

Decarboxylative Cross-Electrophile Coupling of *N*-Hydroxyphthalimide Esters
with Aryl Iodides

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I. General Information

Reagents.

Metals.

Zinc flake (-325 mesh, Alfa Aesar) and nickel(II) bromide 2-methoxyethyl ether (NiBr₂(diglyme), Aldrich) were used as received and stored in a nitrogen filled glovebox. The amount of diglyme present in the NiBr₂(diglyme) was determined by elemental analysis and the amount of NiBr₂(diglyme) was calculated accordingly. (dtbbpy)NiBr₂ was synthesized from NiBr₂•3H₂O and dtbbpy in ethanol in analogy to a published procedure.¹ Ni(cod)₂ (Stem Chemicals) was used soon after receiving as this material decomposes over time. Although we had previously experienced success with material from Aldrich, recent (Jan 2016) lots from Aldrich were of poor quality.

Ligands.

4-4'-di-*tert*-butyl-2,2'-bipyridine (Aldrich) was used as received. Other ligands tested were from commercial suppliers and used as received.

Solvents.

Anhydrous *N,N*-dimethylacetamide (DMA), *N,N*-dimethylformamide (DMF), pentane, and THF were obtained by passage through activated alumina and molecular sieves in a solvent purification system and were stored over 4 Å molecular sieves in a nitrogen filled glovebox. Solvents used for organometallic work were further degassed by 3-6 freeze-pump-thaw cycles. DMF-*d*₇ and acetone-*d*₆ (Cambridge Isotope Laboratories, Inc.) were degassed before use and stored in an argon glovebox.

Other Reagents.

Dodecane (Aldrich), *N*-(*tert*-butoxycarbonyl)proline (Alfa Aesar), *N,N'*-dicyclohexylcarbodiimide (Alfa Aesar), *N,N'*-diisopropylcarbodiimide (Chem-Impex), *N*-hydroxyphthalimide (Alfa Aesar), DMAP (Alfa Aesar), 4-phenylbutyric acid (Aldrich), 3,3-dimethylbutyric acid (Alfa Aesar), cyclopentane carboxylic acid (Combi-Blocks), Boc-Asp-OtBu (Combi-Blocks), Boc-Glu-OtBu (Combi-Blocks), *N*-Boc-Pro-OH (Alfa Aesar), 4-acetylbutyric acid (Combi-Blocks), cholic acid (Sigma Aldrich), and piperidine-3-carboxylic acid (Combi-Blocks) were used as received.

¹ Durandetti, M.; Devaud, M.; Périchon, J. *New J. Chem.* **1996**, *20*, 659-667.

Substrates.

1-(5-iodo-1H-indol-1-yl)ethanone² and 4-iodophenylboronic acid pinacol ester³ were prepared according to literature procedures. Iodobenzene (Alfa Aesar), 2-iodotoluene (Aldrich), 4-iodoacetophenone (Alfa Aesar), ethyl-3-iodobenzoate (Combi-Blocks), and ethyl succinyl chloride (TCI America) were used as received.

Methods.

NMR Spectroscopy.

¹H and ¹³C NMR spectra were acquired on 400 and 500 MHz Bruker NMR instruments. NMR chemical shifts are reported in ppm and are referenced to TMS ($\delta = 0.00$ ppm, ¹H NMR) or the residual solvent peak for CDCl₃ ($\delta = 7.26$ ppm, ¹H NMR; $\delta = 77.16$ ppm, ¹³C NMR). Coupling constants (*J*) are reported in Hertz. For substrates that existed as rotamers at ambient temperature, the ¹H NMR spectrum was obtained at 55 °C.

Gas Chromatography.

GC analyses were performed on an Agilent 7890A GC equipped with dual DB-5 columns (20 m x 180 μ m x 0.18 μ m), dual FID detectors, and hydrogen as the carrier gas. A sample volume of 1 μ L was injected at a temperature of 300 °C and a 100:1 split ratio. The initial inlet pressure was 20.3 psi but varied as the column flow was held constant at 1.8 mL/min for the duration of the run. The initial oven temperature of 50 °C was held for 0.46 min followed by a temperature ramp of 65 °C/min up to 300 °C. The temperature was held at 300 °C for 3 min. The total run time was ~7.3 min and the FID temperature was 325 °C.

GC/MS Analysis

GC/MS analyses were performed on a Shimadzu GCMS-QP2010 equipped with an RTX-XLB column (30 m x 0.25 mm x 0.28 μ m) with a quadrupole mass analyzer using helium as the carrier gas. The analysis method used in all cases was 5 μ L injection of sample, an injection temp of 225 °C, and a 25:1 split ratio. The initial inlet pressure was 7.8 psi, but varied as the column flow was held constant at 1.0 mL/min for the duration of the run. The interface temperature was held at 250 °C, and the ion source (EI+, 30 eV) was held at 250 °C. The initial

² Lai, A.; Kahraman, M.; Govek, S.; Nagasawa, J.; Bonnefous, C.; Julien, J.; Douglas, K.; Sensintaffar, J.; Lu, N.; Lee, K.-J.; Aparicio, A.; Kaufman, J.; Qian, J.; Shao, G.; Prudente, R.; Moon, M. J.; Joseph, J. D.; Darimont, B.; Brigham, D.; Grillot, K.; Heyman, R.; Rix, P. J.; Hager, J. H.; Smith, N. D. *J. Med. Chem.* **2015**, *58*, 4888–4904.

³ Matteson, D. S.; Man, H.-W. *J. Org. Chem.* **1994**, *59*, 5734–5741.

oven temperature was held at 50 °C for 2 min with the detector off, followed by a temperature ramp, with the detector on, to 280 °C at 40 °C/min. The temperature was held at 280 °C for 3 min. Total run time was 11.75 min.

Supercritical Fluid Chromatography (SFC) Analysis

SFC analysis was performed on a Jasco Analytical and Semi-Preparative SFC instrument equipped with a column oven (35 °C), photodiode array detector, a back pressure regulator (12.0 MPa), and a carbon dioxide pump. Chiralpak IA and IC columns were used for separation of enantiomers. All analyses were performed on isolated samples. For each analysis, ~1-2 mg of material was used and diluted with 1 mL of diethyl ether. Racemic samples were used for method determination and were prepared by combining equal amounts of enantiopure materials.

Low Resolution Mass Spectrometry (LRMS) Analysis

LRMS analyses were performed on a Thermo LTQ Velos LC/MS equipped with an electrospray (ESI) probe operating in positive ion mode (ESI+) with an ion trap mass analyzer. Direct injection analysis was employed in all cases with a sample solution in methanol.

Elemental Analysis.

Elemental analyses were performed by CENTC Elemental Analysis Facility at University of Rochester, funded by NSF CHE-0650456.

Infrared Spectroscopy.

Infrared (IR) spectra were recorded on a Shimadzu IRAffinity-1 Fourier Transform Infrared Spectrophotometer and are reported in wavenumbers (cm^{-1}).

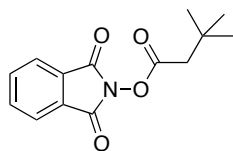
UV-Vis spectroscopy.

UV-Vis spectra (300-900 nm) were recorded on a HP 8452A spectrometer using quartz, screw-cap cuvettes to exclude oxygen. The samples were prepared in a glove box under Ar.

Chromatography.

Chromatography was performed on silica gel (EMD, silica gel 60, particle size 0.040-0.063 mm) using standard flash techniques or on a Teledyne Isco Rf-200 (detection at 210 nm). Products were visualized by UV, iodine stain, ceric ammonium molybdate stain, or KMnO_4 stain.

II. Synthesis of *N*-Hydroxyphthalimide esters (NHP esters)



1,3-dioxoisindolin-2-yl 3,3-dimethylbutanoate (1a).

A round bottom flask containing a teflon-coated magnetic stir bar was charged with tert-butylacetic acid (5.50 mL, 43.0 mmol, 1.00 equiv) and dry EtOAc (420 mL). After sequential addition of *N,N'*-dicyclohexylcarbodiimide (10.5 g, 64.5 mmol, 1.50 equiv), DMAP (263 mg, 2.15 mmol, 0.0500 equiv), and *N*-hydroxyphthalimide (4.33g, 26.6 mmol, 1.66 equiv), the reaction mixture was allowed to stir overnight at room temperature. After this time, the heterogeneous mixture was filtered and the filtrate was concentrated under reduced pressure. Recrystallization from acetone yielded product (10.0 g, 38.4 mmol, 89%) as a colorless solid.

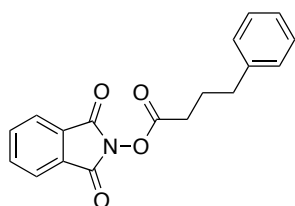
$^1\text{H NMR}$ (400 MHz; CDCl_3): δ 7.89 (dd, $J = 5.4, 3.0$ Hz, 2H), 7.79 (dd, $J = 5.5, 3.0$ Hz, 2H), 2.53 (s, 2H), 1.17 (s, 9H).

$^{13}\text{C NMR}$ (126 MHz, CDCl_3): δ 168.0, 162.2, 134.8, 129.1, 124.1, 44.7, 31.4, 29.6.

mp 92–93 °C

IR (cm^{-1}): 2936, 2361, 1809, 1782, 1736, 1624, 1470, 1366, 1346, 1319, 1180, 1088, 1034, 968, 876, 810, 787, 698.

LRMS (ESI+) m/z : 262.2 [$\text{M}+\text{H}^+$], 284.2 [$\text{M}+\text{Na}^+$].



1,3-dioxoisindolin-2-yl 4-phenylbutanoate (1b).

The procedure was adapted from the method of Overman and coworkers.⁴ A round bottom flask containing a teflon-coated magnetic stir bar was charged with 4-phenylbutyric acid (2.63 g, 16.0 mmol, 1.00 equiv) and dry THF (75 mL) under argon. After sequential addition of *N*-hydroxyphthalimide (4.34 g, 26.6 mmol, 1.66 equiv), DMAP (98.0 mg, 0.800 mmol, 0.0500 equiv), and *N,N'*-diisopropylcarbodiimide (3.03 g, 2.40 mmol, 1.50 equiv), the reaction mixture was allowed to stir overnight at room temperature. After this time, the heterogeneous mixture was filtered and the filtrate was concentrated under reduced pressure. The crude product was

⁴ Pratsch, G.; Lackner, G. L.; Overman, L. E. *J. Org. Chem.* **2015**, *80*, 6025–6036.

purified by silica gel chromatography (80:20 hexanes/EtOAc, $R_f = 0.31$) to yield product (3.86 g, 12.5 mmol, 78%) as a colorless solid.

$^1\text{H NMR}$ (400 MHz; CDCl_3): δ 7.90 (dd, $J = 5.2, 3.1$ Hz, 2H), 7.79 (dd, $J = 5.4, 3.0$ Hz, 2H), 7.31 (t, $J = 7.4$ Hz, 2H), 7.24 (t, $J = 7.9$ Hz, 3H), 2.78 (t, $J = 7.5$ Hz, 2H), 2.67 (t, $J = 7.3$ Hz, 2H), 2.17-2.08 (m, 2H).

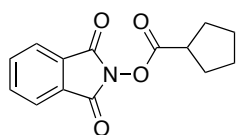
$^1\text{H NMR}$ (500 MHz; $\text{DMF-}d_7$): δ 7.32 (dd, $J = 11.6, 5.8$ Hz, 5H), 7.24 (dd, $J = 6.7, 5.0$ Hz, 1H), 2.80 (dd, $J = 6.2, 4.6$ Hz, 6H), 2.06 (dd, $J = 13.2, 6.9$ Hz, 3H).

$^{13}\text{C NMR}$ (126 MHz, CDCl_3): δ 169.6, 162.1, 140.8, 134.9, 129.1, 128.7, 128.7, 126.4, 124.1, 34.8, 30.4, 26.5.

mp 83–86 °C

IR (cm^{-1}): 2928, 2855, 1805, 1778, 1732, 1612, 1458, 1366, 1219, 1184, 1146, 1123, 1088, 1072, 1030, 918, 760, 706, 664.

LRMS (ESI+) m/z : 310.2 [$\text{M}+\text{H}^+$], 332.2 [$\text{M}+\text{Na}^+$].



1,3-dioxoisindolin-2-yl cyclopentanecarboxylate (1c).

The procedure was adapted from the method of Overman and coworkers.⁴ A round bottom flask containing a teflon-coated magnetic stir bar was charged with cyclopentane carboxylic acid (4.33 mL, 40.0 mmol, 1.00 equiv) and dry THF (150 mL) under nitrogen. After sequential addition of *N*-hydroxyphthalimide (10.8 g, 66.4 mmol, 1.66 equiv), DMAP (977 mg, 8.00 mmol, 0.200 equiv), and *N,N'*-diisopropylcarbodiimide (9.30 mL, 60.0 mmol, 1.50 equiv), the reaction mixture was allowed to stir overnight at room temperature. After this time, the heterogeneous mixture was filtered and the filtrate was concentrated under reduced pressure. The crude product was purified by silica gel chromatography (90:10 hexanes/EtOAc, $R_f = 0.13$) to yield product (2.89 g, 11.2 mmol, 28%) as a colorless solid.

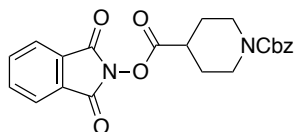
$^1\text{H NMR}$ (400 MHz; CDCl_3): δ 7.89 (dd, $J = 5.4, 3.1$ Hz, 2H), 7.79 (dt, $J = 5.9, 3.2$ Hz, 2H), 3.16-3.08 (m, 1H), 2.11-1.99 (m, 4H), 1.81-1.75 (m, 2H), 1.72-1.65 (m, 2H).

$^{13}\text{C NMR}$ (126 MHz, CDCl_3): δ 173.0, 162.3, 134.8, 129.2, 124.0, 40.8, 30.4, 26.1.

mp 62–65 °C

IR (cm^{-1}): 2967, 2874, 1813, 1782, 1740, 1608, 1589, 1524, 1466, 1450, 1362, 1288, 1258, 1184, 1080, 972, 876, 694.

LRMS (ESI+) m/z : 260.1 [$\text{M}+\text{H}^+$], 282.1 [$\text{M}+\text{Na}^+$].



1-benzyl 4-((1,3-dioxoisindolin-2-yl)oxy)carbamate (**1d**).

1-((benzyloxy)carbonyl)piperidine-4-carboxylic acid was prepared from piperidine-4-carboxylic acid (3.23 g, 25.0 mmol) based on the literature procedure and was used without purification.⁵

The NHP ester was prepared by an adapted procedure from Overman and co-workers.⁴

To an oven dried round bottom flask equipped with a stirbar was added a solution of 1-((benzyloxy)carbonyl)piperidine-4-carboxylic acid (crude, approximately 25.0 mmol) in dry THF (248 mL) under nitrogen. *N*-hydroxyphthalimide (6.12 g, 37.5 mmol, 1.5 equiv), DMAP (0.611 g, 5.00 mmol, 0.200 equiv), and *N,N'*-diisopropylcarbodiimide (4.65 mL, 30.0 mmol, 1.20 equiv) were sequentially added, and the reaction mixture was stirred overnight. Upon completion, the reaction mixture was filtered and concentrated under reduced pressure. The resulting solid that formed was then transferred to a filter funnel and washed using ethyl acetate (200 mL), and the filtrate was concentrated under reduced pressure and purified by column chromatography (70:30, hexanes/EtOAc, $R_f = 0.21$) to afford a viscous liquid. Hot methylcyclohexane was added, and the resulting solution was concentrated under reduced pressure. This process was repeated several times until a white solid was obtained, which was dried under high vacuum (2.90 g, 7.10 mmol, 28% yield).

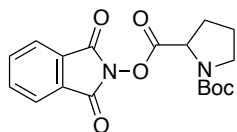
¹H NMR (500 MHz; CDCl₃; 55 °C): δ 7.90-7.79 (m, 4H), 7.37-7.31 (m, 5H), 5.14 (s, 2H), 4.10 (s, 2H), 3.12 (t, $J = 10.2$ Hz, 2H), 2.94 (tt, $J = 9.6, 4.5$ Hz, 1H), 2.09 (d, $J = 10.5$ Hz, 2H), 1.90 (t, $J = 10.0$ Hz, 2H).

¹³C NMR (126 MHz, CDCl₃): δ 170.6, 162.0, 155.2, 136.8, 134.9, 129.0, 128.7, 128.2, 128.0, 124.1, 67.4, 42.9, 38.5, 27.8.

mp 96–98 °C

IR (cm⁻¹): 2951, 2338, 1813, 1786, 1744, 1686, 1470, 1450, 1362, 1227, 1130, 1065, 1018, 995, 880, 756, 698.

LRMS (ESI+) m/z : 431.2 [M+Na⁺], 447.1 [M+K⁺].



1-(*tert*-butyl) 2-((1,3-dioxoisindolin-2-yl)oxy)carbamate (**1e**).

⁵ Reich, M.; Schunk, S.; Jostock, R.; Hees, S.; Germann, T.; Engels, M. F.-M. Substituted Disulfonamide Compounds US2010152158 (A1) — 2010-06-17.

A round bottom flask equipped with a teflon-coated stirbar was charged with *N*-hydroxyphthalimide (1.52 g, 9.29 mmol, 1.00 equiv), *N,N'*-dicyclohexylcarbodiimide (1.92 g, 9.29 mmol, 1.00 equiv), and dry EtOAc (25 mL). After the reaction mixture was stirred, *N*-(tert-butoxycarbonyl)proline (2.00 g, 9.29 mmol, 1.00 equiv) and additional EtOAc (25 mL) was added and the reaction mixture was allowed to stir overnight at room temperature. Stirring was stopped and the reaction mixture was allowed to stand for one day, then filtered through a short silica plug and concentrated under reduced pressure to afford a white solid (2.26 g, 6.27 mmol, 67% yield).

Due to the existence of rotamers at ambient temperature, the ¹H NMR spectrum was obtained at 55 °C:

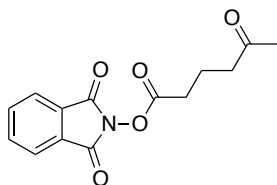
¹H NMR (500 MHz; CDCl₃; 55 °C): δ 7.86 (dd, *J* = 5.0, 2.6 Hz, 2H), 7.76 (dd, *J* = 4.7, 2.3 Hz, 2H), 4.61 (s, 1H), 3.60 (s, 1H), 3.50 (s, 1H), 2.38 (dd, *J* = 13.5, 7.3 Hz, 2H), 2.13–2.04 (m, 1H), 1.96 (dt, *J* = 11.7, 5.6 Hz, 1H), 1.51 (s, 9H).

¹³C NMR (126 MHz, CDCl₃): δ 169.7, 161.8, 153.6, 134.9, 128.9, 124.0, 81.2, 57.3, 46.3, 31.5, 28.2, 23.6.

mp 155–157 °C (lit.⁶ mp 68–69 °C)

IR (cm⁻¹): 2936, 2361, 1786, 1736, 1690, 1431, 1389, 1366, 1273, 1223, 1123, 1072, 1015, 880, 749, 698.

LRMS (ESI+) *m/z*: 383.2 [M+Na⁺], 399.1 [M+K⁺].



1,3-dioxoisindolin-2-yl 5-oxohexanoate (1i).

The procedure was adapted from the method of Overman and coworkers.⁴ A round bottom flask containing a teflon-coated magnetic stir bar was charged with 4-acetylbutyric acid (650 mg, 5.00 mmol, 1.00 equiv) and dry THF (25 mL) under argon. After sequential addition of *N*-hydroxyphthalimide (1.35 g, 8.30 mmol, 1.66 equiv), DMAP (30.0 mg, 0.250 mmol, 0.0500 equiv) and *N,N'*-diisopropylcarbodiimide (946 mg, 7.50 mmol, 1.50 equiv), the reaction was allowed to stir overnight at room temperature. After this time, the heterogeneous mixture was filtered and the filtrate was concentrated under reduced pressure. The crude product was purified by silica gel chromatography (80:20 hexanes/EtOAc, *R*_f = 0.12) to yield product as a colorless solid (812 mg, 2.95 mmol, 59% yield).

⁶ Il'ina, A. V.; Davidovich, Y. A.; Rogozhin, S. V. *Bull. Acad. Sci. USSR, Div. Chem. Sci. (Engl. Transl.)* **1984**, 33, 69–70.

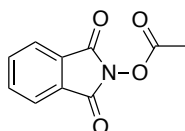
¹H NMR (400 MHz; CDCl₃): δ 7.89 (dd, *J* = 5.5, 3.1 Hz, 2H), 7.79 (dd, *J* = 5.4, 3.1 Hz, 2H), 2.73 (t, *J* = 7.0 Hz, 2H), 2.65 (t, *J* = 7.1 Hz, 2H), 2.18 (s, 3H), 2.05 (quintet, *J* = 7.0 Hz, 2H).

¹³C NMR (126 MHz, CDCl₃): δ 207.7, 169.4, 162.1, 134.9, 129.0, 124.1, 41.6, 30.2, 30.1, 18.7.

mp 90–91 °C

IR (cm⁻¹): 2951, 1813, 1786, 1736, 1709, 1609, 1362, 1184, 1134, 1096, 1053, 972, 880, 795, 698.

LRMS (ESI+) *m/z*: 276.2 [M+H⁺], 298.1 [M+Na⁺].



1,3-dioxoisindolin-2-yl acetate (1j).

The procedure was modified from the method of Seligman and coworkers.⁷ Instead of DCC, DIC was used. A round bottom flask containing a teflon-coated magnetic stir bar was charged with *N*-hydroxyphthalimide (2.80 g, 17.4 mmol, 1.00 equiv), and *N,N'*-diisopropylcarbodiimide (1.79 mL, 17.4 mmol, 1.00 equiv). Dry EtOAc (250 mL) was then added followed by acetic acid (1.00 mL, 17.4 mmol, 1.00 equiv) and the reaction was stirred open to air at room temperature overnight. The reaction mixture became cloudy and a white solid precipitated from the solution, which was removed via vacuum filtration. The filtrate was dried with Na₂SO₄ and concentrated under reduced pressure to give the crude product. Recrystallization of the residue from hot ethanol provided product as a colorless solid (3.10 g, 15.1 mmol, 87% yield). Analytical data matched those reported in the literature.

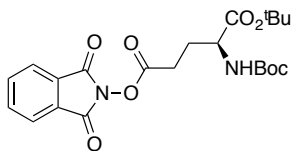
¹H NMR (500 MHz; CDCl₃): δ 7.89 (s, 2H), 7.80 (s, 2H), 2.40 (d, *J* = 0.5 Hz, 3H).

¹³C NMR (126 MHz, CDCl₃): δ 166.7, 162.0, 134.9, 129.0, 124.1, 17.8.

mp 160–165 °C (lit⁷ mp 185 °C)

IR (cm⁻¹): 1809, 1786, 1736, 1373, 1157, 1080, 1007, 968, 880, 837, 694.

LRMS (ESI+) *m/z*: 206.1 [M+H⁺], 228.1 [M+Na⁺].



(*S*)-1-(*tert*-butyl) 5-(1,3-dioxoisindolin-2-yl) (*tert*-butoxycarbonyl)-glutamate (1k).

The procedure was adapted from the method of Overman and coworkers.⁴ A round bottom flask containing a teflon-coated magnetic stir bar was charged with Boc-Glu-OtBu (1.52 g, 5.00

⁷ Saljoughian, M.; Morimoto, H.; Williams, P. G.; Than, C.; Seligman, S. J. *J. Org. Chem.* **1996**, *61*, 9625–9628.

mmol, 1.00 equiv) and dry THF (25 mL) under argon. After sequential addition of *N*-hydroxyphthalimide (1.35 g, 8.3 mmol, 1.66 equiv), DMAP (30.0 mg, 0.250 mmol, 0.0500 equiv), and *N,N'*-diisopropylcarbodiimide (946 mg, 7.50 mmol, 1.50 equiv), the reaction was allowed to stir overnight at room temperature. After this time, the heterogeneous mixture was filtered and the filtrate was concentrated under reduced pressure. The crude product was purified by silica gel chromatography (80:20 hexanes/EtOAc, $R_f = 0.23$) to yield product as a colorless solid (1.74 g, 3.88 mmol, 72% yield).

$[\alpha]_D^{23} +13.3$ ($c=1.08$, CHCl_3)

$^1\text{H NMR}$ (400 MHz; CDCl_3): δ 7.89 (dd, $J = 5.5, 3.1$ Hz, 2H), 7.79 (dd, $J = 5.4, 3.1$ Hz, 2H), 5.19 (d, $J = 6.7$ Hz, 1H), 4.28 (d, $J = 5.0$ Hz, 1H), 2.85-2.68 (m, 2H), 2.35-2.29 (m, 1H), 2.11-2.02 (m, 1H), 1.47 (d, $J = 14.3$ Hz, 18H).

$^{13}\text{C NMR}$ (126 MHz, CDCl_3): δ 170.9, 169.1, 161.9, 155.5, 134.9, 129.0, 124.1, 82.7, 80.1, 53.2, 28.4, 28.1, 27.5.

mp 84–85 °C

IR (cm^{-1}): 3368, 2978, 2936, 2361, 2338, 1813, 1786, 1740, 1690, 1508, 1366, 1150, 1072, 1018, 976, 876, 787, 698.

LRMS (ESI+) m/z : 471.2 $[\text{M}+\text{Na}^+]$.

SFC analysis (Daicel Chiralpak IA (0.46 cm ID \times 25 cm L), 25% *i*-PrOH in CO_2 , 3 mL/min, $\lambda = 220$ nm, 35 °C, 12.0 MPa): t_R [min] = 1.9 (1.55%), 2.5 (98.45%), 97% *ee*.

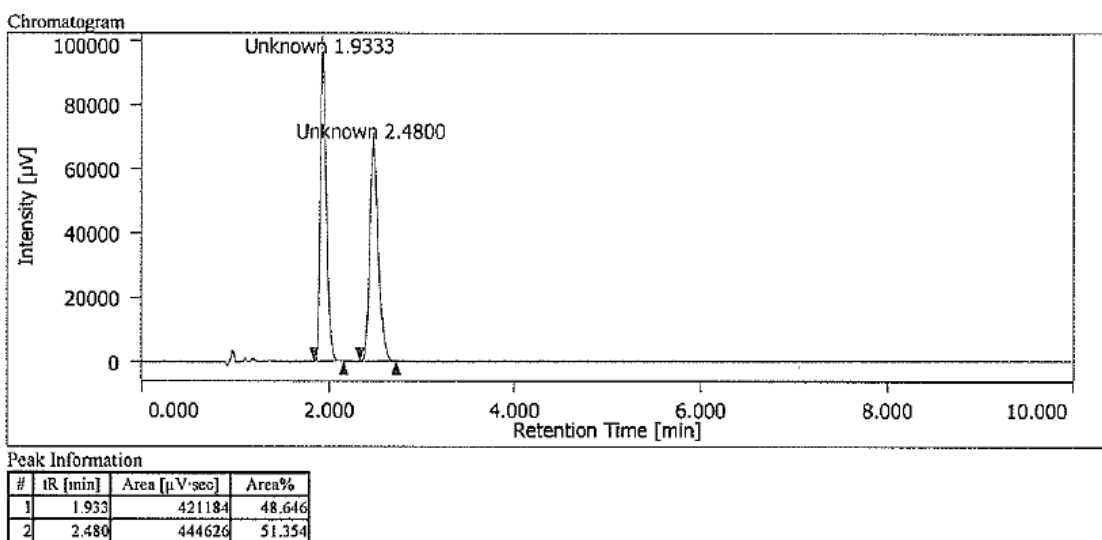


Figure S1. Enantiomeric mixture of **1k**.

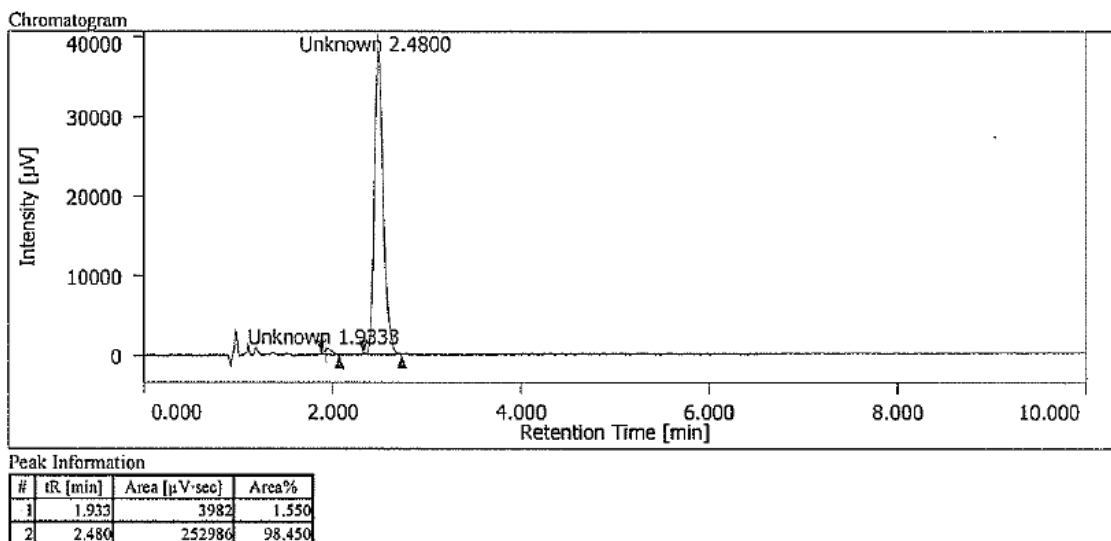
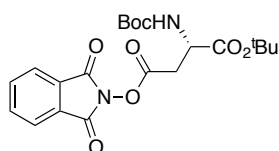


Figure S2. (*S*)-1k.



(*S*)-1-(*tert*-butyl) 3-(1,3-dioxoisindolin-2-yl)-2-((*tert*-butoxycarbonyl)amino)malonate (11).

The procedure was adapted from the method of Overman and coworkers.⁴ A round bottom flask containing a teflon-coated magnetic stir bar was charged with Boc-Asp-OtBu (4.63 g, 16.0 mmol, 1.00 equiv) and dry THF (75 mL) under argon. After sequential addition of *N*-hydroxyphthalimide (4.34 g, 26.6 mmol, 1.66 equiv), DMAP (98.0 mg, 0.800 mmol, 0.0500 equiv), and *N,N'*-diisopropylcarbodiimide (3.03 g, 24.0 mmol, 1.50 equiv), the reaction was allowed to stir overnight at room temperature. After this time, the heterogeneous mixture was filtered and the filtrate was concentrated under reduced pressure. The crude product was purified by silica gel chromatography (80:20 hexanes/EtOAc, $R_f = 0.23$) to yield product (5.60 g, 12.9 mmol, 81% yield) as a white solid.

$[\alpha]_D^{23} +32.6$ ($c=1.01$, CHCl_3)

$^1\text{H NMR}$ (400 MHz; CDCl_3): δ 7.89 (dd, $J = 5.1, 3.1$ Hz, 2H), 7.79 (dd, $J = 5.2, 3.1$ Hz, 2H), 5.51–5.49 (m, 1H), 4.59–4.57 (m, 1H), 3.28 (dd, $J = 24.4, 4.1$ Hz, 2H), 1.47 (d, $J = 7.6$ Hz, 18H).

$^{13}\text{C NMR}$ (126 MHz, CDCl_3): δ 168.8, 167.6, 161.7, 155.4, 134.9, 128.9, 124.1, 83.4, 80.3, 50.3, 34.3, 28.4, 27.9.

mp 124–125 °C

IR (cm^{-1}): 3372, 2970, 2361, 1809, 1786, 1748, 1694, 1501, 1362, 1246, 1215, 1153, 1103, 1065, 968, 787, 694.

LRMS (ESI+) m/z : 457.2 [M+Na⁺].

SFC analysis (Daicel Chiralpak IA (0.46 cm ID × 25 cm L), 10% *i*-PrOH in CO₂, 4 mL/min, λ = 220 nm, 35 °C, 12.0 MPa): tR [min] = 3.2 (0.2%), 3.9 (99.8%), >98% *ee*.

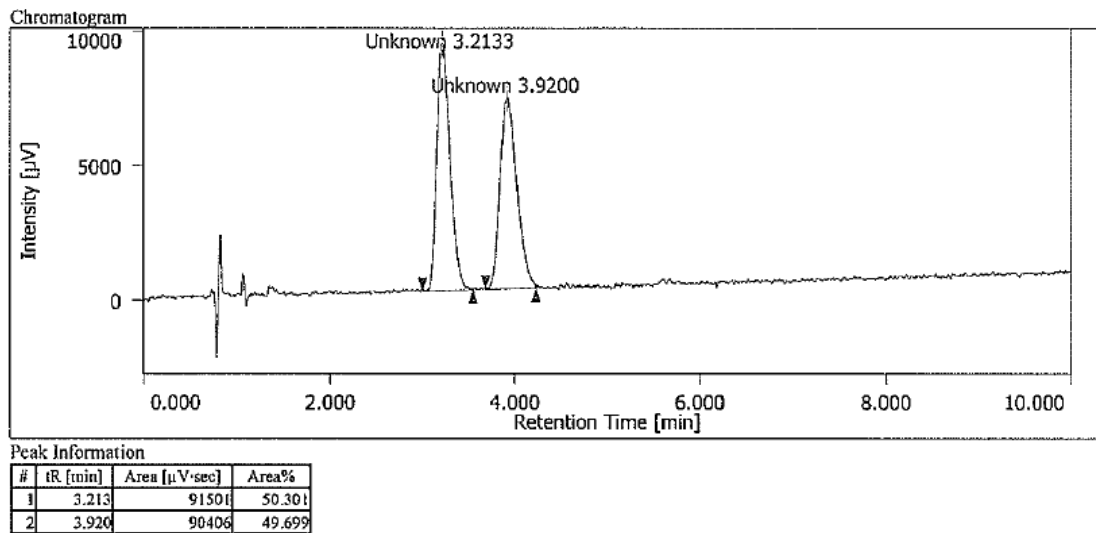


Figure S3. Enantiomeric mixture of **11**.

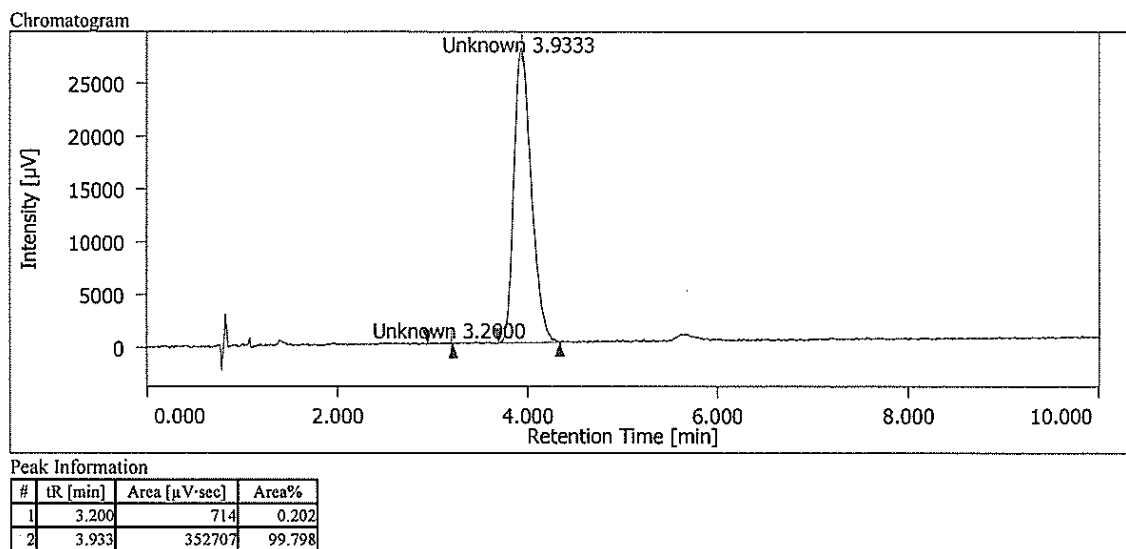
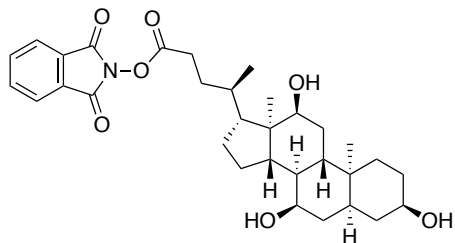


Figure S4. (*S*)-**11**.



1,3-dioxoisindolin-2-yl (*R*)-4-((*3R,5S,7R,8R,9S,10S,12S,13R,14S,17R*)-3,7,12-trihydroxy-10,13-dimethylhexadecahydro-1*H*-cyclopenta[*a*]phenanthren-17-yl)pentanoate (1m**).**

The procedure was adapted from the method of Pratsch and coworkers.⁴ A round bottom flask containing a teflon-coated magnetic stir bar was charged with cholic acid (4.09 g, 10.0 mmol, 1.00 equiv) and dry DMF (100 mL) under nitrogen. After sequential addition of *N*-hydroxyphthalimide (2.71 g, 16.6 mmol, 1.66 equiv), DMAP (244 mg, 2.00 mmol, 0.200 equiv), and *N,N'*-diisopropylcarbodiimide (2.33 mL, 15.0 mmol, 1.50 equiv), the reaction was allowed to stir overnight at room temperature. After this time, the heterogeneous mixture was filtered and the filtrate was concentrated under reduced pressure. The crude viscous liquid was diluted with hot methylcyclohexane and concentrated under reduced pressure. This process was repeated several times until a red solid formed. The solid was purified by silica gel chromatography (100% EtOAc, $R_f = 0.31$) to yield the product as a colorless solid (1.17 g, 2.12 mmol, 21% yield).

¹H NMR (400 MHz; CDCl₃): δ 7.89 (dd, $J = 5.4, 3.1$ Hz, 2H), 7.79 (dd, $J = 5.5, 3.1$ Hz, 2H), 4.01 (s, 2H), 3.85 (s, 2H), 3.49-3.43 (m, 1H), 2.76-2.70 (m, 1H), 2.66-2.60 (m, 1H), 2.26-2.17 (m, 2H), 1.35 (dd, $J = 40.6, 27.6$ Hz, 5H), 1.14 (d, $J = 6.5$ Hz, 4H), 0.99-0.96 (m, 2H), 0.90 (s, 3H), 0.73 (s, 3H).

¹³C NMR (126 MHz, CDCl₃): δ 170.2, 162.2, 134.9, 129.1, 124.1, 76.9, 73.1, 72.1, 68.5, 47.1, 46.8, 42.4, 41.6, 39.9, 39.8, 35.4, 35.1, 34.8, 34.7, 30.8, 30.7, 28.6, 28.2, 27.6, 26.8, 23.3, 22.7, 17.5, 12.7.

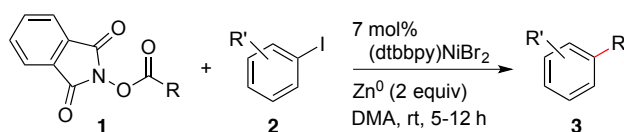
mp 99–105 °C

IR (cm⁻¹): 3337, 2932, 2866, 2361, 1786, 1740, 1616, 1466, 1366, 1184, 1130, 1076, 972, 910, 876, 729, 698.

LRMS (ESI+) m/z : 576.3 [M+Na⁺].

III. Coupling of NHP Esters with Aryl Iodides

General Procedure for the Coupling of *N*-(acyloxy)Phthalimides and Aryl Iodides.



Reactions were set up in a nitrogen filled glove box. To an oven-dried 1-dram vial fitted with a Teflon-coated stir-bar was added (dtbbpy)NiBr₂ (27.3 mg, 0.0560 mmol, 0.0700 equiv), *N*-(acyloxy)phthalimide (1.20 mmol, 1.50 equiv), aryl iodide (0.800 mmol, 1.00 equiv), dodecane (as an internal standard, 10.0 μ L), zinc flake (105 mg, 1.60 mmol, 2.00 equiv), and DMA (1.00 mL). The vial was capped with a screw cap fitted with a PTFE-faced silicone septum, removed from the glove box, and heated in a reaction block set to 28 °C on the benchtop with stirring at 1195 rpm until the reaction was judged complete (<5% *N*-(acyloxy)phthalimide or aryl iodide remaining) by GC analysis, typically 5–11 h.

Alternatively, the catalyst could be generated by pre-stirring NiBr₂(diglyme) (0.0560 mmol, 0.0700 equiv) and 4-4'-di-*tert*-butyl-2,2'-bipyridine (15.0 mg, 0.0560 mmol, 0.0700 equiv) in DMA (1.00 mL) for ~10 min. The remaining reagents were then added, following the order of addition above.

GC Analysis.

After 5–11 h, the reaction was vented to an oil bubbler out before removing a 25 μ L aliquot of the reaction mixture with a 50 μ L gas-tight syringe. The aliquot was diluted with diethyl ether (1.5 mL) and filtered through a short silica pad (1.5 cm) in a pipette packed with glass wool. The filtrate was analyzed by gas chromatography and percent yield was calculated versus dodecane as the internal standard.

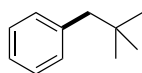
Isolation and Purification.

Upon reaction completion (judged as <5% *N*-(acyloxy)phthalimide or aryl iodide remaining by GC analysis) the reaction mixture was filtered through a short plug of silica gel (1.5 cm wide \times 2 cm high) to remove metal salts and eluted with diethyl ether (75 mL). DMA was removed by adding deionized water (30 mL) to the organic layer and extracting the aqueous layer with diethyl ether (3 \times 30 mL). The combined organic layers were dried over MgSO₄, filtered, and concentrated under reduced pressure. The resulting residue was purified by column chromatography on silica gel to afford the pure product.

Large-Scale Procedure conducted on the benchtop in a round-bottom flask.

To a 25 mL round-bottom flask containing a Teflon-coated stir-bar was added nickel pre-catalyst (87 mg of NiBr₂(diglyme), 0.28 mmol) and 4,4'-di-*tert*-butyl-2,2'-bipyridine (75 mg, 0.28 mmol). The reaction flask was sealed with a rubber septum, and the septum was fitted with a needle connected to an oil bubbler and a needle connected to an argon manifold. The headspace of the flask was purged with argon gas for ten minutes and then the needle to the bubbler was removed. DMA (5 mL), was added via syringe and the resulting mixture was stirred on the benchtop (~1200 rpm) at rt under Ar for 15 minutes to allow ligation of the nickel. The color of the reaction mixture became blue-green. Iodobenzene (0.448 mL, 816 mg, 4.00 mmol) was added via syringe, and 1,3-dioxoisindolin-2-yl 3,3-dimethylbutanoate (**1a**) (1.57 g, 6.00 mmol) and zinc dust (0.52 g, 8.0 mmol) were added in one portion to the reaction vessel by quickly removing the septum and replacing it. The reaction mixture was warmed to 28 °C in an oil bath and stirred at that temperature under Ar. After the reaction was judged complete by GC analysis (~12 h), the reaction mixture was filtered through a plug of silica. The pad was washed with Et₂O (100 mL) and concentrated. The resulting residue was purified by chromatography on SiO₂ (pentane) to yield 480 mg of **3a** (81% yield). Characterization data matched those obtained on 0.8 mmol scale (vide infra).

Product Characterization



t-butylmethylbenzene [1007-26-7] (**3a**).

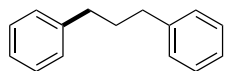
The general procedure was followed with (dtbbpy)NiBr₂ (27.3 mg, 0.0560 mmol, 0.0700 equiv), 1,3-dioxoisindolin-2-yl 3,3-dimethylbutanoate (314 mg, 1.20 mmol, 1.50 equiv), and iodobenzene (89.5 μL, 0.800 mmol, 1.00 equiv). After 5 h, the reaction mixture was worked up and purified by flash chromatography (100% pentane, R_f = 0.54) to afford a colorless oil (103 mg, 87% yield). Analytical data matched those in the literature.⁸

¹H NMR (500 MHz; CDCl₃): δ 7.28-7.12 (m, 5H), 2.50 (s, 2H), 0.91 (s, 9H).

¹³C NMR (126 MHz, CDCl₃): δ 139.9, 130.6, 127.7, 125.8, 50.4, 31.9, 29.5.

GC-MS m/z (% relative intensity, ion): 149.10 (2.32, M⁺), 133.10 (15.93, M⁺-CH₃), 92.10 (100.0, M⁺-C₄H₈), 57.10 (89.08, M⁺-C₇H₇).

⁸ Everson, D. A.; Shrestha, R.; Weix, D. J. *J. Am. Chem. Soc.* **2010**, *132*, 920–921.



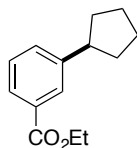
1,3-diphenylpropane [1081-75-0] (3b).

The general procedure was followed with NiBr₂(diglyme) (17.7 mg, 0.0560 mmol, 0.0700 equiv), 4-4'-di-*tert*-butyl-2,2'-bipyridine (15.0 mg, 0.0560 mmol, 0.0700 equiv), 1,3-dioxoisindolin-2-yl 4-phenylbutanoate (247.5 mg, 0.800 mmol, 1.00 equiv), and iodobenzene (89.5 μ L, 0.800 mmol, 1.00 equiv). After 11 h, the reaction mixture was worked up and purified by flash chromatography (100% pentane, R_f = 0.50) to afford a colorless oil (152 mg, 97% yield). Analytical data matched those in the literature.⁹

¹H NMR (400 MHz; CDCl₃): δ 7.31-7.26 (m, 4H), 7.20 (d, *J* = 6.4 Hz, 6H), 2.67 (t, *J* = 7.7 Hz, 4H), 1.98 (quintet, *J* = 7.7 Hz, 2H).

¹³C NMR (126 MHz, CDCl₃): δ 142.4, 128.6, 128.4, 125.9, 35.6, 33.1.

GC-MS *m/z* (% relative intensity, ion): 197.20 (12.21, M⁺), 92.15 (100.00, M⁺-C₈H₉), 77.05 (12.58, M⁺-C₉H₁₄).



3-cyclopentyl-benzoic acid ethyl ester [1027294-28-5] (3c).

The general procedure was followed with NiBr₂(diglyme) (17.7 mg, 0.0560 mmol, 0.0700 equiv), 4-4'-di-*tert*-butyl-2,2'-bipyridine (15.0 mg, 0.0560 mmol, 0.0700 equiv), 1,3-dioxoisindolin-2-yl cyclopentanecarboxylate (311 mg, 1.20 mmol, 1.50 equiv), and ethyl 3-iodobenzoate (135 μ L, 0.800 mmol, 1.00 equiv). After 11 h, the reaction mixture was filtered through a silica plug with diethyl ether, concentrated under reduced pressure, and purified by flash chromatography (2% Et₂O in pentane, R_f = 0.31) to afford a pale yellow oil (155 mg, 89% yield). Analytical data matched those in the literature.¹⁰

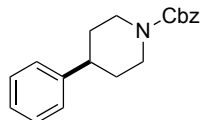
¹H NMR (400 MHz; CDCl₃): δ 7.92 (s, 1H), 7.85 (d, *J* = 7.6 Hz, 1H), 7.43 (d, *J* = 7.7 Hz, 1H), 7.34 (t, *J* = 7.6 Hz, 1H), 4.38 (q, *J* = 7.1 Hz, 2H), 3.04 (quintet, *J* = 8.6 Hz, 1H), 2.13-2.06 (m, 2H), 1.87-1.77 (m, 2H), 1.70 (dd, *J* = 12.4, 7.8 Hz, 2H), 1.66-1.57 (m, 2H), 1.40 (t, *J* = 7.1 Hz, 3H).

¹³C NMR (126 MHz, CDCl₃): δ 167.1, 147.0, 131.8, 130.6, 129.7, 128.4, 127.1, 61.0, 45.9, 34.8, 25.7, 14.5.

⁹ Gieshoff, T. M.; Villa, M.; Welther, A.; Polis, M.; Chakraborty, U.; Wolf, R.; von Wangelin, A. *J. Green Chem.* **2015**, *17*, 1408–1413.

¹⁰ Cuisiat, S.; Bourdiol, N.; Lacharme, V.; Newman-Tancredi, A.; Colpaert, F.; Vacher, B. *J. Med. Chem.* **2007**, *50*, 865–876.

GC-MS m/z (% relative intensity, ion): 219.15 (12.11, M^+), 189.10 (56.46, $M^+ - C_2H_5$), 173.15 (59.21, $M^+ - C_2H_5O$), 145.15 (100.00, $M^+ - C_3H_5O_2$), 117.10 (73.46, $M^+ - C_5H_9O_2$), 69.05 (12.00, $M^+ - C_9H_9O_2$).



4-phenylpiperidine-1-carboxylic acid benzyl ester [733810-73-6] (3d).

The general procedure was followed with $NiBr_2$ (diglyme) (15.2 mg, 0.0480 mmol, 0.120 equiv), 4-4'-di-*tert*-butyl-2,2'-bipyridine (12.9 mg, 0.0480 mmol, 0.120 equiv), 1-benzyl 4-(1,3-dioxoisindolin-2-yl) piperidine-1,4-dicarboxylate (163 mg, 0.400 mmol, 1.00 equiv), iodobenzene (44.8 μ L, 0.400 mmol, 1.00 equiv), Zn (52.3 mg, 0.800 mmol, 2.00 equiv), and DMA (0.500 mL). After 9 h, the reaction mixture was filtered through a silica plug with diethyl ether, concentrated under reduced pressure, and purified by flash chromatography (90:10, hexanes/acetone, R_f = 0.31) to afford a white solid (75.4 mg, 64% yield). Analytical data matched those in the literature.¹¹

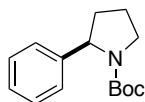
1H NMR (500 MHz; $CDCl_3$): δ 7.38-7.29 (m, 7H), 7.20 (dd, J = 12.7, 7.4 Hz, 3H), 5.16 (s, 2H), 4.34 (s, 2H), 2.89 (s, 2H), 2.67 (t, J = 12.2 Hz, 1H), 1.84 (d, J = 11.6 Hz, 2H), 1.65 (d, J = 10.6 Hz, 2H).

^{13}C NMR (126 MHz, $CDCl_3$): δ 155.4, 145.7, 137.2, 128.7, 128.6, 128.1, 128.0, 126.9, 126.6, 67.2, 44.8, 42.8, 33.3.

mp 56–57 °C

IR (cm^{-1}): 3028, 2936, 2851, 2361, 1682, 1493, 1431, 1362, 1277, 1223, 1123, 1080, 1015, 748, 698.

LRMS (ESI+) m/z : 431.2 [$M+Na^+$], 447.1 [$M+K^+$].



N-(*tert*-butoxycarbonyl)-2-phenylpyrrolidine [154874-88-1] (3e).

The general procedure was followed with $NiBr_2$ (diglyme) (14.9 mg, 0.0480 mmol, 0.120 equiv), 4-4'-di-*tert*-butyl-2,2'-bipyridine (12.9 mg, 0.0480 mmol, 0.120 equiv), 1-(*tert*-butyl) 2-(1,3-dioxoisindolin-2-yl) pyrrolidine-1,2-dicarboxylate (216 mg, 0.600 mmol, 1.50 equiv), iodobenzene (44.8 μ L, 0.400 mmol, 1.00 equiv), Zn (52.3 mg, 0.800 mmol, 2.00 equiv), and DMA (0.500 mL). After 8 h, the reaction mixture was filtered through a silica plug with diethyl

¹¹ Powell, D. A.; Fu, G. C. *J. Am. Chem. Soc.* **2004**, *126*, 7788–7789.

ether, concentrated under reduced pressure, and purified by flash chromatography (90:10, hexanes/acetone, $R_f = 0.31$) to afford a white solid (66.5 mg, 67% yield). The isolated product was contaminated with a small amount of *N*-Boc-pyrrolidine. The actual yield of product was determined to be 63.8 mg (65% yield). Analytical data matched those in the literature.¹²

Due to the existence of rotamers at ambient temperature, the ^1H NMR spectrum was obtained at 55 °C.

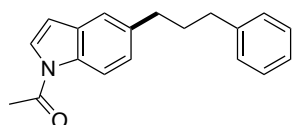
^1H NMR (500 MHz; CDCl_3 ; 55 °C): δ 7.26 (q, $J = 6.5$ Hz, 2H), 7.19-7.14 (m, 3H), 4.82 (s, 1H), 3.59 (t, $J = 6.3$ Hz, 2H), 2.32-2.26 (m, 1H), 1.95-1.80 (m, 3H), 1.27 (s, 9H).

^{13}C NMR (126 MHz, CDCl_3): δ 154.7, 145.3, 128.2, 126.6, 125.6, 79.3, 61.5, 47.2, 36.2, 28.3, 23.3.

mp 47–49 °C (lit.¹³ mp 62–63 °C)

IR (cm^{-1}): 2970, 2886, 2158, 2021, 1975, 1678, 1449, 1398, 1362, 1256, 1165, 1155, 1113, 876, 764, 737, 700.

LRMS (ESI+) m/z : 270.2 [$\text{M}+\text{Na}^+$].



1-(5-(3-phenylpropyl)-1*H*-indol-1-yl)ethan-1-one (3f).

The general procedure was followed with $\text{NiBr}_2(\text{diglyme})$ (17.7 mg, 0.0560 mmol, 0.0700 equiv), 4-4'-di-*tert*-butyl-2,2'-bipyridine (15.0 mg, 0.0560 mmol, 0.0700 equiv), 1,3-dioxoisindolin-2-yl 4-phenylbutanoate (371 mg, 1.20 mmol, 1.50 equiv), and 1-(5-iodo-1*H*-indol-1-yl)ethanone (228 mg, 0.800 mmol, 1.00 equiv). After 8 h, the reaction mixture was worked up and purified by flash chromatography (85:15, hexanes/acetone, $R_f = 0.33$) to afford a light yellow oil (198 mg, 89% yield).

^1H NMR (500 MHz; CDCl_3): δ 8.32 (d, $J = 7.0$ Hz, 1H), 7.37 (d, $J = 13.6$ Hz, 2H), 7.27 (dd, $J = 13.4, 6.3$ Hz, 2H), 7.18 (t, $J = 7.2$ Hz, 4H), 6.58 (d, $J = 3.7$ Hz, 1H), 2.75 (t, $J = 7.6$ Hz, 2H), 2.66 (t, $J = 7.8$ Hz, 2H), 2.62 (s, 3H), 2.00 (quintet, $J = 7.7$ Hz, 2H).

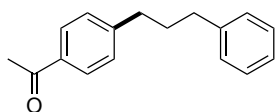
^{13}C NMR (126 MHz, CDCl_3): δ 168.6, 142.5, 137.9, 134.1, 130.8, 128.6, 128.4, 126.0, 125.8, 125.4, 120.4, 116.4, 109.2, 35.5, 35.5, 33.5, 24.0.

IR (cm^{-1}): 3387, 3340, 2936, 2866, 2361, 1813, 1786, 1740, 1466, 1377, 1327, 1076, 910, 880, 729, 698.

LRMS (ESI+) m/z : 278.2 [$\text{M}+\text{H}^+$], 300.2 [$\text{M}+\text{Na}^+$].

¹² Beak, P.; Wu, S.; Yum, E. K.; Jun, Y. M. *J. Org. Chem.* **1994**, *59*, 276–277.; Dieter, R. K.; Li, S. *J. Org. Chem.* **1997**, *62*, 7726–7735.

¹³ Barker, G.; O'Brien, P.; Campos, K. R. *Org. Lett.* **2010**, *12*, 4176–4179



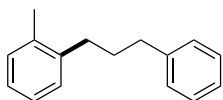
1-(*p*-Acetylphenyl)-3-phenylpropane [113138-08-2] (3g).

The general procedure was followed with (dtbbpy)NiBr₂ (27.3 mg, 0.0560 mmol, 0.0700 equiv), 1,3-dioxoisindolin-2-yl 4-phenylbutanoate (371 mg, 1.20 mmol, 1.50 equiv), and 4-iodoacetophenone (197 μ L, 0.800 mmol, 1.00 equiv). After 5 h, the reaction mixture was worked up and purified by flash chromatography (95:5 hexanes/acetone, R_f = 0.14) to afford a colorless oil (135 mg, 71% yield). Analytical data matched those in the literature.¹⁴

¹H NMR (400 MHz; CDCl₃): δ 7.88 (d, J = 8.2 Hz, 2H), 7.31-7.26 (m, 4H), 7.19 (t, J = 8.4 Hz, 3H), 2.68 (dt, J = 20.3, 7.7 Hz, 4H), 2.58 (s, 3H), 1.98 (quintet, J = 7.7 Hz, 2H).

¹³C NMR (126 MHz, CDCl₃): δ 197.9, 148.2, 142.0, 135.2, 128.8, 128.6, 128.5, 128.5, 126.0, 35.5, 35.5, 32.7, 26.7.

GC-MS m/z (% relative intensity, ion): 238.10 (70.99, M⁺), 223.05 (100.00, M⁺-CH₃), 147.05 (75.15, M⁺-C₇H₇), 134.05 (84.36), 105.05 (94.62, M⁺-C₉H₉O).



1-methyl-2-(3-phenylpropyl)benzene [1520-39-4] (3h).

The general procedure was followed with NiBr₂(diglyme) (17.7 mg, 0.0560 mmol, 0.0700 equiv), 4-4'-di-*tert*-butyl-2,2'-bipyridine (15.0 mg, 0.0560 mmol, 0.0700 equiv), 1,3-dioxoisindolin-2-yl 4-phenylbutanoate (248 mg, 0.800 mmol, 1.00 equiv), and 2-iodotoluene (102 μ L, 0.800 mmol, 1.00 equiv). After 4 h, the reaction mixture was filtered through a silica plug with diethyl ether, concentrated under reduced pressure, and purified by flash chromatography (100% pentane, R_f = 0.47). Mixed fractions of the desired product were obtained. The mixed fractions were combined, concentrated under reduced pressure and the residue was resubjected to flash chromatography (100% pentane) to afford a colorless oil (153 mg, 91% yield). Analytical data matched those in the literature.¹⁵

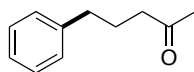
¹H NMR (500 MHz; CDCl₃): δ 7.31-7.25 (m, 3H), 7.20 (dt, J = 8.8, 4.7 Hz, 3H), 7.14-7.10 (m, 4H), 2.71 (t, J = 7.7 Hz, 2H), 2.64 (t, J = 7.9 Hz, 2H), 2.27 (s, 3H), 1.92 (quintet, J = 7.8 Hz, 2H).

¹³C NMR (126 MHz, CDCl₃): δ 142.4, 140.6, 136.0, 130.3, 128.9, 128.6, 128.5, 128.4, 126.0, 126.0, 125.9, 36.0, 33.0, 31.9, 19.4.

¹⁴ Molander, G.; Ito, T. *Org. Lett.* **2001**, *3*, 393–396.

¹⁵ Moriya, T.; Kentaro, T.; Konakahara, T.; Ogiaware, Y.; Sakai, N. *Eur. J. Org. Chem.* **2015**, *10*, 2277–2281.

GC-MS m/z (% relative intensity, ion): 211.15 (8.35, M⁺), 119.10 (53.90, M⁺-C₇H₇), 106.10 (100.00, M⁺-C₈H₉), 91.10 (47.45, M⁺-C₇H₇).



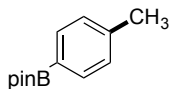
5-phenyl-2-pentanone [2235-83-8] (3i).

The general procedure was followed with NiBr₂(diglyme) (17.7 mg, 0.0560 mmol, 0.0700 equiv), 4-4'-di-*tert*-butyl-2,2'-bipyridine (15.0 mg, 0.0560 mmol, 0.0700 equiv), 1,3-dioxoisindolin-2-yl 5-oxohexanoate (330 mg, 1.20 mmol, 1.50 equiv), and iodobenzene (89.5 μL, 0.800 mmol, 1.00 equiv). After 14 h, the reaction mixture was filtered through a silica plug with diethyl ether, concentrated under reduced pressure, and purified by flash chromatography (20:1 Pentane/Et₂O, R_f = 0.18) to afford a light yellow oil (90.9 mg, 70% yield). Analytical data matched those in the literature.¹⁶

¹H NMR (400 MHz; CDCl₃): δ 7.28 (dd, *J* = 12.6, 5.1 Hz, 3H), 7.19 (dd, *J* = 12.4, 7.1 Hz, 3H), 2.63 (t, *J* = 7.6 Hz, 2H), 2.44 (t, *J* = 7.4 Hz, 2H), 2.12 (s, 3H), 1.91 (quintet, *J* = 7.5 Hz, 2H).

¹³C NMR (126 MHz, CDCl₃): δ 208.8, 141.7, 128.6, 128.5, 126.0, 42.9, 35.1, 30.0, 25.3.

GC-MS m/z (% relative intensity, ion): 163.15 (8.31, M⁺), 104.10 (100.00, M⁺-C₃H₅O), 91.10 (14.71, M⁺-C₇H₇).



4,4,5,5-tetramethyl-2-(*p*-tolyl)-1,3,2-dioxaborolane [195062-57-8] (3j).

The general procedure was followed with NiBr₂(diglyme) (17.7 mg, 0.0560 mmol, 0.0700 equiv), 4-4'-di-*tert*-butyl-2,2'-bipyridine (15.0 mg, 0.0560 mmol, 0.0700 equiv), 1,3-dioxoisindolin-2-yl acetate (246 mg, 1.20 mmol, 1.50 equiv), and 4-iodophenylboronic acid pinacol ester (264 mg, 0.800 mmol, 1.00 equiv). After 6 h, the reaction mixture was worked up and purified by flash chromatography (97:3 hexanes/acetone, R_f = 0.30) to afford a white solid (72.2 mg, 41% yield). The actual yield of the reaction was higher, but ~19 mg (11%) product was collected in fractions that also contained the hydrodehalogenation byproduct, 4,4,5,5-tetramethyl-2-phenyl-1,3,2-dioxaborolane and we were unable to separate this mixture further after repeated attempts. Analytical data matched those in the literature.¹⁷ In the ¹³C NMR spectrum, the carbon attached to boron was not observed.¹⁸

¹⁶ Moriyama, K.; Takemura, M.; Togo, H. *J. Org. Chem.* **2014**, *79*, 6094–6104.

¹⁷ Mo, F.; Jiang, Y.; Qiu, D.; Zhang, Y.; Wang, J. *Angew. Chem. Int. Ed.* **2010**, *49*, 1846–1849.

¹⁸ Zhao, C.-J.; Xue, D.; Jia, Z.-H.; Wang, C.; Xiao, J. *Synlett.* **2014**, *25*, 1577–1584.

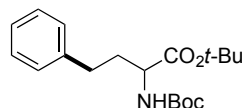
¹H NMR (400 MHz; CDCl₃): δ 7.70 (d, *J* = 7.8 Hz, 2H), 7.19 (d, *J* = 7.6 Hz, 2H), 2.36 (s, 3H), 1.34 (s, 12H).

¹³C NMR (126 MHz, CDCl₃): δ 141.5, 134.9, 128.7, 83.7, 25.0, 21.9.

mp 48–49 °C (lit.¹⁹ mp 47.2–48.0 °C)

IR (cm⁻¹): 2976, 2924, 2158, 2021, 1977, 1610, 1439, 1396, 1358, 1319, 1265, 1213, 1142, 1088, 1022, 962, 858, 816, 725, 700.

LRMS (ESI+) *m/z*: 219.2 [M+H⁺], 241.2 [M+Na⁺].



(S)-tert-butyl 2-((tert-butoxycarbonyl)amino)-4-phenylbutanoate [111652-08-5] (3k).

The general procedure was followed with NiBr₂(diglyme) (17.7 mg, 0.0560 mmol, 0.0700 equiv), 4-4'-di-*tert*-butyl-2,2'-bipyridine (15.0 mg, 0.0560 mmol, 0.0700 equiv), 1-(*tert*-butyl) 5-(1,3-dioxoisindolin-2-yl) (*tert*-butoxycarbonyl)-glutamate (538 mg, 1.20 mmol, 1.50 equiv), and iodobenzene (89.5 μL, 0.800 mmol, 1.00 equiv). After 14 h, the reaction mixture was filtered through a silica plug with diethyl ether, concentrated under reduced pressure, and purified by flash chromatography (95:5, hexanes/acetone, R_f = 0.31) to afford a white solid (75.4 mg, 64% yield). Analytical data matched those in the literature.²⁰

[α]_D²³ +30.3 (c=1.03, CHCl₃)

¹H NMR (400 MHz; CDCl₃): δ 7.29 (d, *J* = 7.5 Hz, 2H), 7.19 (t, *J* = 8.0 Hz, 3H), 5.07 (d, *J* = 7.3 Hz, 1H), 4.25 (d, *J* = 5.5 Hz, 1H), 2.73–2.59 (m, 2H), 2.10 (dt, *J* = 11.0, 5.9 Hz, 1H), 1.90 (tt, *J* = 11.9, 6.0 Hz, 1H), 1.47 (d, *J* = 8.9 Hz, 18H).

¹³C NMR (126 MHz, CDCl₃): δ 171.9, 155.5, 141.3, 128.6, 128.5, 126.2, 82.0, 79.7, 54.0, 34.9, 31.7, 28.4, 28.1.

mp 71–72 °C (lit.²⁰ mp 68–69 °C)

IR (cm⁻¹): 3395, 2974, 2927, 2361, 1728, 1694, 1497, 1362, 1150, 1030, 860, 845, 721, 698.

LRMS (ESI+) *m/z*: 336.3 [M+H⁺], 358.3 [M+Na⁺], 374.2 [M+K⁺].

SFC analysis (Daicel Chiralpak IA (0.46 cm ID × 25 cm L), 10% *i*-PrOH in CO₂, 4 mL/min, λ = 220 nm, 35 °C, 12.0 MPa): tR [min] = 2.3 (1.4%), 2.7 (98.6%), 97% *ee*.

¹⁹ Labre, F.; Gimbert, Y.; Bannwarth, P.; Olivero, S.; Duñach, E.; Chavant, P. Y. *Org. Lett.* **2014**, *16*, 2366–2369.

²⁰ Münster, P.; Steglich, W. *Synthesis* **1987**, 223–225.

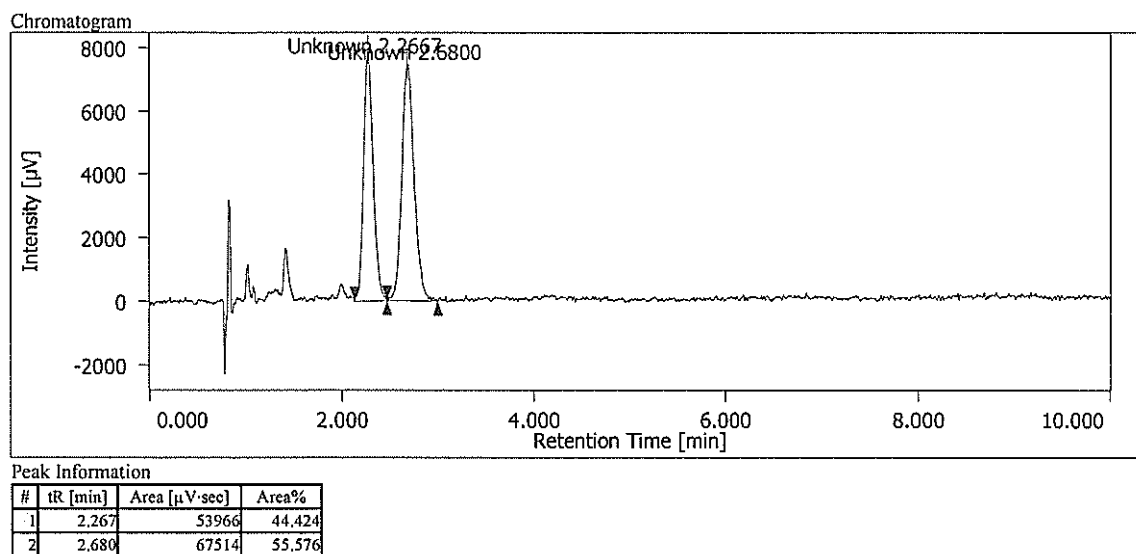


Figure S5. Enantiomeric mixture of **3k**.

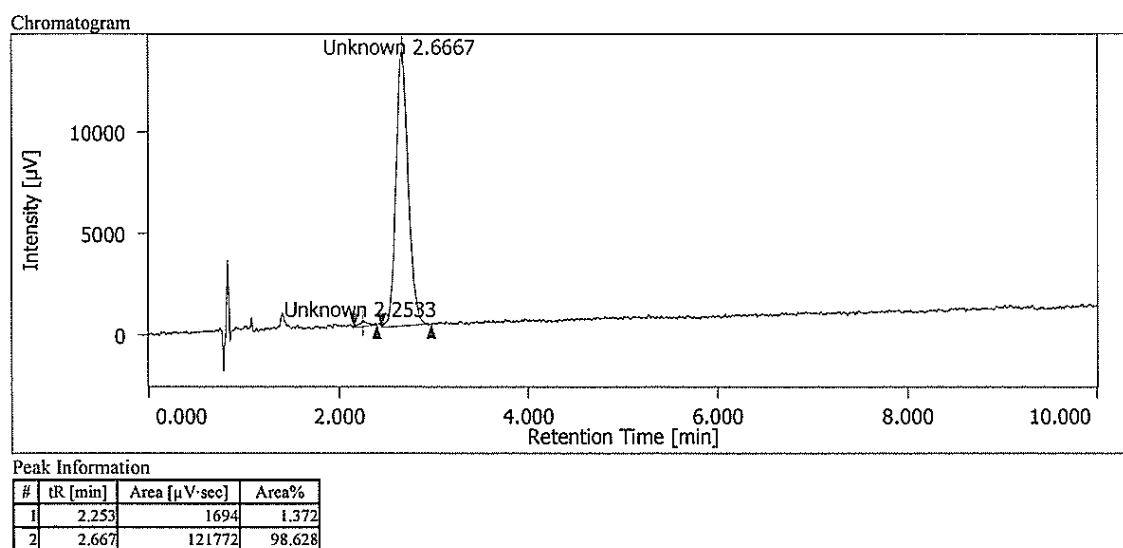
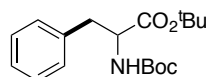


Figure S6. (*S*)-**3k**.



(*S*)-tert-butyl *N*-Boc-phenylalaninate (3l**).**

The general procedure was followed with NiBr₂(diglyme) (17.7 mg, 0.0560 mmol, 0.0700 equiv), 4-4'-di-*tert*-butyl-2,2'-bipyridine (15.0 mg, 0.0560 mmol, 0.0700 equiv), 1-(*tert*-butyl) 3-(1,3-dioxoisindolin-2-yl)-2-((*tert*-butoxycarbonyl)amino)malonate (521 mg, 1.20 mmol, 1.50 equiv), and iodobenzene (89.5 µL, 0.800 mmol, 1.00 equiv). After 11 h, the reaction mixture was filtered through a silica plug with diethyl ether, concentrated under reduced pressure, and

purified by flash chromatography (95:5 hexane/acetone, $R_f = 0.24$) to afford a light yellow oil (192 mg, 75%). Analytical data matched those in the literature.²¹

$[\alpha]_D^{23}$ 15.2 ($c=1.05$, CHCl_3), which corresponds to 48-52% *ee* depending upon which literature value is used (32²¹ to 29.5²² have been reported). Chiral-phase SFC analysis demonstrates that the material is 97% *ee* (vide infra).

¹H NMR (400 MHz; CDCl_3): δ 7.27 (q, $J = 9.5$ Hz, 4H), 7.17 (d, $J = 6.8$ Hz, 2H), 4.99 (d, $J = 7.1$ Hz, 1H), 4.45 (q, $J = 6.5$ Hz, 1H), 3.05 (d, $J = 5.8$ Hz, 2H), 1.41 (d, $J = 9.4$ Hz, 18H).

¹³C NMR (126 MHz, CDCl_3): δ 171.1, 155.2, 136.5, 129.6, 128.4, 126.9, 82.1, 79.7, 55.0, 38.66, 28.4, 28.1.

LRMS (ESI+) m/z : 322.2 $[\text{M}+\text{H}^+]$, 344.2 $[\text{M}+\text{Na}^+]$.

SFC analysis (Daicel Chiralpak IC (0.46 cm ID \times 25 cm L), 10% modifier (4:1 hexanes/EtOH) in CO_2 , 4 mL/min, $\lambda = 220$ nm, 35 °C, 12.0 MPa): tR [min] = 2.9 (1.3%) 3.2 (98.7%), 97% *ee*.

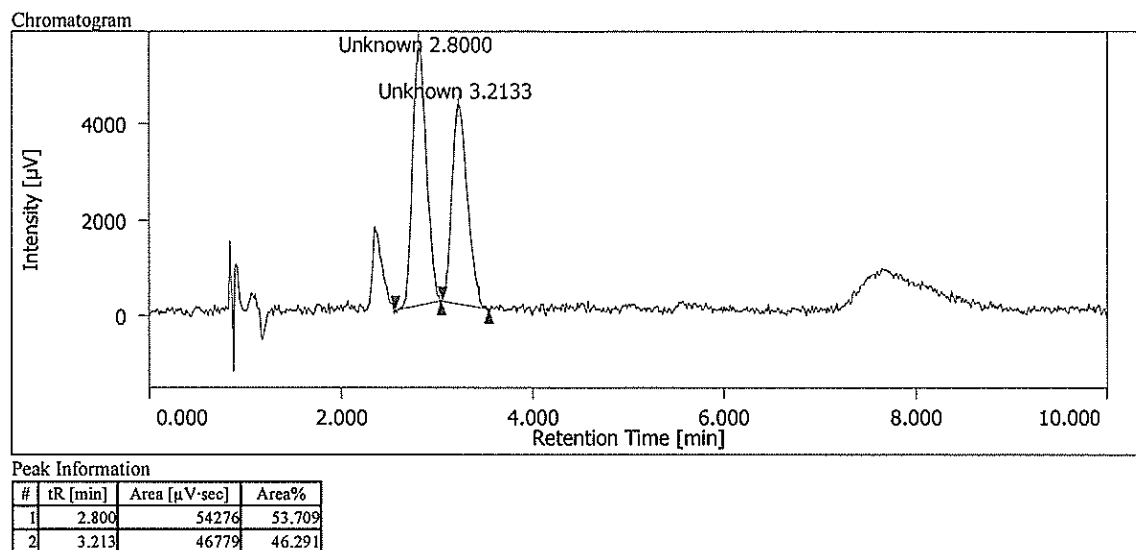


Figure S7. Enantiomeric mixture of **31**.

²¹ Konda, Y.; Takahashi, Y.; Arima, S.; Sato, N. Takeda, K.; Dobashi, K.; Baba, M.; Harigaya, Y. *Tetrahedron* **2001**, *57*, 4311–4321.

²² Strazzolini, P.; Melloni, T.; Giumanini, A. G. *Tetrahedron* **2001**, *57*, 9033.

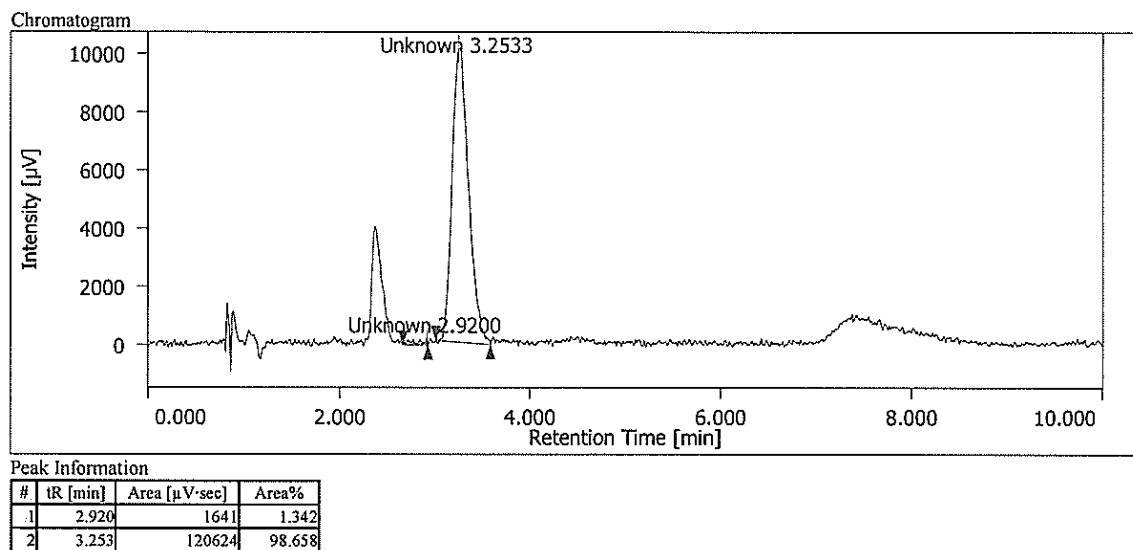
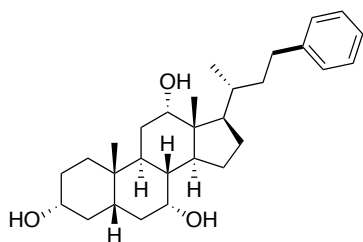


Figure S8. (*S*)-**3l**.



(3*R*,5*S*,7*R*,8*R*,9*S*,10*S*,12*S*,13*R*,14*S*,17*R*)-10,13-dimethyl-17-((*R*)-4-phenylbutan-2-yl)hexadecahydro-1*H*-cyclopenta[*a*]phenanthrene-3,7,12-triol (3m**).**

The general procedure was followed with NiBr₂(diglyme) (8.86 mg, 0.0282 mmol, 0.0700 equiv), 4-4'-di-*tert*-butyl-2,2'-bipyridine (7.52 mg, 0.0282 mmol, 0.0700 equiv), 1,3-dioxoisindolin-2-yl (*R*)-4-((3*R*,5*S*,7*R*,8*R*,9*S*,10*S*,12*S*,13*R*,14*S*,17*R*)-3,7,12-trihydroxy-10,13-dimethylhexadecahydro-1*H*-cyclopenta[*a*]phenanthren-17-yl)pentanoate (221 mg, 0.600 mmol, 1.33 equiv), iodobenzene (91.0 mg, 0.450 mmol, 1.00 equiv), Zn (52.3 mg, 0.800 mmol, 2.00 equiv), and DMA (0.500 mL). After 5 h, the reaction mixture was filtered through a silica plug, the plug was washed with diethyl ether, and the filtrate was concentrated under reduced pressure. The residue was purified by flash chromatography (100% EtOAc, R_f = 0.44) to afford a colorless solid (221 mg) that contained *N,N*-diisopropylurea (~10 wt%) and phthalimide (~4 wt%).²³ Because we had difficulty separating these impurities from **3m**, we analyzed the product mixture by ¹H NMR with an internal standard (trimethoxybenzene) to determine the actual yield of product: (191 mg, 97%). Peaks reported are for **3m** only.

¹H NMR (400 MHz; CDCl₃): δ 7.29-7.25 (m, 3H), 7.17 (d, *J* = 6.0 Hz, 2H), 4.01 (s, 1H), 3.85 (s,

²³ The identity of these species was confirmed by GC analysis vs. authentic samples, GC-MS, and comparison of ¹H NMR chemical shifts.

1H), 3.45 (ddd, $J = 9.7, 6.9, 5.2$ Hz, 1H), 2.72-2.68 (m, 1H), 2.51-2.45 (m, 1H), 2.25-2.16 (m, 1H), 1.99-1.86 (m, 2H), 1.84-1.58 (m, 8H), 1.57-1.48 (m, 3H), 1.46-1.34 (m, 3H), 1.29-1.23 (m, 1H), 1.02-0.94 (m, 1H), 0.89-0.86 (m, 3H), 0.68 (s, 2H).

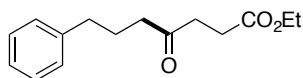
^{13}C NMR (126 MHz, CDCl_3): δ 143.4, 134.9, 128.5, 128.4, 125.7, 73.2, 72.1, 68.6, 47.42, 46.7, 42.0, 41.6, 39.8, 39.7, 38.1, 35.6, 35.4, 34.9, 34.8, 32.8, 30.7, 28.4, 27.7, 26.7, 23.4, 22.7, 17.9, 12.7.

mp 88–94 °C

IR (cm^{-1}): 3352, 2932, 2862, 2338, 1790, 1744, 1640, 1555, 1450, 1369, 1234, 1165, 1076, 1042, 1018, 980, 748, 698.

LRMS (ESI+) m/z : 463.3 [$\text{M}+\text{Na}^+$].

Coupling of NHP ester with an acid chloride.



ethyl 4-oxo-7-phenylheptanoate [108972-13-0] (5).

The reaction was set up in a nitrogen filled glove box. To an oven-dried 1-dram vial, a Teflon-coated stir-bar was added. The catalyst was generated by pre-stirring $\text{NiBr}_2(\text{diglyme})$ (17.7 mg, 0.0560 mmol, 0.0700 equiv) and 4-4'-di-*tert*-butyl-2,2'-bipyridine (15.0 mg, 0.0560 mmol, 0.0700 equiv) in DMA (1.00 mL) for ~10 min. Next, 1,3-dioxoisindolin-2-yl 4-phenylbutanoate (248 mg, 0.800 mmol, 1.00 equiv), ethyl succinyl chloride (362 μL , 2.40 mmol, 3.00 equiv), dodecane as an internal standard (10.0 μL), and zinc flake (105 mg, 1.60 mmol, 2.00 equiv) were consecutively added. The vial was capped with a screw cap fitted with a PTFE-faced silicone septum, removed from the glove box, and heated in a reaction block set to 28 °C on the benchtop with stirring at 1195 rpm. After 1 h, the reaction mixture was worked up and purified by flash chromatography (10% EtOAc in hexanes, $R_f = 0.21$) to afford a yellow oil (167 mg, 84% yield). Analytical data matched those in the literature.²⁴

^1H NMR (400 MHz; CDCl_3): δ 7.28 (t, $J = 7.4$ Hz, 2H), 7.18 (t, $J = 8.4$ Hz, 3H), 4.12 (q, $J = 7.1$ Hz, 2H), 2.62 (ddt, $J = 32.2, 15.9, 7.6$ Hz, 6H), 2.46 (t, $J = 7.3$ Hz, 2H), 1.93 (quintet, $J = 7.4$ Hz, 2H), 1.25 (t, $J = 7.0$ Hz, 3H).

^{13}C NMR (126 MHz, CDCl_3): δ 208.7, 172.8, 141.6, 128.5, 128.4, 126.0, 60.6, 41.9, 37.2, 35.1, 28.0, 25.3, 14.2.

LRMS (ESI+) m/z : 249.6 [$\text{M}+\text{H}^+$], 271.5 [$\text{M}+\text{Na}^+$].

²⁴ Debien, L.; Quiclet-Sire, B.; Zard, S. Z. *Org. Lett.* **2011**, *13*, 5676–5679.

IV. Synthesis and reactions of (dtbbpy)Ni^{II}(2-tolyl)I (**6**)

(dtbbpy)Ni^{II}(2-tolyl)I (**6**).

A solution of (dtbbpy)Ni(cod) was generated by stirring 138 mg of Ni(cod)₂ (0.5 mmol) and 134 mg of 4,4'-di-*tert*-butyl-2,2'-bipyridine (0.5 mmol) in 5 mL of THF overnight at room temperature in an argon-filled glovebox. Upon dissolution of the solids, the reaction mixture became dark purple. To this purple mixture was added 0.076 mL of 2-iodotoluene (131 mg, 0.6 mmol) and the color rapidly changed to red, indicating formation of **6**. The solution was stirred for an additional 2 h before the solvent was removed under vacuum. The solid was triturated with dry, degassed pentane three times to remove residual cyclooctadiene and 2-iodotoluene and then dried under vacuum overnight to provide 230 mg of **6** (85% yield). The ¹H and ¹³C NMR spectra are consistent with [(dtbbpy)Ni(2-tolyl)(O=C(CD₃)₂)]I being the predominant species in solution, most notably the bound acetone-*d*₆ in the ¹³C NMR gives rise to characteristic peaks at 209.9 (s) and 54.6 (apparent q, expected septet for -CD₃). The propensity of Ni(II) halide complexes to exist as solvated cations is well documented.²⁵

¹H NMR (500 MHz; acetone-*d*₆): δ 9.56 (d, *J* = 2.9 Hz, 1H), 8.40 (d, *J* = 16.4 Hz, 2H), 7.65 (s, 1H), 7.57 (d, *J* = 6.9 Hz, 1H), 7.38 (s, 1H), 6.84 (d, *J* = 2.8 Hz, 1H), 6.76 (d, *J* = 5.7 Hz, 1H), 6.70-6.69 (m, 1H), 6.63 (d, *J* = 6.8 Hz, 1H), 2.95 (s, 3H), 1.43 (s, 9H), 1.37 (s, 9H).

¹³C NMR (126 MHz, acetone-*d*₆): δ 209.94, 164.42, 164.01, 156.64, 154.20, 154.04, 149.82, 148.97, 143.42, 138.49, 127.80, 124.37, 124.28, 123.63, 122.62, 119.66, 119.25, 69.15, 54.64 (q, *J* = 19.1 Hz), 36.18 (2C), 30.37, 27.20.

Anal. Calcd for C₂₅H₃₁N₂NiI: 55.08% C, 5.73% H, 5.14% N; found 53.75% C, 5.69% H, 4.80% N.

UV-Vis spectrum in DMF (**Figure S9**): ε₄₃₀ = 2598 M⁻¹cm⁻¹.

²⁵ (a) Osakada, K.; Yamamoto, T. *Coord. Chem. Rev.* **2000**, *198*, 379-399; (b) Ishiguro, S.-i.; Ozutsumi, K. *Bull. Chem. Soc. Jpn.* **1989**, *62*, 2392-2393.

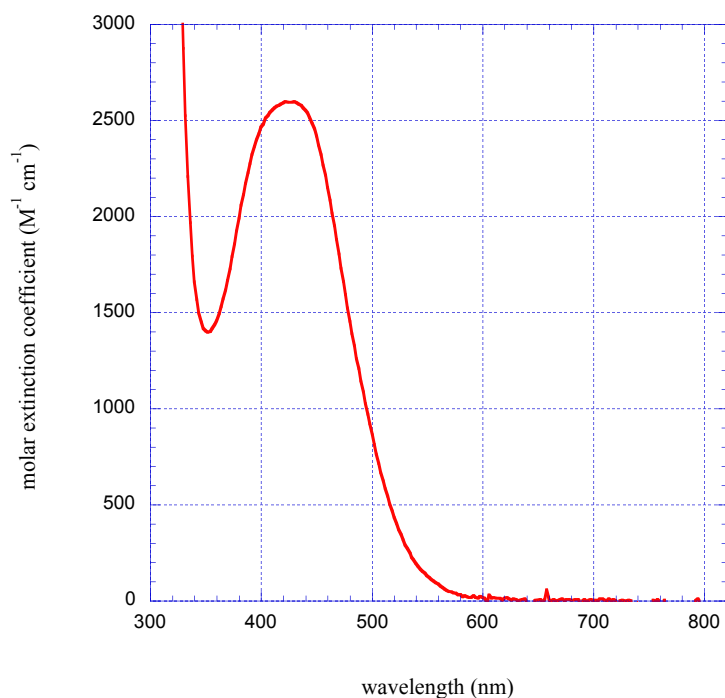


Figure S9. UV-vis of **6** recorded in DMF at rt.

NMR analysis of reaction of **6 with **1b**.**

A solution of 0.0125 mmol (6.8mg) (dtbbpy)Ni^{II}(2-tolyl)(I) (**6**) was generated in 0.75 mL of DMF-*d*₇. To this solution was added 1,3-dioxoisindolin-2-yl 4-phenylbutanoate (**1b**) (0.13 mmol, 40 mg). During this time the color changed from red to orange indicating reaction. The resulting orange homogenous solution was then analyzed by ¹H NMR using paramagnetic parameters. Consumption of **6** was confirmed in the diamagnetic region (**Figure S10**). A paramagnetic species was present in the reaction mixture as indicated by broad peaks at 60, 41, and 19 ppm (**Figure S11**). Examination of this material by EPR spectroscopy at both rt and 15 K found no signal, consistent with an integer-spin system.

UV-Vis (**Figure S12**): $\epsilon_{440} = 1931 \text{ M}^{-1}\text{cm}^{-1}$.

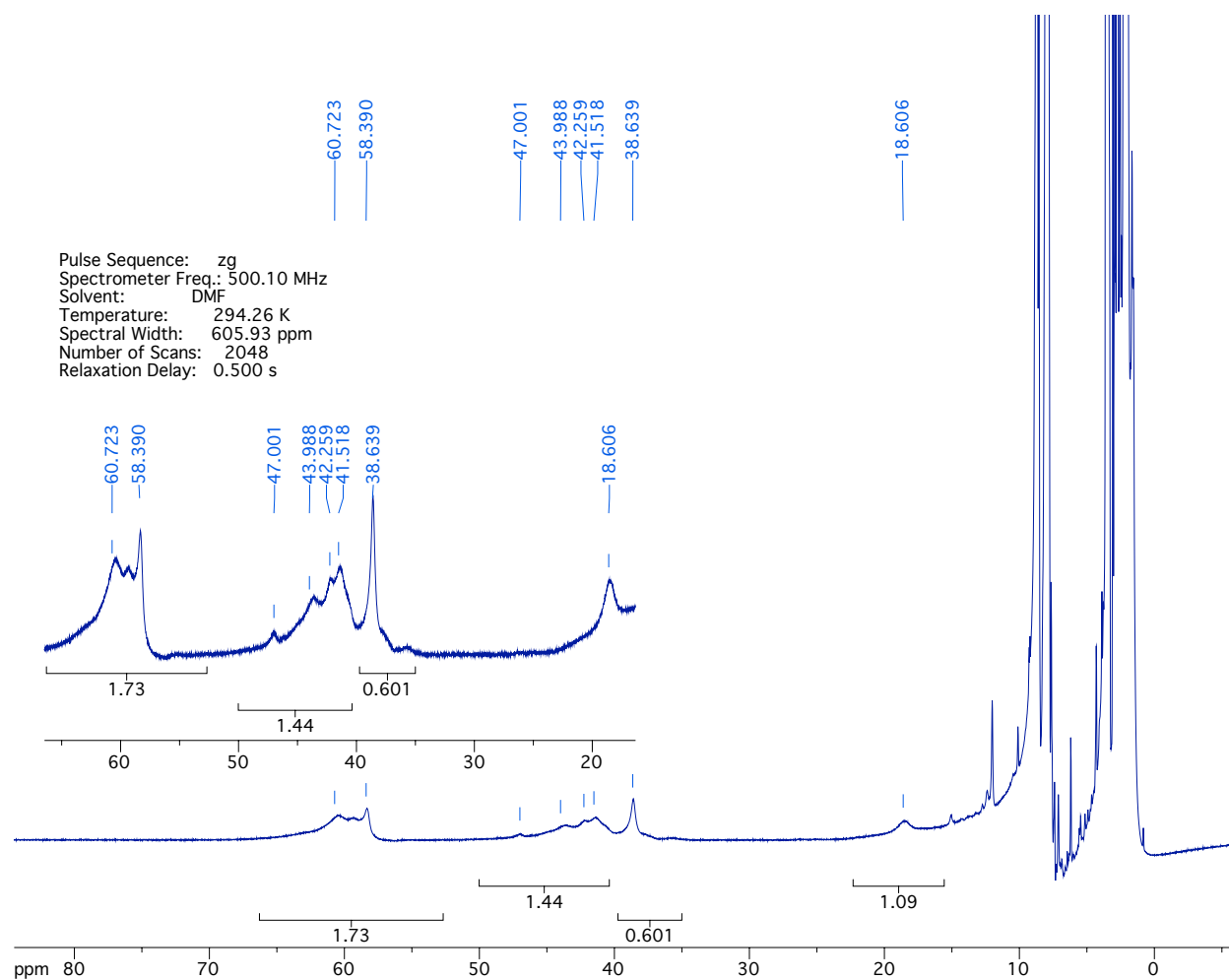


Figure S11. Paramagnetic ^1H NMR spectrum of **6+1b** after stirring overnight in $\text{DMF-}d_7$ at rt.

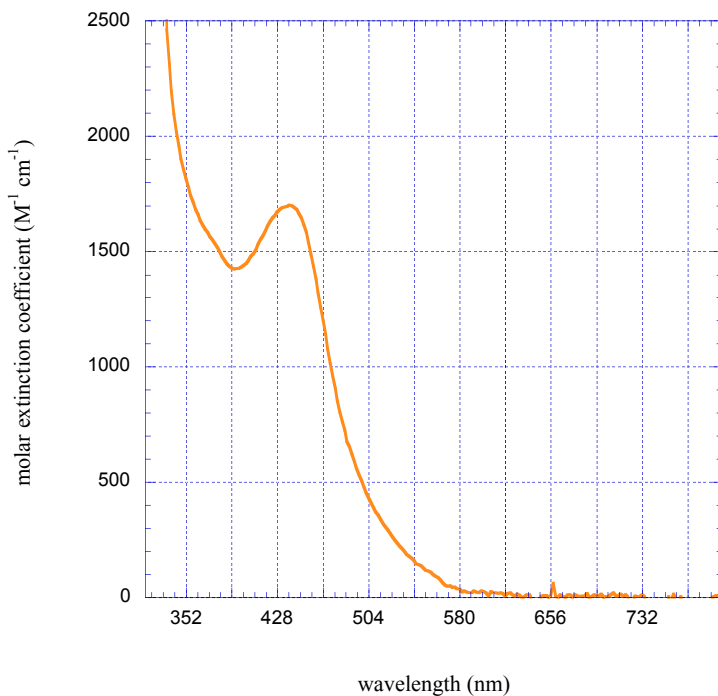


Figure S12. UV-vis spectrum of **6+1b** after stirring overnight in DMF-*d*₇ at rt.

Reaction of (dtbbpy)Ni^{II}(2-tolyl)(I) (**6**) with **1b**.

To a 1 mL oven-dried conical vial equipped with a PTFE-coated stir-vane was added (dtbbpy)Ni^{II}(2-tolyl)(I) (**6**) (6.8 mg, 0.0125 mmol), 1,3-dioxoisindolin-2-yl 4-phenylbutanoate (**1b**) (40 mg, 0.13 mmol), dodecane (10 μL, 0.044 mmol), and 250 μL of DMF. The vial was capped with a PTFE-faced silicone septum, removed from the glovebox, and set to stir at room temperature. GC analysis of acid-quenched aliquots of this reaction mixture showed product **3h** (47% average yield over 3 runs, corrected GC yield). We could not account for all of the mass of **6** added to the reaction mixture – only trace toluene and no 2,2'-bitoluene were observed.

Reaction of (dtbbpy)Ni^{II}(2-tolyl)(I) (**6**) with **1b** and Zn.

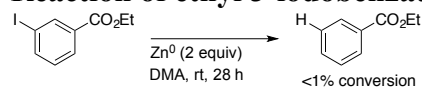
In a 1 mL oven-dried conical vial equipped with a PTFE-coated stir-vane was added (dtbbpy)Ni^{II}(2-tolyl)(I) (**6**) (6.8 mg, 0.0125 mmol), 1,3-dioxoisindolin-2-yl 4-phenylbutanoate (**1b**) (40 mg, 0.13 mmol), zinc (1.6 mg, 0.025 mmol), dodecane (10 μL, 0.044 mmol), and 250 μL of DMF. The vial was capped with a PTFE-faced silicone septum, removed from the

glovebox, and set to stir at room temperature. GC analysis of a acid-quenched (NaHSO_4 (aq)) aliquots of this reaction mixture showed product **3h** (98% average yield over 3 runs, corrected GC yield). At later reaction points, propylbenzene and 1,6-diphenylhexane started growing in, presumably due to the action of zinc and nickel in the absence of an aryl electrophile.

Catalytic reaction of 2-iodotoluene with **1b** in DMF.

Run as the general procedure on 0.4 mmol scale with **1b** and 2-iodotoluene in a 1:1 ratio (vide supra) except in dry DMF. Yield was calculated by GC vs. an internal standard (dodecane). After 4 h, **1b** had been completely consumed but 2-iodotoluene remained. In addition to a 46% yield of **3h**, a substantial amount of 1,6-diphenylhexane (the dimer derived from **1b**) was also present.

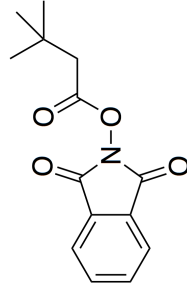
Reaction of ethyl 3-iodobenzoate with zinc.



Ethyl 3-iodobenzoate was subjected to standard reaction conditions (vide supra) except that nickel and ligand were omitted from the reaction. The mixture was stirred at rt for 28 hours and monitored by GC analysis. Comparison of the chromatograms to chromatograms of authentic starting material and ethyl benzoate confirmed that <1% of the aryl iodide was reduced in 28 h. For comparison, catalytic reactions are complete in 12 h or less.

V. NMR Spectra

7.897
7.890
7.884
7.876
7.798
7.791
7.785
7.777
7.777
7.260

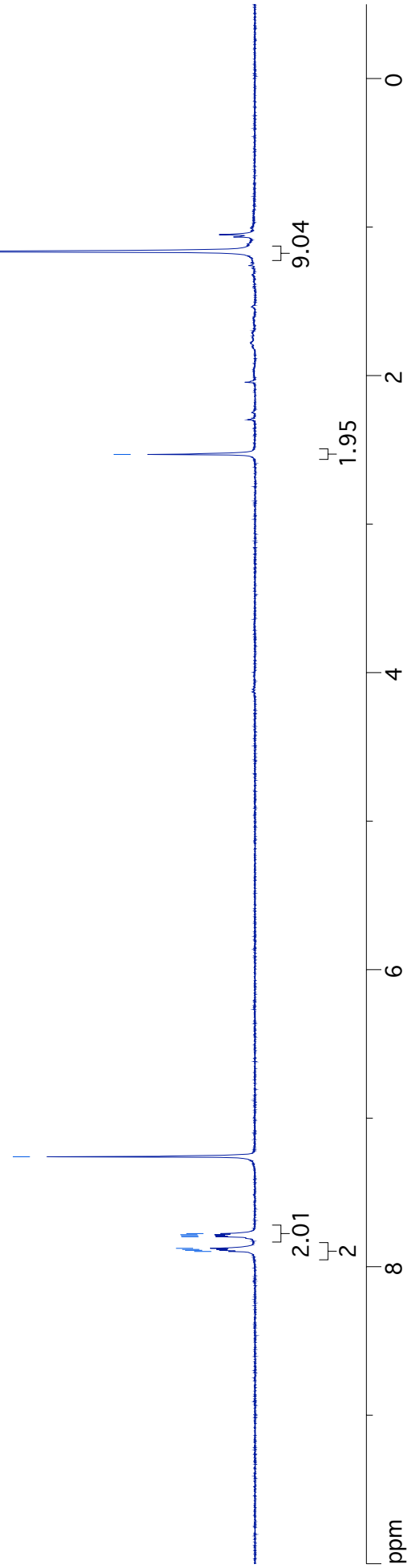


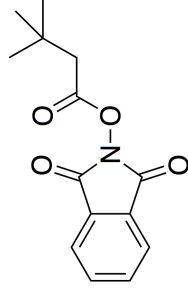
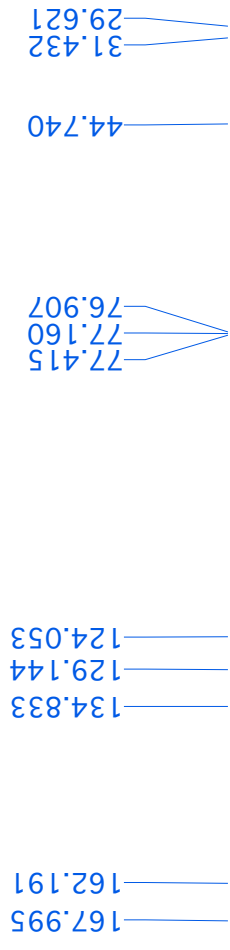
1a

Spectrometer Freq.: 400.13 MHz
Solvent: CDCl₃
Temperature: 298.16 K
Relaxation Delay: 1.000 s

CS3

2.531
1.167

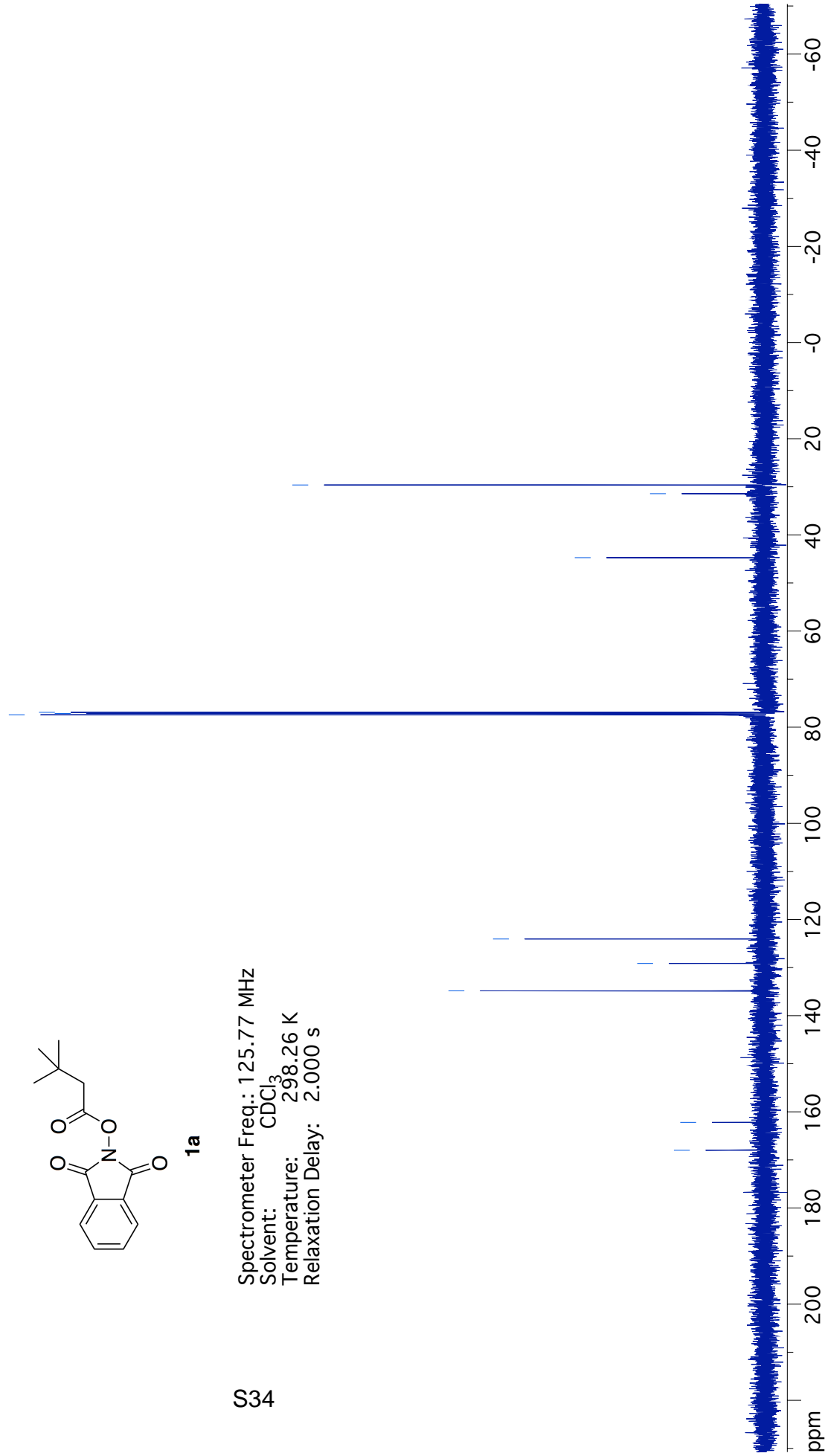




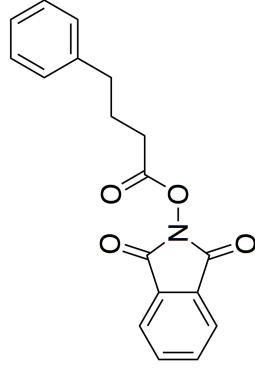
1a

S34

Spectrometer Freq.: 125.77 MHz
 Solvent: CDCl₃
 Temperature: 298.26 K
 Relaxation Delay: 2.000 s



7.906
7.898
7.893
7.885
7.805
7.798
7.792
7.784
7.334
7.314
7.296
7.260
7.239
7.220

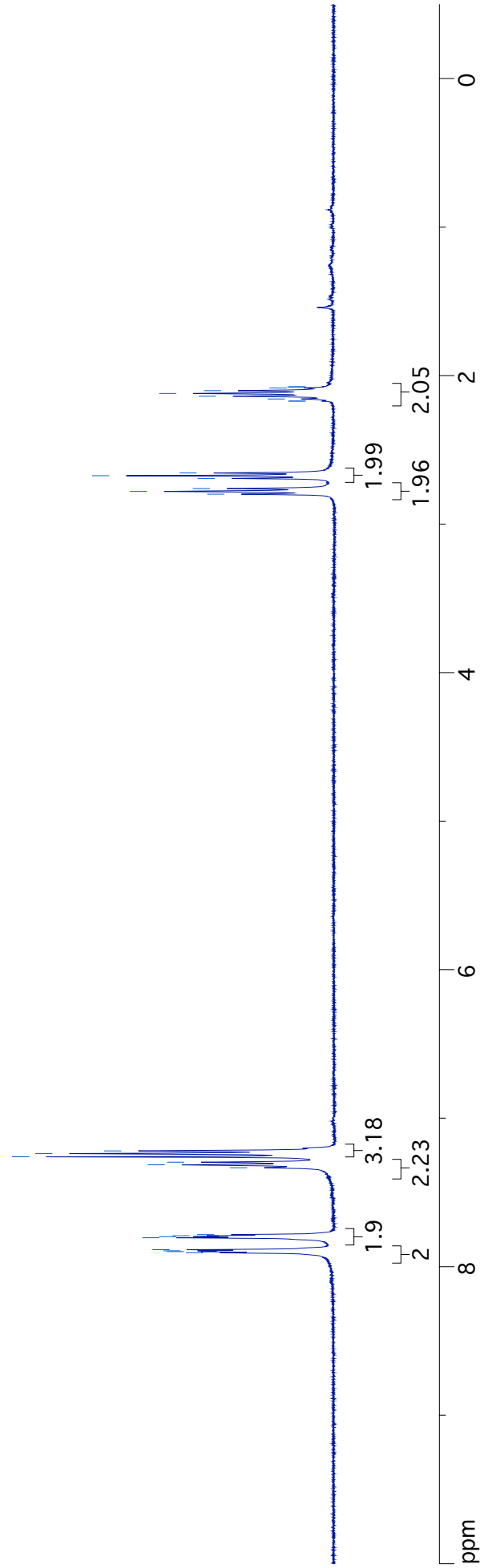


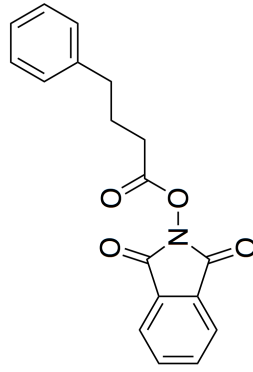
1b

S35

Spectrometer Freq.: 400.13 MHz
Solvent: CDCl₃
Temperature: 298.16 K
Relaxation Delay: 1.000 s

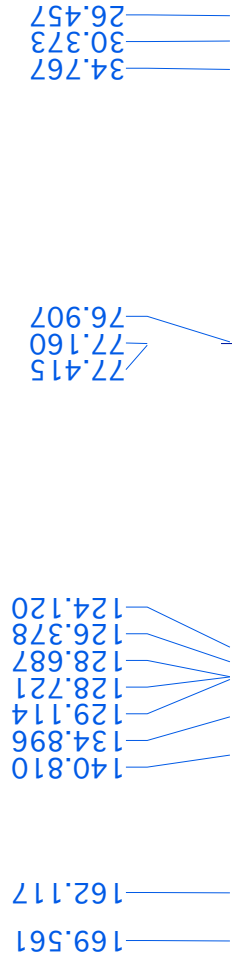
2.799
2.780
2.692
2.674
2.656
2.172
2.171
2.158
2.139
2.120
2.102
2.083
2.077
2.075

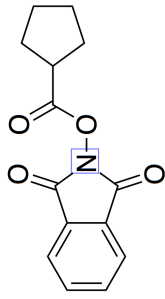
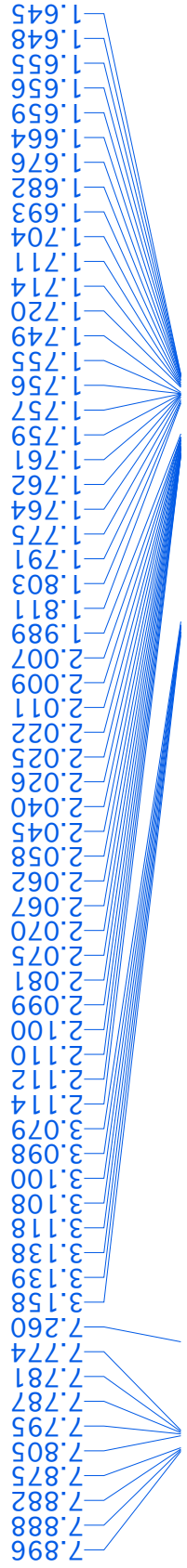




1b

Spectrometer Freq.: 125.77 MHz
Solvent: CDCl₃
Temperature: 298.26 K
Relaxation Delay: 2.000 s

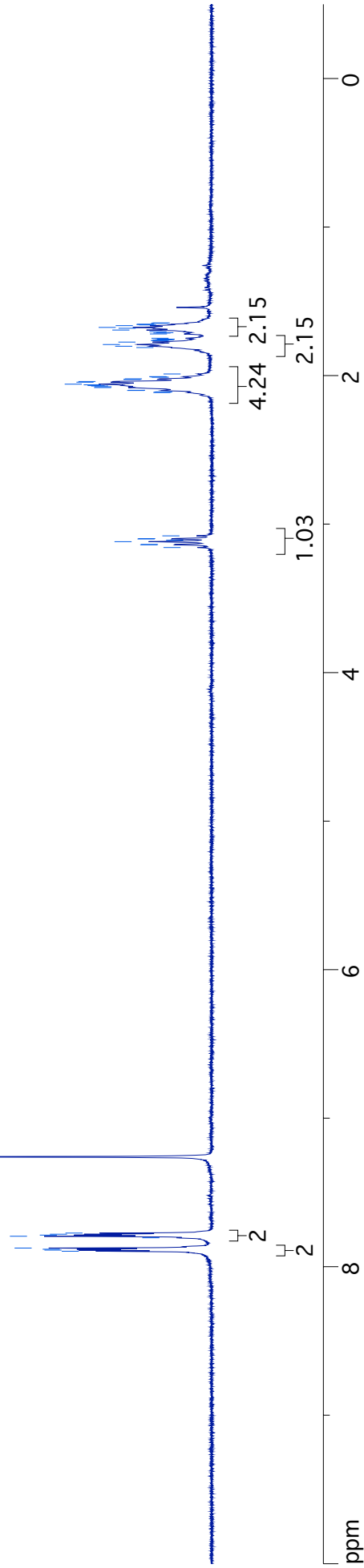




1c

Spectrometer Freq.: 400.13 MHz
 Solvent: CDCl₃
 Temperature: 298.16 K
 Relaxation Delay: 1.000 s

S37

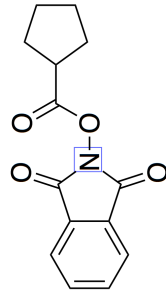


26.079
30.370
40.811

76.905
77.160
77.413

124.038
129.166
134.811

162.255
172.999



1c

Spectrometer Freq.: 125.77 MHz
Solvent: CDCl₃
Temperature: 298.26 K
Relaxation Delay: 2.000 s

S38

ppm

200

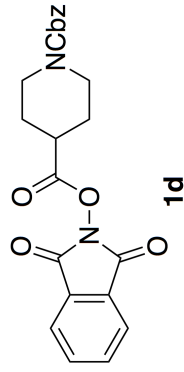
150

100

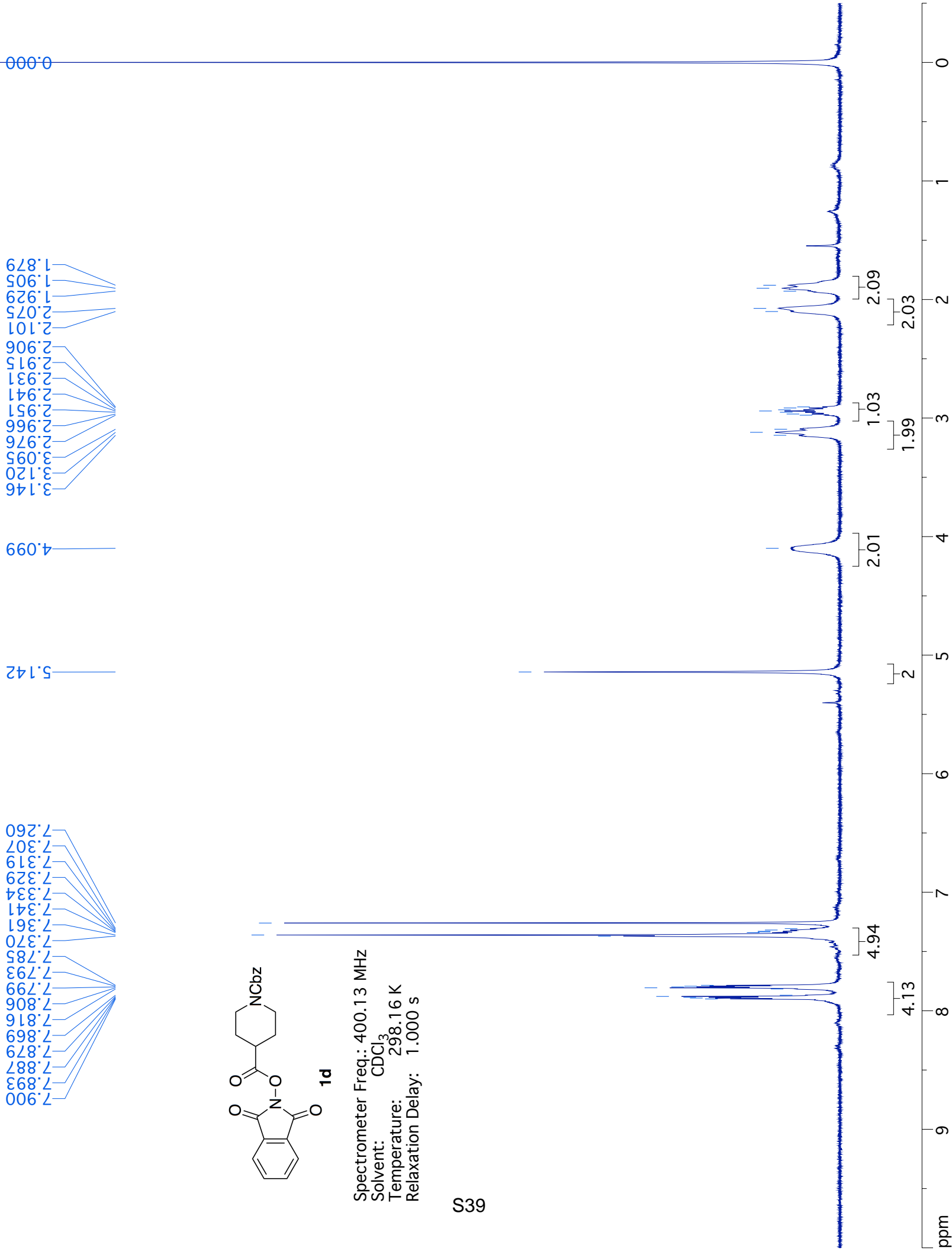
50

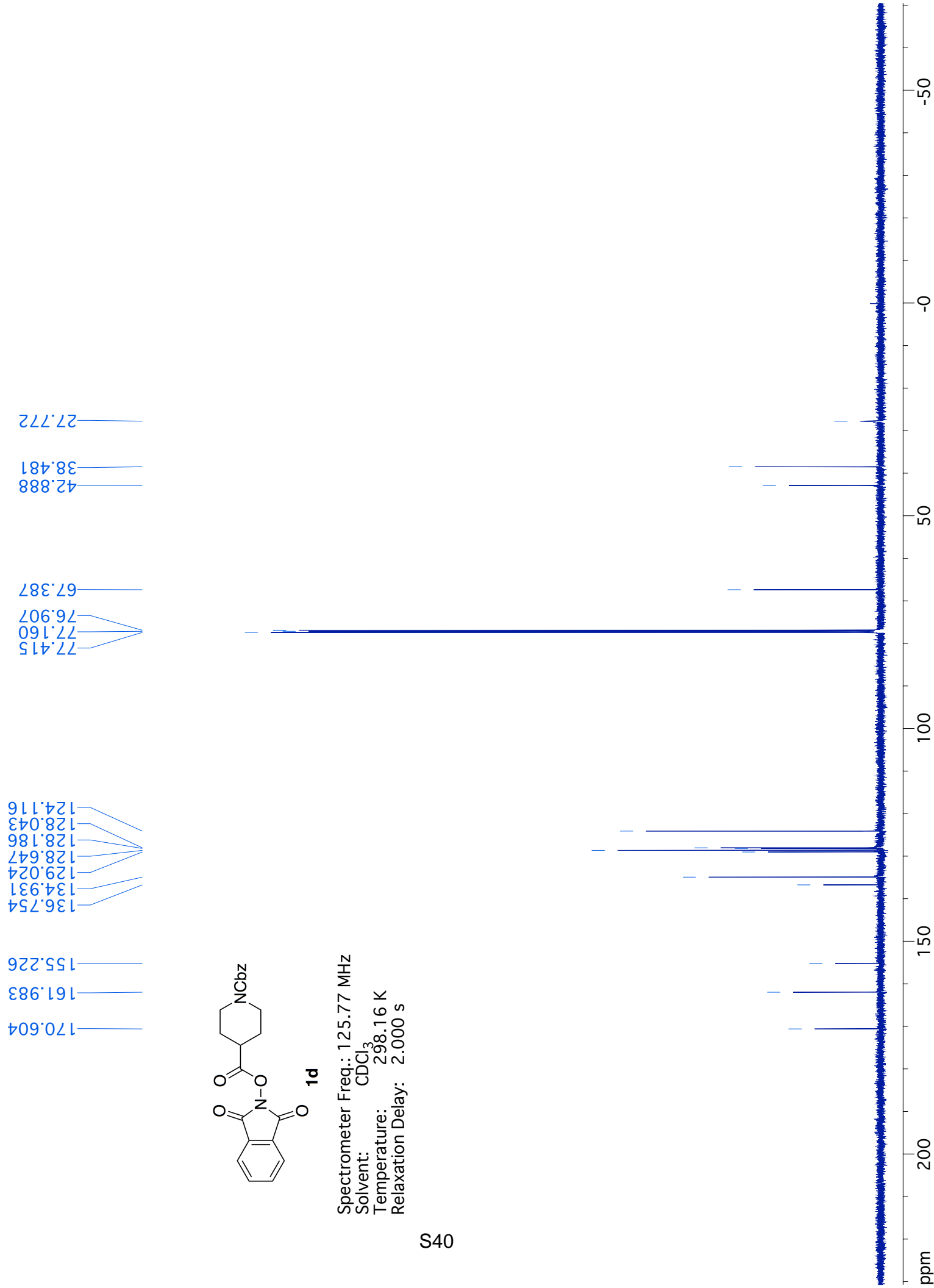
-0

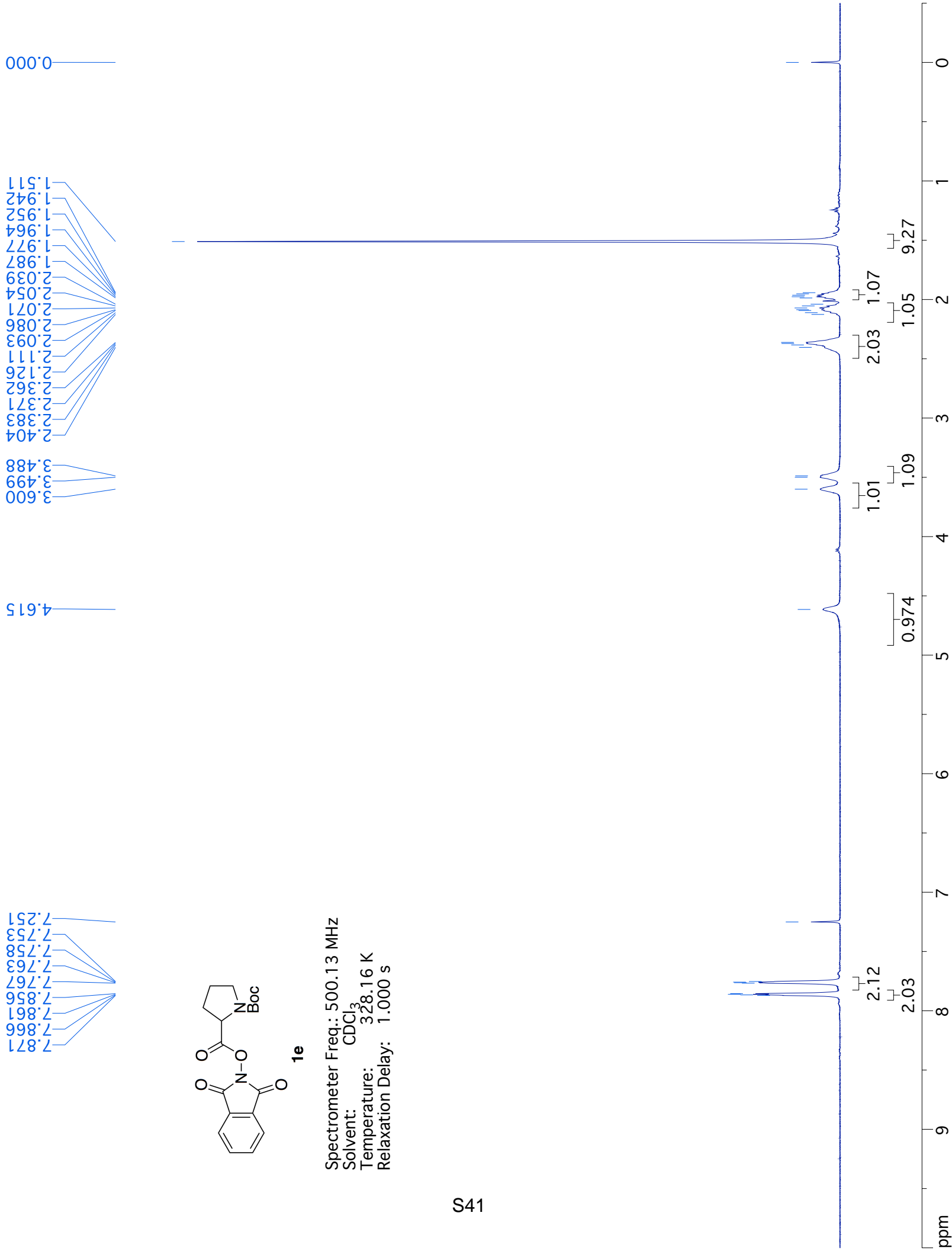
-50

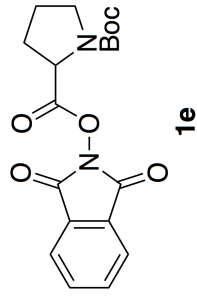


Spectrometer Freq.: 400.13 MHz
 Solvent: CDCl₃
 Temperature: 298.16 K
 Relaxation Delay: 1.000 s

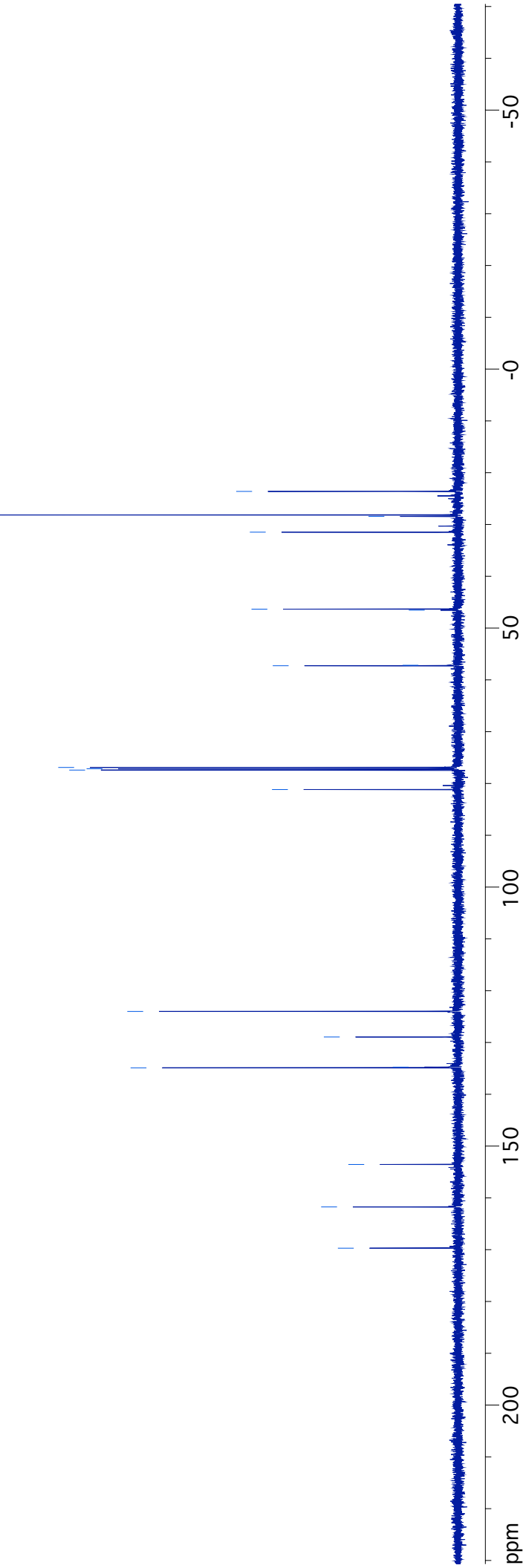




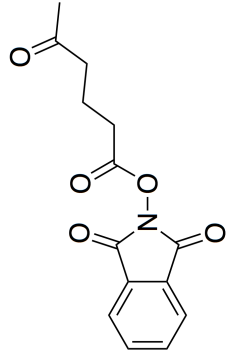




Spectrometer Freq.: 125.77 MHz
 Solvent: CDCl₃
 Temperature: 298.26 K
 Relaxation Delay: 2.000 s



7.897
7.889
7.883
7.876
7.804
7.796
7.790
7.782
7.260

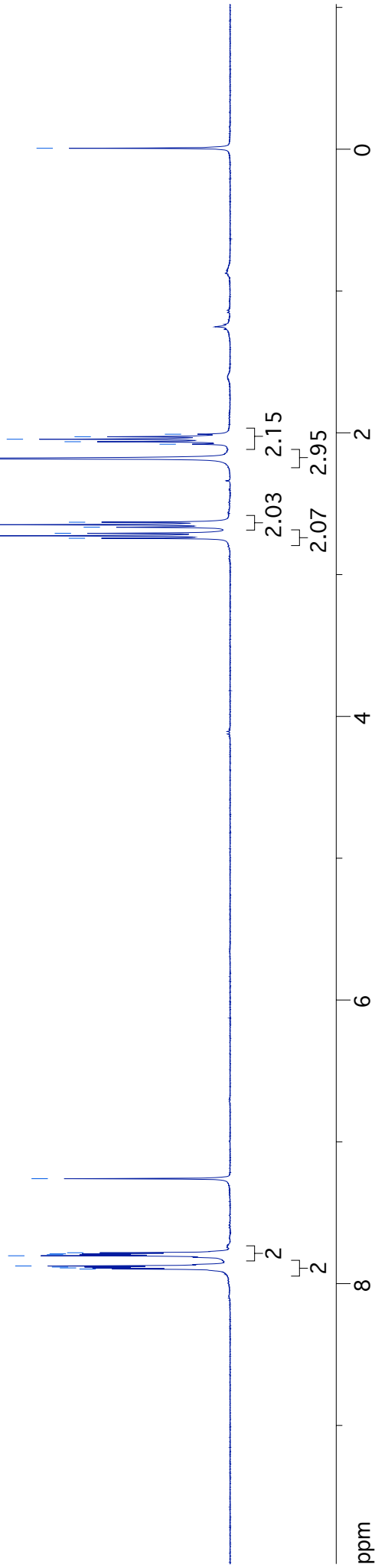


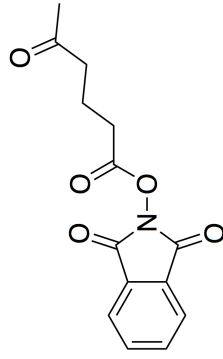
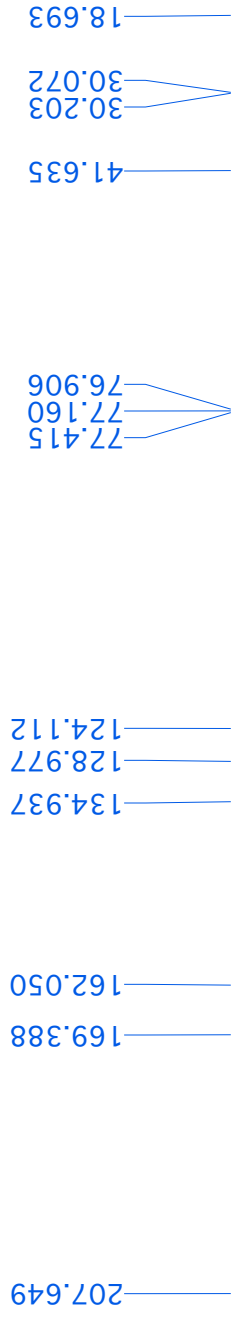
1i

Spectrometer Freq.: 400.13 MHz
Solvent: CDCl₃
Temperature: 298.16 K
Relaxation Delay: 1.000 s

2.744
2.726
2.709
2.666
2.648
2.630
2.181
2.080
2.063
2.045
2.028
2.010

-0.007

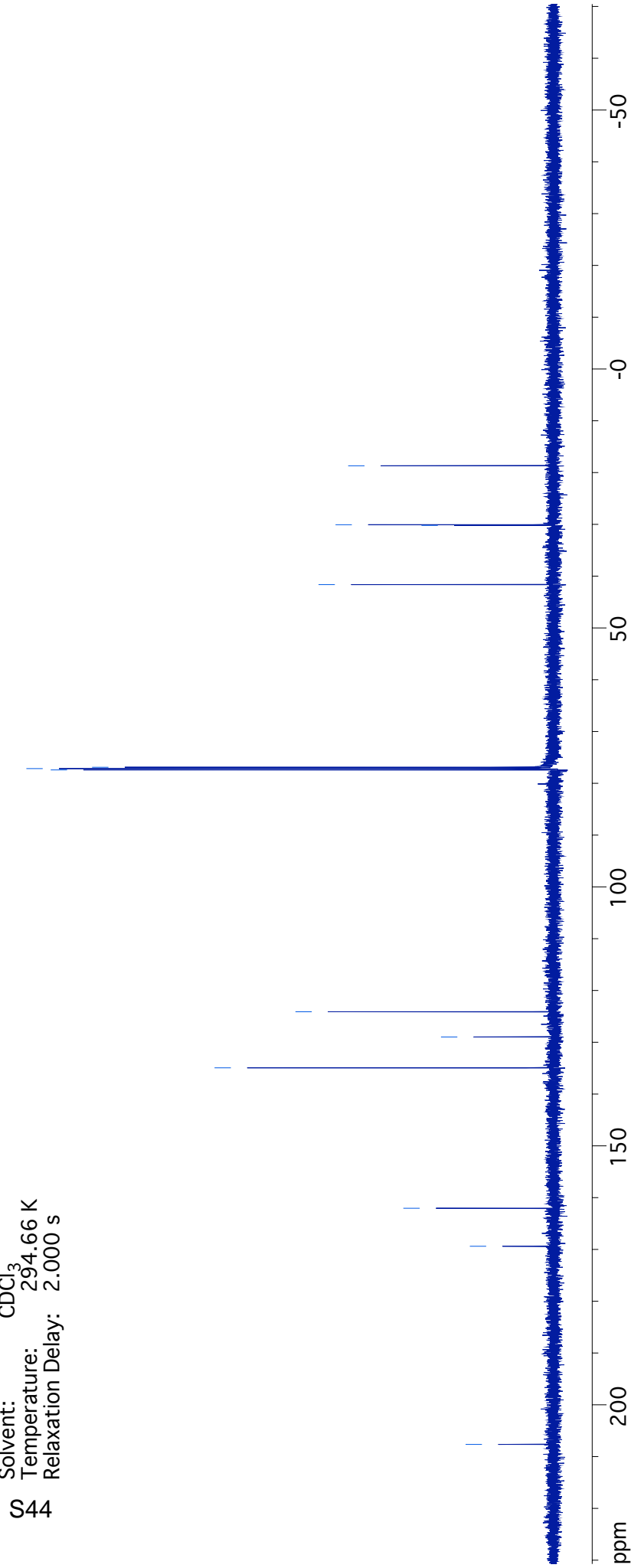


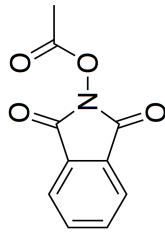


1i

Spectrometer Freq.: 125.77 MHz
Solvent: CDCl₃
Temperature: 294.66 K
Relaxation Delay: 2.000 s

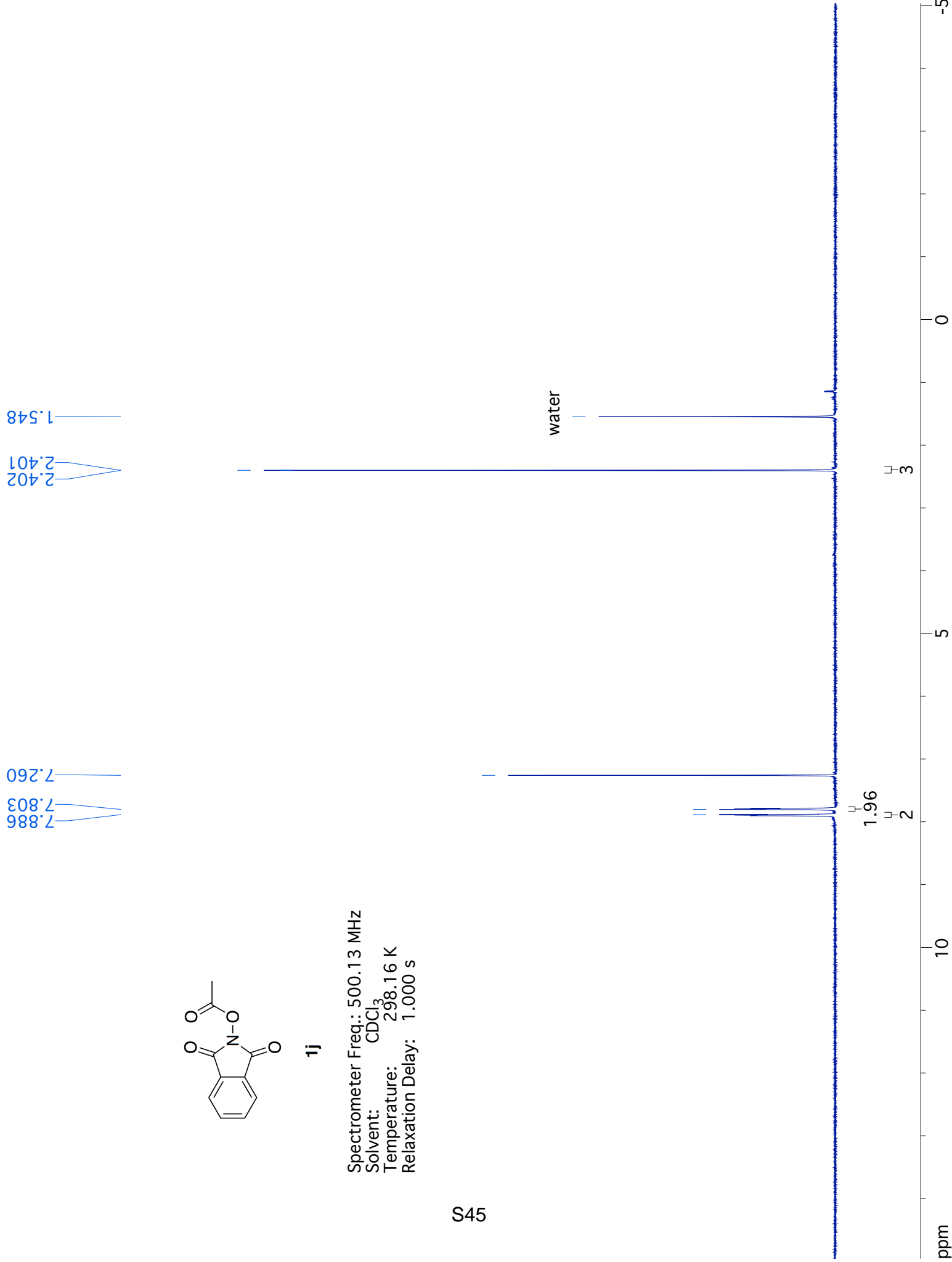
449





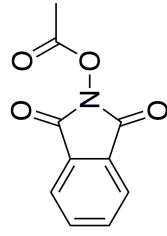
1j

Spectrometer Freq.: 500.13 MHz
Solvent: CDCl₃
Temperature: 298.16 K
Relaxation Delay: 1.000 s



S45

ppm

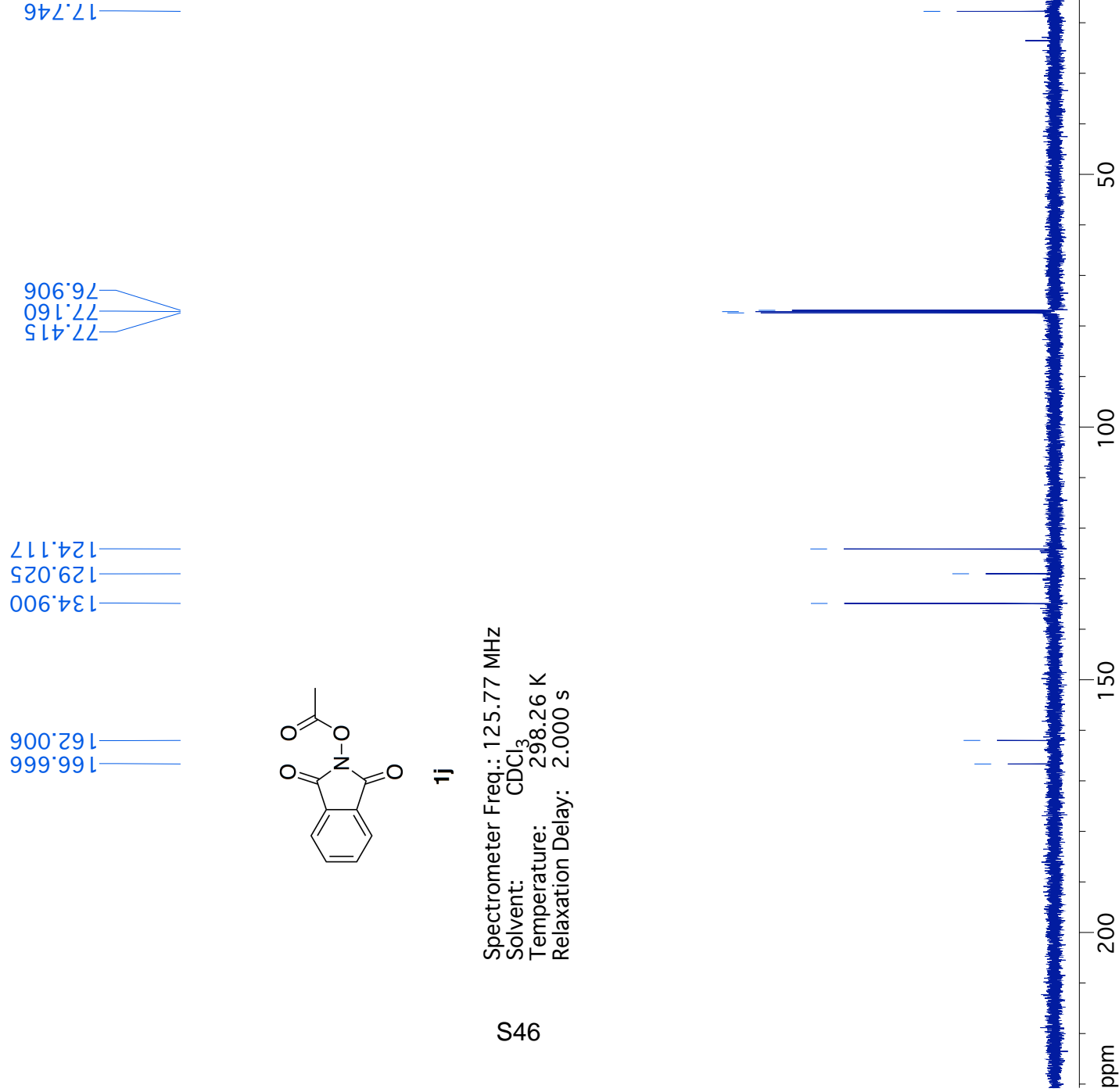
**1j**

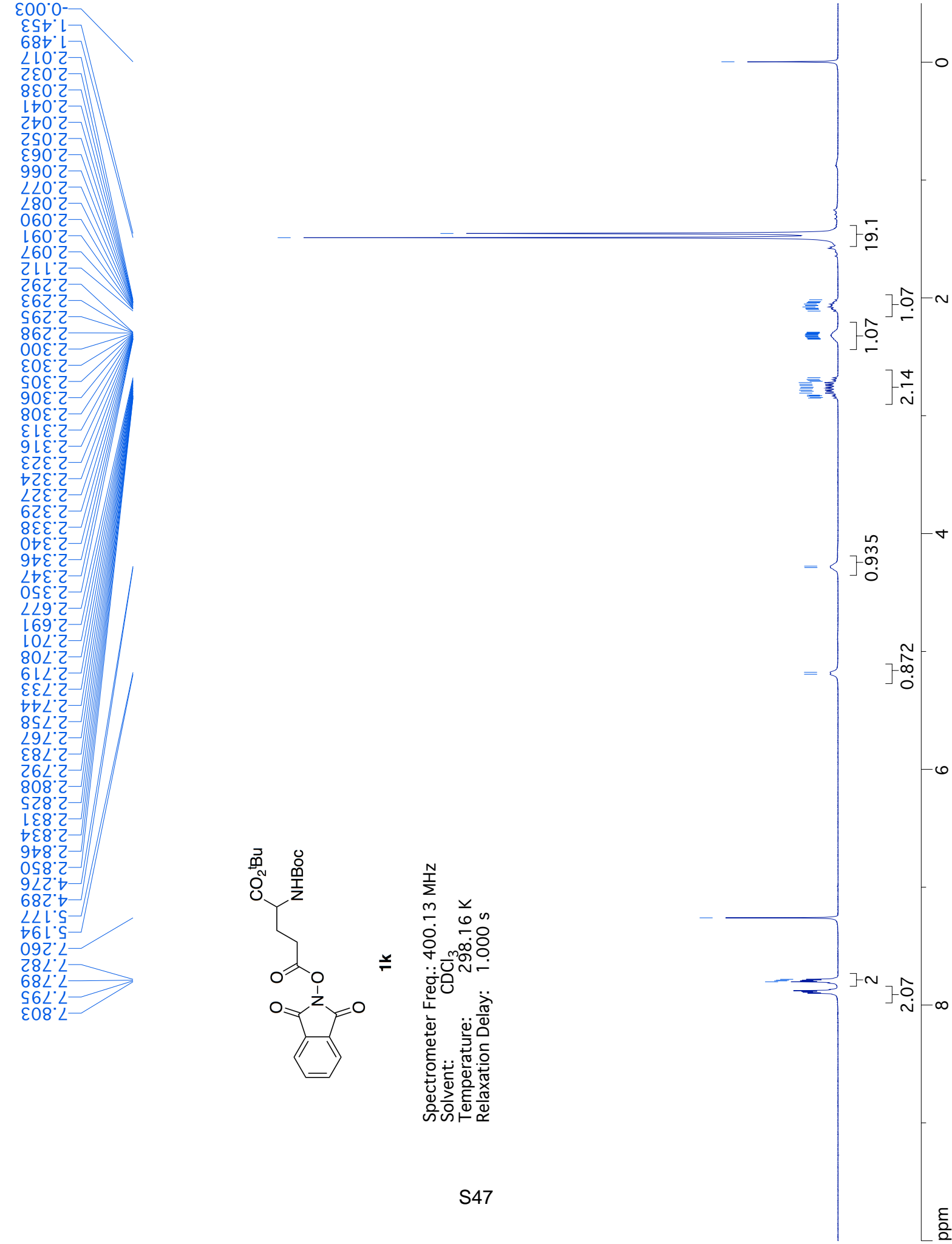
Spectrometer Freq.: 125.77 MHz

Solvent: CDCl₃

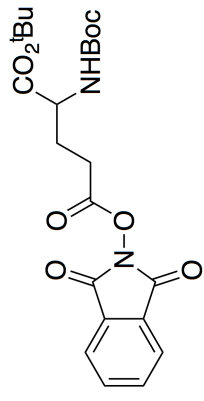
Temperature: 298.26 K

Relaxation Delay: 2.000 s





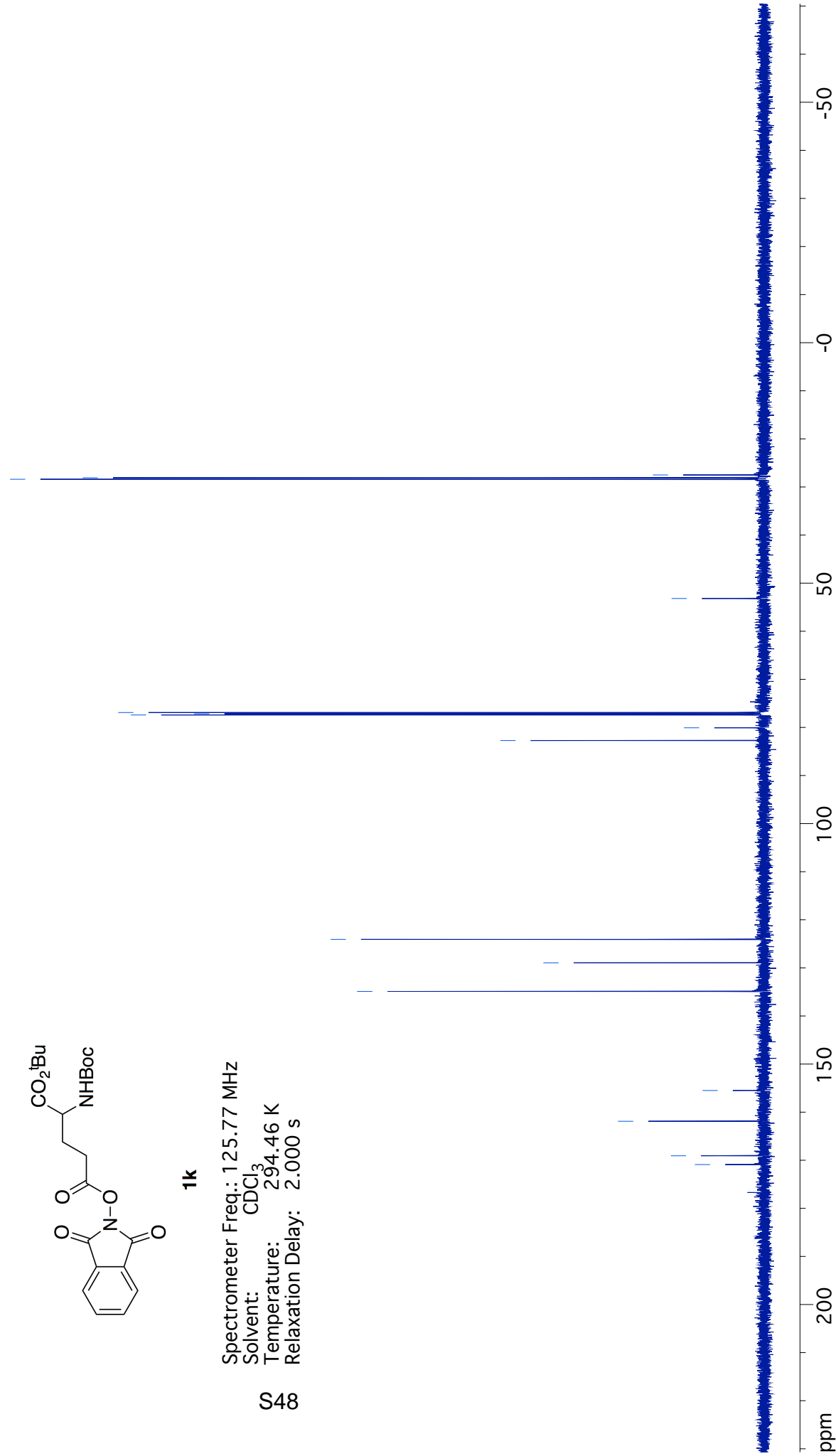
170.897
 169.071
 161.894
 155.496
 134.896
 128.949
 124.078
 82.725
 80.079
 77.413
 77.160
 76.906
 53.189
 28.396
 28.088
 27.500

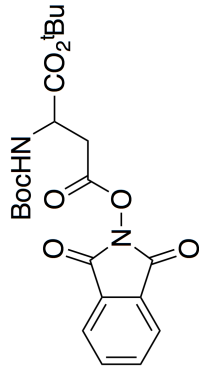


1k

Spectrometer Freq.: 125.77 MHz
 Solvent: CDCl₃
 Temperature: 294.46 K
 Relaxation Delay: 2.000 s

S48





11

Spectrometer Freq.: 400.13 MHz
 Solvent: CDCl₃
 Temperature: 298.16 K
 Relaxation Delay: 1.000 s

1.483
1.464

3.310
3.301
3.250
3.239

4.572
4.574
4.576
4.579
4.581
4.584
4.588
4.589
4.591
5.493
5.512
5.513

7.900
7.892
7.887
7.879
7.879
7.804
7.796
7.791
7.783
7.760

19.2

2.16

0.97

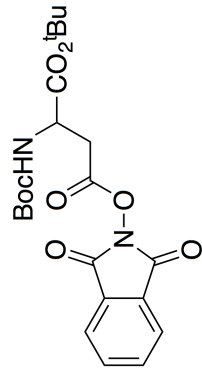
0.947

2

2.09

ppm

168.824
167.558
161.657
155.417
134.925
128.935
124.108

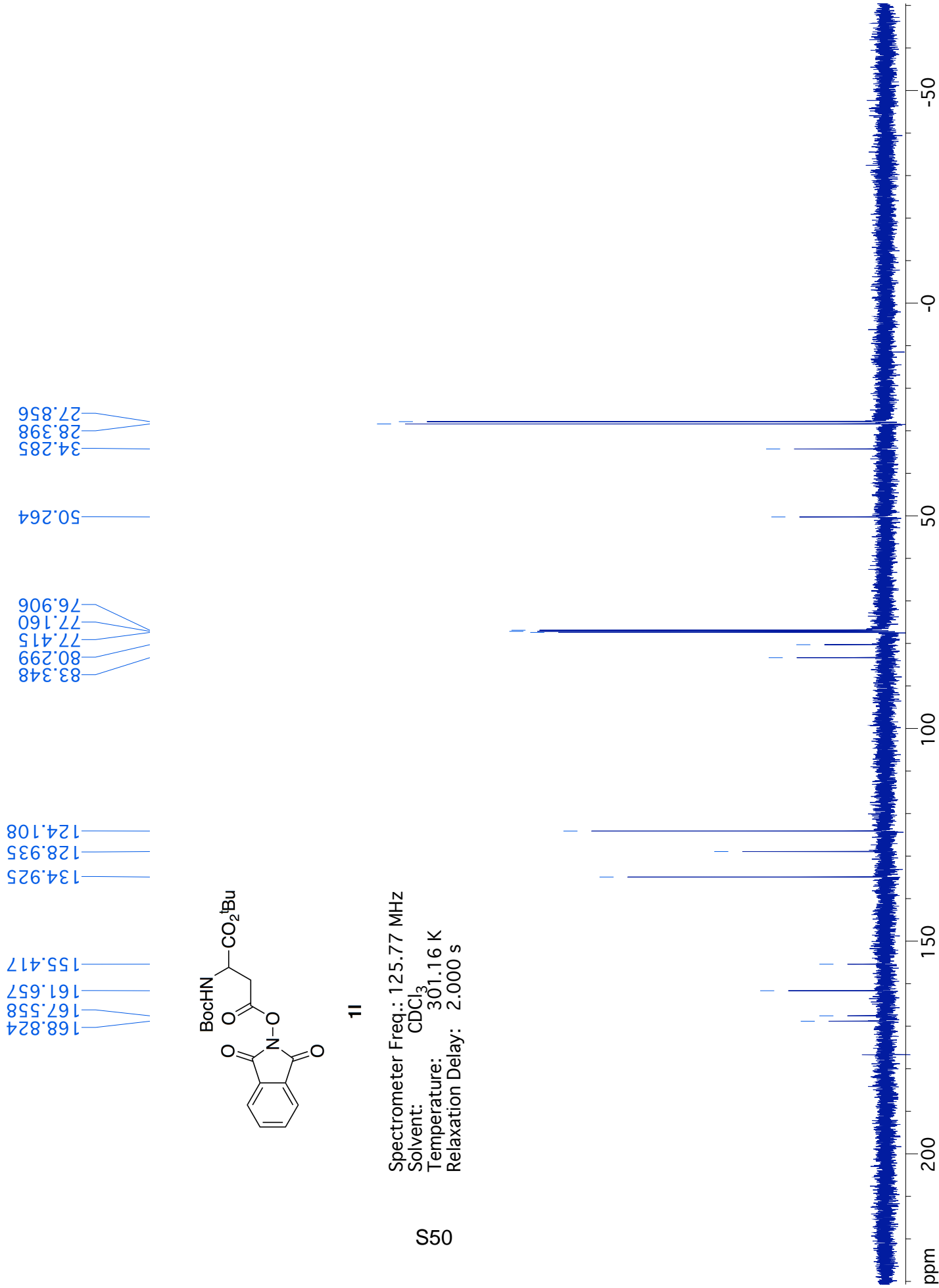


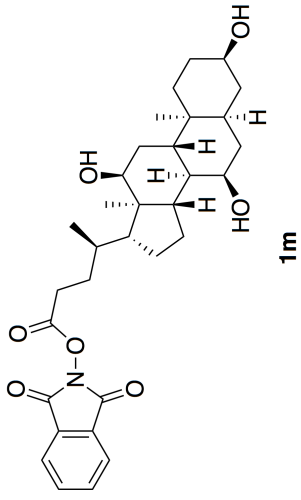
11

Spectrometer Freq.: 125.77 MHz
Solvent: CDCl₃
Temperature: 301.16 K
Relaxation Delay: 2.000 s

S50

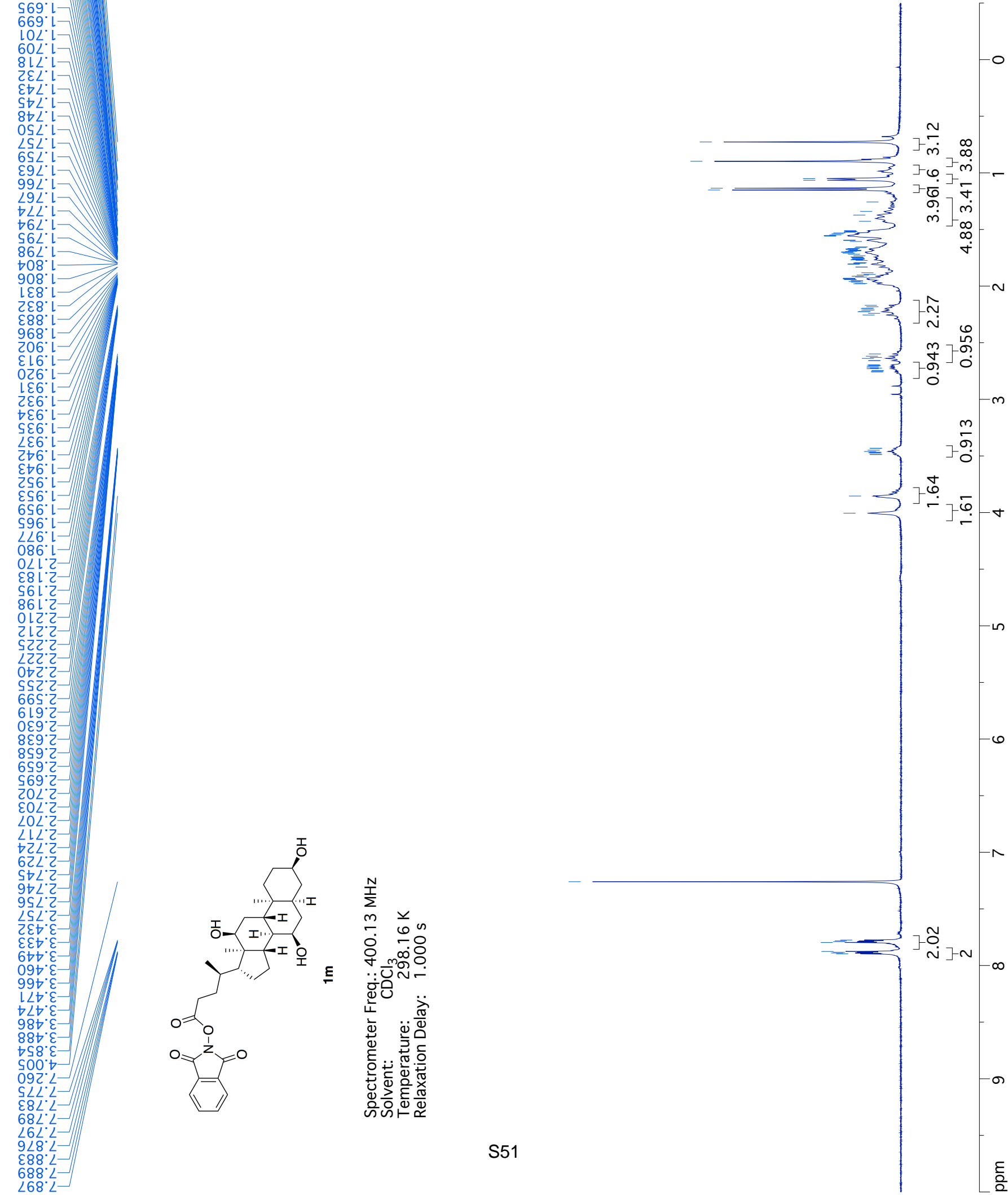
83.348
80.299
77.415
77.160
76.906
50.264
34.285
28.398
27.856

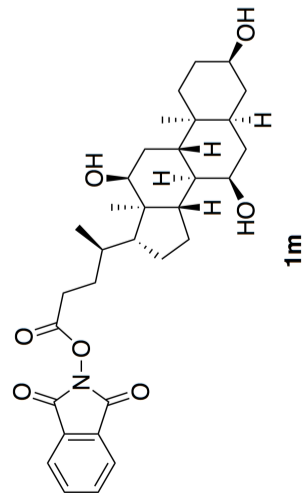




Spectrometer Freq.: 400.13 MHz
 Solvent: CDCl₃
 Temperature: 298.16 K
 Relaxation Delay: 1.000 s

S51





1m

Spectrometer Freq.: 125.77 MHz
 Solvent: CDCl₃
 Temperature: 298.16 K
 Relaxation Delay: 2.000 s

77.413
 77.160
 76.905
 73.046
 72.138
 68.521
 47.134
 46.748
 42.438
 42.120
 41.619
 39.890
 39.769
 35.368
 35.111
 34.840
 34.698
 30.781
 30.720
 28.576
 28.210
 27.549
 26.832
 23.636
 23.338
 22.711
 17.464
 12.717

170.193
 162.153
 134.864
 129.110
 124.104

ppm

150

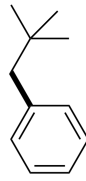
100

50

-0

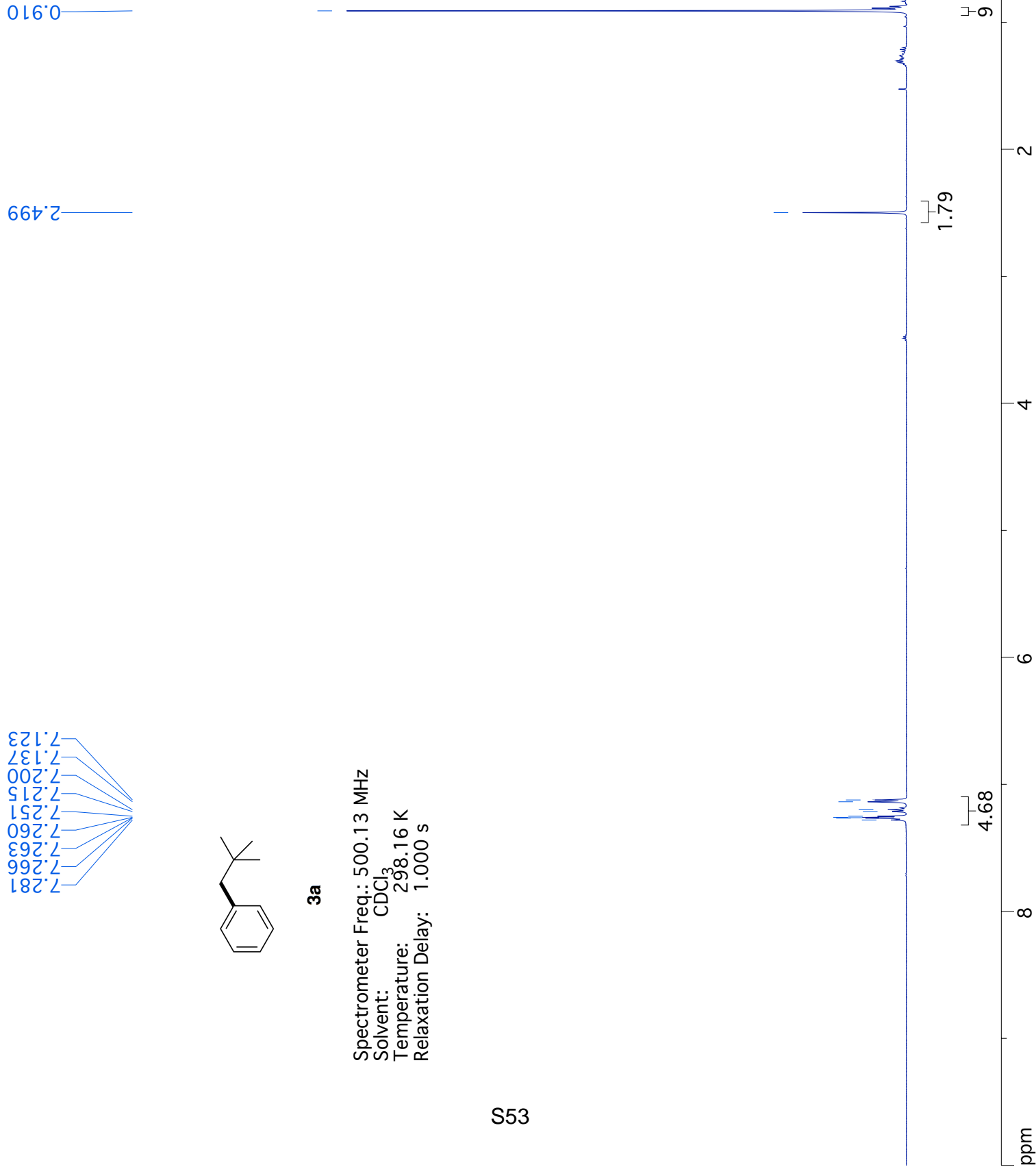
-50

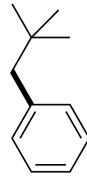
7.281
7.266
7.263
7.260
7.251
7.215
7.200
7.137
7.123



3a

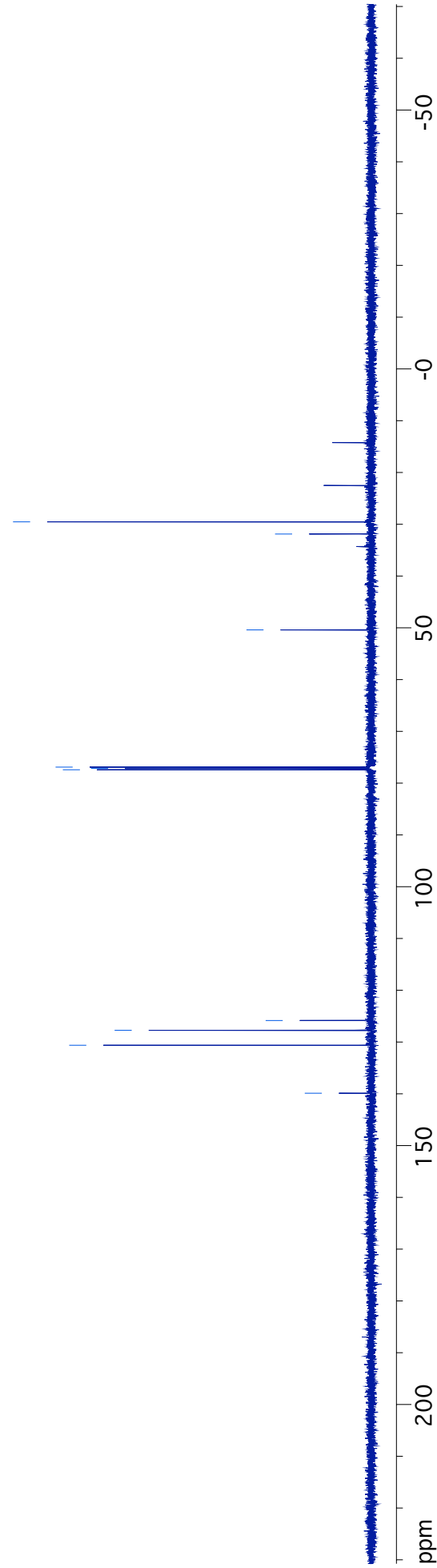
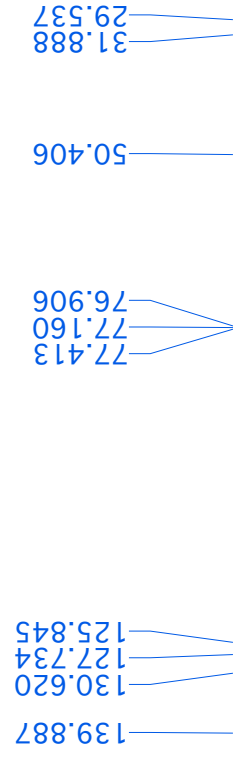
Spectrometer Freq.: 500.13 MHz
Solvent: CDCl₃
Temperature: 298.16 K
Relaxation Delay: 1.000 s





3a

Spectrometer Freq.: 125.77 MHz
Solvent: CDCl₃
Temperature: 298.26 K
Relaxation Delay: 2.000 s



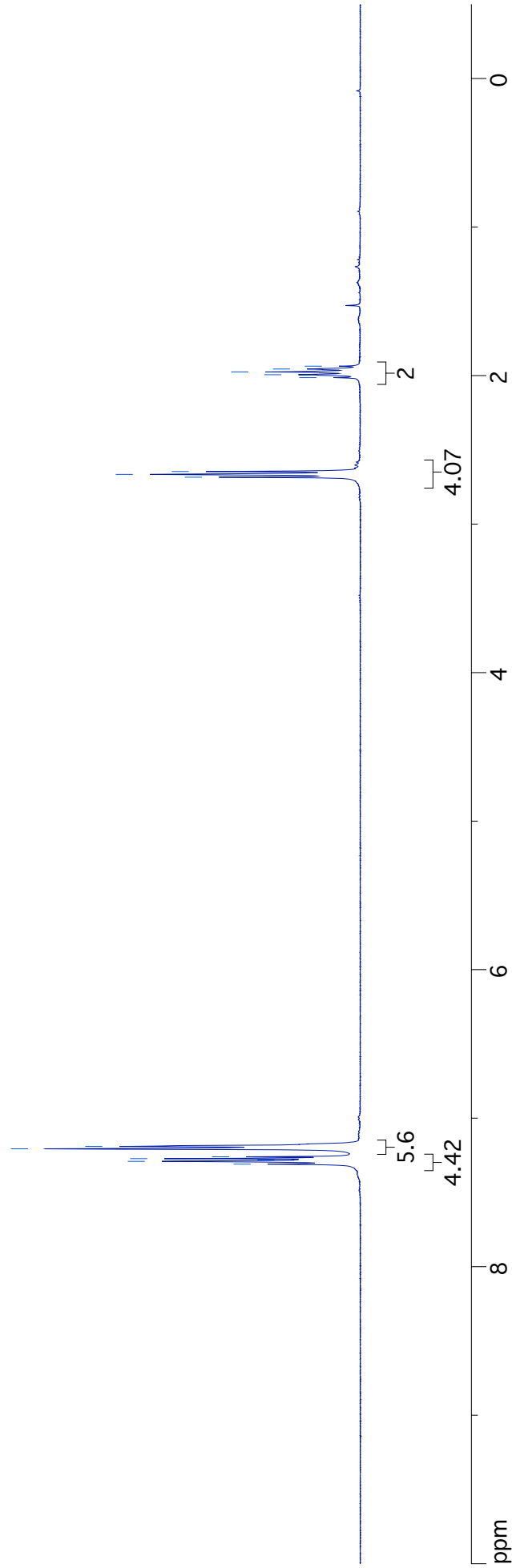


3b

Spectrometer Freq.: 400.13 MHz
Solvent: CDCl₃
Temperature: 298.16 K
Relaxation Delay: 1.000 s

S55

7.310
7.291
7.281
7.272
7.260
7.206
7.190
2.684
2.665
2.646
2.014
1.994
1.975
1.956
1.937





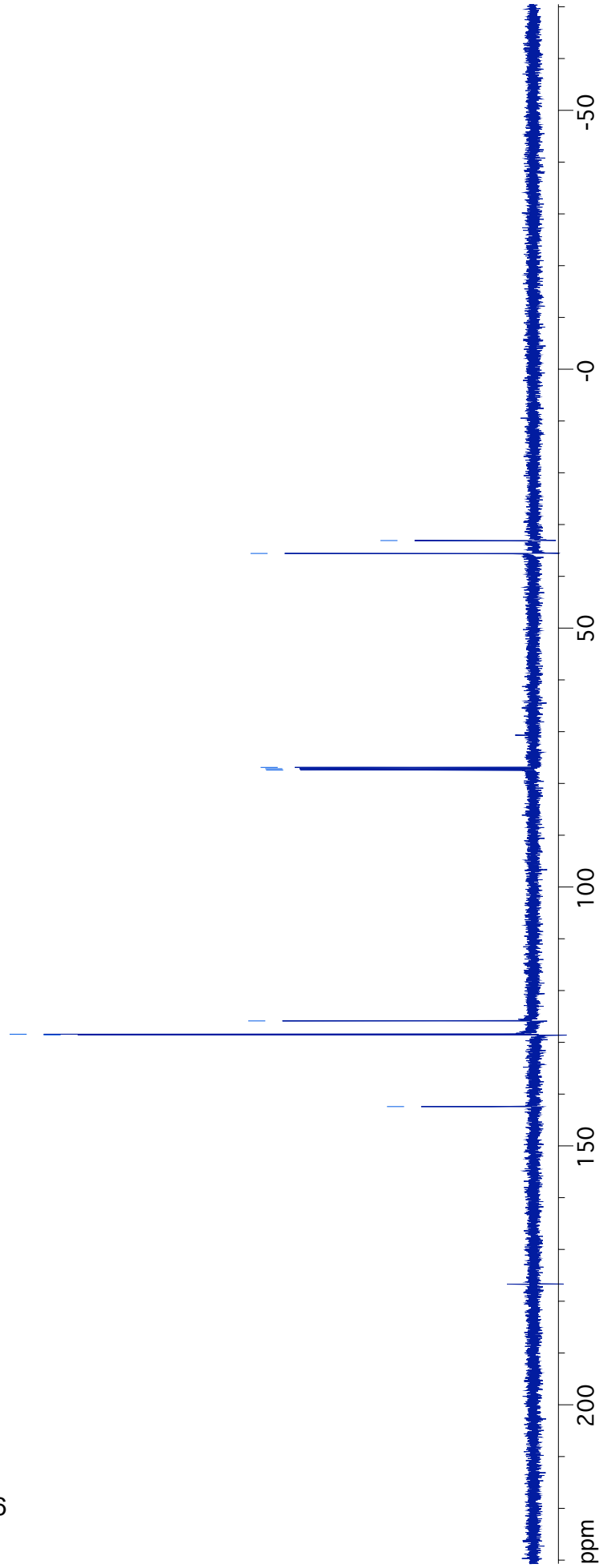
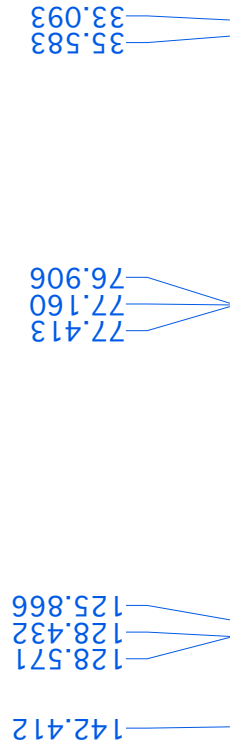
3b

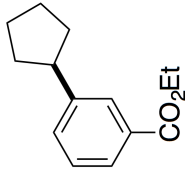
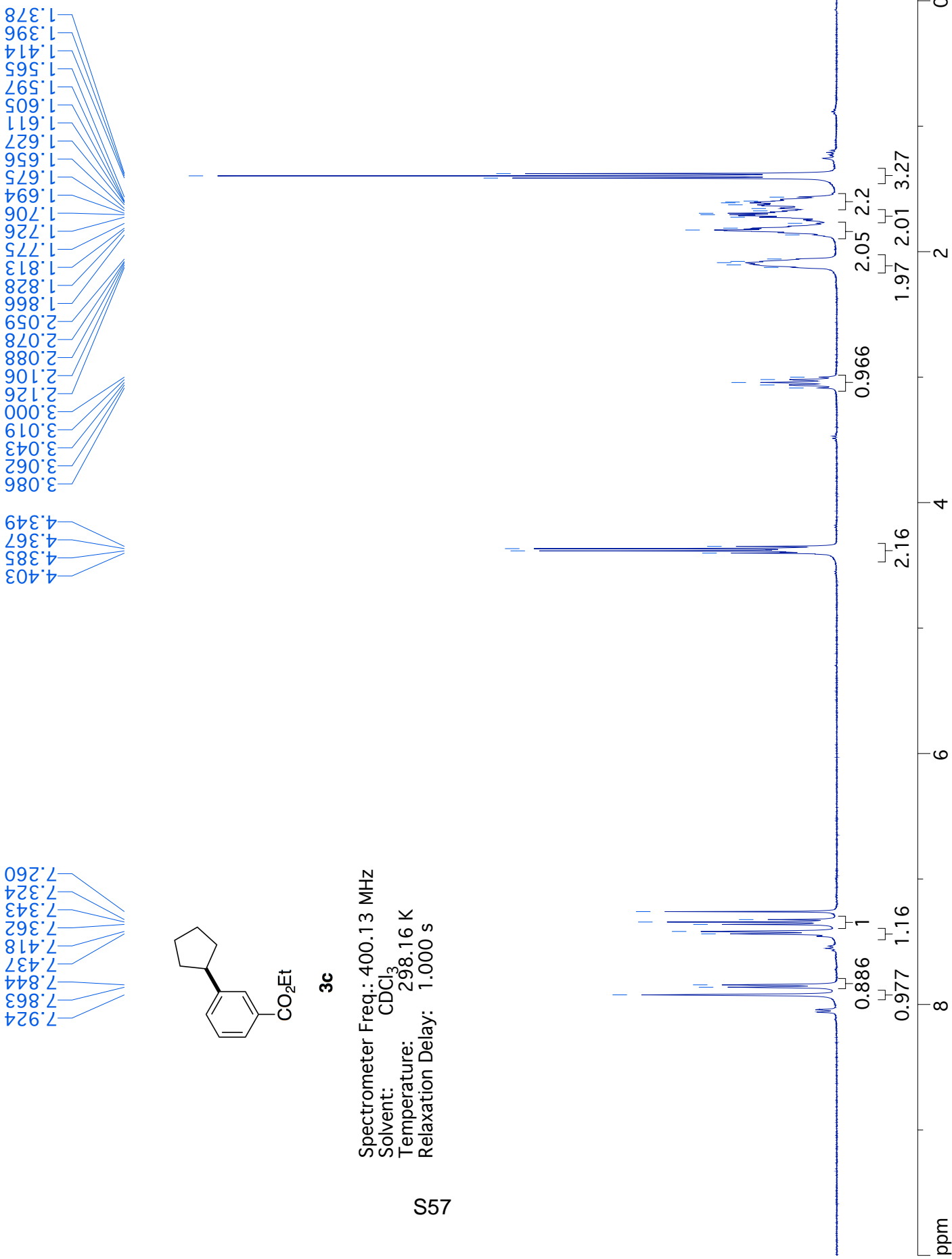
Spectrometer Freq.: 125.77 MHz

Solvent: CDCl₃

Temperature: 298.16 K

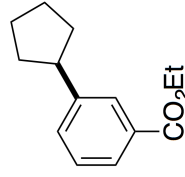
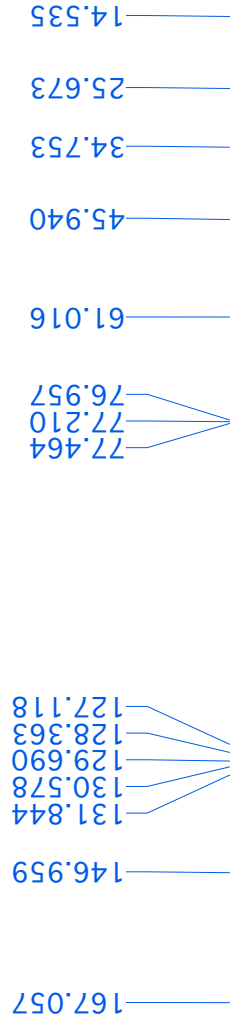
Relaxation Delay: 2.000 s





3c

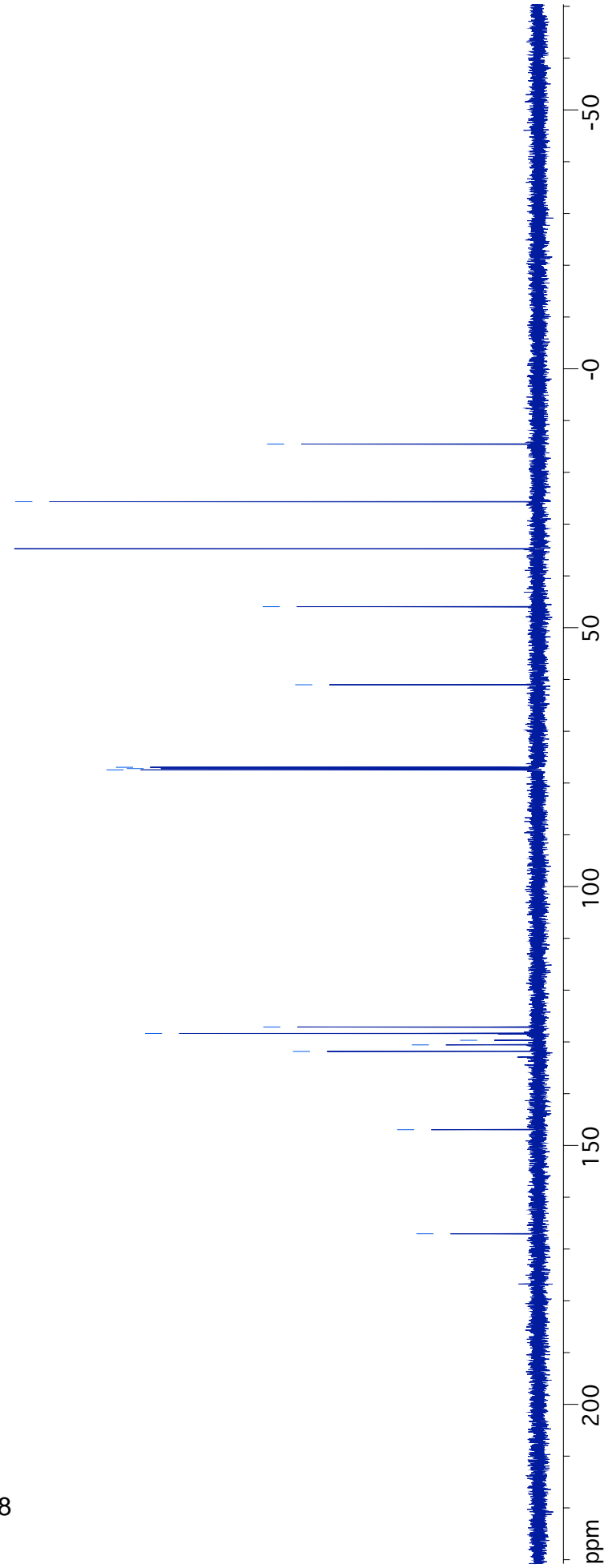
Spectrometer Freq.: 400.13 MHz
 Solvent: CDCl₃
 Temperature: 298.16 K
 Relaxation Delay: 1.000 s

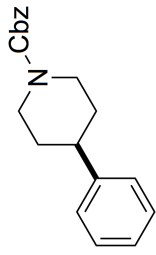


3c

Spectrometer Freq.: 125.77 MHz
 Solvent: CDCl₃
 Temperature: 298.16 K
 Relaxation Delay: 2.000 s

558

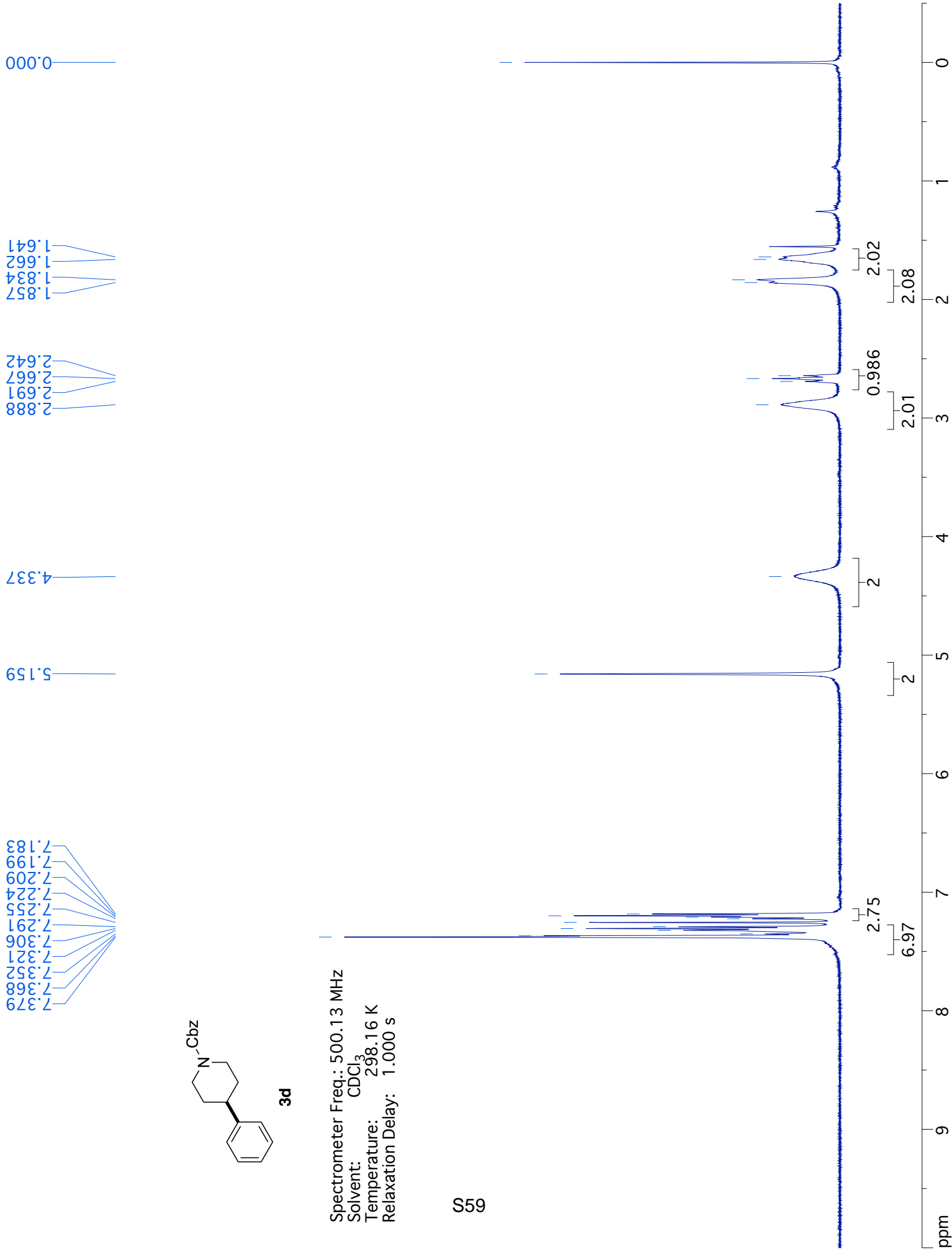


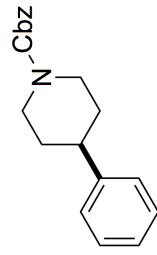


3d

Spectrometer Freq.: 500.13 MHz
Solvent: CDCl₃
Temperature: 298.16 K
Relaxation Delay: 1.000 s

559

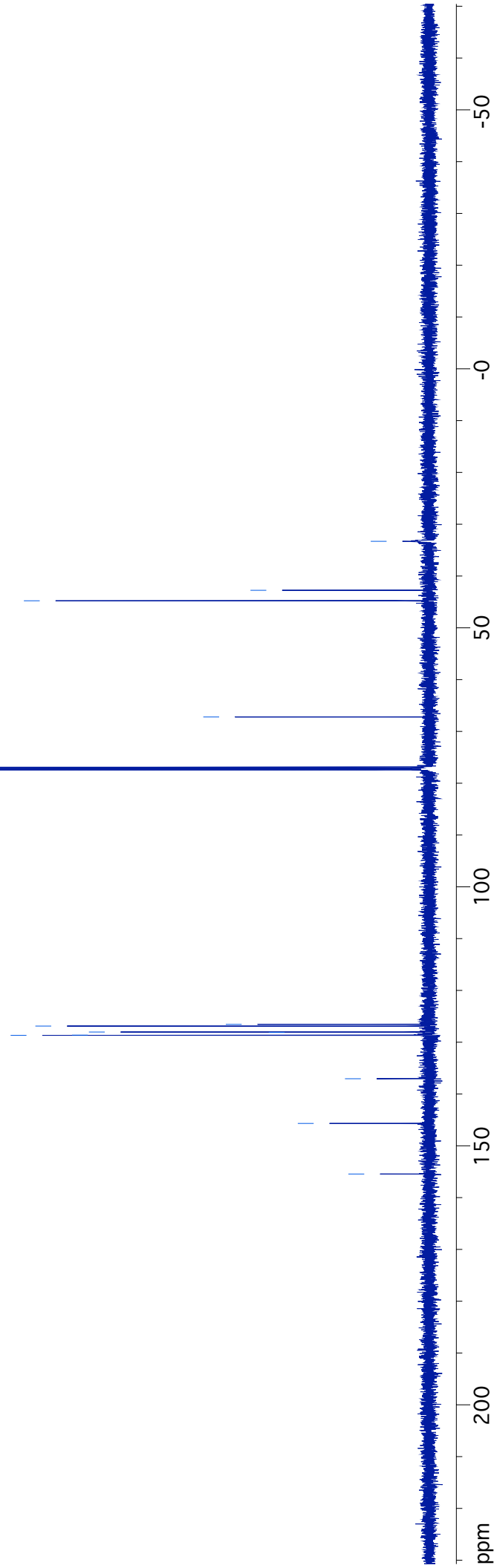




3d

Spectrometer Freq.: 125.77 MHz
Solvent: CDCl₃
Temperature: 298.16 K
Relaxation Delay: 2.000 s

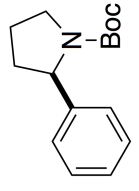
155.444
145.680
137.051
128.676
128.630
128.105
128.033
126.884
126.554
77.415
77.160
76.906
67.214
44.779
42.758
33.299



0.000
 1.268
 1.458
 1.796
 1.805
 1.807
 1.815
 1.821
 1.824
 1.826
 1.828
 1.833
 1.836
 1.845
 1.855
 1.868
 1.876
 1.893
 1.897
 1.909
 1.921
 1.934
 1.948
 2.262
 2.274
 2.274
 2.291
 2.301
 2.306
 2.317
 2.305
 3.382
 3.582
 3.595
 3.607

7.278
 7.264
 7.248
 7.242
 7.188
 7.186
 7.173
 7.154
 7.140

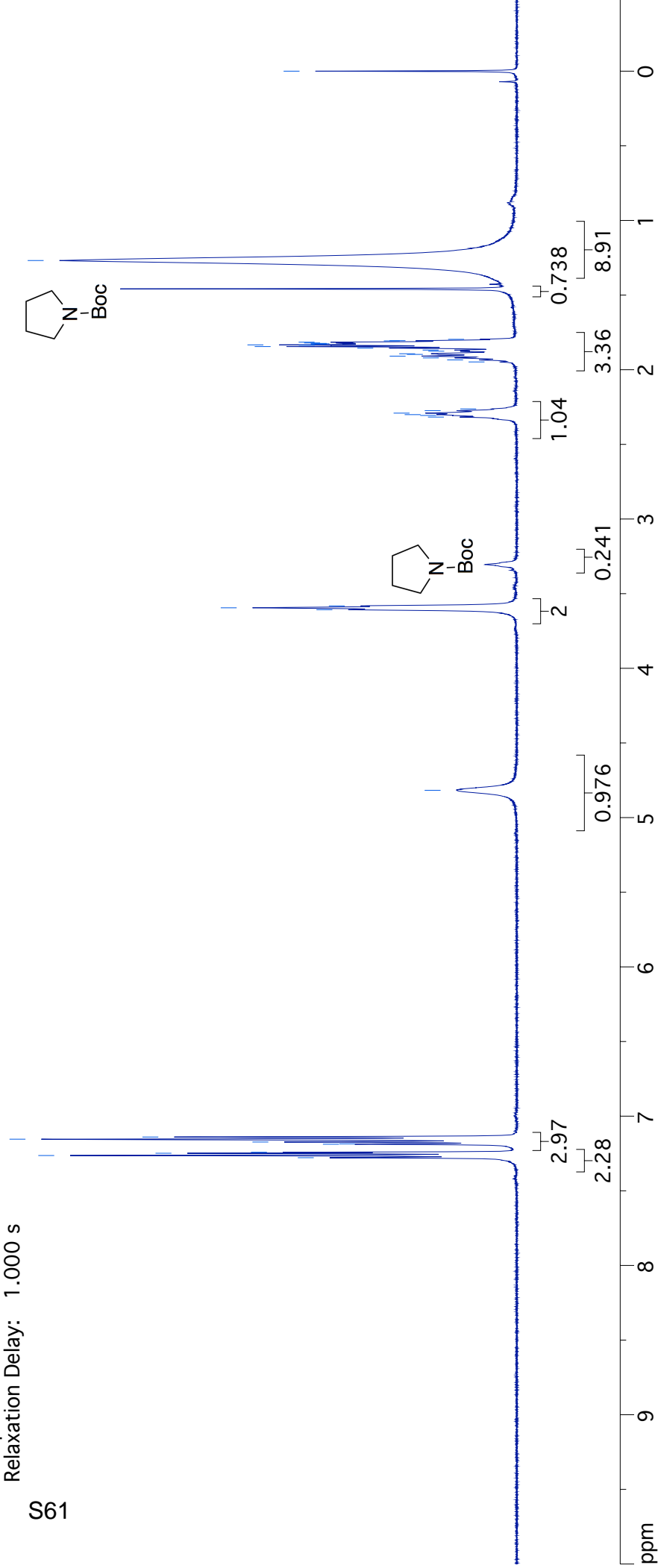
4.817

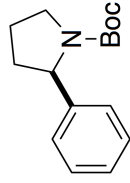


3e

Spectrometer Freq.: 500.13 MHz
 Solvent: CDCl₃
 Temperature: 328.26 K
 Relaxation Delay: 1.000 s

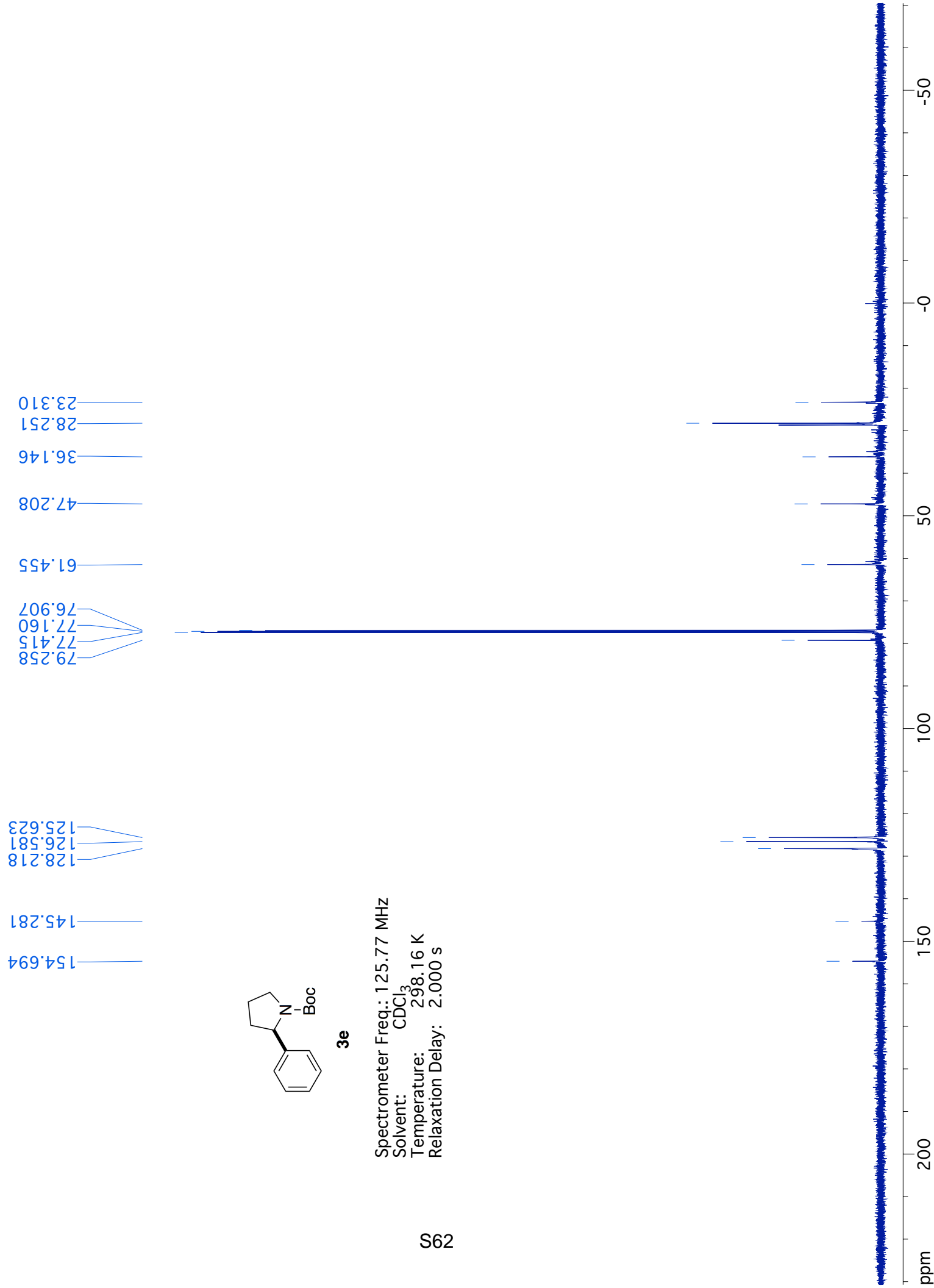
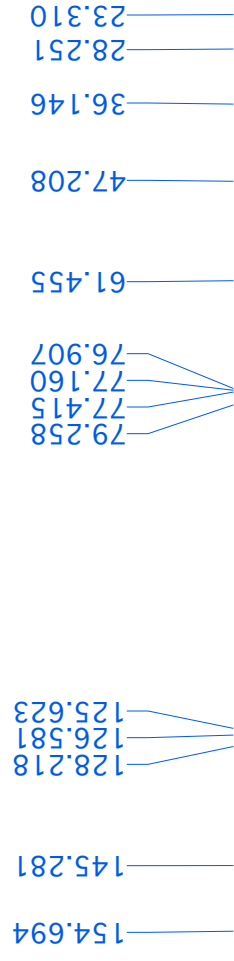
S61

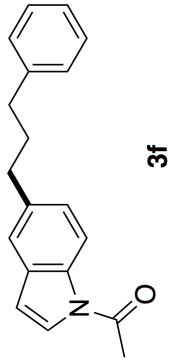




3e

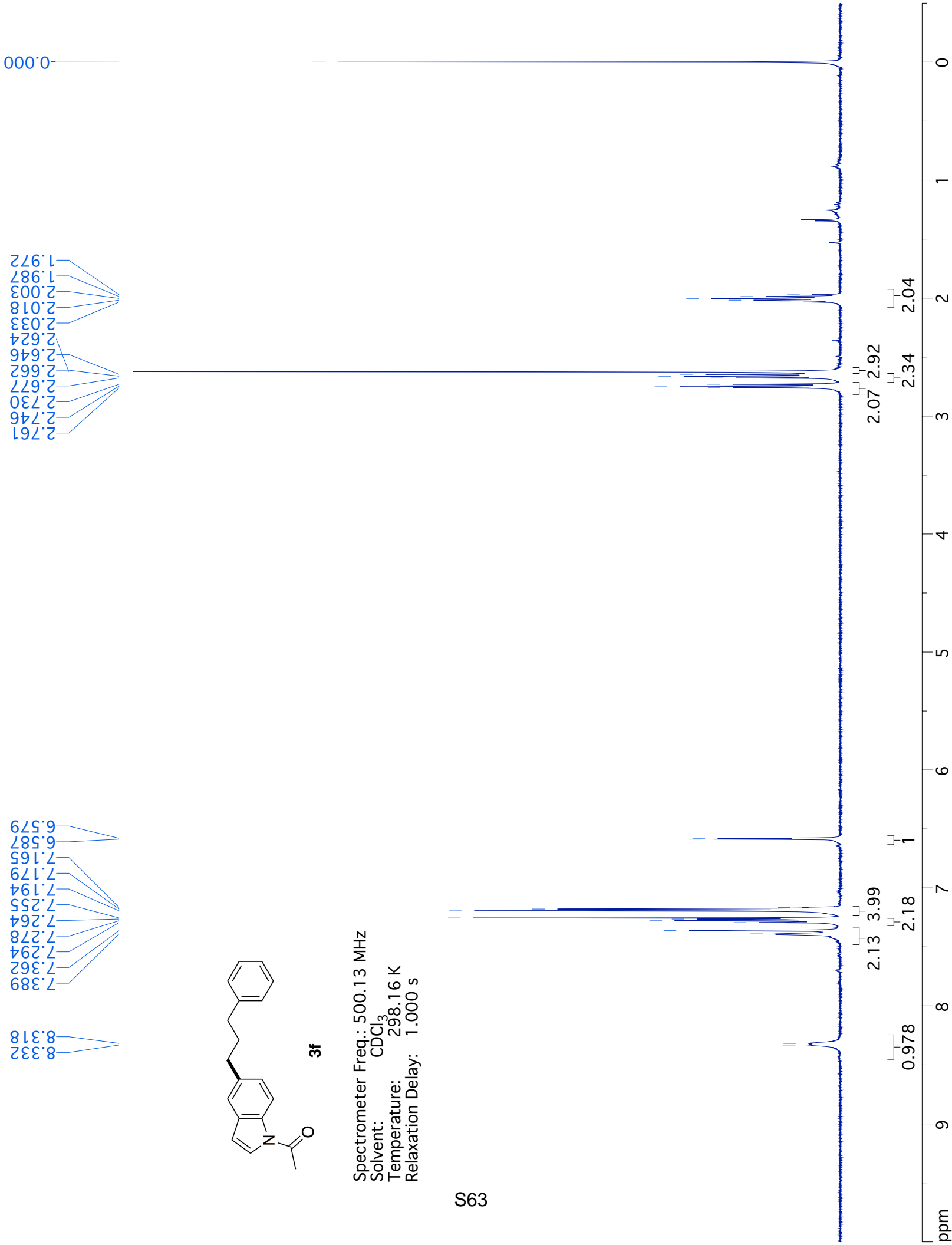
Spectrometer Freq.: 125.77 MHz
Solvent: CDCl₃
Temperature: 298.16 K
Relaxation Delay: 2.000 s

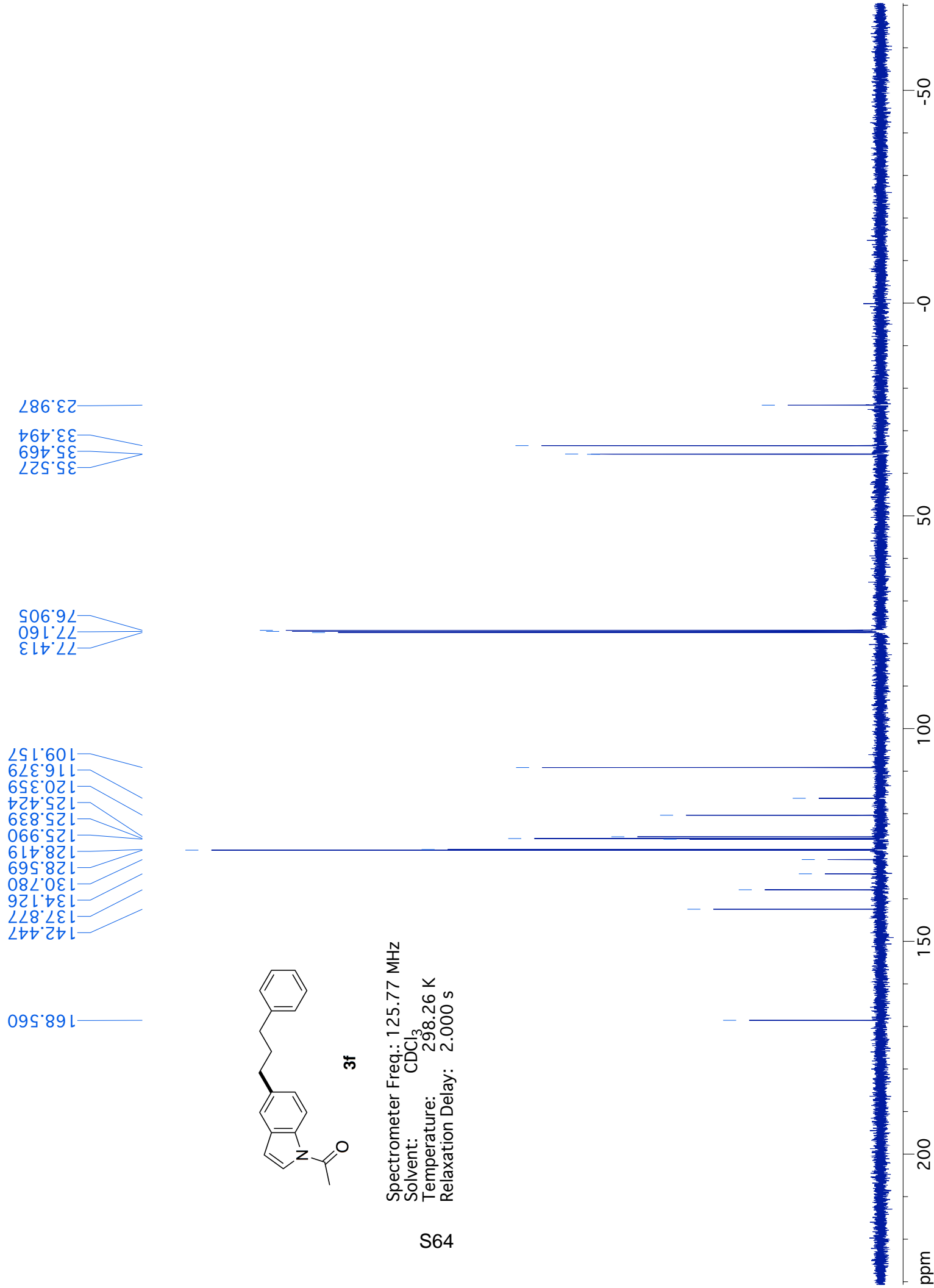




Spectrometer Freq.: 500.13 MHz
Solvent: CDCl₃
Temperature: 298.16 K
Relaxation Delay: 1.000 s

S63

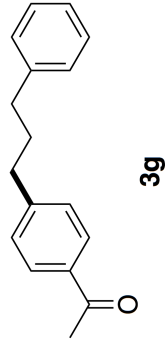




0.000

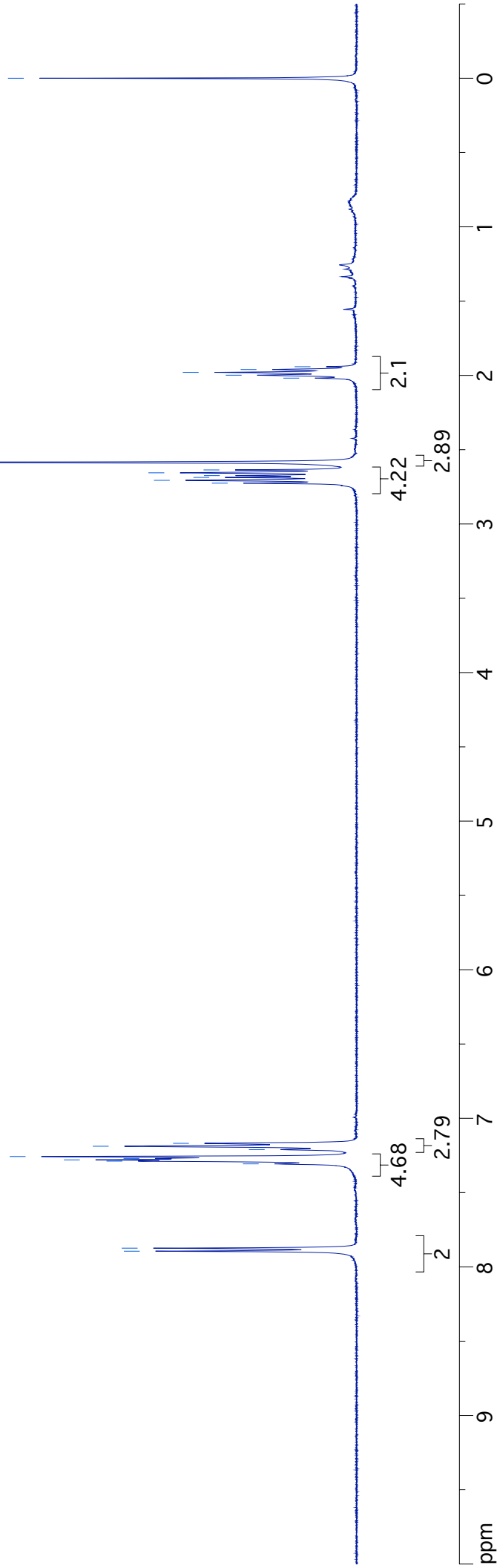
1.942
1.960
1.980
1.999
2.018
2.585
2.636
2.656
2.675
2.687
2.706
2.725

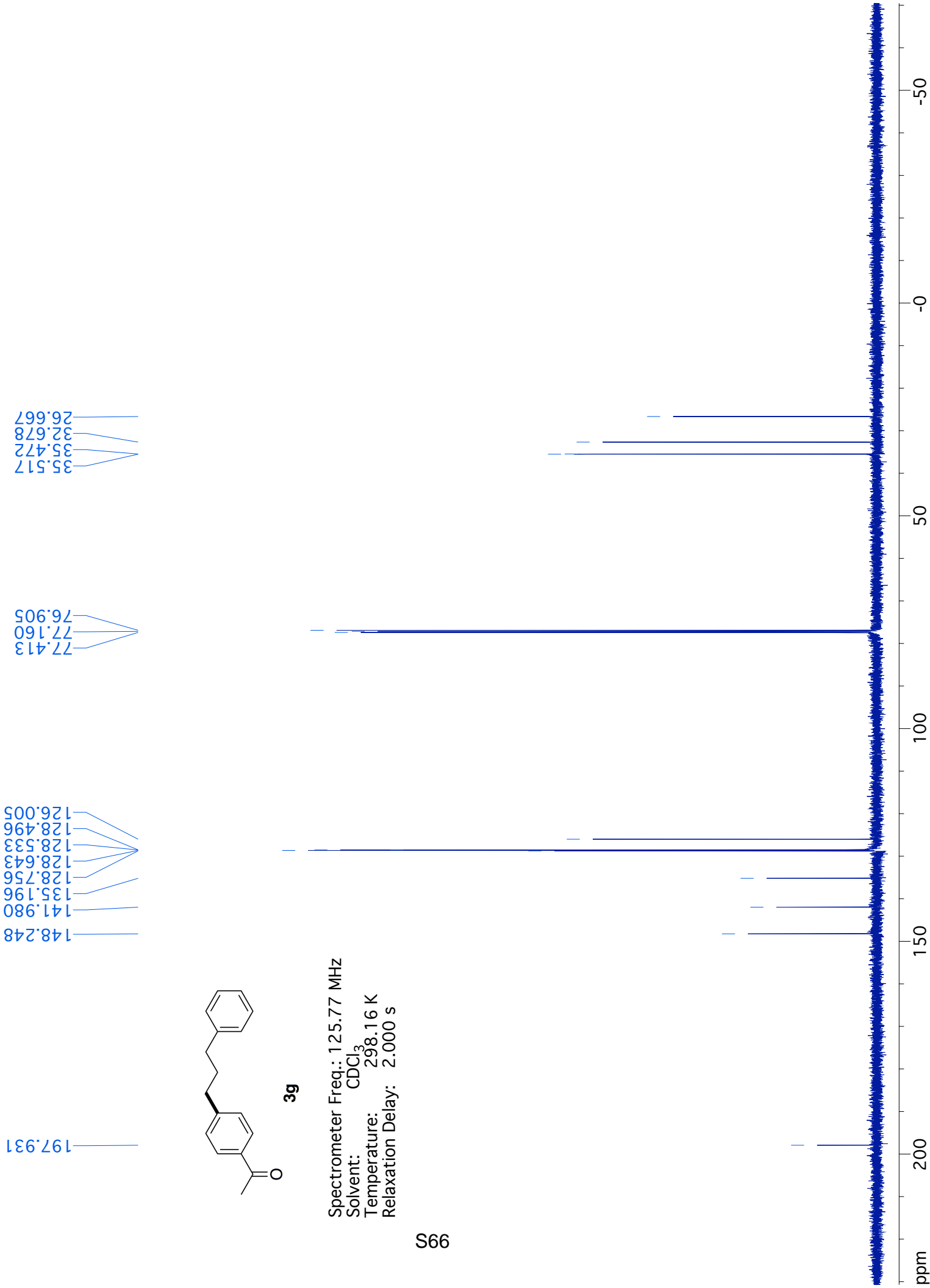
7.169
7.188
7.210
7.257
7.270
7.280
7.288
7.307
7.874
7.894



Spectrometer Freq.: 400.13 MHz
Solvent: CDCl₃
Temperature: 298.16 K
Relaxation Delay: 1.000 s

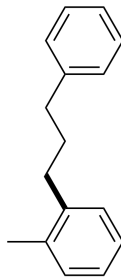
S65





1.892
1.907
1.923
1.939
1.954
1.954
2.273
2.273
2.628
2.644
2.660
2.694
2.709
2.724

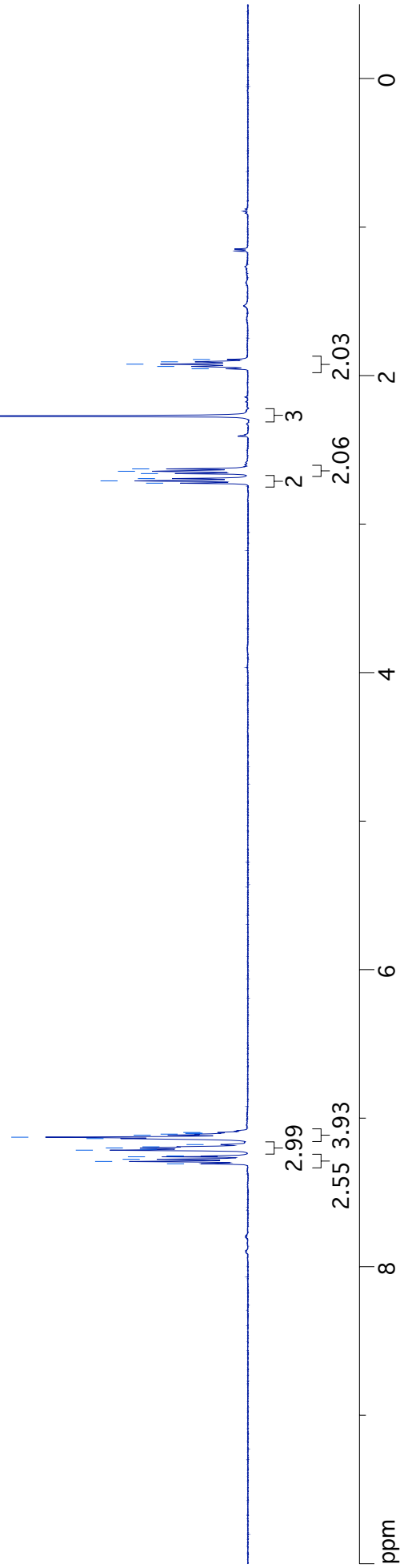
7.307
7.292
7.277
7.260
7.255
7.254
7.216
7.209
7.201
7.193
7.178
7.137
7.128
7.114
7.108
7.102
7.102
7.096

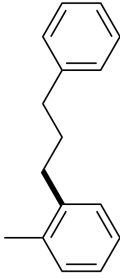


3h

Spectrometer Freq.: 500.13 MHz
Solvent: CDCl₃
Temperature: 298.16 K
Relaxation Delay: 1.000 s

S67





3h

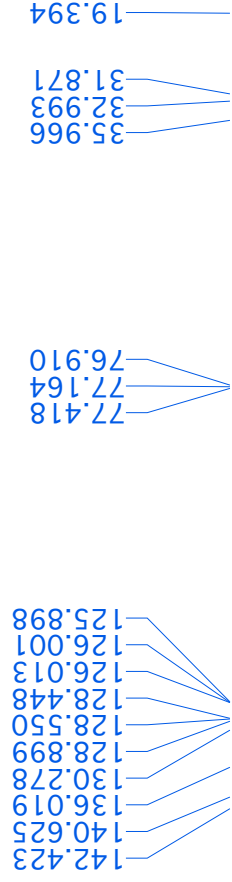
Spectrometer Freq.: 125.77 MHz

Solvent: CDCl₃

Temperature: 298.26 K

Relaxation Delay: 2.000 s

568



ppm

200

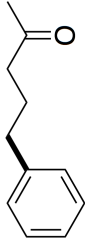
150

100

50

-0

-50



3i

Spectrometer Freq.: 400.13 MHz

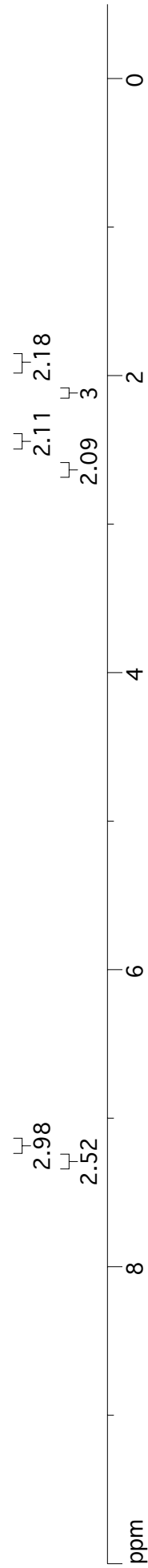
Solvent: CDCl₃

Temperature: 298.16 K

Relaxation Delay: 1.000 s

2.644
2.625
2.606
2.455
2.437
2.419
2.118
1.950
1.931
1.913
1.894
1.876

7.304
7.286
7.268
7.260
7.211
7.193
7.180
7.163





3i

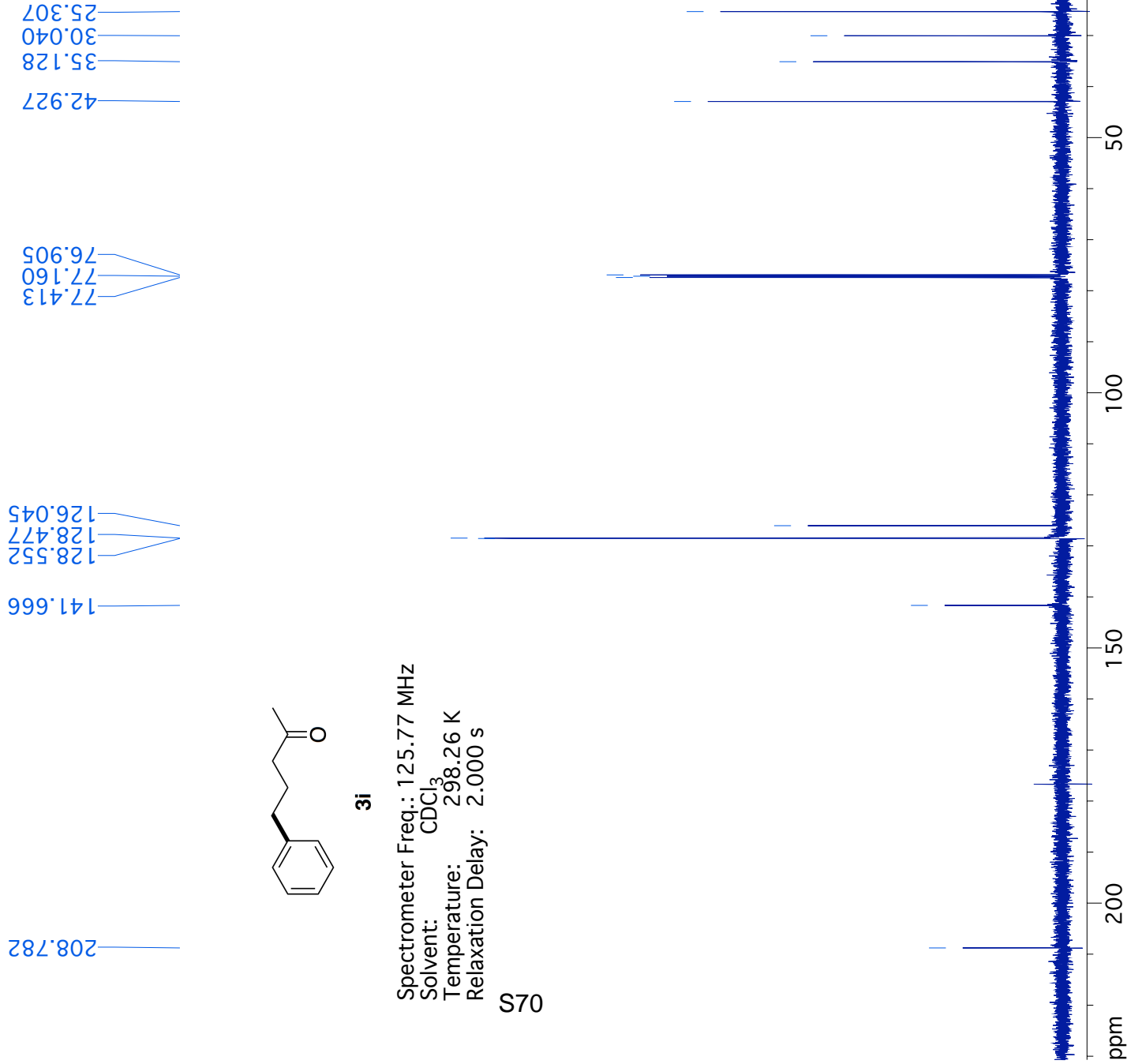
Spectrometer Freq.: 125.77 MHz

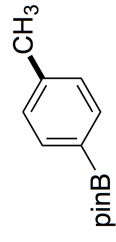
Solvent: CDCl₃

Temperature: 298.26 K

Relaxation Delay: 2.000 s

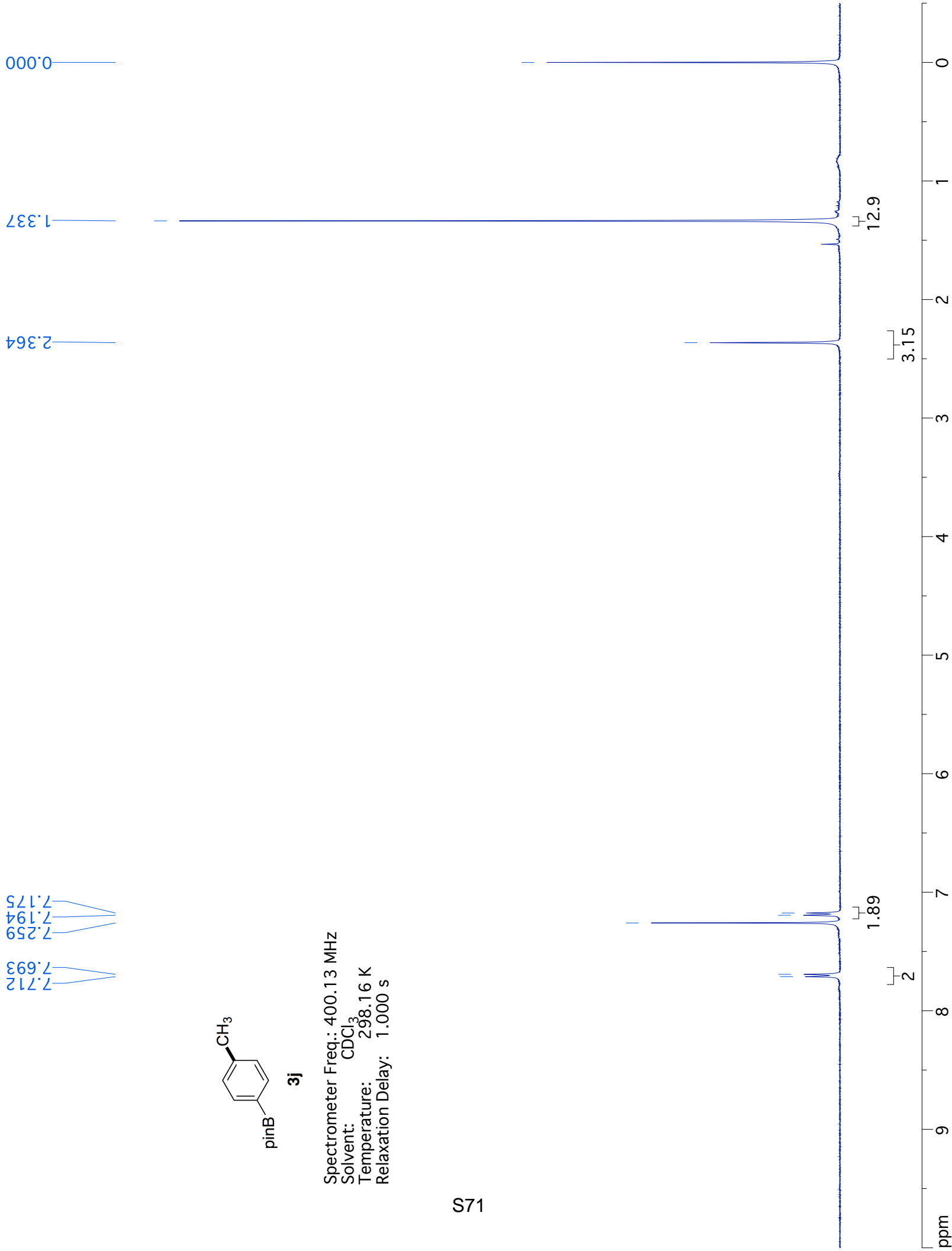
S70

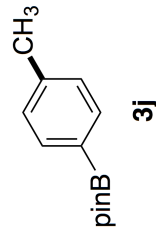




3j

Spectrometer Freq.: 400.13 MHz
Solvent: CDCl₃
Temperature: 298.16 K
Relaxation Delay: 1.000 s



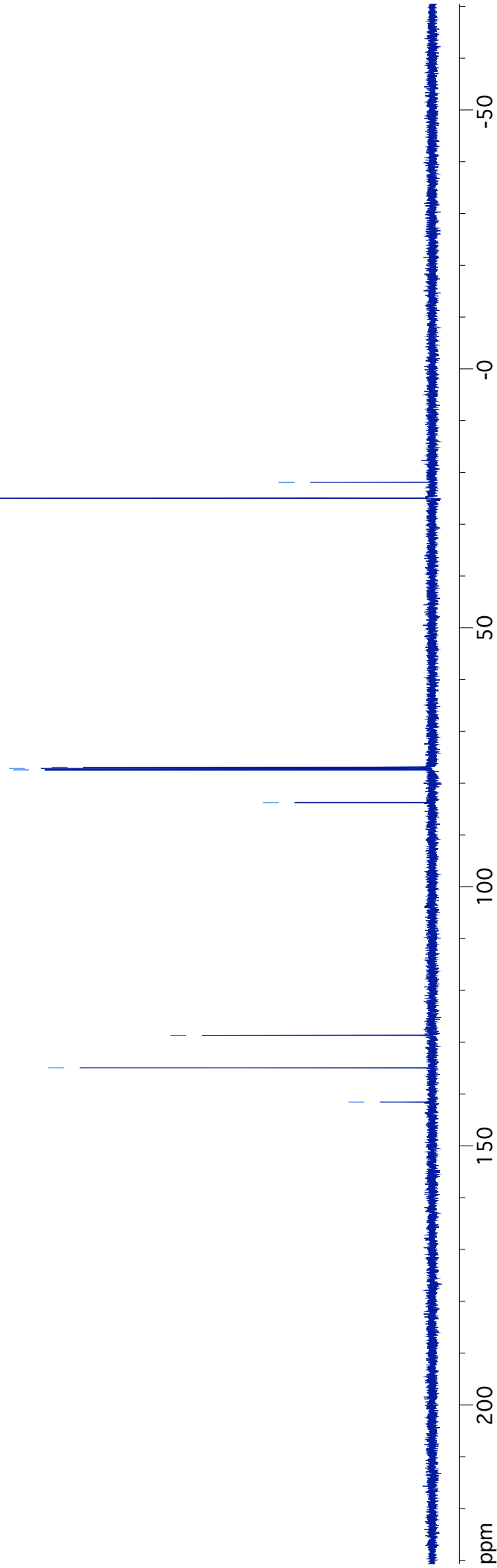
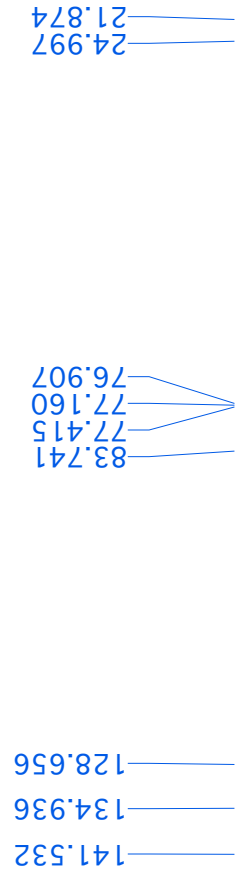


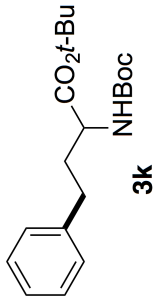
Spectrometer Freq.: 125.77 MHz

Solvent: CDCl₃

Temperature: 294.66 K

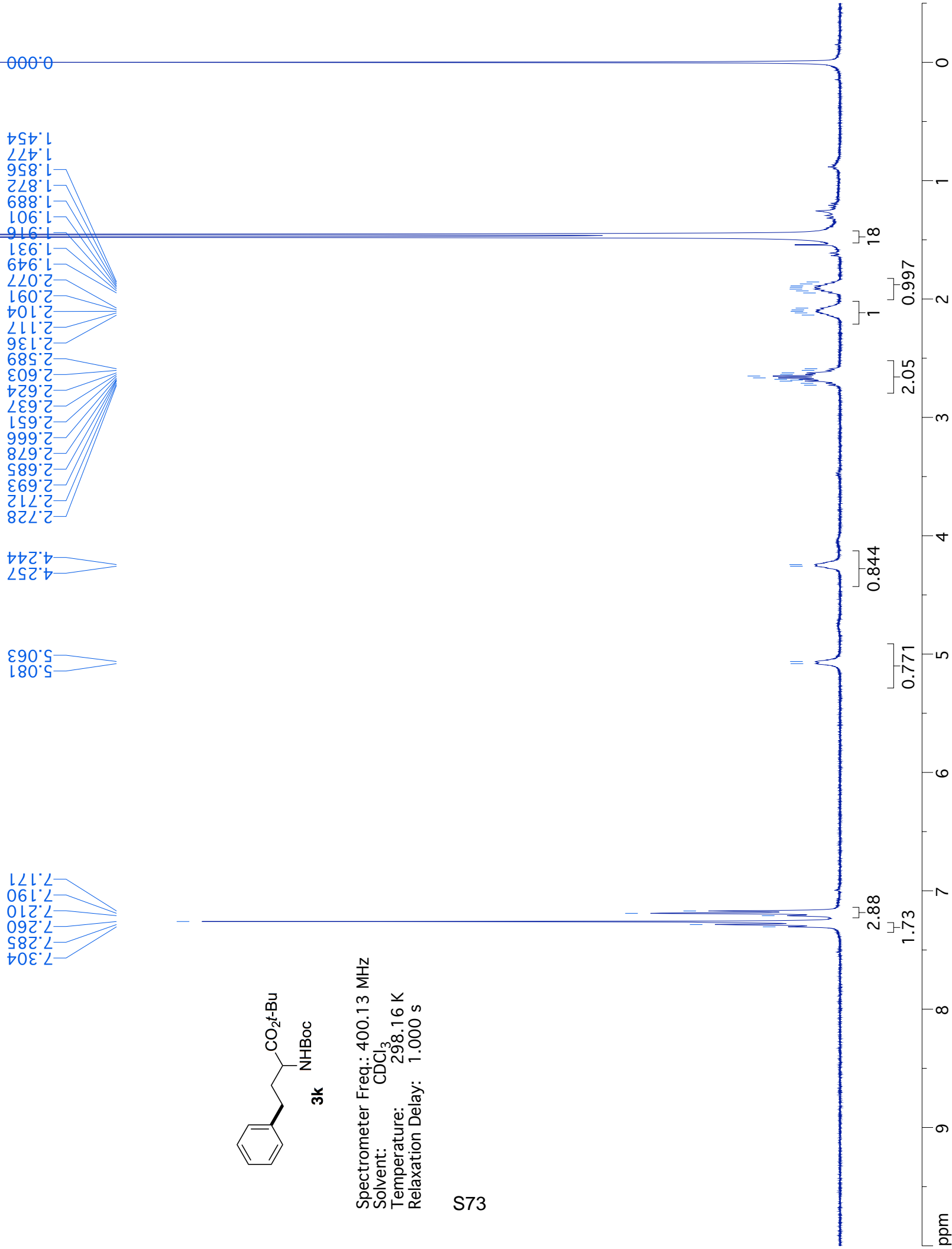
Relaxation Delay: 2.000 s

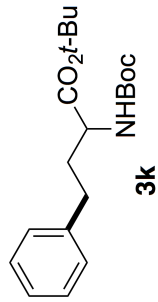




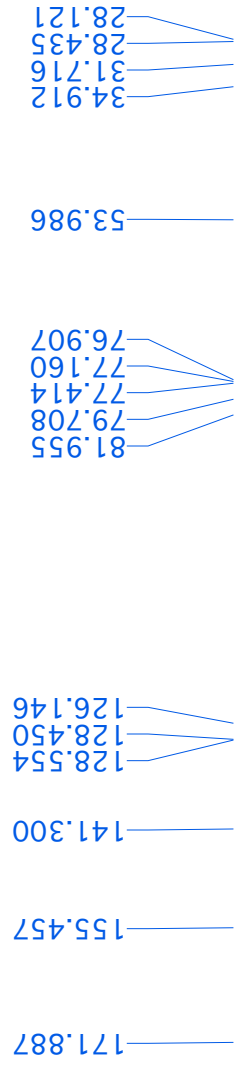
Spectrometer Freq.: 400.13 MHz
 Solvent: CDCl₃
 Temperature: 298.16 K
 Relaxation Delay: 1.000 s

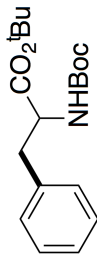
S73





Spectrometer Freq.: 125.77 MHz
 Solvent: CDCl₃
 Temperature: 298.46 K
 Relaxation Delay: 2.000 s

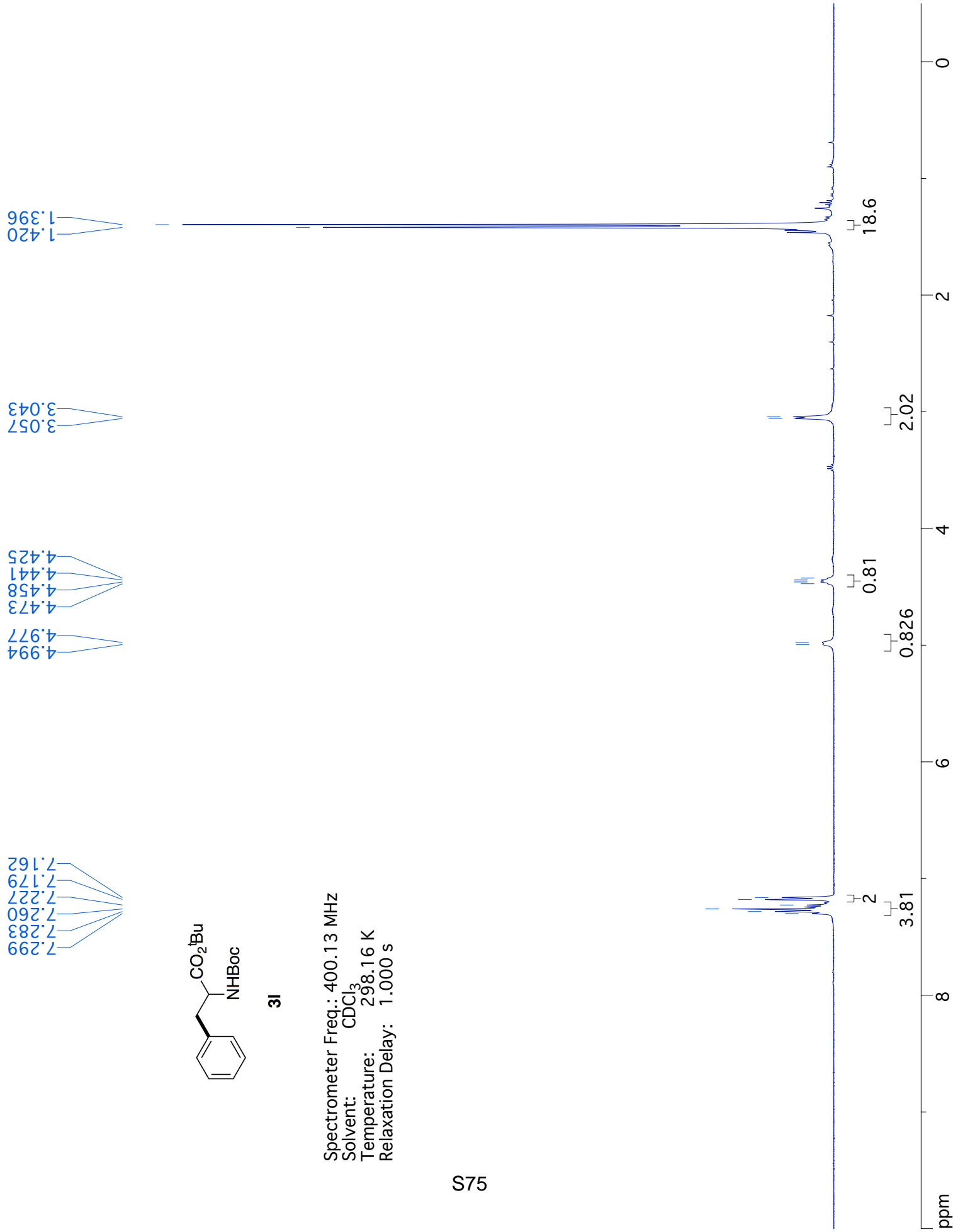


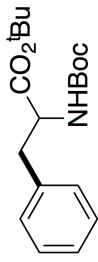


31

Spectrometer Freq.: 400.13 MHz
Solvent: CDCl₃
Temperature: 298.16 K
Relaxation Delay: 1.000 s

S75





3l

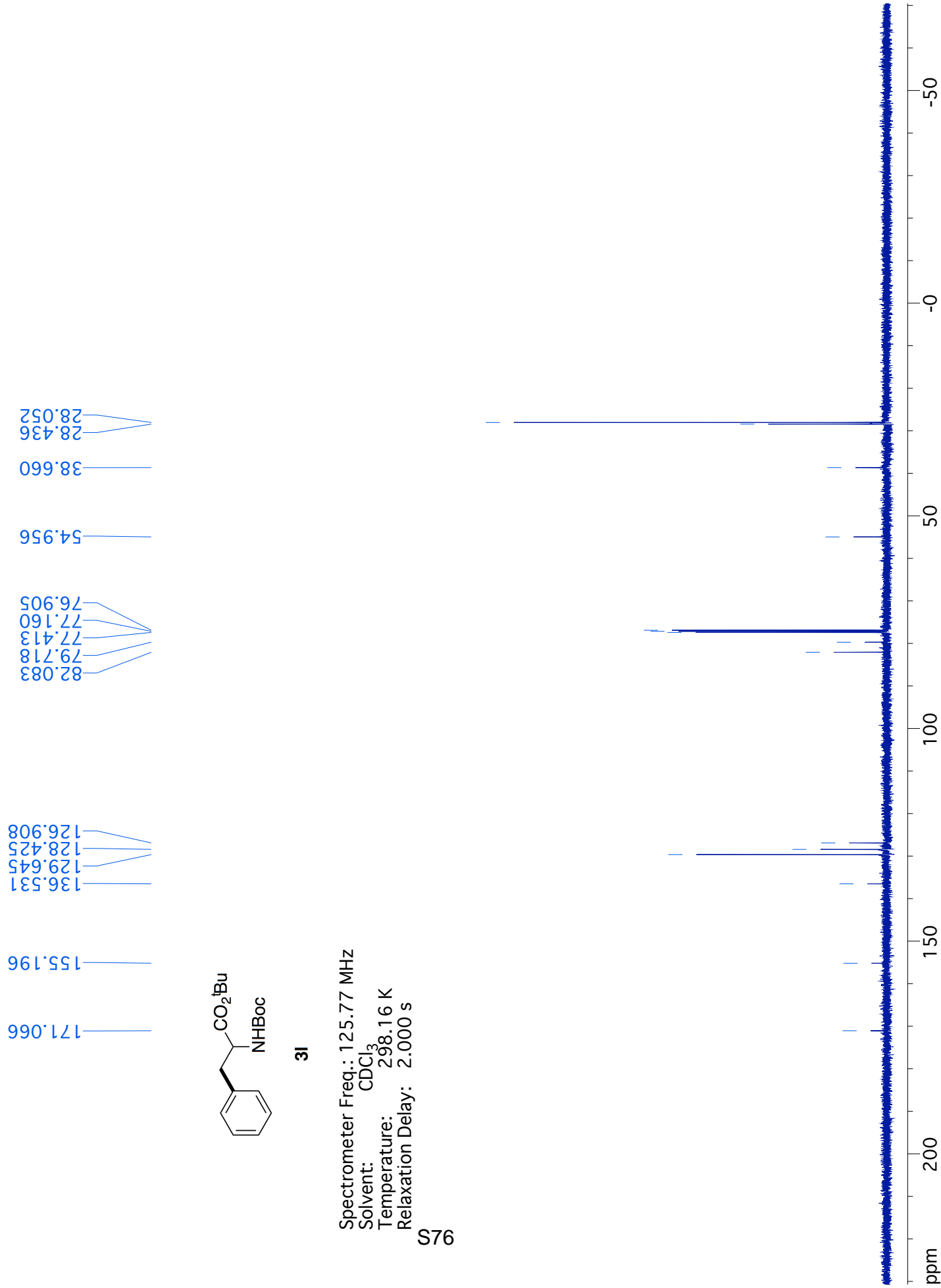
Spectrometer Freq.: 125.77 MHz

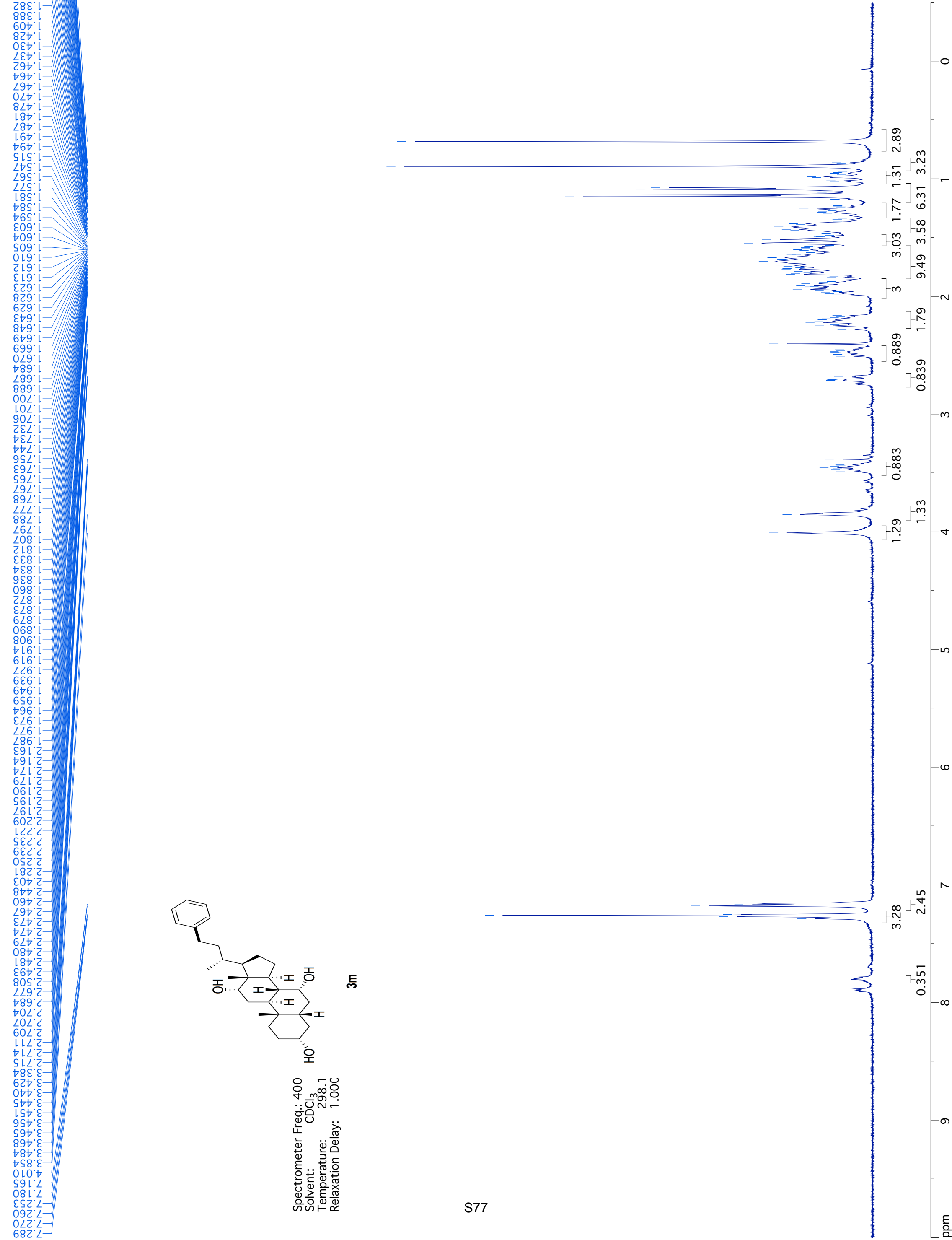
Solvent: CDCl₃

Temperature: 298.16 K

Relaxation Delay: 2.000 s

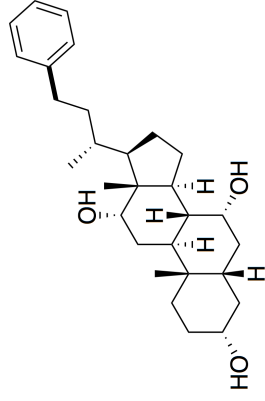
S76





77.414
77.160
76.907
73.230
72.111
68.600
47.422
46.650
42.396
42.001
41.622
39.804
39.737
38.121
35.623
35.390
34.876
34.756
32.783
30.676
28.393
27.687
26.715
23.629
23.356
22.668
17.892
12.682

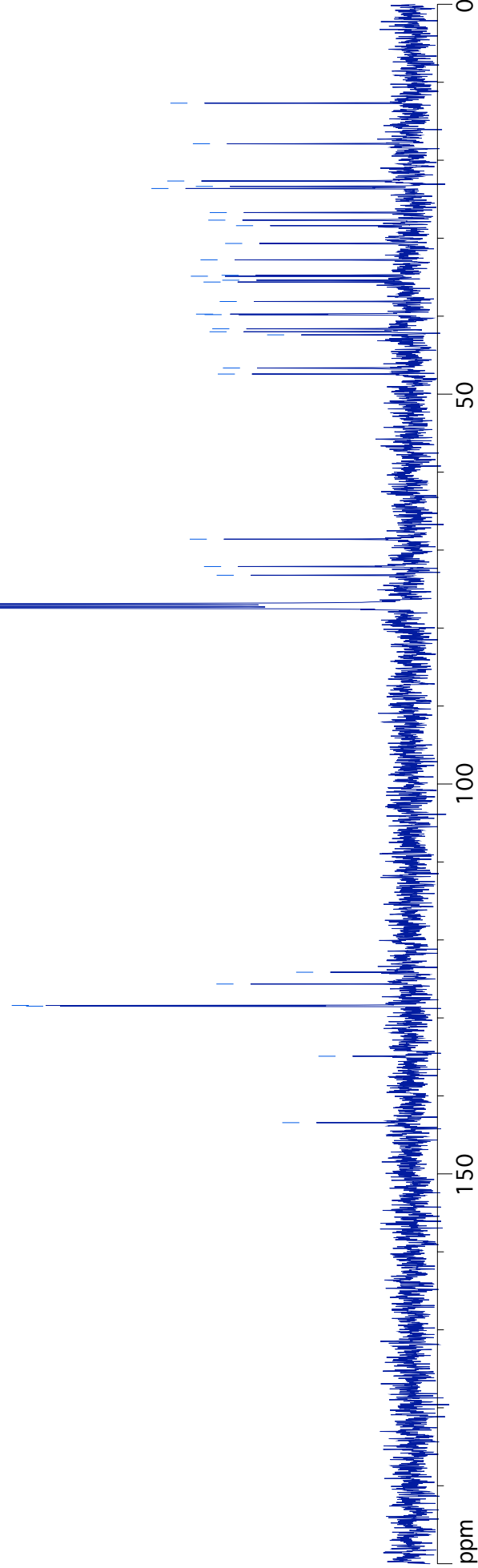
143.433
134.913
128.494
128.402
125.652
124.142

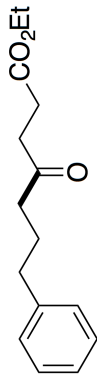


3m

Spectrometer Freq.: 125.77 MHz
Solvent: CDCl₃
Temperature: 298.16 K
Relaxation Delay: 2.000 s

S78



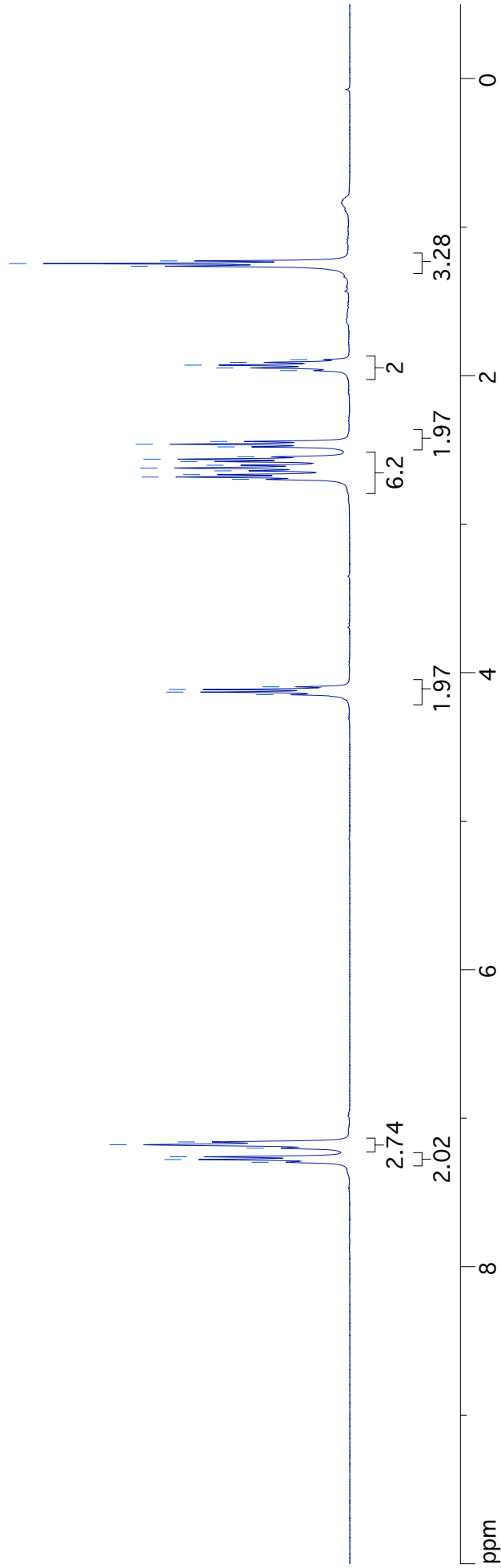


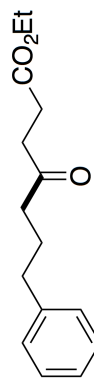
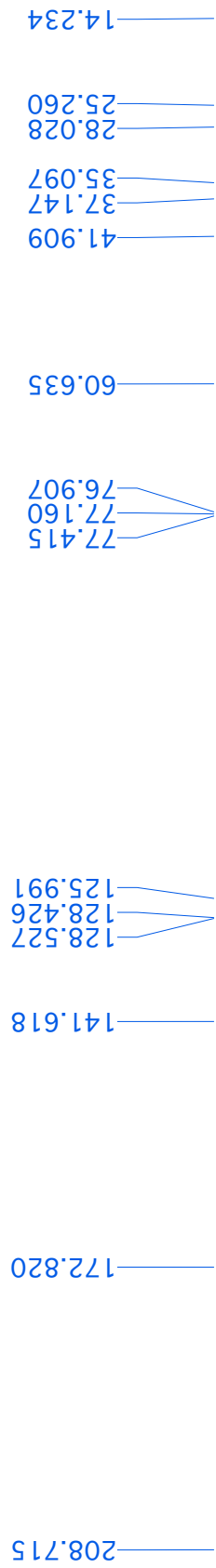
5

Spectrometer Freq.: 400.13 MHz
Solvent: CDCl₃
Temperature: 298.16 K
Relaxation Delay: 1.000 s

4.149
4.131
4.113
4.096
2.699
2.683
2.667
2.641
2.623
2.604
2.579
2.563
2.547
2.480
2.462
2.444
1.967
1.948
1.930
1.911
1.893
1.264
1.246
1.228

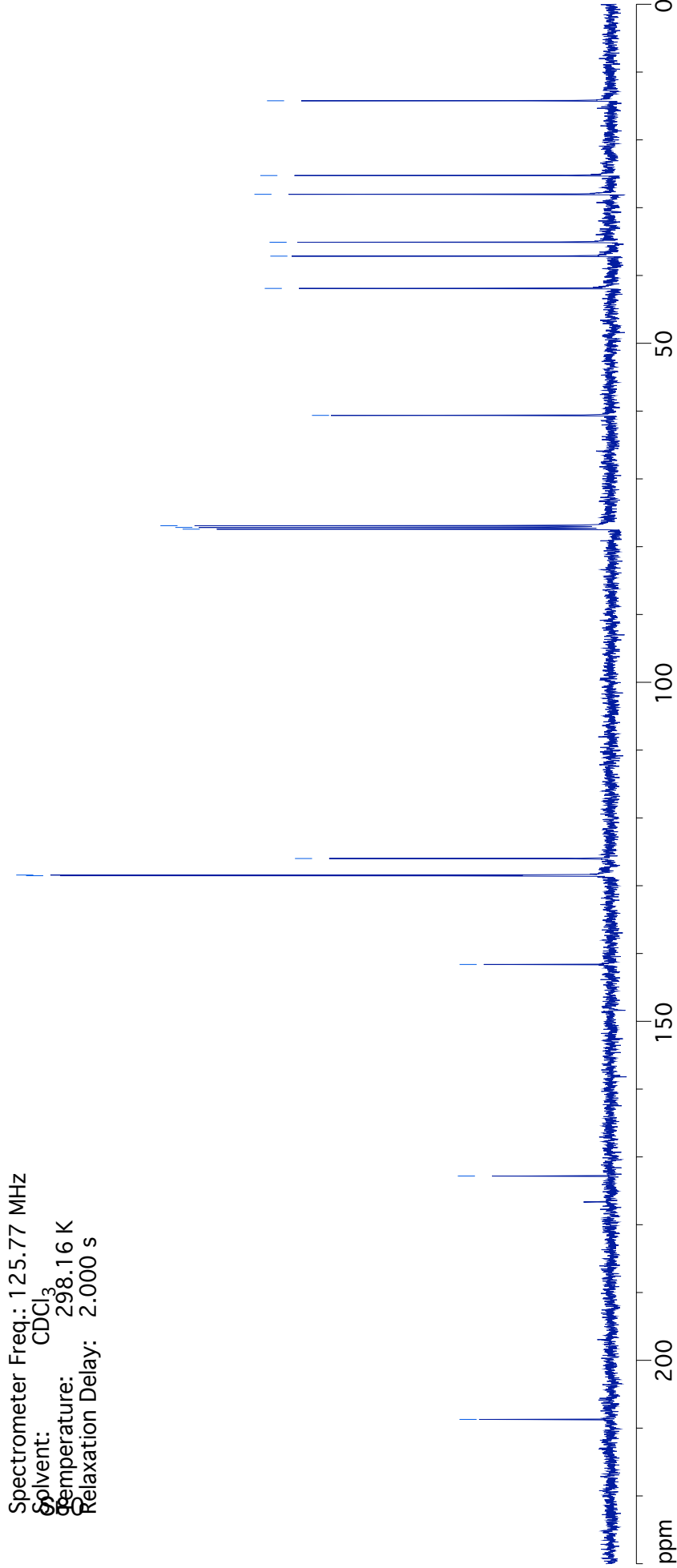
7.297
7.279
7.260
7.202
7.179
7.160

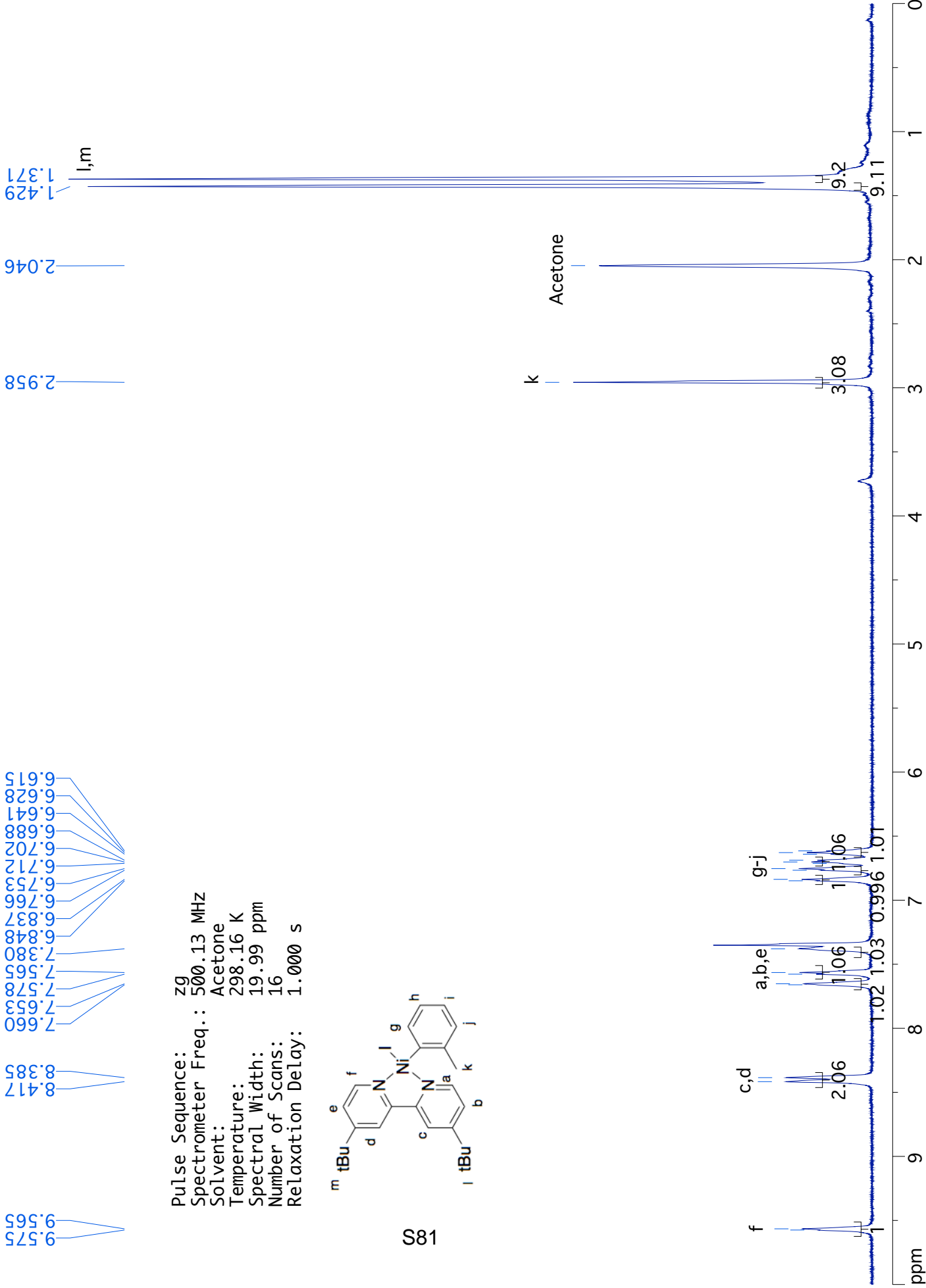




5

Spectrometer Freq.: 125.77 MHz
Solvent: CDCl₃
Temperature: 298.16 K
Relaxation Delay: 2.000 s





Pulse Sequence: zg
 Spectrometer Freq.: 500.13 MHz
 Solvent: Acetone
 Temperature: 298.16 K
 Spectral Width: 19.99 ppm
 Number of Scans: 16
 Relaxation Delay: 1.000 s

