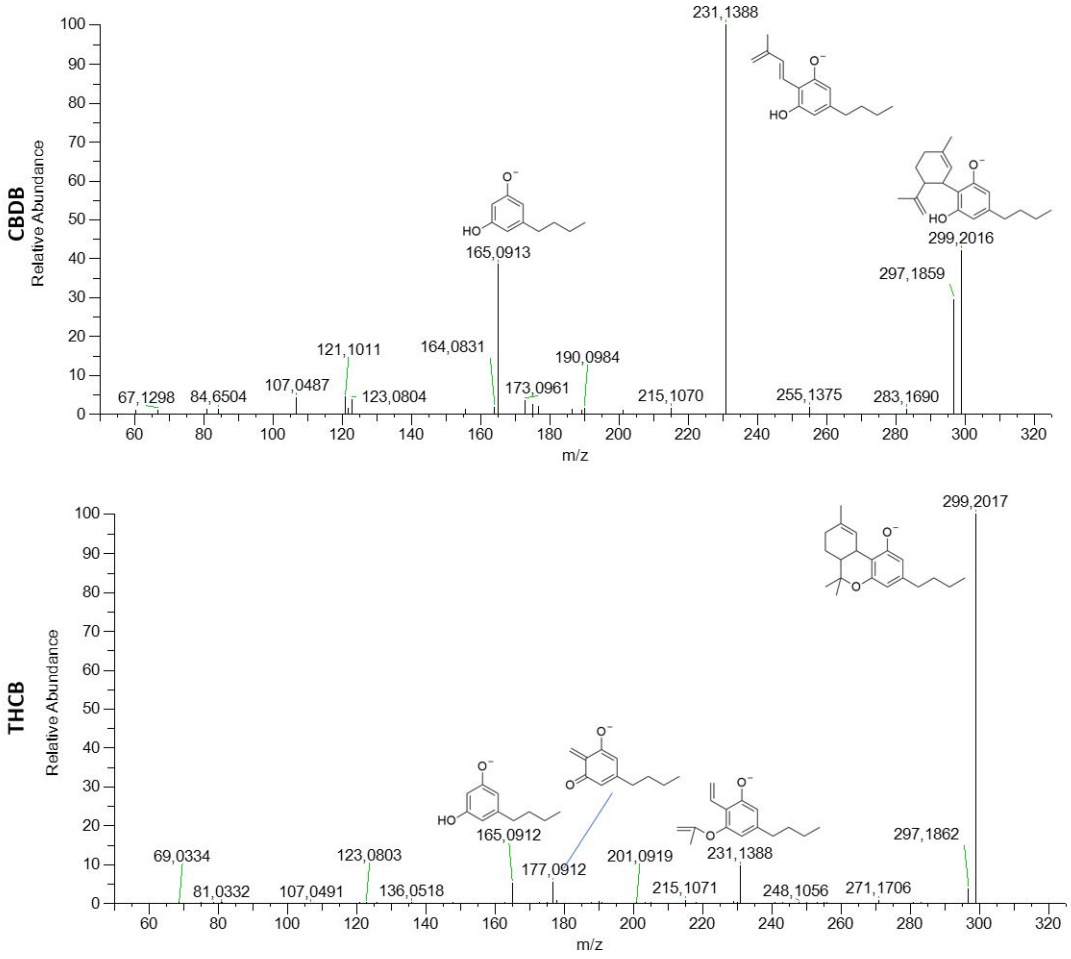
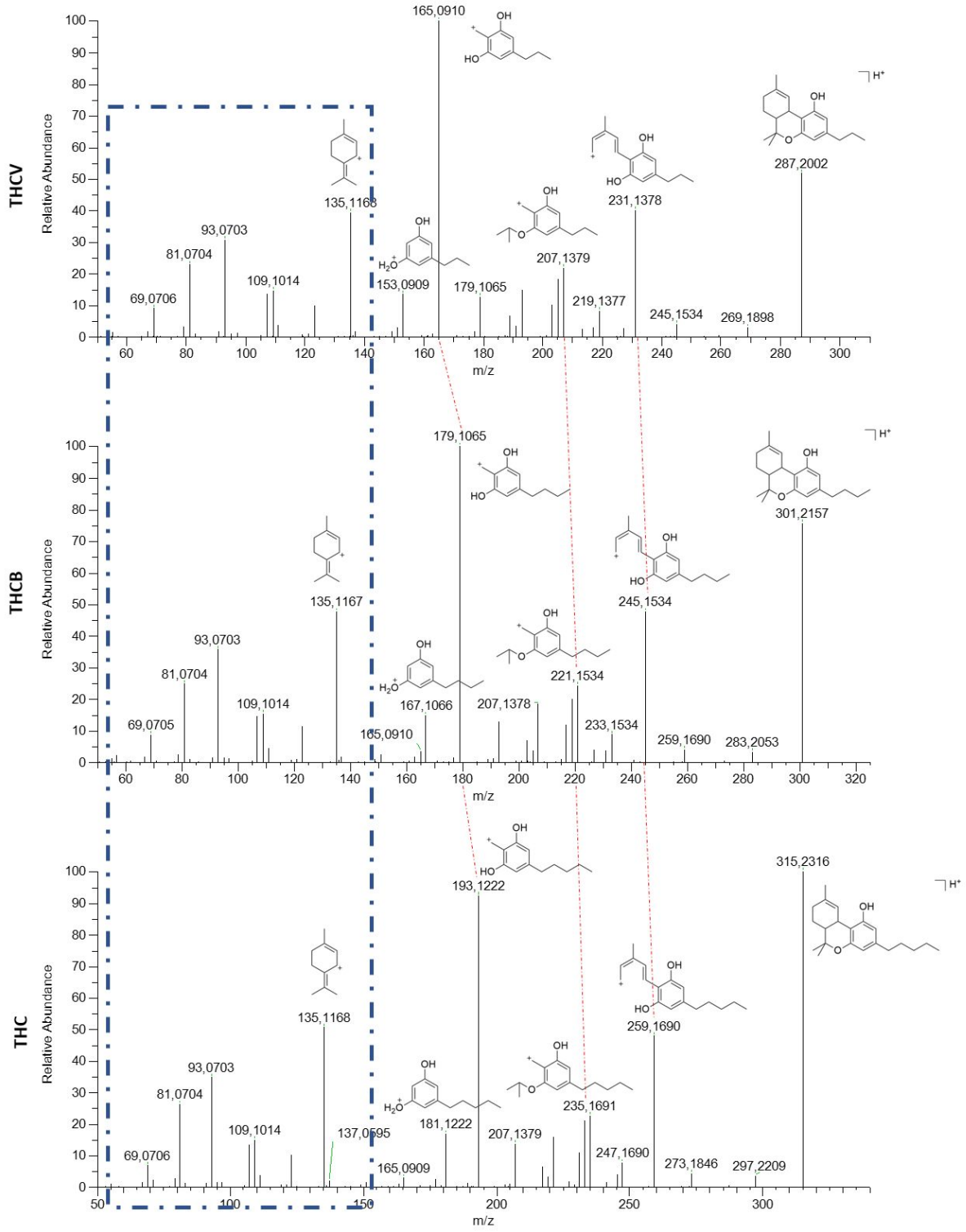


Figure S6. HRMS spectra of Δ^9-THC, Δ^9-THCB and Δ^9-THCV in positive ionization mode. A putative structure is given for each fragment. Dotted red lines indicate correspondence of fragments between pentyl (*m/z*), butyl (*m/z*-CH_3) and propyl (*m/z*-C_2H_5) forms.



NMR spectra of synthetic (-)-*trans*-Δ^9-THCB

Figure S7

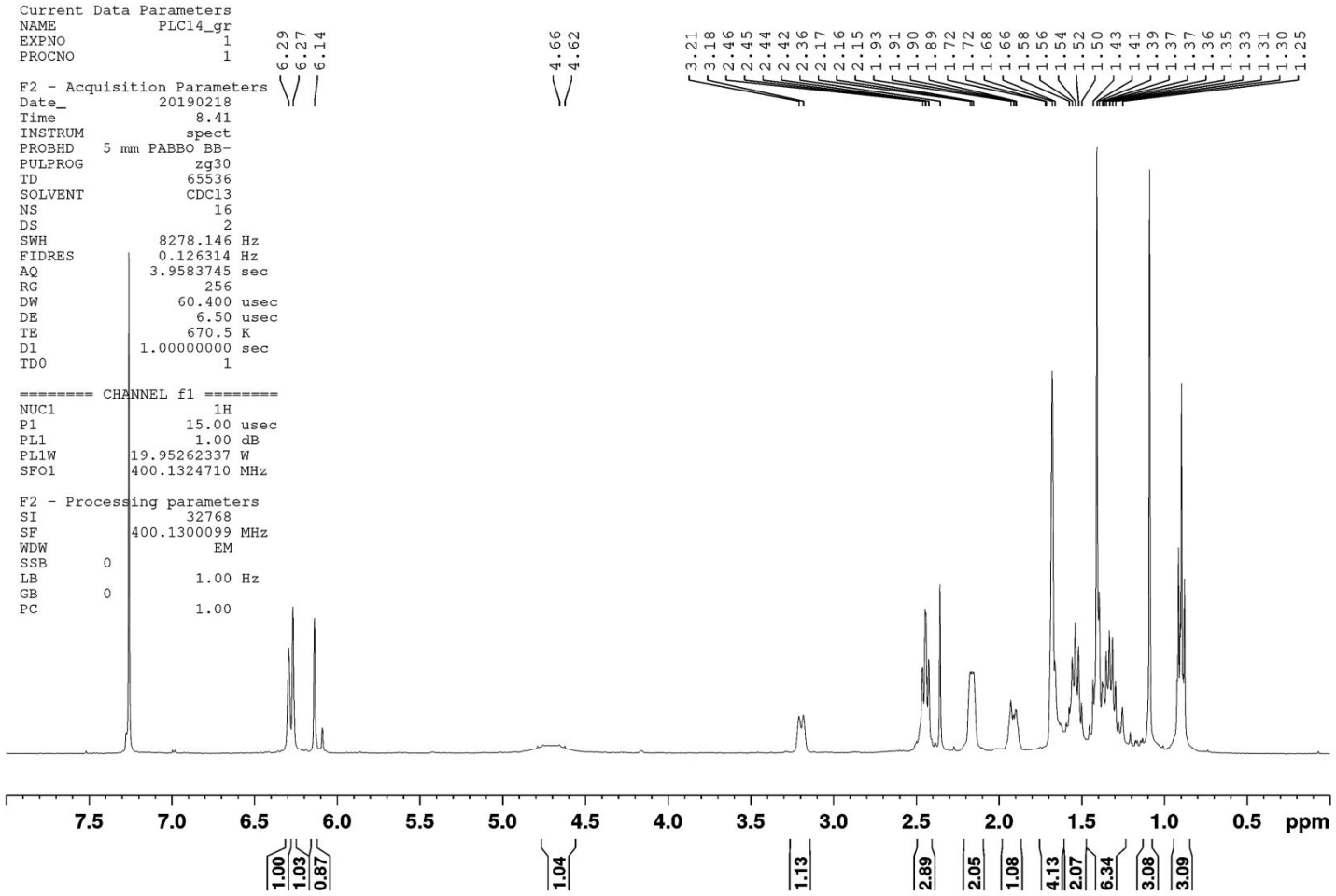
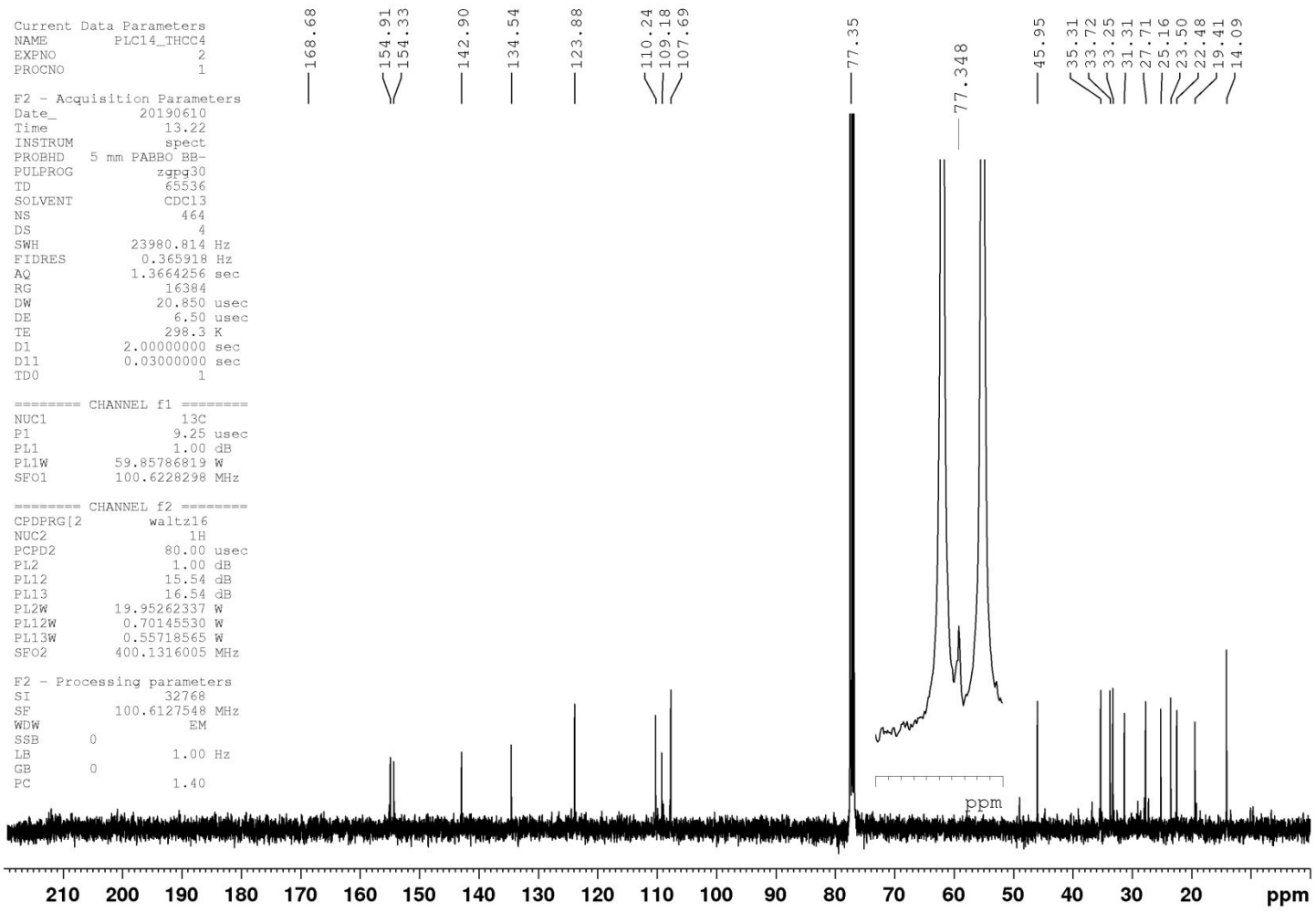


Figure S8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SOLVENT CDCl3
NS 464
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FIDRES 0.365918 Hz
AQ 1.3664256 sec
RG 16384
DW 20.850 usec
DE 6.50 usec
TE 298.3 K
D1 2.00000000 sec
D11 0.03000000 sec
TD0 1
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P1 9.25 usec
PL1 1.00 dB
PL1W 59.85786819 W
SFO1 100.6228298 MHz
======== CHANNEL f2 ========
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NUC2 1H
PCPD2 80.00 usec
PL2 1.00 dB
PL12 15.54 dB
PL13 16.54 dB
PL2W 19.95262337 W
PL12W 0.70145530 W
PL13W 0.55718565 W
SFO2 400.1316005 MHz
F2 - Processing parameters
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SF 100.6127548 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40
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123.88
110.24
109.18
107.69
77.35
77.348
45.95
35.31
33.72
33.25
31.31
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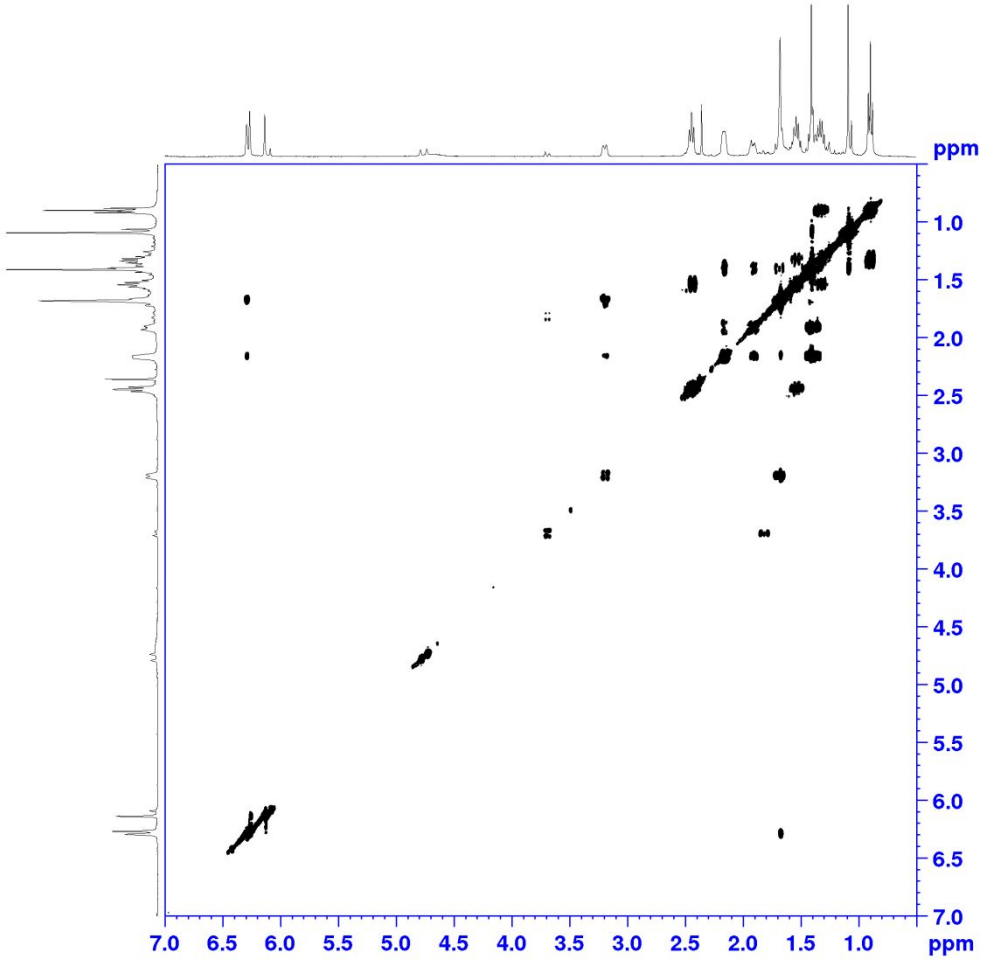
Figure S9

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PULPROG         cosygpqf
TD                  2048
SOLVENT             CDCl3
NS                     2
DS                     8
SWH              5341.880 Hz
FIDRES           2.608340 Hz
AQ               0.1916928 sec
RG                 228.1
DW                93.600 usec
DE                 6.50 usec
TE                297.8 K
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D1            1.00000000 sec
D13           0.00000400 sec
D16           0.00020000 sec
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======== CHANNEL f1 ========
NUC1                  1H
P0                 15.00 usec
P1                 15.00 usec
PL1                 1.00 dB
PL1W         19.95262337 W
SFO1        400.1324057 MHz

====== GRADIENT CHANNEL =====
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GPZ1                10.00 %
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SFO1            400.1324 MHz
FIDRES         41.733440 Hz
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FnMODE                QF

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SF          400.1300130 MHz
WDW                  SINE
SSB       0
LB        0 Hz
GB        0
PC                  1.40

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MC2                    QF
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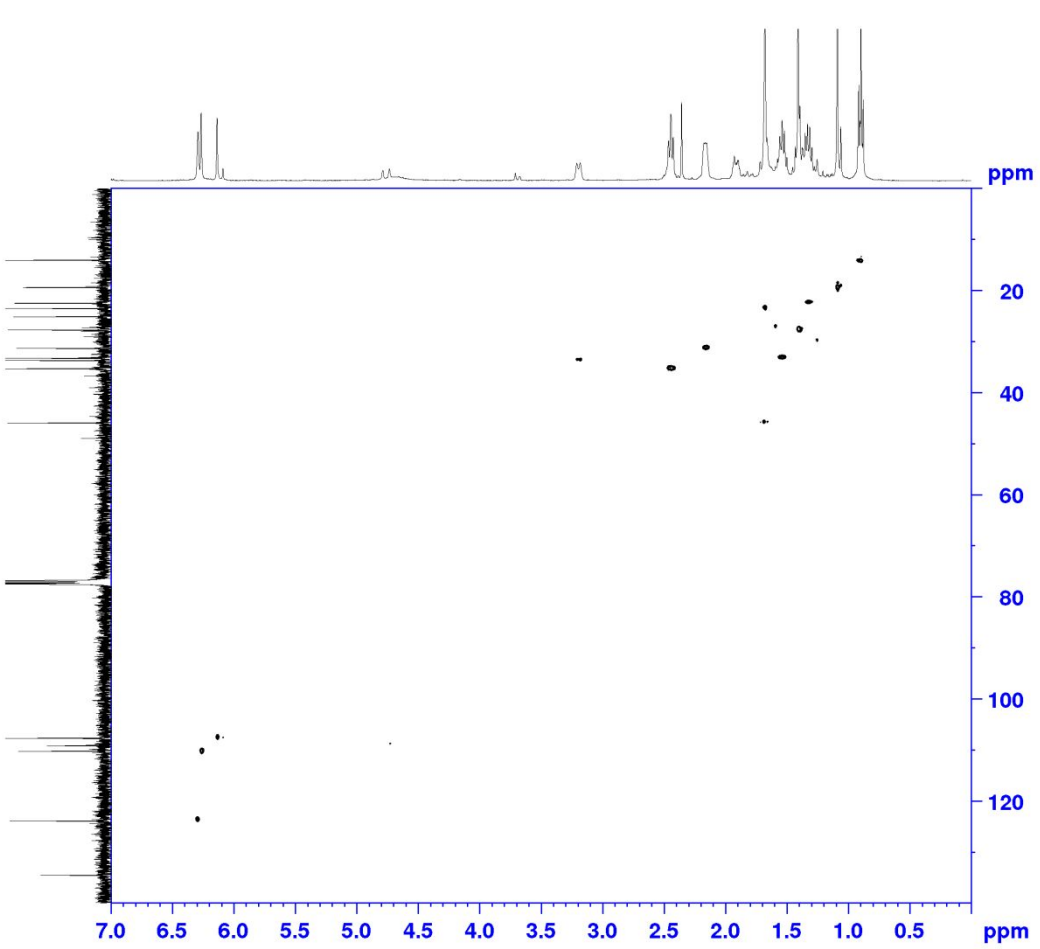
Figure S10

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PROCNO                  1

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TD                   2048
SOLVENT              CDCl3
NS                      4
DS                     16
SWH               5341.880 Hz
FIDRES            2.608340 Hz
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RG                     4096
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TE                 298.2 K
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D4                0.00172414 sec
D11               0.03000000 sec
D13               0.00000400 sec
D16               0.00020000 sec
D21               0.00345000 sec
IN0               0.00003000 sec
ZGOPTNS

======== CHANNEL f1 ========
NUC1                    1H
P1                   15.00 usec
P2                   30.00 usec
P28                   1.00 usec
PL1                   1.00 dB
PL1W         19.95262337 W
SFO1         400.1324057 MHz

======== CHANNEL f2 ========
CPDPRG[2              garp
NUC2                   13C
P3                    9.25 usec
P4                   18.50 usec
PCPD2                70.00 usec
PL2                   1.00 dB
PL12                 18.00 dB
PL2W         59.85786819 W
PL12W         1.19432151 W
SFO2         100.6202727 MHz

====== GRADIENT CHANNEL =====
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GPNAM[2]         SINE.100
GPZ1                80.00 %
GPZ2                20.10 %
P16               1000.00 usec

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TD                     256
SFO1            100.6203 MHz
FIDRES         130.208328 Hz
SW                165.639 ppm
FnMODE     Echo-Antiecho

F2 - Processing parameters
SI                    2048
SF              400.1300123 MHz
WDW                   QSINE
SSB                       2
LB         0 Hz
GB         0
PC                     1.40

F1 - Processing parameters
SI                    1024
MC2         echo-antiecho
SF              100.6127690 MHz
WDW                   QSINE
SSB                       2
LB         0 Hz
GB         0
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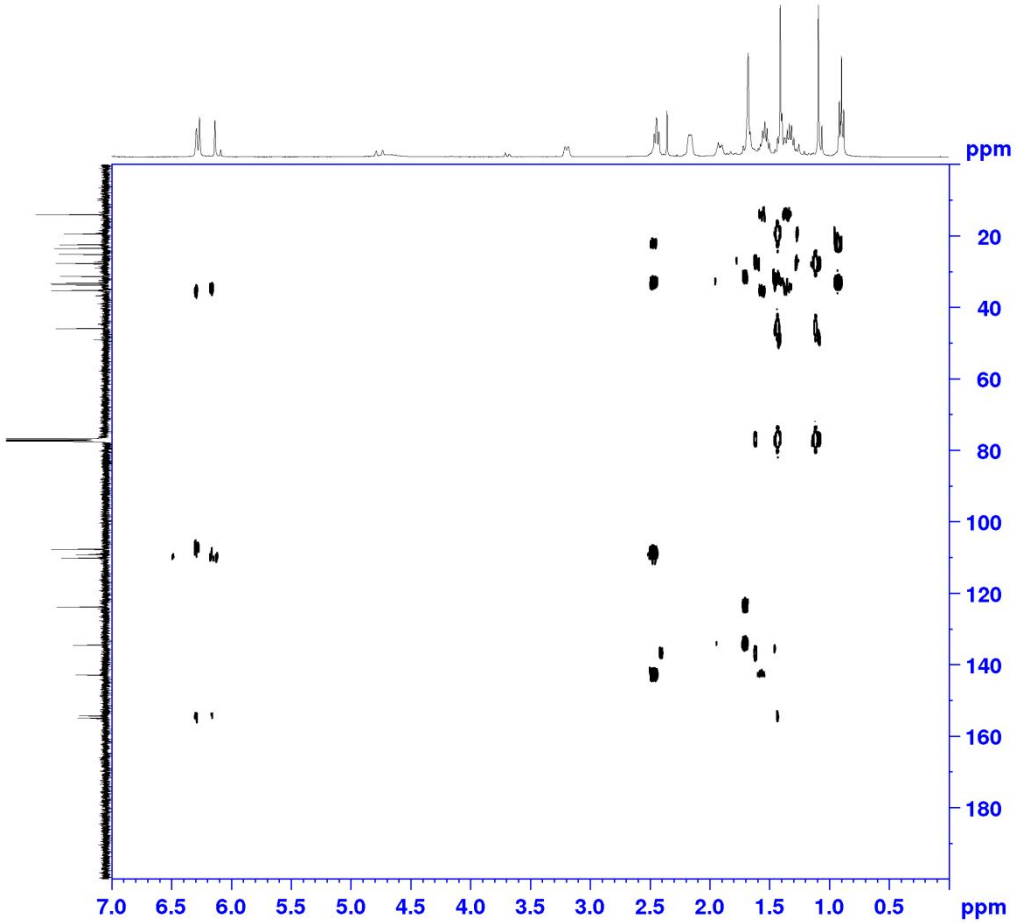
Figure S11

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INSTRUM           spect
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PULPROG    hmbcgplpndqf
TD                 4096
SOLVENT            CDCl3
NS                   16
DS                   16
SWH             5208.333 Hz
FIDRES          1.271566 Hz
AQ              0.3932160 sec
RG                  4096
DW                96.000 usec
DE                 6.50 usec
TE                298.0 K
CNST2         145.0000000
CNST13          8.0000000
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D1              1.00000000 sec
D2              0.00344828 sec
D6              0.06250000 sec
D16             0.00020000 sec
IN0             0.00002235 sec

======== CHANNEL f1 ========
NUC1                1H
P1                 15.00 usec
P2                 30.00 usec
PL1                 1.00 dB
PLW          19.95262337 W
SFO1         400.1325208 MHz

======== CHANNEL f2 ========
NUC2               13C
P3                  9.25 usec
PL2                 1.00 dB
PLW          59.85786819 W
SFO2         100.6228138 MHz

====== GRADIENT CHANNEL =====
GPNAM[1]        SINE.100
GPNAM[2]        SINE.100
GPNAM[3]        SINE.100
GPZ1               50.00 %
GPZ2               30.00 %
GPZ3               40.10 %
P16              1000.00 usec

F1 - Acquisition parameters
TD                   65
SFO1          100.6228 MHz
FIDRES        687.625549 Hz
SW            222.095 ppm
FnMODE               QF

F2 - Processing parameters
SI                 4096
SF          400.1300000 MHz
WDW                SINE
SSB       0
LB        0 Hz
GB        0
PC                 1.40

F1 - Processing parameters
SI                 1024
MC2                  QF
SF          100.6127690 MHz
WDW                SINE
SSB       0
LB        0 Hz
GB        0
```

NMR spectra of extracted (-)-*trans*-Δ^9-THCB

Figure S12

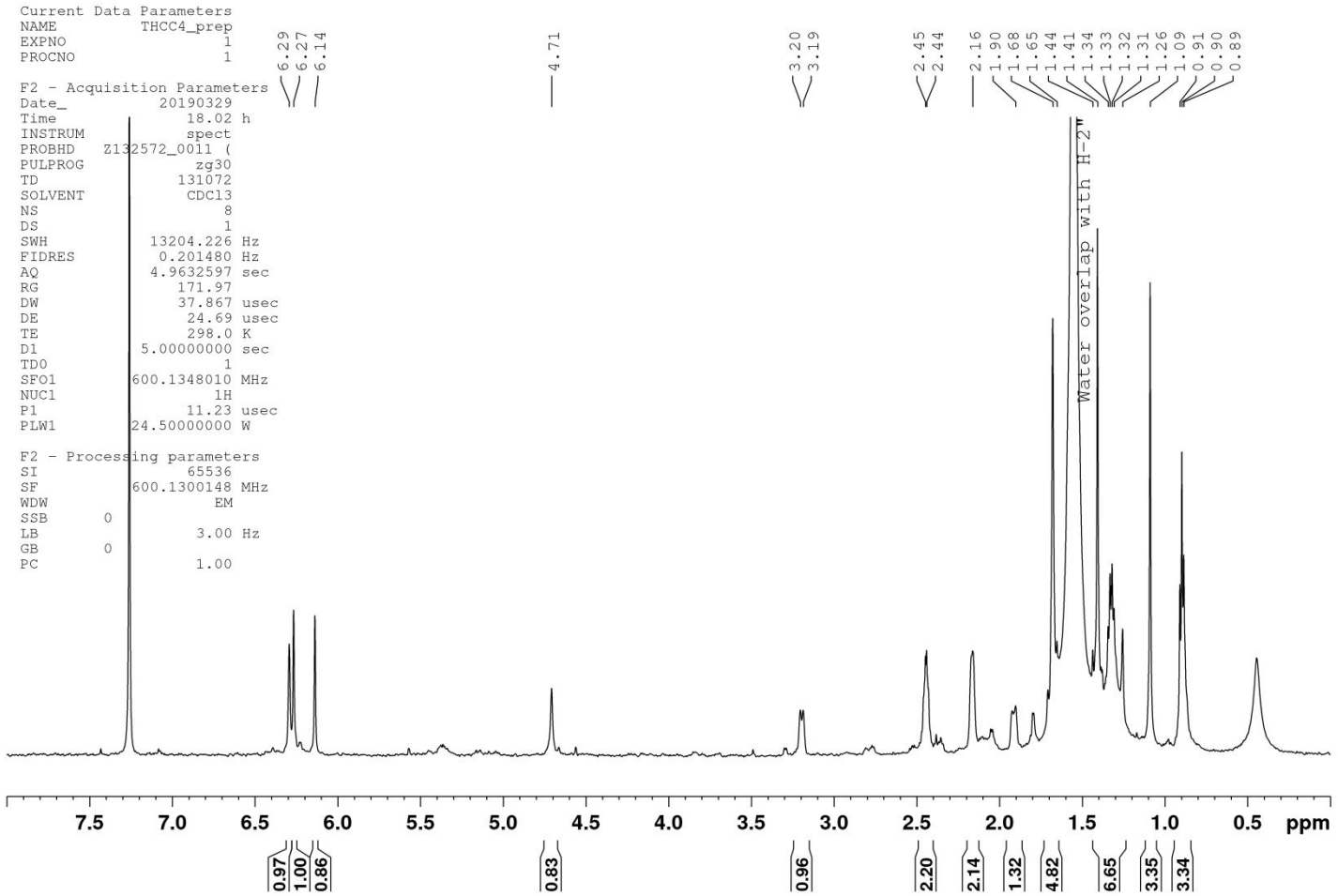
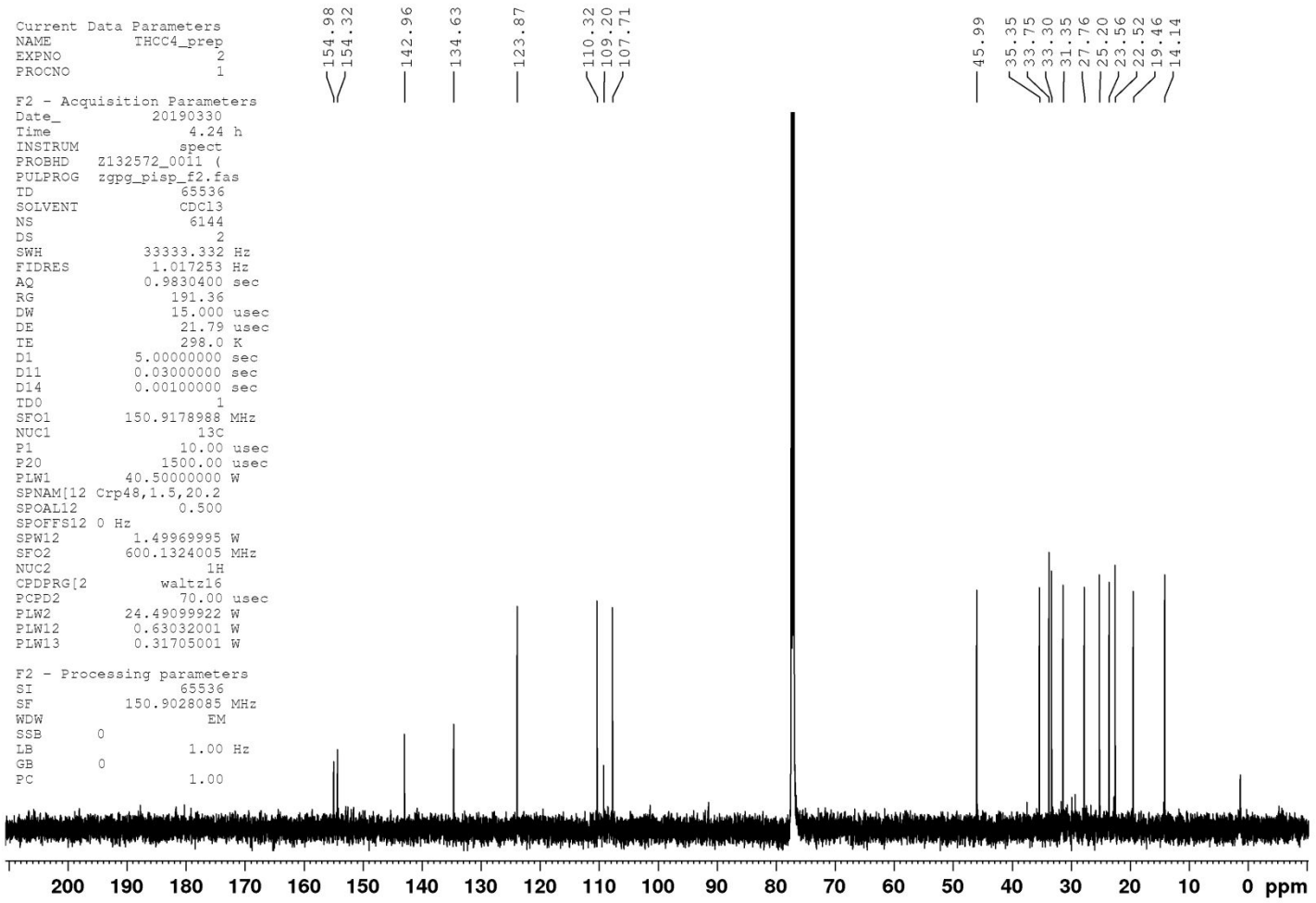


Figure S13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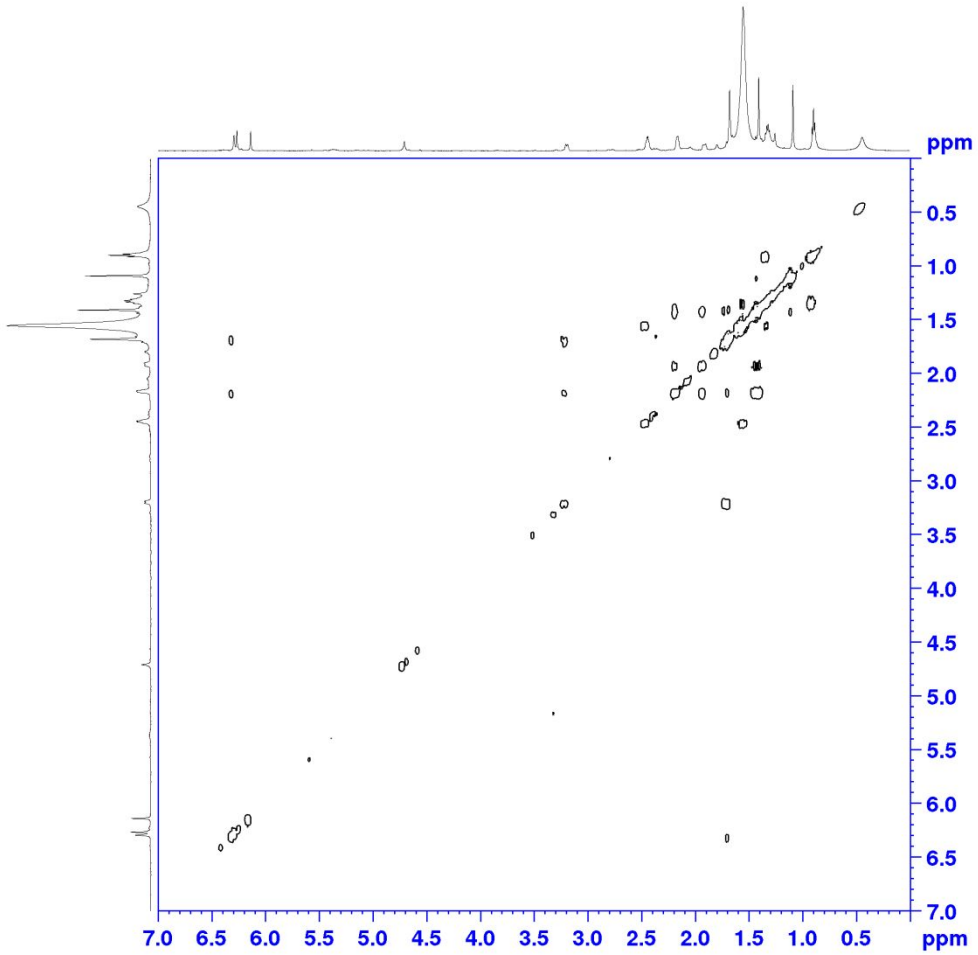
TD 65536
SOLVENT CDCl3
NS 6144
DS 2
SWH 33333.332 Hz
FIDRES 1.017253 Hz
AQ 0.9830400 sec
RG 191.36
DW 15.000 usec
DE 21.79 usec
TE 298.0 K
D1 5.00000000 sec
D11 0.03000000 sec
D14 0.00100000 sec
TD0 1
SFO1 150.9178988 MHz
NUC1 13C
P1 10.00 usec
P20 1500.00 usec
PLW1 40.50000000 W
SPNAM[12 Crp48,1.5,20.2
SPOAL12 0.500
SPOFFS12 0 Hz
SPW12 1.49969995 W
SFO2 600.1324005 MHz
NUC2 1H
CPDPRG[2 waltz16
PCPD2 70.00 usec
PLW2 24.49099922 W
PLW12 0.63032001 W
PLW13 0.31705001 W
F2 - Processing parameters
SI 65536
SF 150.9028085 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.00
154.98
154.32
142.96
134.63
123.87
110.32
109.20
107.71
45.99
35.35
33.75
33.30
31.35
27.76
25.20
23.56
22.52
19.46
14.14
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

Figure S14

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PULPROG       cosygpppqf
TD                  2048
SOLVENT             CDC13
NS                     4
DS                     8
SWH              7812.500 Hz
FIDRES           7.629395 Hz
AQ               0.1310720 sec
RG                  54.87
DW                 64.000 usec
DE                 20.00 usec
TE                298.0 K
D0             0.00000300 sec
D1             1.00000000 sec
D11            0.03000000 sec
D12            0.00002000 sec
D13            0.00000400 sec
D16            0.00020000 sec
IN0            0.00012800 sec
TDav                   1
SFO1         600.1324005 MHz
NUC1                1H
P0                 11.23 usec
P1                 11.23 usec
P17              2500.00 usec
PLW1         24.49099922 W
PLW10         4.94169998 W
GPNAM[1]      SMSQ10.100
GPZ1               10.00 %
P16              1000.00 usec

F1 - Acquisition parameters
TD                   256
SFO1            600.1324 MHz
FIDRES          61.035156 Hz
SW                13.018 ppm
FnMODE                QF

F2 - Processing parameters
SI                  2048
SF           600.1300000 MHz
WDW                 QSINE
SSB       0
LB        0 Hz
GB        0
PC                  1.00

F1 - Processing parameters
SI                  1024
MC2                   QF
SF           600.1300000 MHz
WDW                 QSINE
SSB       0
LB        0 Hz
GB        0
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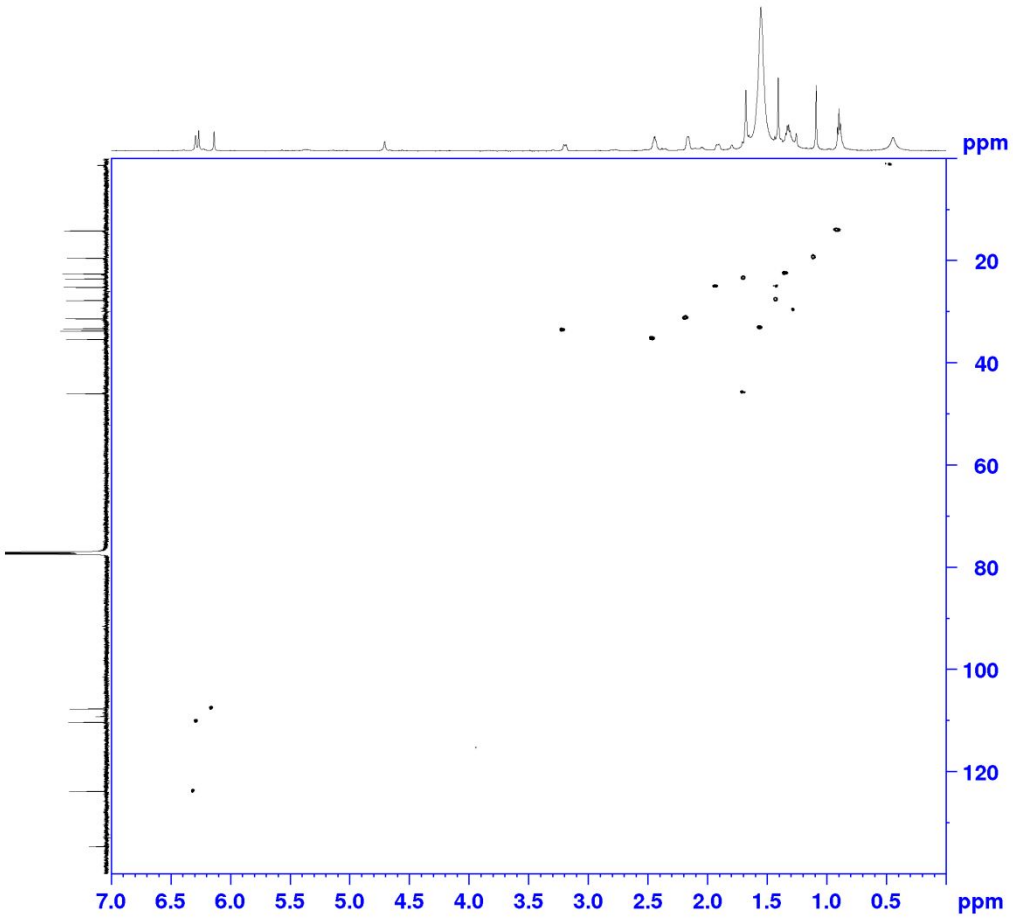
Figure S15

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TD                  2048
SOLVENT            CDCl3
NS                     8
DS                    16
SWH             7812.500 Hz
FIDRES             7.629395 Hz
AQ              0.1310720 sec
RG                 191.36
DW                64.000 usec
DE                20.00 usec
TE                298.0 K
CNST2          145.0000000
D0              0.00000300 sec
D1              0.50000000 sec
D4              0.00172414 sec
D11             0.03000000 sec
D16             0.00020000 sec
D21             0.00345000 sec
IN0             0.00001840 sec
TDav                   1
SFO1          600.1324005 MHz
NUC1                  1H
P1                 11.23 usec
P2                 22.46 usec
P28       0 usec
PLW1         24.49099922 W
SFO2         150.9148808 MHz
NUC2                 13C
CPDPRG[2             garp4
P3                 10.00 usec
P14               500.00 usec
P31              1730.00 usec
PCPD2              60.00 usec
PLW0       0 W
PLW2          40.50000000 W
PLW12          1.12500000 W
SPNAM[3] Crp60,0.5,20.1
SPOAL3               0.500
SPOFFS3    0 Hz
SFW3           6.18790007 W
SPNAM[18   Crp60_xfilt.2
SPOAL18              0.500
SPOFFS18   0 Hz
SFW18          1.78840005 W
GPNAM[1]       SMSQ10.100
GPZ1                80.00 %
GPNAM[2]       SMSQ10.100
GPZ2                20.10 %
P16               1000.00 usec

F1 - Acquisition parameters
TD                    512
SFO1            150.9149 MHz
FIDRES         106.148094 Hz
SW              180.061 ppm
FnMODE     Echo-Antiecho

F2 - Processing parameters
SI                   2048
SF            600.1300000 MHz
WDW                  QSINE
SSB                      2
LB         0 Hz
GB         0
PC                    1.00

F1 - Processing parameters
SI                   1024
MC2         echo-antiecho
SF             150.9028085 MHz
WDW                  QSINE
SSB                      2
LB         0 Hz
GB         0
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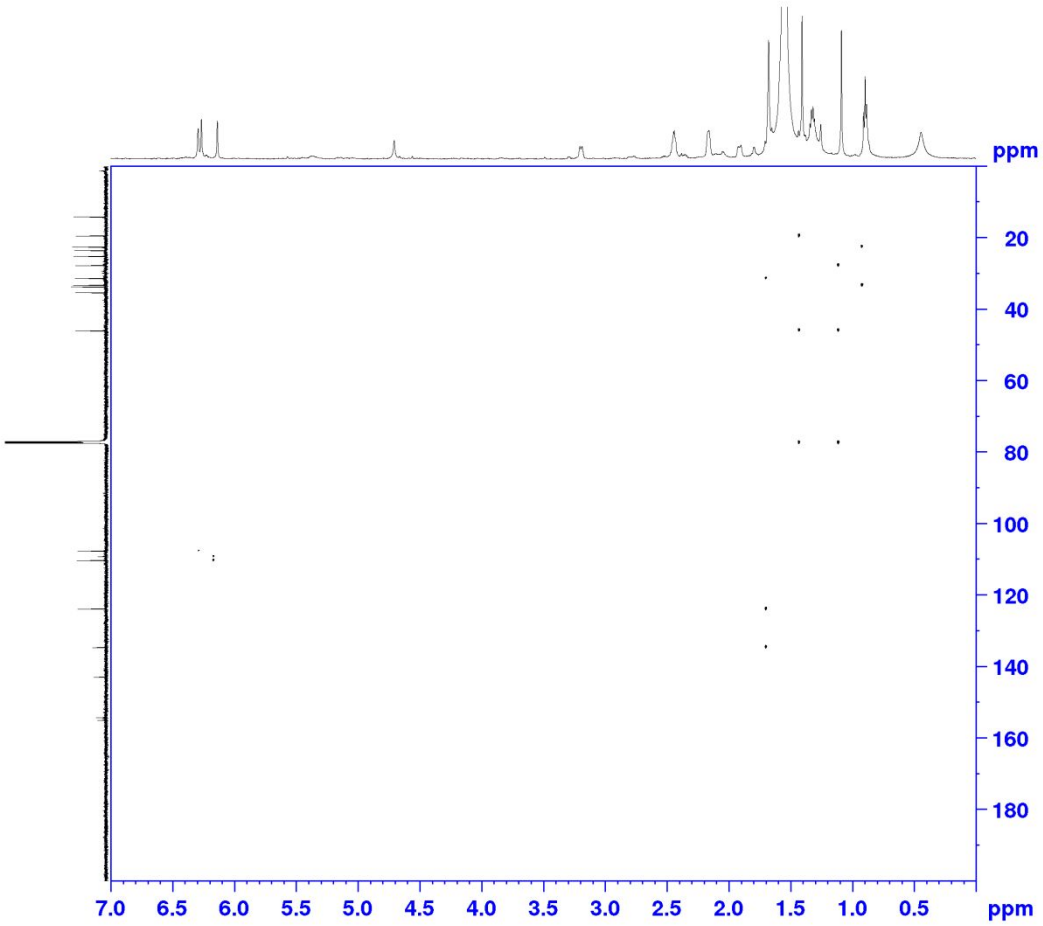
Figure S16

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PULPROG    hmbcetgpl3nd
TD                      4096
SOLVENT                 CDCl3
NS                        16
DS                        16
SWH                 7812.500 Hz
FIDRES              3.814697 Hz
AQ                  0.2621440 sec
RG                     191.36
DW                     64.000 usec
DE                     20.00 usec
TE                     298.0 K
CNST6              120.0000000
CNST7              170.0000000
CNST13               8.0000000
D0                  0.00000300 sec
D1                  0.50000000 sec
D6                  0.06250000 sec
D16                 0.00020000 sec
IN0                 0.00001510 sec
TDav                          1
SFO1               600.1324005 MHz
NUC1                        1H
P1                     11.23 usec
P2                     22.46 usec
PLW1               24.49099922 W
SFO2               150.9178988 MHz
NUC2                       13C
P3                     10.00 usec
P24                  2000.00 usec
PLW2               40.50000000 W
SPNAM[7]           Crp60comp.4
SPOAL7                   0.500
SPOFFS7  0 Hz
SPW7                6.18790007 W
GPNAM[1]           SMSQ10.100
GP21                    80.00 %
GPNAM[3]           SMSQ10.100
GP23                    14.00 %
GPNAM[4]           SMSQ10.100
GP24                    -8.00 %
GPNAM[5]           SMSQ10.100
GP25                    -4.00 %
GPNAM[6]           SMSQ10.100
GP26                    -2.00 %
P16                  1000.00 usec

F1 - Acquisition parameters
TD                            512
SFO1               150.9179 MHz
FIDRES             129.346024 Hz
SW                 219.408 ppm
FnMODE     Echo-Antiecho

F2 - Processing parameters
SI                          2048
SF                 600.1300000 MHz
WDW                         SINE
SSB                            4
LB          0 Hz
GB          0
PC                          1.00

F1 - Processing parameters
SI                          1024
MC2             echo-antiecho
SF                 150.9028085 MHz
WDW                        QSINE
SSB                            2
LB          0 Hz
GB          0
```

Figure S17. Superimposition of ^{1}H NMR (A) and ^{13}C NMR (B) of extracted (-)-*trans*-Δ^{9}-THCB (red spectra) and synthetic (-)-*trans*-Δ^{9}-THCB (blue spectra).

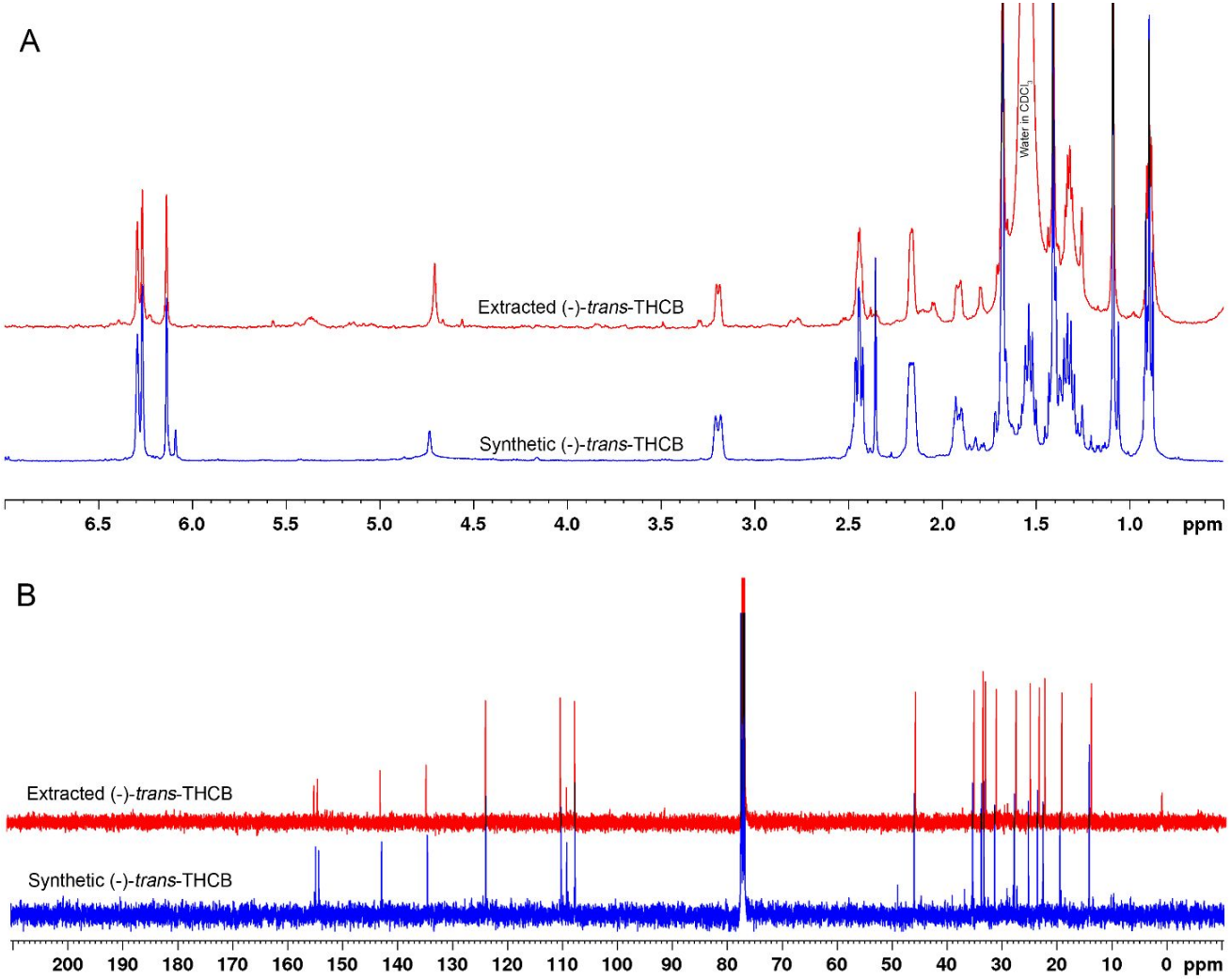

Figure S18. Superimposition of the Circular Dichroism (CD) spectra of isolated (green) and synthesized (blue) Δ^9-THCB, in acetonitrile at 10 µg/mL.