

Supplementary Material

Inhibition of 11 β -HSD1 by Tetracyclic Triterpenoids from *Euphorbia kansui*

Figure S1. ¹H-NMR Spectrum of 3 in CDCl₃.

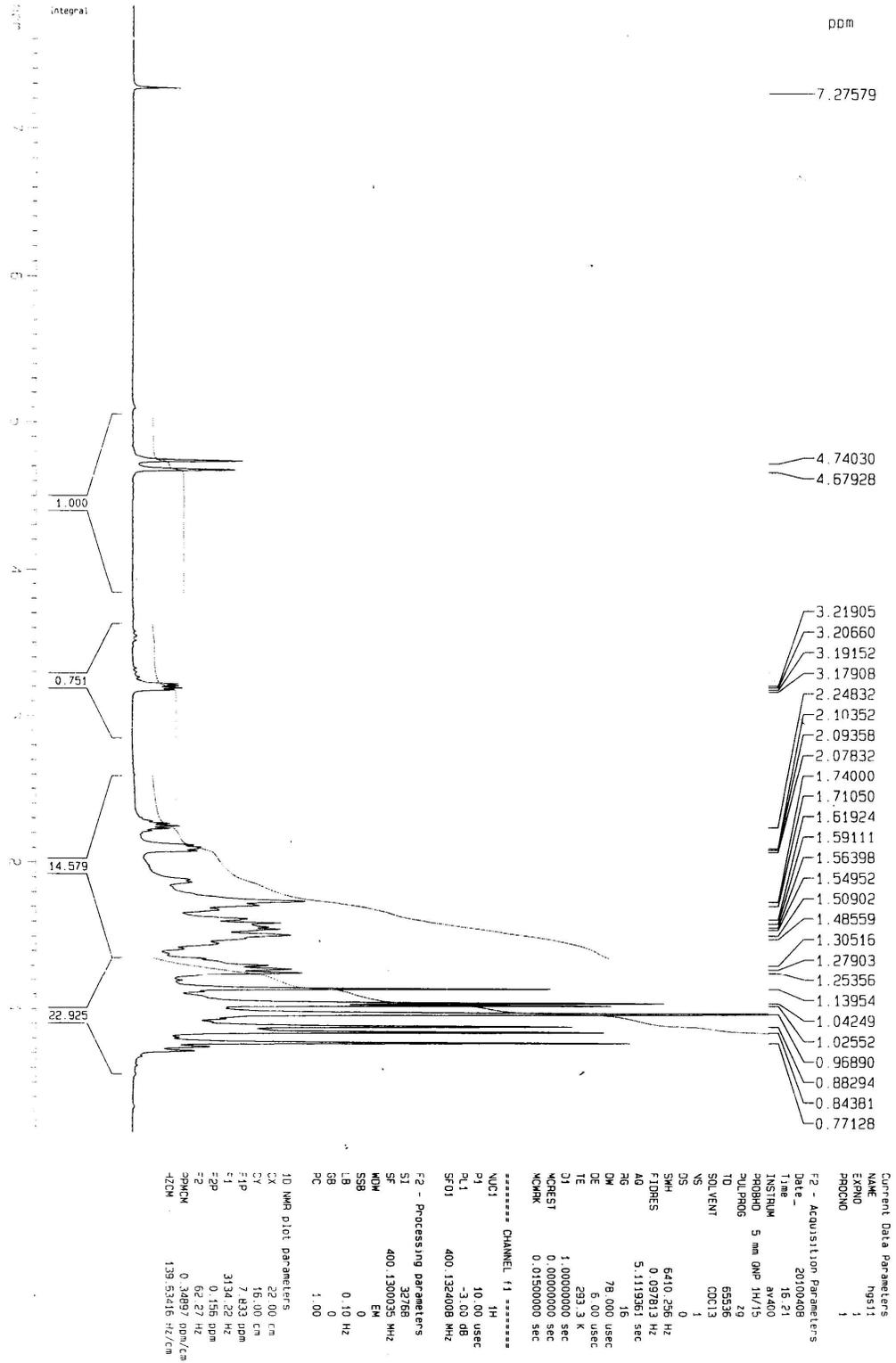


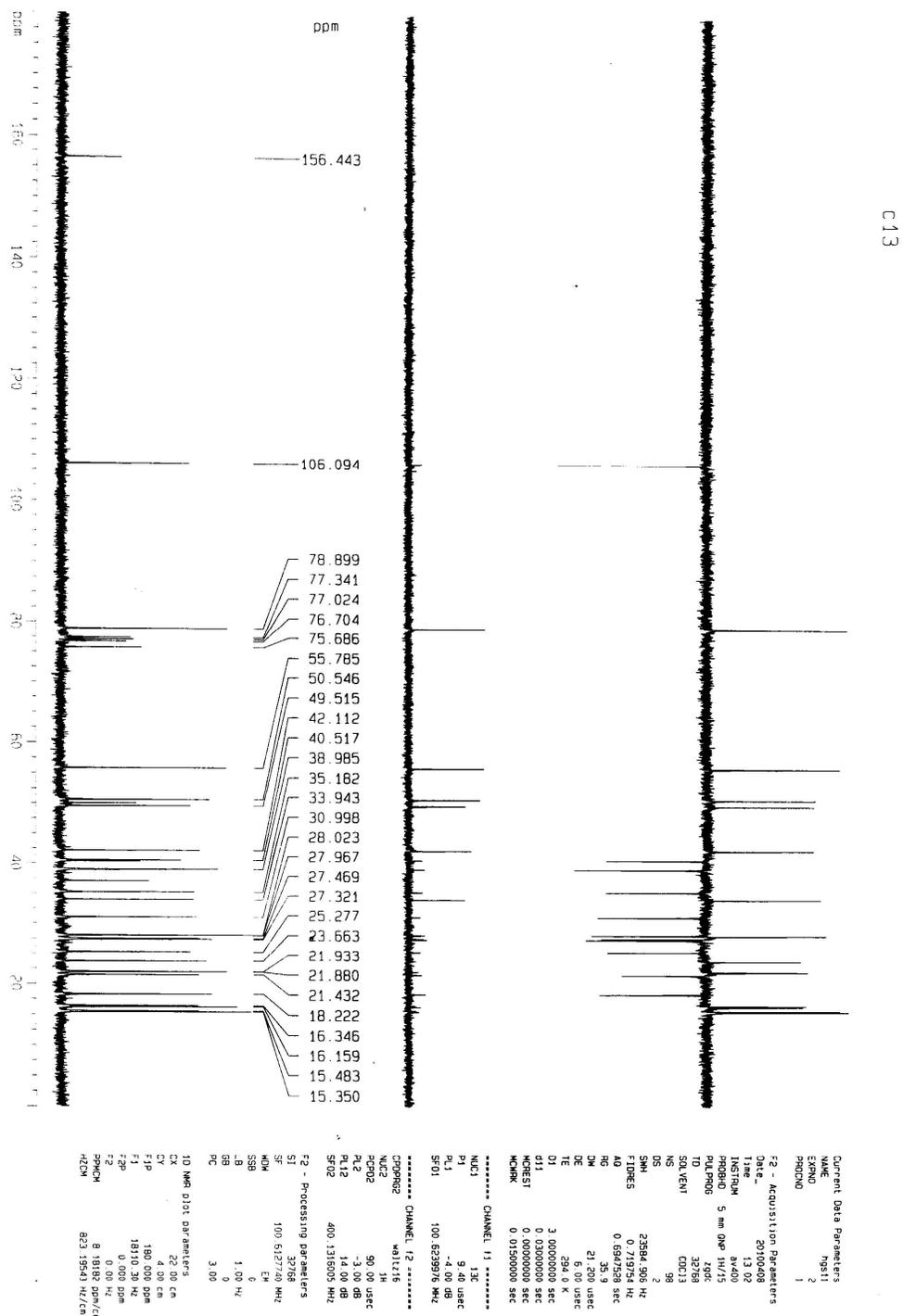
Figure S2. ^{13}C and DEPT NMR Spectrum of **3** in CDCl_3 .

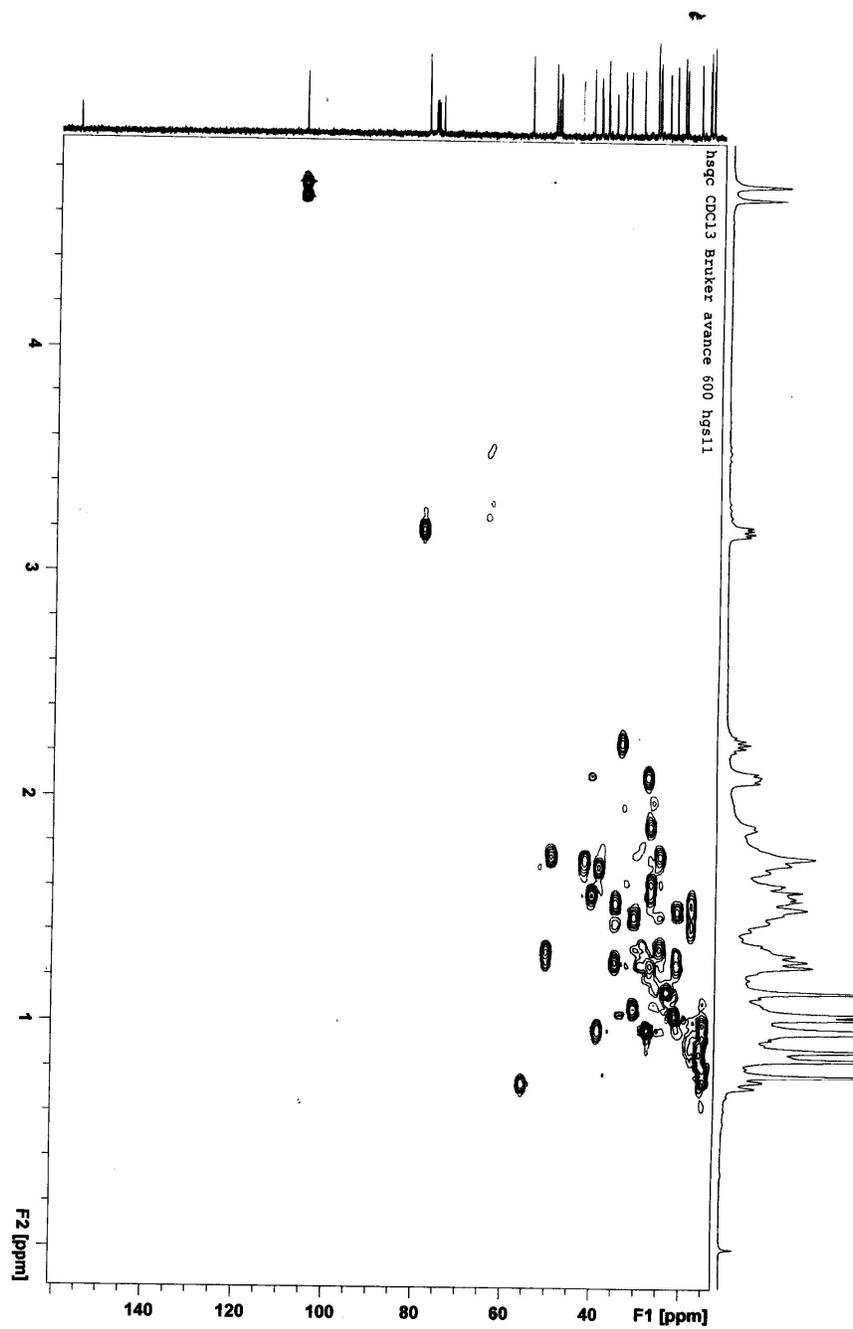
Figure S3. HSQC Spectrum of 3 in CDCl₃.

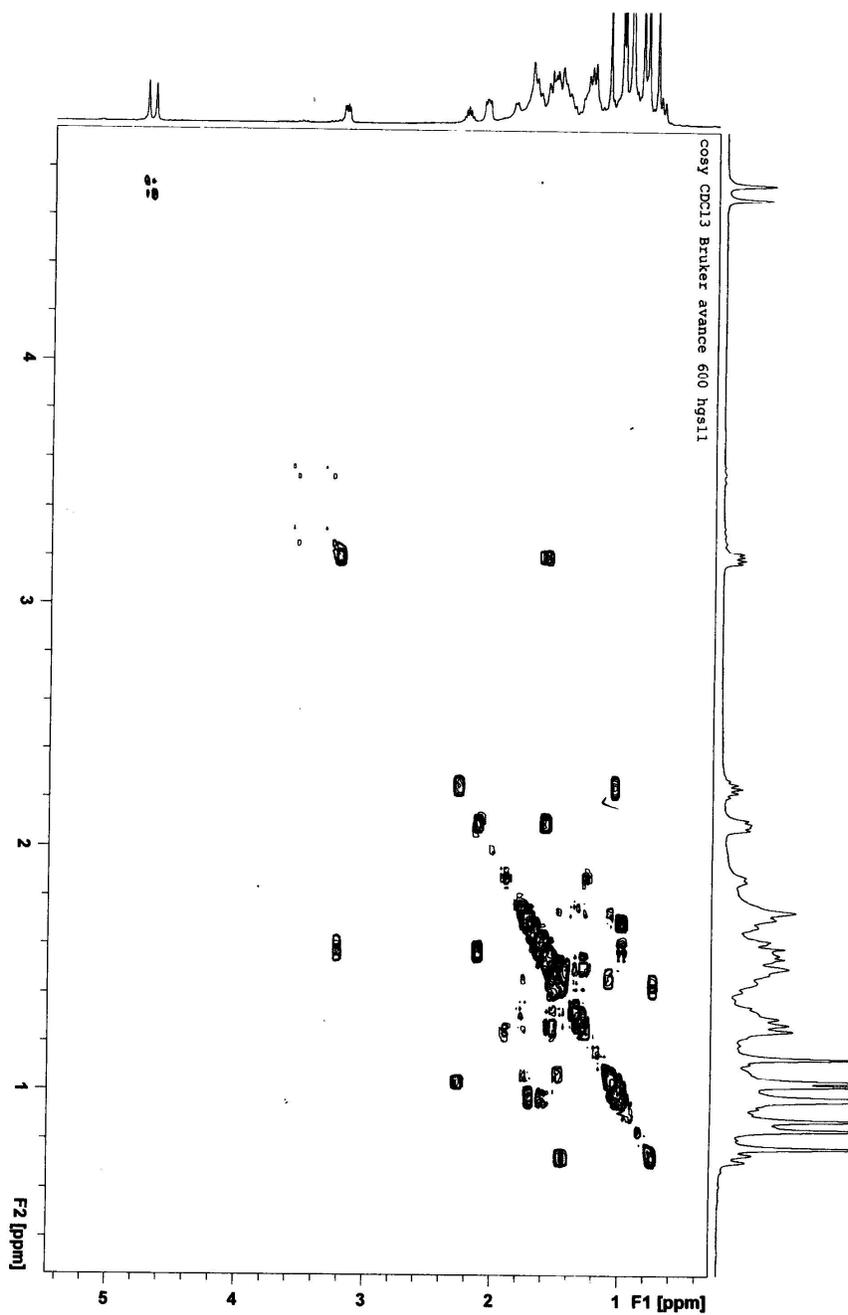
Figure S4. ^1H - ^1H COSY Spectrum of **3** in CDCl_3 .

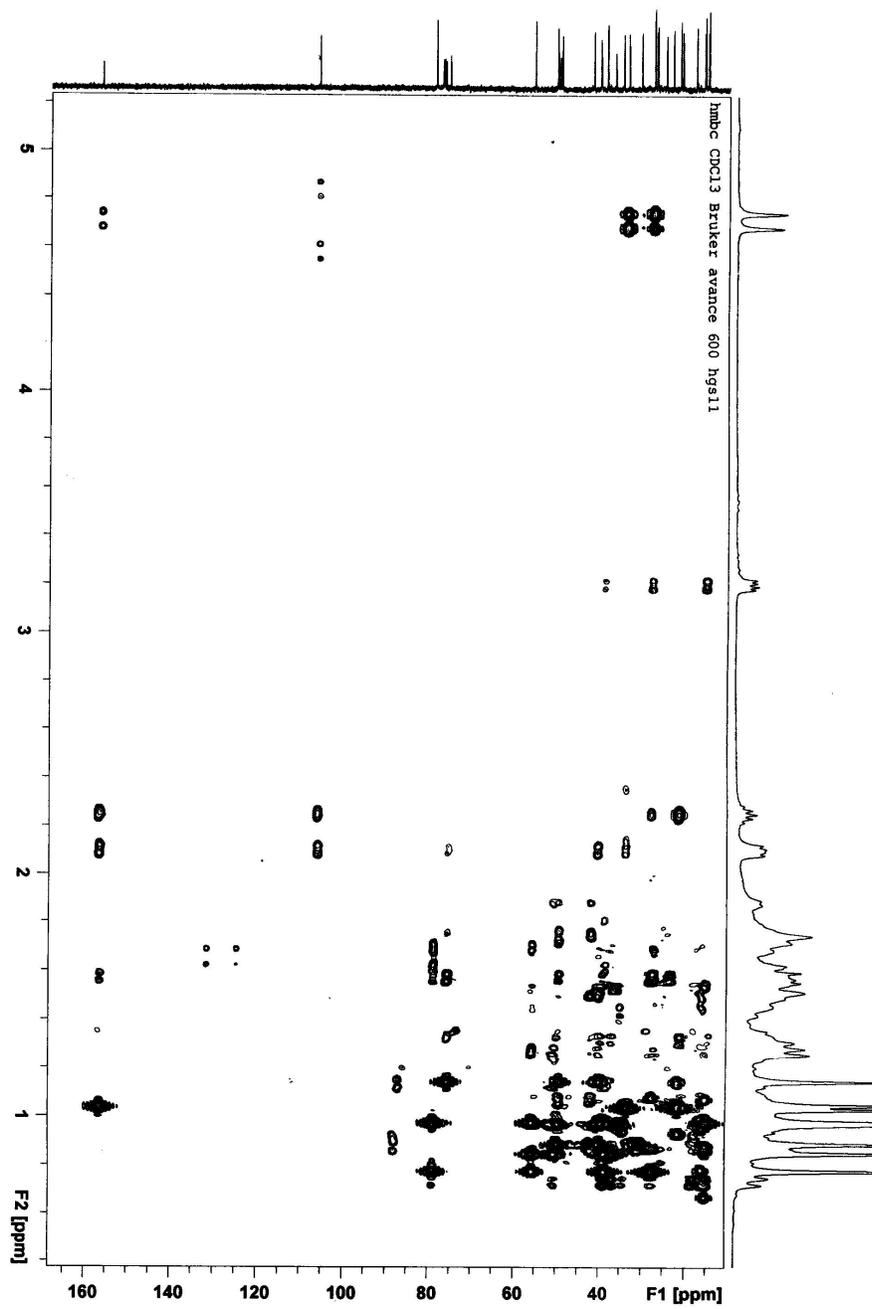
Figure S5. HMBC Spectrum of 3 in CDCl₃.

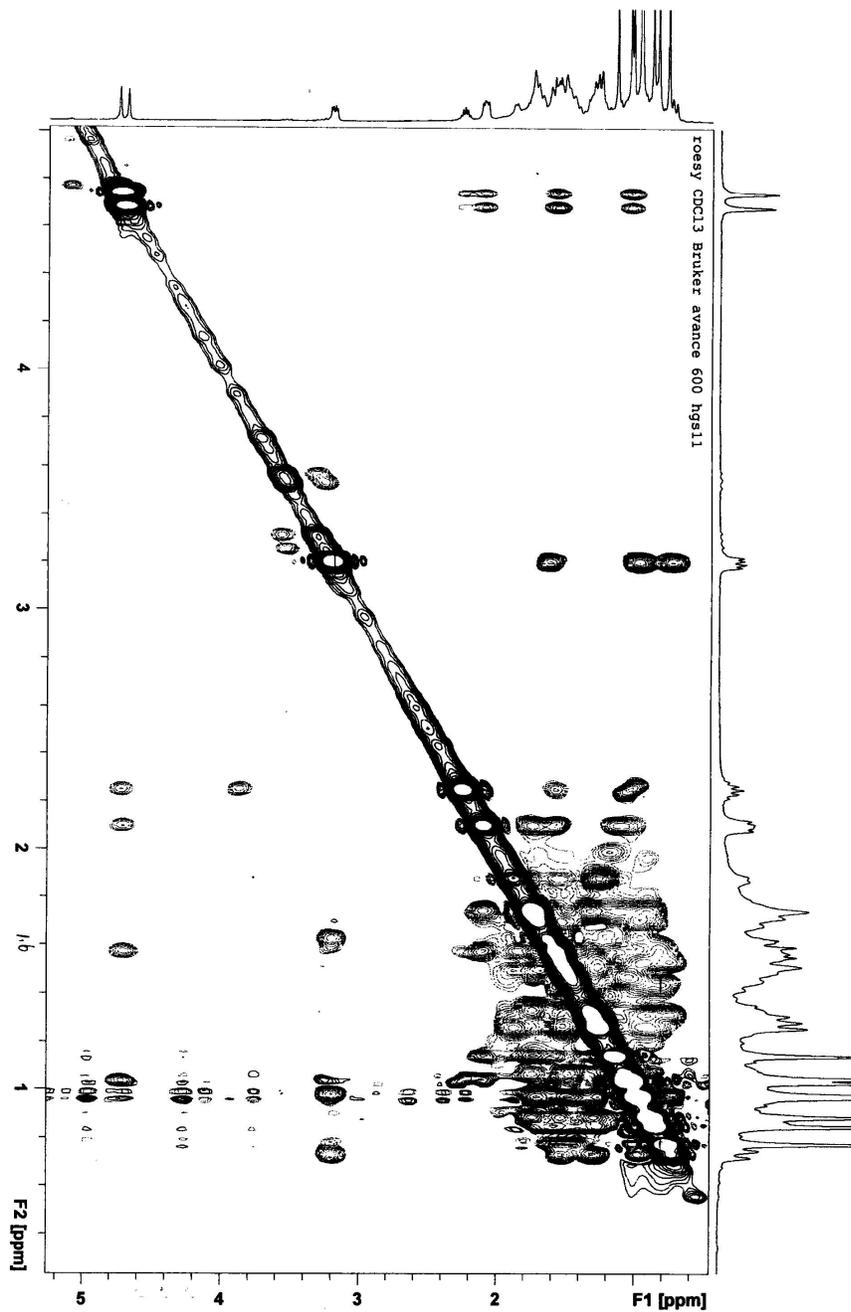
Figure S6. ROESY Spectrum of 3 in CDCl₃.

Figure S7. EI Mass Spectrometry of 3.

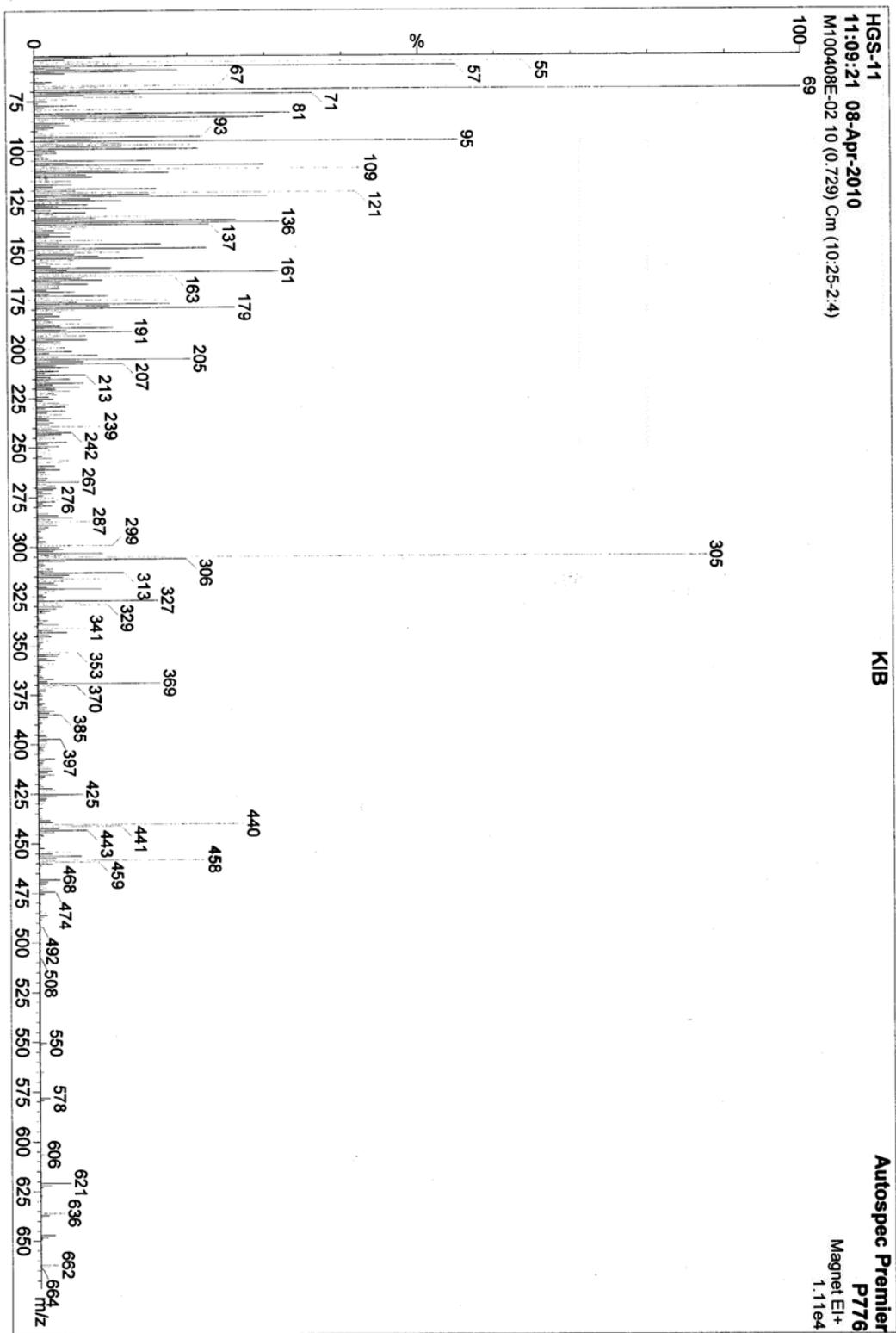
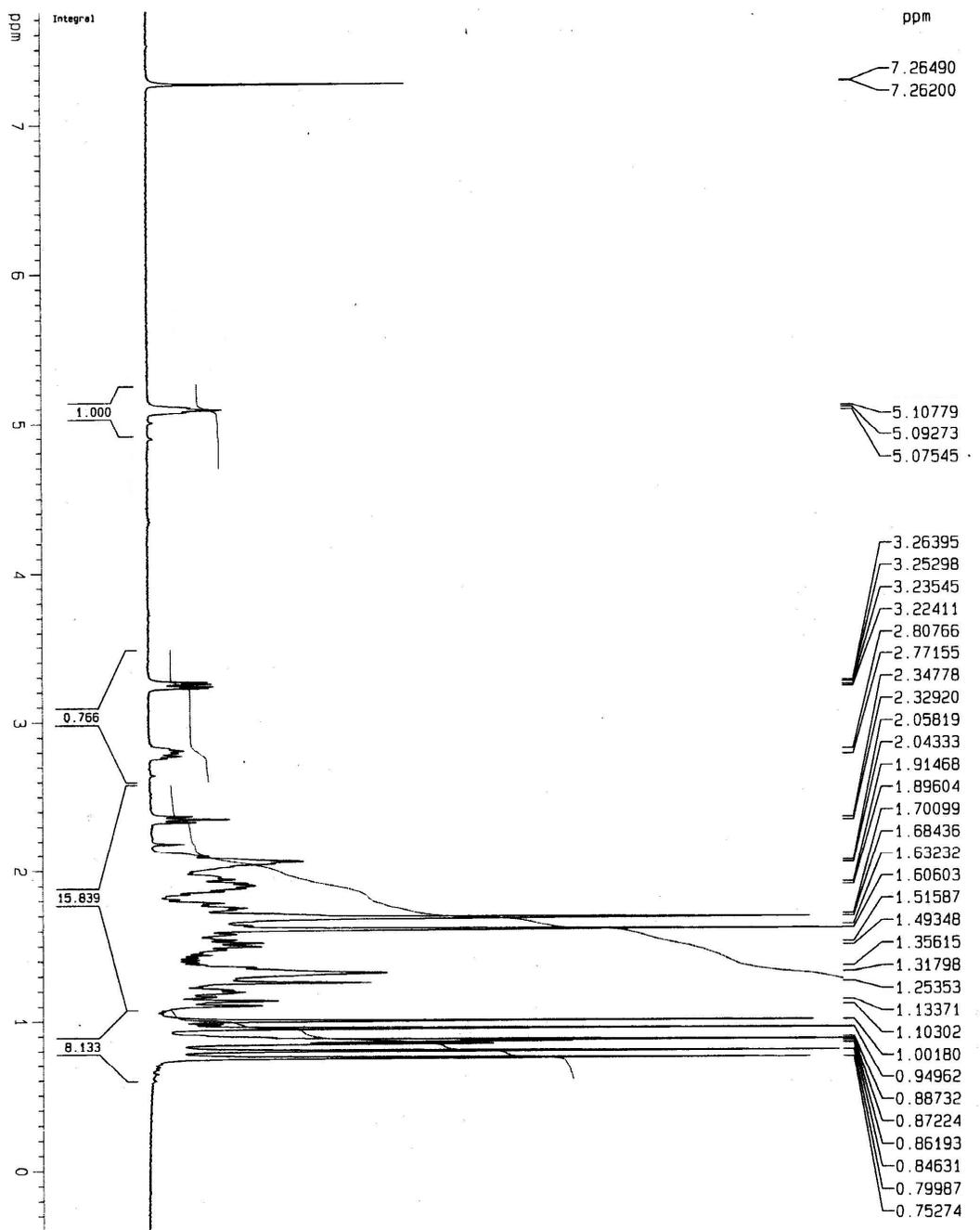


Figure S8. ¹H-NMR Spectrum of 1 in CDCl₃.

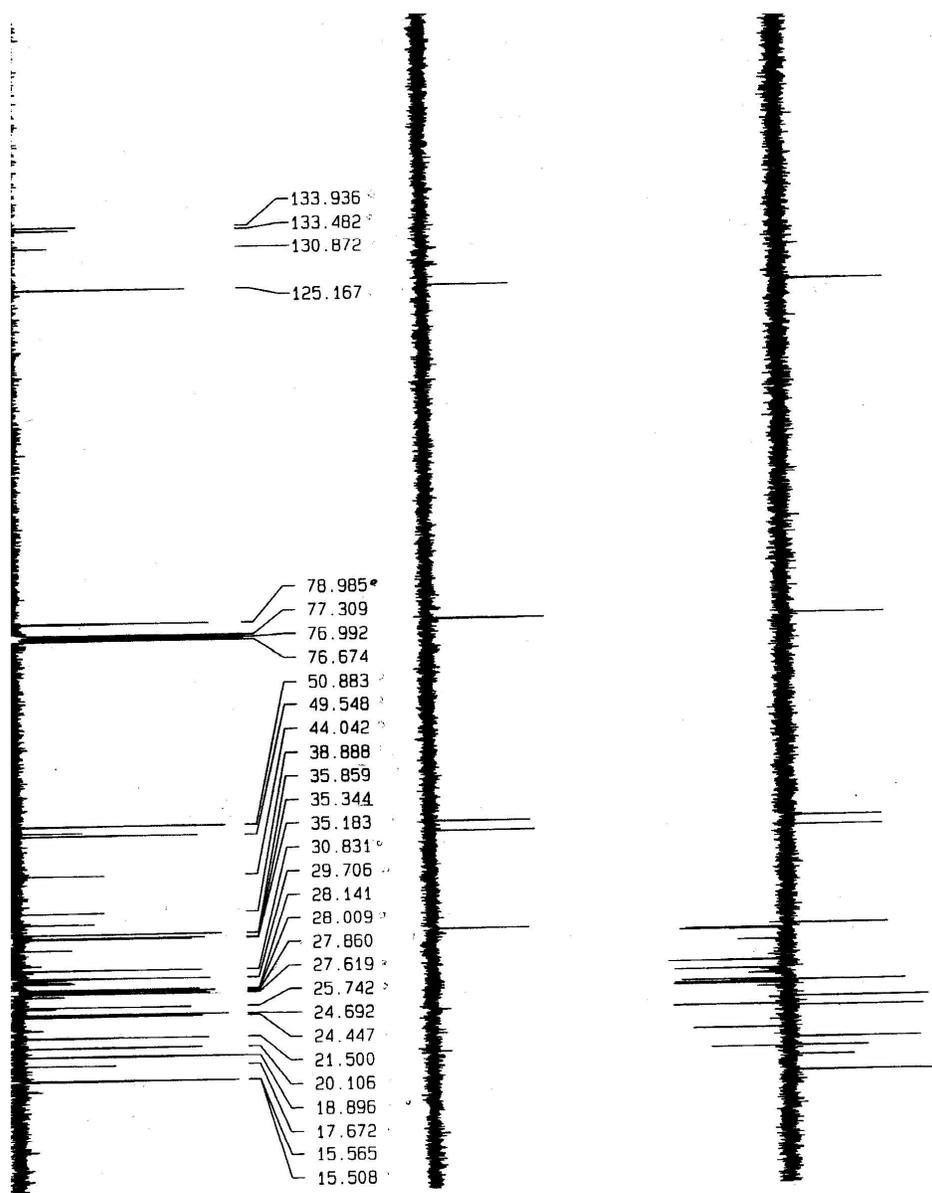
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EXPNO 1
PROCNO 1

F2 - Acquisition Parameters
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INSTRUM av400
PROBHD 5 mm QNP 1H/15
PULPROG zg
TD 65536
SOLVENT CDCl3
NS 1
DS 0
SFO 6410.266 Hz
FIDRES 0.097813 Hz
AQ 5.119361 sec
RG 71.8
DM 78.000 usec
DE 6.00 usec
TE 291.4 K
D1 2.00000000 sec
MCHEST 0.00000000 sec
KCHXK 0.01500000 sec

***** CHANNEL f1 *****
NUC1 1H
P1 10.00 usec
PL1 -3.00 dB
SFO1 400.1324008 MHz

F2 - Processing parameters
SI 32768
SF 400.1305965 MHz
MDM EM
SSB 0
LB 0.30 Hz
GB 0
FC 1.00

1D NMR plot parameters
CX 22.00 cm
CY 13.00 cm
F1P 7.754 ppm
F1 3102.60 Hz
F2P -0.396 ppm
F2 -158.61 Hz
PPMCH 0.37047 ppm/cm
HZCM 148.23591 Hz/cm

Figure S9. ^{13}C -NMR Spectrum of 1 in CDCl_3 .

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Current Data Parameters
NAME      f9s1
EXPNO    2
PROCNO   1

F2 - Acquisition Parameters
Date_    20080313
Time     11.43
INSTRUM  spect
PROBHD   5 mm QNP 1H/1
PULPROG  zgpg30
PCPRG06  jmod
TD        32768
SOLVENT  CDCl3
NS        400
DS        2
SWH       23564.306 Hz
FIDRES    0.719754 Hz
AQ         0.6947528 sec
RG         8192
DM         21.200 usec
DE         6.00 usec
TE         292.0 K
D1         3.50000000 sec
d11        0.03000000 sec
MCKEYEST  0.00000000 sec
MCKEY     0.01500000 sec

***** CHANNEL f1 *****
NUC1       13C
P1         9.40 usec
PL1        -4.00 dB
SFO1      100.6289975 MHz

***** CHANNEL f2 *****
CPDPRG2   waltz16
NUC2       1H
PCPD2     30.00 usec
PL2        -3.00 dB
PL12       14.00 dB
SFO2      400.1315005 MHz

F2 - Processing Parameters
SI         32768
SF         100.628216 MHz
WDW        EM
SSB        0
LB         1.00 Hz
GB         0
PC         2.00

1D NMR plot parameters
CX         22.00 cm
CY         1.00 cm
C1P        180.000 ppm
F1         18110.33 Hz
F2         0.000 ppm
F2         0.00 Hz
SFO1CM    8.18182 ppm/cm
SFO2CM    823.15666 Hz/cm
  
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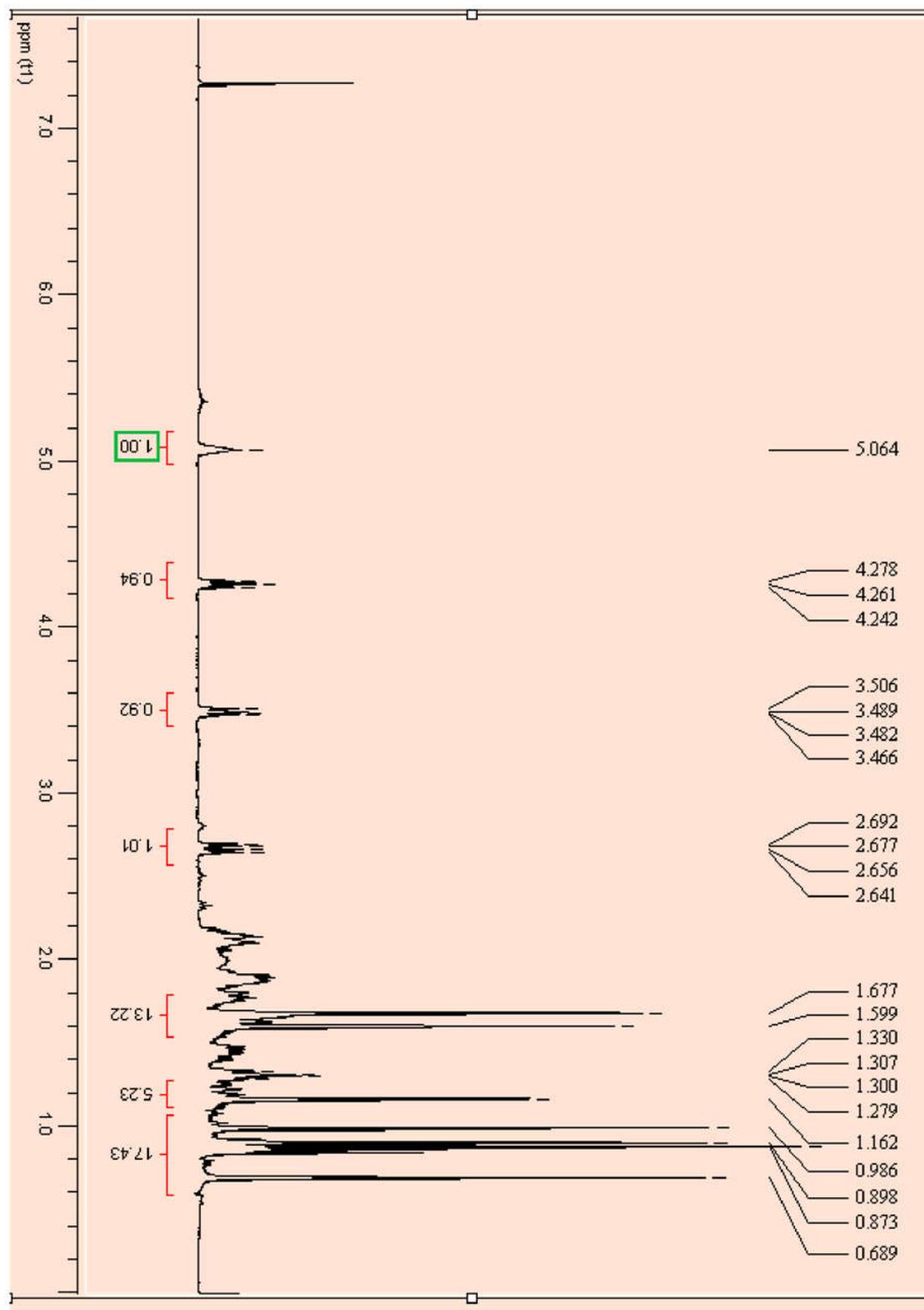
Figure S10. $^1\text{H-NMR}$ Spectrum of **2** in CDCl_3 .

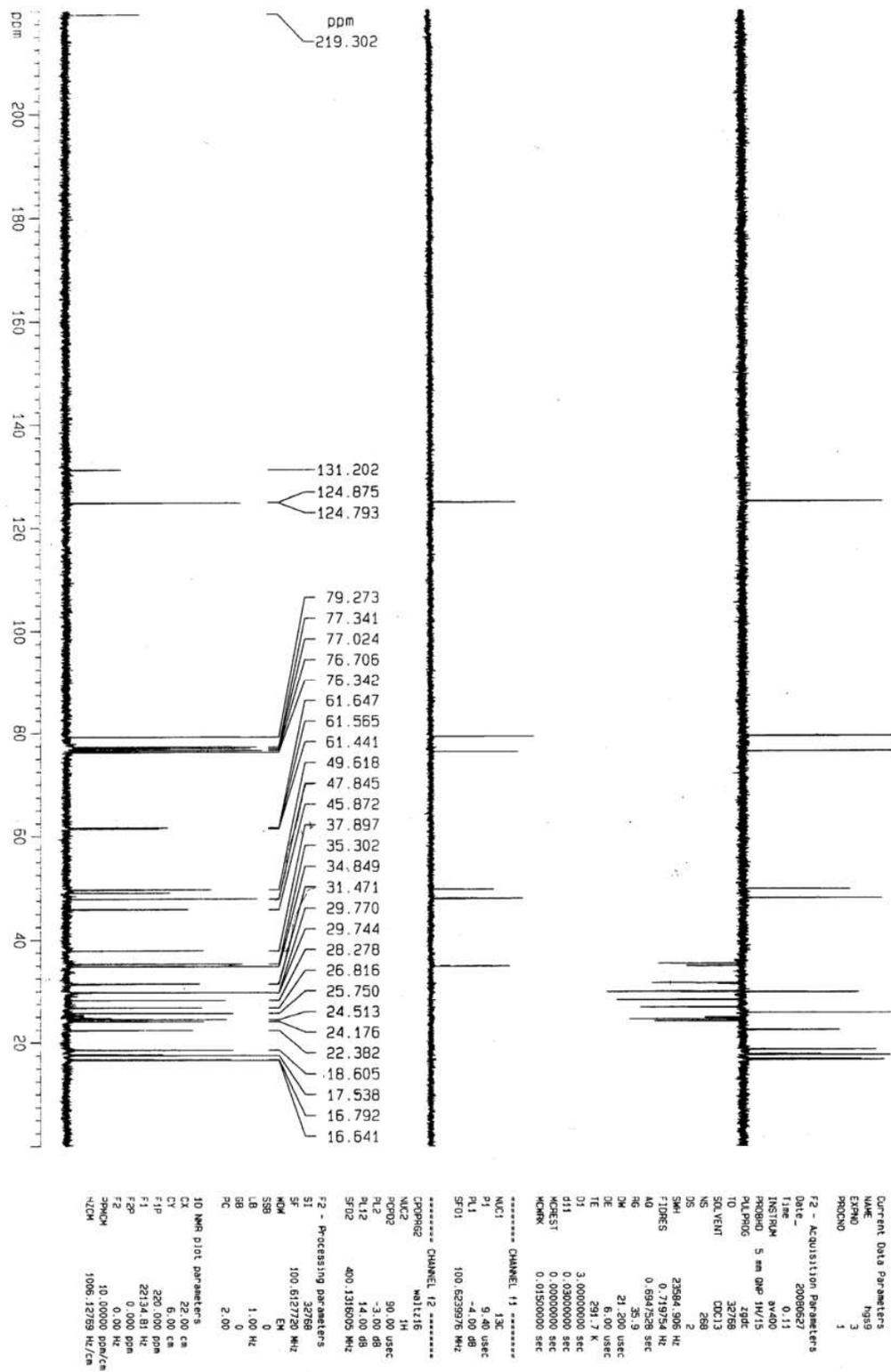
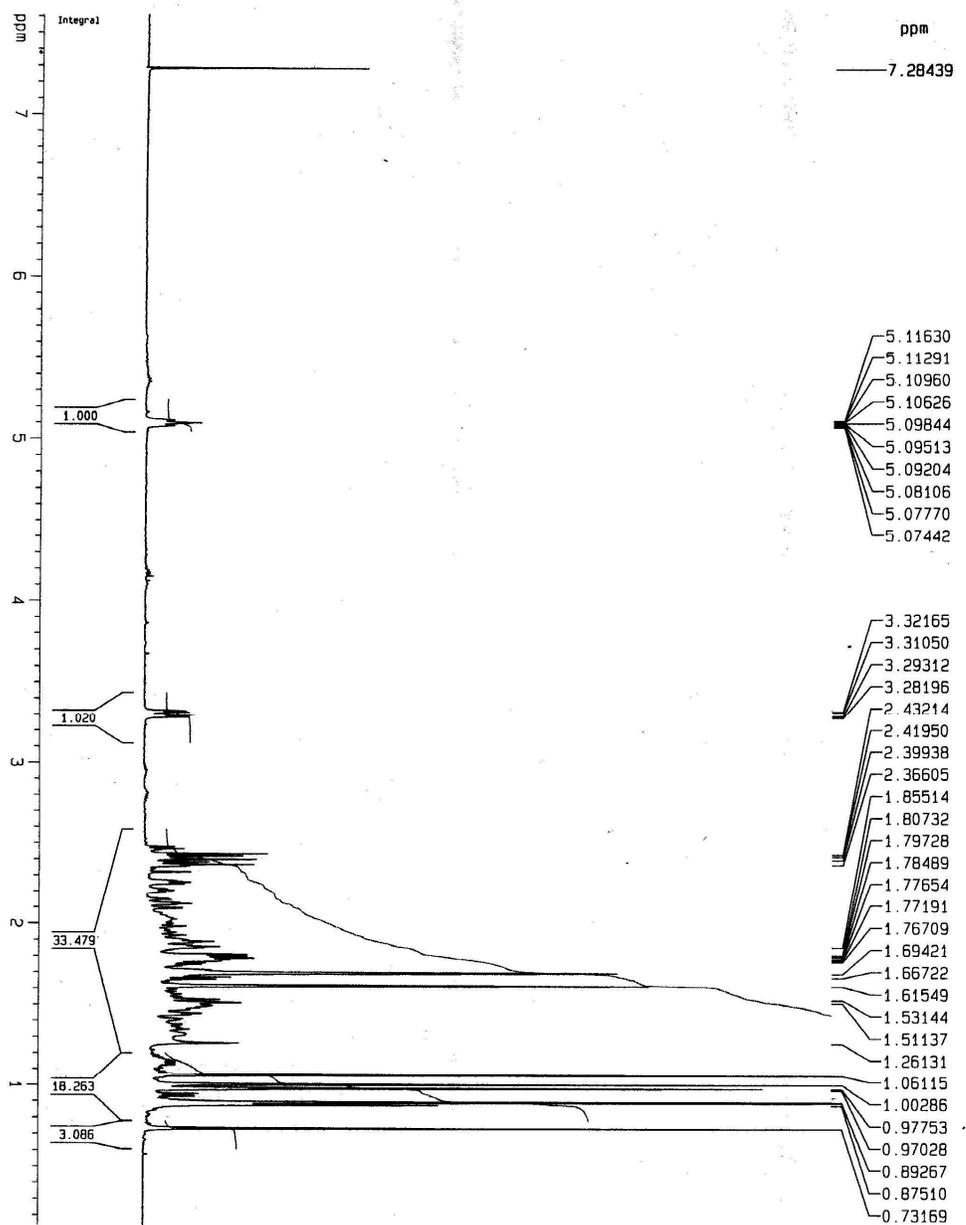
Figure S11. ^{13}C -NMR Spectrum of **2** in CDCl_3 .

Figure S12. ¹H-NMR Spectrum of 4 in CDCl₃.

Current Data Parameters

NAME	h937
EXPNO	1
PROCNO	1

F2 - Acquisition Parameters

Date_	20081121
Time	12.31
INSTRUM	av400
PROBHD	5 mm QNP 1H/13
PULPROG	zg
TD	65536
SOLVENT	MeD
NS	1
DS	0
SHF	540.256 Hz
FIDRES	0.097813 Hz
AQ	5.115581 sec
HG	22.5
DM	78.000 usec
DE	6.00 usec
TE	292.0 K
D1	2.0000000 sec
DELTA	0.0000000 sec
MCHEST	0.0150000 sec
MCPRK	0.0150000 sec

***** CHANNEL f1 *****

NUC1	¹ H
P1	10.00 usec
PL1	-3.00 dB
SFO1	400.1324008 MHz

F2 - Processing parameters

SI	32768
SF	400.1300000 MHz
WDW	GM
SSB	0
LB	-0.20 Hz
GB	0.2
PC	1.00

10 NMR plot parameters

CX	22.00 cm
CY	18.00 cm
CP	7.611 ppm
F1	3045.48 Hz
F2	0.138 ppm
PRNOM	0.33859 ppm/cm
HZCM	135.51972 Hz/cm

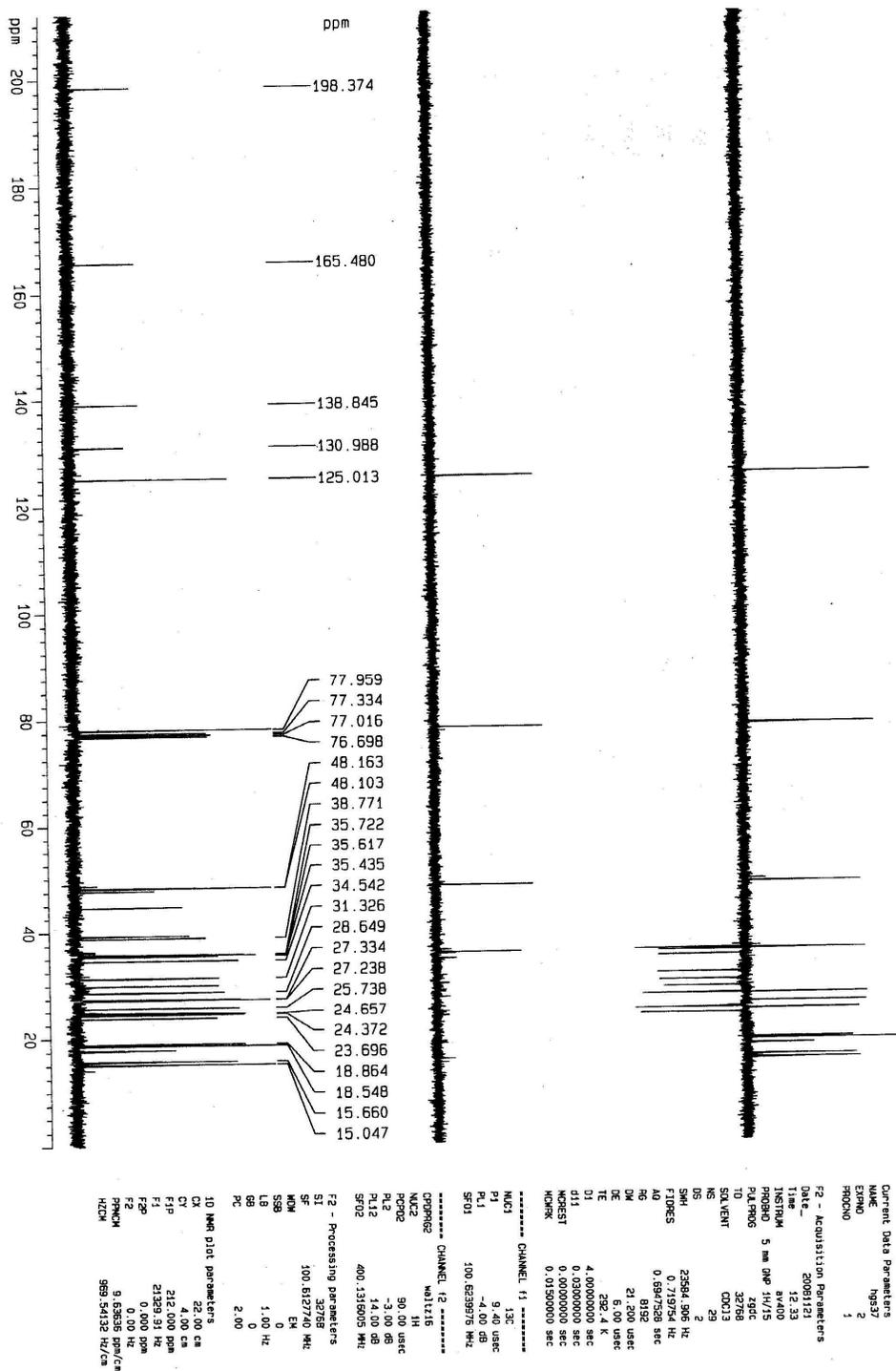
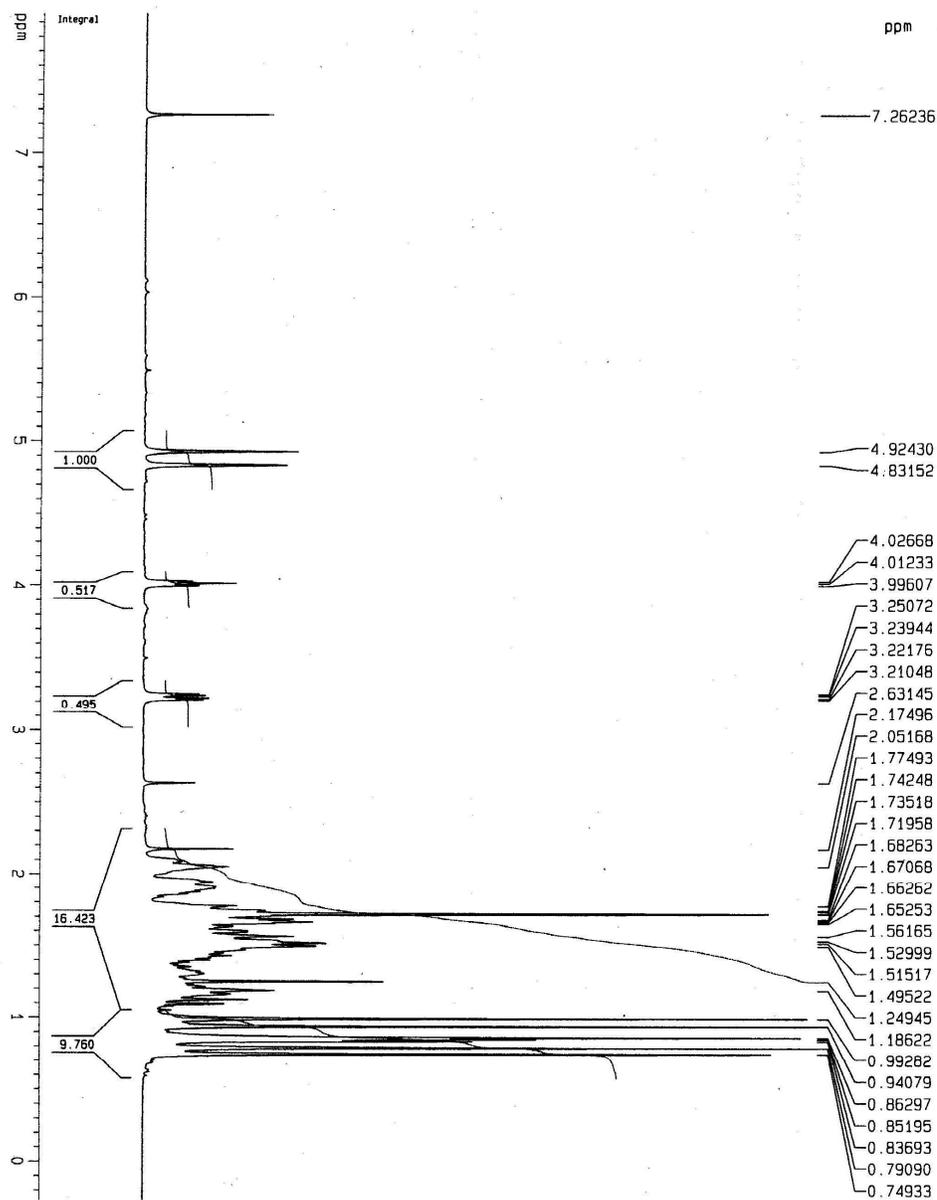
Figure S13. ¹³C-NMR Spectrum of 4 in CDCl₃.

Figure S14. ¹H-NMR Spectrum of 5 in CDCl₃.

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Current Data Parameters
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EXPNO        1
PROCNO       1

F2 - Acquisition Parameters
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Time         10.07
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PROBHD      5 mm QNP 1H/15
PULPROG     zg
TD           65536
SOLVENT     MeOD
NS           1
DS           0
SMH          9615.385 Hz
FIDRES       0.146719 Hz
AQ           3.4079740 sec
RG           35.9
DM           52.000 usec
DE           6.00 usec
TE           673.2 K
D1           2.00000000 sec
MCREST1     0.00000000 sec
MCMRK       0.01500000 sec

***** CHANNEL f1 *****
NUC1         1H
P1           10.00 usec
PL1         -3.00 dB
SFO1        400.1320007 MHz

F2 - Processing parameters
SI          32768
SF          400.1300990 MHz
RG          64
AQ          0.30 Hz
SFO         400.1300990 MHz
PC          1.00

ID NMR plot parameters
CY          32.00 cm
CV          13.00 cm
F1P         7.959 ppm
F1          3184.70 Hz
F2P        -10.268 ppm
F2         -107.30 Hz
PPHCH       0.37397 ppm/cm
HZCM        149.63838 Hz/cm

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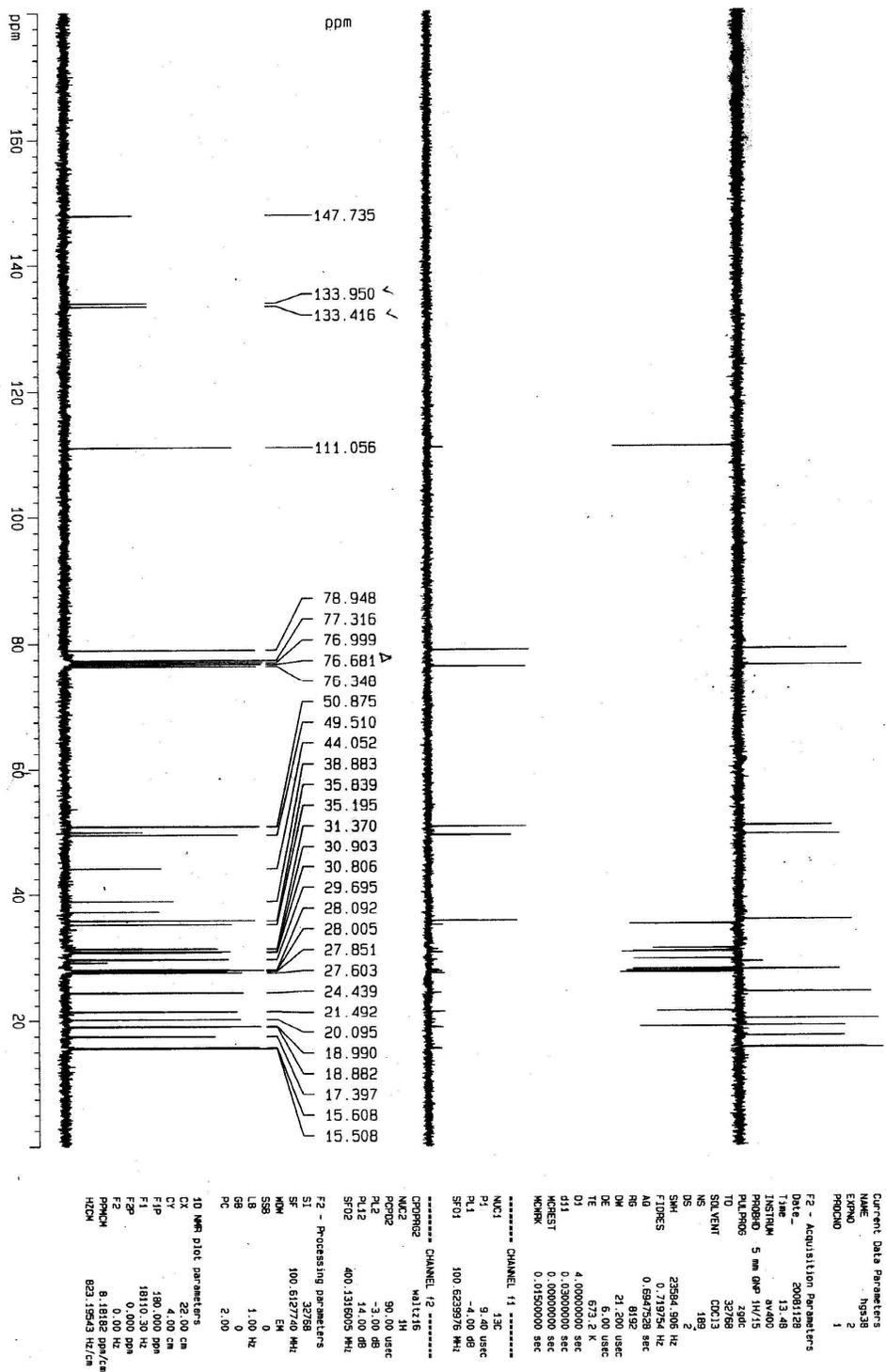
Figure S15. ^{13}C -NMR Spectrum of **5** in CDCl_3 .

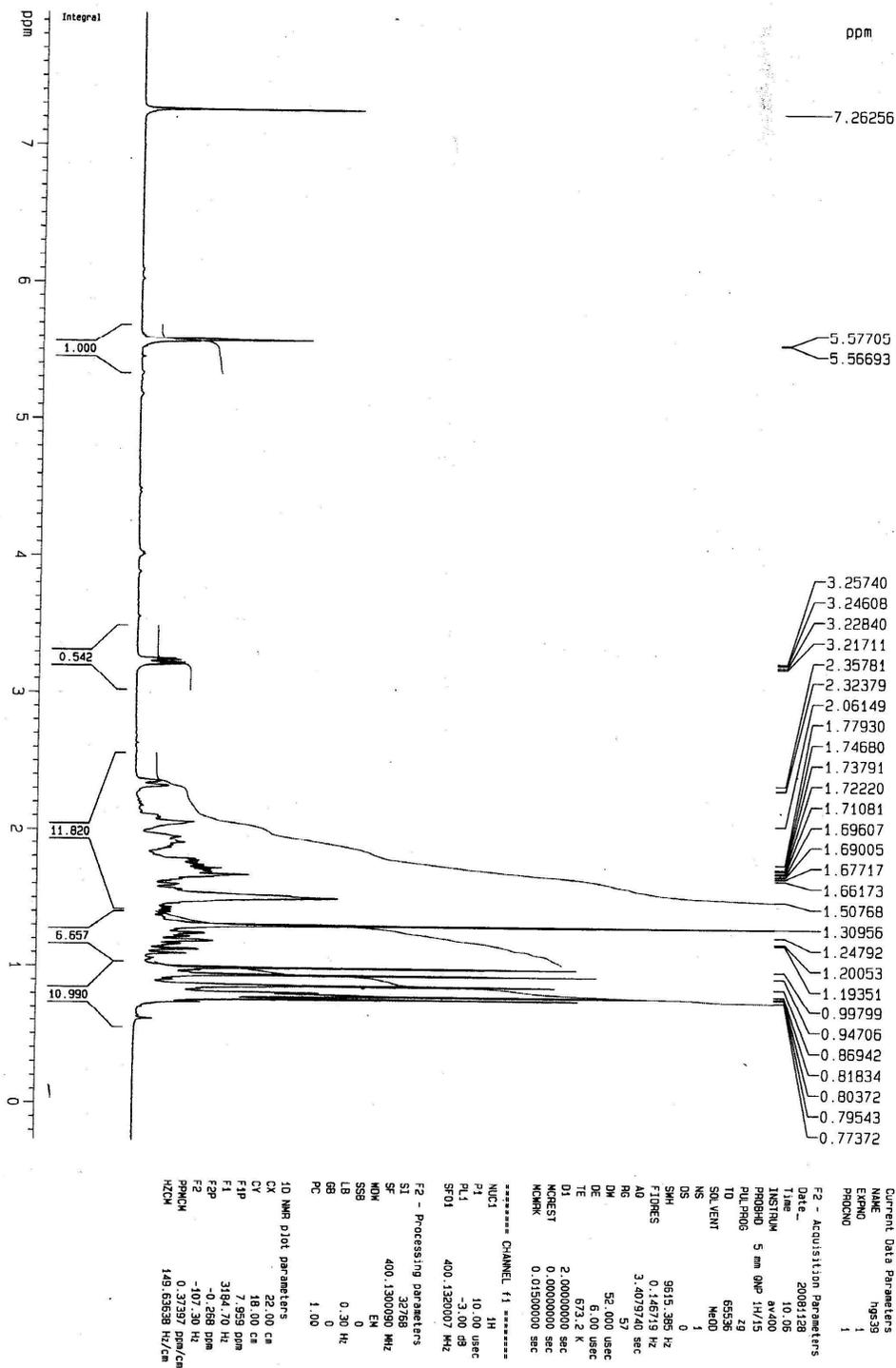
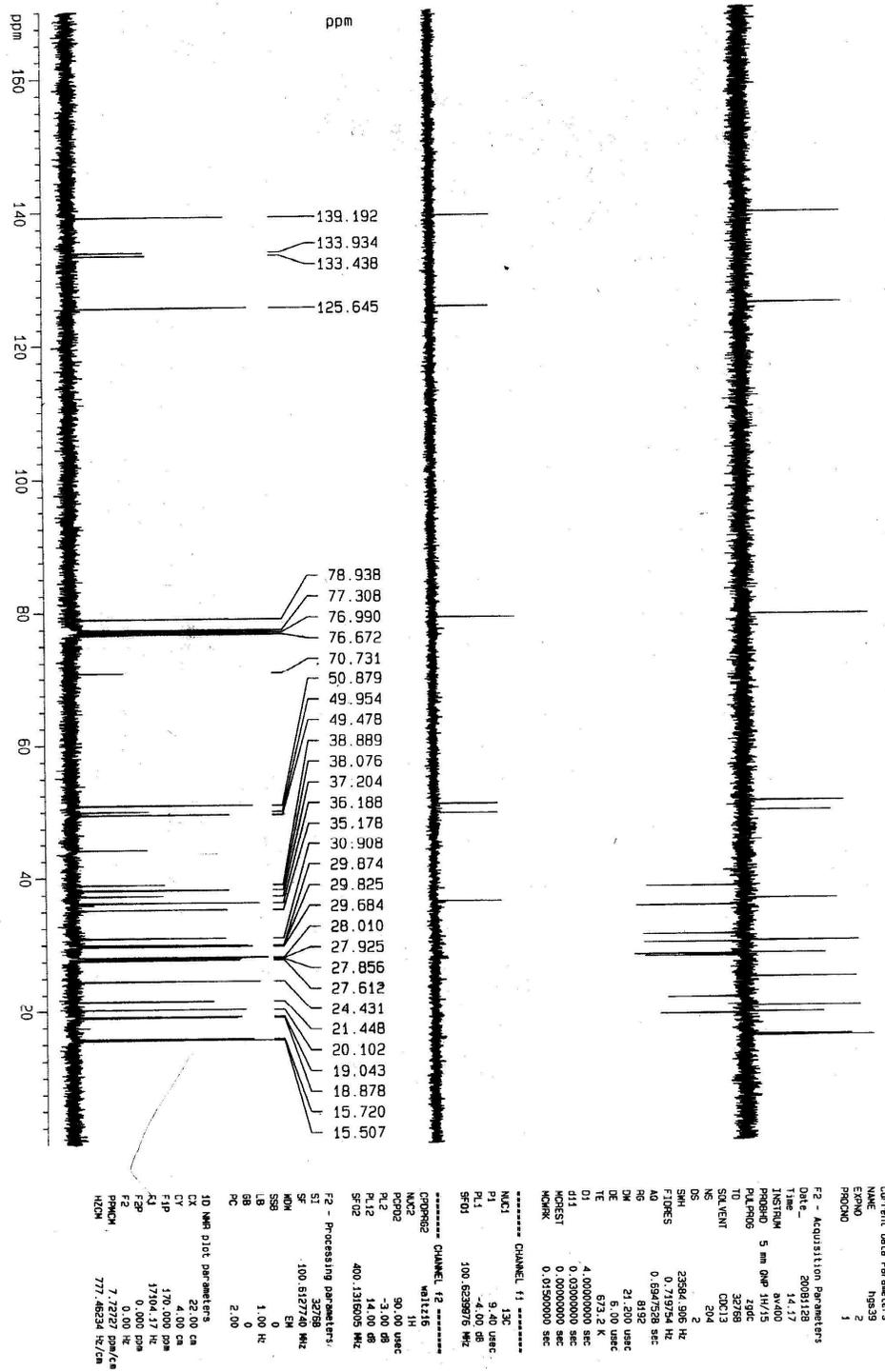
Figure S16. ¹H-NMR Spectrum of 6 in CDCl₃.

Figure S17. ¹³C-NMR Spectrum of 6 in CDCl₃.

Result of Biological Testing of 1–6.

Table 1. Inhibition of 11 β -HSD1.

Compounds and dose	Mouse 11 β -HSD1	Human 11 β -HSD1
Compound-1 1 μ M	90.99%	85.76%
Compound-1 10 μ M	99.75%	95.72%
Compound-2 1 μ M	42.52%	40.29%
Compound-2 10 μ M	93.61%	78.08%
Compound-3 1 μ M	95.74%	96.85%
Compound-3 10 μ M	100.49%	97.67%
Compound-4 1 μ M	99.00%	96.97%
Compound-4 10 μ M	100.17%	96.00%
Compound-5 1 μ M	95.40%	93.10%
Compound-5 10 μ M	100.08%	97.10%
Compound-6 1 μ M	92.90%	96.83%
Compound-6 10 μ M	100.17%	97.93%
glycyrrhizinic acid 1 nM	27.43%	13.48%
glycyrrhizinic acid 10 nM	56.62%	48.34%
glycyrrhizinic acid 100 nM	91.47%	84.45%

Table 2. IC₅₀ for mouse 11 β -HSD1(X \pm SD, n = 2).

Compounds and dose	Mean	SD	IC ₅₀
Compound-1 0.01 μ M	13.69%	4.55%	
Compound-1 0.03 μ M	27.94%	5.31%	
Compound-1 0.1 μ M	53.48%	0.71%	78.44 nM
Compound-1 0.3 μ M	72.93%	0.51%	
Compound-1 1 μ M	89.37%	0.13%	
Compound-2 0.1 μ M	16.21%	0.77%	
Compound-2 0.3 μ M	28.98%	4.37%	
Compound-2 1 μ M	46.71%	0.03%	1.077 μ M
Compound-2 3 μ M	70.48%	3.49%	
Compound-2 10 μ M	90.75%	0.76%	
Compound-3 0.01 μ M	21.44%	3.85%	
Compound-3 0.03 μ M	29.00%	3.15%	
Compound-3 0.1 μ M	57.01%	4.76%	80.52 nM
Compound-3 0.3 μ M	80.27%	0.55%	
Compound-3 1 μ M	95.34%	0.45%	
Compound-4 0.003 μ M	20.72%	0.87%	
Compound-4 0.01 μ M	42.25%	3.83%	
Compound-4 0.03 μ M	72.02%	2.13%	13.36 nM
Compound-4 0.1 μ M	92.55%	0.82%	
Compound-4 0.3 μ M	97.02%	1.58%	

Table 2. *Cont.*

Compounds and dose	Mean	SD	IC ₅₀
Compound-5 0.01 μM	25.25%	2.71%	
Compound-5 0.03 μM	40.53%	0.20%	
Compound-5 0.1 μM	58.85%	2.69%	
Compound-5 0.3 μM	79.71%	0.58%	49.46 nM
Compound-5 1 μM	94.14%	2.23%	
Compound-6 0.01 μM	28.95%	0.97%	
Compound-6 0.03 μM	24.50%	0.85%	
Compound-6 0.1 μM	44.58%	1.76%	
Compound-6 0.3 μM	69.55%	1.48%	294.7 nM
Compound-6 1 μM	91.49%	2.25%	
glycyrrhizininc acid 1 nM	27.40%	0.61%	
glycyrrhizininc acid 10 nM	64.74%	4.65%	
glycyrrhizininc acid 100 nM	92.93%	3.09%	3.601 nM

Table 3. IC₅₀ for human 11β-HSD1(X ± SD, n = 2).

Compounds and dose	Mean	SD	IC ₅₀
Compound-1 0.01 μM	35.06%	1.55%	
Compound-1 0.03 μM	40.01%	3.19%	
Compound-1 0.1 μM	60.09%	0.57%	34.86 nM
Compound-1 0.3 μM	80.31%	2.48%	
Compound-1 1 μM	88.50%	3.46%	
Compound-2 0.1 μM	13.88%	4.84%	
Compound-2 0.3 μM	28.09%	2.37%	
Compound-2 1 μM	42.10%	6.37%	1.115 μM
Compound-2 3 μM	59.31%	5.51%	
Compound-2 10 μM	82.58%	3.56%	
Compound-3 0.001 μM	16.42%	4.67%	
Compound-3 0.003 μM	24.21%	0.36%	
Compound-3 0.01 μM	41.73%	3.03%	16.08 nM
Compound-3 0.03 μM	67.99%	1.18%	
Compound-3 0.1 μM	91.82%	3.12%	
Compound-4 0.0003 μM	15.74%	4.77%	
Compound-4 0.001 μM	26.63%	0.41%	
Compound-4 0.003 μM	51.49%	5.33%	2.815 nM
Compound-4 0.01 μM	75.03%	1.42%	
Compound-4 0.03 μM	90.37%	0.87%	
Compound-5 0.003 μM	20.54%	2.49%	
Compound-5 0.01 μM	28.39%	3.41%	
Compound-5 0.03 μM	56.15%	0.05%	26.47 nM
Compound-5 0.1 μM	82.07%	0.72%	
Compound-5 0.3 μM	95.27%	2.67%	

Table 3. *Cont.*

Compounds and dose	Mean	SD	IC ₅₀
Compound-6 0.01 μM	36.41%	6.95%	
Compound-6 0.03 μM	67.93%	1.02%	
Compound-6 0.1 μM	91.16%	2.25%	15.99 nM
Compound-6 0.3 μM	96.00%	2.24%	
Compound-6 1 μM	99.30%	1.38%	
glycyrrhizinic acid 1 nM	15.32%	0.28%	
glycyrrhizinic acid 10 nM	46.94%	2.05%	8.626 nM
glycyrrhizinic acid 100 nM	81.71%	0.54%	

Table 4. IC₅₀ for mouse 11β-HSD2(X ± SD, n = 2).

Compounds and dose	Mean	SD	IC ₅₀
Compound-1 1 mM	20.94%	5.78%	
Compound-1 100 μM	7.04%	3.02%	>1 mM
Compound-2 1 mM	33.38%	13.44%	
Compound-2 100 μM	22.09%	1.02%	
Compound-2 10 μM	8.65%	0.48%	>1 mM
Compound-3 1 mM	28.00%	12.62%	
Compound-3 100 μM	35.55%	7.49%	
Compound-3 10 μM	6.57%	0.43%	>1 mM
Compound-4 1 mM	16.24%	5.71%	
Compound-4 100 μM	23.82%	0.75%	>1mM
Compound-5 1 mM	16.00%	0.35%	
Compound-5 100 μM	30.11%	3.64%	
Compound-5 10 μM	15.32%	2.77%	>1 mM
Compound-6 1 mM	5.65%	4.60%	
Compound-6 100 μM	32.96%	1.60%	
Compound-6 10 μM	22.76%	1.31%	>1 mM
carbenoxolone 1 nM	3.90%	2.06%	
carbenoxolone 10 nM	21.11%	3.50%	
carbenoxolone 100 nM	47.75%	5.98%	
carbenoxolone 1 μM	64.68%	10.20%	59.16 nM
carbenoxolone 10 μM	84.31%	1.36%	

Table 5. IC₅₀ for human 11β-HSD2 (X ± SD, n = 2).

Compounds and dose	Mean	SD	IC ₅₀
Compound-1 30 μM	94.44%	4.33%	8.179 μM
Compound-1 10 μM	57.44%	3.43%	
Compound-1 3 μM	39.24%	2.43%	
Compound-1 1 μM	21.70%	2.18%	
Compound-2 100 μM	103.39%	14.83%	2.626 μM
Compound-2 30 μM	83.33%	4.60%	
Compound-2 10 μM	52.52%	2.51%	
Compound-2 3 μM	31.43%	2.65%	
Compound-3 3 μM	103.59%	15.43%	0.3952 μM
Compound-3 1 μM	66.20%	8.04%	
Compound-3 0.3 μM	52.11%	1.71%	
Compound-3 0.1 μM	32.47%	2.12%	
Compound-4 0.3 μM	97.51%	5.20%	0.107 μM
Compound-4 0.1 μM	58.39%	5.33%	
Compound-4 0.03 μM	36.08%	2.54%	
Compound-4 0.01 μM	24.88%	4.28%	
Compound-5 10 μM	98.14%	0.52%	1.687 μM
Compound-5 3 μM	75.21%	3.89%	
Compound-5 1 μM	42.46%	3.33%	
Compound-5 0.3 μM	13.84%	5.85%	
Compound-6 3 μM	73.75%	3.11%	0.6664 μM
Compound-6 1 μM	51.03%	4.83%	
Compound-6 0.3 μM	30.78%	2.77%	
Compound-6 0.1 μM	7.44%	4.64%	
glycyrrhizinic acid 0.01 nM	0.054304	0.55%	2.246 nM
glycyrrhizinic acid 0.1 nM	0.205319	5.75%	
glycyrrhizinic acid 1 nM	0.38055	1.37%	
glycyrrhizinic acid 10 nM	0.698451	3.45%	
glycyrrhizinic acid 100 nM	0.981153	2.55%	