

## Supplementary Information

### **[<sup>18</sup>F]- and [<sup>11</sup>C]N-benzyl-isatin sulfonamide analogues as PET tracers for Apoptosis: Synthesis, radiolabeling mechanism, and *in vivo* imaging study of Apoptosis in Fas-treated mice using [<sup>11</sup>C]WC-98**

Dong Zhou,<sup>a</sup> Wenhua Chu,<sup>a</sup> Delphine L. Chen,<sup>a</sup> Qi Wang,<sup>a</sup> David E. Reichert,<sup>a</sup> Justin Rothfuss,<sup>a</sup> Andre D'Avignon,<sup>a</sup> Michael J. Welch<sup>a</sup> and Robert H. Mach<sup>a,\*</sup>

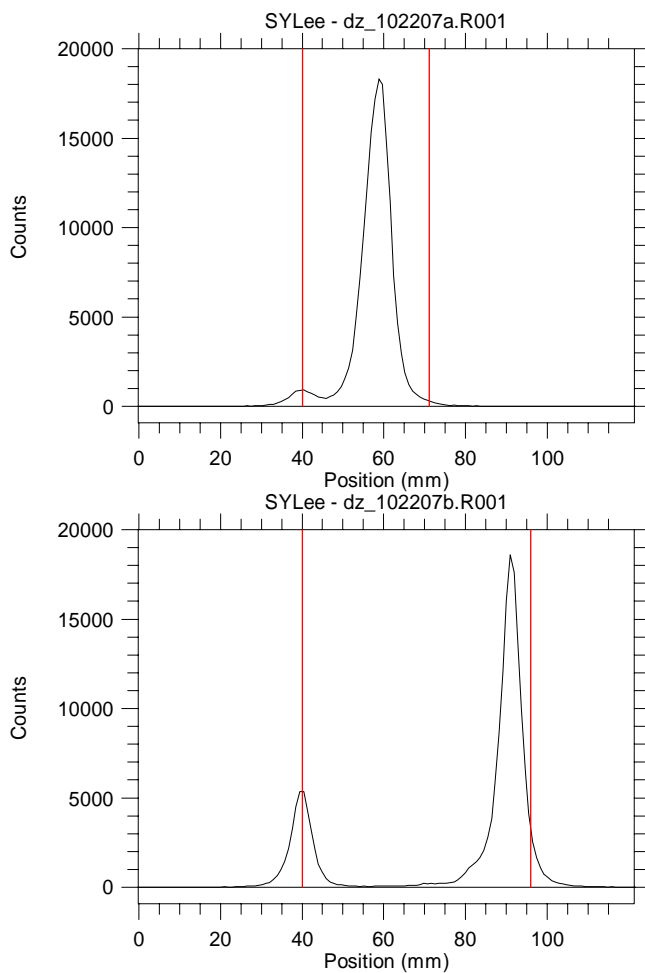
<sup>a</sup>*Division of Radiological Sciences, Washington University School of Medicine, 510 South Kingshighway Boulevard, St. Louis, Missouri 63110*

<sup>b</sup>*Department of Chemistry, Washington University, One Brookings Dr., St. Louis, Missouri 63130*

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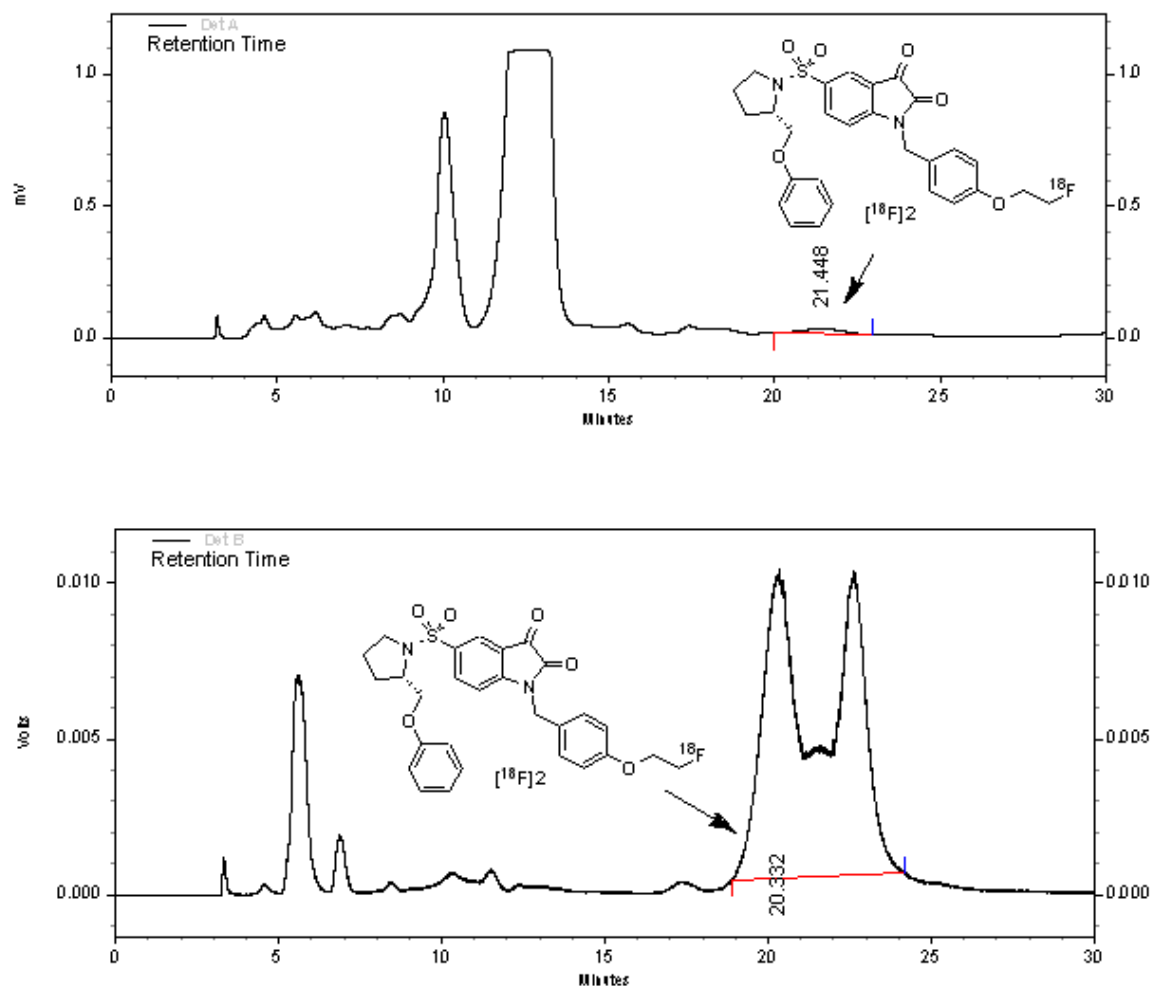


**Figure S1.** RadioTLCs of the reaction mixture of radiosynthesis of [ $^{18}\text{F}$ ] **2**.

Above: Precursor **7a**, [ $^{18}\text{F}$ ]fluoride,  $\text{K}_{222}$ ,  $\text{K}_2\text{CO}_3$ , DMSO, Microwave;

Bottom: 1 N HCl, Microwave.

Silica Gel TLC plate; solvent: 20% MeOH, 80%  $\text{CH}_2\text{Cl}_2$ .

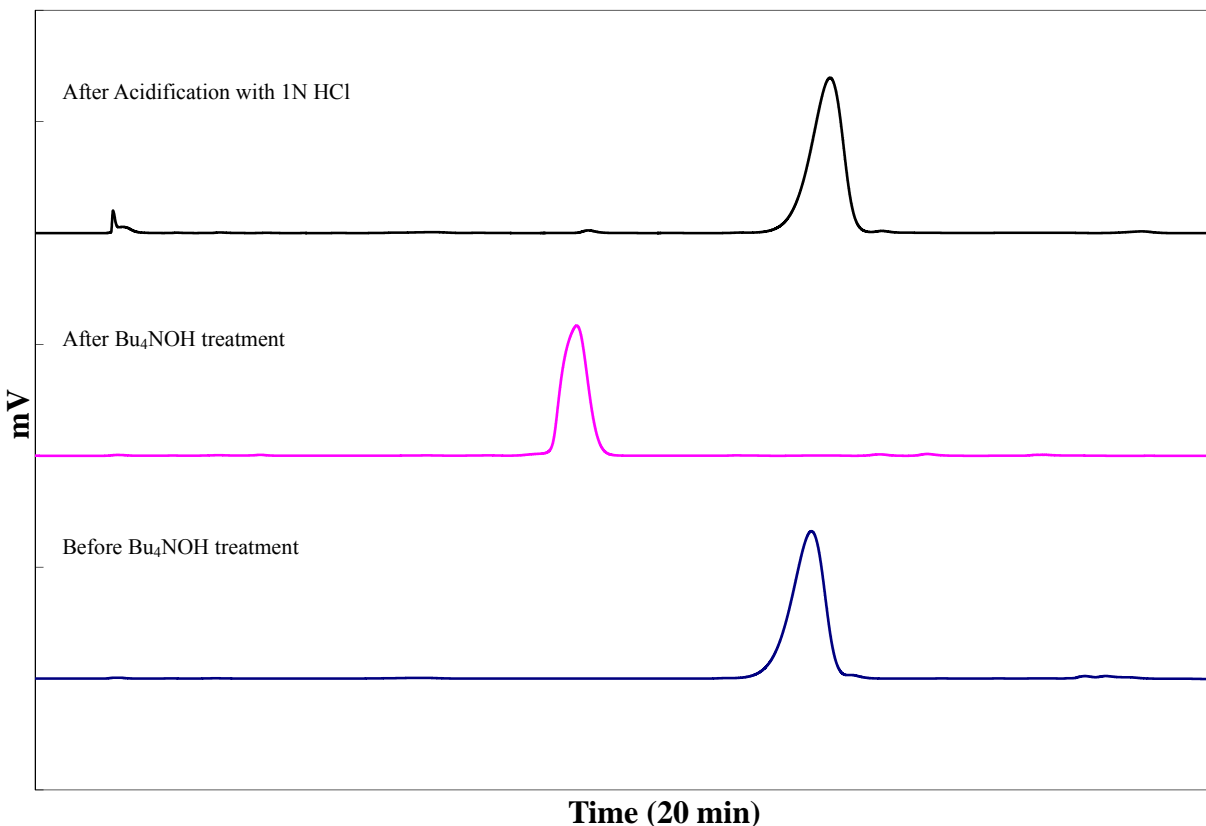


**Figure S2.** Typical HPLC chromatograms for  $[^{18}\text{F}]\mathbf{2}$  purification

Above: UV absorbance at 251 nm;

Bottom: radioactivity (The “rabbit” ears are due to saturation of the radioactive detector)

Alltech Econosil 250×10 mm, 10 $\mu$ ; 4.0 mL/min, 251 nm, 800 psi; 24% Acetonitrile, 44% methanol, 32% Ammonium formate buffer (pH = 4.5)



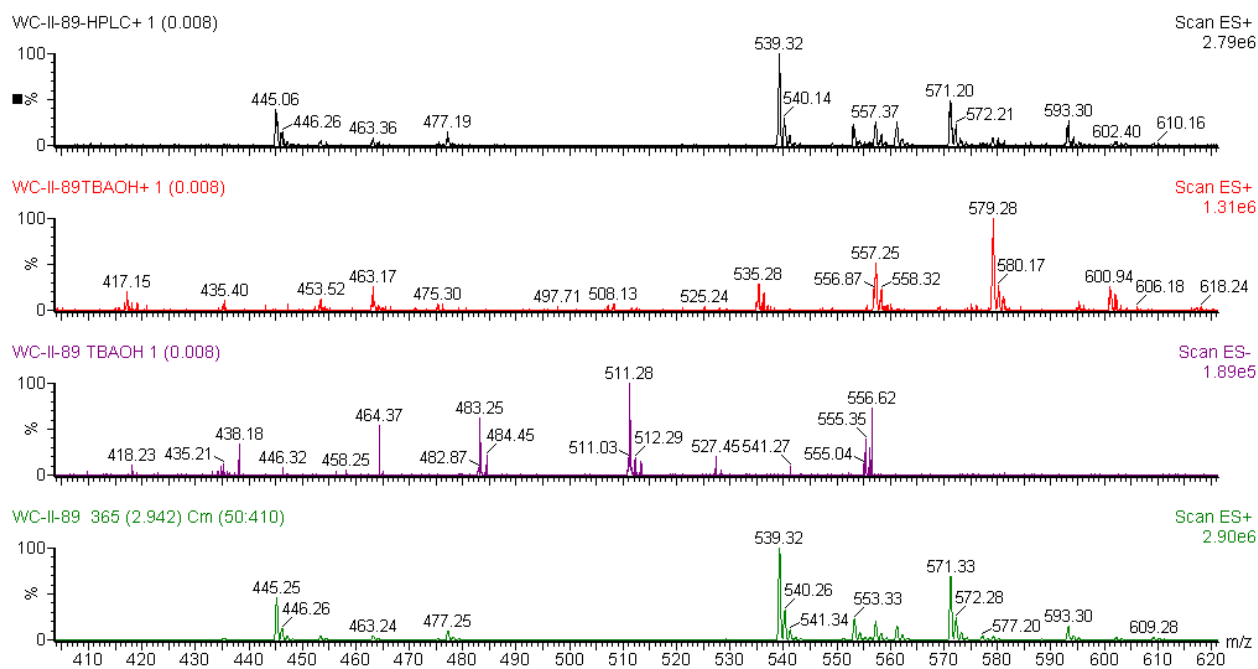
**Figure S3.** HPLC chromatograms of isatin analogue **2** (bottom), isatinate **17** (middle) and isatin **2** recycled from isatinate **17** (top).

HPLC condition: Alltech Altima C18 250 × 4.6 mm 10 $\mu$ , gradient: 25% Acetonitrile, 40% ammonium formate buffer (pH = 4.5), 35% Methanol to 35% Acetonitrile, 20% ammonium formate buffer (pH = 4.5), 45% Methanol over 15 min, 1.0 mL/min, 251 nm.

Before Bu<sub>4</sub>NOH treatment: 20  $\mu$ L 1000 ppm **2** injected

Bu<sub>4</sub>NOH treatment: 0.1 mg **2** in 100  $\mu$ L acetonitrile treated with 2  $\mu$ L 1 M Bu<sub>4</sub>NOH/H<sub>2</sub>O, 20  $\mu$ L 1000 ppm injected

1 N HCl treatment: 100  $\mu$ L 1 N HCl, 1 hour at ambient temperature, 40  $\mu$ L 500 ppm injected.



**Figure S4.** ESI/MS of isatin analogue **2** (bottom), isatinate **17** (middle, negative and positive) and isatin **2** recycled from isatinate **17** (top).

Isatinate and isatin recycled from isatinate were purified by HPLC (see above)

19F OBSERVE  
STANDARD PARAMETERS

Pulse Sequence: s2pul

Solvent: DMSO  
Ambient temperature  
File: isatin\_TBAF\_F  
Mercury-300 "m300"

PULSE SEQUENCE

Relax. delay 4.000 sec  
Pulse 19.5 degrees  
Acq. time 0.300 sec  
Width 50000.0 Hz  
64 repetitions

OBSERVE F19, 282.3941399 MHz

DATA PROCESSING

Line broadening 0.3 Hz  
FT size 32768  
Total time 1 hr, 16 min, 2 sec

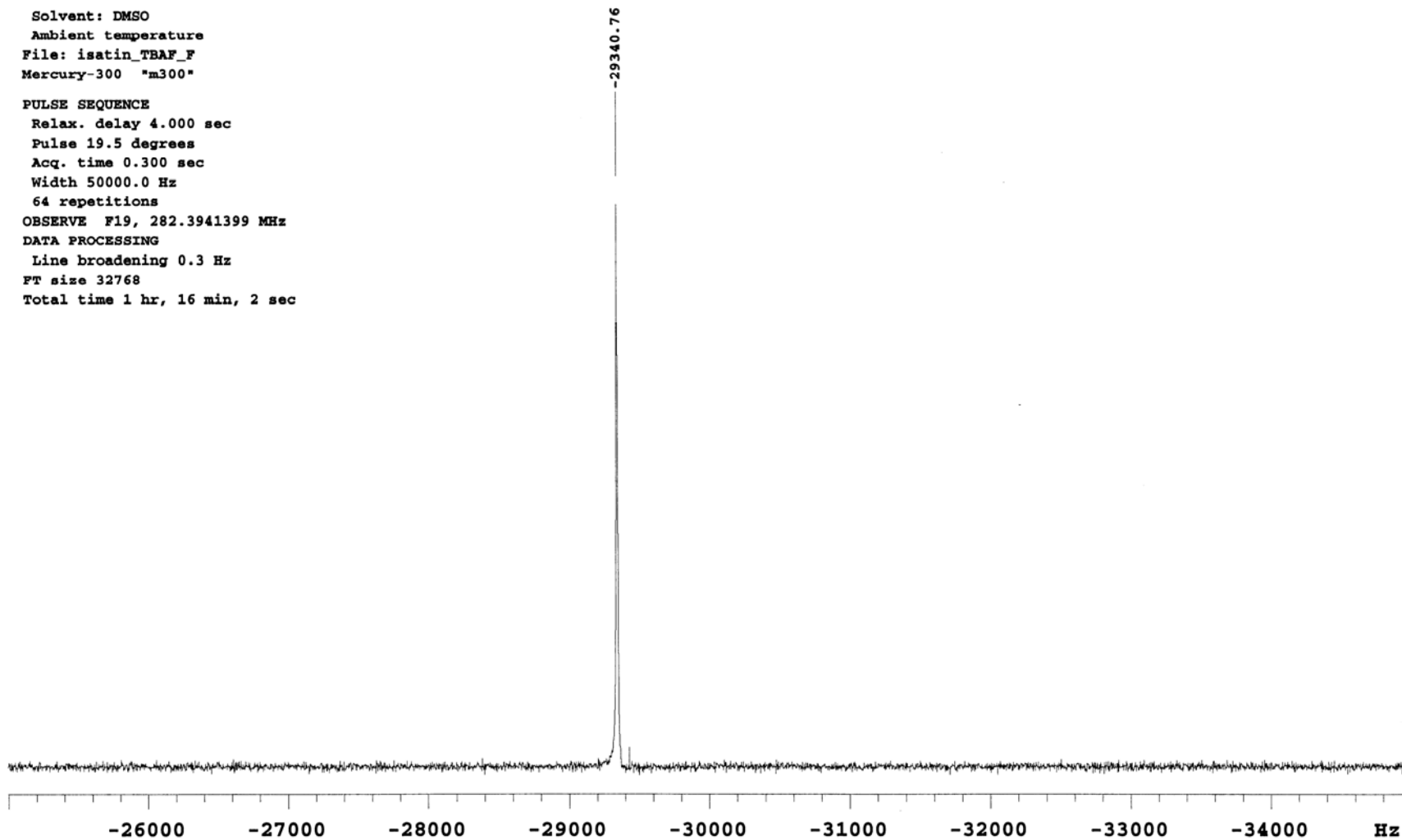


Figure S5. 282 MHz <sup>19</sup>F NMR spectrum (DMSO-d<sub>6</sub>) of Bu<sub>4</sub>NF

19F OBSERVE  
STANDARD PARAMETERS  
  
Pulse Sequence: s2pul  
  
Solvent: DMSO  
Ambient temperature  
File: isatin\_plustBAF300ul\_F  
Mercury-300 "m300"  
  
PULSE SEQUENCE  
Relax. delay 4.000 sec  
Pulse 19.5 degrees  
Acq. time 0.300 sec  
Width 50000.0 Hz  
64 repetitions  
OBSERVE F19, 282.3941399 MHz  
DATA PROCESSING  
Line broadening 0.3 Hz  
FT size 32768  
Total time 1 hr, 16 min, 2 sec

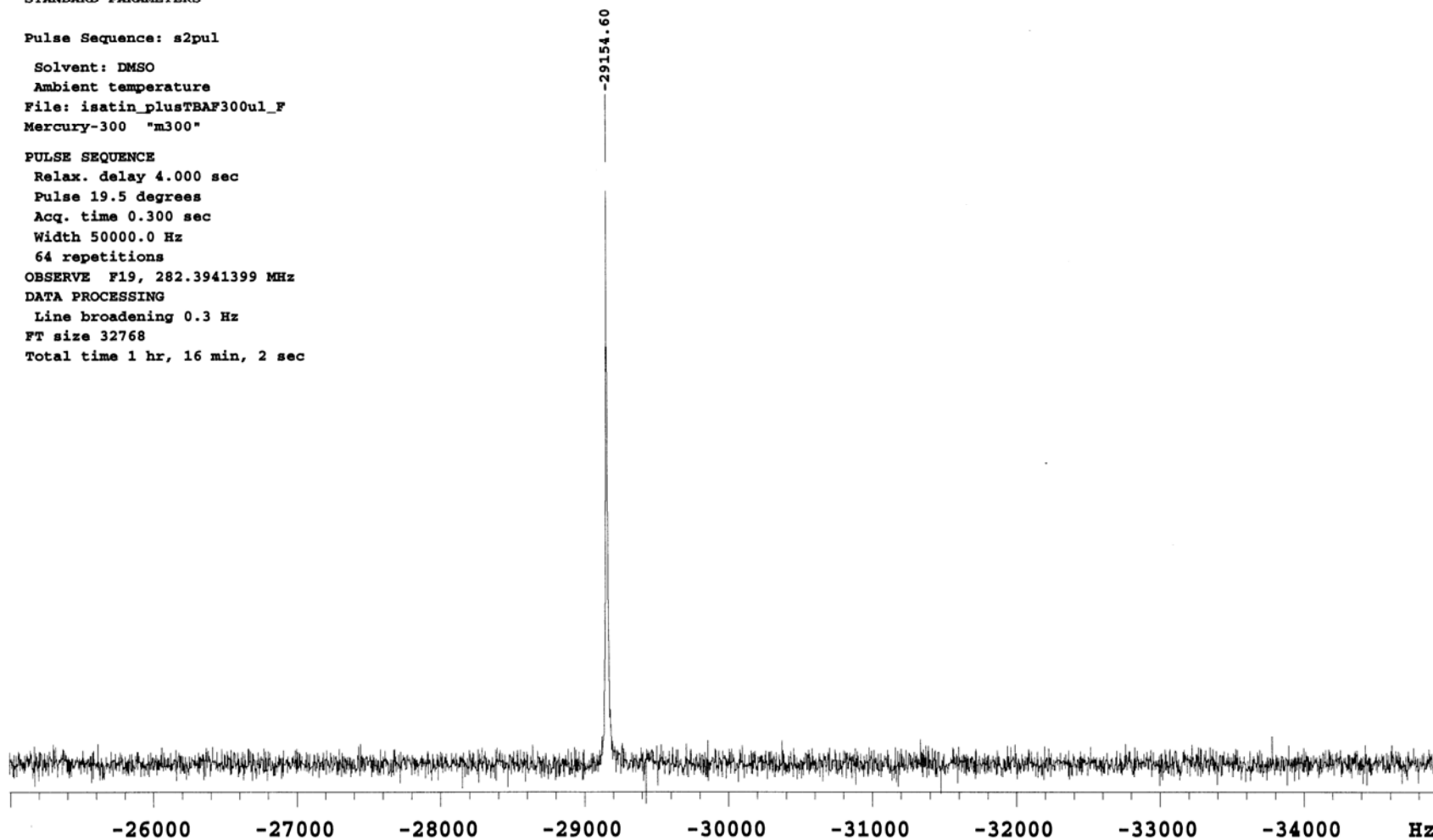


Figure S6. 282 MHz <sup>19</sup>F NMR spectrum (DMSO-d6) of Bu<sub>4</sub>NF with addition of N-benzyl isatin **21**



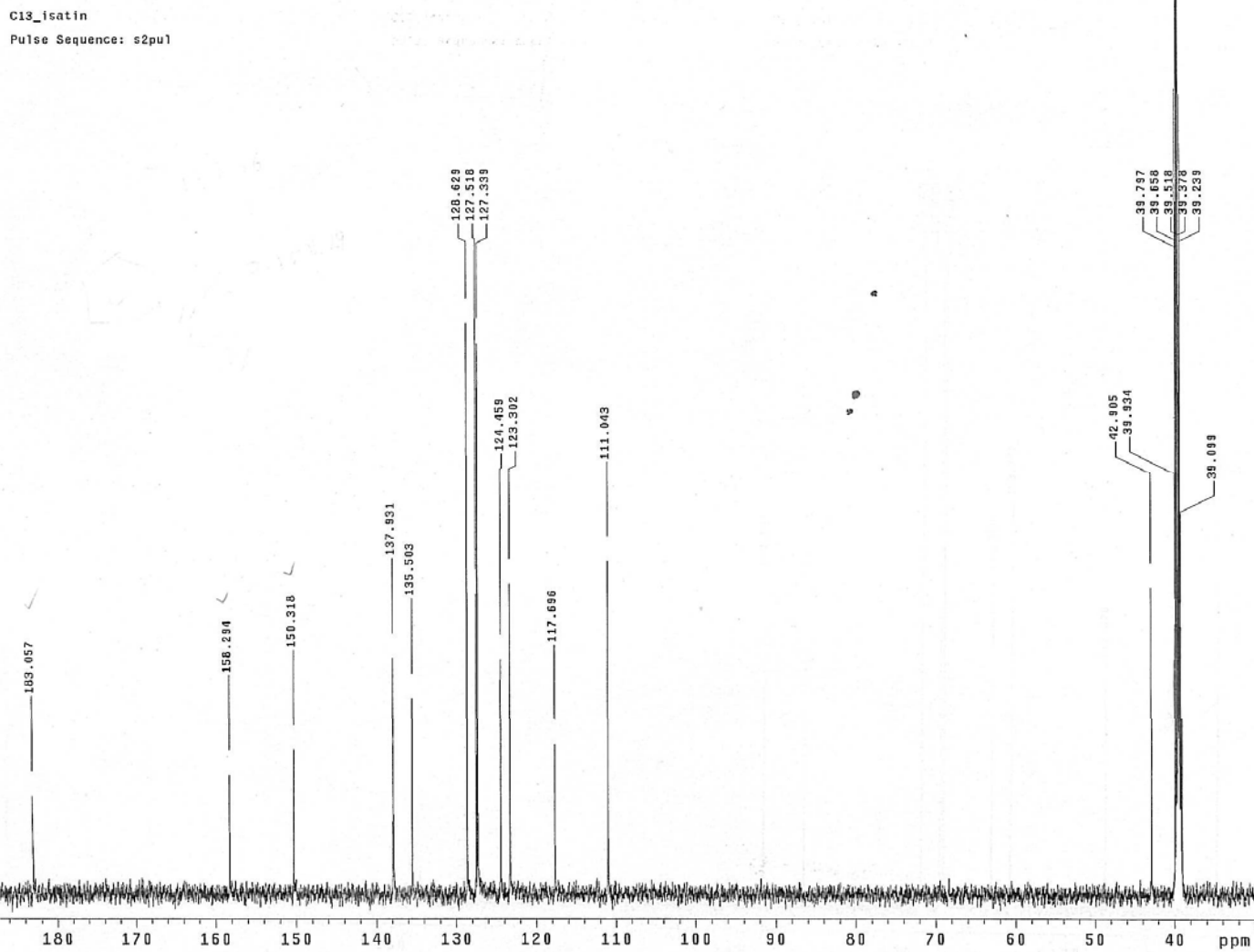
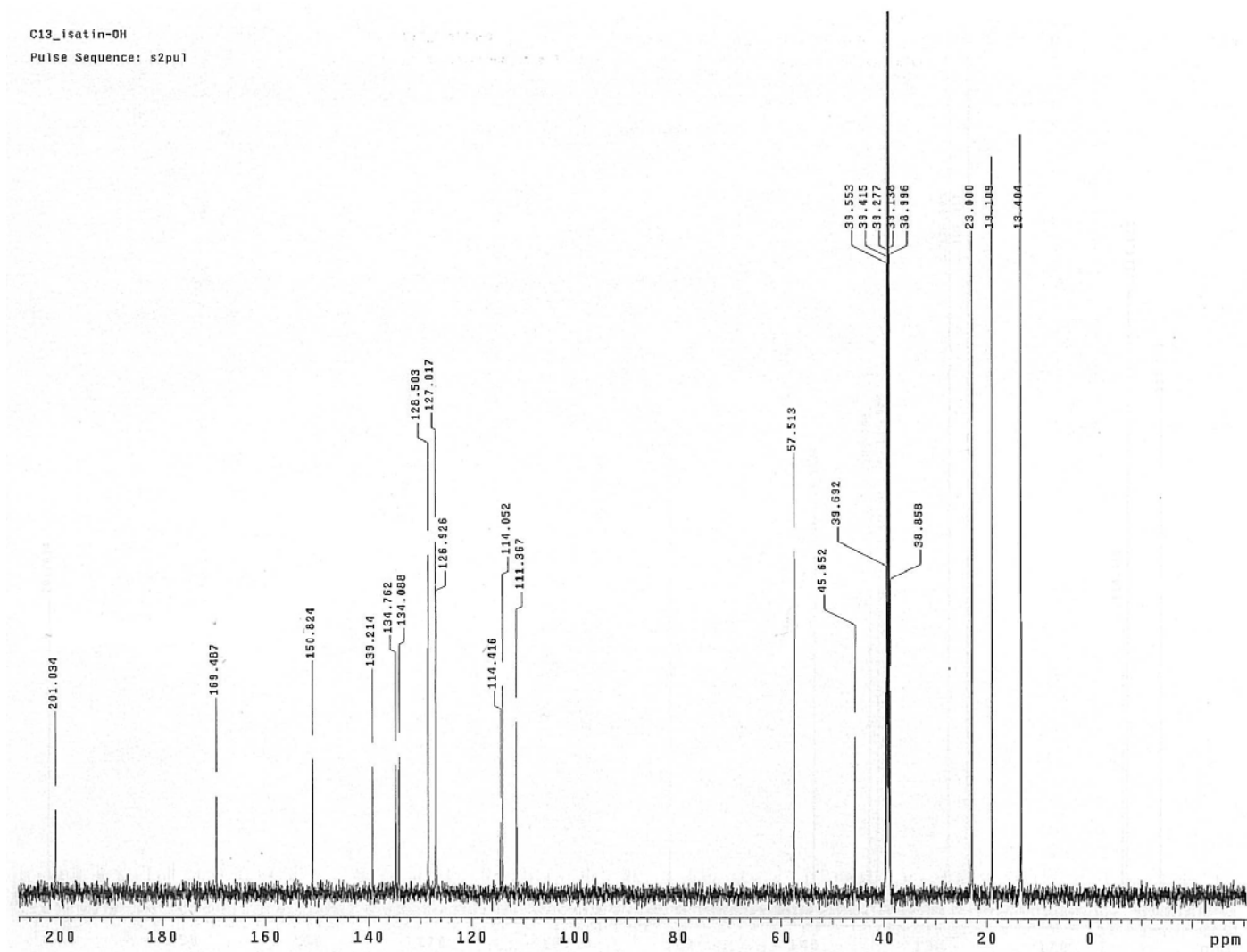
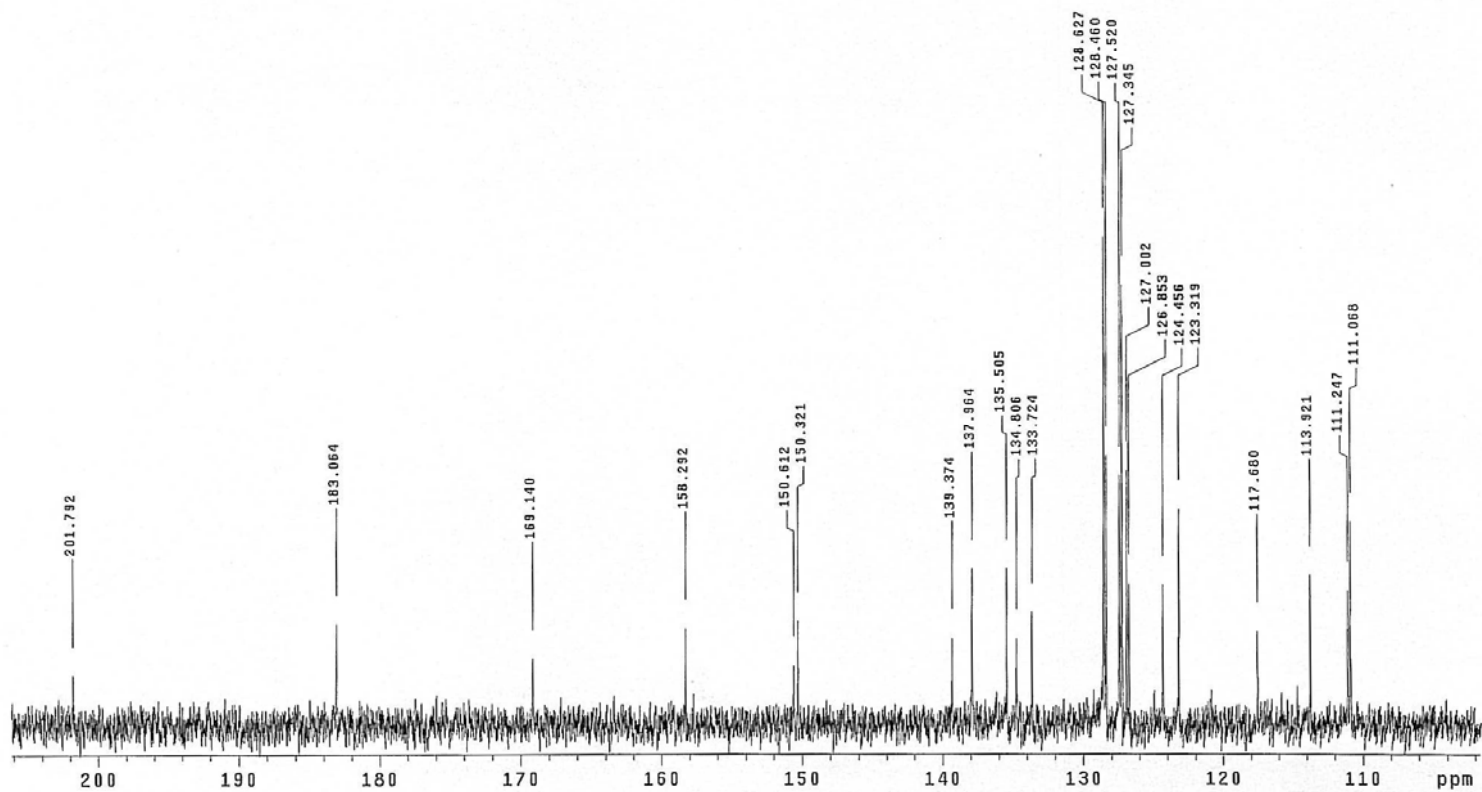


Figure S7. 150 MHz  $^{13}\text{C}$  NMR (DMSO- $d_6$ ) Spectrum of N-benzyl isatin **21**.

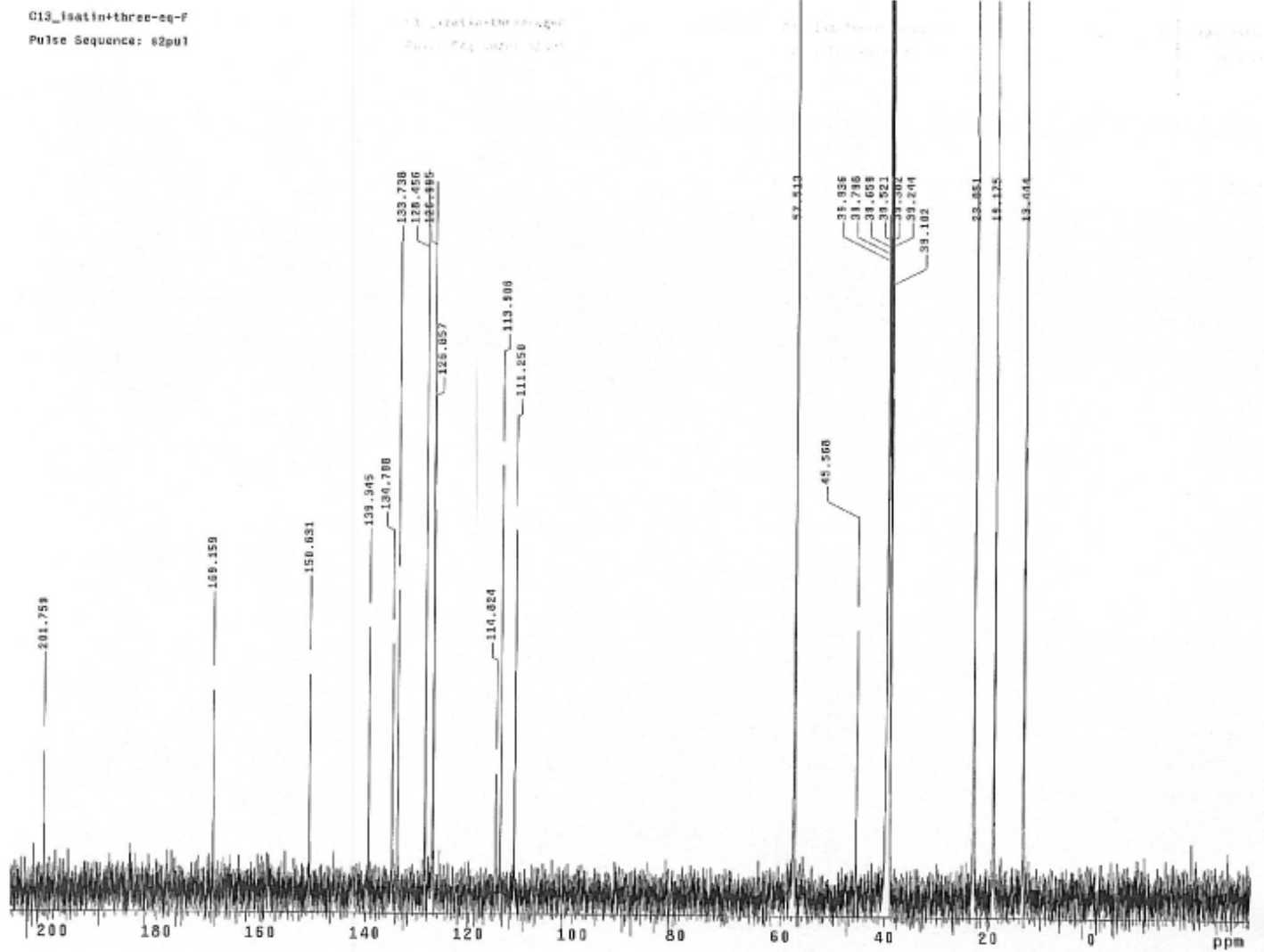


**Figure S8.** 150 MHz  $^{13}\text{C}$  NMR Spectrum (DMSO- $d_6$ ) of N-benzyl isatin **21** treated with 1M  $\text{Bu}_4\text{NOH}/\text{H}_2\text{O}$  (10 mg **21** in 0.6 mL DMSO- $d_6$ )

C13\_isatin+one-eq-F  
Pulse Sequence: s2pu1



**Figure S9.** 150 MHz <sup>13</sup>C NMR Spectrum (DMSO-d<sub>6</sub>) of N-benzyl isatin **21** treated with 1 equivalent Bu<sub>4</sub>NF/H<sub>2</sub>O (10 mg **21** in 0.6 mL DMSO-d<sub>6</sub>)



**Figure S10.** 150 MHz <sup>13</sup>C NMR Spectrum (DMSO-d<sub>6</sub>) of N-benzyl isatin **21** treated with 3 equivalents Bu<sub>4</sub>NF/H<sub>2</sub>O (10 mg **21** in 0.6 mL DMSO-d<sub>6</sub>)

C13\_WC2-89\_OMs  
Pulse Sequence: s2pu1  
Solvent: DMSO  
Temp. 25.0 C / 298.1 K  
User: 1-14-87  
File: C13\_WC2-89\_OMs  
INNOVA-600 "khan"  
  
Relax. delay 1.000 sec  
Pulse 86.5 degrees  
Acq. time 1.300 sec  
Width 29996.3 Hz  
344 repetitions  
OBSERVE C13, 150.8063061 MHz  
DECOUPLE H1, 599.7479451 MHz  
Power 44 dB  
continuously on  
WALTZ-16 modulated  
DATA PROCESSING  
Line broadening 2.0 Hz  
FT size 131072  
Total time 641 hr, 30 min, 5 sec

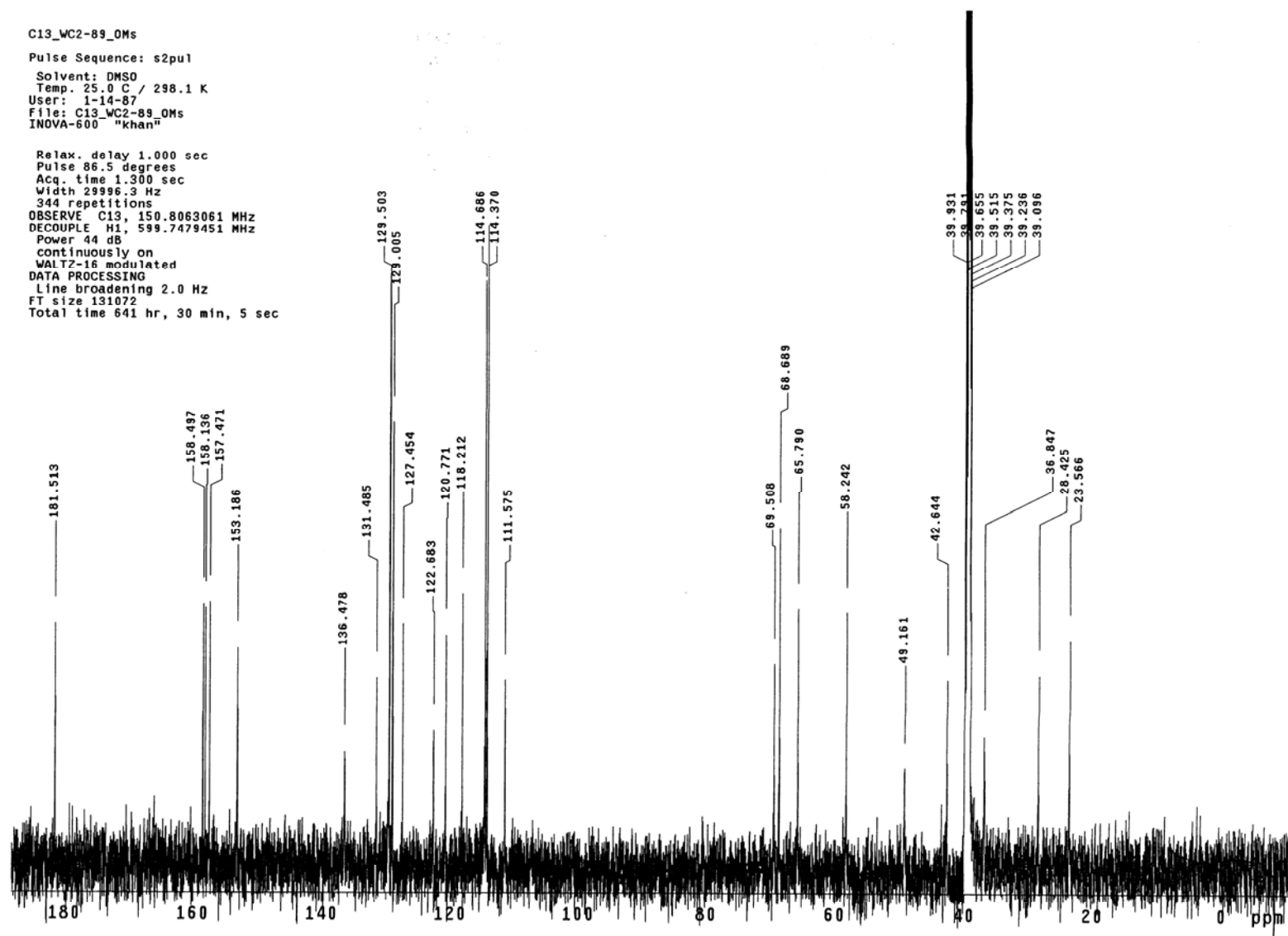
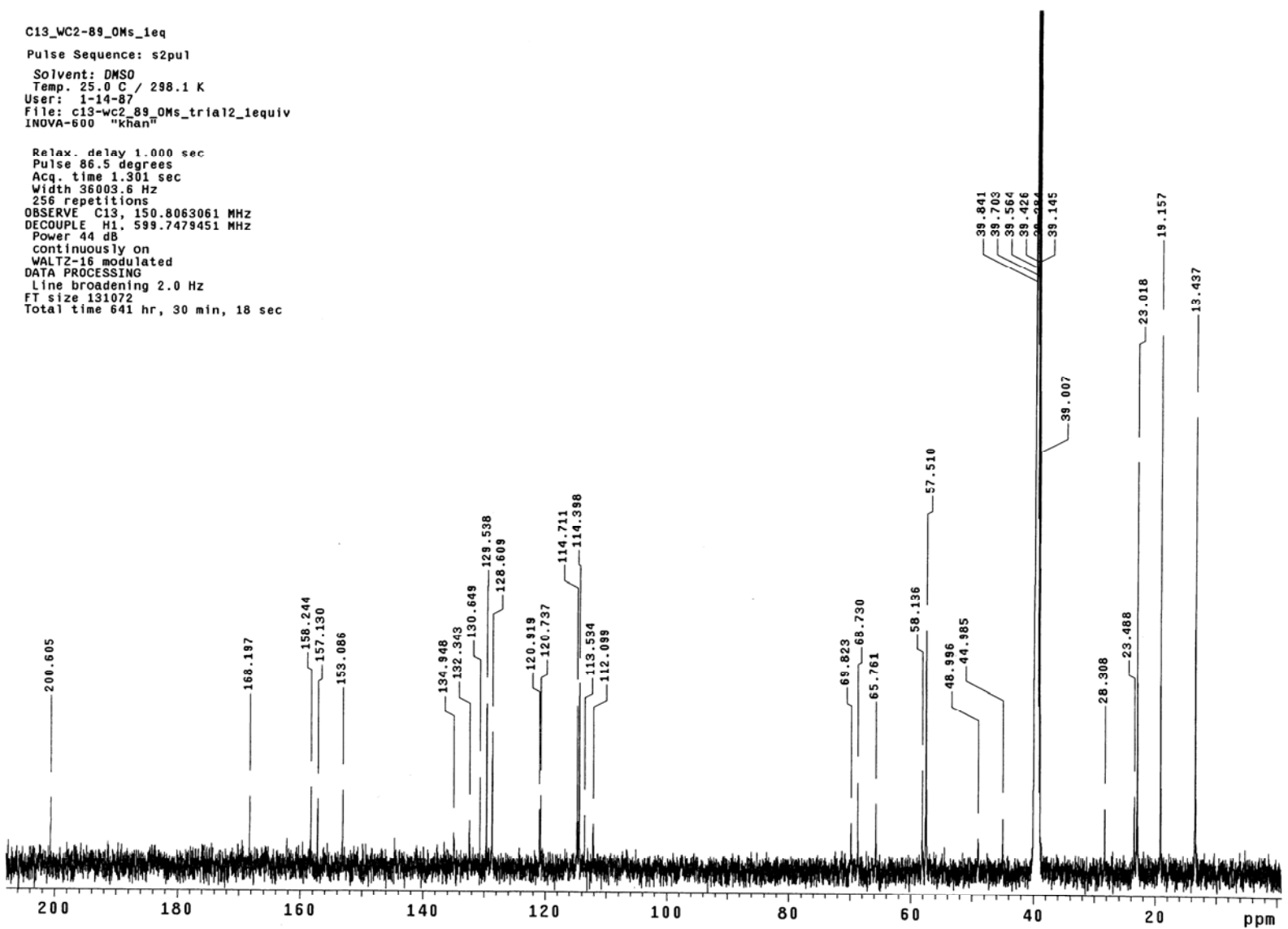


Figure S11. 150 MHz  $^{13}\text{C}$  NMR spectrum (DMSO- $d_6$ ) of **7a** (10 mg **7a** in 0.6 mL DMSO- $d_6$ )



**Figure S12.** 150 MHz  $^{13}\text{C}$  NMR spectrum (DMSO- $d_6$ ) of ring-opened **7a** (10 mg **7a** in 0.6 mL DMSO- $d_6$  treated with 20  $\mu\text{L}$  1M  $\text{Bu}_4\text{NOH}/\text{H}_2\text{O}$ )

C13\_WC2-89  
 Pulse Sequence: s2pul  
 Solvent: DMSO  
 Temp. 25.0 C / 298.1 K  
 User: 1-14-87  
 File: C13\_WC2-89  
 INOVA-600 "khan"  
  
 Relax. delay 1.000 sec  
 Pulse 86.5 degrees  
 Acq. time 1.301 sec  
 Width 36003.6 Hz  
 112 repetitions  
 OBSERVE C13, 150.8063061 MHz  
 DECOUPLE H1, 599.7478451 MHz  
 Power 44 dB  
 continuously on  
 WALTZ-16 modulated  
 DATA PROCESSING  
 Line broadening 2.0 Hz  
 FT size 131072  
 Total time 641 hr, 30 min, 18 sec

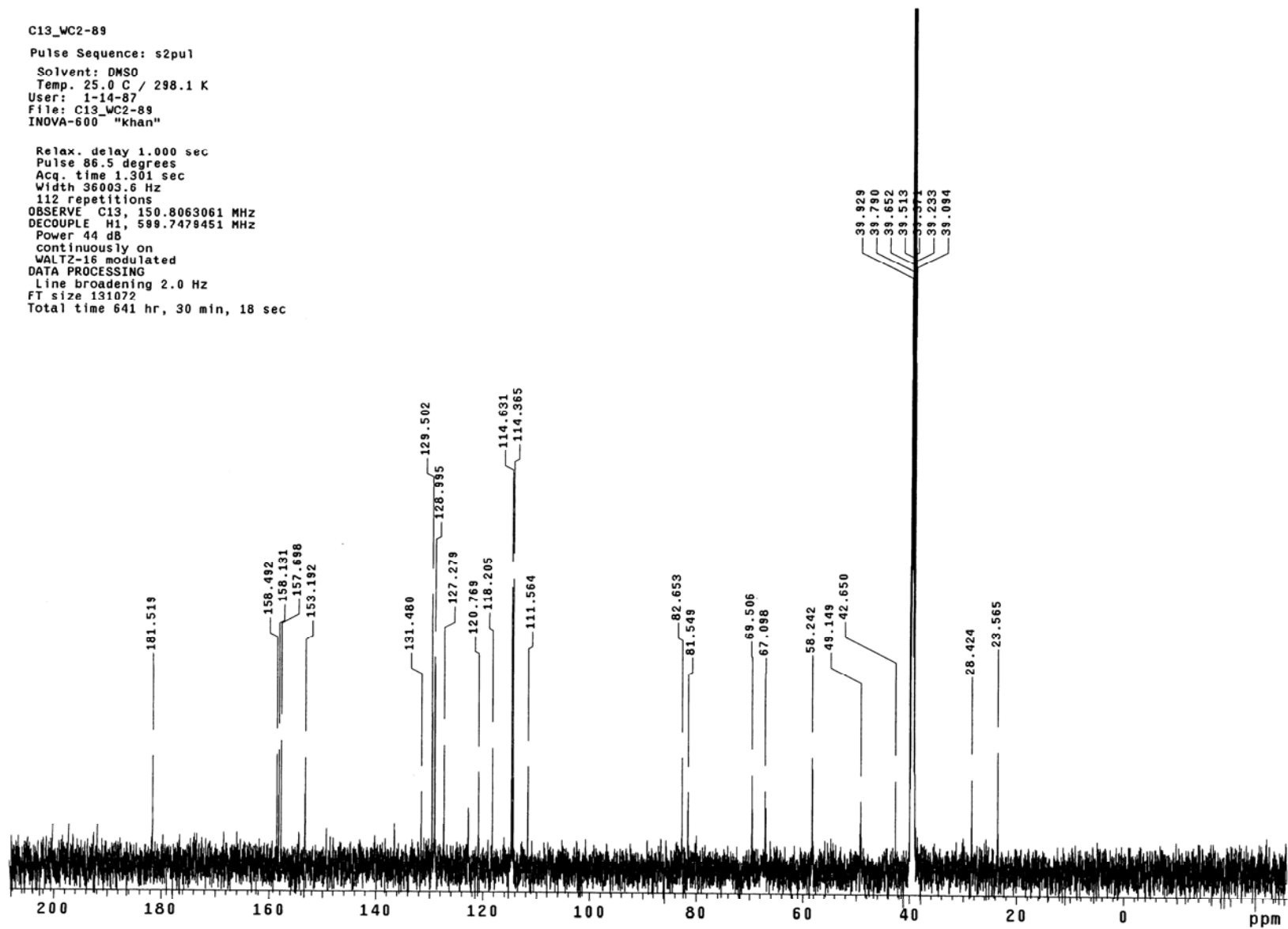
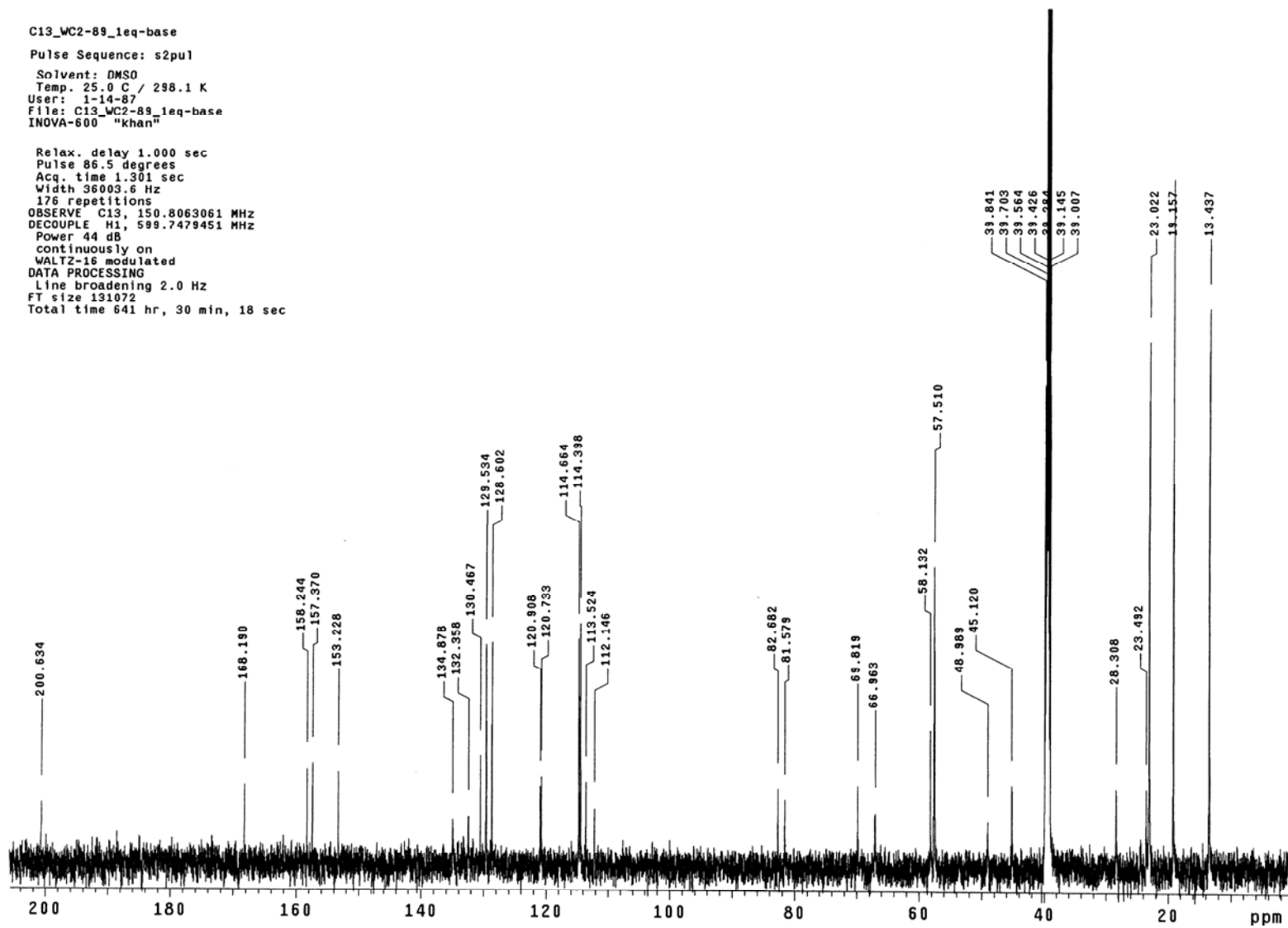


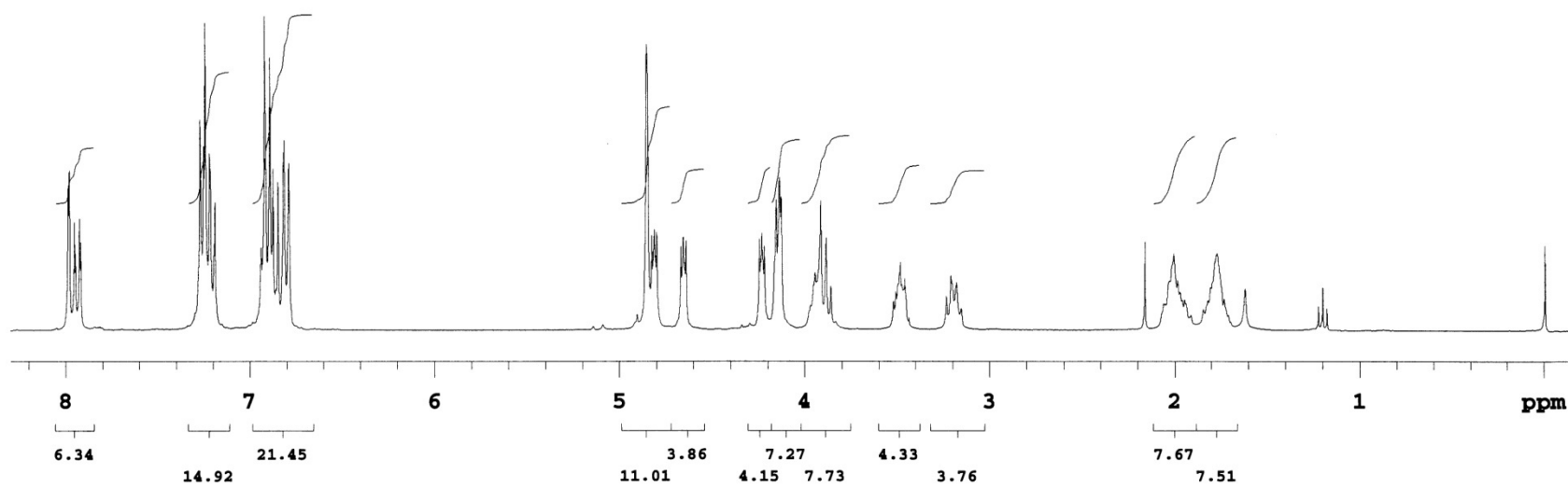
Figure S13. 150 MHz  $^{13}\text{C}$  NMR spectrum (DMSO- $d_6$ ) of **2** (10 mg **2** in 0.6 mL DMSO- $d_6$ )

C13\_WC2-89\_1eq-base  
Pulse Sequence: s2pul  
Solvent: DMSO  
Temp: 25.0 C / 298.1 K  
User: 1-14-87  
File: C13\_WC2-89\_1eq-base  
INOVA-600 "khan"  
  
Relax. delay 1.000 sec  
Pulse 86.5 degrees  
Acq. time 1.301 sec  
Width 36003.6 Hz  
176 repetitions  
OBSERVE C13, 150.8063061 MHz  
DECOUPLE H1, 599.7479451 MHz  
Power 44 dB  
continuously on  
WALTZ-16 modulated  
DATA PROCESSING  
Line broadening 2.0 Hz  
FT size 131072  
Total time 641 hr, 30 min, 18 sec

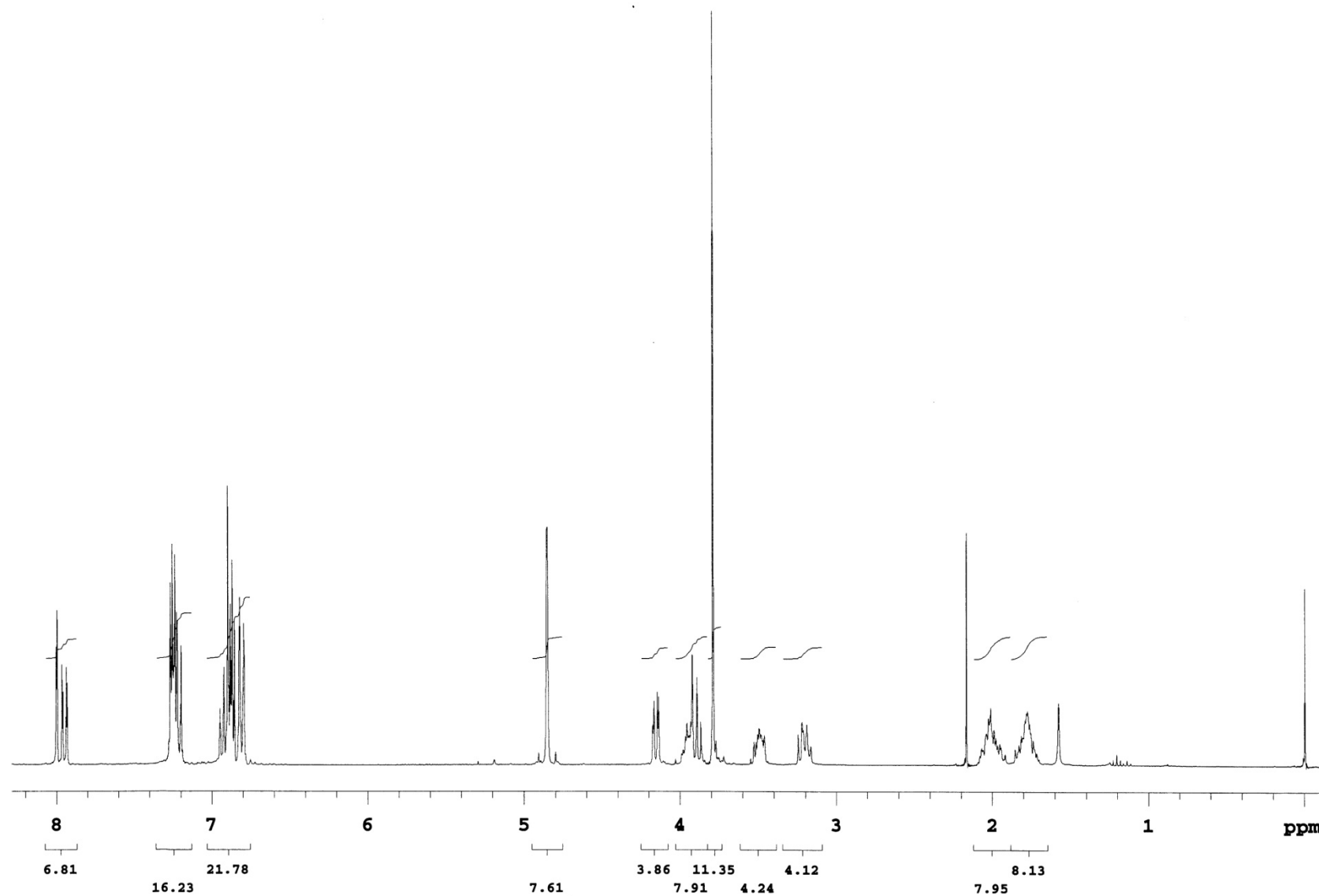


**Figure S14.** 150 MHz  $^{13}\text{C}$  NMR spectrum (DMSO- $d_6$ ) of ring-opened **2** (10 mg **2** in 0.6 mL DMSO- $d_6$  treated with 20  $\mu\text{L}$  1M  $\text{Bu}_4\text{NOH}/\text{H}_2\text{O}$ )





**Figure S15.** 300 MHz  $^1\text{H}$  NMR spectrum (CDCl<sub>3</sub>) of 2



**Figure S16.** 300 MHz  $^1\text{H}$  NMR spectrum (CDCl<sub>3</sub>) of **4**

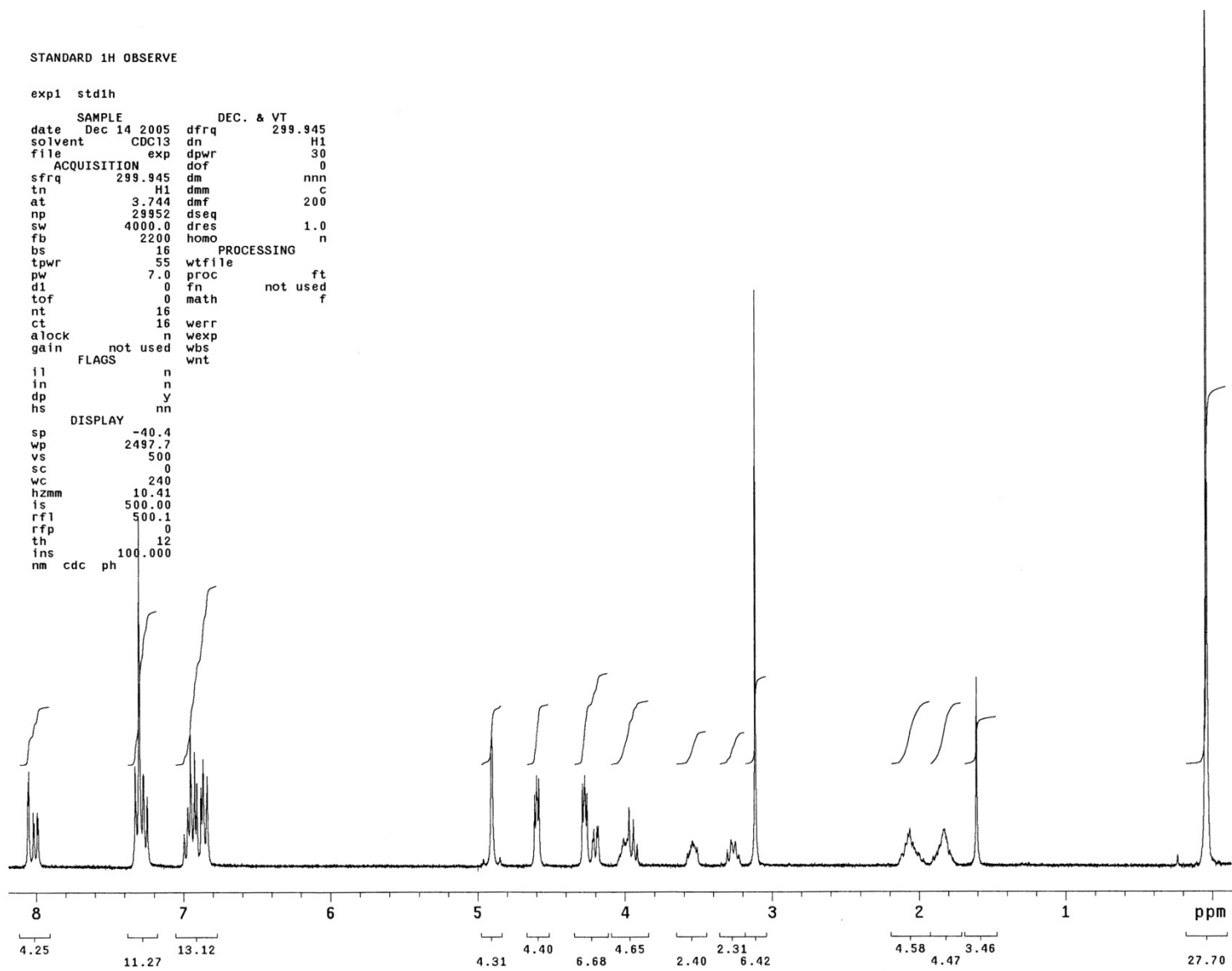
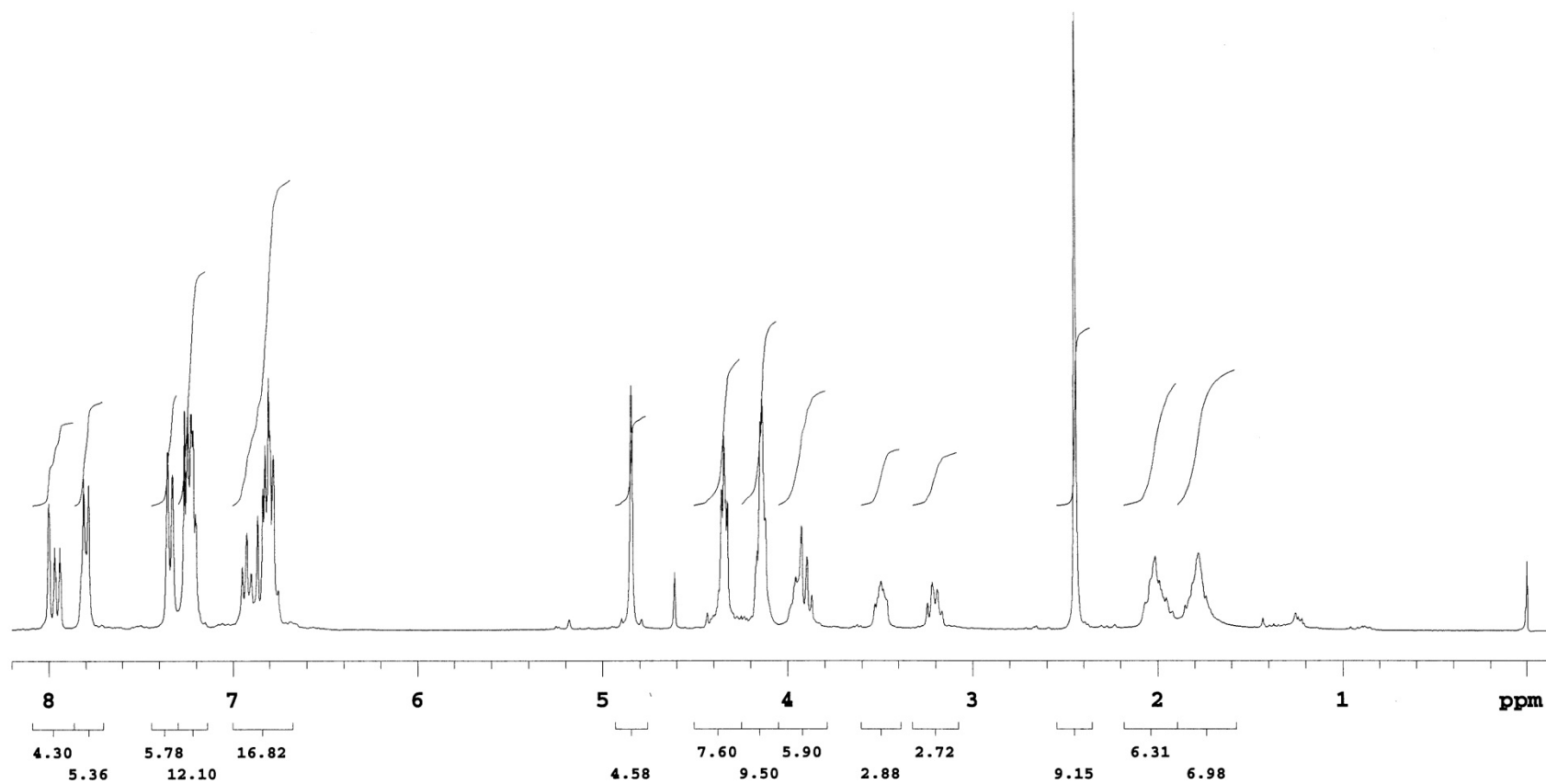


Figure S17. 300 MHz  $^1\text{H}$  NMR spectrum ( $\text{CDCl}_3$ ) of **7a**



**Figure S18.** 300 MHz  $^1\text{H}$  NMR spectrum ( $\text{CDCl}_3$ ) of **7b**

STANDARD 1H OBSERVE

exp1 std1h

SAMPLE DEC. & VT  
date Apr 22 2007 dfrq 300.119  
solvent CDCl3 dn H1  
file exp dpwr 43  
ACQUISITION dof 0  
sfrq 300.119 dm nnn  
tn H1 dmm c  
at 1.998 dmf 11500  
np 17984 PROCESSING  
sw 4500.5 wtfile  
fb 2600 proc ft  
bs 16 fn not used  
ss 2  
tpwr 55 werr  
pw 7.0 wexp  
d1 1.000 wbs  
tof 0 wnt wft f ds vp=12-  
nt 16 dscale vsadj aph  
ct 16

alock n  
gain not used

FLAGS

il n  
in n  
dp y

DISPLAY

sp -36.2  
wp 2490.2  
vs 50  
sc 0  
wc 250  
lgmm 9.96  
ls 240.82  
rf1 795.5  
rtp 0

th 3

ins 100.000

gm cdc ph

7 6 5 4 3 2 1 ppm

6.82

17.94

22.08

3.30

7.86

4.06

8.02

4.12

4.16

8.47

8.23

4.93

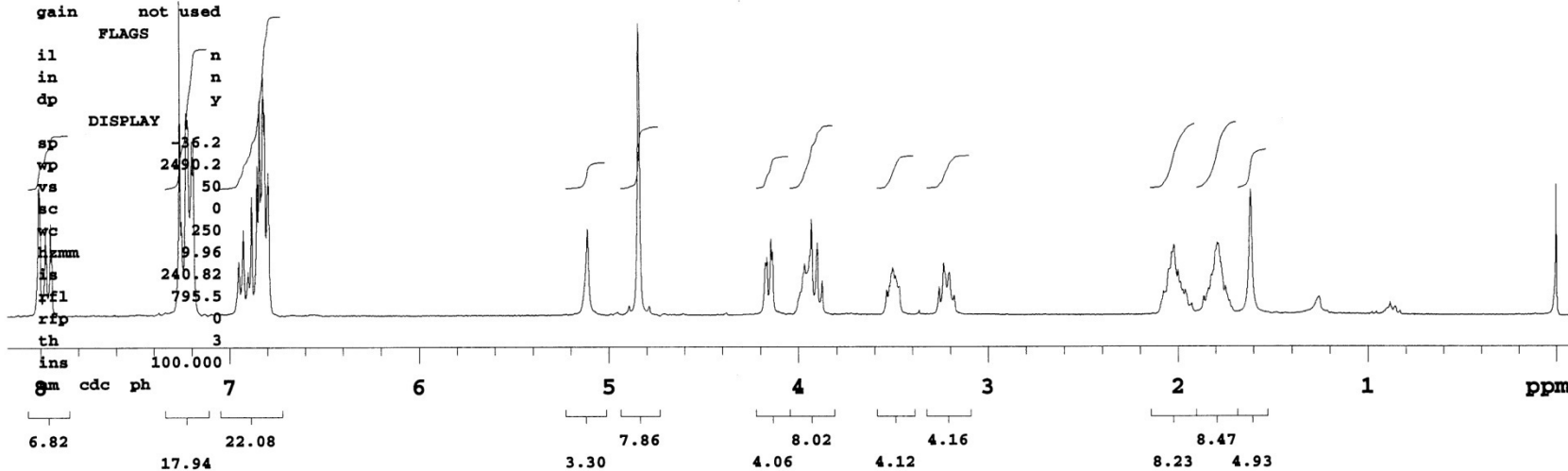
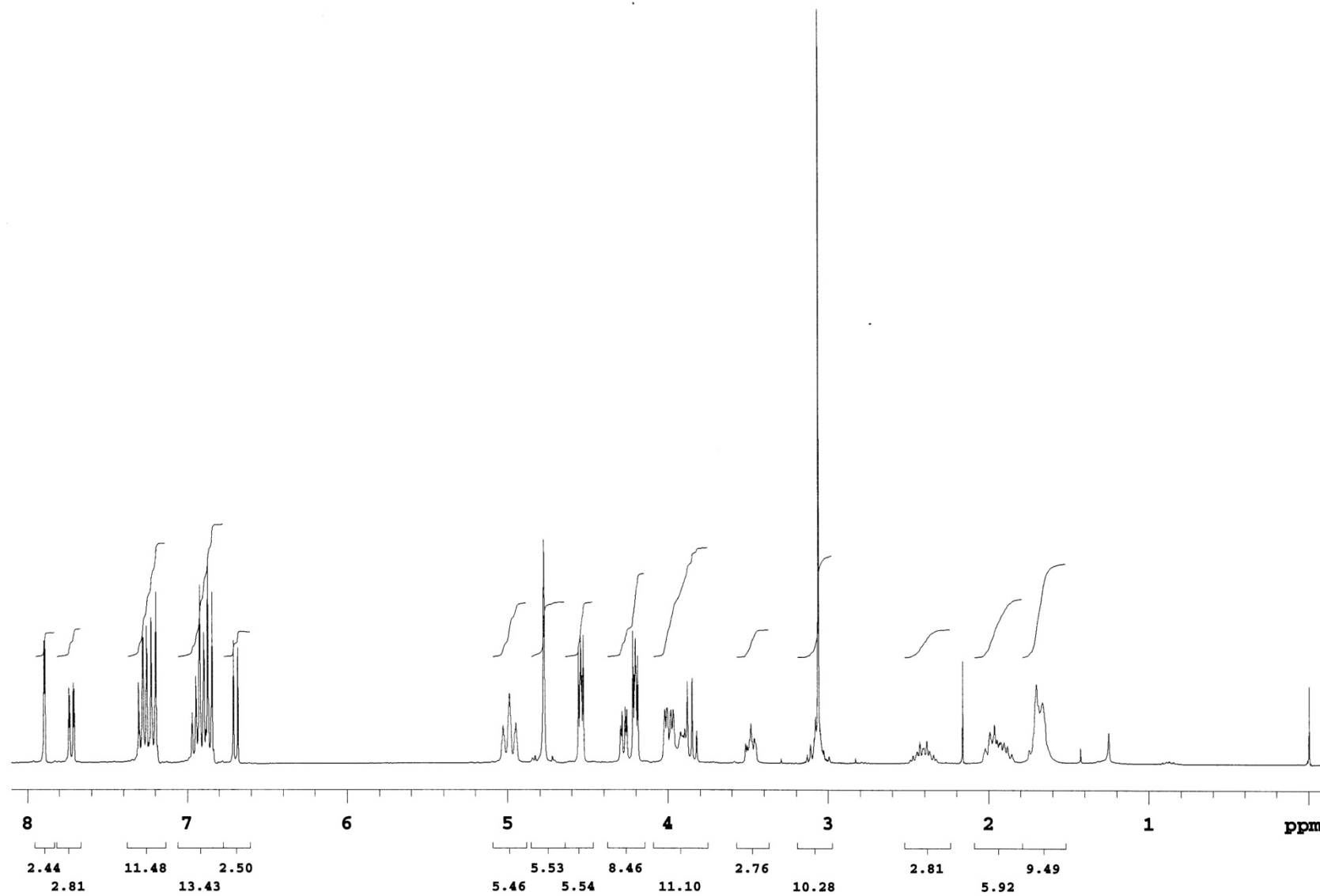
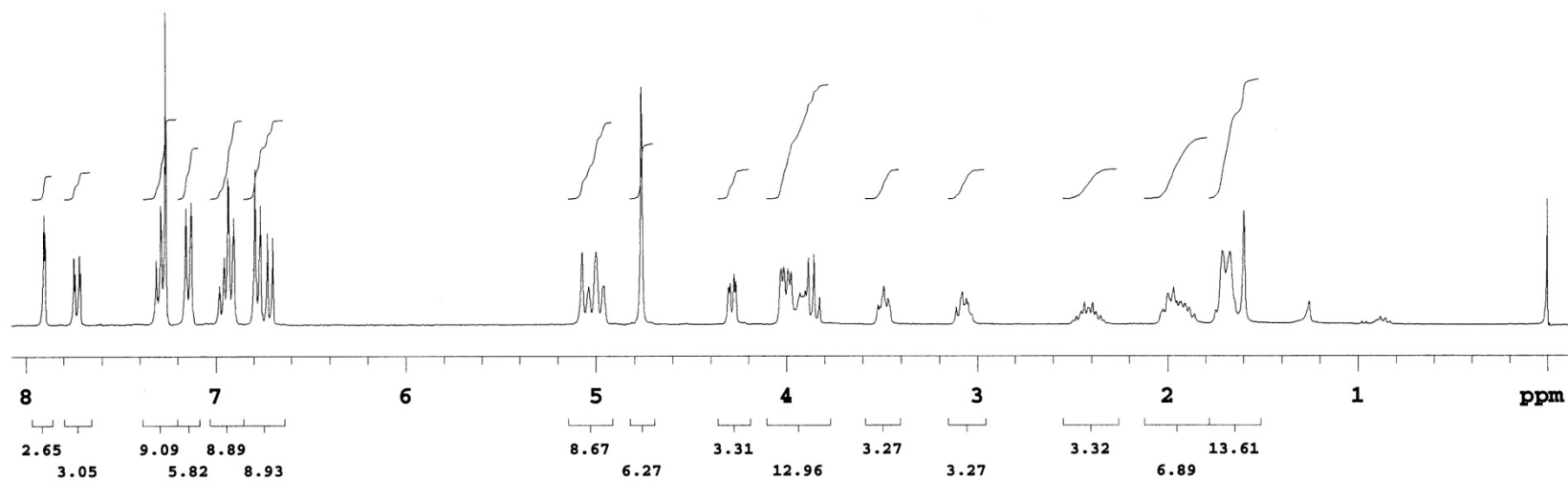


Figure S19. 300 MHz  $^1\text{H}$  NMR spectrum ( $\text{CDCl}_3$ ) of **8**



**Figure S20.** 300 MHz  $^1\text{H}$  NMR spectrum ( $\text{CDCl}_3$ ) of **12**



**Figure S21.** 300 MHz  $^1\text{H}$  NMR spectrum ( $\text{CDCl}_3$ ) of **13**