Supplementary Material (ESI) for Organic & Biomolecular Chemistry

Supplementary Information

[^{18}F]- and [^{11}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 [^{11}C]WC-98

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

[a]*Division of Radiological Sciences, Washington University School of Medicine, 510 South Kingshighway Boulevard, St. Louis, Missouri 63110*

[b]*Department of Chemistry, Washington University, One Brookings Dr., St. Louis, Missouri 63130*

Table of Contents

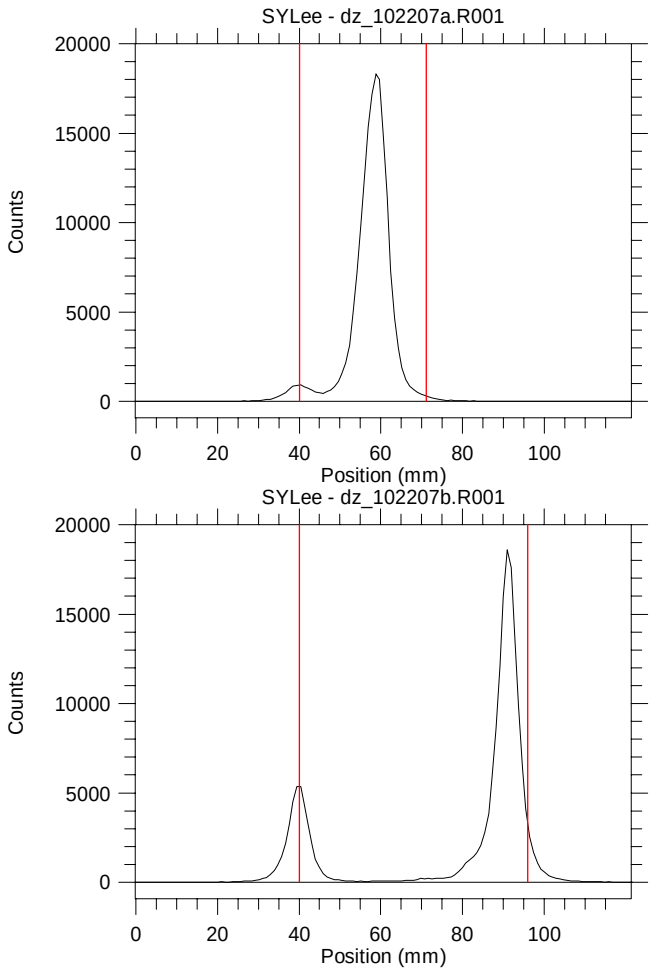

Figure S**1**. RadioTLCs of the reaction mixture of radiosynthesis of [^{18}F] **2**.

Above: Precursor **7a**, [^{18}F]fluoride, K_{222}, K_2CO_3, DMSO, Microwave;

Bottom: 1 N HCl, Microwave.

Silica Gel TLC place; solvent: 20% MeOH, 80% CH_2Cl_2.

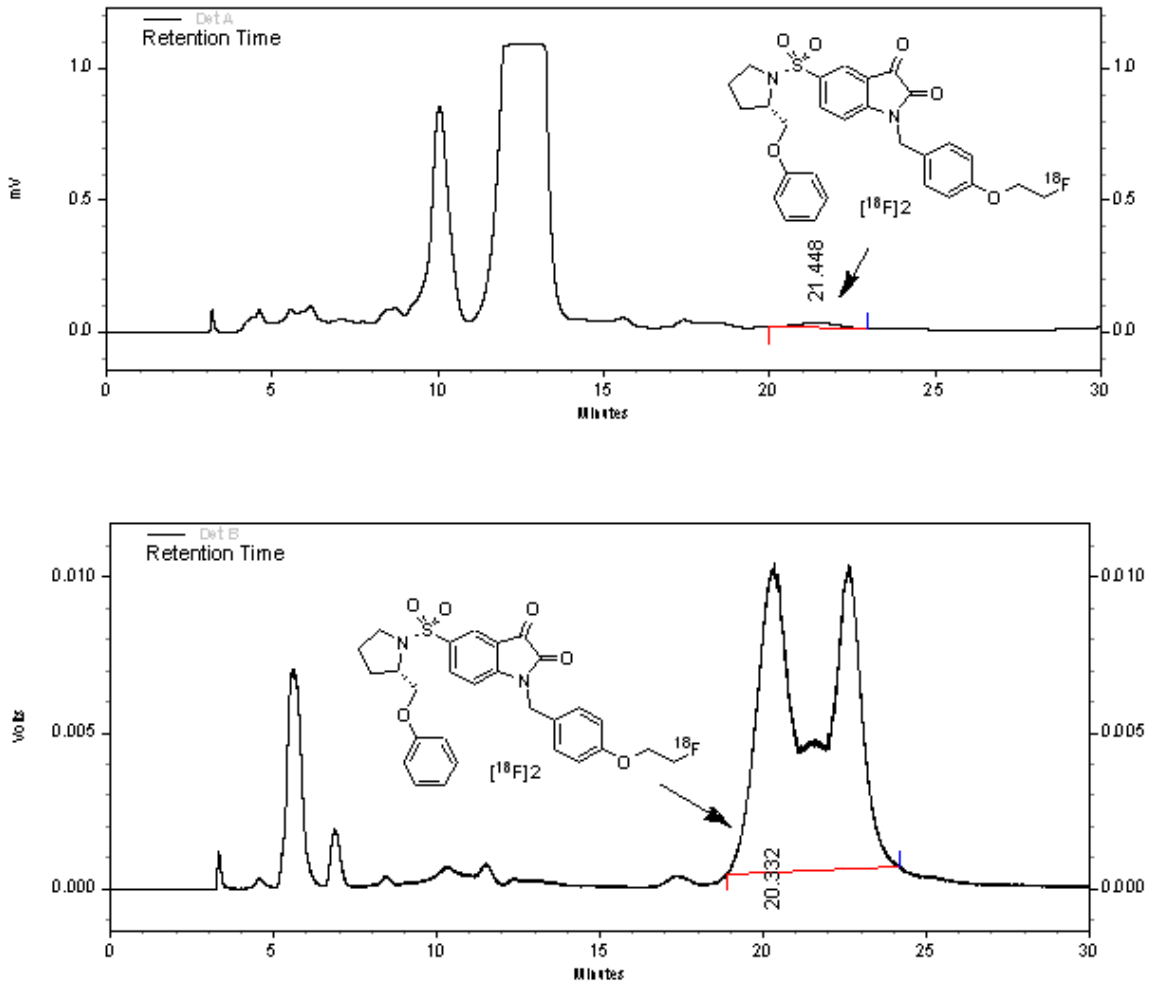

Figure S**2**. Typical HPLC chromatograms for [^{18}F]**2** purification

Above: UV absorbance at 251 nm;

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

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

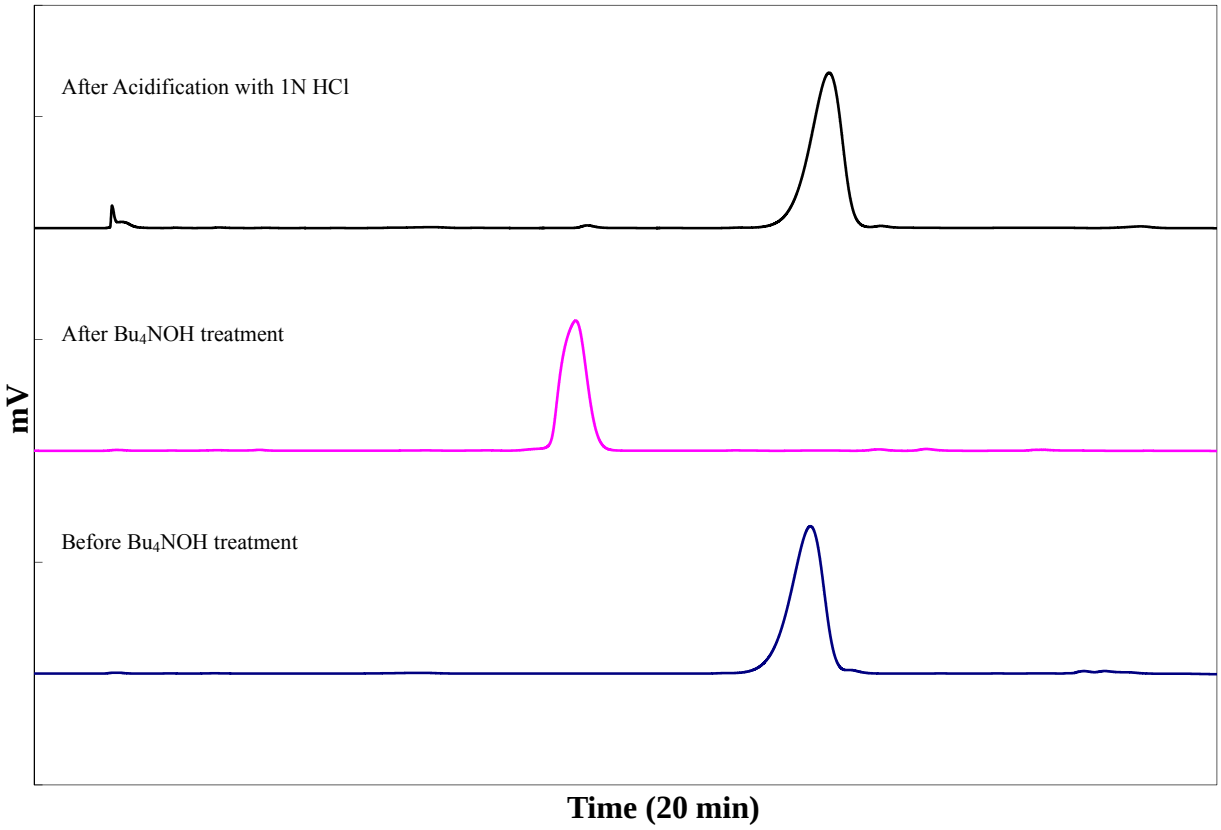

Figure S**3**. HPLC chromatograms of isatin analogue **2** (bottom), isatinate **17** (middle) and isatin **2** recyclized from isatinate **17** (top).

HPLC condition: Alltech Altima C18 250 × 4.6 mm 10μ, 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_4NOH treatment: 20 μL 1000 ppm **2** injected

Bu_4NOH treatment: 0.1 mg **2** in 100 μL acetonitrile treated with 2 μL 1 M Bu_4NOH/H_2O, 20 μL 1000 ppm injected

1 N HCl treatment: 100 μL 1 N HCl, 1 hour at ambient temperature, 40 μL 500 ppm injected.

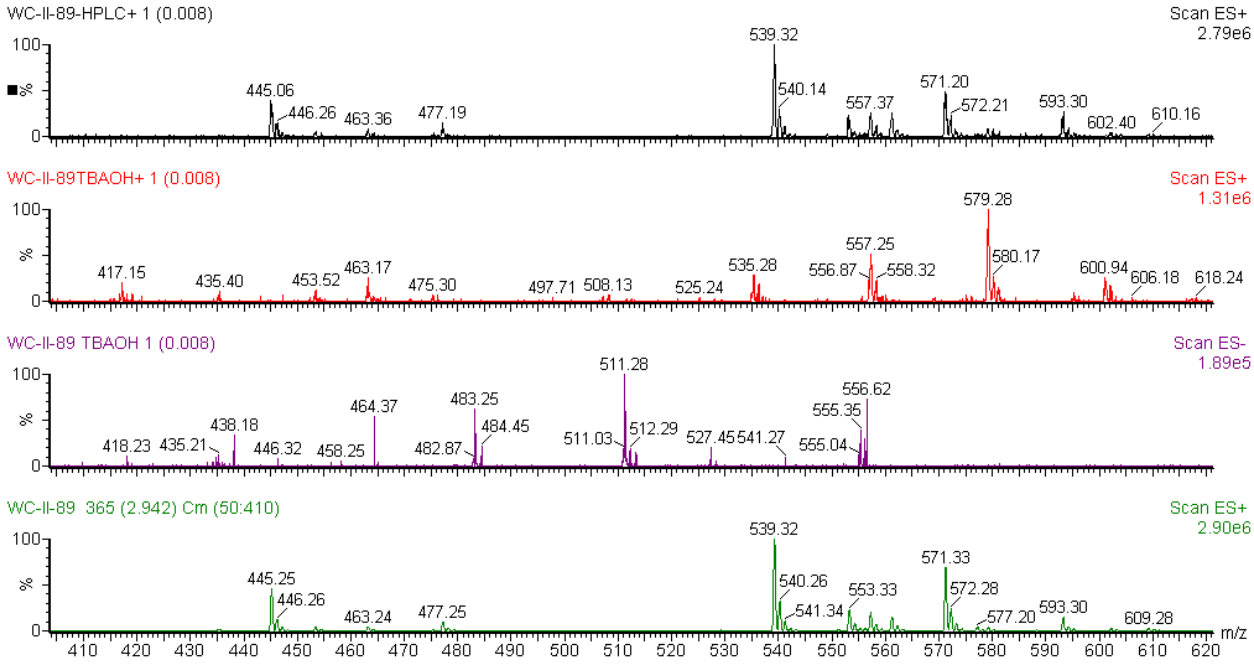

Figure S4. ESI/MS of isatin analogue **2** (bottom), isatinate **17** (middle, negative and positive) and isatin **2** recyclized from isatinate **17** (top).

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

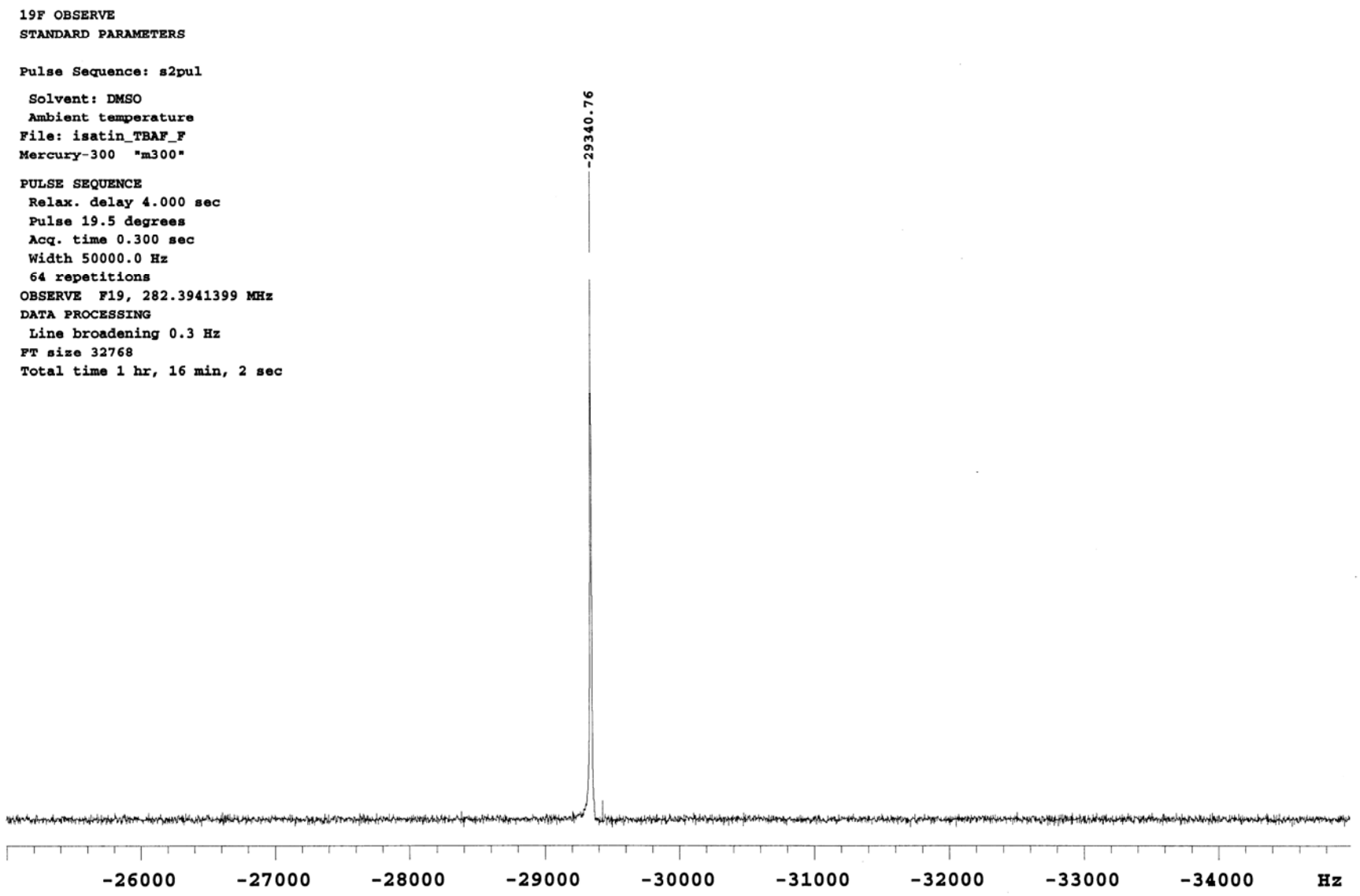

Figure S5. 282 MHz ^{19}F NMR spectrum (DMSO-d6) of Bu_4NF

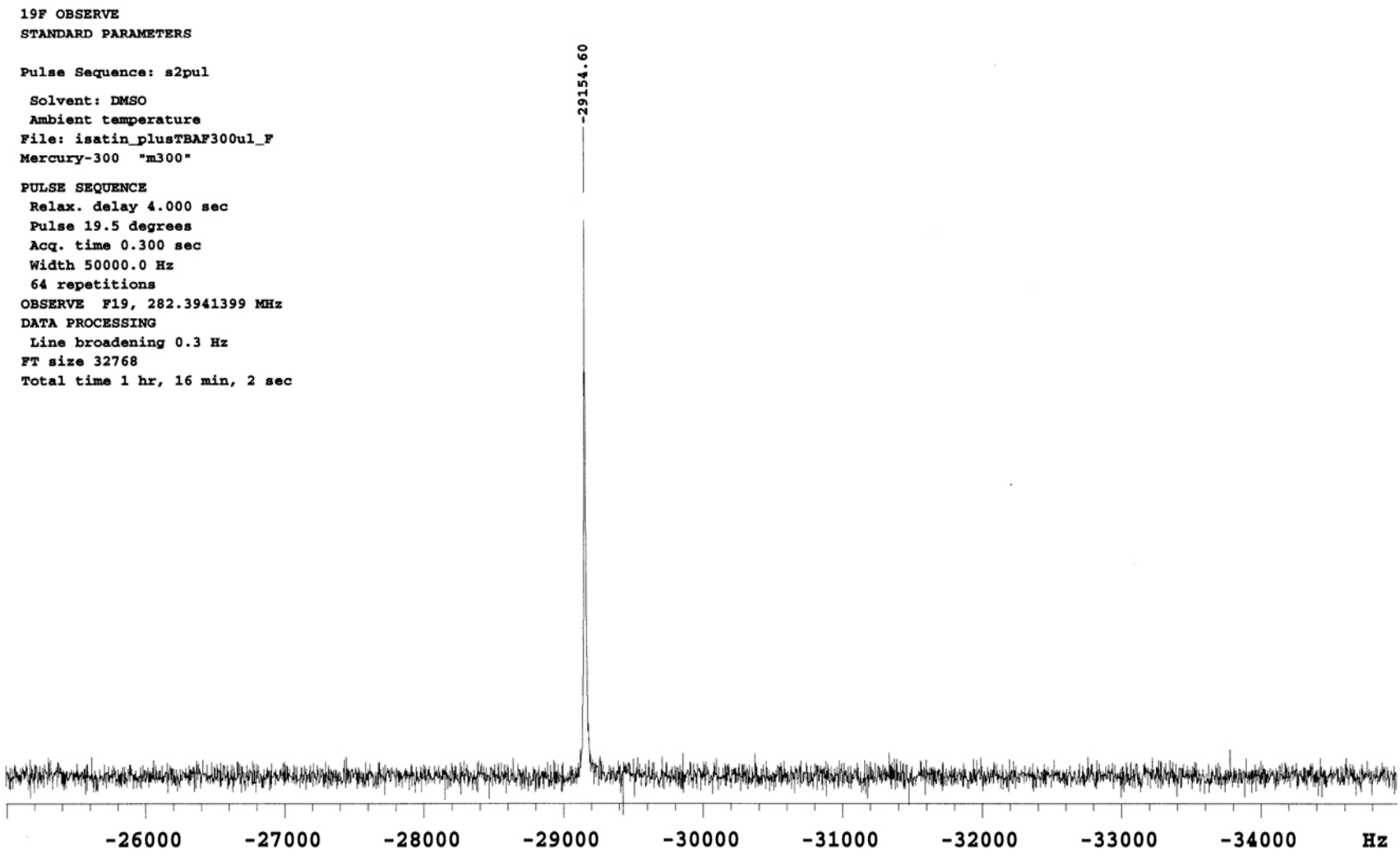

Figure S6. 282 MHz ^{19}F NMR spectrum (DMSO-d6) of Bu_4NF with addition of N-benzyl isatin **21**

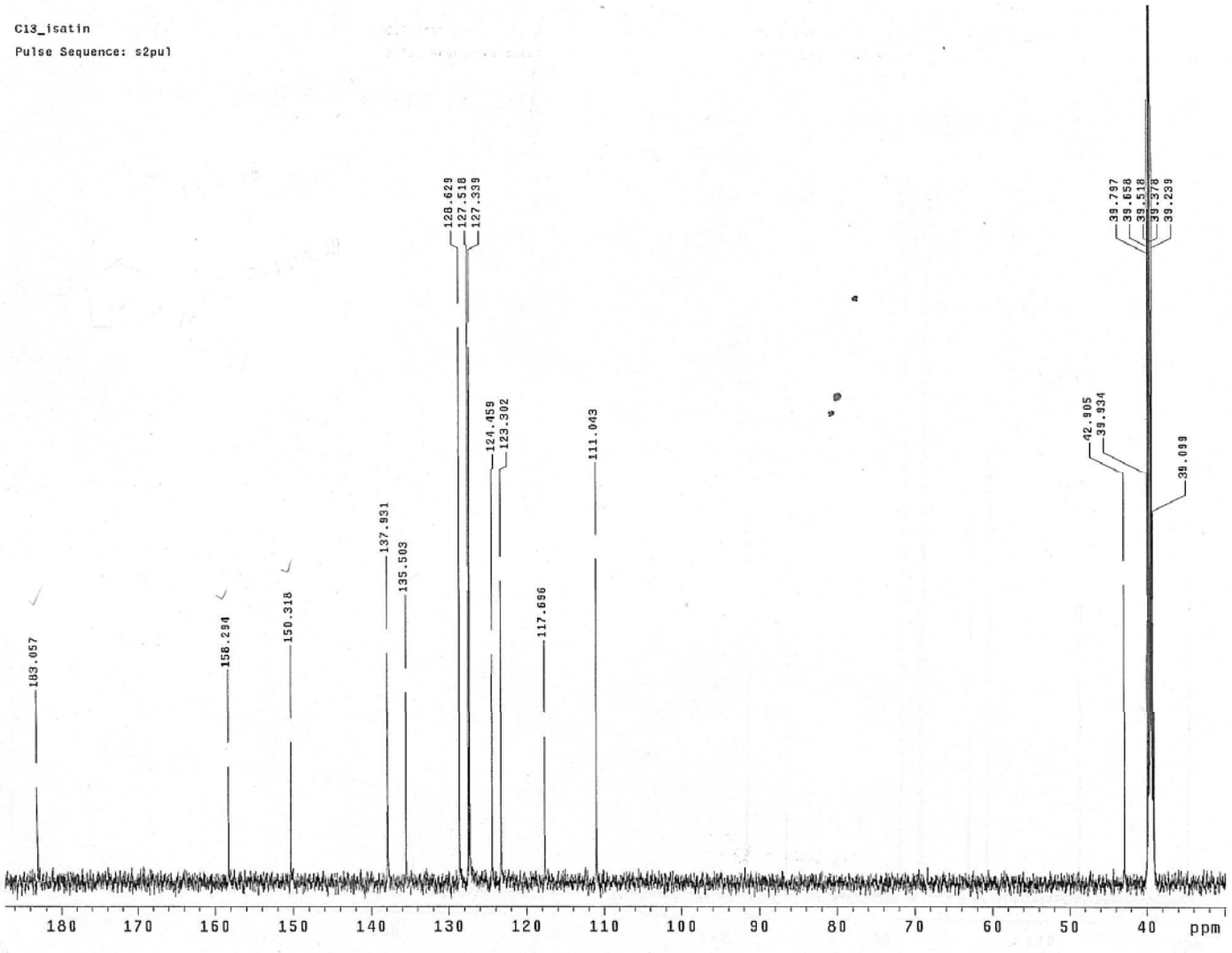

Figure S7. 150 MHz ^{13}C NMR (DMSO-d6) Spectrum of N-benzyl isatin **21**.

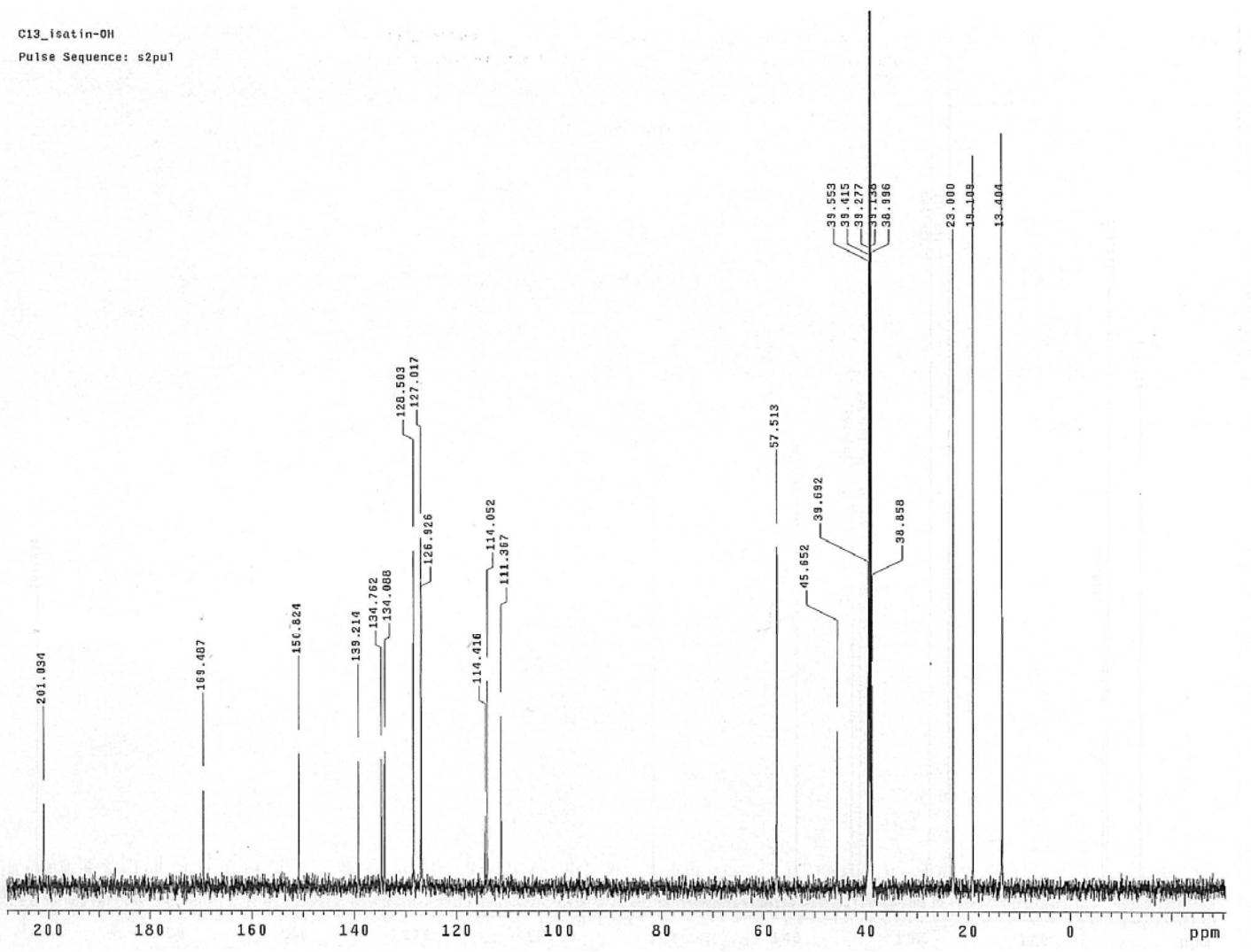

Figure S8. 150 MHz ^{13}C NMR Spectrum (DMSO-d6) of N-benzyl isatin **21** treated with 1M Bu_4NOH/H_2O (10 mg **21** in 0.6 mL DMSO-d6)

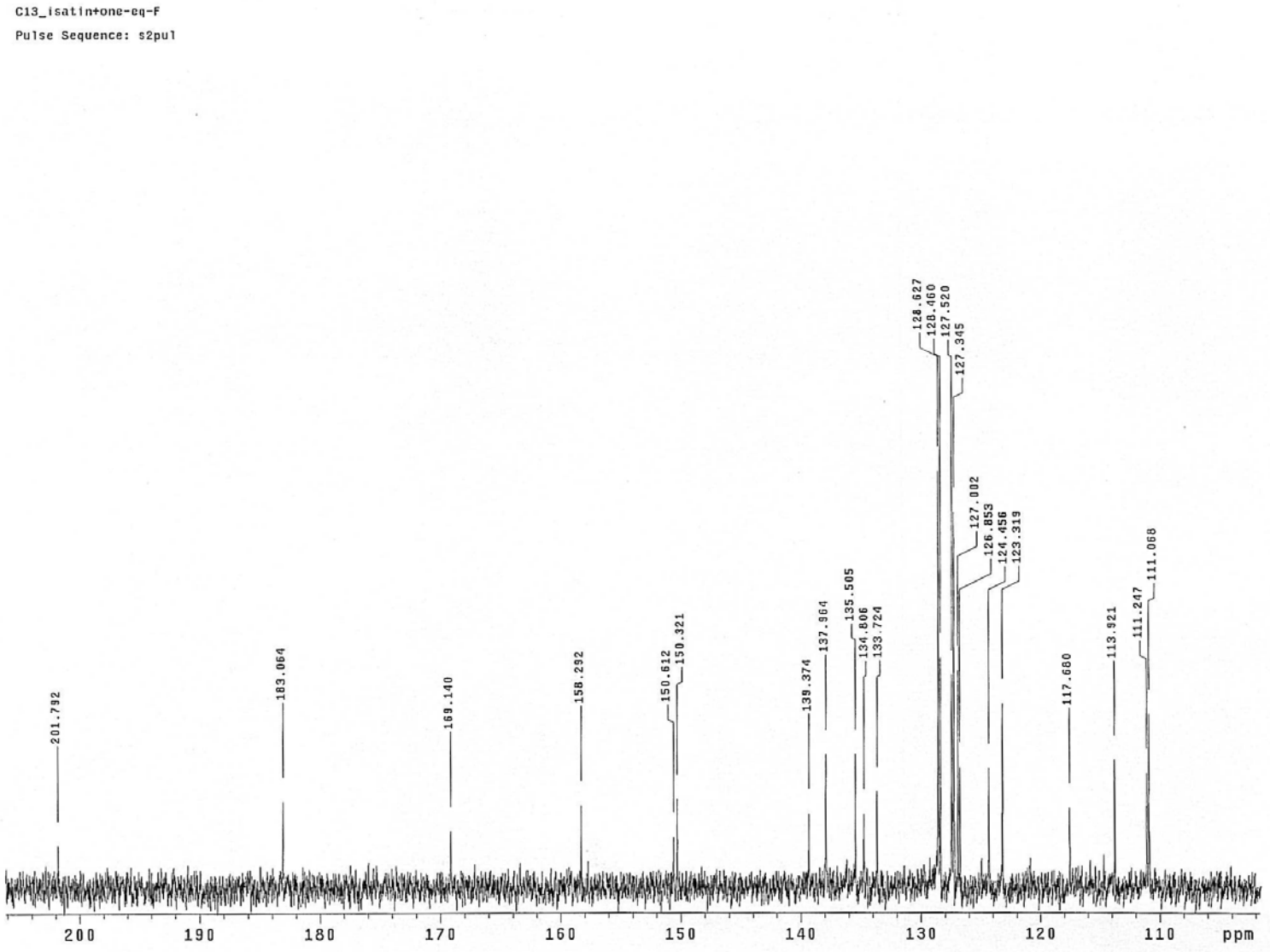

Figure S9. 150 MHz ^{13}C NMR Spectrum (DMSO-d6) of N-benzyl isatin **21** treated with 1 equivalent Bu_4NF/H_2O (10 mg **21** in 0.6 mL DMSO-d6)

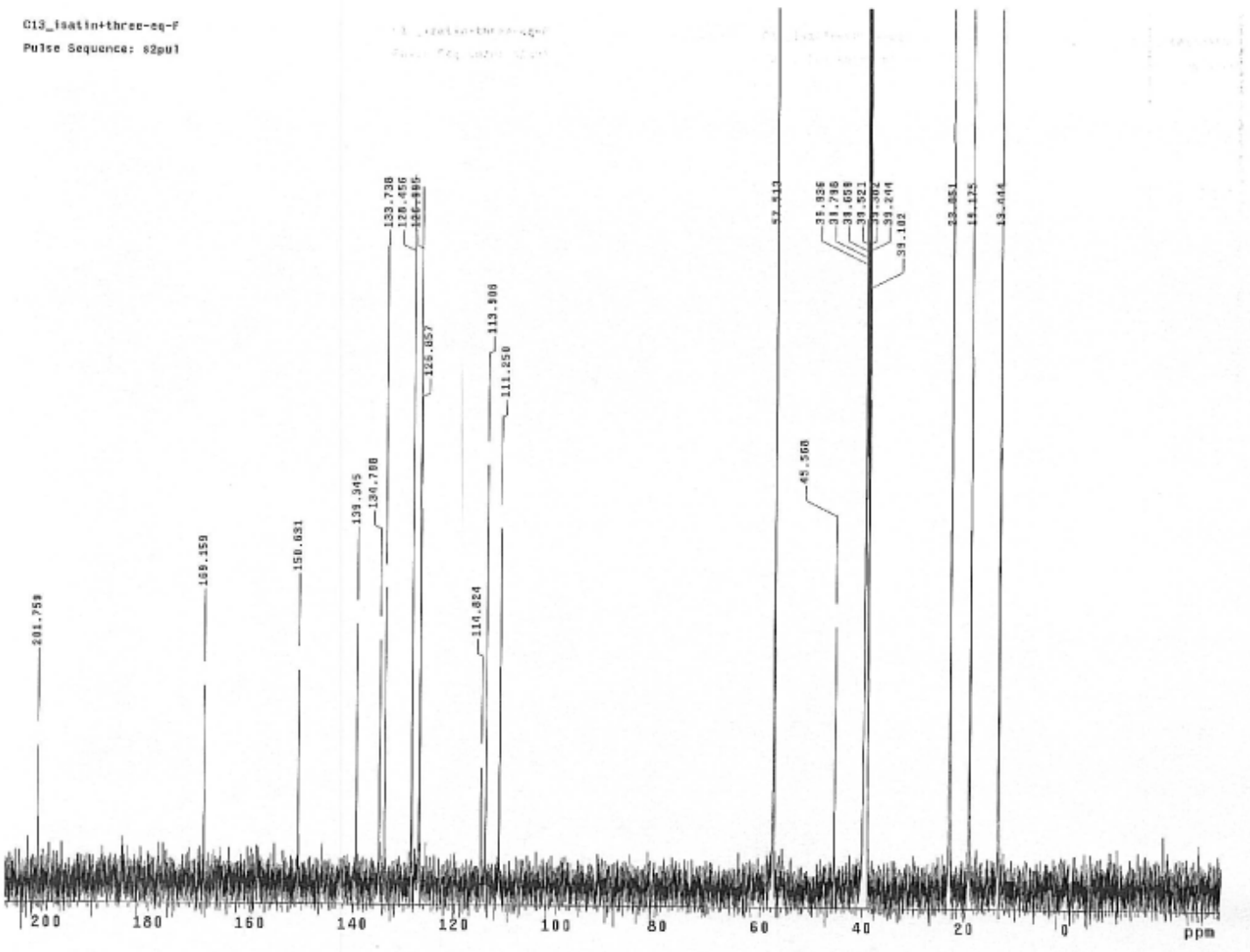

Figure S10. 150 MHz ^{13}C NMR Spectrum (DMSO-d6) of N-benzyl isatin **21** treated with 3 equivalents Bu_4NF/H_2O (10 mg **21** in 0.6 mL DMSO-d6)

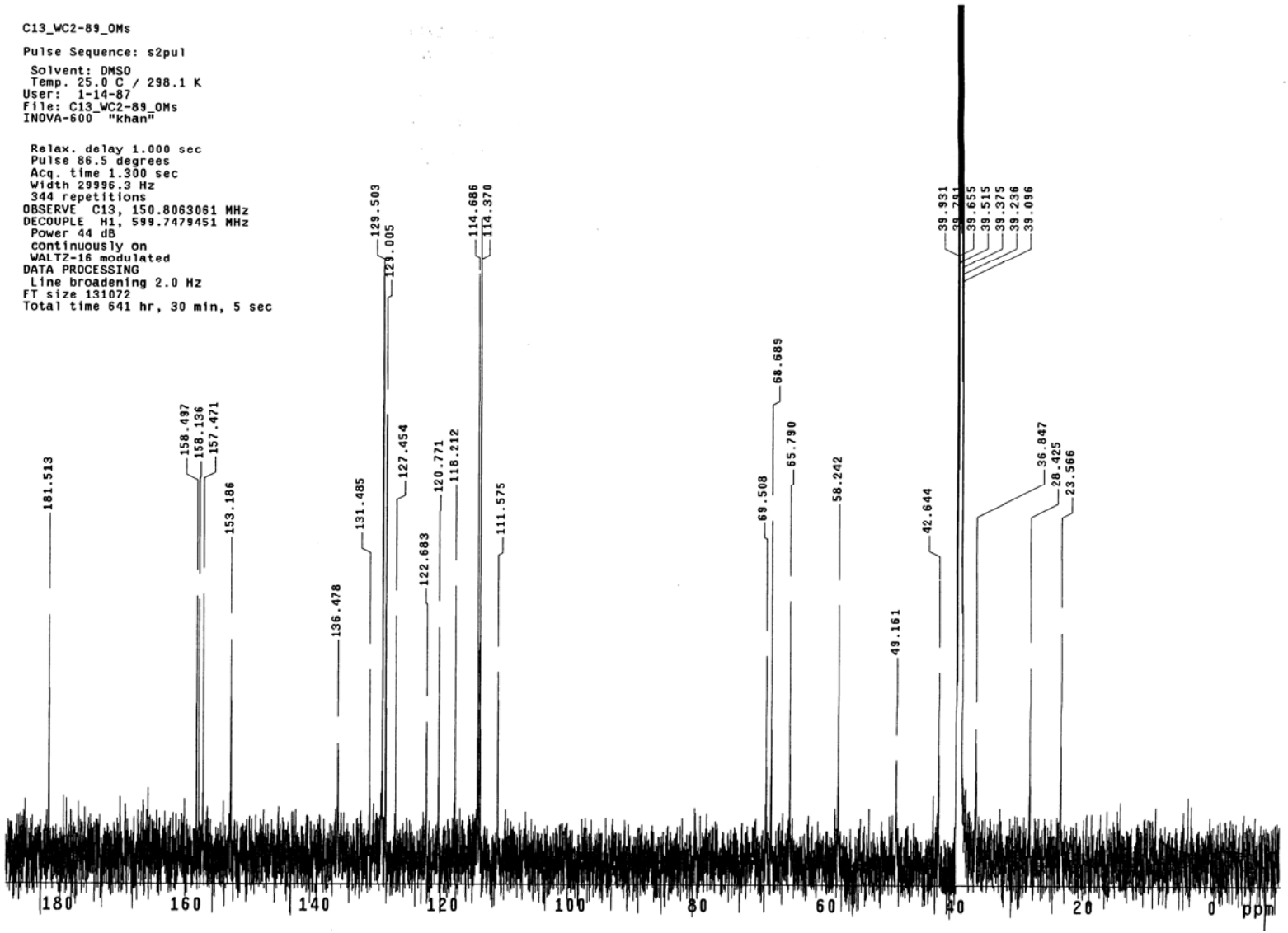

Figure S11. 150 MHz ^{13}C NMR spectrum (DMSO-d6) of **7a (**10 mg **7a** in 0.6 mL DMSO-d6)

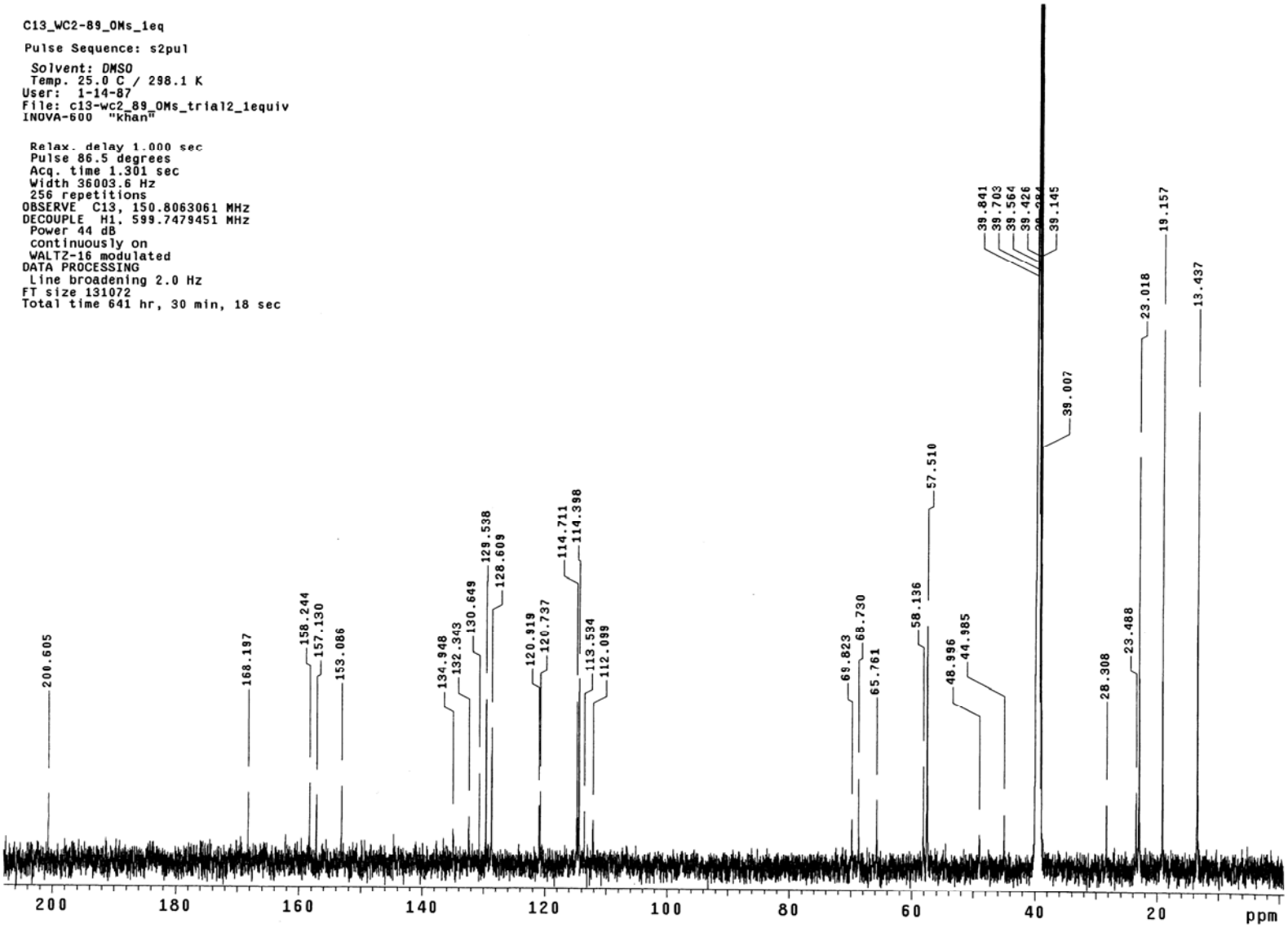

Figure S12. 150 MHz ^{13}C NMR spectrum (DMSO-d6) of ring-opened **7a** (10 mg **7a** in 0.6 mL DMSO-d6 treated with 20 µL 1M Bu_4NOH/H_2O)

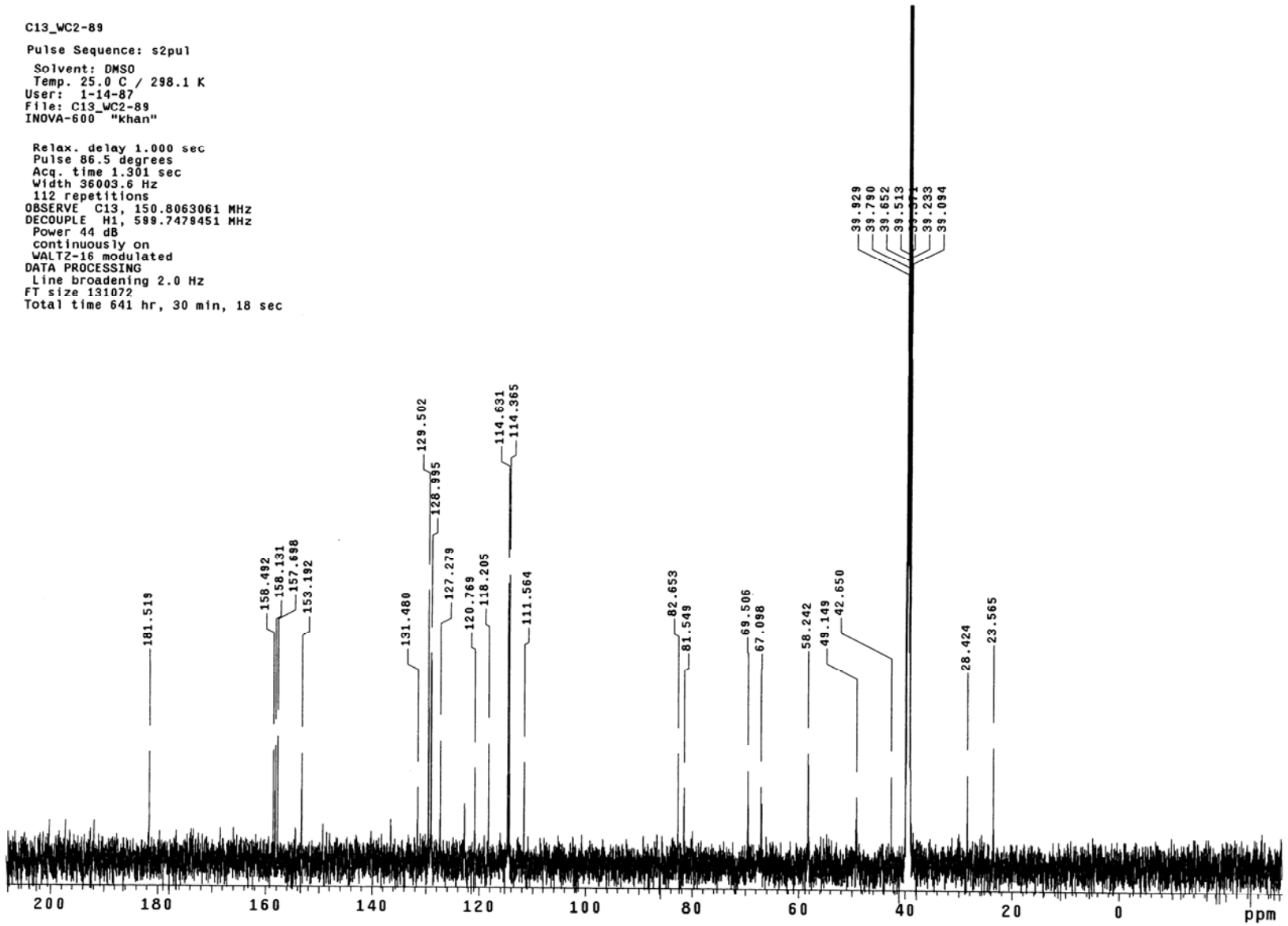

Figure S13. 150 MHz ^{13}C NMR spectrum (DMSO-d6) of **2 (**10 mg **2** in 0.6 mL DMSO-d6)

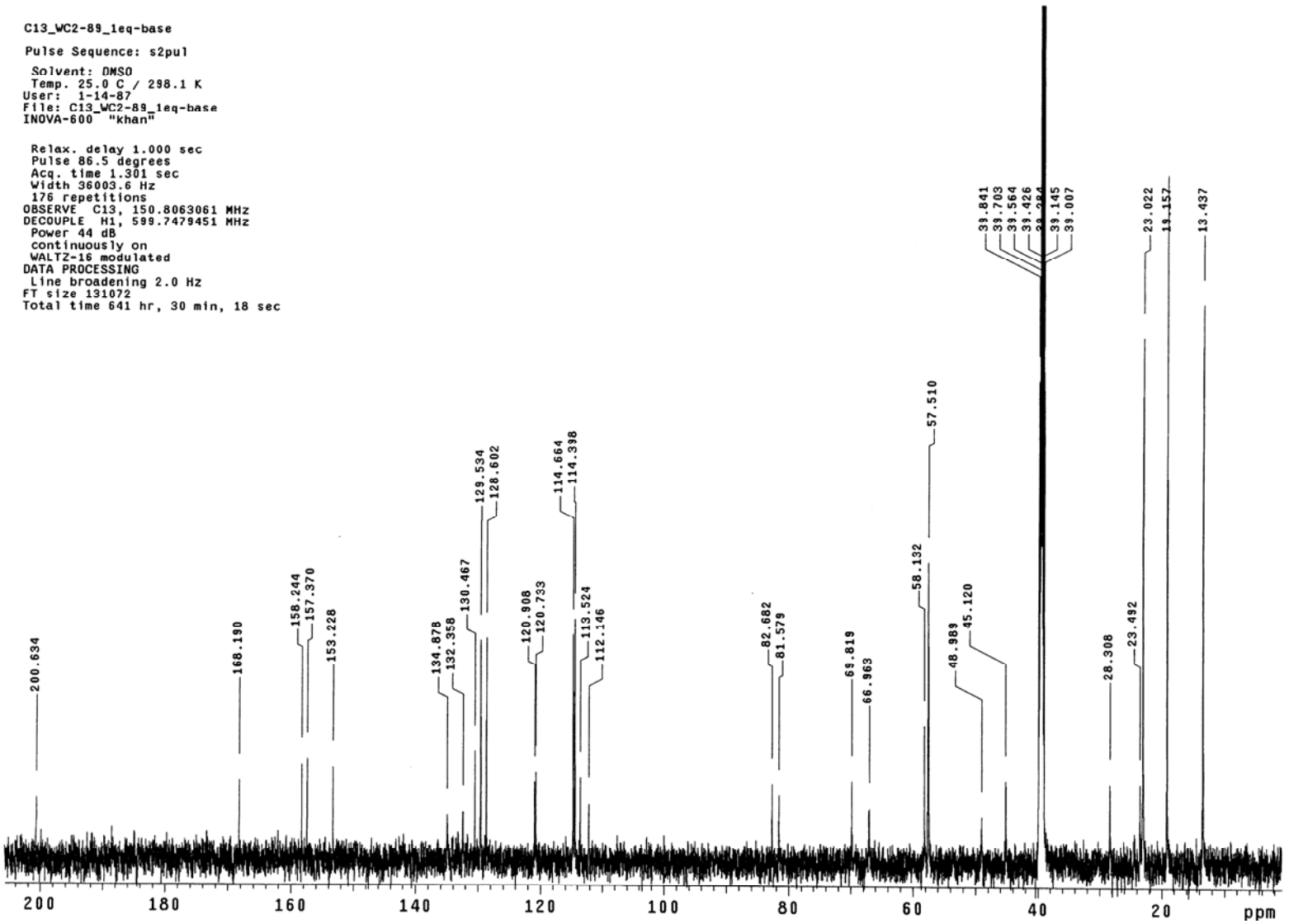

Figure S14. 150 MHz ^{13}C NMR spectrum (DMSO-d6) of ring-opened **2**(10 mg **2** in 0.6 mL DMSO-d6 treated with 20 µL 1M Bu_4NOH/H_2O)

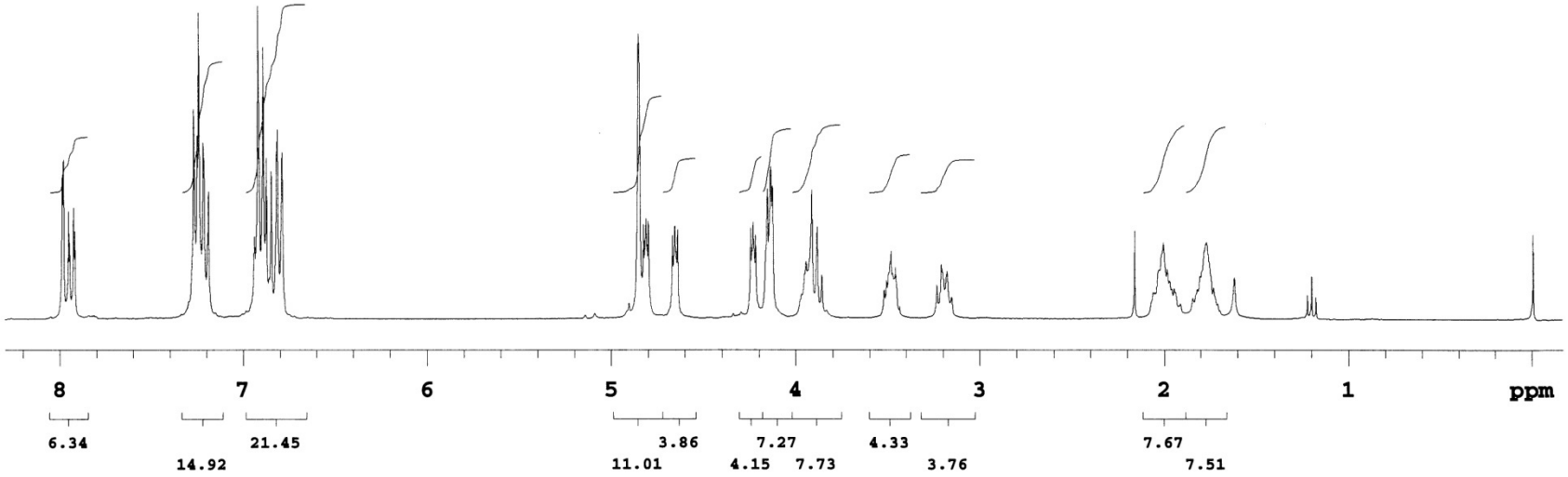

Figure S15. 300 MHz ^{1}H NMR spectrum ($CDCl_3$) of **2**

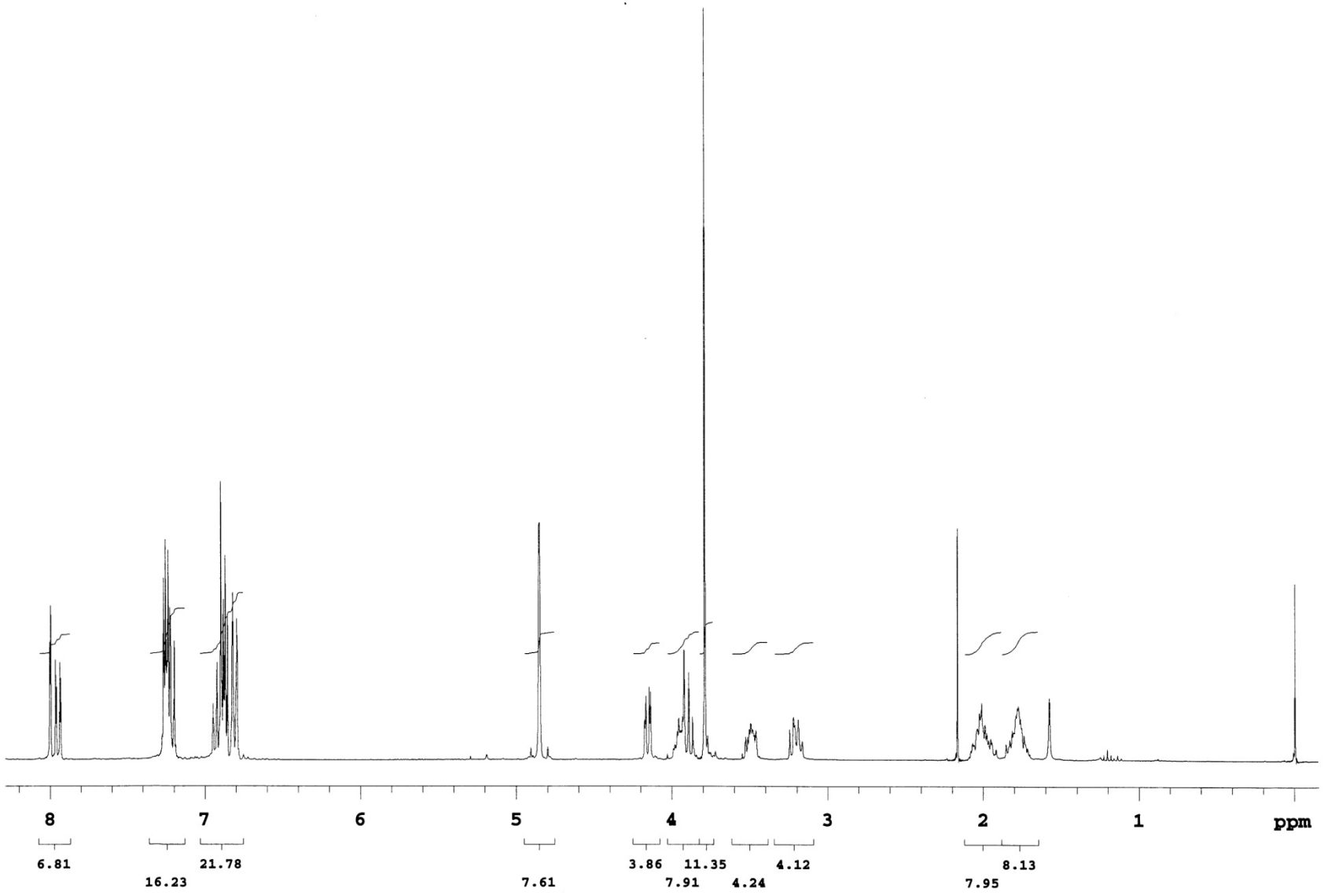

Figure S16. 300 MHz ^{1}H NMR spectrum ($CDCl_3$) of **4**

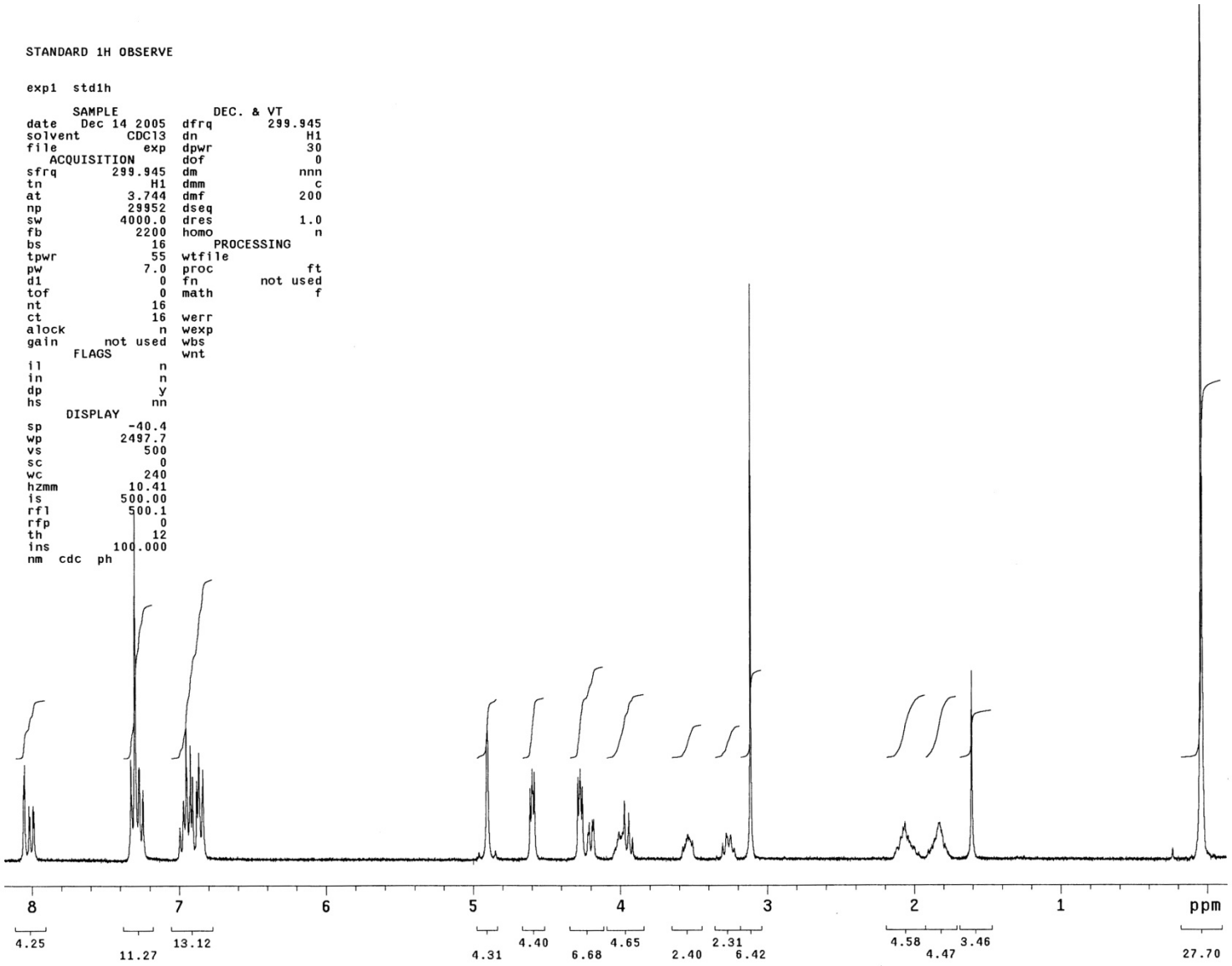

Figure S17. 300 MHz ^{1}H NMR spectrum ($CDCl_3$) of **7a**

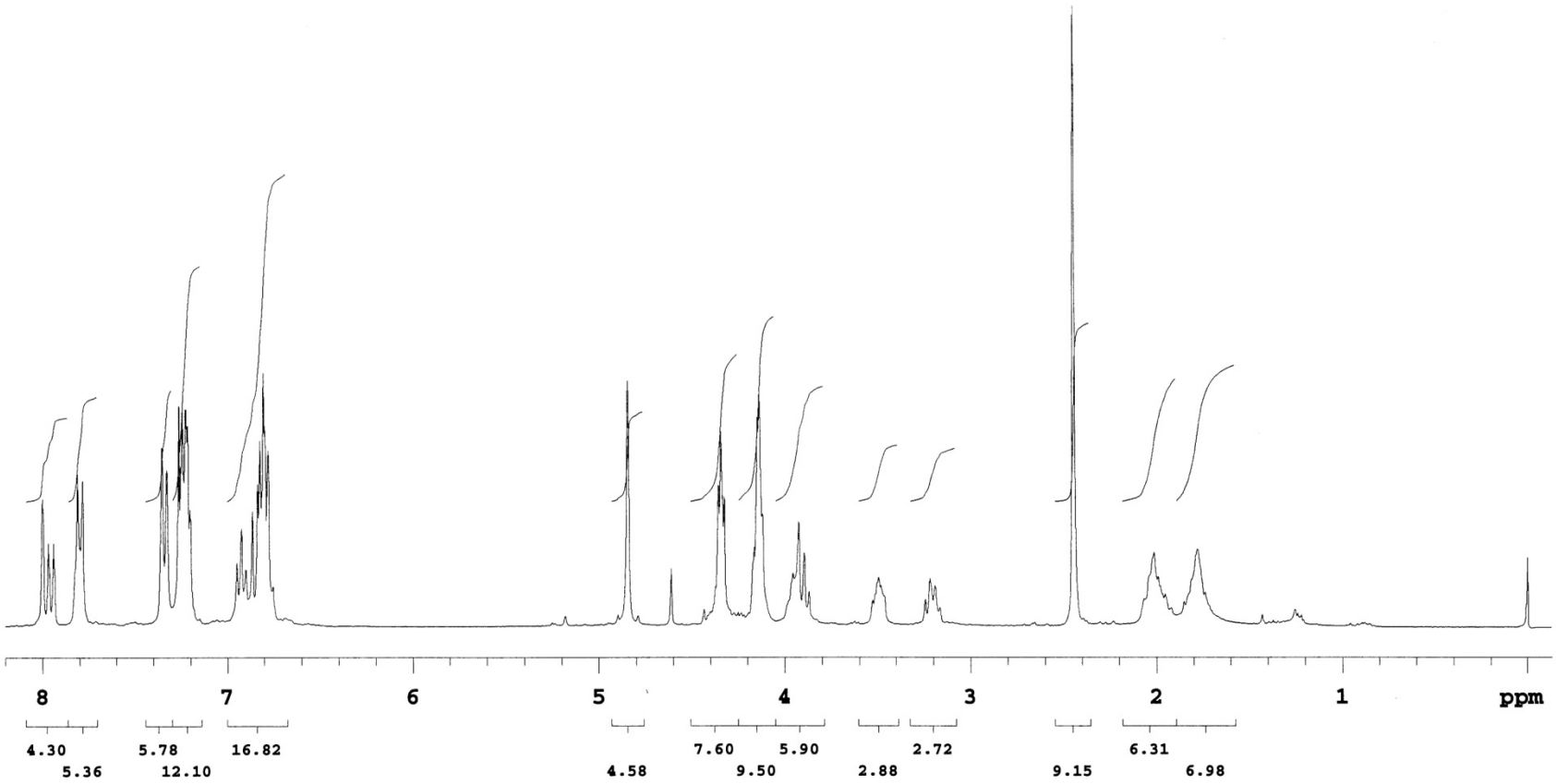

Figure S18. 300 MHz ^{1}H NMR spectrum ($CDCl_3$) of **7b**

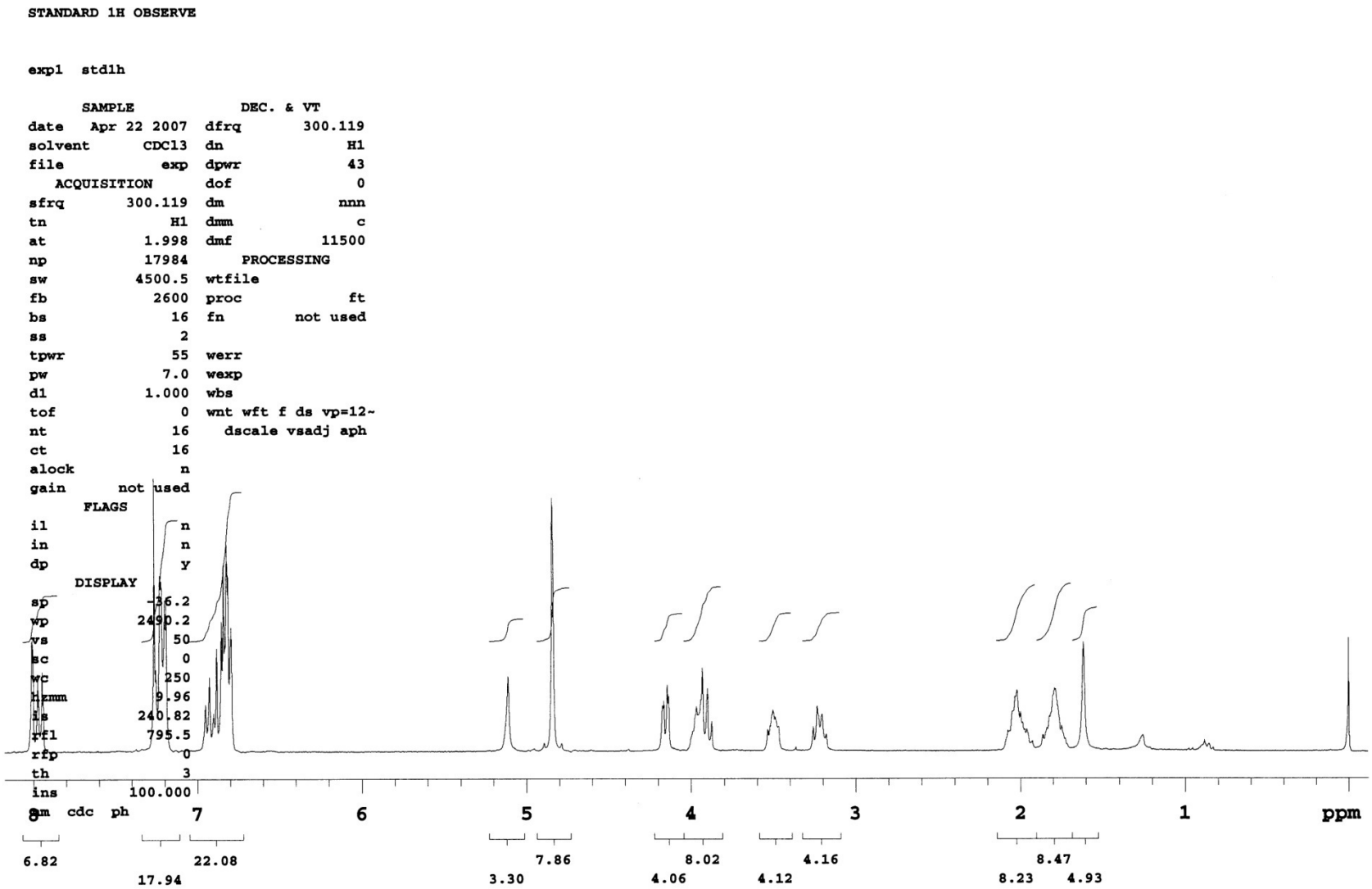

Figure S19. 300 MHz ^{1}H NMR spectrum ($CDCl_3$) of **8**

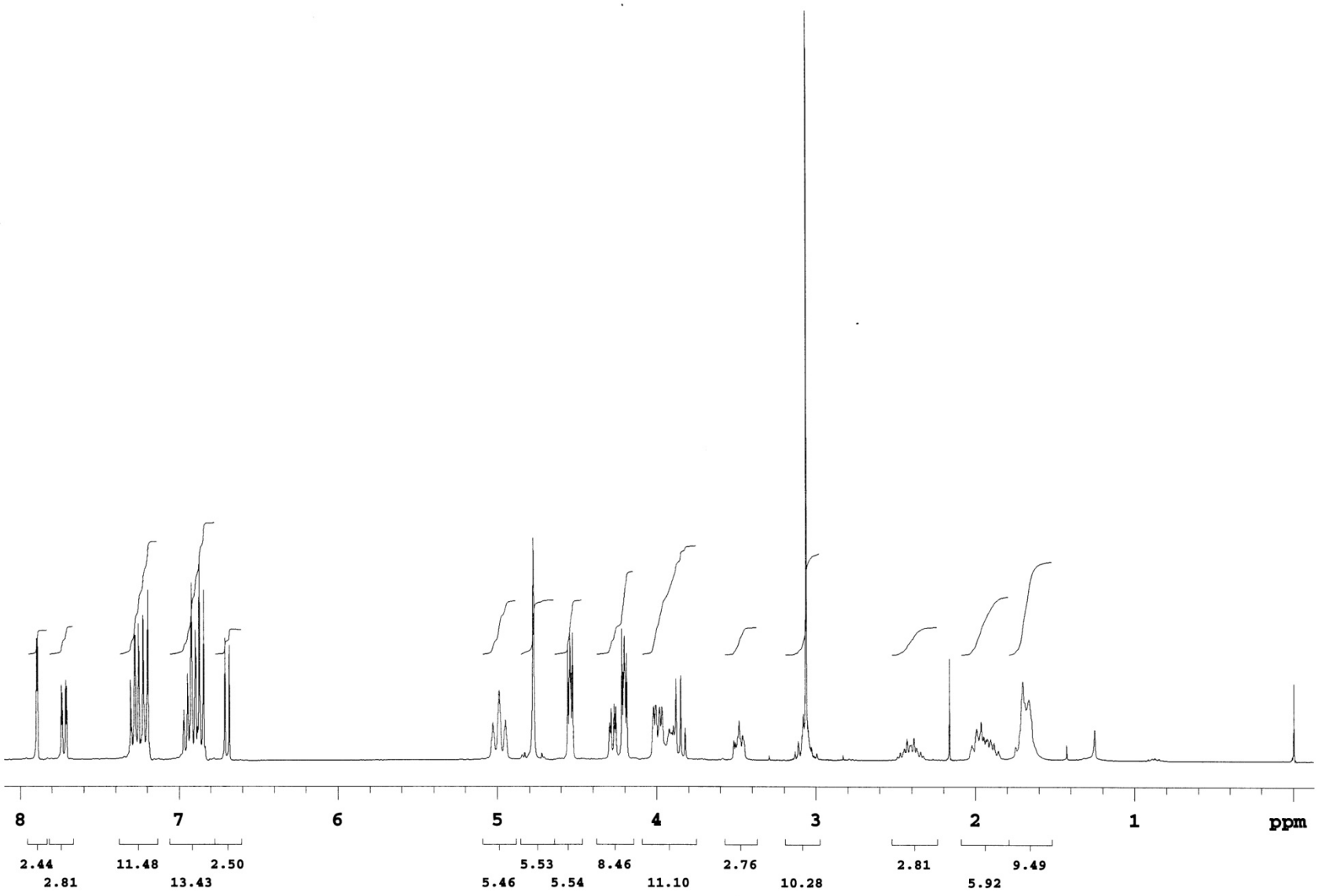

Figure S20. 300 MHz ^{1}H NMR spectrum ($CDCl_3$) of **12**

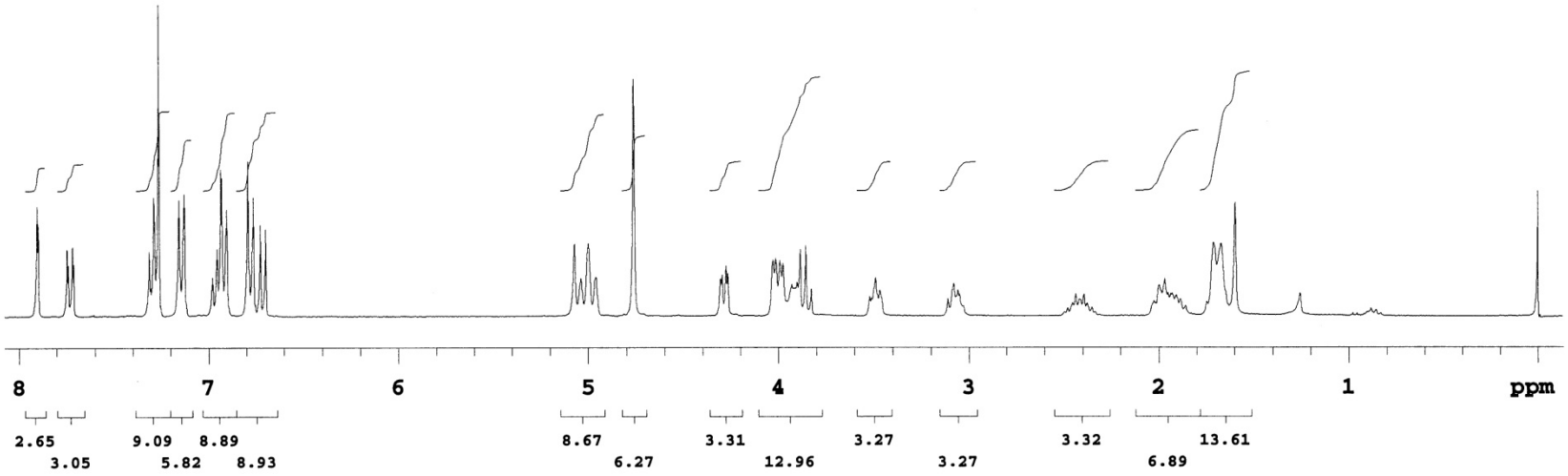

Figure S21. 300 MHz ^{1}H NMR spectrum ($CDCl_3$) of **13**