Supplementary Material

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

Figure S1. ^{1}H-NMR Spectrum of **3** in $CDCl_3$.

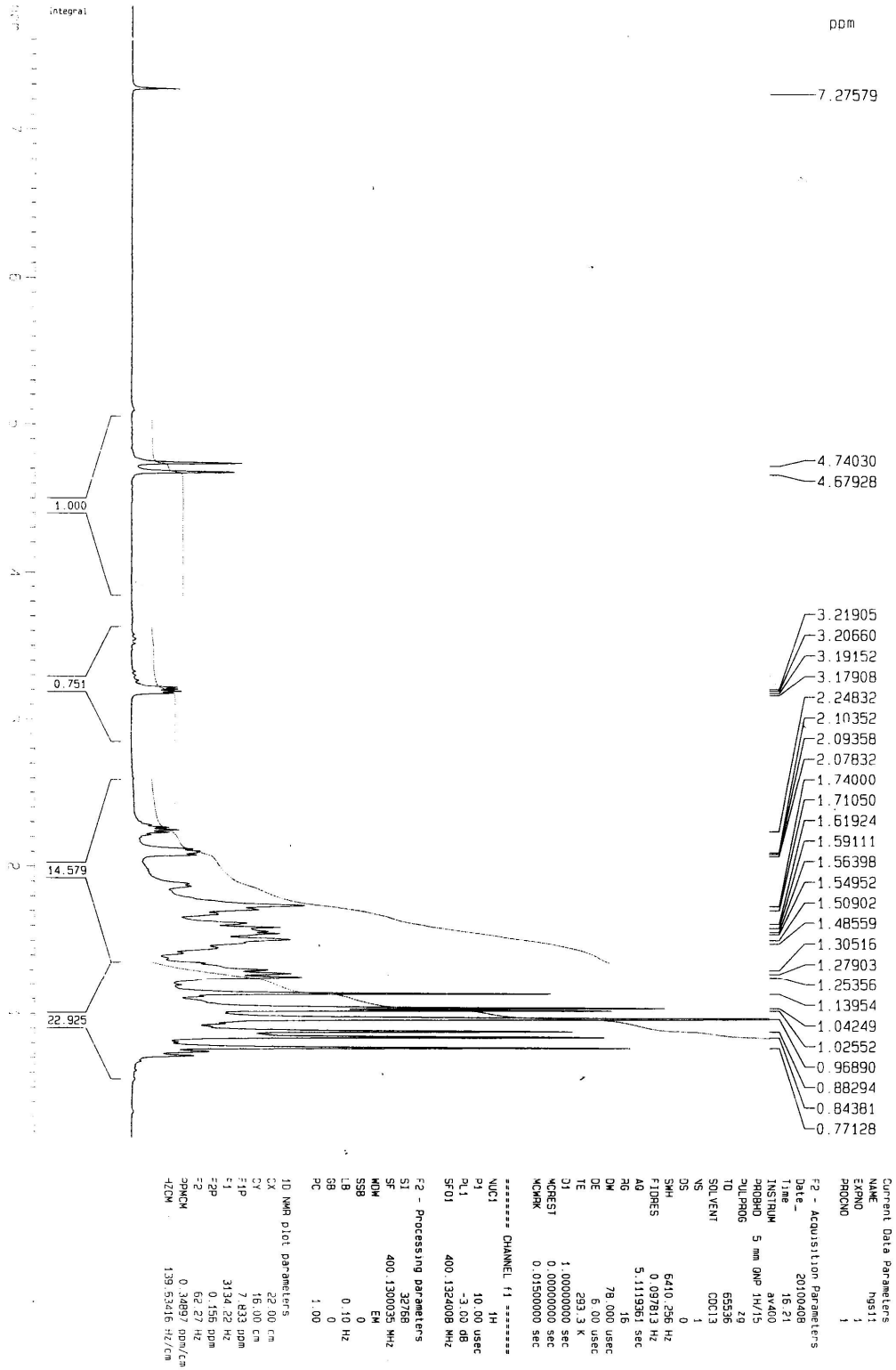


Figure S2. ^{13}C and DEPT NMR Spectrum of **3** in $CDCl_3$.

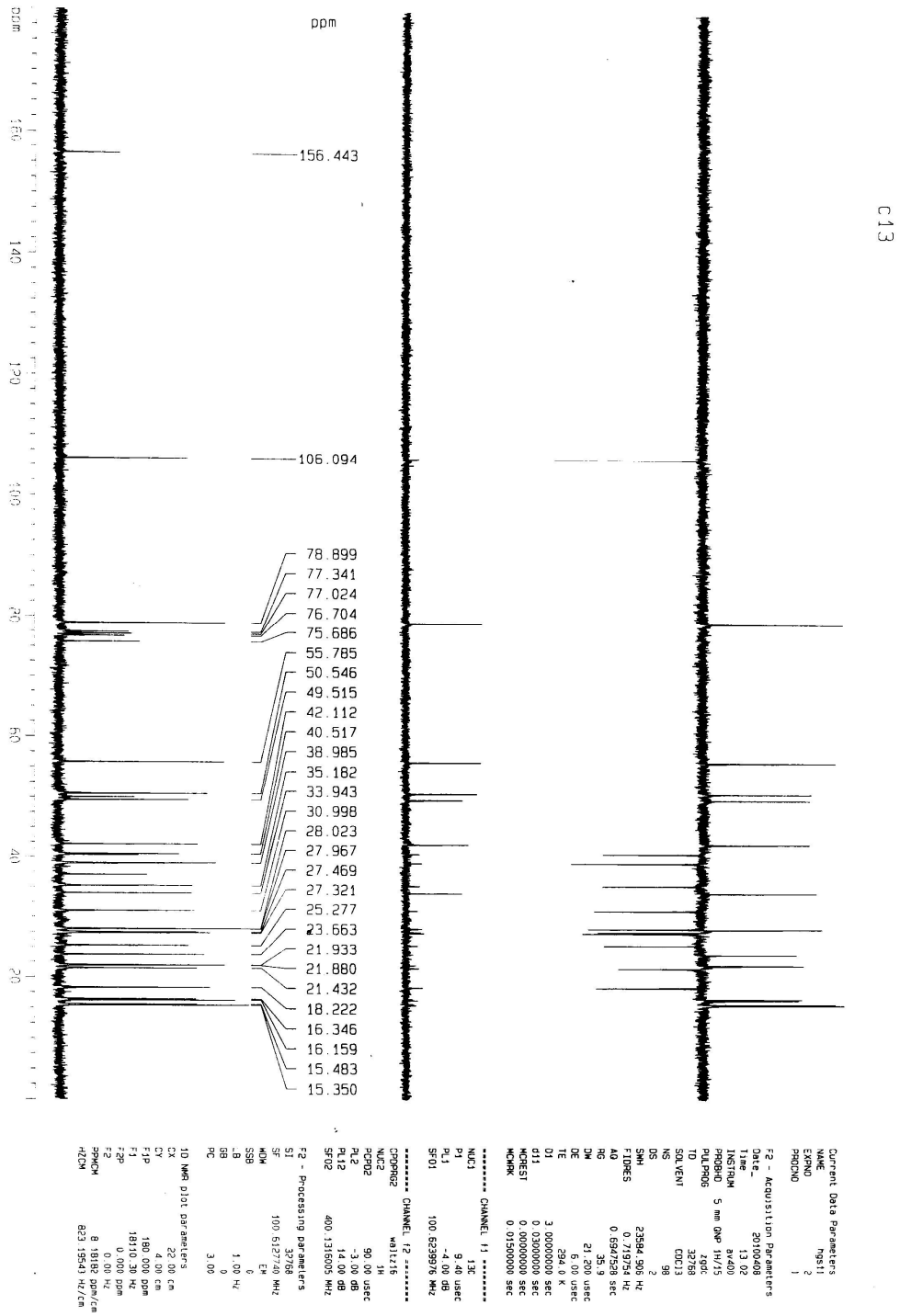


Figure S3. HSQC Spectrum of **3** in $CDCl_3$.

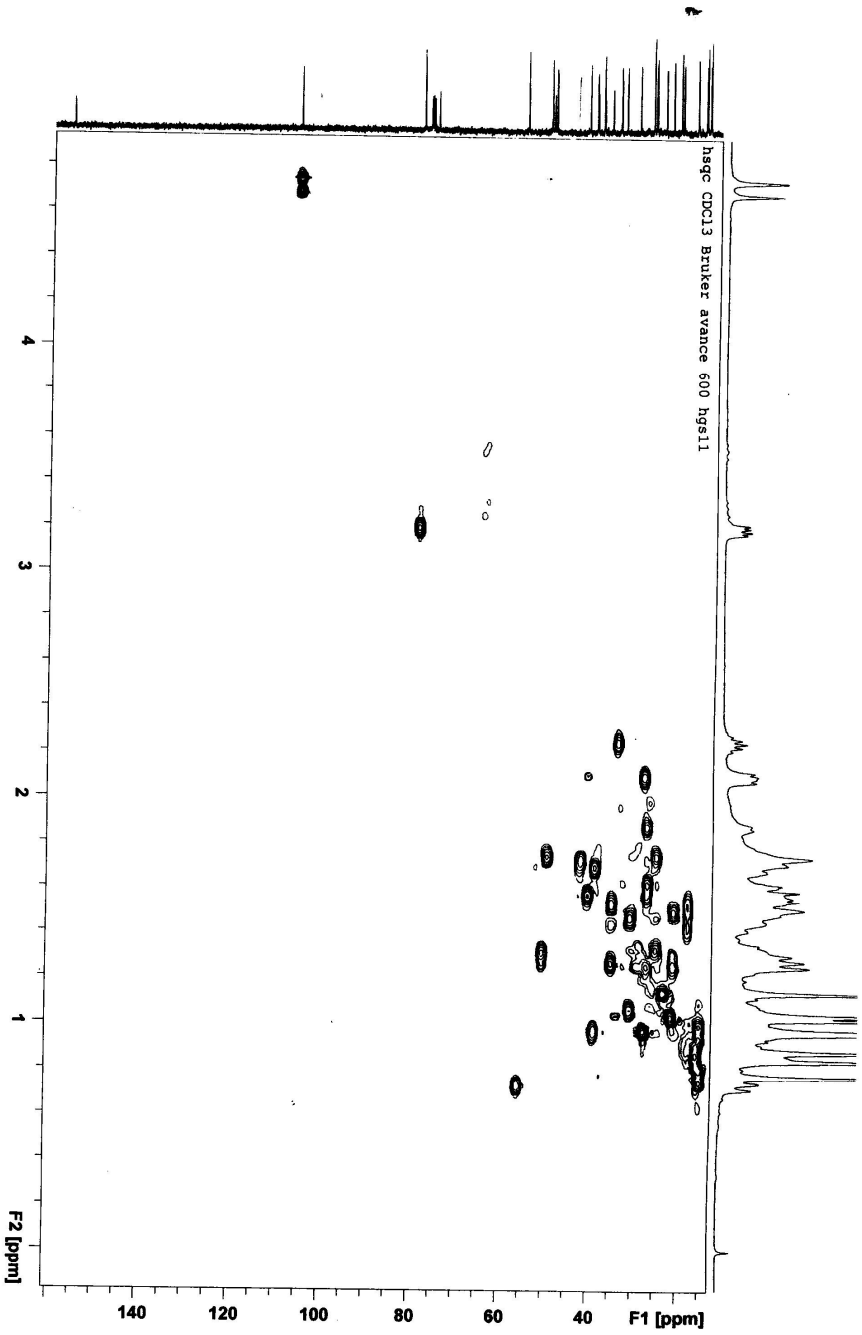


Figure S4. ^{1}H-^{1}H COSY Spectrum of **3** in $CDCl_3$.

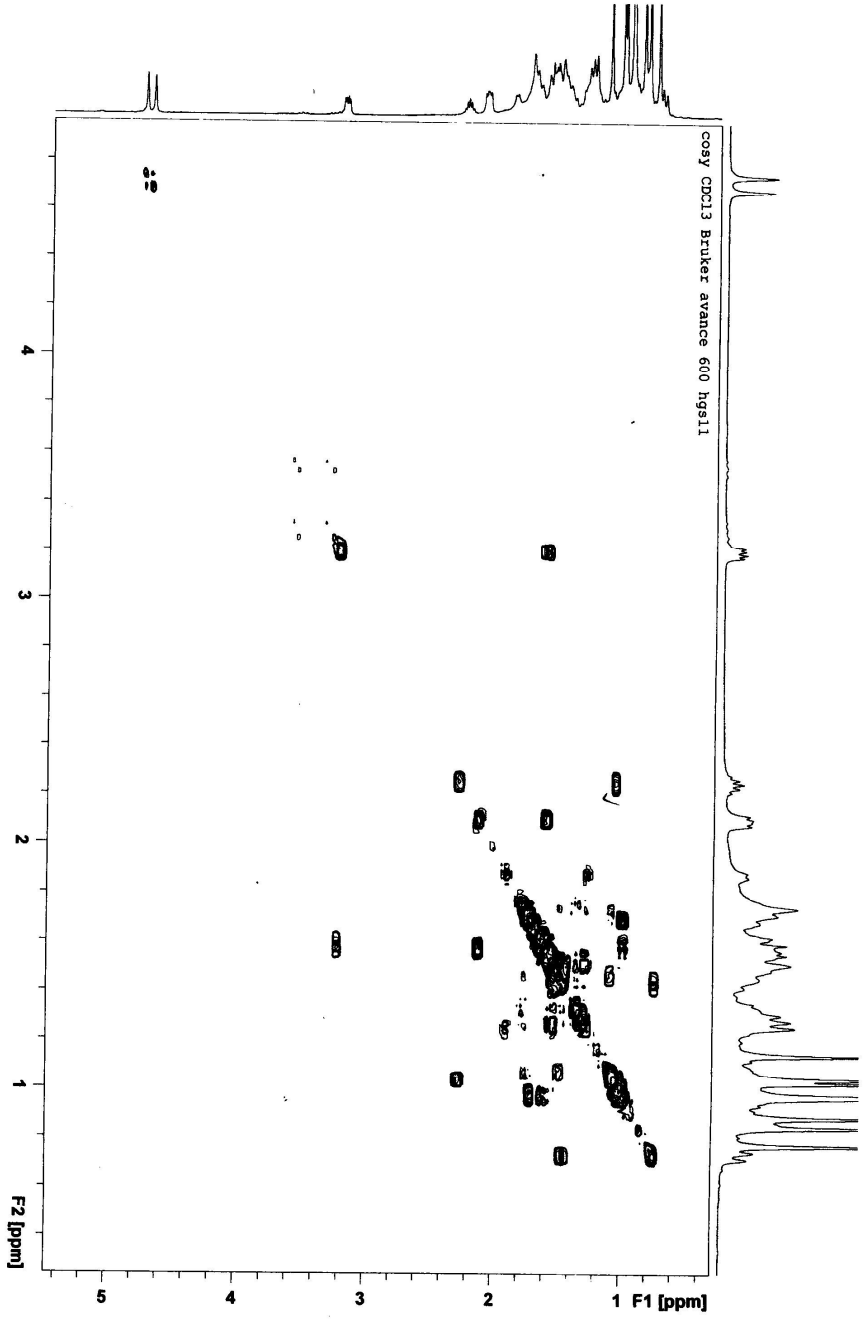


Figure S5. HMBC Spectrum of **3** in $CDCl_3$.

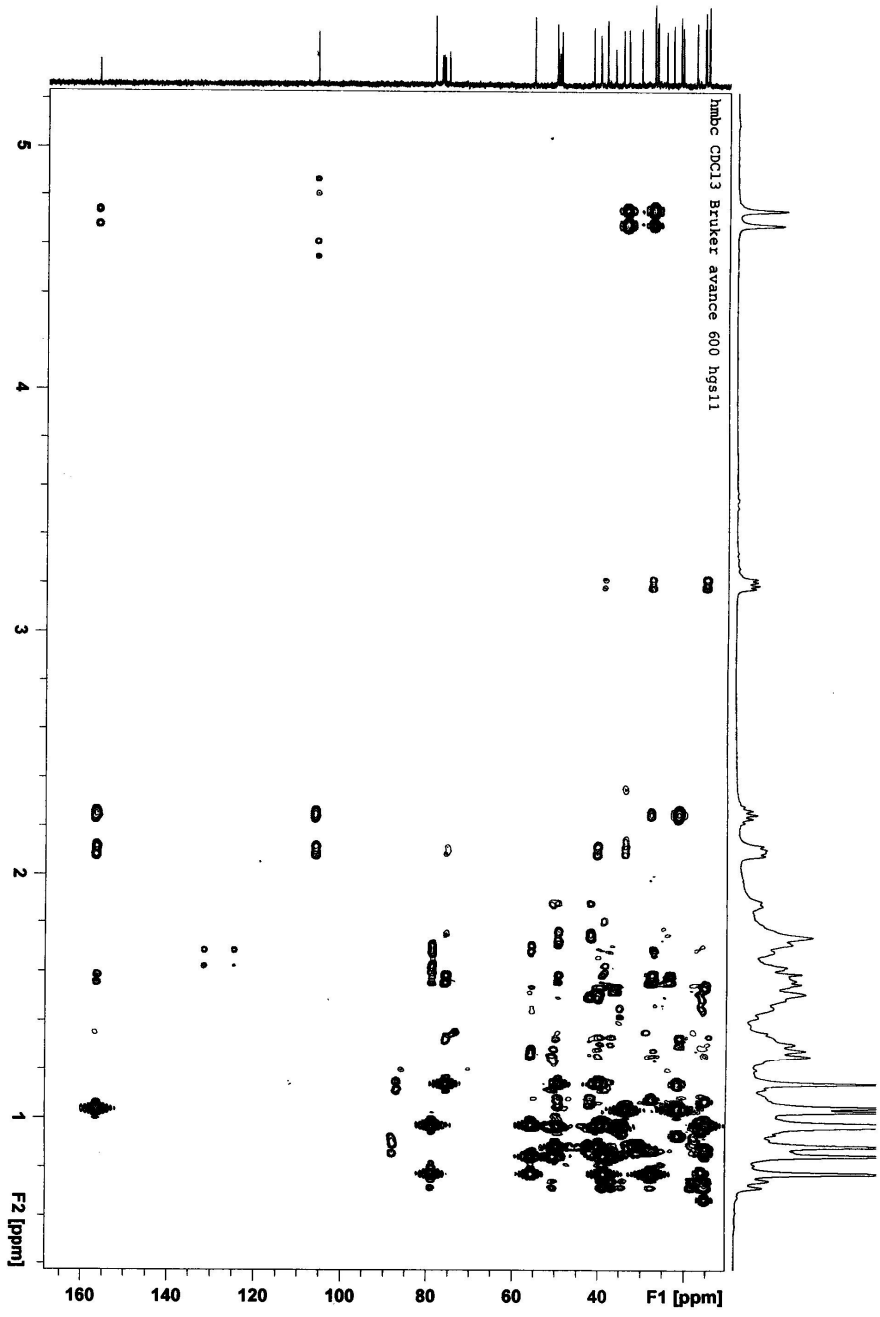


Figure S6. ROESY Spectrum of **3** in $CDCl_3$.

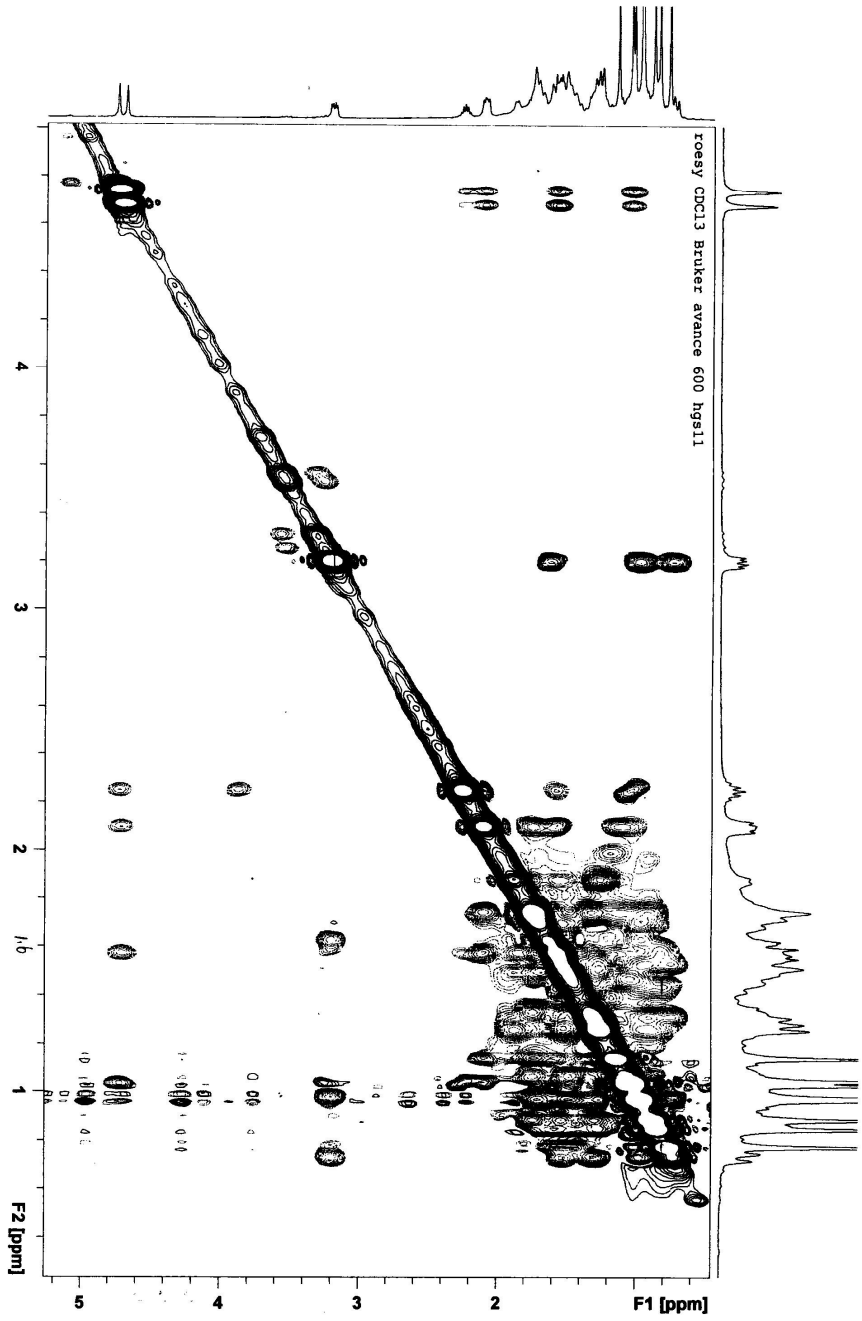


Figure S7. EI Mass Spectrometry of **3**.

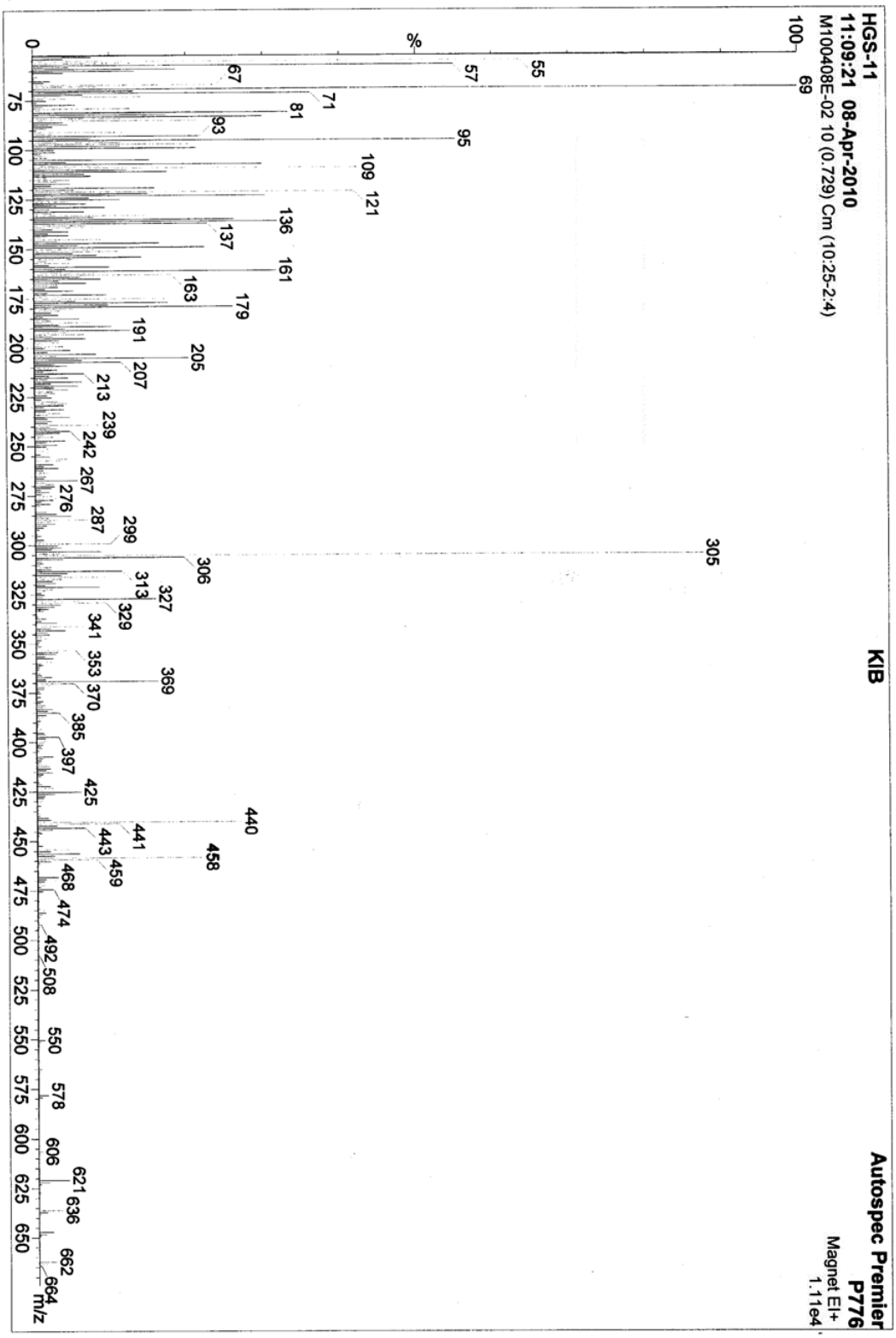


Figure S8. ^{1}H-NMR Spectrum of **1** in $CDCl_3$.

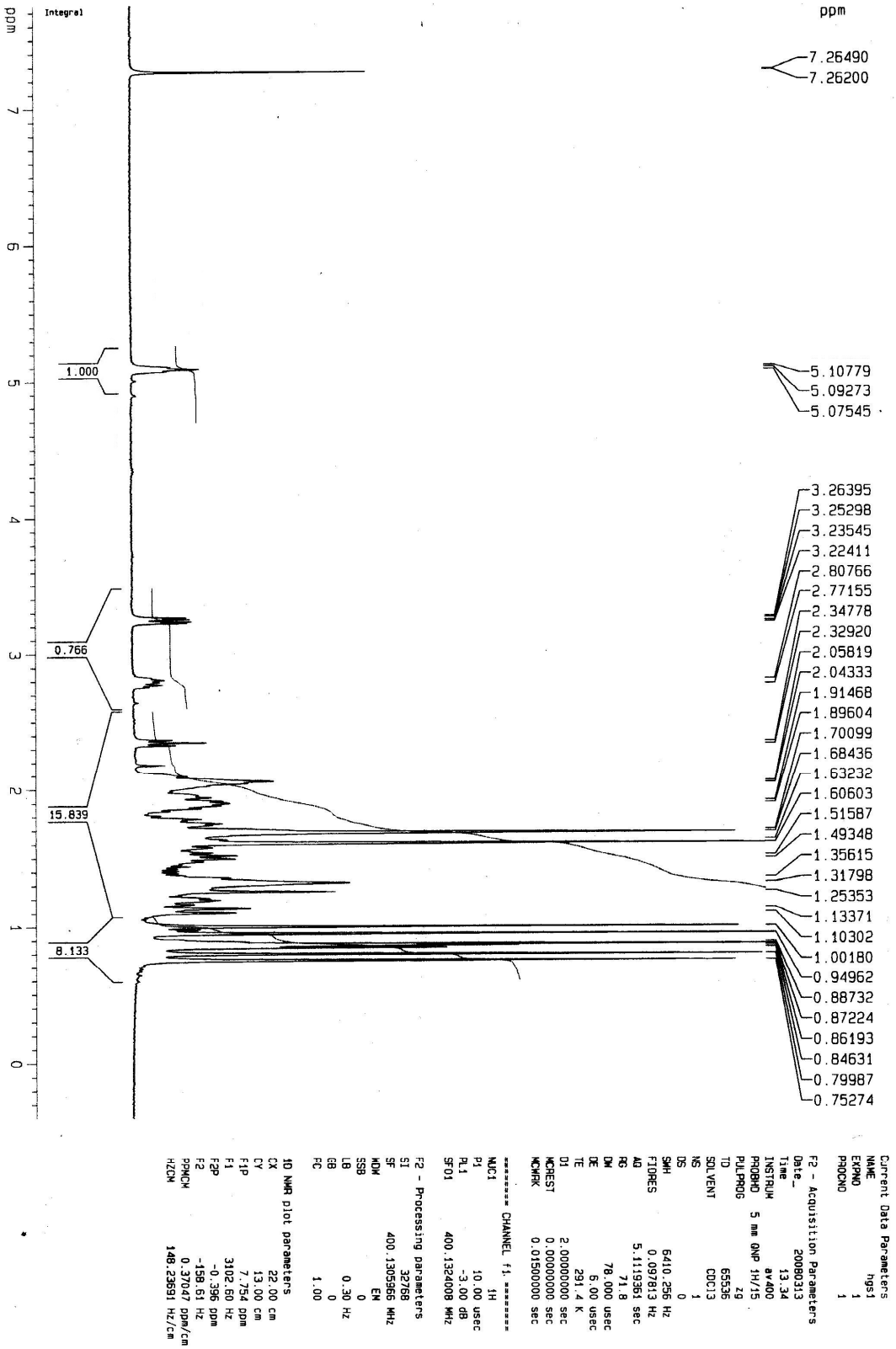


Figure S9. ^{13}C-NMR Spectrum of **1** in $CDCl_3$.

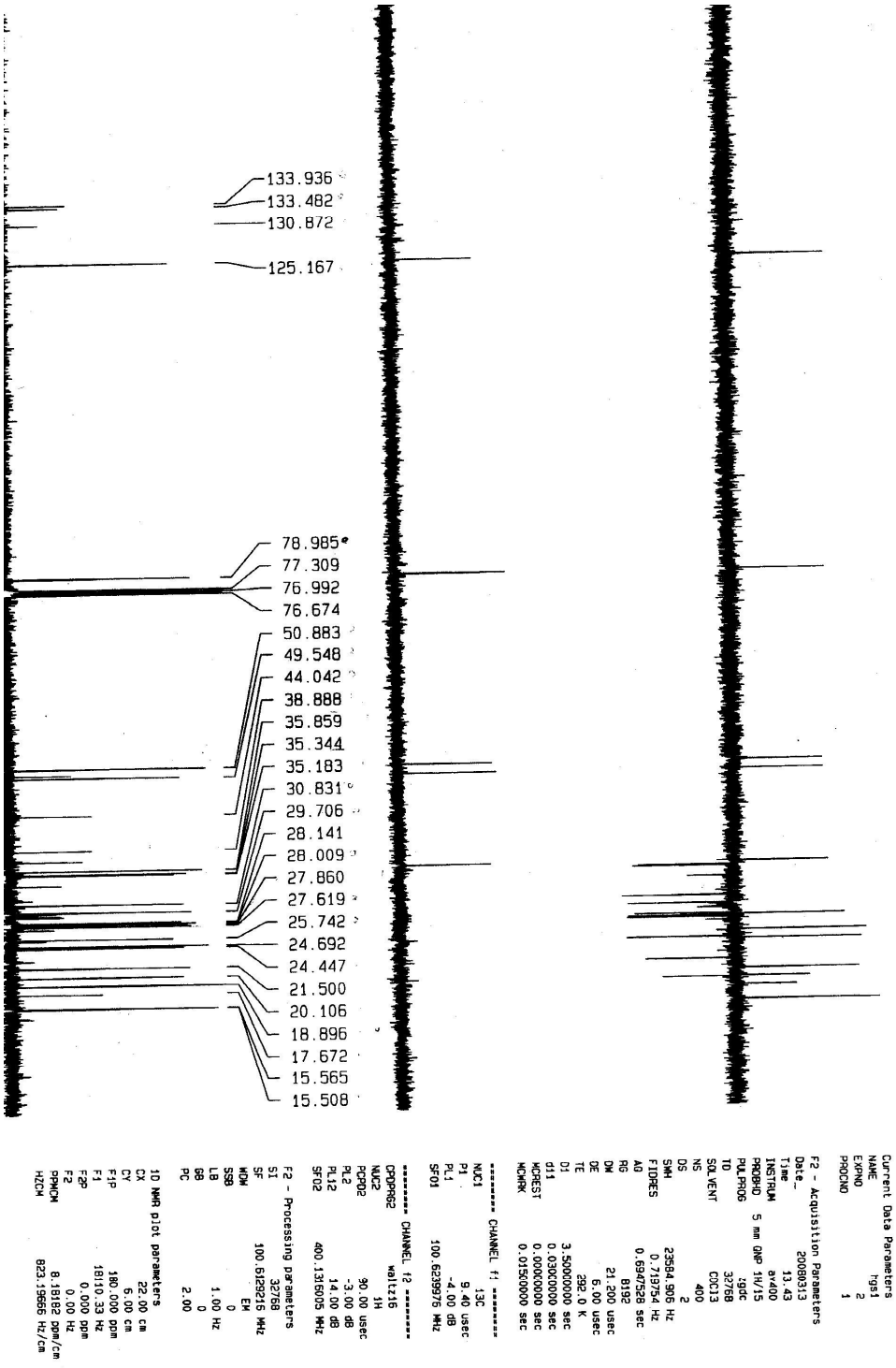


Figure S10. ^{1}H-NMR Spectrum of **2** in $CDCl_3$.

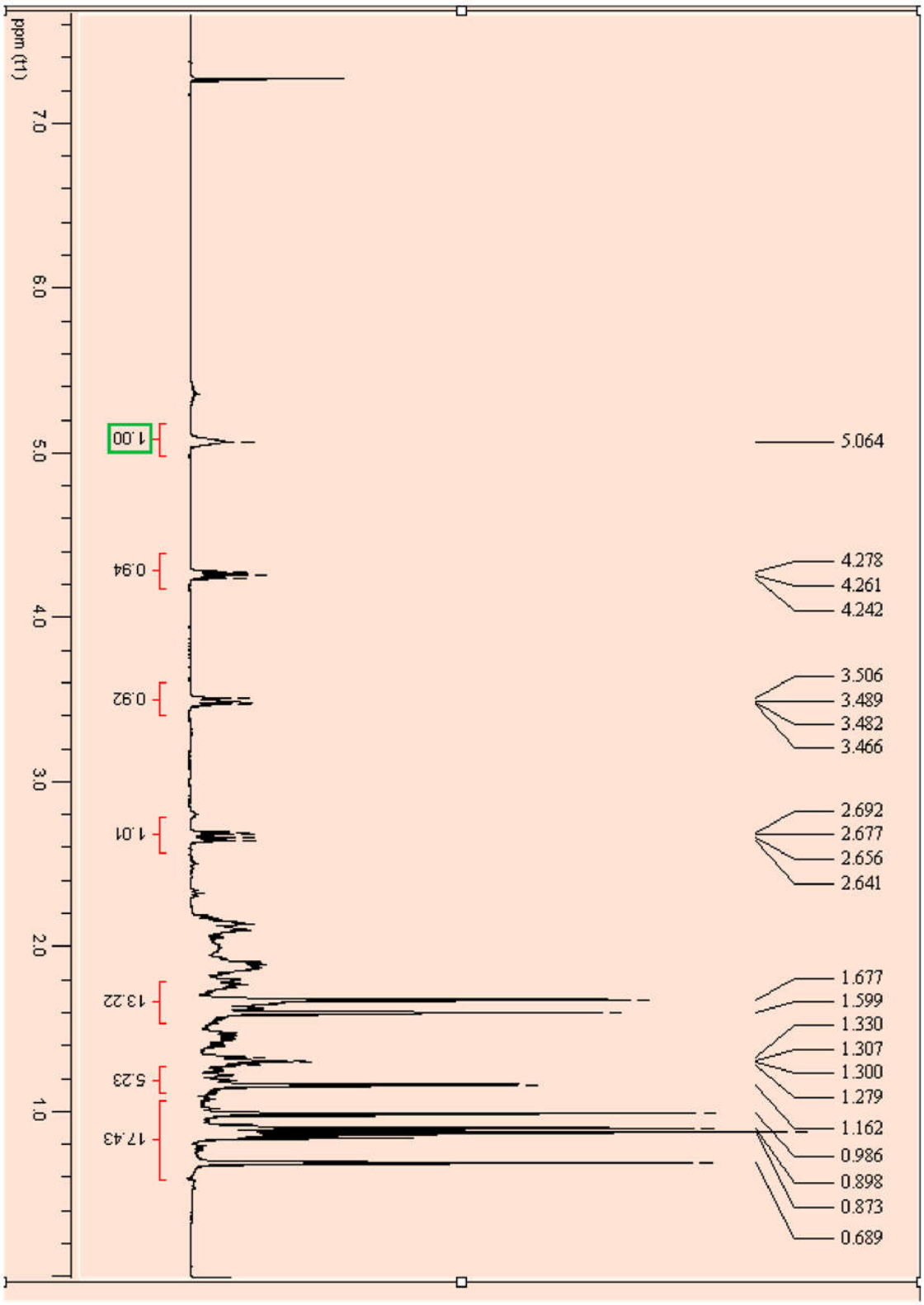


Figure S11. ^{13}C-NMR Spectrum of **2** in $CDCl_3$.

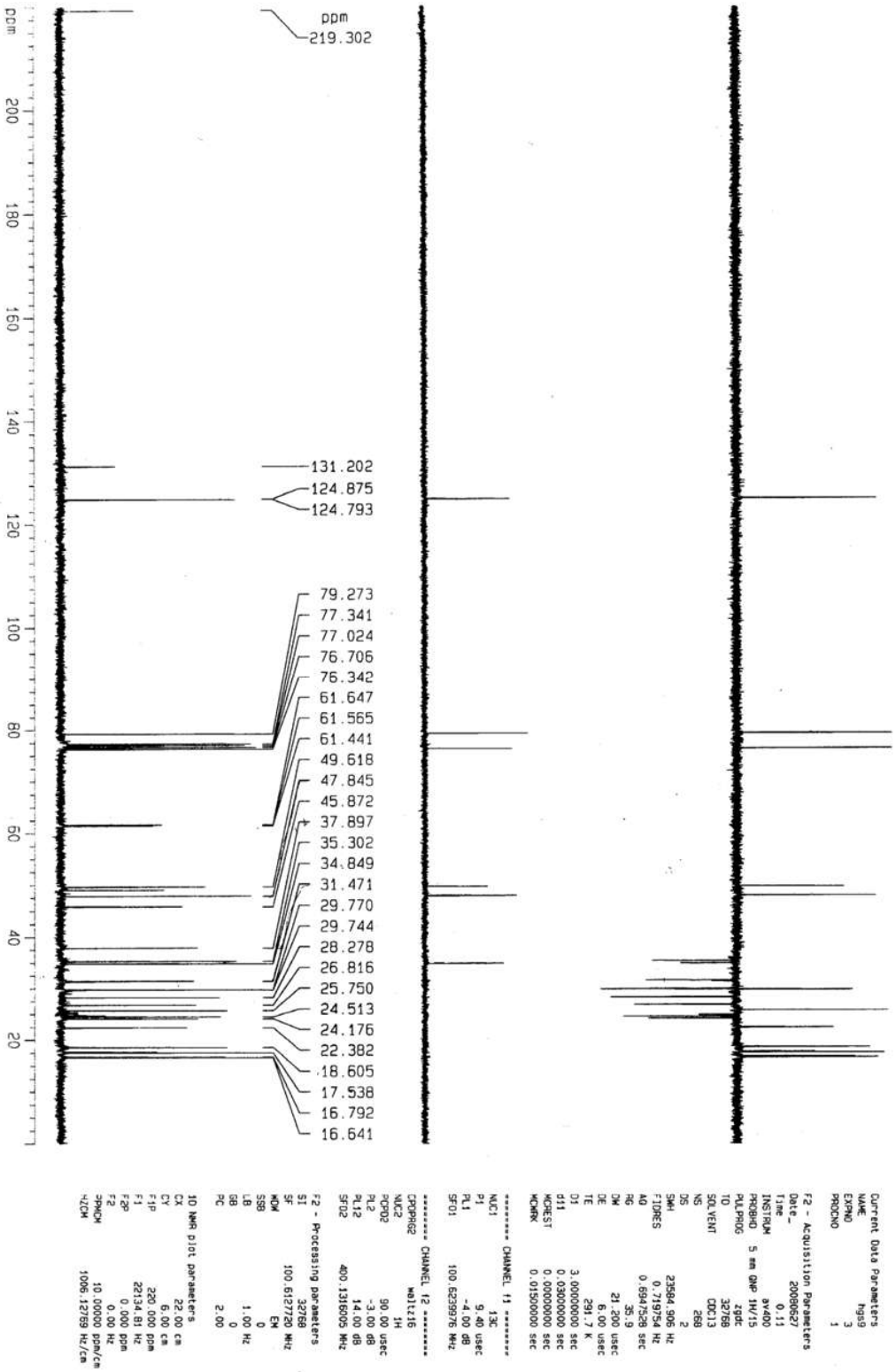


Figure S12. ^{1}H-NMR Spectrum of **4** in $CDCl_3$.

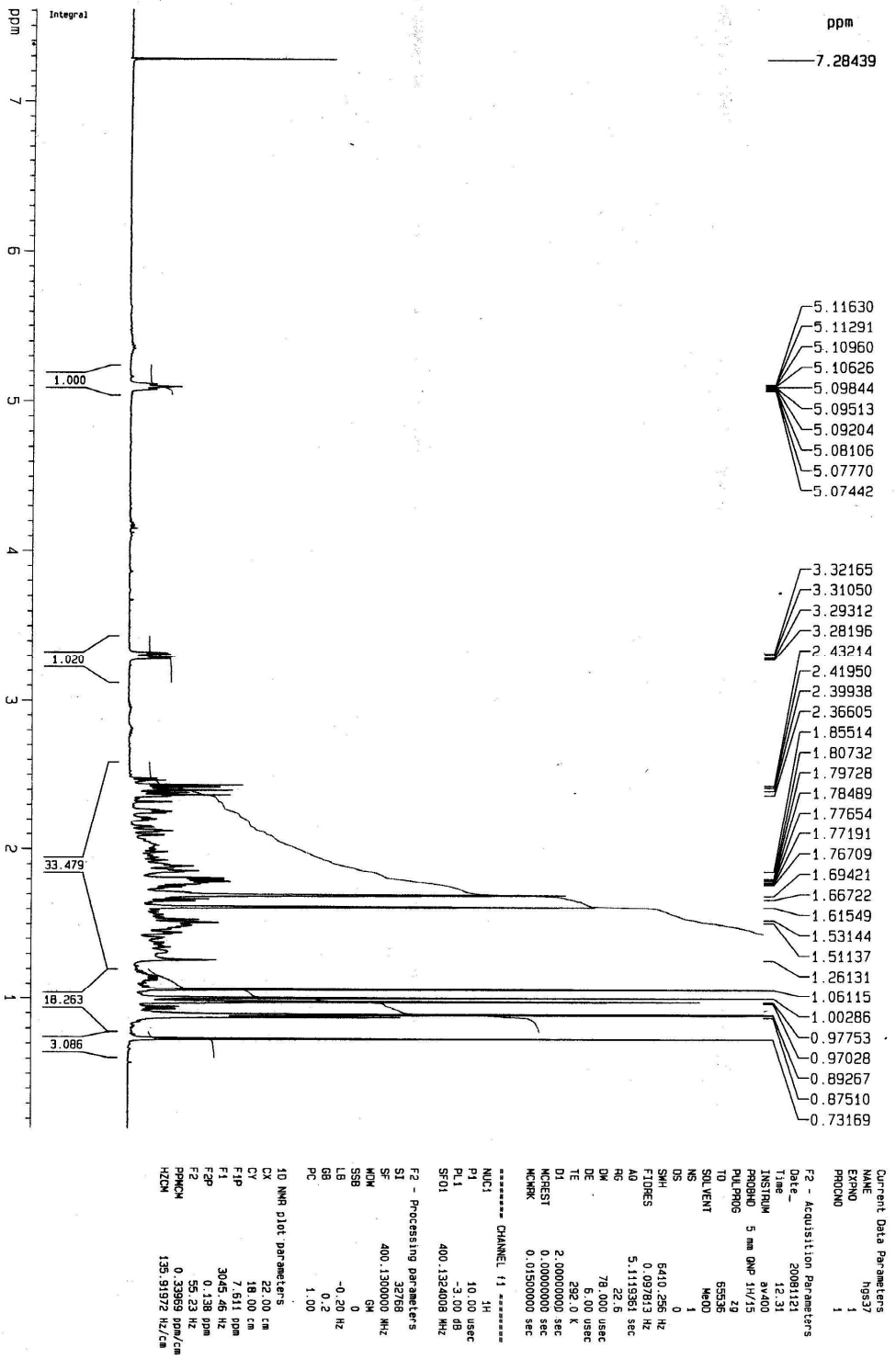


Figure S13. ^{13}C-NMR Spectrum of **4** in $CDCl_3$.

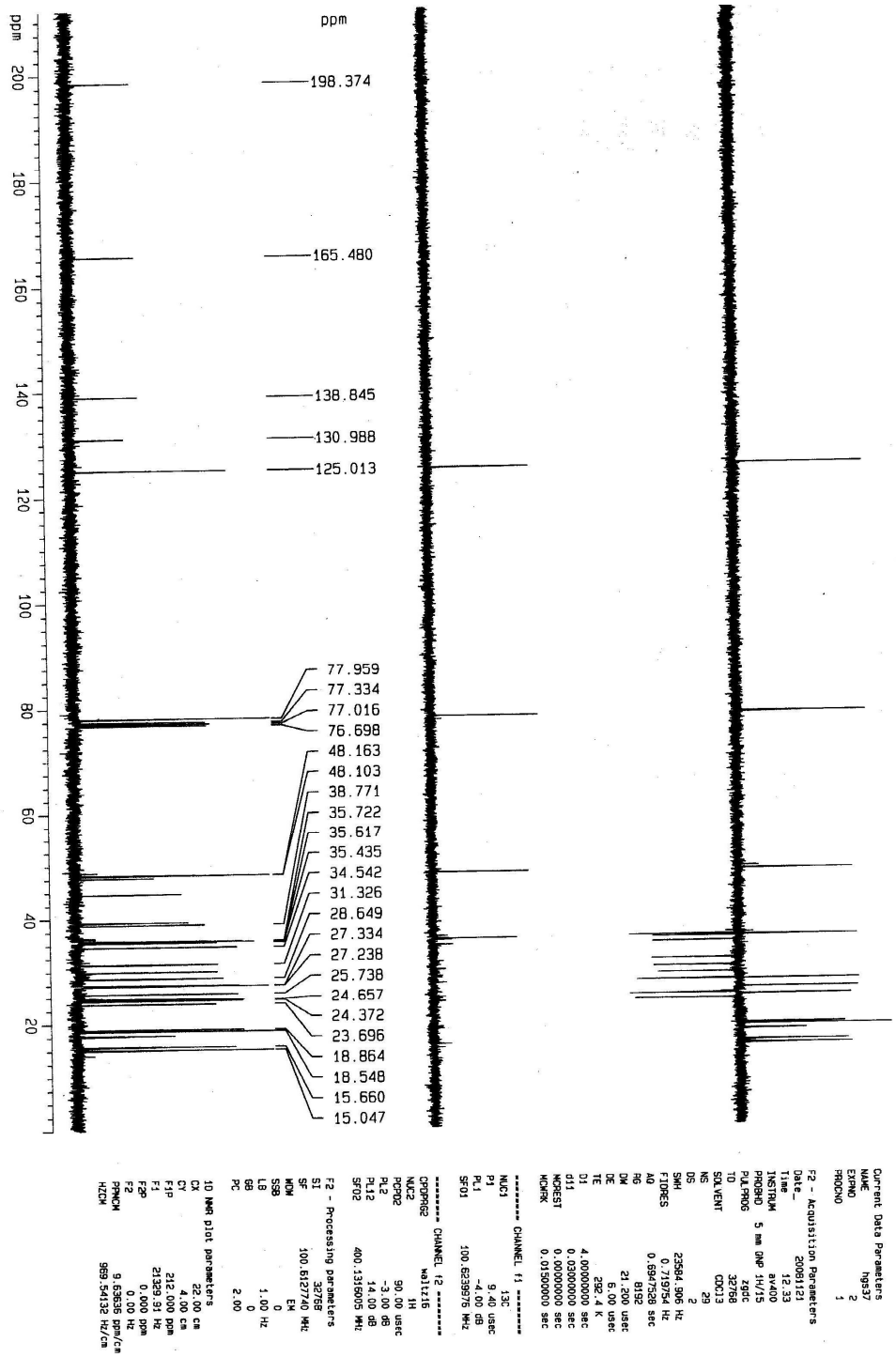


Figure S14. ^{1}H-NMR Spectrum of **5** in $CDCl_3$.

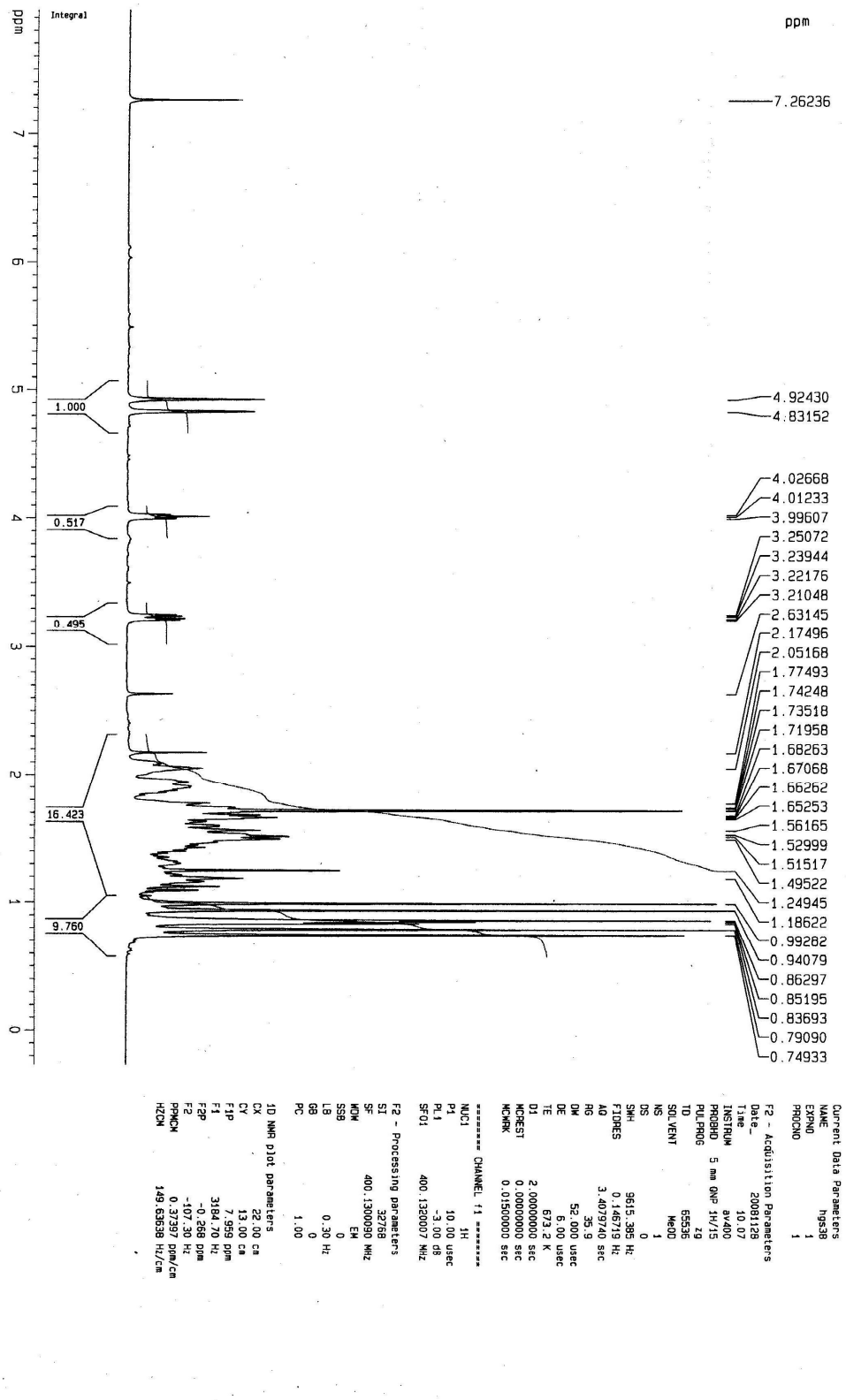


Figure S15. ^{13}C-NMR Spectrum of **5** in $CDCl_3$.

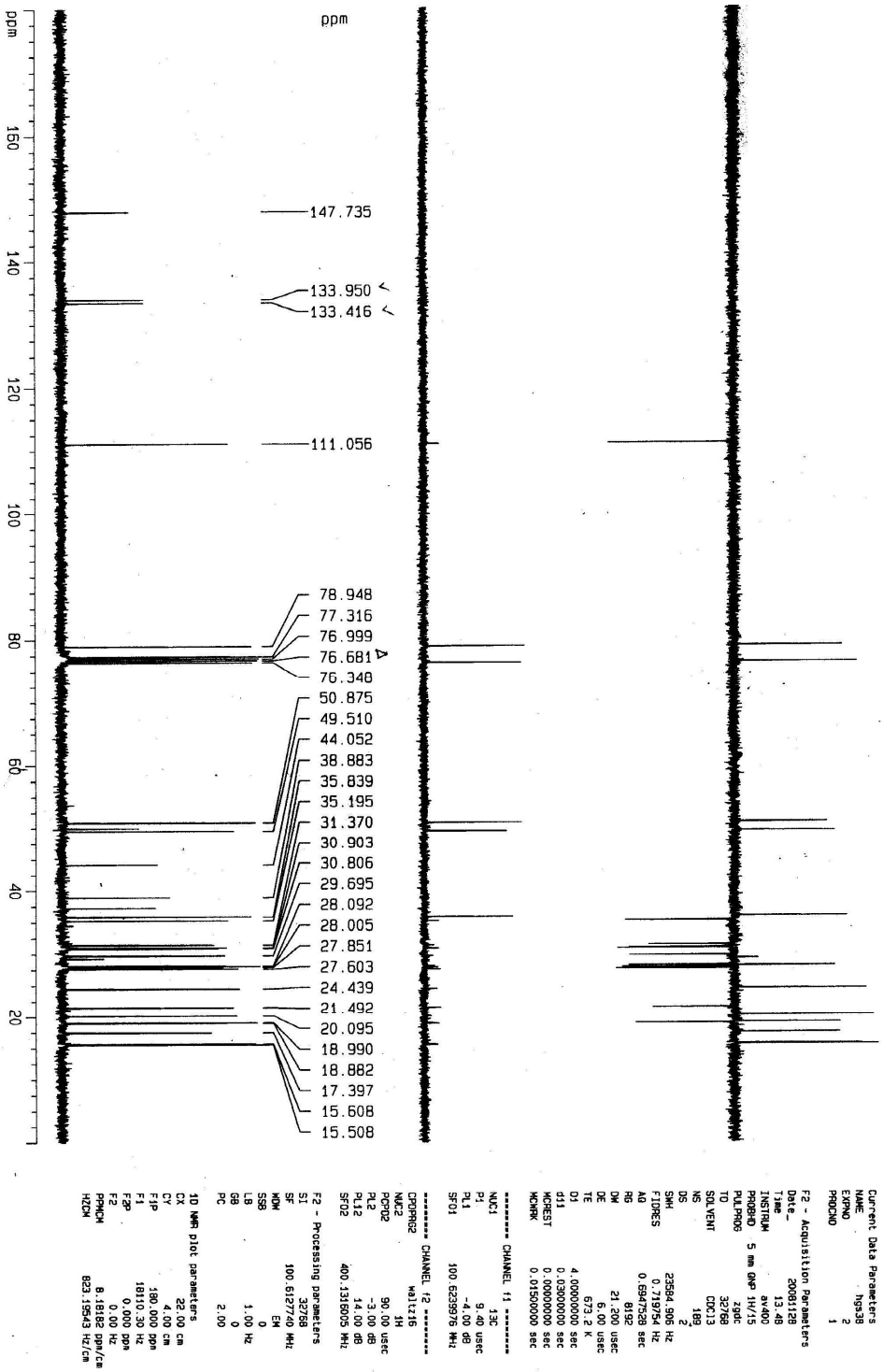


Figure S16. ^{1}H-NMR Spectrum of **6** in $CDCl_3$.

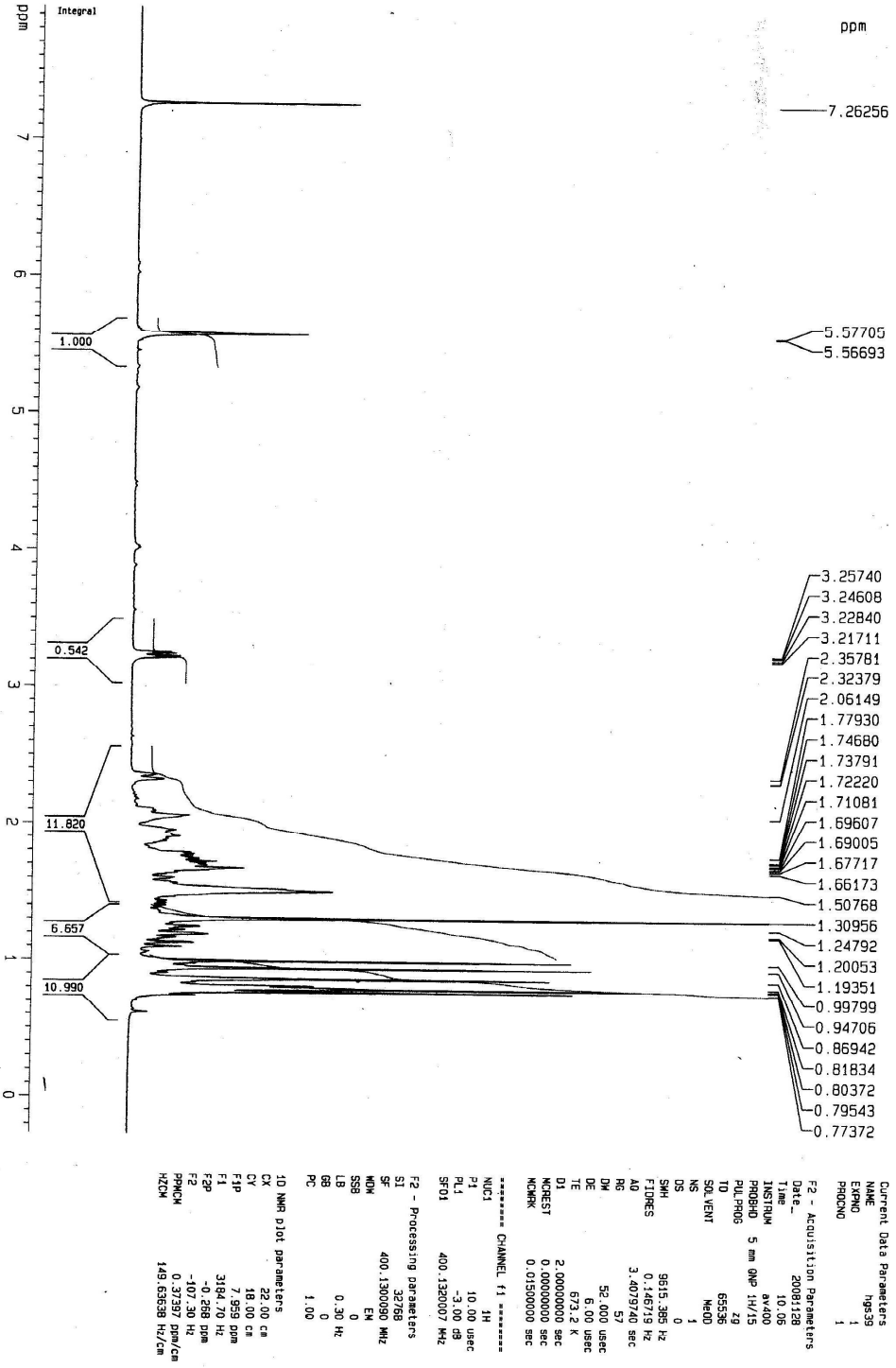
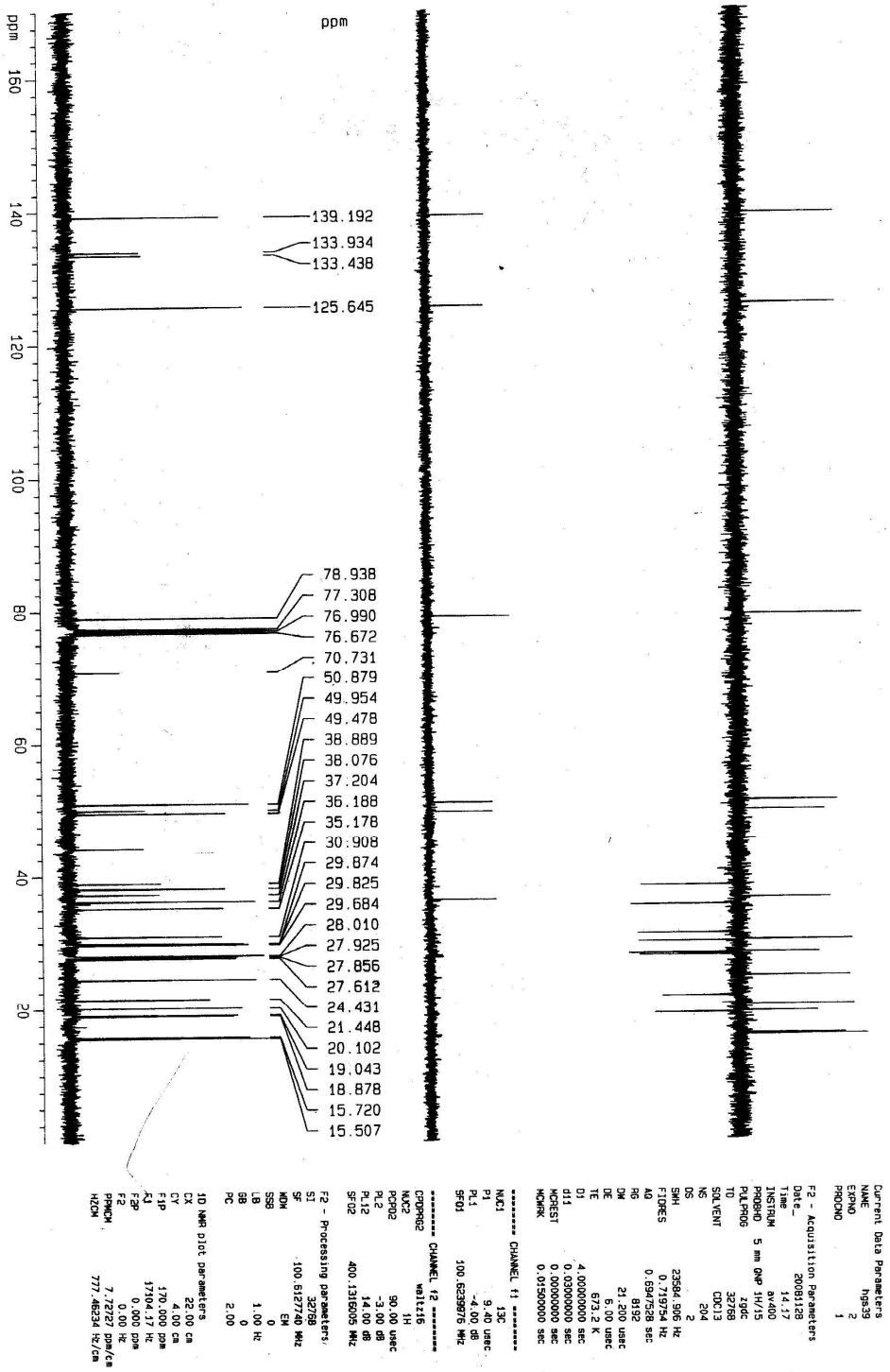


Figure S17. ^{13}C-NMR Spectrum of **6** in $CDCl_3$.



Result of Biological Testing of 1–6.

Table 1. Inhibition of 11β-HSD1.

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

Table 2. IC_{50} for mouse 11β-HSD1(X ± SD, n = 2).

Compounds and dose	Mean	SD	IC_{50}
Compound-1 0.01 μM	13.69%	4.55%	
Compound-1 0.03 μM	27.94%	5.31%	
Compound-1 0.1 μM	53.48%	0.71%	78.44 nM
Compound-1 0.3 μM	72.93%	0.51%	
Compound-1 1 μM	89.37%	0.13%	
Compound-2 0.1 μM	16.21%	0.77%	
Compound-2 0.3 μM	28.98%	4.37%	
Compound-2 1 μM	46.71%	0.03%	1.077 μM
Compound-2 3 μM	70.48%	3.49%	
Compound-2 10 μM	90.75%	0.76%	
Compound-3 0.01 μM	21.44%	3.85%	
Compound-3 0.03 μM	29.00%	3.15%	
Compound-3 0.1 μM	57.01%	4.76%	80.52 nM
Compound-3 0.3 μM	80.27%	0.55%	
Compound-3 1 μM	95.34%	0.45%	
Compound-4 0.003 μM	20.72%	0.87%	
Compound-4 0.01 μM	42.25%	3.83%	
Compound-4 0.03 μM	72.02%	2.13%	13.36 nM
Compound-4 0.1 μM	92.55%	0.82%	
Compound-4 0.3 μM	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%	3.601 nM
glycyrrhizininc acid 100 nM	92.93%	3.09%	

Table 3. IC_{50} 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%	15.99 nM
Compound-6 0.03 μM	67.93%	1.02%	
Compound-6 0.1 μM	91.16%	2.25%	
Compound-6 0.3 μM	96.00%	2.24%	
Compound-6 1 μM	99.30%	1.38%	
glycyrrhizininc acid 1 nM	15.32%	0.28%	8.626 nM
glycyrrhizininc acid 10 nM	46.94%	2.05%	
glycyrrhizininc acid 100 nM	81.71%	0.54%	

Table 4. IC_{50} for mouse 11β-HSD2(X ± SD, n = 2).

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

Table 5. IC_{50} for human 11β-HSD2 (X ± SD, n = 2).

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