

# ***Copper-Catalyzed Alkylation of Nitroalkanes with $\alpha$ -Bromonitriles: Synthesis of $\beta$ -Cyanonitroalkanes***

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## **Supporting Information**

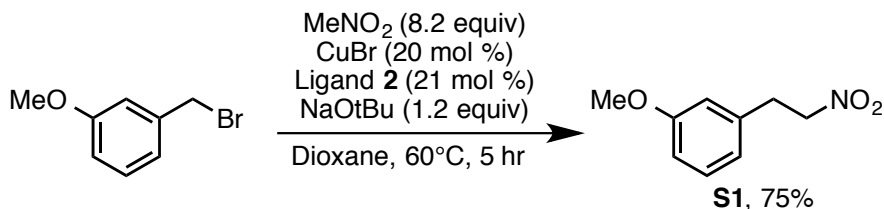
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**1. General Experimental Details.** Diethyl ether, dimethylformamide, dichloromethane, hexanes, tetrahydrofuran and dioxane were dried on alumina according to a published procedure.<sup>1</sup> 1,2-Dichloroethane was purchased in a sure-seal bottle and used as received. Copper bromide and sodium tert-butoxide were purchased commercially; the bulk was stored in a N<sub>2</sub> filled glovebox; samples were removed from the glovebox and stored in a desiccator under air for up to two weeks prior to use. Triethylamine was distilled from calcium hydride and sparged with N<sub>2</sub> prior to use. All hot glassware was oven dried for a minimum of two hours or flame-dried under vacuum prior to use.  $\beta$ -Diketiminatate ligand **2** was synthesized according to a published procedure.<sup>2</sup> Methyl-4-nitrobutyrate,<sup>3</sup> *N,N*-dimethyl-4-nitrobutanamide,<sup>4</sup> 4-nitrobutyl acetate,<sup>5</sup> 1-nitrohexene,<sup>6</sup> 1-nitroheptene<sup>6</sup> and 1-phenyl-2-nitrobutane<sup>7</sup> were synthesized according to published procedures. All other substrates and reagents were purchased in highest analytical purity from commercial suppliers and used as received. All yields in optimization reactions were determined using <sup>1</sup>H NMR using 1,3,5-trimethoxybenzene as an internal standard. Diastereomeric ratios were also determined using <sup>1</sup>H NMR of unpurified products. All other reactions were set up using standard Schlenk technique and heated with stirring in temperature controlled oil baths. "Double manifold" refers to a standard Schlenk-line gas manifold equipped with N<sub>2</sub> and vacuum (ca. 0.1 mm Hg). Note: any product yields listed in the main text that do not match those listed in the supporting information are the average of multiple isolated yields.

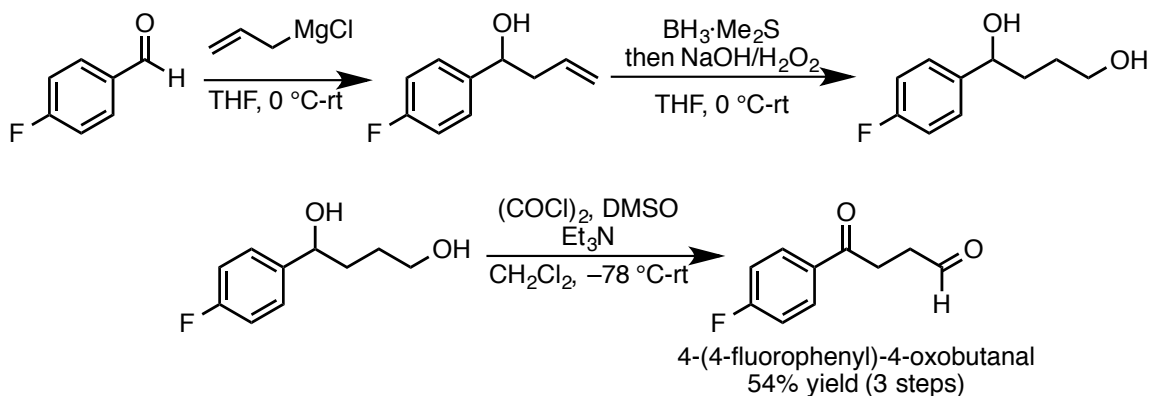
**2. Instrumentation and Chromatography.** 400 MHz <sup>1</sup>H, 101 MHz <sup>13</sup>C, and 376 MHz <sup>19</sup>F spectra were obtained on a 400 MHz FT-NMR spectrometer equipped with a Bruker CryoPlatform. 600 MHz <sup>1</sup>H and 151 MHz <sup>13</sup>C spectra were obtained on a 600 MHz FT-NMR spectrometer equipped with a Bruker SMART probe. All samples were analyzed in the indicated deuterio-solvent and were recorded at ambient temperatures. Chemical shifts are reported in ppm. <sup>1</sup>H NMR spectra were calibrated using the residual protio-signal in deuterio-solvents as a standard. <sup>13</sup>C NMR spectra were calibrated using the deuterio-solvent as a standard. IR spectra were recorded on a Nicolet Magma-IR 560 FT-IR spectrometer as thin films on KBr plates. Column chromatography was performed with 40-63  $\mu$ m silica gel or basic Al<sub>2</sub>O<sub>3</sub> (Brockmann type I, 50-200  $\mu$ m) with the eluent reported in parentheses. Analytical thin-layer chromatography (TLC) was performed on precoated glass plates and visualized by UV or by staining with KMnO<sub>4</sub>. GC/MS data was collected using an Agilent 6850 series GC and 5973 MS detector. Low resolution ESI data was collected on a Thermo LCQ Advantage running in positive ion mode. High resolution MS data was obtained on a Thermo Q-Exactive Orbitrap using electrospray ionization (ESI) or a Waters GCT Premier spectrometer using chemical ionization (CI) or liquid injection field desorption ionization (LIFDI).

### 3. Synthesis of Miscellaneous Starting Materials

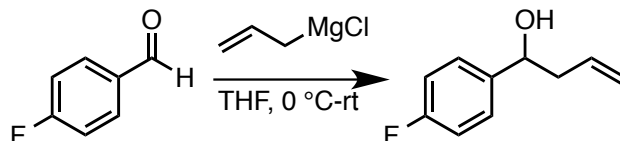
Nitroalkanes **S1** was prepared via the previously reported alkylation of nitroalkanes with benzylic halides.<sup>7</sup>



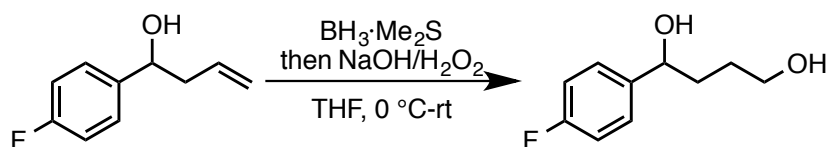
**(S1)**: An oven-dried 200 mL Schlenk flask equipped with a magnetic stir bar and a rubber septum was cooled under vacuum. Once cool, the flask was back-filled with nitrogen. The septum was briefly removed under air and the flask was charged with CuBr (629 mg, 4.4 mmol, 0.20 equiv), ligand **2** (1.408 g, 4.6 mmol, 0.21 equiv), and sodium *tert*-butoxide (2.53 g, 26.4 mmol, 1.2 equiv). The septum was replaced, and the flask was evacuated and refilled with nitrogen 5 times. Anhydrous dioxane (110 mL), nitromethane (9.8 mL, 180 mmol, 8.2 equiv), and 3-methoxybenzyl bromide (3.08 mL, 22 mmol, 1.0 equiv) were added sequentially via syringe, resulting in a thick suspension. The flask was placed in a 60 °C oil bath and the reaction was stirred vigorously for 5 hours. The reaction was then cooled to room temperature and diluted with diethyl ether (100 mL, ACS grade). The suspension was added to a separatory funnel and washed twice with saturated aqueous NH<sub>4</sub>Cl (~100 mL) and once with brine (~100 mL). The organic layer was dried over magnesium sulfate, filtered, and concentrated *in vacuo*. The crude product was purified by flash silica gel chromatography (91:9:1 hexanes-ethyl acetate-trifluoroacetic acid) to give the pure product along with several fractions containing the product and the over-alkylated product. The impure fractions were purified by a second chromatographic purification on silica gel (96:4 hexanes-ethyl acetate). The pure fractions were combined to give the product as a clear to yellow oil (2.99 g, 75%). <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>) δ 7.24 (d, *J* = 7.9 Hz, 1H), 6.86 – 6.77 (m, 2H), 6.77 – 6.70 (m, 1H), 4.61 (t, *J* = 7.5 Hz, 2H), 3.80 (s, 3H), 3.30 (t, *J* = 7.4 Hz, 2H). All spectra were in agreement with published data.<sup>8</sup>



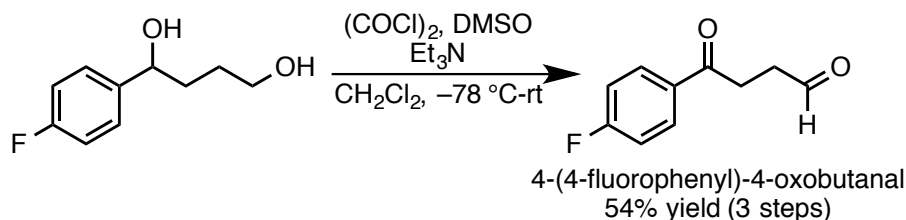
4-(4-Fluorophenyl)-4-oxobutanal was prepared from 4-fluorobenzaldehyde via a three-step sequence consisting of Grignard addition, hydroboration/oxidation followed by Swern oxidation.

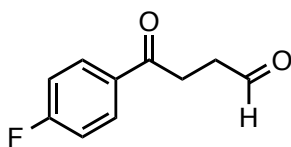


**Grignard addition:** A flame dried 500 mL round bottom flask equipped with a magnetic stir bar and a rubber septum was cooled under a stream of N<sub>2</sub> for 15 minutes. 4-Fluorobenzaldehyde (5.36 mL, 50 mmol, 1.0 equiv) and anhydrous THF (80 mL) were added sequentially via syringe. The flask was cooled to 0 °C in an ice-water bath. A separate flame dried 50 mL round bottom flask was equipped with a rubber septum and purged with nitrogen for 5 minutes. Allylmagnesium chloride (32.3 ml of a 1.7M solution in THF, 55 mmol, 1.1 equiv) was added to this flask and added dropwise to the flask containing the aldehyde via cannula using a positive pressure of N<sub>2</sub>. After the addition was complete, the flask was warmed to room temperature and stirred for 3 hours. The mixture was cooled to 0 °C in an ice-water bath, the septum was removed, and diluted with diethyl ether (100 mL, ACS grade). The reaction was quenched with saturated aqueous NH<sub>4</sub>Cl (50 mL) and H<sub>2</sub>O (50 mL). The layers were separated and the combined aqueous layers were extracted with diethyl ether (100 mL). The combined organic layers were washed with brine (150 mL), dried with magnesium sulfate, filtered and concentrated *in vacuo* to afford the homoallylic alcohol as a yellow oil (8.3 g).<sup>9</sup> The crude product was sufficiently pure by <sup>1</sup>H and <sup>19</sup>F NMR and was carried on without further purification.



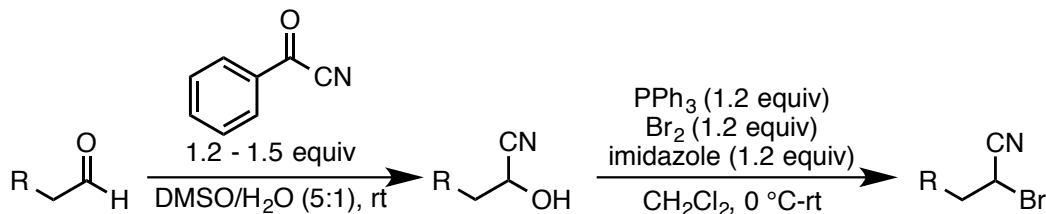
**Hydroboration:** A flame-dried 500 mL round bottom flask equipped with a magnetic stir bar and a rubber septum was charged with the crude homoallylic alcohol (~8.3g, 50 mmol assumed, 1.0 equiv) and the flask was purged with a stream of nitrogen for 5 minutes and cooled to 0 °C in an ice-water bath. Anhydrous THF (200 mL) was added via syringe. A separate flame dried 50 mL round bottom flask was equipped with a rubber septum and purged with nitrogen for 5 minutes. Borane-dimethylsulfide complex (38 mL of a 2M solution in THF, 75 mmol, 1.5 equiv) was added to this flask and added dropwise to the flask containing the alkene via cannula using a positive pressure of N<sub>2</sub>. The mixture was stirred at 0 °C for 15 minutes, then warmed to room temperature and stirred for 2.5 hours. The mixture was cooled to 0 °C in an ice-water bath and 3M NaOH (75 mmol, 25 mL) was added slowly via syringe (*caution: vigorous gas evolution*). Next, 30% aqueous H<sub>2</sub>O<sub>2</sub> (8.6 mL, 80 mmol, 1.6 equiv) was added via syringe. The mixture was warmed to room temperature and stirred for 2 hours. The septum was removed, and the mixture was diluted with ethyl acetate (150 mL) and the layers were separated. The organic layer was washed with brine (100 mL). The combined aqueous layers were extracted with ethyl acetate (100 mL). The combined organic layers were again washed with brine (100 mL), dried with magnesium sulfate, filtered and concentrated to give the diol as a thick yellow oil which solidified after several hours on high-vacuum (9.2 g).<sup>10</sup> The diol was carried forward without further purification.



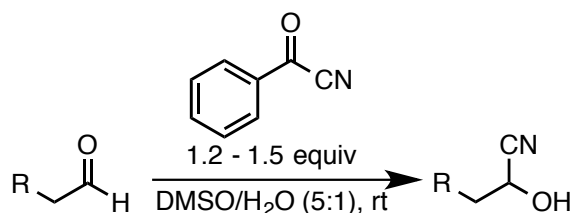


**Swern Oxidation:** A flame-dried 1 L round bottom flask equipped with a magnetic stir bar and a rubber septum was cooled under a stream of nitrogen and charged with anhydrous dichloromethane (400 mL) and DMSO (21.3 mL, 300 mmol, 6.0 equiv) via syringe. The mixture was cooled to  $-78\text{ }^{\circ}\text{C}$  in a dry-ice/acetone bath. A separate flame dried 50 mL round bottom flask was equipped with a rubber septum and purged with nitrogen for 5 minutes. Oxalyl chloride (17.2 mL, 200 mmol, 4.0 equiv) and anhydrous dichloromethane (20 mL) were added to this flask via syringe. The solution of oxalyl chloride was added dropwise via cannula to the flask containing DMSO and the mixture was allowed to stir for 20 minutes at  $-78\text{ }^{\circ}\text{C}$ . In a separate flask, the above diol (9.2 g, 50 mmol assumed, 1.0 equiv) was dissolved in anhydrous dichloromethane (90 mL). This solution was added dropwise via cannula using a positive pressure of  $\text{N}_2$  to the flask and the mixture was stirred for 30 minutes at  $-78\text{ }^{\circ}\text{C}$ . Triethylamine (70 mL, 500 mmol, 10 equiv) was added via syringe and the mixture was allowed to warm to room temperature. After 30 minutes, TLC indicated full conversion of the starting material. The septum was removed and the reaction was quenched with water (150 mL). The layers were separated and the organic layer was washed with water (200 mL) and brine (2 x 200 mL). The combined aqueous layers were back-extracted with dichloromethane (100 mL). The combined organic layers were dried with magnesium sulfate, filtered and evaporated. The crude product was purified by flash silica chromatography (85 : 15 hexanes : ethyl acetate – 75 : 25 hexanes : ethyl acetate) to afford 4-(4-fluorophenyl)-4-oxobutanal as a yellow/orange oil (4.9 g, 54% over 3 steps from 4-fluorobenzaldehyde).  $^1\text{H}$  NMR (600 MHz,  $\text{CDCl}_3$ )  $\delta$  9.90 (s, 1H), 8.02 (dd,  $J = 8.8, 5.4$  Hz, 2H), 7.14 (t,  $J = 8.6$  Hz, 2H), 3.29 (t,  $J = 6.3$  Hz, 2H), 2.94 (t,  $J = 6.3$  Hz, 2H);  $^{13}\text{C}$  NMR (151 MHz,  $\text{CDCl}_3$ )  $\delta$  200.6, 196.3, 166.8, 165.1, 133.01, 139.99, 130.9, 130.8, 116.0, 115.8, 37.7, 31.0;  $^{19}\text{F}$  NMR (565 MHz,  $\text{CDCl}_3$ )  $\delta$  -104.9; FTIR ( $\text{cm}^{-1}$ ): 2910, 2833, 2730, 1721, 1685, 1506, 1231; GC/MS (EI) 161.0 (M-F) $^+$ . HRMS (CI)  $m/z$ , calculated for  $[\text{C}_{10}\text{H}_{10}\text{O}_2\text{F}]^+$ : 181.0671; found: 181.0665.

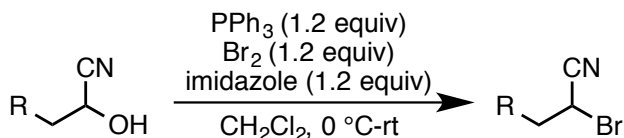
#### 4. General Protocol for the Synthesis of Previously Unknown $\alpha$ -Bromonitriles.



$\alpha$ -Bromonitriles were prepared from aldehydes in a two-step procedure involving formation of a cyanohydrin followed by a modified Appel reaction to generate the  $\alpha$ -bromonitrile. Cyanohydrins were prepared using an established literature procedure using benzoyl cyanide in a 5:1 mixture of DMSO and water.<sup>11</sup>

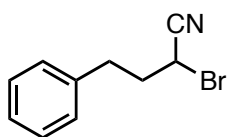


**General Protocol A:** The aldehyde (1 equiv) and DMSO:water (5:1) were combined in a round bottom flask containing a magnetic stir bar. A rubber septum was added and the flask was purged with nitrogen for 5 minutes. A solution of benzoyl cyanide (1.2-1.5 equiv) in DMSO and water (5:1) was added to the flask containing the aldehyde *via* cannula using a positive pressure of  $N_2$ . The reaction was stirred at room temperature. TLC analysis was performed by removing a small aliquot, quenching with phosphate buffer, extracting with diethyl ether and analyzing the organic layer by TLC. When the reaction was judged complete by TLC analysis, the reaction was quenched by adding pH 7 phosphate buffer. The mixture was extracted two times with the indicated solvent. The organic layers were combined and washed twice with saturated aqueous  $NaHCO_3$  to remove remaining benzoic acid, then twice with brine to remove DMSO. The combined organic layers were dried over magnesium sulfate, filtered and concentrated *in vacuo* to give the crude product. If NMR analysis of the crude mixture revealed that the aldehyde had been completely consumed, the crude mixture could be taken on directly to the bromination step. If some aldehyde remained, a short silica gel column was run to separate the aldehyde from the product cyanohydrin.



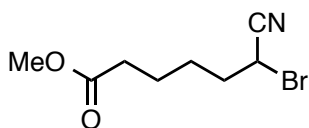
**General Protocol B:** Triphenylphosphine (1.2 equiv) was added to a flame-dried round bottom flask equipped with a magnetic stir bar and a rubber septum, and the flask was purged with a stream of nitrogen for ~5 minutes. Dichloromethane (ACS grade, stored over molecular sieves) was added via syringe, and the solution was cooled to 0 °C in an ice-water bath. Bromine ( $Br_2$ , 1.2 equiv) was added dropwise via syringe, forming a yellow suspension, and this suspension was stirred at 0 °C for 30 minutes. The septum was removed, imidazole (1.2 equiv) was added quickly, and the septum was replaced. The cyanohydrin (1 equiv) was added as a solution in dichloromethane *via* cannula or syringe in a single portion. The resulting mixture was warmed to room temperature and stirred overnight or until TLC indicated complete conversion of the starting material. The reaction was quenched with saturated aqueous  $NH_4Cl$  and saturated aqueous

$\text{Na}_2\text{S}_2\text{O}_3$ . The mixture was extracted twice with dichloromethane. The combined organic layers were washed with brine, dried over magnesium sulfate, filtered and concentrated *in vacuo*. The product was purified by silica gel chromatography.



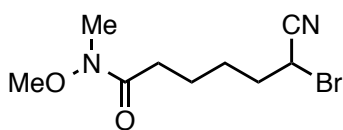
**(32)** According to general protocol B: triphenylphosphine (3.77 g, 14.4 mmol), bromine (0.74 mL, 14.4 mmol), dichloromethane (60 mL), imidazole (980 mg, 14.4 mmol), and 2-hydroxy-4-phenylbutanenitrile<sup>11</sup> (1.93 g, 12 mmol) were combined and stirred at room temperature overnight. The reaction was worked up according to the general procedure and purified by flash silica chromatography (91:9 hexanes : diethyl ether) to afford  $\alpha$ -bromonitrile **32** as a pale yellow oil (2.14 g, 80%). <sup>1</sup>H NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.37 – 7.31 (m, 2H), 7.29 – 7.24 (m, 1H), 7.23 – 7.18 (m, 2H), 4.17 (t,  $J$  = 7.2 Hz, 1H), 2.90 (t,  $J$  = 7.4 Hz, 2H), 2.41 (qd,  $J$  = 7.2, 1.8 Hz, 2H); <sup>13</sup>C NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  138.4, 129.0, 128.6, 127.1, 117.4, 38.1, 32.9, 26.4; FTIR ( $\text{cm}^{-1}$ ): 3028, 2956, 2243, 1496, 1454, 700; GC/MS (EI) 225.0 ( $\text{M}^+$ ). HRMS (CI)  $m/z$ , calculated for  $[\text{C}_{10}\text{H}_{11}\text{NBr}]^+$ : 224.0075; found: 224.0061.

NOTE: the product was stored in a freezer under air and showed no signs of decomposition by <sup>1</sup>H or <sup>13</sup>C NMR after ~9 months.



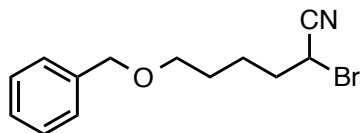
**(S2)** According to general protocol A: a solution of benzoyl cyanide (3.50 g, 26.6 mmol, 1.2 equiv) in 5:1 DMSO:H<sub>2</sub>O (60 mL) was added via cannula to a solution of 6-oxo-hexanoic acid methyl ester (3.20 g, 22.2 mmol, 1.0 equiv) in 5:1 DMSO:H<sub>2</sub>O (60 mL) under N<sub>2</sub> and stirred at room temperature for 6 hours. After extractive workup with diethyl ether, the crude cyanohydrin was taken on without further purification.

According to general protocol B: triphenylphosphine (3.35 g, 12.8 mmol), bromine (0.67 mL, 12.8 mmol), dichloromethane (50 mL), imidazole (870 mg, 12.8 mmol), and methyl 6-cyano-6-hydroxyhexanoate were combined and stirred at room temperature for 6 hours. The reaction was worked up according to the general procedure and purified by flash silica chromatography (75:25 hexanes : ethyl acetate) to afford  $\alpha$ -bromonitrile **S2** as a light yellow oil (2.08 g, 83%). <sup>1</sup>H NMR (600 MHz,  $\text{CDCl}_3$ )  $\delta$  4.31 (t,  $J$  = 6.9 Hz, 1H), 3.69 (s, 3H), 2.36 (t,  $J$  = 7.2 Hz, 2H), 2.15 – 2.09 (m, 2H), 1.71 (p,  $J$  = 7.2 Hz, 2H), 1.66 – 1.59 (m, 2H); <sup>13</sup>C NMR (151 MHz,  $\text{CDCl}_3$ )  $\delta$  173.5, 117.3, 51.8, 36.2, 33.6, 26.9, 26.5, 23.8; FTIR ( $\text{cm}^{-1}$ ): 2952, 2868, 2243, 1734, 1437, 1173; GC/MS (EI) 204.0 ( $\text{M-OMe}^+$ ). HRMS (CI)  $m/z$ , calculated for  $[\text{C}_8\text{H}_{13}\text{NO}_2\text{Br}]^+$ : 234.0130; found: 234.0132.



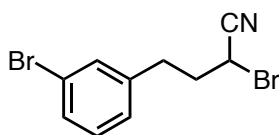
**(S3)** According to general protocol A: a solution of benzoyl cyanide (2.60 g, 20 mmol, 1.2 equiv) in 5:1 DMSO:H<sub>2</sub>O (45 mL) was added to a solution of aldehyde (2.83 g, 16.4 mmol, 1.0 equiv) in 5:1 DMSO:H<sub>2</sub>O (45 mL) via cannula under N<sub>2</sub> and stirred for 24 hours. After extractive workup with dichloromethane, the product was isolated as a yellow oil (2.78 g, 85%) which was taken on without further purification.

According to general protocol B: triphenylphosphine (4.32 g, 16.5 mmol), bromine (0.86 mL, 16.5 mmol), dichloromethane (60 mL), imidazole (1.12 g, 16.5 mmol), and 6-cyano-6-hydroxy-*N*-methoxy-*N*-methylhexanamide (2.80 g, 14 mmol) were combined and stirred at room temperature overnight. The reaction was worked up according to the general procedure and purified by flash silica chromatography (60:40 hexanes : ethyl acetate) to afford **S3** as an orange oil (2.84 g, 77%). <sup>1</sup>H NMR (600 MHz,  $\text{CDCl}_3$ )  $\delta$  4.32 (t,  $J$  = 6.9 Hz, 1H), 3.69 (s, 3H), 3.18 (s, 3H), 2.47 (t,  $J$  = 7.3 Hz, 2H), 2.16 – 2.10 (m, 2H), 1.71 (p,  $J$  = 7.1 Hz, 2H), 1.67 – 1.59 (m, 2H); <sup>13</sup>C NMR (151 MHz,  $\text{CDCl}_3$ )  $\delta$  173.8, 117.4, 61.3, 36.3, 32.3, 31.4, 27.0, 26.8, 23.3; FTIR ( $\text{cm}^{-1}$ ): 2941, 2868, 2242, 1660, 1462, 999; GC/MS (EI) 204.0 ( $\text{M-MeNOMe}^+$ ). HRMS (CI)  $m/z$ , calculated for  $[\text{C}_9\text{H}_{16}\text{N}_2\text{O}_2\text{Br}]^+$ : 263.0395; found: 263.0388.



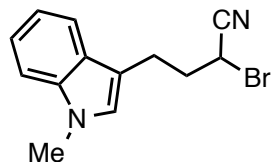
**(S4)** According to general protocol A: a solution of benzoyl cyanide (5.50 g, 42 mmol, 1.2 equiv) in 5:1 DMSO:H<sub>2</sub>O (50 mL) was added to a solution of aldehyde<sup>12</sup> (6.72 g, 35 mmol, 1.0 equiv) in 5:1 DMSO:H<sub>2</sub>O (150 mL) via cannula under N<sub>2</sub> and stirred at room temperature for 20 hours. After extractive workup with diethyl ether, TLC showed significant remaining starting material. The product was purified by flash silica gel chromatography (80:20 hexanes : ethyl acetate) to afford the product as a yellow oil (3.61 g, 47%).

According to general protocol B: triphenylphosphine (4.72 g, 18 mmol), bromine (0.93 mL, 18 mmol), dichloromethane (60 mL), imidazole (1.23 g, 18 mmol), and 6-(benzyloxy)-2-hydroxyhexanenitrile (3.29 g, 15 mmol) were combined and stirred at room temperature overnight. The reaction was worked up according to the general procedure and purified by flash silica chromatography (80:20 hexanes : diethyl ether) to afford **S4** as a yellow oil (4.06 g, 96%). <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>) δ 7.38 – 7.32 (m, 4H), 7.31 – 7.28 (m, 1H), 4.50 (s, 2H), 4.30 (t, *J* = 6.9 Hz, 1H), 3.50 (t, *J* = 5.7 Hz, 2H), 2.15 – 2.08 (m, 2H), 1.71 – 1.66 (m, 4H); <sup>13</sup>C NMR (151 MHz, CDCl<sub>3</sub>) δ 138.4, 128.6, 127.8, 117.4, 73.2, 69.6, 36.4, 28.6, 27.1, 24.2; FTIR (cm<sup>-1</sup>): 2941, 2863, 2242, 1454, 1103, 698; GC/MS (EI) 283.0 (M)<sup>+</sup>. HRMS (CI) *m/z*, calculated for [C<sub>13</sub>H<sub>17</sub>NOBr]<sup>+</sup>: 282.0494; found: 282.0487.



**(S5)** According to general protocol A: a solution of benzoyl cyanide (4.72 g, 36 mmol, 1.2 equiv) in 5:1 DMSO:H<sub>2</sub>O (100 mL) was added to a solution of aldehyde (6.39 g, 30 mmol, 1.0 equiv) in 5:1 DMSO:H<sub>2</sub>O (100 mL) via cannula under N<sub>2</sub> and stirred at room temperature for 24 hours. After extractive workup with diethyl ether the crude cyanohydrin was taken on without further purification.

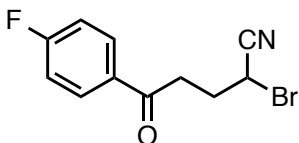
According to general protocol B: triphenylphosphine (6.44 g, 24.6 mmol), bromine (1.28 mL, 24.6 mmol), dichloromethane (80 mL), imidazole (1.68 g, 24.6 mmol), and 4-(3-bromophenyl)-2-hydroxybutanenitrile (4.92 g, 20.5 mmol) were combined and stirred at room temperature for 3 hours. The reaction was worked up according to the general procedure and purified by flash silica chromatography (87:13 hexanes : diethyl ether) to afford **S5** as a colorless oil (5.4 g, 87%). <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>) δ 7.40 (d, *J* = 8.0 Hz, 1H), 7.37 (s, 1H), 7.20 (t, *J* = 7.8 Hz, 1H), 7.14 (d, *J* = 7.6 Hz, 1H), 4.20 (t, *J* = 7.0 Hz, 1H), 2.88 (td, *J* = 7.3, 2.0 Hz, 2H), 2.40 (qd, *J* = 7.1, 1.9 Hz, 2H); <sup>13</sup>C NMR (151 MHz, CDCl<sub>3</sub>) δ 140.8, 131.6, 130.6, 130.3, 127.3, 123.1, 117.1, 37.8, 32.6, 26.2; FTIR (cm<sup>-1</sup>): 3059, 2956, 2864, 2243, 1596, 1568, 1474, 1072; GC/MS (EI) 302.9 (M)<sup>+</sup>. HRMS (CI) *m/z* calculated for [C<sub>10</sub>H<sub>10</sub>NBr<sub>2</sub>]<sup>+</sup>: 303.9160; found: 303.9149.



**(S6)** According to general protocol A: a solution of benzoyl cyanide (5.24 g, 39 mmol, 1.2 equiv) in 5:1 DMSO:H<sub>2</sub>O (110 mL) was added to a solution of aldehyde<sup>13,14</sup> (6.07 g, 32.5 mmol, 1.0 equiv) via cannula under N<sub>2</sub> and stirred at room temperature for 38 hours. After extractive workup with diethyl ether and ethyl acetate, TLC showed significant remaining starting material. The product was purified by flash silica gel chromatography (80:20 hexanes:ethyl acetate) to afford the product as a yellow oil (4.05 g, 58%).

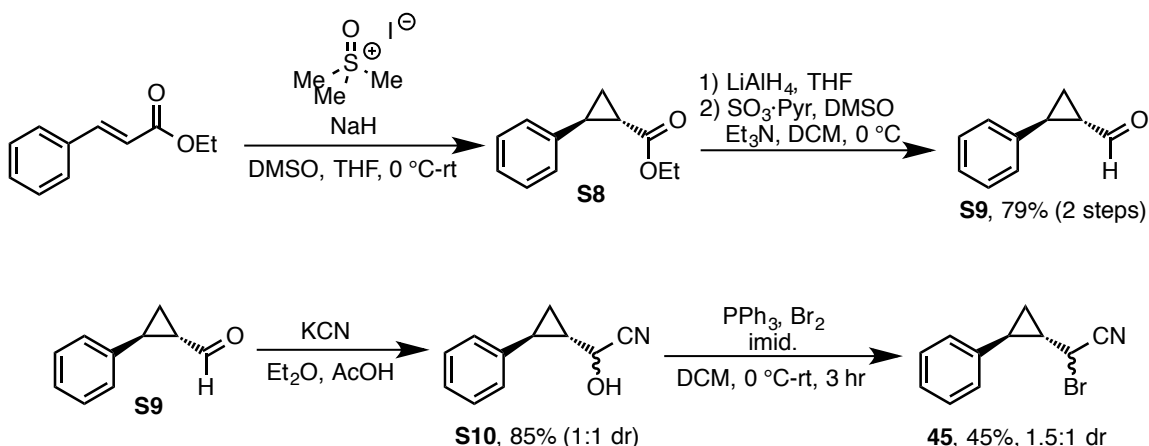
According to general protocol B: triphenylphosphine (5.90 g, 22.5 mmol), bromine (1.16 mL, 22.5 mmol), dichloromethane (95 mL), imidazole (1.53 g, 22.5 mmol) and 2-hydroxy-4-(1-methyl-1*H*-indol-3-yl)butanenitrile (4.05 g, 19 mmol) were combined and stirred at room temperature for 4 hours. The reaction was worked up according to the general procedure and purified by flash silica chromatography (80:20 hexanes : diethyl ether) to afford **S6** as a viscous yellow oil (4.6 g, 88%). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.58 (d, *J* = 7.9 Hz, 1H), 7.33 (d, *J* = 8.2 Hz, 1H), 7.29 ? 7.22 (m, 1H), 7.14 (t, *J* = 7.4 Hz, 1H), 6.93 (s, 1H), 4.19 (t, *J* = 7.3 Hz, 1H), 3.77 (s, 3H), 3.05 (t, *J* = 6.9 Hz, 2H), 2.54 ? 2.40 (m, 2H); <sup>13</sup>C NMR (151 MHz, CDCl<sub>3</sub>) δ 137.3, 127.3, 127.1, 122.1, 119.3, 118.7, 117.6, 110.7, 109.6, 37.1, 32.8, 26.9, 22.6; FTIR (cm<sup>-1</sup>): 3054, 2938, 2852, 2242, 1744, 741; GC-MS (EI): 302.9 (M)<sup>+</sup>. HRMS (CI) *M/Z* calculated for [C<sub>13</sub>H<sub>14</sub>N<sub>2</sub>Br]<sup>+</sup>: 277.0340; found: 277.0322.



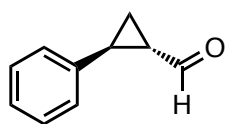


**(S7)** According to general protocol B: triphenylphosphine (2.93 g, 11.2 mmol), bromine (0.58 mL, 11.2 mmol), dichloromethane (45 mL), imidazole (762 mg, 11.2 mmol) and 5-(4-fluorophenyl)-2-hydroxy-5-oxopentanenitrile (1.90 g, 9.40 mmol) were combined and stirred for at room temperature for 6 hours. The reaction was worked up according to the general procedure and purified by flash silica chromatography (85:15 hexanes : diethyl ether) to afford **S7** as a light yellow solid (1.97 g, 78%).  $^1\text{H}$  NMR (600 MHz,  $\text{CDCl}_3$ )  $\delta$  8.01 (ddd,  $J = 8.9, 5.2, 2.5$  Hz, 2H), 7.17 (t,  $J = 8.6$  Hz, 2H), 4.63 (t,  $J = 6.9$  Hz, 1H), 3.35 – 3.22 (m, 2H), 2.55 (hept,  $J = 7.8$  Hz, 2H);  $^{13}\text{C}$  NMR (151 MHz,  $\text{CDCl}_3$ )  $\delta$  195.7, 167.1, 165.4, 132.70, 132.68, 130.9, 130.8, 117.2, 116.2, 116.1, 35.1, 30.9, 26.6;  $^{19}\text{F}$  NMR (565 MHz,  $\text{CDCl}_3$ )  $\delta$  -103.9; FTIR ( $\text{cm}^{-1}$ ): 3076, 2972, 2244, 1685, 1598, 1158; mp = 56-58 °C; GC/MS (EI) 251.9 (M-F) $^+$ . HRMS (CI)  $m/z$  calculated for  $[\text{C}_{11}\text{H}_{10}\text{NOBrF}]^+$ : 269.9930; found: 269.9904

## Synthesis of Radical Clock Substrate 45



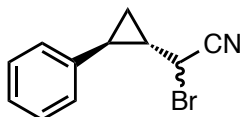
Ester **S8** was prepared according to a literature procedure.<sup>15</sup>



(**S9**) LiAlH<sub>4</sub> (692 mg, 18.2 mmol, 2.6 equiv) was placed in a flame-dried 100 mL round-bottom flask equipped with a magnetic stir bar and a rubber septum and the flask was purged with nitrogen for 10 minutes. Anhydrous THF (25 mL) was added via syringe and the flask was cooled to 0 °C in an ice-water bath. A solution of ester **S8** (1.33 g, 7 mmol, 1 equiv) in anhydrous THF (10 mL) was added dropwise via syringe, the bath was removed, and the resulting grey suspension was allowed to stir at room temperature for 90 minutes, when TLC showed full conversion of the ester. A vent needle was placed in the septum and the reaction was cooled to 0 °C and *carefully* quenched by sequentially slowly adding 700 μL H<sub>2</sub>O, 700 μL 3.75M NaOH, and 2.10 mL H<sub>2</sub>O via syringe and warmed to room temperature. The reaction was stirred vigorously until a white granular precipitate was observed (~15 minutes). The reaction was filtered through a Celite pad, washing with ethyl acetate (30 mL). The solvent was evaporated *in vacuo* to provide the crude alcohol (1.04 g), which was taken on to the oxidation step without further purification.

The crude alcohol (assumed 7 mmol, 1 equiv), anhydrous DMSO (2.49 mL, 35 mmol, 5 equiv), triethylamine (3.9 mL, 28 mmol, 4 equiv) and anhydrous dichloromethane (30 mL) were combined in a 100 mL round bottom flask equipped with a magnetic stir bar and a rubber septum. The mixture was cooled to 0 °C in an ice-water bath and sulfur trioxide pyridine complex (2.23 g, 14 mmol, 2 equiv) was added portion-wise over 10 minutes. The bath was removed and the reaction was stirred at room temperature for 90 minutes when TLC showed full conversion of the alcohol. The septum was removed and the reaction was quenched by the addition of water (20 mL) and brine (20 mL). The mixture was extracted twice with dichloromethane (30 mL) and the combined organic layers were washed with brine (30 mL), dried over magnesium sulfate, filtered and concentrated *in vacuo*. The aldehyde was purified by flash silica gel chromatography (95:5 hexanes : ethyl acetate) to provide the product as a clear oil (801 mg, 79% yield over two steps). <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>) δ 9.34 (d, *J* = 4.6 Hz, 1H), 7.30 (t, *J* = 7.5 Hz, 2H), 7.23 (t, *J* = 7.4 Hz, 1H), 7.12 (d, *J* = 7.4 Hz, 2H), 2.69 – 2.60 (m, 1H), 2.23 – 2.13 (m, 1H), 1.74 (dt, *J* = 10.0, 5.1 Hz, 1H), 1.60 – 1.49 (m, 1H). All spectra were consistent with published data.<sup>16,17</sup>

Because cyanohydrin synthesis using the aforementioned method with benzoyl cyanide was very sluggish, an alternate procedure was utilized.



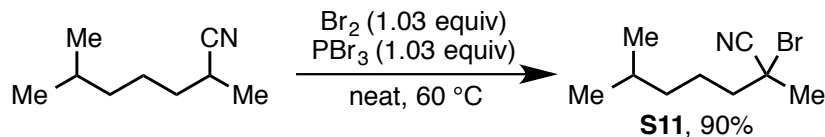
**(45)** Potassium cyanide (520 mg, 8 mmol, 1.6 equiv) was placed in a flame-dried 100 mL round bottom flask with a magnetic stir bar and a rubber septum and the flask was purged with nitrogen for 5 minutes. Anhydrous diethyl ether (15 mL) was added via syringe. A solution of aldehyde **S9** (750 mg, 5.1 mmol, 1 equiv) in anhydrous diethyl ether (5 mL) was added dropwise via syringe with vigorous stirring. Acetic acid (460  $\mu$ L, 8 mmol, 1.6 equiv) was added via syringe. After a short time, a thick white suspension formed. The mixture was stirred vigorously for 24 hours at room temperature (**CAUTION: HCN IS FORMED DURING THE REACTION**). The reaction was quenched by slowly adding distilled water (3 mL) and saturated aqueous  $\text{NaHCO}_3$  (4 mL) via syringe. The layers were separated and the aqueous layer was extracted twice with diethyl ether (15 mL). The combined organic layers were dried with magnesium sulfate and concentrated *in vacuo* to yield the crude cyanohydrin **S10** as a 1:1 mixture of diastereomers, which was taken onto the bromination without further purification.

Triphenylphosphine (1.36 g, 5.2 mmol, 1.2 equiv) and imidazole (354 mg, 5.2 mmol, 1.2 equiv) were added to a flame-dried 100 mL round bottom flask equipped with a magnetic stir bar and a rubber septum and the flask was purged with nitrogen for 5 minutes. Anhydrous dichloromethane (15 mL) was added via syringe and the solution was cooled to 0  $^{\circ}\text{C}$  in an ice-water bath. Bromine (260  $\mu$ L, 5.1 mmol, 1.2 equiv) was added dropwise via syringe and the mixture was stirred for 30 minutes at 0  $^{\circ}\text{C}$ . A solution of cyanohydrin **S10** (750 mg, 4.3 mmol, 1 equiv) in dichloromethane (5 mL) was added via syringe. The mixture was allowed to warm to room temperature and stirred for 3 hours, when TLC showed full conversion of the cyanohydrin. The reaction was worked up according to general protocol B (above). The product was isolated using automated silica gel chromatography on a Biotage isolera automated chromatography machine to provide **45** as a yellow oil (453 mg, 45%).  $^1\text{H}$  NMR (600 MHz,  $\text{CDCl}_3$ )  $\delta$  7.35 – 7.27 (m, 2H), 7.25 – 7.20 (m, 1H), 7.18 – 7.08 (m, 2H), 4.34 (ap dd,  $J$  = 7.5, 1.7 Hz, 1H), 2.29 (p,  $J$  = 9.9, 5.4 Hz, 0.6H), 2.22 (p,  $J$  = 9.9, 5.3 Hz, 0.4H), 1.93 – 1.71 (m, 1H), 1.44 – 1.24 (m, 2H).  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  139.37, 139.36, 128.74, 128.72, 126.9, 126.7, 126.4, 115.78, 115.75, 30.9, 30.8, 27.0, 26.8, 26.1, 25.4, 16.8, 16.4; FTIR ( $\text{cm}^{-1}$ ): 3029, 2962, 2244, 2214, 1604, 1498, 697. HRMS (CI)  $m/z$  calculated for  $[\text{C}_{11}\text{H}_{11}\text{NBr}]^+$ : 236.0075; found: 236.0074.

## 5. Synthesis of $\alpha$ -Bromonitriles by Direct Bromination of Alkyl Nitriles

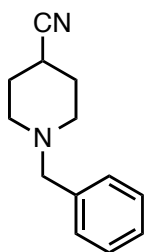
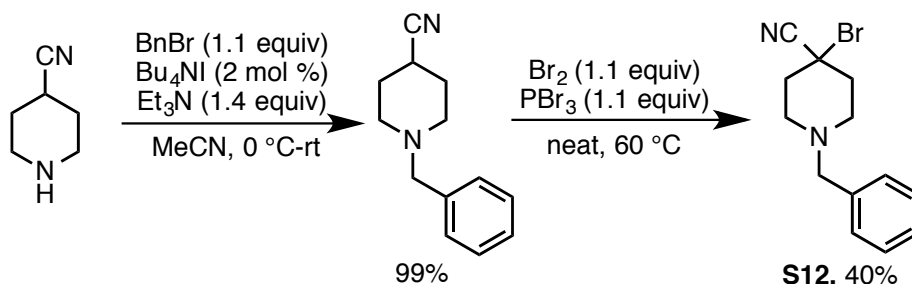
1-Bromocyclohexanecarbonitrile and  $\alpha$ -bromoisobutyronitrile were prepared according to a literature procedure.<sup>18</sup>

NOTE: all yields in this section are unoptimized

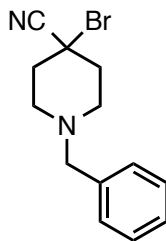


**(S11)** A flame dried 250 mL round bottom flask equipped with a magnetic stir bar and a rubber septum was cooled under a stream of  $\text{N}_2$  for 15 minutes. Phosphorus tribromide ( $\text{PBr}_3$ , 1.93 mL, 20.5 mmol, 1.03 equiv) was added via syringe. The flask was cooled to 0  $^{\circ}\text{C}$  in an ice-water bath and bromine (1.06 mL, 20.5 mmol, 1.03) was added dropwise via syringe, forming an orange solid. 2,6-dimethylheptanenitrile (2.8 g, 20 mmol) was added to the flask via syringe and the flask was placed in a 60  $^{\circ}\text{C}$  oil bath and stirred rapidly overnight. During the reaction, the flask was connected to an oil bubbler and a very slow stream of  $\text{N}_2$  was introduced in order to purge the  $\text{HBr}$  created during the course of the reaction. A dark red homogeneous mixture was formed

during the reaction. The mixture was cooled to room temperature and quenched by pouring carefully onto ice water. The mixture was extracted twice with diethyl ether (50 mL). The combined organic layers were washed with saturated aqueous  $\text{NaHCO}_3$  (40 mL) and brine (40 mL), dried over magnesium sulfate and concentrated *in vacuo*. The crude product was purified by passing through a short plug of silica gel (eluting with 98:2 hexanes : diethyl ether) to afford **S11** as a light yellow oil (3.93 g, 90%).  $^1\text{H}$  NMR (600 MHz,  $\text{CDCl}_3$ )  $\delta$  2.07 (s, 3H), 2.06 – 1.92 (m, 2H), 1.71 – 1.52 (m, 3H), 1.35 – 1.16 (m, 2H), 0.91 (s, 3H), 0.90 (s, 3H);  $^{13}\text{C}$  NMR (151 MHz,  $\text{CDCl}_3$ )  $\delta$  120.4, 44.9, 44.5, 38.1, 31.8, 27.9, 24.6, 22.62, 22.60; FTIR ( $\text{cm}^{-1}$ ): 2956, 2871, 2237, 1462, 1384; GC/MS (EI) 218.1 ( $\text{M}^+$ ). HRMS (CI)  $m/z$  calculated for  $[\text{C}_9\text{H}_{17}\text{NBr}]^+$ : 218.0544; found: 218.0528.

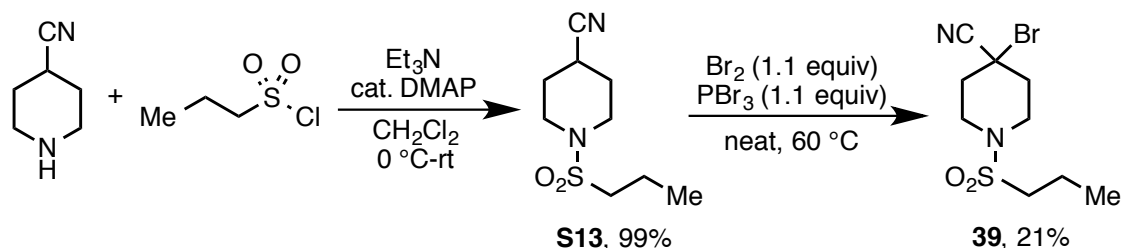


4-Cyanopiperidine (6.2 mL, 55 mmol, 1.0 equiv), triethylamine (9.8 mL, 70 mmol, 1.3 equiv) and tetrabutylammonium iodide (500 mg, 1.4 mmol, 2.5 mol %) and acetonitrile (140 mL) were combined in a 250 mL round bottom flask and cooled to 0 °C in an ice-water bath. Benzyl bromide (7.2 mL, 60 mmol, 1.1 equiv) was added slowly via syringe and the mixture was warmed to room temperature and stirred overnight. The crude reaction mixture was poured into a separatory funnel containing water (200 mL) and extracted twice with ethyl acetate (100 mL). The layers were separated and the organic layer was washed twice with 3M HCl (150 mL). The organic layer was then discarded. The aqueous layer containing the ammonium salt of the product was then basified to  $\text{pH} > 9$  by slowly adding 8M NaOH at 0 °C. The aqueous layer was then extracted twice with diethyl ether (50 mL) to extract the free amine. The organic layer was dried over magnesium sulfate and concentrated *in vacuo* to afford the product as a light yellow oil (10.9 g, 99% yield).  $^1\text{H}$  NMR (600 MHz,  $\text{CDCl}_3$ )  $\delta$  7.34 – 7.23 (m, 5H), 3.50 (s, 2H), 2.66 (s, 3H), 2.31 (s, 2H), 1.98 – 1.90 (m, 2H), 1.91 – 1.79 (m, 2H). All spectra were in agreement with published data.<sup>19</sup>



**(S12)** A flame dried 250 mL round bottom flask equipped with a magnetic stir bar and a rubber septum was cooled under a stream of  $\text{N}_2$  for 15 minutes. Phosphorus tribromide ( $\text{PBr}_3$ , 2.60 mL, 27.5 mmol, 1.1 equiv) was added via syringe. The flask was cooled to 0 °C in an ice-water bath and bromine (1.42 mL, 27.5 mmol, 1.1 equiv) was added dropwise via syringe, forming an orange solid. *N*-Benzyl-4-cyanopiperidine (5.0 g, 25 mmol, 1.0 equiv) was added to the flask via syringe and the flask was placed in a 60 °C oil bath and stirred rapidly overnight. During the reaction, the flask was connected to an oil bubbler and a very slow stream of  $\text{N}_2$  was introduced in order to purge the HBr created during the course of the reaction. The flask was cooled to room temperature and the solidified mixture was diluted with diethyl ether (150 mL) and quenched by pouring carefully onto ice water. The mixture was extracted twice with diethyl ether (50 mL). The combined organic layers were washed with saturated aqueous  $\text{NaHCO}_3$  (100 mL) and brine (100 mL), dried over magnesium sulfate and concentrated *in vacuo*. The crude product was purified by flash silica gel chromatography (85:15 hexanes : ethyl acetate) to afford product **S12** as an off-white solid (2.77

g, 40% yield).  $^1\text{H}$  NMR (600 MHz,  $\text{CDCl}_3$ )  $\delta$  7.41 – 7.27 (m, 5H), 3.54 (s, 2H), 2.70 (s, 2H), 2.50 (s, 2H), 2.44 – 2.35 (m, 2H), 2.36 – 2.27 (m, 2H).  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  137.7, 128.9, 128.4, 127.4, 119.5, 62.4, 50.5, 43.5, 40.2; FTIR ( $\text{cm}^{-1}$ ): 2811, 2769, 2239, 1653, 740; mp = 58–60 °C; GC/MS (EI) 278.0 (M) $^+$ . HRMS (CI) m/z calculated for  $[\text{C}_{13}\text{H}_{16}\text{N}_2\text{Br}]^+$ : 279.0497; found: 279.0470.

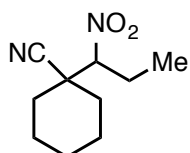


**(S13)** 4-Cyanopiperidine (5.62 mL, 50 mmol, 1 equiv), 4-dimethylaminopyridine (DMAP, ~10 mg), triethylamine (10.5 mL, 75 mmol, 1.5 equiv) and dichloromethane (75 mL) were combined in a 200 mL round bottom flask equipped with a magnetic stir bar and a rubber septum. The mixture was cooled to 0 °C in an ice-water bath and freshly distilled 1-propanesulfonyl chloride (5.9 mL, 52 mmol, 1.04 equiv) was added dropwise via syringe, forming a white precipitate. The mixture was warmed to room temperature, stirred for 2.5 hours and quenched with water (50 mL). The mixture was extracted with dichloromethane (50 mL) and the organic layer was washed with saturated aqueous  $\text{NaHCO}_3$  (50 mL), twice with 1M HCl (50 mL), and once with brine (50 mL). The combined organic layers were dried over magnesium sulfate and concentrated *in vacuo* to give the *N*-1-propanesulfonyl-4-cyanopiperidine (**S13**) as a viscous yellow oil which crystallized upon agitation (10.8 g, 99% yield).  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  3.46 – 3.30 (m, 4H), 2.97 – 2.80 (m, 3H), 2.06 – 1.90 (m, 4H), 1.90 – 1.78 (m, 2H), 1.06 (t,  $J = 7.4$  Hz, 3H).  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  120.6, 51.6, 43.5, 28.5, 25.7, 17.0, 13.3; FTIR ( $\text{cm}^{-1}$ ): 2969, 2937, 2859, 2241, 1457, 1322, 1146; mp = 39–41 °C; GC/MS (EI): 216.1 (M) $^+$ . HRMS (CI) m/z calculated for  $[\text{C}_9\text{H}_{17}\text{N}_2\text{O}_2\text{S}]^+$ : 217.1011; found: 217.1027.

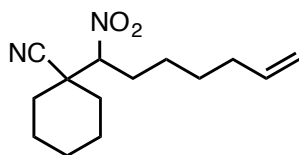
**(39)** A flame dried 250 mL round bottom flask equipped with a magnetic stir bar and a rubber septum was cooled under a stream of  $\text{N}_2$  for 15 minutes. Phosphorus tribromide ( $\text{PBr}_3$ , 2.76 mL, 29.4 mmol, 1.1 equiv) was added via syringe. The flask was cooled to 0 °C in an ice-water bath and bromine (1.53 mL, 29.4 mmol, 1.1 equiv) was added dropwise via syringe, forming an orange solid. The septum was removed, *N*-1-propanesulfonyl-4-cyanopiperidine (**S13**, 6.1 g, 28 mmol, 1.0 equiv) was quickly added to the flask in a single portion, and the septum was replaced. The flask was placed in a 60 °C oil bath and stirred rapidly overnight. During the reaction, the flask was connected to an oil bubbler and a very slow stream of  $\text{N}_2$  was introduced in order to purge the HBr created during the course of the reaction. The mixture was cooled to room temperature and quenched by pouring carefully onto ice water. The mixture was extracted twice with ethyl acetate (75 mL). The combined organic layers were washed with saturated aqueous  $\text{NaHCO}_3$  (100 mL) and brine (50 mL), dried over magnesium sulfate and evaporated. The crude product was purified by flash silica gel chromatography (75:25 hexanes : ethyl acetate) to afford product **39** as an off-white solid (1.77 g, 21% yield). Note: the starting material could be recovered cleanly and resubjected to the bromination reaction without incident.  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  3.64 – 3.49 (m, 2H), 3.46 – 3.33 (m, 2H), 3.00 – 2.84 (m, 2H), 2.53 – 2.40 (m, 2H), 2.40 – 2.27 (m, 2H), 1.94 – 1.73 (m, 2H), 1.07 (t,  $J = 7.4$  Hz, 3H).  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  118.7, 52.4, 43.1, 41.9, 39.7, 17.0, 13.2; FTIR ( $\text{cm}^{-1}$ ): 2975, 2846, 2234, 1338, 1162; mp = 116–118 °C; GC/MS (EI) 295.6 (M) $^+$ . HRMS (CI) m/z calculated for  $[\text{C}_9\text{H}_{16}\text{N}_2\text{O}_2\text{SBr}]^+$ : 295.0116; found: 295.0093.

## 6. General Protocol for Alkylation.

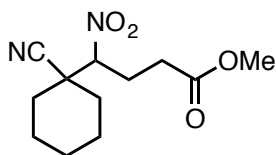
An oven-dried (or flame-dried) Schlenk flask equipped with a magnetic stir bar and a rubber septum was attached to a double manifold and cooled under vacuum. Once cool, the rubber septum was removed and the flask was charged with CuBr (0.2 equiv), ligand **2** (0.25 equiv) and sodium *tert*-butoxide (1.2 equiv). The septum was replaced and the flask was attached to a double manifold and evacuated and refilled with N<sub>2</sub> five times. Anhydrous solvent and nitroalkane (1.25 equiv) were added sequentially via syringe. The mixture was stirred for ~5 min, forming a thick suspension. The  $\alpha$ -bromonitrile (1 equiv) was added neat as an oil via syringe. If the  $\alpha$ -bromonitrile was a solid, it was added as an air-free solution in the specified anhydrous solvent via syringe (the solution was prepared either by evacuating and refilling a vial containing the solid with N<sub>2</sub> and adding anhydrous solvent or by preparing a solution in anhydrous solvent and sparging with N<sub>2</sub>). The mixture was stirred at the designated temperature using an oil bath for 24 h. The reaction was cooled to room temperature and diluted with diethyl ether or dichloromethane. The mixture was filtered through a short pad of Celite washing with diethyl ether or dichloromethane. After concentrating *in vacuo*, the product was purified by silica gel chromatography.



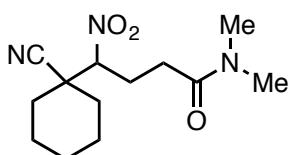
(**3**) According to the general protocol: CuBr (85.8 mg, 600  $\mu$ mol), ligand **2** (230 mg, 750  $\mu$ mol), sodium *tert*-butoxide (346 mg, 3.60 mmol), anhydrous hexanes (18 mL), 1-nitropropane (334  $\mu$ L, 3.75 mmol) and 1-bromocyclohexanecarbonitrile (564 mg, 3.00 mmol) were combined under N<sub>2</sub> and stirred rapidly at room temperature for 24 hours. The reaction was worked up according to the general protocol and purified by flash silica gel chromatography (90:10:1 hexanes : ethyl acetate : acetic acid) to afford product **3** (552 mg, 94%) as a white solid: <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>)  $\delta$  4.27 (dd, *J* = 11.9, 2.8 Hz, 1H), 2.30 (ddq, *J* = 14.4, 12.0, 7.2 Hz, 1H), 2.10 – 2.04 (m, 1H), 1.99 (dq, *J* = 14.8, 7.4, 2.9 Hz, 1H), 1.91 – 1.76 (m, 4H), 1.76 – 1.60 (m, 2H), 1.48 (td, *J* = 13.1, 3.5 Hz, 1H), 1.31 (td, *J* = 12.9, 3.6 Hz, 1H), 1.25 – 1.12 (m, 1H), 1.02 (t, *J* = 7.3 Hz, 3H); <sup>13</sup>C NMR (151 MHz, CDCl<sub>3</sub>)  $\delta$  119.2, 95.5, 42.4, 33.8, 32.1, 24.9, 23.1, 22.50, 22.48, 10.6; FTIR (cm<sup>-1</sup>): 2947, 2864, 2237, 1554, 1376; mp = 96–98 °C; GC/MS (EI) 150.2 (M-NO<sub>2</sub>)<sup>+</sup>. HRMS (CI) *m/z*, calculated for [C<sub>10</sub>H<sub>17</sub>N<sub>2</sub>O<sub>2</sub>]<sup>+</sup>: 197.1290; found: 197.1269.



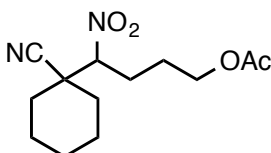
(**4**) According to the general protocol: CuBr (85.8 mg, 600  $\mu$ mol), ligand **2** (230 mg, 750  $\mu$ mol), sodium *tert*-butoxide (346 mg, 3.60 mmol), anhydrous hexanes (18 mL), 7-nitro-1-heptene (537 mg, 3.75 mmol) and 1-bromocyclohexanecarbonitrile (564 mg, 3.00 mmol) were combined under N<sub>2</sub> and heated at 50 °C with rapid stirring for 24 hours. The reaction was worked up according to the general protocol and purified by flash silica gel chromatography (96:4:1 hexanes : ethyl acetate : acetic acid) to afford product **4** as an off-white solid (695 mg, 93%). <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>)  $\delta$  5.75 (ddt, *J* = 16.9, 10.2, 6.7 Hz, 1H), 5.00 (dd, *J* = 17.1, 1.6 Hz, 1H), 4.97 (d, *J* = 10.2 Hz, 1H), 4.33 (dd, *J* = 11.9, 2.6 Hz, 1H), 2.30 (ddt, *J* = 14.4, 12.0, 7.3 Hz, 1H), 2.11 – 1.99 (m, 3H), 1.95 – 1.76 (m, 5H), 1.76 – 1.58 (m, 2H), 1.52 – 1.40 (m, 3H), 1.36 (h, *J* = 7.6, 7.2 Hz, 2H), 1.30 (td, *J* = 12.9, 3.5 Hz, 1H), 1.24 – 1.12 (m, 1H); <sup>13</sup>C NMR (151 MHz, CDCl<sub>3</sub>)  $\delta$  138.0, 119.2, 115.3, 93.8, 42.4, 33.9, 33.3, 32.0, 29.4, 28.1, 25.4, 24.8, 22.51, 22.49; FTIR (cm<sup>-1</sup>): 2936, 2862, 2238, 1554, 1367; mp = 41–43 °C; GC/MS (EI) 204.3 (M-NO<sub>2</sub>)<sup>+</sup>. HRMS (CI) *m/z* calculated for [C<sub>14</sub>H<sub>23</sub>N<sub>2</sub>O<sub>2</sub>]<sup>+</sup>: 251.1760; found: 251.1762.



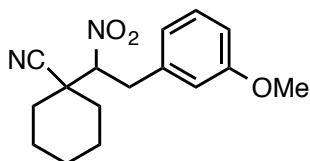
(5) According to the general protocol: CuBr (85.8 mg, 600  $\mu$ mol), ligand **2** (230 mg, 750  $\mu$ mol), sodium *tert*-butoxide (346 mg, 3.60 mmol), anhydrous hexanes (18 mL), methyl 4-nitrobutyrate (552 mg, 3.75 mmol) and 1-bromocyclohexanecarbonitrile (564 mg, 3.00 mmol) were combined under N<sub>2</sub> and stirred rapidly at room temperature for 24 hours. The reaction was worked up according to the general protocol and purified by flash silica gel chromatography (83:17:1 hexanes : ethyl acetate : acetic acid) to afford product **5** as an off-white solid (606 mg, 79% yield): <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>)  $\delta$  4.53 (dd, *J* = 11.4, 2.3 Hz, 1H), 3.71 (s, 3H), 2.54 – 2.45 (m, 2H), 2.39 – 2.27 (m, 2H), 2.13 (dd, *J* = 13.2, 3.1 Hz, 1H), 1.89 – 1.77 (m, 4H), 1.69 (dddd, *J* = 30.0, 26.7, 15.5, 8.3 Hz, 2H), 1.47 (td, *J* = 12.9, 3.5 Hz, 1H), 1.39 (td, *J* = 12.9, 3.7 Hz, 1H), 1.21 (qq, *J* = 12.9, 3.9 Hz, 1H). <sup>13</sup>C NMR (151 MHz, CDCl<sub>3</sub>)  $\delta$  172.2, 119.0, 92.5, 77.4, 52.2, 42.3, 33.7, 32.3, 29.5, 24.9, 24.8, 22.42, 22.40; FTIR (cm<sup>-1</sup>): 2944, 2864, 2238, 1738, 1555; mp = 72-74 °C; GC/MS (EI) 223.0 (M-OMe)<sup>+</sup>. HRMS (CI) *m/z*, calculated for [C<sub>12</sub>H<sub>19</sub>N<sub>2</sub>O<sub>4</sub>]<sup>+</sup>: 255.1345; found: 255.1326.



(6) According to the general protocol: CuBr (85.8 mg, 600  $\mu$ mol), ligand **2** (230 mg, 750  $\mu$ mol), sodium *tert*-butoxide (346 mg, 3.60 mmol), anhydrous dichloromethane (18 mL), *N,N*-dimethyl-4-nitrobutanamide (600 mg, 3.75 mmol) and 1-bromocyclohexanecarbonitrile (564 mg, 3.00 mmol) were combined under N<sub>2</sub> and stirred rapidly at room temperature for 24 hours. The reaction was worked up according to the general protocol and purified by flash silica gel chromatography (45:55:1 hexanes : ethyl acetate : acetic acid) to afford product **6** as a yellow solid (581 mg, 73%). <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>)  $\delta$  4.67 (dd, *J* = 11.5, 2.2 Hz, 1H), 2.96 (s, 3H), 2.95 (s, 3H), 2.56 – 2.45 (m, 2H), 2.43 – 2.33 (m, 1H), 2.29 – 2.15 (m, 2H), 1.89 – 1.74 (m, 4H), 1.74 – 1.58 (m, 2H), 1.46 (tdd, *J* = 12.9, 9.6, 3.6 Hz, 2H), 1.20 (dddd, *J* = 16.4, 12.7, 8.9, 4.1 Hz, 1H); <sup>13</sup>C NMR (151 MHz, CDCl<sub>3</sub>)  $\delta$  170.4, 119.3, 93.0, 42.2, 37.1, 35.7, 33.7, 32.6, 28.3, 25.2, 24.9, 22.43, 22.38; FTIR (cm<sup>-1</sup>): 2939, 2863, 2237, 1647, 1554; mp = 78-82 °C; GC/MS (EI) 221.0 (M-NO<sub>2</sub>)<sup>+</sup>. HRMS (CI) *m/z* calculated for [C<sub>13</sub>H<sub>22</sub>N<sub>3</sub>O<sub>3</sub>]<sup>+</sup>: 268.1661; found: 268.1656.

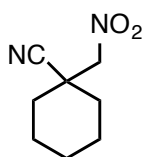


(7) According to the general protocol: CuBr (85.8 mg, 600  $\mu$ mol), ligand **2** (230 mg, 750  $\mu$ mol), sodium *tert*-butoxide (346 mg, 3.60 mmol), anhydrous hexanes (18 mL), 4-nitrobutyl acetate (604 mg, 3.75 mmol) and 1-bromocyclohexanecarbonitrile (564 mg, 3.00 mmol) were combined under N<sub>2</sub> and stirred rapidly at room temperature for 24 hours. The reaction was worked up according to the general protocol and purified by flash silica gel chromatography (84:15:1 hexanes : ethyl acetate : acetic acid) to afford product **7** as a yellow oil (660 mg, 82%). <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>)  $\delta$  4.40 (dd, *J* = 12.0, 2.6 Hz, 1H), 4.20 – 4.14 (m, 1H), 4.06 (dt, *J* = 11.5, 6.3 Hz, 1H), 2.42 – 2.33 (m, 1H), 2.09 – 1.97 (m, 5H), 1.91 – 1.76 (m, 4H), 1.75 – 1.59 (m, 4H), 1.48 (td, *J* = 13.0, 3.4 Hz, 1H), 1.32 (td, 1H), 1.25 – 1.14 (m, 1H); <sup>13</sup>C NMR (151 MHz, CDCl<sub>3</sub>)  $\delta$  171.1, 119.1, 93.3, 62.8, 42.5, 33.8, 32.1, 26.4, 25.2, 24.8, 22.50, 22.48, 21.0; FTIR (cm<sup>-1</sup>): 2941, 2864, 2238, 1738, 1556, 1367, 1239; GC/MS (EI) 222.0 (M-NO<sub>2</sub>)<sup>+</sup>. HRMS (CI) *m/z* calculated for [C<sub>13</sub>H<sub>21</sub>N<sub>2</sub>O<sub>4</sub>]<sup>+</sup>: 269.1501; found: 269.1486.

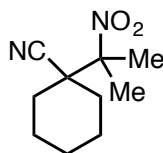


(8) According to the general protocol: CuBr (85.8 mg, 600  $\mu$ mol), ligand **2** (230 mg, 750  $\mu$ mol), sodium *tert*-butoxide (346 mg, 3.60 mmol), anhydrous hexanes (18 mL), 1-methoxy-3-(2-nitroethyl)benzene (**S1**, 679 mg, 3.75 mmol) and 1-bromocyclohexanecarbonitrile (564 mg, 3.00 mmol) were combined under N<sub>2</sub> and heated at 50 °C with rapid stirring for 24 hours. The reaction was worked up according to the general protocol and purified by flash silica gel chromatography (90:10:1 hexanes : ethyl acetate : acetic acid) to afford product **8** as a white solid (743 mg, 86%). <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>)  $\delta$  7.23 (t, *J* = 7.9 Hz, 1H), 6.81 (dd, *J* = 8.2, 2.4 Hz,

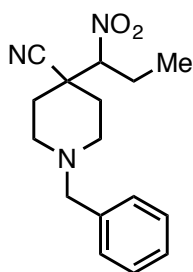
1H), 6.74 (d,  $J = 7.6$  Hz, 1H), 6.70 – 6.65 (m, 2H), 4.58 (dd,  $J = 11.6, 2.9$  Hz, 1H), 3.78 (s, 3H), 3.48 (dd,  $J = 14.5, 11.6$  Hz, 1H), 3.27 (dd,  $J = 14.6, 2.9$  Hz, 1H), 2.18 (dd,  $J = 12.9, 2.9$  Hz, 1H), 1.94 – 1.60 (m, 5H), 1.53 (td,  $J = 13.0, 3.5$  Hz, 1H), 1.41 (td,  $J = 12.8, 3.7$  Hz, 1H), 1.22 (dddd,  $J = 16.6, 12.9, 9.0, 4.1$  Hz, 1H);  $^{13}\text{C}$  NMR (151 MHz,  $\text{CDCl}_3$ )  $\delta$  160.1, 136.0, 130.3, 121.0, 119.1, 114.7, 113.3, 95.1, 55.4, 42.5, 36.0, 34.0, 32.1, 24.8, 22.6, 22.5; FTIR ( $\text{cm}^{-1}$ ): 2940, 2862, 2237, 1556, 1264; mp = 108-110 °C; GC/MS (EI) 287.8 ( $\text{M}^+$ ). HRMS (CI)  $m/z$  calculated for  $[\text{C}_{16}\text{H}_{21}\text{N}_2\text{O}_3]^+$ : 289.1552; found: 289.1562.



**(9)** According to the general protocol: CuBr (85.8 mg, 600  $\mu\text{mol}$ ), ligand **2** (230 mg, 750  $\mu\text{mol}$ ), sodium *tert*-butoxide (346 mg, 3.60 mmol), anhydrous hexanes (18 mL), nitromethane (980  $\mu\text{L}$ , 18 mmol) and 1-bromocyclohexanecarbonitrile (564 mg, 3.00 mmol) were combined under  $\text{N}_2$  and stirred rapidly at room temperature for 24 hours. The reaction was worked up according to the general protocol and purified by flash silica gel chromatography (83:17:1 hexanes : ethyl acetate : acetic acid) to afford product **9** as an off-white solid (447 mg, 89%).  $^1\text{H}$  NMR (600 MHz,  $\text{CDCl}_3$ )  $\delta$  4.48 (s, 2H), 2.07 (d,  $J = 12.4$  Hz, 2H), 1.89 – 1.78 (m, 3H), 1.77 – 1.65 (m, 2H), 1.43 (td,  $J = 13.1, 3.5$  Hz, 2H), 1.32 – 1.18 (m, 1H);  $^{13}\text{C}$  NMR (151 MHz,  $\text{CDCl}_3$ )  $\delta$  119.8, 81.5, 38.6, 33.3, 24.8, 22.3; FTIR ( $\text{cm}^{-1}$ ): 2939, 2862, 2236, 1558, 1383; mp = 93-94 °C; GC/MS (EI) 122.1 ( $\text{M}-\text{NO}_2$ ) $^+$ . HRMS (CI)  $m/z$ , calculated for  $[\text{C}_8\text{H}_{13}\text{N}_2\text{O}_2]^+$ : 169.0977; found: 169.0969;

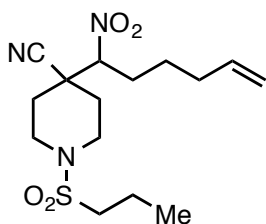


**(10)** According to the general protocol: CuBr (85.8 mg, 600  $\mu\text{mol}$ ), ligand **2** (230 mg, 750  $\mu\text{mol}$ ), sodium *tert*-butoxide (346 mg, 3.60 mmol), anhydrous hexanes (18 mL), 2-nitropropane (334  $\mu\text{L}$ , 3.75 mmol) and 1-bromocyclohexanecarbonitrile (564 mg, 3.00 mmol) were combined under  $\text{N}_2$  and heated at 50 °C with rapid stirring for 24 hours. The reaction was worked up according to the general protocol and purified by flash silica gel chromatography (83:17:1 hexanes : ethyl acetate : acetic acid) to afford product **10** as a yellow solid (260 mg, 44%).  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  1.92 (d,  $J = 11.7$  Hz, 2H), 1.85 (dt,  $J = 14.3, 3.7$  Hz, 2H), 1.76 (s, 6H), 1.75 – 1.65 (m, 3H), 1.42 (td,  $J = 13.1, 3.6$  Hz, 2H), 1.13 (qt,  $J = 13.0, 3.9$  Hz, 1H);  $^{13}\text{C}$  NMR (151 MHz,  $\text{CDCl}_3$ )  $\delta$  119.9, 91.3, 47.3, 30.5, 24.8, 23.1, 23.0; FTIR ( $\text{cm}^{-1}$ ): 2941, 2865, 2233, 1536, 1383; mp = 116-119 °C; GC/MS (EI) 150.2 ( $\text{M}-\text{NO}_2$ ) $^+$ . HRMS (CI)  $m/z$  calculated for  $[\text{C}_{10}\text{H}_{17}\text{N}_2\text{O}_2]^+$ : 197.1290; found: 197.1300.

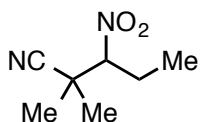


**(11)** According to the general protocol: CuBr (85.8 mg, 600  $\mu\text{mol}$ ), ligand **2** (230 mg, 750  $\mu\text{mol}$ ), sodium *tert*-butoxide (346 mg, 3.60 mmol), anhydrous dichloromethane (15 mL), and 1-nitropropane (334  $\mu\text{L}$ , 3.75 mmol) were combined under  $\text{N}_2$ . To this mixture was added a solution of bromonitrile **S13** (857 mg, 3.00 mmol) in anhydrous dichloromethane (4 mL) and the reaction was heated at 50 °C with rapid stirring for 24 hours. The reaction was worked up according to the general protocol and purified by flash silica gel chromatography (60:40:1 hexanes : ethyl acetate : triethylamine) to afford product **11** as a brown oil which slowly solidified to a light brown solid over time (751 mg, 87%).  $^1\text{H}$  NMR (600 MHz,  $\text{CDCl}_3$ )  $\delta$  7.35 – 7.24 (m, 5H), 4.26 (dd,  $J = 11.9, 2.8$  Hz, 1H), 3.54 (d,  $J = 2.8$  Hz, 2H), 2.92 (d,  $J = 12.4$  Hz, 2H), 2.43 – 2.24 (m, 3H), 2.07 – 1.92 (m, 2H), 1.86 – 1.74 (m, 2H), 1.64 (td,  $J = 12.6, 4.0$  Hz, 1H), 1.03 (t,  $J = 7.3$  Hz, 3H);  $^{13}\text{C}$  NMR (151 MHz,  $\text{CDCl}_3$ )  $\delta$  137.9, 129.1, 128.5, 127.5, 118.7, 95.1, 62.7, 49.6, 49.5, 41.1, 33.4, 31.9, 23.1, 10.5; FTIR ( $\text{cm}^{-1}$ ): 2944, 2815, 2239, 2020, 1636, 1555; mp = 68-70 °C; GC/MS (EI) 287.1 ( $\text{M}^+$ ). HRMS (CI)  $m/z$  calculated for  $[\text{C}_{16}\text{H}_{22}\text{N}_3\text{O}_2]^+$ : 288.1712; found: 288.1706.

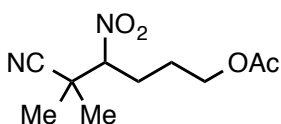




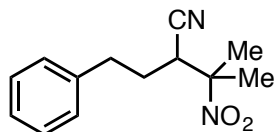
**(40)** According to the general protocol: CuBr (193 mg, 1.35 mmol), ligand **2** (514 mg, 1.68 mmol), sodium *tert*-butoxide (776 mg, 8.08 mmol), anhydrous dichloromethane (30 mL), and 6-nitro-1-hexene (1.09 g, 8.41 mmol) were combined under N<sub>2</sub>. To this mixture was added a solution of bromonitrile **39** (2.00 g, 6.73 mmol) in anhydrous dichloromethane (11 mL) and the reaction was heated at 50 °C with rapid stirring for 24 hours. The reaction was worked up according to the general protocol and purified by flash silica gel chromatography (78:22:1 hexanes : ethyl acetate : acetic acid) to afford product **40** as a yellow solid (1.95 g, 84%). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 5.80 – 5.60 (m, 1H), 5.06 (d, *J* = 8.9 Hz, 1H), 5.02 (s, 1H), 4.36 (dd, *J* = 11.9, 2.7 Hz, 1H), 3.93 (t, *J* = 11.6 Hz, 2H), 3.20 – 3.01 (m, 2H), 2.97 – 2.85 (m, 2H), 2.36 – 2.23 (m, 1H), 2.20 – 2.02 (m, 3H), 1.99 – 1.78 (m, 5H), 1.68 (td, *J* = 12.8, 4.3 Hz, 1H), 1.55 – 1.41 (m, 2H), 1.07 (t, *J* = 7.4 Hz, 3H); <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 136.7, 117.5, 116.3, 92.5, 52.0, 42.4, 42.2, 40.9, 32.8, 32.5, 31.6, 28.5, 24.6, 16.9, 13.1; FTIR (cm<sup>-1</sup>): 2969, 2937, 2084, 1636, 1558; mp = 172–175 °C; GC/MS (EI) 343.4 (M)<sup>+</sup>. HRMS (CI) *m/z* calculated for [C<sub>15</sub>H<sub>26</sub>N<sub>3</sub>O<sub>4</sub>S]<sup>+</sup>: 344.1644; found: 344.1624.



**(12)** According to the general protocol: CuBr (85.8 mg, 600 μmol), ligand **2** (230 mg, 750 μmol), sodium *tert*-butoxide (346 mg, 3.60 mmol), anhydrous hexanes (18 mL), 1-nitropropane (334 μL, 3.75 mmol) and 2-bromo-2-methylpropanenitrile (444 mg, 3.00 mmol) were combined under N<sub>2</sub> and heated at 50 °C with rapid stirring for 24 hours. The reaction was worked up according to the general protocol and purified by flash silica gel chromatography (85:15:1 hexanes : ethyl acetate : acetic acid) to afford product **12** as a yellow solid (362 mg, 77%). <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>) δ 4.28 (dd, *J* = 11.8, 2.8 Hz, 1H), 2.28 (ddq, *J* = 14.4, 11.9, 7.2 Hz, 1H), 1.99 (dq, *J* = 14.8, 7.4, 2.7 Hz, 1H), 1.49 (s, 3H), 1.46 (s, 3H), 1.04 (t, *J* = 7.3 Hz, 3H); <sup>13</sup>C NMR (151 MHz, CDCl<sub>3</sub>) δ 120.9, 95.0, 35.9, 25.3, 23.7, 23.6, 10.7; FTIR (cm<sup>-1</sup>): 2978, 2946, 2242, 1556, 1374, 812; mp = 54–55 °C; GC/MS (EI) 110.2 (M-NO<sub>2</sub>)<sup>+</sup>. HRMS (CI) *m/z* calculated for [C<sub>7</sub>H<sub>13</sub>N<sub>2</sub>O<sub>2</sub>]<sup>+</sup>: 157.0977; found: 157.0969.

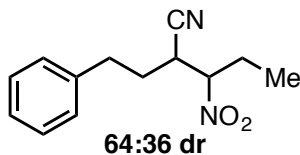


**(13)** According to the general protocol: CuBr (85.8 mg, 600 μmol), ligand **2** (230 mg, 750 μmol), sodium *tert*-butoxide (346 mg, 3.60 mmol), anhydrous dichloromethane (18 mL), 4-nitrobutyl acetate (604 mg, 3.75 mmol) and 2-bromo-2-methylpropanenitrile (444 mg, 3.00 mmol) were combined under N<sub>2</sub> and heated at 50 °C with rapid stirring for 24 hours. The reaction was worked up according to the general protocol and purified by flash silica gel chromatography (70:30:1 hexanes : ethyl acetate : acetic acid) to afford product **13** as a yellow oil (296 mg, 43%). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 4.41 (dd, *J* = 12.0, 2.6 Hz, 1H), 4.17 (dt, *J* = 12.3, 6.1 Hz, 1H), 4.07 (dt, *J* = 11.5, 6.0 Hz, 1H), 2.35 (dddd, *J* = 14.3, 12.0, 8.3, 5.9 Hz, 1H), 2.07 (s, 3H), 2.06 – 1.94 (m, 1H), 1.79 – 1.63 (m, 2H), 1.50 (s, 3H), 1.47 (s, 3H); <sup>13</sup>C NMR (151 MHz, CDCl<sub>3</sub>) δ 171.0, 120.7, 92.7, 62.7, 36.0, 26.9, 25.3, 25.2, 23.5, 21.0; FTIR (cm<sup>-1</sup>): 2990, 2241, 1738, 1557, 1366, 1239; GC/MS (EI) 182.1 (M-NO<sub>2</sub>)<sup>+</sup>. HRMS (CI) *m/z* calculated for [C<sub>10</sub>H<sub>17</sub>N<sub>2</sub>O<sub>4</sub>]<sup>+</sup>: 229.1188; found: 229.1182.



**(14)** According to the general procedure: CuBr (85.8 mg, 600 μmol), ligand **2** (230 mg, 750 μmol), sodium *tert*-butoxide (346 mg, 3.60 mmol), anhydrous hexanes (18 mL), 2-nitropropane (334 μL, 3.75 mmol), and 2-bromo-4-phenylbutanenitrile (672 mg, 3.00 mmol) were combined under N<sub>2</sub> and heated at 50 °C with rapid stirring for 24 hours. The reaction was worked up according to the general protocol and purified by flash silica gel chromatography (93:7:1 hexanes : ethyl acetate : acetic acid) to afford product **14** as a light yellow solid (629 mg, 90%). <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>) δ 7.33 (t, *J* = 7.5 Hz, 2H), 7.27 – 7.22 (m, 1H), 7.19 (d, *J* = 7.1 Hz, 2H), 3.31 (dd, *J* = 12.0, 3.4 Hz, 1H), 3.02 (ddd, *J* = 13.7, 9.0, 4.5 Hz, 1H),

2.73 (dt,  $J = 14.0, 8.5$  Hz, 1H), 1.98 – 1.90 (m, 1H), 1.75 (s, 3H), 1.74 – 1.71 (m, 1H), 1.70 (s, 3H);  $^{13}\text{C}$  NMR (151 MHz,  $\text{CDCl}_3$ )  $\delta$  139.0, 129.0, 128.5, 127.0, 118.1, 88.0, 40.9, 33.5, 29.6, 26.4, 22.2; FTIR ( $\text{cm}^{-1}$ ): 3029, 2932, 2245, 1545, 1348, 701; mp = 72-74 °C; GC/MS (EI) 186.2 ( $\text{M-NO}_2$ ) $^+$ . HRMS (CI)  $m/z$  calculated for  $[\text{C}_{13}\text{H}_{16}\text{N}_2\text{O}_2]^+$ : 232.1212, found: 232.1215. HRMS (CI)  $m/z$  calculated for  $[\text{C}_{13}\text{H}_{17}\text{N}_2\text{O}_2]^+$ : 233.1290, found: 233.1262.

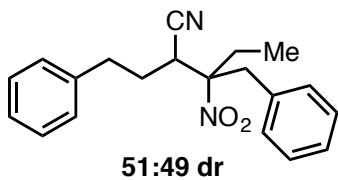


**(15)** According to the general protocol: CuBr (85.8 mg, 600  $\mu\text{mol}$ ), ligand **2** (230 mg, 750  $\mu\text{mol}$ ), sodium *tert*-butoxide (346 mg, 3.60 mmol), anhydrous hexanes (18 mL), 1-nitropropane (334  $\mu\text{L}$ , 3.75 mmol), and 2-bromo-4-phenylbutanenitrile (672 mg, 3.00 mmol) were combined under  $\text{N}_2$  and heated at 50 °C with rapid stirring for 24 hours. The reaction was worked up according to the general protocol.

NMR analysis of the crude reaction mixture revealed a 64:36 ratio of diastereomers. The products were separated and purified by flash silica gel chromatography (91:9:1 hexanes : ethyl acetate : acetic acid) to afford two diastereomerically pure products **(15)** (607 mg, 87% combined).

**15A** (Diastereomer 1) (364 mg, 52%, yellow solid):  $^1\text{H}$  NMR (600 MHz,  $\text{CDCl}_3$ )  $\delta$  7.32 (t,  $J = 7.5$  Hz, 2H), 7.24 (t,  $J = 7.3$  Hz, 1H), 7.18 (d,  $J = 7.3$  Hz, 2H), 4.49 (td,  $J = 9.8, 3.7$  Hz, 1H), 3.17 (td,  $J = 10.0, 4.2$  Hz, 1H), 2.99 (ddd,  $J = 13.9, 9.1, 4.8$  Hz, 1H), 2.77 (dt,  $J = 14.0, 8.4$  Hz, 1H), 2.19 – 2.05 (m, 2H), 2.01 – 1.94 (m, 1H), 1.87 (dtd,  $J = 13.4, 8.5, 4.2$  Hz, 1H), 1.02 (t,  $J = 7.4$  Hz, 3H).  $^{13}\text{C}$  NMR (151 MHz,  $\text{CDCl}_3$ )  $\delta$  138.8, 129.0, 128.5, 127.0, 117.4, 89.2, 35.1, 32.8, 31.3, 26.1, 10.1; FTIR ( $\text{cm}^{-1}$ ): 3030, 2937, 2246, 1558, 699; GC/MS (EI): 186.0 ( $\text{M-NO}_2$ ) $^+$ . HRMS (CI)  $m/z$  calculated for  $[\text{C}_{13}\text{H}_{17}\text{N}_2\text{O}_2]^+$ : 233.1290; found: 233.1307.

**15B** (Diastereomer 2) (242 mg, 35%, yellow oil):  $^1\text{H}$  NMR (600 MHz,  $\text{CDCl}_3$ )  $\delta$  7.33 (t,  $J = 7.5$  Hz, 2H), 7.29 – 7.22 (m, 1H), 7.20 (d,  $J = 7.3$  Hz, 2H), 4.45 (dt,  $J = 9.8, 5.0$  Hz, 1H), 3.00 – 2.91 (m, 2H), 2.84 – 2.74 (m, 1H), 2.29 – 2.17 (m, 1H), 2.06 – 1.97 (m, 1H), 1.97 – 1.86 (m, 2H), 1.00 (t,  $J = 7.4$  Hz, 3H);  $^{13}\text{C}$  NMR (151 MHz,  $\text{CDCl}_3$ )  $\delta$  138.9, 129.1, 128.5, 127.1, 117.1, 88.5, 34.2, 32.9, 30.6, 25.5, 10.2; FTIR ( $\text{cm}^{-1}$ ): 3029, 2937, 2246, 1557, 1456, 701; GC/MS (EI): 186.1 ( $\text{M-NO}_2$ ) $^+$ . HRMS (CI)  $m/z$  calculated for  $[\text{C}_{13}\text{H}_{17}\text{N}_2\text{O}_2]^+$ : 233.1290; found: 233.1278.



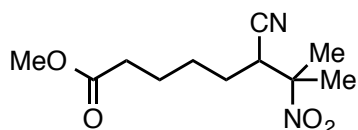
**(16)** According to the general protocol: CuBr (85.8 mg, 600  $\mu\text{mol}$ ), ligand **2** (230 mg, 750  $\mu\text{mol}$ ), sodium *tert*-butoxide (346 mg, 3.60 mmol), anhydrous hexanes (18 mL), (2-nitrobutyl)benzene (672 mg, 3.75 mmol), and 2-bromo-4-phenylbutanenitrile (672 mg, 3.00 mmol) were combined under  $\text{N}_2$  and heated at 50 °C with rapid stirring for 24 hours. The reaction was worked up according to the

general protocol. NMR analysis of the crude reaction mixture revealed a 51:49 ratio of diastereomers. The products were separated and purified by flash silica gel chromatography (93:7:1 hexanes : ethyl acetate : acetic acid) to afford two diastereomerically pure products **(16)** (833 mg, 86% combined)

**16A** (Diastereomer 1) (404 mg, 42%, off-white solid):  $^1\text{H}$  NMR (600 MHz,  $\text{CDCl}_3$ )  $\delta$  7.32 (t,  $J = 7.4$  Hz, 2H), 7.29 – 7.22 (m, 4H), 7.19 (d,  $J = 7.1$  Hz, 2H), 6.99 (d,  $J = 7.0$  Hz, 2H), 3.41 (d,  $J = 14.5$  Hz, 1H), 3.30 (d,  $J = 14.5$  Hz, 1H), 3.22 (dd,  $J = 11.6, 3.6$  Hz, 1H), 3.02 (ddd,  $J = 13.5, 8.5, 4.7$  Hz, 1H), 2.71 (dt,  $J = 13.9, 8.4$  Hz, 1H), 2.29 (dq,  $J = 15.0, 7.5$  Hz, 1H), 1.98 (dq,  $J = 14.9, 7.5$  Hz, 1H), 1.93 – 1.82 (m, 2H), 1.13 (t,  $J = 7.5$  Hz, 3H);  $^{13}\text{C}$  NMR (151 MHz,  $\text{CDCl}_3$ )  $\delta$  139.2, 133.1, 129.9, 129.1, 129.0, 128.7, 128.2, 127.0, 118.6, 94.4, 40.0, 37.3, 33.5, 29.7, 27.6, 8.9; FTIR ( $\text{cm}^{-1}$ ): 3031, 2981, 2243, 1653, 1544; mp = 105-106 °C. HRMS (LIFDI)  $m/z$  calculated for  $[\text{C}_{20}\text{H}_{22}\text{N}_2\text{O}_2]^+$ : 322.1681; found: 322.1676;

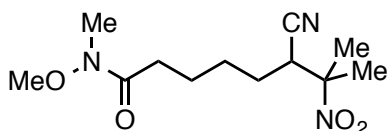
**16B** (Diastereomer 2) (429 mg, 44%, off-white solid):  $^1\text{H}$  NMR (600 MHz,  $\text{CDCl}_3$ )  $\delta$  7.33 (t,  $J = 7.5$  Hz, 2H), 7.30 – 7.24 (m, 4H), 7.20 (d,  $J = 7.2$  Hz, 2H), 7.04 (dd,  $J = 7.4, 1.8$  Hz, 2H), 3.49 (d,  $J = 14.7$  Hz, 1H), 3.21 (d,  $J = 14.7$  Hz, 1H), 3.11 – 3.00 (m, 2H), 2.73 (dt,  $J = 13.9, 8.4$  Hz, 1H), 2.04 (dq,  $J = 15.1, 7.6$  Hz, 1H), 2.00 – 1.84 (m, 3H), 0.89 (t,  $J = 7.5$  Hz, 3H);  $^{13}\text{C}$  NMR (151 MHz,  $\text{CDCl}_3$ )  $\delta$  139.2, 133.1, 130.0, 129.03, 129.01, 128.6, 128.2, 127.0, 118.3, 94.3, 41.2, 36.9, 33.4,

29.5, 27.1, 8.5; FTIR (cm<sup>-1</sup>): 3030, 2945, 2243, 1545, 1455, 701; mp = 86-89 °C. HRMS (LIFDI) m/z calculated for [C<sub>20</sub>H<sub>22</sub>N<sub>2</sub>O<sub>2</sub>]<sup>+</sup>: 322.1681; found: 322.1658.



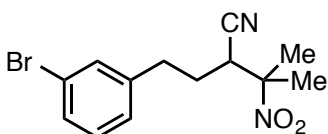
(**17**) According to the general protocol: CuBr (85.8 mg, 600 μmol), ligand **2** (230 mg, 750 μmol), sodium *tert*-butoxide (346 mg, 3.60 mmol), anhydrous hexanes (18 mL), 2-nitropropane (334 μL, 3.75 mmol), and methyl 6-bromo-6-cyanoheptanoate (**S2**, 702 mg, 3.00 mmol) were combined under N<sub>2</sub> and heated at

50 °C with rapid stirring for 24 hours. The reaction was worked up according to the general protocol and purified by flash silica gel chromatography (85:15:1 hexanes : ethyl acetate : acetic acid) to afford product **17** as a yellow oil that solidified after storage in a freezer. (607 mg, 84%). <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>) δ 3.68 (s, 3H), 3.37 (dd, *J* = 11.7, 3.4 Hz, 1H), 2.34 (td, *J* = 6.5, 2.6 Hz, 2H), 1.78 (s, 3H), 1.72 – 1.61 (m, 7H), 1.51 – 1.45 (m, 1H), 1.44 – 1.37 (m, 1H); <sup>13</sup>C NMR (151 MHz, CDCl<sub>3</sub>) δ 173.6, 118.2, 88.1, 51.8, 41.5, 33.6, 27.6, 27.2, 26.5, 24.2, 22.0; FTIR (cm<sup>-1</sup>): 2952, 2870, 2244, 1734, 1542; mp = 44-46 °C; GC/MS (EI) 196.0 (M-NO<sub>2</sub>)<sup>+</sup>. HRMS (CI) m/z calculated for [C<sub>11</sub>H<sub>19</sub>N<sub>2</sub>O<sub>4</sub>]<sup>+</sup>: 243.1345; found: 243.1331.



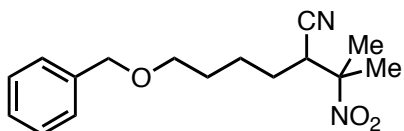
(**18**) According to the general protocol: CuBr (85.8 mg, 600 μmol), ligand **2** (230 mg, 750 μmol), sodium *tert*-butoxide (346 mg, 3.60 mmol), anhydrous hexanes (18 mL), 2-nitropropane (334 μL, 3.75 mmol), and 6-bromo-6-cyano-*N*-methoxy-*N*-methylhexanamide (**S3**, 789 mg, 3.00 mmol) were combined

under N<sub>2</sub> and stirred rapidly at room temperature for 24 hours. The reaction was worked up according to the general protocol and purified by flash silica gel chromatography (60:40:1 hexanes : ethyl acetate : acetic acid) to afford product **18** as a pale light red oil (684 mg, 84%). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 3.68 (s, 3H), 3.38 (dd, *J* = 11.6, 3.4 Hz, 1H), 3.18 (s, 3H), 2.45 (t, *J* = 6.1 Hz, 2H), 1.77 (s, 3H), 1.74 – 1.60 (m, 7H), 1.55 – 1.37 (m, 2H); <sup>13</sup>C NMR (151 MHz, CDCl<sub>3</sub>) δ 173.9, 118.2, 88.1, 77.4, 41.5, 31.3, 27.6, 27.3, 26.2, 23.7, 22.2; FTIR (cm<sup>-1</sup>): 2941, 2871, 2243, 1662, 1546, 1350, 995; GC/MS (EI) 225.0 (M-NO<sub>2</sub>)<sup>+</sup>. HRMS (CI) m/z calculated for [C<sub>12</sub>H<sub>22</sub>N<sub>3</sub>O<sub>4</sub>]<sup>+</sup>: 272.1610; found: 272.1599.



(**19**) According to the general protocol: CuBr (85.8 mg, 600 μmol), ligand **2** (230 mg, 750 μmol), sodium *tert*-butoxide (346 mg, 3.60 mmol), anhydrous dichloromethane (18 mL), 2-nitropropane (334 μL, 3.75 mmol), and 2-bromo-4-(3-bromophenyl)butanenitrile (**S5**, 909 mg, 3.00 mmol) were combined under N<sub>2</sub> and heated at 50 °C

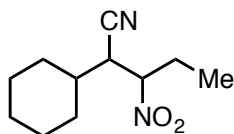
with rapid stirring for 24 hours. The reaction was worked up according to the general protocol and purified by flash silica gel chromatography (94:6:1 hexanes : ethyl acetate : acetic acid) to afford product **19** as a light brown solid (774 mg, 83%). <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>) δ 7.39 (d, *J* = 8.0 Hz, 1H), 7.34 (s, 1H), 7.20 (t, *J* = 7.8 Hz, 1H), 7.12 (d, *J* = 7.6 Hz, 1H), 3.32 (dd, *J* = 12.0, 3.3 Hz, 1H), 2.98 (ddd, *J* = 13.8, 9.4, 4.4 Hz, 1H), 2.74 – 2.64 (m, 1H), 1.99 – 1.89 (m, 1H), 1.77 (s, 3H), 1.74 – 1.66 (m, 4H); <sup>13</sup>C NMR (151 MHz, CDCl<sub>3</sub>) δ 141.3, 131.6, 130.5, 130.2, 127.2, 123.0, 117.9, 87.9, 40.9, 33.2, 29.4, 26.5, 22.1; FTIR (cm<sup>-1</sup>): 2941, 2245, 1545, 1474, 1348; mp = 65-67 °C; GC/MS (EI) 264.0 (M-NO<sub>2</sub>)<sup>+</sup>. HRMS (CI) m/z calculated for [C<sub>13</sub>H<sub>15</sub>N<sub>2</sub>O<sub>2</sub>Br]<sup>+</sup>: 310.0317; found: 310.0327. HRMS (CI) m/z calculated for [C<sub>13</sub>H<sub>16</sub>N<sub>2</sub>O<sub>2</sub>Br]<sup>+</sup>: 311.0395; found: 311.0379.



(**20**) According to the general protocol: CuBr (85.8 mg, 600 μmol), ligand **2** (230 mg, 750 μmol), sodium *tert*-butoxide (346 mg, 3.60 mmol), anhydrous hexanes (18 mL), 2-nitropropane (334 μL, 3.75 mmol), and 6-(benzyloxy)-2-bromohexanenitrile (**S4**, 846 mg, 3.00 mmol) were combined

under N<sub>2</sub> and heated at 50 °C with rapid stirring for 24 hours. The reaction was worked up according to the general protocol and purified by flash silica gel chromatography (92:8:1 hexanes : ethyl acetate : acetic acid) to afford product **20** as a yellow oil (747 mg, 86%). <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>) δ 7.34 (dt, *J* = 13.3, 7.1 Hz, 4H), 7.29 (d, *J* = 7.0 Hz, 1H), 4.49 (s, 2H), 3.48 (td, *J* =

6.2, 2.8 Hz, 2H), 3.37 (dd,  $J = 11.7, 3.5$  Hz, 1H), 1.81 – 1.72 (m, 4H), 1.71 – 1.59 (m, 6H), 1.59 – 1.49 (m, 1H), 1.42 (ddt,  $J = 13.4, 7.2, 3.7$  Hz, 1H);  $^{13}\text{C}$  NMR (151 MHz,  $\text{CDCl}_3$ )  $\delta$  138.5, 128.6, 127.83, 127.78, 118.4, 73.2, 69.7, 41.7, 29.0, 27.7, 26.4, 24.7, 22.0; FTIR ( $\text{cm}^{-1}$ ): 2940, 2866, 2244, 1546, 1102; GC/MS (EI) 243.0 (M- $\text{HNO}_2$ ) $^+$ . HRMS (CI)  $m/z$  calculated for  $[\text{C}_{16}\text{H}_{23}\text{N}_2\text{O}_3]^+$ : 291.1709; found: 291.1699.

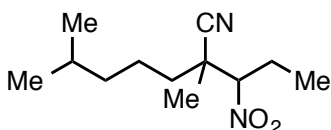


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**(21)** According to the general protocol: CuBr (572 mg, 4.00 mmol), ligand **2** (1.53 g, 5.00 mmol), sodium *tert*-butoxide (2.30 g, 24.0 mmol), anhydrous hexanes (120 mL), 1-nitropropane (2.72 mL, 25.0 mmol), and 2-bromo-2-cyclohexylacetone (4.04 g, 20.00 mmol) were combined under  $\text{N}_2$  and stirred rapidly at room temperature for 24 hours. The reaction was worked up according to the general protocol. NMR analysis of the crude reaction mixture revealed a 59:41 ratio of diastereomers. The products were separated and purified by flash silica gel chromatography (91:9:1 hexanes : ethyl acetate : acetic acid) to provide two diastereomerically pure products (**21**) (3.85 g combined yield 92%). NOTE: the same reaction was carried out on a 3 mmol scale with a combined yield of 96%.

**21A** (Diastereomer 1) (1.60 g, 38%, beige solid):  $^1\text{H}$  NMR (600 MHz,  $\text{CDCl}_3$ )  $\delta$  4.64 (td,  $J = 10.3, 3.3$  Hz, 1H), 3.17 (dd,  $J = 10.2, 3.7$  Hz, 1H), 2.17 (dq,  $J = 14.9, 7.5, 3.3$  Hz, 1H), 2.08 (ddq,  $J = 14.5, 10.5, 7.2$  Hz, 1H), 1.92 – 1.74 (m, 3H), 1.72 – 1.60 (m, 2H), 1.48 – 1.40 (m, 1H), 1.36 (qd,  $J = 11.9, 3.3$  Hz, 1H), 1.32 – 1.13 (m, 4H), 1.03 (t,  $J = 7.4$  Hz, 3H);  $^{13}\text{C}$  NMR (151 MHz,  $\text{CDCl}_3$ )  $\delta$  116.7, 86.9, 42.5, 36.9, 31.8, 28.1, 26.7, 25.9, 25.7, 25.6, 10.1; FTIR ( $\text{cm}^{-1}$ ): 2929, 2855, 2242, 1560, 808; mp = 54-57  $^\circ\text{C}$ ; GC/MS (EI): 164.2 (M- $\text{NO}_2$ ) $^+$ . HRMS (CI)  $m/z$  calculated for  $[\text{C}_{11}\text{H}_{19}\text{N}_2\text{O}_2]^+$ : 211.1447; found: 211.1418.

**21B** (Diastereomer 2) (2.25 g, 54%, yellow solid):  $^1\text{H}$  NMR (600 MHz,  $\text{CDCl}_3$ )  $\delta$  4.64 (ddd,  $J = 9.6, 6.5, 4.7$  Hz, 1H), 2.82 (t,  $J = 7.0$  Hz, 1H), 2.19 (ddq,  $J = 14.6, 9.5, 7.3$  Hz, 1H), 2.01 – 1.88 (m, 2H), 1.88 – 1.76 (m, 3H), 1.74 – 1.66 (m, 1H), 1.59 (tdt,  $J = 11.0, 7.0, 3.5$  Hz, 1H), 1.32 – 1.22 (m, 2H), 1.22 – 1.13 (m, 3H), 1.04 (t,  $J = 7.4$  Hz, 3H);  $^{13}\text{C}$  NMR (151 MHz,  $\text{CDCl}_3$ )  $\delta$  116.7, 86.5, 41.7, 36.7, 31.4, 30.3, 25.9, 25.8, 25.6, 10.2; FTIR ( $\text{cm}^{-1}$ ): 2927, 2856, 2241, 1636, 1558; mp = 85-87  $^\circ\text{C}$ ; GC/MS (EI): 164.1 (M- $\text{NO}_2$ ) $^+$ . HRMS (CI)  $m/z$  calculated for  $[\text{C}_{11}\text{H}_{19}\text{N}_2\text{O}_2]^+$ : 211.1447; found: 211.1447.



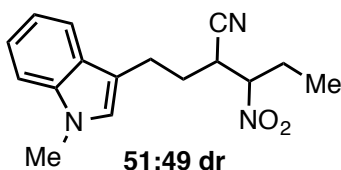
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**(22)** According to the general protocol: CuBr (85.8 mg, 600  $\mu\text{mol}$ ), ligand **2** (230 mg, 750  $\mu\text{mol}$ ), sodium *tert*-butoxide (346 mg, 3.60 mmol), anhydrous hexanes (18 mL), 1-nitropropane (334  $\mu\text{L}$ , 3.75 mmol), and 2-bromo-2,6-dimethylheptanenitrile (654 mg, 3.00 mmol) were combined under  $\text{N}_2$  and heated at 50  $^\circ\text{C}$  with rapid stirring for 24 hours. The reaction was worked up according to the general protocol. NMR analysis of the crude reaction mixture revealed a 59:41 mixture of diastereomers. The products were separated and purified by flash silica gel chromatography (95:5:1 hexanes : ethyl acetate : acetic acid) to afford two diastereomerically pure products (**22**) (554 mg, 82% combined).

**22A** (Diastereomer 1) (333 mg, 49%, colorless oil):  $^1\text{H}$  NMR (600 MHz,  $\text{CDCl}_3$ )  $\delta$  4.39 (dd,  $J = 11.9, 2.6$  Hz, 1H), 2.28 (ddq,  $J = 14.4, 12.0, 7.2$  Hz, 1H), 2.01 (dq,  $J = 14.8, 7.4, 2.7$  Hz, 1H), 1.70 (td,  $J = 12.9, 12.3, 4.1$  Hz, 1H), 1.64 – 1.54 (m, 2H), 1.52 – 1.45 (m, 2H), 1.43 (s, 3H), 1.25 – 1.18 (m, 2H), 1.03 (t,  $J = 7.3$  Hz, 3H), 0.90 (s, 3H), 0.89 (s, 3H);  $^{13}\text{C}$  NMR (151 MHz,  $\text{CDCl}_3$ )  $\delta$  120.4, 93.8, 40.6, 38.7, 37.6, 27.8, 23.7, 22.61, 22.58, 22.5, 20.3, 10.7; FTIR ( $\text{cm}^{-1}$ ): 2956, 2871, 2239, 1635, 1558, 1463; GC/MS (EI) 180.2 (M- $\text{NO}_2$ ) $^+$ . HRMS (CI)  $m/z$  calculated for  $[\text{C}_{12}\text{H}_{23}\text{N}_2\text{O}_2]^+$ : 227.1760; found: 227.1739.

**22B** (Diastereomer 2) (221 mg, 33%, yellow solid):  $^1\text{H}$  NMR (600 MHz,  $\text{CDCl}_3$ )  $\delta$  4.32 (dd,  $J = 11.9, 2.8$  Hz, 1H), 2.28 (ddq,  $J = 14.4, 11.9, 7.2$  Hz, 1H), 2.03 – 1.92 (m, 1H), 1.67 – 1.61 (m, 1H), 1.60 – 1.46 (m, 4H), 1.44 (s, 3H), 1.20 (hept,  $J = 6.4$  Hz, 2H), 1.03 (t,  $J = 7.3$  Hz, 3H), 0.89 (d,  $J = 1.1$  Hz, 3H), 0.88 (d,  $J = 1.0$  Hz, 3H);  $^{13}\text{C}$  NMR (151 MHz,  $\text{CDCl}_3$ )  $\delta$  120.3, 94.6, 40.3, 38.7,

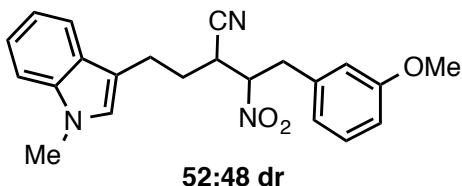
36.1, 27.8, 23.3, 22.6, 22.5, 22.3, 21.9, 10.7; FTIR (cm<sup>-1</sup>): 2956, 2871, 2239, 1557, 1466, 811; mp = 43-45 °C; GC/MS (EI) 180.2 (M-NO<sub>2</sub>)<sup>+</sup>. HRMS (CI) m/z calculated for [C<sub>12</sub>H<sub>23</sub>N<sub>2</sub>O<sub>2</sub>]<sup>+</sup>: 227.1760; found: 227.1749.



**(23)** According to the general protocol: CuBr (85.8 mg, 600 μmol), ligand **2** (230 mg, 750 μmol), sodium *tert*-butoxide (346 mg, 3.60 mmol), anhydrous dichloromethane (18 mL), 1-nitropropane (334 μL, 3.75 mmol), and 2-bromo-4-(1-methyl-1*H*-indol-3-yl)butanenitrile (831 mg, 3.00 mmol) were combined under N<sub>2</sub> and heated at 50 °C with rapid stirring for 24 hours. The reaction was worked up according to the general protocol. NMR analysis of the crude reaction mixture revealed 51:49 ratio of diastereomers. The products were separated and purified by flash silica gel chromatography (85:15:1 hexanes : ethyl acetate : acetic acid) to afford two diastereomerically pure products (**23**) (757 mg, 89% combined)

**23A** (Diastereomer 1) (307 mg, 36%, brown oil): <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>) δ 7.54 (d, *J* = 7.9 Hz, 1H), 7.31 (d, *J* = 8.1 Hz, 1H), 7.24 (d, *J* = 8.0 Hz, 1H), 7.13 (t, *J* = 7.4 Hz, 1H), 6.89 (s, 1H), 4.49 (td, *J* = 8.9, 4.6 Hz, 1H), 3.76 (s, 3H), 3.23 (ddd, *J* = 10.2, 8.7, 4.4 Hz, 1H), 3.12 (ddd, *J* = 13.5, 8.1, 4.8 Hz, 1H), 3.01 – 2.91 (m, 1H), 2.16 – 1.92 (m, 4H), 1.01 (t, *J* = 7.4 Hz, 3H). <sup>13</sup>C NMR (151 MHz, CDCl<sub>3</sub>) δ 137.3, 127.4, 126.9, 122.1, 119.3, 118.7, 117.7, 111.4, 109.5, 89.1, 35.2, 32.8, 30.3, 25.9, 22.4, 10.1; FTIR (cm<sup>-1</sup>): 3055, 2937, 2245, 1555, 1327, 743; GC/MS (EI): 284.9 (M)<sup>+</sup>. HRMS (CI) m/z calculated for [C<sub>16</sub>H<sub>20</sub>N<sub>3</sub>O<sub>2</sub>]<sup>+</sup>: 286.1556; found: 286.1563. Note: this diastereomer was isolated along with ~5% of the protodebrominated starting material (triplet at δ=2.34) which was inseparable by chromatography.

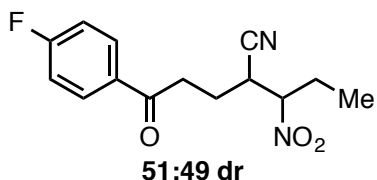
**23B** (Diastereomer 2) (450 mg, 53%, light brown oil): <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>) δ 7.56 (d, *J* = 7.9 Hz, 1H), 7.32 (d, *J* = 8.2 Hz, 1H), 7.29 – 7.23 (m, 1H), 7.13 (t, *J* = 7.4 Hz, 1H), 6.94 (s, 1H), 4.40 (dt, *J* = 9.8, 4.9 Hz, 1H), 3.77 (s, 3H), 3.13 (dt, *J* = 14.8, 5.8 Hz, 1H), 3.01 – 2.91 (m, 2H), 2.19 (ddt, *J* = 14.6, 9.8, 7.3 Hz, 1H), 2.06 – 2.00 (m, 2H), 1.86 (dq, *J* = 14.8, 7.5, 4.5 Hz, 1H), 0.95 (t, *J* = 7.4 Hz, 3H); <sup>13</sup>C NMR (151 MHz, CDCl<sub>3</sub>) δ 137.4, 127.34, 127.28, 122.1, 119.3, 118.7, 117.4, 111.3, 109.6, 88.7, 34.3, 32.9, 29.6, 25.7, 22.4, 10.2; FTIR (cm<sup>-1</sup>): 3055, 2937, 2245, 1554, 1327, 744; mp = 100-102 °C; GC/MS (EI): 285.1 (M)<sup>+</sup>. HRMS (CI) m/z calculated for [C<sub>16</sub>H<sub>20</sub>N<sub>3</sub>O<sub>2</sub>]<sup>+</sup>: 286.1556; found: 286.1539.



**(24)** According to the general protocol: CuBr (85.8 mg, 600 μmol), ligand **2** (230 mg, 750 μmol), sodium *tert*-butoxide (346 mg, 3.60 mmol), anhydrous dichloromethane (18 mL), 1-methoxy-3-(2-nitroethyl)benzene (**S1**, 679 mg, 3.75 mmol), and 2-bromo-4-(1-methyl-1*H*-indol-3-yl)butanenitrile (**S6**, 831 mg, 3.00 mmol) were combined under N<sub>2</sub> and heated at 50 °C with rapid stirring for 24 hours. The reaction was worked up according to the general protocol. NMR analysis of the crude reaction mixture revealed a 52:48 ratio of diastereomers. The products were separated and purified by flash silica gel chromatography (88:12:1 hexanes : ethyl acetate : acetic acid) to afford product **24** (999 mg, 88%)

**24A** (Diastereomer 1) (417 mg, 37%, yellow gum): <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>) δ 7.55 (d, *J* = 7.9 Hz, 1H), 7.32 (d, *J* = 8.2 Hz, 1H), 7.29 – 7.24 (m, 1H), 7.19 (t, *J* = 8.1 Hz, 1H), 7.14 (t, *J* = 7.4 Hz, 1H), 6.89 (s, 1H), 6.81 (d, *J* = 9.8 Hz, 1H), 6.65 (s, 2H), 4.82 – 4.72 (m, 1H), 3.77 (s, 3H), 3.76 (s, 3H), 3.36 – 3.28 (m, 2H), 3.28 – 3.21 (m, 1H), 3.18 – 3.10 (m, 1H), 2.96 (dt, *J* = 15.2, 8.2 Hz, 1H), 2.09 – 1.93 (m, 2H); <sup>13</sup>C NMR (151 MHz, CDCl<sub>3</sub>) δ 160.1, 137.3, 135.3, 130.2, 127.4, 127.0, 122.1, 121.1, 119.3, 118.7, 117.8, 114.6, 113.5, 111.3, 109.6, 88.7, 55.4, 38.2, 35.0, 32.8, 30.0, 22.4; FTIR (cm<sup>-1</sup>): 3055, 2923, 2852, 2245, 1557, 743; GC/MS (EI): 330.1 (M-HNO<sub>2</sub>)<sup>+</sup>. HRMS (CI) m/z calculated for [C<sub>22</sub>H<sub>24</sub>N<sub>3</sub>O<sub>3</sub>]<sup>+</sup>: 378.1818; found: 378.1816.

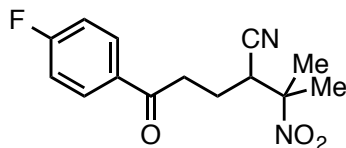
**24B** (Diastereomer 2) (582 mg, 51% (~95:5 dr), yellow gum):  $^1\text{H}$  NMR (600 MHz,  $\text{CDCl}_3$ )  $\delta$  7.54 (d,  $J = 7.9$  Hz, 1H), 7.31 (d,  $J = 8.1$  Hz, 1H), 7.27 – 7.24 (m, 1H), 7.18 (t,  $J = 7.9$  Hz, 1H), 7.13 (t,  $J = 7.2$  Hz, 1H), 6.83 (s, 1H), 6.80 (dd,  $J = 8.2, 2.0$  Hz, 1H), 6.69 (d,  $J = 7.6$  Hz, 1H), 6.66 (s, 1H), 4.70 – 4.64 (m, 1H), 3.76 (s, 3H), 3.73 (s, 3H), 3.43 (dd,  $J = 14.2, 8.3$  Hz, 1H), 3.15 (dd,  $J = 14.2, 6.8$  Hz, 1H), 3.09 (dt,  $J = 14.6, 6.1$  Hz, 1H), 2.96 – 2.89 (m, 2H), 2.11 – 1.98 (m, 2H);  $^{13}\text{C}$  NMR (151 MHz,  $\text{CDCl}_3$ )  $\delta$  160.2, 137.3, 135.2, 130.3, 127.3, 127.1, 122.1, 121.1, 119.3, 118.7, 117.3, 114.5, 113.6, 111.2, 109.6, 87.8, 55.4, 38.3, 33.8, 32.8, 29.8, 22.3; FTIR ( $\text{cm}^{-1}$ ): 3056, 2933, 2245, 1556, 742; GC/MS (EI): 329.9 (M- $\text{HNO}_2$ ) $^+$ . HRMS (CI)  $m/z$  calculated for  $[\text{C}_{22}\text{H}_{24}\text{N}_3\text{O}_3]^+$ : 378.1818; found: 378.1837.



**(25)** According to the general protocol: CuBr (85.8 mg, 600  $\mu\text{mol}$ ), ligand **2** (230 mg, 750  $\mu\text{mol}$ ), sodium *tert*-butoxide (346 mg, 3.60 mmol), anhydrous dichloromethane (15 mL), and 1-nitropropane (334  $\mu\text{L}$ , 3.75 mmol) were combined under  $\text{N}_2$ . To this mixture was added a solution of 2-bromo-5-(4-fluorophenyl)-5-oxopentanenitrile (810 mg, 3.00 mmol) in anhydrous dichloromethane (3 mL) and the reaction was heated at 50  $^\circ\text{C}$  with rapid stirring for 24 hours. The reaction was worked up according to the general protocol. NMR analysis of the crude reaction mixture revealed a 51:49 ratio of diastereomers. The products were separated and purified by flash silica gel chromatography (85:15:1 hexanes : ethyl acetate : acetic acid) to afford two diastereomerically pure products (**25**) (729 mg, 87% combined)

**25A** (Diastereomer 1) (349 mg, 42%, light brown solid):  $^1\text{H}$  NMR (600 MHz,  $\text{CDCl}_3$ )  $\delta$  7.99 (ddd,  $J = 10.0, 5.2, 2.5$  Hz, 2H), 7.18 – 7.13 (m, 2H), 4.55 (dt,  $J = 8.2, 6.9$  Hz, 1H), 3.50 (ddd,  $J = 10.6, 8.5, 4.4$  Hz, 1H), 3.27 (ddd,  $J = 18.1, 7.4, 5.2$  Hz, 1H), 3.20 (dt,  $J = 18.1, 7.5$  Hz, 1H), 2.21 – 2.13 (m, 3H), 2.04 – 1.96 (m, 1H), 1.07 (t,  $J = 7.4$  Hz, 3H);  $^{13}\text{C}$  NMR (151 MHz,  $\text{CDCl}_3$ )  $\delta$  195.7, 167.1, 165.4, 132.71, 132.69, 130.9, 130.8, 117.4, 116.2, 116.0, 89.2, 35.0, 34.9, 25.9, 23.9, 10.1;  $^{19}\text{F}$  NMR (565 MHz,  $\text{CDCl}_3$ )  $\delta$  -104.0; FTIR ( $\text{cm}^{-1}$ ): 2977, 2246, 1686, 1599, 1556, 1232; mp = 74-75  $^\circ\text{C}$ ; GC/MS (EI) 232.0 (M- $\text{NO}_2$ ) $^+$ . HRMS (CI)  $m/z$  calculated for  $[\text{C}_{14}\text{H}_{16}\text{N}_2\text{O}_3\text{F}]^+$ : 279.1145; found: 279.1137.

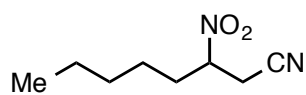
**25B** (Diastereomer 2) (380 mg, 46%, yellow oil):  $^1\text{H}$  NMR (600 MHz,  $\text{CDCl}_3$ )  $\delta$  8.02 – 7.97 (m, 2H), 7.19 – 7.14 (m, 2H), 4.58 (dt,  $J = 9.9, 5.1$  Hz, 1H), 3.39 (dt,  $J = 10.6, 4.9$  Hz, 1H), 3.30 – 3.24 (m, 2H), 2.33 – 2.20 (m, 2H), 2.02 (ddd,  $J = 14.6, 7.4, 4.9$  Hz, 1H), 1.93 (ddt,  $J = 13.8, 10.9, 5.4$  Hz, 1H), 1.08 (t,  $J = 7.4$  Hz, 3H);  $^{13}\text{C}$  NMR (151 MHz,  $\text{CDCl}_3$ )  $\delta$  196.4, 167.1, 165.4, 132.7, 130.9, 130.8, 117.2, 116.2, 116.1, 88.7, 34.7, 34.1, 25.8, 23.3, 10.2;  $^{19}\text{F}$  NMR (565 MHz,  $\text{CDCl}_3$ )  $\delta$  -103.7; FTIR ( $\text{cm}^{-1}$ ): 2978, 2941, 2246, 1686, 1599, 1555, 1233; GC/MS (EI) 232.0 (M- $\text{NO}_2$ ) $^+$ . HRMS (CI)  $m/z$  calculated for  $[\text{C}_{14}\text{H}_{16}\text{N}_2\text{O}_3\text{F}]^+$ : 279.1145; found: 279.1143.



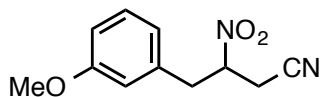
**(26)** According to the general protocol: CuBr (85.8 mg, 600  $\mu\text{mol}$ ), ligand **2** (230 mg, 750  $\mu\text{mol}$ ), sodium *tert*-butoxide (346 mg, 3.60 mmol), anhydrous dichloromethane (15 mL), and 2-nitropropane (334  $\mu\text{L}$ , 3.75 mmol) were combined under  $\text{N}_2$ . To this mixture was added a solution of 2-bromo-5-(4-fluorophenyl)-5-oxopentanenitrile (**S7**, 810 mg, 3.00 mmol) in anhydrous dichloromethane (3 mL) and the reaction was heated at 50  $^\circ\text{C}$  with rapid stirring for 24 hours. The reaction was worked up according to the general protocol and purified by flash silica gel chromatography (89:11:1 hexanes : ethyl acetate : acetic acid) to afford product **26** as a yellow solid (646 mg, 77%).  $^1\text{H}$  NMR (600 MHz,  $\text{CDCl}_3$ )  $\delta$  8.00 (ddd,  $J = 8.8, 5.1, 2.5$  Hz, 2H), 7.19 – 7.13 (m, 2H), 3.58 (dd,  $J = 12.0, 3.8$  Hz, 1H), 3.29 (ddd,  $J = 18.2, 7.2, 5.1$  Hz, 1H), 3.21 (dt,  $J = 18.2, 7.6$  Hz, 1H), 2.13 – 2.05 (m, 1H), 1.99 – 1.91 (m, 1H), 1.82 (s, 3H), 1.79 (s, 3H);  $^{13}\text{C}$  NMR (151 MHz,  $\text{CDCl}_3$ )  $\delta$  196.0, 167.0, 165.3, 132.73, 132.71, 130.84, 130.78, 118.1, 116.2, 116.0, 88.0, 40.8, 35.5, 25.4, 23.2, 22.2;  $^{19}\text{F}$  NMR (565 MHz,  $\text{CDCl}_3$ )  $\delta$  -103.9; FTIR ( $\text{cm}^{-1}$ ): 2946, 2245, 1687, 1599, 1547, 1232, 841; mp = 68-70  $^\circ\text{C}$ ; GC/MS (EI) 232.0 (M- $\text{NO}_2$ ) $^+$ . HRMS (CI)  $m/z$  calculated for  $[\text{C}_{14}\text{H}_{16}\text{N}_2\text{O}_3\text{F}]^+$ : 279.1145; found: 279.1145.

## 7. General Protocol for Alkylation of Nitroalkanes with Bromoacetonitrile

An oven-dried (or flame-dried) Schlenk flask equipped with a magnetic stir bar and a rubber septum was attached to a double manifold and cooled under vacuum. Once cool, the rubber septum was removed and the flask was charged with CuBr (0.2 equiv), ligand **2** (0.22 equiv) and sodium trimethylsilanolate (1.1 equiv). The septum was replaced and the flask was attached to a double manifold and evacuated and refilled with N<sub>2</sub> five times. Anhydrous solvent and nitroalkane (1.0 equiv) were added sequentially via syringe. The mixture was stirred for 1 hour at 50 °C. To this suspension was added bromoacetonitrile (2.0 equiv) via syringe. The mixture was stirred at 50 °C using an oil bath for 24 hours. The reaction was cooled to room temperature and diluted with diethyl ether or dichloromethane. The mixture was filtered through a short pad of Celite washing with diethyl ether or dichloromethane. After concentrating *in vacuo*, the product was purified by silica gel chromatography.

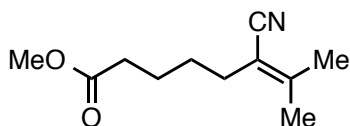


**(27)** According to the general protocol for alkylation of nitroalkanes with bromoacetonitrile, CuBr (57.2 mg, 400 μmol), ligand **2** (135 mg, 440 μmol), sodium trimethylsilanolate (246 mg, 2.20 mmol), anhydrous dichloromethane (12 mL), 1-Nitrohexane (262 mg, 2.00 mmol), and bromoacetonitrile (278 μL, 4.00 mmol) were combined under N<sub>2</sub> and heated at 50 °C with rapid stirring for 24 hours. The reaction was worked up according to the general protocol and purified by flash silica gel chromatography (85:15:1 hexanes : ethyl acetate : acetic acid) to afford product **27** as an orange oil (184 mg, 54%). <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>) δ 4.73 – 4.65 (m, 1H), 3.02 (dd, *J* = 17.2, 7.0 Hz, 1H), 2.93 (dd, *J* = 17.2, 5.9 Hz, 1H), 2.16 – 2.05 (m, 1H), 2.01 – 1.89 (m, 1H), 1.46 – 1.23 (m, 6H), 0.90 (t, *J* = 7.1 Hz, 3H); <sup>13</sup>C NMR (151 MHz, CDCl<sub>3</sub>) δ 114.9, 82.4, 33.1, 30.9, 25.0, 22.3, 21.6, 13.9; FTIR (cm<sup>-1</sup>): 2959, 2933, 1863, 2256, 1557, 1379; GC/MS (EI) 124.2 (M-NO<sub>2</sub>)<sup>+</sup>. HRMS (CI) *m/z* calculated for [C<sub>8</sub>H<sub>15</sub>N<sub>2</sub>O<sub>2</sub>]<sup>+</sup>: 171.1134; found: 171.1125.

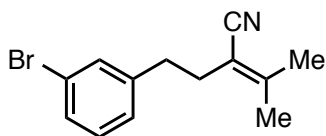


**(28)** According to the general protocol for alkylation of nitroalkanes with bromoacetonitrile, CuBr (57.2 mg, 400 μmol), ligand **2** (135 mg, 440 μmol), sodium trimethylsilanolate (246 mg, 2.20 mmol), anhydrous dichloromethane (12 mL), 1-methoxy-3-(2-nitroethyl)benzene (362 mg, 2.00 mmol), and bromoacetonitrile (278 μL, 4.00 mmol) were combined under N<sub>2</sub> and heated at 50 °C with rapid stirring for 24 hours. The reaction was worked up according to the general protocol and purified by flash silica gel chromatography (78:22:1 hexanes : ethyl acetate : acetic acid) to afford product **28** as a brown oil (250 mg, 57%). <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>) δ 7.28 (t, *J* = 7.9 Hz, 1H), 6.87 (dd, *J* = 8.3, 2.4 Hz, 1H), 6.78 (d, *J* = 7.5 Hz, 1H), 6.74 ? 6.71 (m, 1H), 4.87 (dq, *J* = 7.5, 6.2 Hz, 1H), 3.81 (s, 3H), 3.47 (dd, *J* = 14.1, 6.2 Hz, 1H), 3.25 (dd, *J* = 14.1, 7.8 Hz, 1H), 2.91 (d, *J* = 6.2 Hz, 2H); <sup>13</sup>C NMR (151 MHz, CDCl<sub>3</sub>) δ 160.4, 134.6, 130.6, 121.3, 115.0, 114.9, 113.7, 82.8, 55.4, 38.8, 20.6; FTIR (cm<sup>-1</sup>): 2967, 2940, 2839, 2255, 1557, 1264; GC/MS (EI) 220.1 (M)<sup>+</sup>. HRMS (CI) *m/z* calculated for [C<sub>11</sub>H<sub>13</sub>N<sub>2</sub>O<sub>3</sub>]<sup>+</sup>: 221.0926; found: 221.0917.

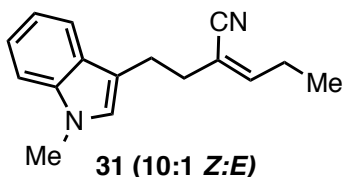
## 8. Synthesis of Cyanoalkenes



**(29)** 1,8-Diazabicyclo[5.4.0]undec-7-ene (DBU, 134  $\mu$ L, 900  $\mu$ mol, 3 equiv.) was added to a solution of methyl 6-cyano-7-methyl-7-nitrooctanoate (**17**, 73.0 mg, 300  $\mu$ mol) in dichloromethane (1.5 mL) and the mixture was stirred at room temperature for 1 hour, when TLC showed complete conversion of the starting material. The mixture was diluted with water (3 mL), transferred to a separatory funnel and washed twice with 1M HCl (3 mL) and once with brine (3 mL), dried with magnesium sulfate, filtered and evaporated to afford **29** as a yellow oil (60 mg, 100% yield).  $^1\text{H}$  NMR (600 MHz,  $\text{CDCl}_3$ )  $\delta$  3.67 (s, 3H), 2.34 (t,  $J = 7.4$  Hz, 2H), 2.22 (t,  $J = 7.6$  Hz, 2H), 2.07 (s, 3H), 1.83 (s, 3H), 1.69 – 1.61 (m, 2H), 1.59 – 1.50 (m, 2H);  $^{13}\text{C}$  NMR (151 MHz,  $\text{CDCl}_3$ )  $\delta$  173.9, 152.2, 119.3, 109.2, 51.7, 33.9, 29.6, 27.8, 24.9, 24.3, 20.2; FTIR ( $\text{cm}^{-1}$ ): 2951, 2865, 2209, 1738, 1437; GC/MS (EI) 195.1 ( $\text{M}^+$ ). HRMS (CI)  $m/z$  calculated for  $[\text{C}_{11}\text{H}_{18}\text{NO}_2]^+$ : 196.1338; found: 196.1339.

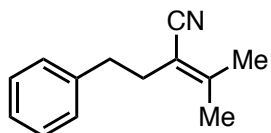


**(30)** 1,8-Diazabicyclo[5.4.0]undec-7-ene (DBU, 134  $\mu$ L, 900  $\mu$ mol, 3 equiv.) was added to a solution of 2-(3-bromophenethyl)-3-methyl-3-nitrobutanenitrile (**19**, 93.3 mg, 300  $\mu$ mol) in dichloromethane (1 mL) and the mixture was stirred at room temperature for 1 hour, when TLC showed complete conversion of the starting material. The mixture was diluted with water (3 mL), transferred to a separatory funnel and washed twice with 1M HCl (3 mL) and once with brine (3 mL), dried with magnesium sulfate, filtered and evaporated to afford **30** as a light brown solid (77.8 mg, 98% yield).  $^1\text{H}$  NMR (600 MHz,  $\text{CDCl}_3$ )  $\delta$  7.34 (d,  $J = 8.7$  Hz, 2H), 7.16 (t,  $J = 7.6$  Hz, 1H), 7.11 (d,  $J = 7.6$  Hz, 1H), 2.79 (t,  $J = 7.5$  Hz, 2H), 2.48 (t,  $J = 7.8$  Hz, 2H), 2.05 (s, 3H), 1.66 (s, 3H);  $^{13}\text{C}$  NMR (151 MHz,  $\text{CDCl}_3$ )  $\delta$  153.2, 142.8, 131.7, 130.2, 129.6, 127.4, 122.6, 119.2, 108.3, 34.1, 31.8, 24.9, 20.1; FTIR ( $\text{cm}^{-1}$ ): 2935, 2862, 2209, 1637, 1568; mp = 62-64  $^\circ\text{C}$ ; GC/MS (EI) 263.0 ( $\text{M}^+$ ). HRMS (CI)  $m/z$  calculated for  $[\text{C}_{13}\text{H}_{15}\text{NBr}]^+$ : 264.0388; found: 264.0384.



**(31)** 1,8-Diazabicyclo[5.4.0]undec-7-ene (DBU, 134  $\mu$ L, 900  $\mu$ mol, 3 equiv.) was added to a solution of **23** (86 mg, 300  $\mu$ mol, mixture of diastereomers) in dichloromethane (1 mL) and the mixture was stirred at room temperature for 1 hour, when TLC showed complete conversion of the starting material. The mixture was diluted with water (3 mL), transferred to a separatory funnel and washed with 1M HCl (3 mL), brine (3 mL) and dried with magnesium sulfate. The crude mixture was purified by flash silica gel chromatography (91:9 hexanes : ethyl acetate) to afford **31** as 10:1 mixture of alkene isomers as a yellow oil (56.1 mg, 79% yield). NOE experiments determined that the (Z) isomer was the major isomer.  $^1\text{H}$  NMR (600 MHz,  $\text{CDCl}_3$ ): 10:1 Z:E mixture of isomers, useful diagnostic peaks for each isomer are listed. See attached spectra for details)  $\delta$  (**Z**-**31**): 6.85 (s, 0H), 6.03 (t,  $J = 7.6$  Hz, 1H), 2.33 (p,  $J = 7.5$  Hz, 2H), 0.97 (t,  $J = 7.5$  Hz, 1H). (**E**-**31**): 6.89 (s, 1H), 6.31 (t,  $J = 7.6$  Hz, 1H), 1.99 (p,  $J = 7.6$  Hz, 2H), 0.81 (t,  $J = 7.5$  Hz, 3H).  $^{13}\text{C}$  NMR (151 MHz,  $\text{CDCl}_3$ )  $\delta$  (**Z**-**31**): 149.9, 137.2, 127.7, 126.7, 121.7, 118.9, 118.9, 117.9, 113.7, 112.9, 109.4, 35.3, 32.7, 25.1, 24.1, 13.2. (**E**-**31**):  $^{13}\text{C}$  NMR (151 MHz,  $\text{CDCl}_3$ )  $\delta$  150.3, 126.8, 118.7, 29.7, 23.8, 21.9, 12.9; FTIR ( $\text{cm}^{-1}$ ): 2969, 2933, 2853, 2213, 1636, 1473. HRMS (LIFDI) calculated for  $[\text{C}_{16}\text{H}_{18}\text{N}_2]^+$ : 238.1470; found: 238.1471.

## Alkylation/elimination Sequence for the Synthesis of Cyanoalkenes



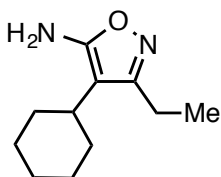
**(33)** According to the general protocol for nitroalkylation: CuBr (28.6 mg, 200  $\mu$ mol), ligand **2** (76.5 mg, 250  $\mu$ mol), sodium *tert*-butoxide (115 mg, 1.20 mmol), anhydrous dichloromethane (6 mL), 2-nitropropane (110  $\mu$ L, 1.25 mmol), and 2-bromo-4-phenylbutanenitrile (224 mg, 1.00



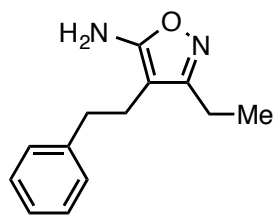
mmol) were combined under N<sub>2</sub> and heated at 50 °C with rapid stirring for 24 hours. The reaction mixture was cooled to room temperature, diluted with diethyl ether (20 mL) and filtered through a short pad of Celite. The crude mixture was concentrated *in vacuo* and dichloromethane (4 mL) and 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU, 450 μL, 3.00 mol, 3 equiv) were added and the reaction was stirred at room temperature for 1 hour until TLC showed complete conversion of the nitroalkane. The reaction was quenched with water and extracted twice with dichloromethane. The combined organic layers were washed with 1M HCl (10 mL, to remove excess DBU), brine and dried with magnesium sulfate, filtered and concentrated *in vacuo*. The product was purified by flash silica chromatography (94:6:1 hexanes : ethyl acetate : acetic acid) to afford product **33** as a yellow oil (145 mg, 78%). <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>) δ 7.29 (t, *J* = 7.5 Hz, 2H), 7.23 – 7.15 (m, 3H), 2.82 (t, *J* = 7.4 Hz, 2H), 2.49 (t, *J* = 7.8 Hz, 2H), 2.04 (s, 3H), 1.64 (s, 3H); <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 153.0, 140.5, 128.65, 128.58, 126.4, 119.4, 108.6, 34.5, 32.2, 24.9, 20.0; FTIR (cm<sup>-1</sup>): 3027, 2923, 2210, 1453, 699; GC/MS (EI) 185.2 (M)<sup>+</sup>. HRMS (CI) *m/z* calculated for [C<sub>13</sub>H<sub>16</sub>N]<sup>+</sup>: 186.1283; found: 186.1265.

### 9. Cyclization of Products to form 5-Aminoisoxazoles

**General protocol:** Potassium carbonate (2.0 equiv), tetrabutylammonium iodide (0.15 equiv) and the β-cyanonitroalkane (1.0 equiv) were added to a flame dried round-bottom flask equipped with a magnetic stir bar and a rubber septum. The flask was evacuated and refilled with N<sub>2</sub> three times. Anhydrous dioxane and benzyl bromide (2.0 equiv) were added and the mixture was stirred vigorously at room temperature under N<sub>2</sub> for the indicated period of time. The heterogeneous mixture was filtered through Celite and concentrated *in vacuo*. The crude mixture was purified by flash silica gel chromatography to yield the isoxazole.

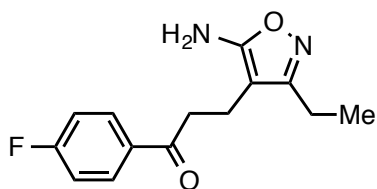


**(34)** According to the general protocol, potassium carbonate (138 mg, 1.0 mmol, 2.0 equiv), tetrabutylammonium iodide (28.0 mg, 75 μmol, 0.15 equiv) and 2-cyclohexyl-3-nitropentanenitrile (mixture of diastereomers; 110 mg, 500 μmol, 1 equiv), anhydrous dioxane (2.5 mL) and benzyl bromide (120 μL, 1.0 mmol, 2.0 equiv) were combined and stirred rapidly under N<sub>2</sub> for 24 hours. The reaction was worked up according to the general protocol and purified by flash silica gel chromatography (70:30 hexanes : ethyl acetate) to afford product **34** as a white solid (62 mg, 62%). <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>) δ 4.12 (s, 2H), 2.55 (q, *J* = 7.5 Hz, 2H), 2.19 (tt, *J* = 12.4, 3.4 Hz, 1H), 1.82 (d, *J* = 13.1 Hz, 2H), 1.75 (t, *J* = 14.0 Hz, 3H), 1.43 (qd, *J* = 12.6, 2.9 Hz, 2H), 1.32 (ddd, *J* = 16.2, 12.9, 9.7 Hz, 2H), 1.25 (t, *J* = 7.5 Hz, 3H), 1.20 (dt, *J* = 12.8, 3.5 Hz, 1H); <sup>13</sup>C NMR (151 MHz, CDCl<sub>3</sub>) δ 165.6, 164.1, 97.1, 33.3, 32.4, 27.0, 26.2, 19.4, 12.5; FTIR (cm<sup>-1</sup>): 3373, 3186, 2925, 2850, 1638, 1491; mp = 98-100 °C; GC/MS (EI) 194.2 (M)<sup>+</sup>. HRMS (CI) *m/z* calculated for [C<sub>11</sub>H<sub>19</sub>N<sub>2</sub>O]<sup>+</sup>: 195.1497; found: 195.1503.

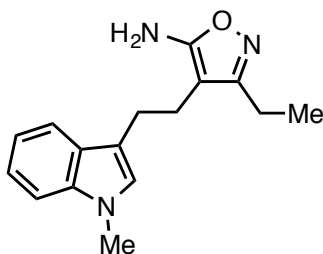


**(35)** According to the general protocol, potassium carbonate (138 mg, 1.0 mmol, 2.0 equiv), tetrabutylammonium iodide (28.0 mg, 75 μmol, 0.15 equiv) and **15** (mixture of diastereomers; 116 mg, 500 μmol, 1 equiv), anhydrous dioxane (2.5 mL) and benzyl bromide (120 μL, 1.0 mmol, 2.0 equiv) were combined and stirred rapidly under N<sub>2</sub> for 48 hours. The reaction was worked up according to the general protocol and purified by flash silica gel chromatography (75:25 hexanes : ethyl acetate) to afford product **35** as a white solid (63 mg, 58%). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.28 (t, *J* = 7.2 Hz, 2H), 7.22 (t, *J* = 7.3 Hz, 1H), 7.12 (d, *J* = 7.0 Hz, 2H), 3.56 (s, 2H), 2.74 (t, *J* = 7.0 Hz, 2H), 2.53 – 2.41 (m, 4H), 1.24 (t, *J* = 7.6 Hz, 3H); <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 165.9, 165.6, 141.5, 128.9, 128.8, 126.5, 91.3, 36.2, 24.2, 19.0, 12.3; mp = 99-101 °C; GC/MS (EI) 216.1 (M)<sup>+</sup>. HRMS (CI) *m/z* calculated for [C<sub>13</sub>H<sub>17</sub>N<sub>2</sub>O]<sup>+</sup>: 217.1341; found: 217.1340.

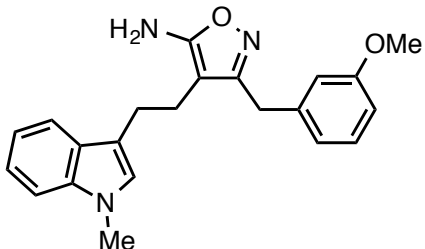
**(36)** According to the general protocol, potassium carbonate (110 mg, 0.8 mmol, 2.0 equiv), tetrabutylammonium iodide (23.0 mg, 60 μmol, 0.15 equiv) and **25** (mixture of diastereomers; 111 mg, 400 μmol, 1 equiv), anhydrous dioxane (2.0 mL) and benzyl bromide (96 μL, 0.8 mmol, 2.0



equiv) were combined and stirred rapidly under N<sub>2</sub> for 48 hours. The reaction was worked up according to the general protocol and purified by flash silica gel chromatography (66:33 hexanes : ethyl acetate) to afford product **36** as a white solid (45 mg, 43%). <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>) δ 7.98 – 7.91 (m, 2H), 7.17 – 7.08 (m, 2H), 4.90 (s, 2H), 3.21 – 3.10 (m, 2H), 2.68 – 2.59 (m, 2H), 2.54 (q, *J* = 7.6 Hz, 2H), 1.27 (t, *J* = 7.6 Hz, 3H). <sup>13</sup>C NMR (151 MHz, CDCl<sub>3</sub>) δ 198.9, 166.9, 166.4, 165.5, 165.2, 133.23, 133.21, 130.8, 130.7, 116.0, 115.9, 90.9, 38.7, 19.1, 15.1, 12.2. <sup>19</sup>F NMR (565 MHz, CDCl<sub>3</sub>) δ -104.4; FTIR (cm<sup>-1</sup>): 3184, 2976, 1681, 1650, 1598, 1497; mp = 103-105 °C; GC/MS (EI) 262.1 (M)<sup>+</sup>. HRMS (CI) *m/z* calculated for [C<sub>14</sub>H<sub>16</sub>N<sub>2</sub>O<sub>2</sub>F]<sup>+</sup>: 263.1196; found: 263.1196.

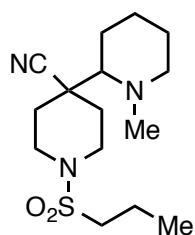
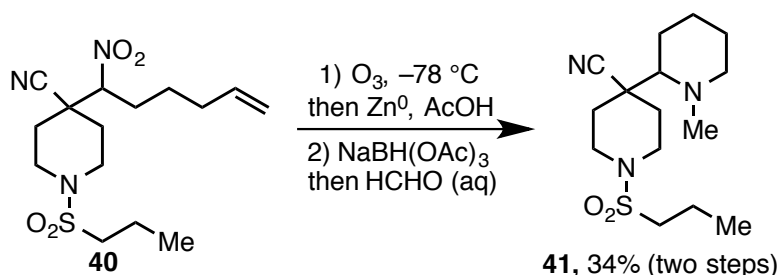


**(37)** According to the general protocol, potassium carbonate (138 mg, 1.0 mmol, 2.0 equiv), tetrabutylammonium iodide (28.0 mg, 75 μmol, 0.15 equiv) and **23** (mixture of diastereomers; 142 mg, 500 μmol, 1 equiv), anhydrous dioxane (2.5 mL) and benzyl bromide (120 μL, 1.0 mmol, 2.0 equiv) were combined and stirred rapidly under N<sub>2</sub> for 40 hours. The reaction was worked up according to the general protocol and purified by flash silica gel chromatography (60:40 hexanes : ethyl acetate) to afford product **37** as a white solid (87 mg, 65%). <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>) δ 7.58 (d, *J* = 7.9 Hz, 1H), 7.30 (d, *J* = 8.2 Hz, 1H), 7.23 (t, *J* = 7.6 Hz, 1H), 7.12 (t, *J* = 7.8 Hz, 1H), 6.75 (s, 1H), 3.73 (s, 3H), 3.55 (s, 2H), 2.89 (t, *J* = 7.0 Hz, 2H), 2.59 (t, *J* = 7.1 Hz, 2H), 2.50 (q, *J* = 7.6 Hz, 2H), 1.26 (t, *J* = 7.6 Hz, 3H). <sup>13</sup>C NMR (151 MHz, CDCl<sub>3</sub>) δ 165.9, 165.6, 137.2, 127.5, 127.0, 121.9, 119.1, 118.8, 113.8, 109.5, 92.0, 32.7, 25.6, 22.7, 19.1, 12.3; FTIR (cm<sup>-1</sup>): 3413, 2970, 1644, 1491, 1472; mp = 147-151 °C; GC/MS (EI) 269.3 (M)<sup>+</sup>. HRMS (CI) *m/z* calculated for [C<sub>16</sub>H<sub>20</sub>N<sub>3</sub>O]<sup>+</sup>: 270.1606; found: 270.1592.



**(38)** According to the general protocol, potassium carbonate (138 mg, 1.0 mmol, 2.0 equiv), tetrabutylammonium iodide (28.0 mg, 75 μmol, 0.15 equiv) and **24** (mixture of diastereomers; 189 mg, 500 μmol, 1 equiv), anhydrous dioxane (2.5 mL) and benzyl bromide (120 μL, 1.0 mmol, 2.0 equiv) were combined and stirred rapidly under N<sub>2</sub> for 24 hours. The reaction was worked up according to the general protocol and purified by flash silica gel chromatography (50:50 hexanes : ethyl acetate) to afford product **38** as a white solid (117 mg, 65%). <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>) δ 7.45 (d, *J* = 7.9 Hz, 1H), 7.27 (d, *J* = 8.3 Hz, 1H), 7.25 – 7.17 (m, 2H), 7.08 (t, *J* = 7.4 Hz, 1H), 6.84 (d, *J* = 7.6 Hz, 1H), 6.81 – 6.75 (m, 2H), 6.57 (s, 1H), 3.78 (s, 3H), 3.77 (s, 2H), 3.71 (s, 3H), 3.54 (s, 2H), 2.56 (t, *J* = 6.9 Hz, 2H), 2.43 (t, *J* = 7.0 Hz, 2H). <sup>13</sup>C NMR (151 MHz, CDCl<sub>3</sub>) δ 166.0, 163.2, 159.8, 138.9, 137.0, 129.5, 127.3, 127.0, 121.7, 121.2, 118.9, 118.7, 114.4, 113.6, 112.2, 109.4, 92.3, 55.2, 32.6, 31.8, 24.9, 22.6; FTIR (cm<sup>-1</sup>): 3347, 2934, 1646, 1600, 1490, 1258; mp = 91-93 °C. HRMS (LIFDI) calculated for [C<sub>22</sub>H<sub>23</sub>N<sub>3</sub>O<sub>2</sub>]<sup>+</sup>: 361.1790; found: 361.1786;

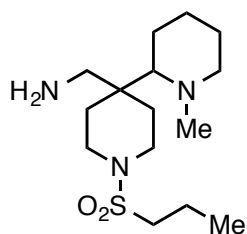
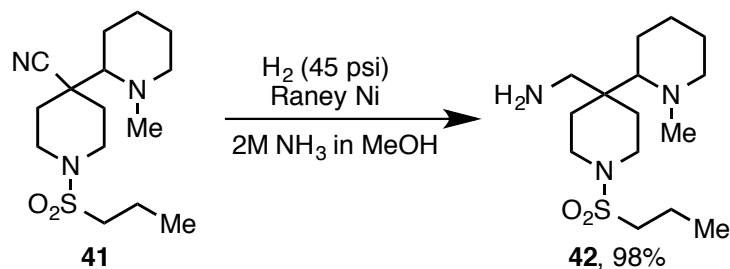
## 10. Synthesis of Gly1 Inhibitor 43.



(**41**) In a 25 mL round bottom flask equipped with a magnetic stir bar and a rubber septum, nitroalkane **40** (138mg, 0.4 mmol, 1.0 equiv) was dissolved in anhydrous dichloromethane (4 mL). The flask was cooled to  $-78\text{ }^\circ\text{C}$  in a dry ice/acetone bath and ozone ( $\text{O}_3$ ) was bubbled through the solution using a steel syringe needle until a blue color persisted (7 minutes), at which point oxygen was bubbled through the solution until the blue color disappeared. At  $-78\text{ }^\circ\text{C}$ , a slurry of zinc dust ( $<10\text{ }\mu\text{m}$ ) (520 mg, 8 mmol, 20 equiv) in glacial acetic acid (4 mL) was added in one portion via pipette and the mixture was stirred for 2 hours while warming to room temperature. The mixture was passed through a short pad of Celite, washing with dichloromethane (20 mL). The mixture was evaporated on high vacuum to remove the bulk of the acetic acid. The mixture was taken up in dichloromethane ( $\sim 1\text{ mL}$ ) and passed through a short pad of basic alumina, eluting with dichloromethane : methanol (20:1, 150 mL). The solution was evaporated to provide a white solid.

A magnetic stir bar and rubber septum were added and anhydrous 1,2-dichloroethane (4 mL) was added via syringe. Sodium triacetoxyborohydride (85 mg, 0.4 mmol, 1.0 equiv) was added in one portion. The mixture was stirred at room temperature for 2 hours. Then, 37% aqueous formaldehyde (65  $\mu\text{L}$ , 0.8 mmol, 2.0 equiv) was added via syringe followed by sodium triacetoxyborohydride (85 mg, 0.4 mmol, 1.0 equiv) in one portion. The mixture was stirred vigorously under  $\text{N}_2$  overnight.

The reaction was quenched by diluting with dichloromethane (10 mL) and saturated aqueous  $\text{NaHCO}_3$  (10 mL). The mixture was extracted twice with dichloromethane and the combined organic layers were washed with brine. The combined organic layers were extracted with 1M HCl (3 x 10 mL). The organic layer was discarded. The combined aqueous layers were carefully basified with 3M NaOH and extracted with dichloromethane (3 x 25 mL). The combined organic layers were dried with magnesium sulfate and evaporated. The crude product was purified by chromatography on basic alumina (80 : 20 hexanes : ethyl acetate) to provide product **41** as a white solid (43 mg, 34%).  $^1\text{H NMR}$  (600 MHz,  $\text{CDCl}_3$ )  $\delta$  3.93 – 3.78 (m, 2H), 3.07 (tdd,  $J = 12.7, 5.8, 2.3\text{ Hz}$ , 2H), 2.99 (dt,  $J = 13.7, 4.3\text{ Hz}$ , 1H), 2.94 – 2.86 (m, 2H), 2.75 – 2.68 (m, 1H), 2.49 (s, 3H), 2.48 – 2.45 (m, 1H), 2.18 (dd,  $J = 13.9, 2.0\text{ Hz}$ , 1H), 2.03 (dd,  $J = 13.5, 2.3\text{ Hz}$ , 1H), 1.99 – 1.91 (m, 1H), 1.90 – 1.79 (m, 2H), 1.77 – 1.51 (m, 5H), 1.50 – 1.36 (m, 2H), 1.07 (dt,  $J = 572.8, 7.4\text{ Hz}$ , 3H);  $^{13}\text{C NMR}$  (151 MHz,  $\text{CDCl}_3$ )  $\delta$  121.9, 67.4, 54.9, 51.3, 43.1, 42.8, 40.8, 38.5, 33.4, 32.5, 23.8, 20.3, 19.1, 17.0, 13.3; FTIR ( $\text{cm}^{-1}$ ): 2931, 2856, 2228, 1652, 1337; mp = 130–132  $^\circ\text{C}$ ; ESI-MS 314.4 ( $\text{M}+\text{H}$ ) $^+$ . HRMS (CI)  $m/z$  calculated for  $[\text{C}_{15}\text{H}_{28}\text{N}_3\text{O}_2\text{S}]^+$ : 314.1902; found: 314.1879.

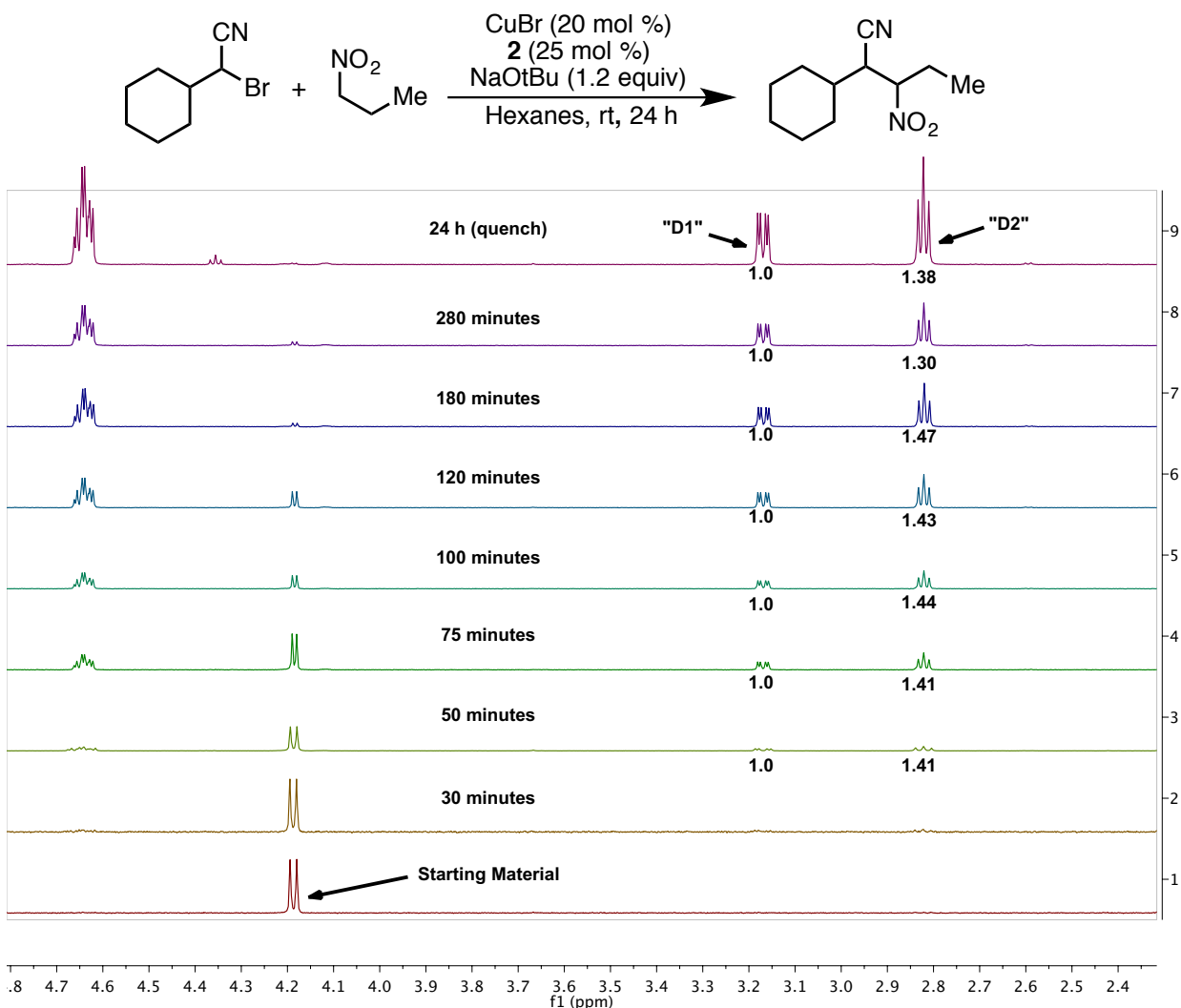


**(42)** Nitrile **41** (17 mg, 54  $\mu$ mol, 1.0 equiv) was added to 2-dram vial with a magnetic stir bar. 2M  $NH_3$  in MeOH (0.5 mL) was added followed by Raney nickel (slurry in  $H_2O$ , 8 drops from a Pasteur pipette). The vial was sealed with a septum cap and pierced with two needles. The vial was placed in a thick-walled glass reactor. The reactor was purged with  $H_2$  (45 psi) ten times, then charged to 45 psi  $H_2$ . The reactor was stirred at room temperature for 23 hours. The mixture was diluted with dichloromethane (5 mL) and filtered through a Celite pad, washing with dichloromethane (20 mL). The filtrate was evaporated to give amine **42** as a clear oil (16.8 mg, 98%).  $^1H$  NMR (600 MHz,  $CDCl_3$ )  $\delta$  3.52 (dd,  $J = 19.5, 14.9$  Hz, 2H), 2.98 (td,  $J = 11.9, 3.1$  Hz, 1H), 2.92 – 2.75 (m, 7H), 2.48 (dd,  $J = 11.3, 2.3$  Hz, 1H), 2.42 (s, 3H), 1.90 – 1.79 (m, 3H), 1.72 (td,  $J = 13.0, 12.4, 4.7$  Hz, 1H), 1.68 – 1.49 (m, 7H), 1.38 (dd,  $J = 45.9, 14.7$  Hz, 3H), 1.05 (t,  $J = 7.4$  Hz, 3H);  $^{13}C$  NMR (151 MHz,  $CDCl_3$ )  $\delta$  65.9, 55.4, 51.0, 42.6, 42.1, 41.7, 39.7, 38.9, 29.9, 29.6, 24.7, 18.7, 18.0, 17.0, 13.3; FTIR ( $cm^{-1}$ ): 2936, 2872, 1587, 1323, 1147; ESI-MS 318.4 ( $M+H$ ) $^+$ . HRMS (LIFDI)  $m/z$  calculated for  $[C_{15}H_{32}N_3O_2S]^+$ : 318.2215; found: 318.2219.

## 11. Studies on Diastereomer Stability

Several studies were undertaken to determine the stability of the diastereomers under the reaction conditions. Because of the lack of diastereoselectivity in the alkylation reaction, the relative configuration of the diastereomers was not rigorously determined. For the following studies, the *syn* and *anti* diastereomers were not assigned and the diastereomers are referred to as "D1" and "D2".

First, the reaction progress was monitored by  $^1\text{H}$  NMR in order to observe whether the diastereomeric ratio of products was constant over time or was degraded over the course of the reaction. In order to determine the diastereomeric ratio, the integration of the  $\alpha$ -cyano protons of the two diastereomers (dd at 3.17 ppm and t at 2.83 ppm) were measured (figure S1). These studies determined that the ratio of products was consistent throughout the course of the reaction and did not degrade, suggesting that the diastereomeric ratio is a kinetic phenomenon, not the result of thermodynamic equilibration of the diastereomers.

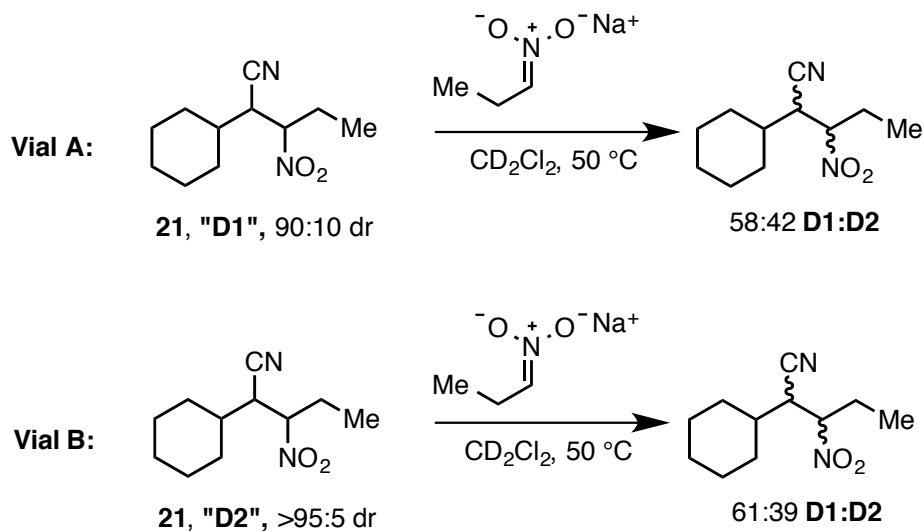


**Figure S1:** Measurement of Diastereomeric Ratio Over Time by  $^1\text{H}$  NMR.

In order to determine the thermodynamic equilibrium of the diastereomers, a stereochemically enriched sample of each diastereomer was exposed to nitronate anion and the epimerization was followed by  $^1\text{H}$  NMR.

In a  $\text{N}_2$ -filled glovebox, a flame dried 1-dram vial was charged with sodium tert-butoxide (9.6 mg, 100  $\mu\text{mol}$ , 1.0 equiv) and  $\text{CD}_2\text{Cl}_2$  (400  $\mu\text{L}$ ). 1-Nitropropane (9  $\mu\text{L}$ , 100  $\mu\text{mol}$ , 1.0 equiv)

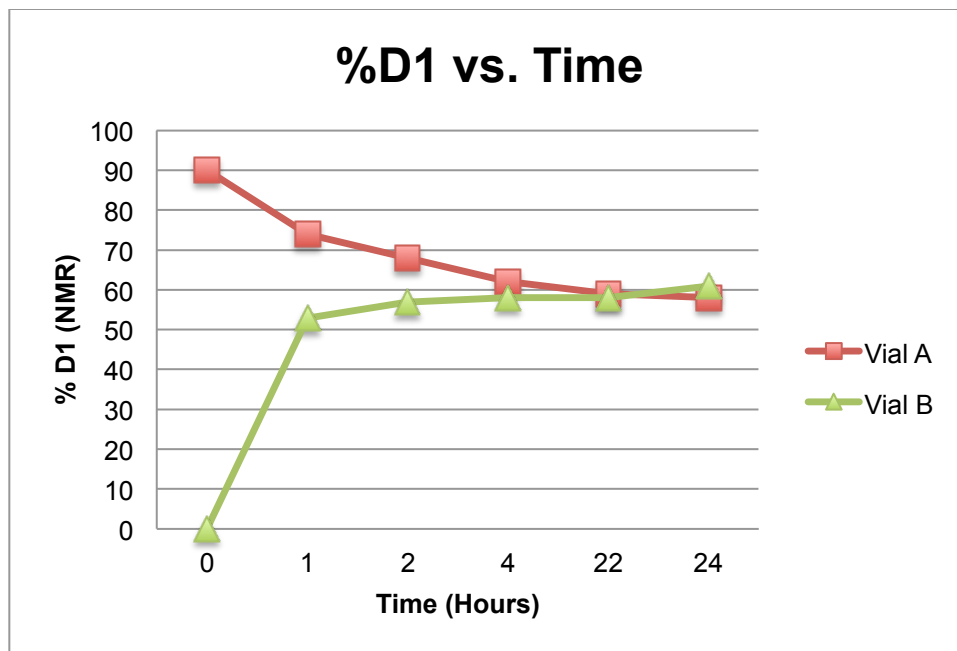
was added, forming a white precipitate immediately. This mixture was stirred vigorously at room temperature for five minutes, then a solution of the pure diastereomer of **21** (21 mg, 100  $\mu\text{mol}$ , 1.0 equiv) in  $\text{CD}_2\text{Cl}_2$  (300  $\mu\text{L}$ ) was added and the vial was placed in an aluminum heating block and stirred at 50  $^\circ\text{C}$  for 24 hours. At the given intervals, a small aliquot (20  $\mu\text{L}$ ) was removed and placed in an NMR tube, diluted with  $\text{CD}_2\text{Cl}_2$ , and analyzed by  $^1\text{H}$  NMR. The diastereomeric ratio was determined by analyzing the  $\alpha$ -cyano protons of the two diastereomers (dd at 3.17 ppm and t at 2.83 ppm).



**Scheme S1:** Epimerization of Diastereomers to the Thermodynamic Equilibrium.

time (hours)	Ratio (D1:D2)	
	Vial A	Vial B
0	90:10	5:>95
1	81:19	54:46
2	71:29	60:40
4	64:36	60:40
22	57:43	62:38
24	58:42	61:39

**Table S1:** Diastereomeric Ratio of Cyanonitroalkane **21** Over Time in the Presence of Sodium Propylnitronate

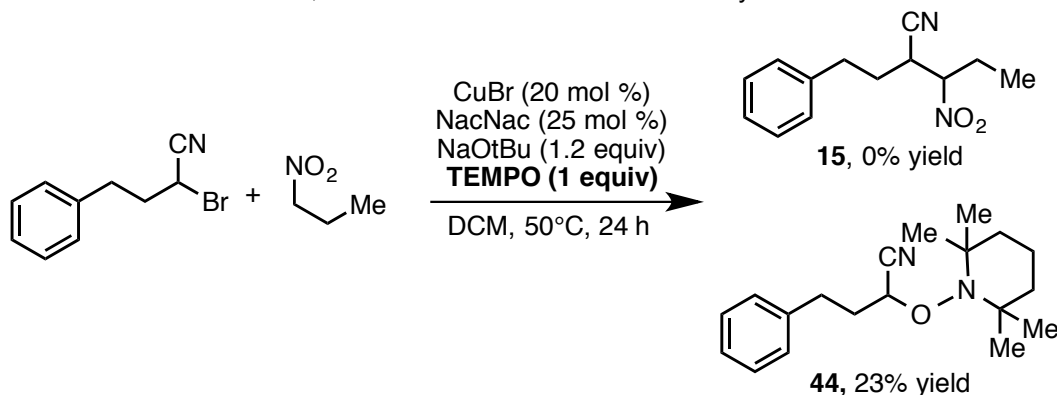


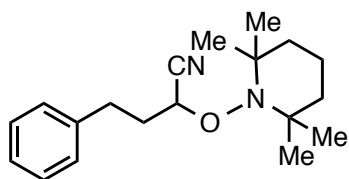
**Chart S1:** Diastereomeric Ratio of Cyanonitroalkane **21** Over Time in the Presence of Sodium Propylnitronate

By combining diastereomerically enriched samples of cyanonitroalkane **21** with sodium propylnitronate, both diastereomers converge to a ~60:40 ratio of D1:D2. This is the opposite sense of enrichment from that observed in the alkylation reaction (41:59 D1:D2). Since both diastereomers converge to a similar ratio, it can be concluded that this ratio is the thermodynamic equilibrium of the mixture. Since the ratio that results from the alkylation reaction is opposite that determined to be the thermodynamic equilibrium, it can be concluded that the reaction is under kinetic control.

## 12. Mechanistic Experiments

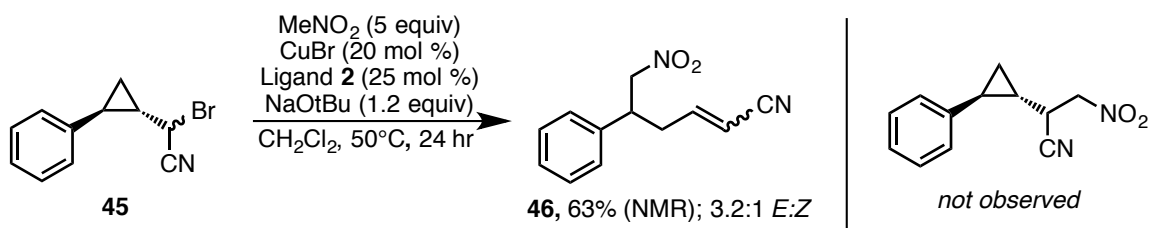
When the reaction was run in the presence of the known radical scavenger 2,2,6,6-tetramethyl-1-piperidinyloxy, free radical (TEMPO), no alkylation product was observed under the standard conditions. However, the adduct **44** was isolated in 23% yield.



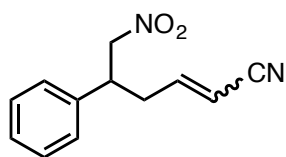


**(44)** According to the general procedure for alkylation, CuBr (28.6 mg, 200  $\mu\text{mol}$ ), ligand **2** (76.5 mg, 250  $\mu\text{mol}$ ), sodium *tert*-butoxide (115 mg, 1.20 mmol), 2,2,6,6-tetramethyl-1-piperidinyloxy, free radical (TEMPO, 156 mg, 1.0 mmol) anhydrous dichloromethane (6 mL), 1-nitropropane (112  $\mu\text{L}$ , 1.25 mmol), and 2-bromo-4-phenylbutanenitrile (224 mg, 1.00 mmol) were combined under  $\text{N}_2$  and heated at 50  $^\circ\text{C}$  with rapid stirring for 24 hours. The reaction was worked up according to the general procedure.  $^1\text{H}$  NMR analysis of the crude reaction mixture revealed that no alkylation product was present. Only starting material and TEMPO adduct in a ~3:1 ratio were present. The title compound (**44**) was isolated by silica gel flash chromatography (97:3:1 hexanes : ethyl acetate : acetic acid) as a yellow oil (68.4 mg, 23%).  $^1\text{H}$  NMR (600 MHz,  $\text{CDCl}_3$ )  $\delta$  7.31 (t,  $J$  = 7.5 Hz, 2H), 7.25 – 7.20 (m, 3H), 4.57 (t,  $J$  = 7.4, 5.6 Hz, 1H), 2.96 – 2.87 (m, 1H), 2.86 – 2.76 (m, 1H), 2.28 – 2.08 (m, 2H), 1.64 – 1.39 (m, 5H), 1.35 (s, 3H), 1.34 – 1.30 (m, 1H), 1.11 (s, 3H), 1.09 (s, 3H), 1.06 (s, 3H);  $^{13}\text{C}$  NMR (151 MHz,  $\text{CDCl}_3$ )  $\delta$  140.2, 128.7, 128.5, 126.5, 119.6, 73.7, 61.0, 60.0, 40.1, 40.0, 34.7, 34.2, 33.7, 31.1, 20.6, 20.4, 17.1; FTIR ( $\text{cm}^{-1}$ ): 2974, 2934, 2871, 1604, 1455, 700; ESI-MS: 301.27 ( $\text{M}+\text{H}$ ) $^+$ . HRMS (LIFDI)  $m/z$  calculated for  $[\text{C}_{19}\text{H}_{28}\text{N}_2\text{O}]^+$ : 300.2202; found: 300.2181.

### Fragmentation/alkylation of Substrate **45**



In order to simplify product identification and isolation, radical clock substrate **45** was reacted with nitromethane under the standard reaction conditions. The direct coupling product was not observed in the crude  $^1\text{H}$  NMR, nor was it isolated from the reaction mixture. The ring-opened product was observed as an inconsequential mixture of *E* and *Z* isomers.



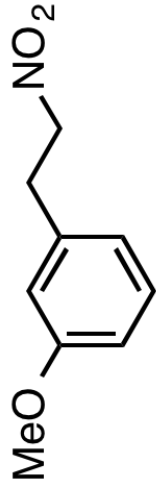
**(46)** In a nitrogen-filled glovebox, an oven-dried 1 dram vial was charged with CuBr (5.70 mg, 40.0  $\mu\text{mol}$ , 0.2 equiv), ligand **2** (15.3 mg, 50  $\mu\text{mol}$ , 0.25 equiv) and sodium *tert*-butoxide (23.0 mg, 240  $\mu\text{mol}$ , 1.2 equiv). Anhydrous dichloromethane (1.2 mL), nitromethane (54  $\mu\text{L}$ , 1.0 mmol, 5.0 equiv) and substrate **45** (47.2 mg, 200  $\mu\text{mol}$ , 1.0 equiv) were added sequentially to the vial. The vial was sealed with a Teflon-lined cap and placed in an aluminum heating block preheated to 50 $^\circ\text{C}$  and stirred vigorously for 24 hours. The mixture was cooled to room temperature and filtered through a short pad of Celite into a vial containing 1,3,5-trimethoxybenzene (internal standard). An aliquot was evaporated and analyzed by  $^1\text{H}$  NMR, showing full conversion of the starting bromide. An aliquot was subjected to silica gel chromatography to confirm the identity of the ring-opened product (**46**).  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.42 – 7.28 (m, 3H), 7.20 – 7.12 (m, 2H), 6.47 (dt,  $J$  = 16.3, 7.3 Hz, 1H), 5.34 (dd,  $J$  = 16.1, 1.5 Hz, 1H), 4.59 (d,  $J$  = 7.6 Hz, 2H), 3.62 (dt,  $J$  = 15.1, 7.6 Hz, 1H), 2.70 – 2.57 (m, 2H);  $^{13}\text{C}$  NMR (151 MHz,  $\text{CDCl}_3$ )  $\delta$  150.7, 137.2, 129.6, 128.6, 127.5, 116.7, 103.1, 79.7, 43.1, 36.7; FTIR ( $\text{cm}^{-1}$ ): 2224, 1635, 1552, 1379, 968, 701; GC/MS (EI) 169.1 ( $\text{M}-\text{HNO}_2$ ) $^+$ . HRMS (CI)  $m/z$  calculated for  $[\text{C}_{12}\text{H}_{13}\text{N}_2\text{O}_2]^+$ : 217.0977; found: 217.0976.



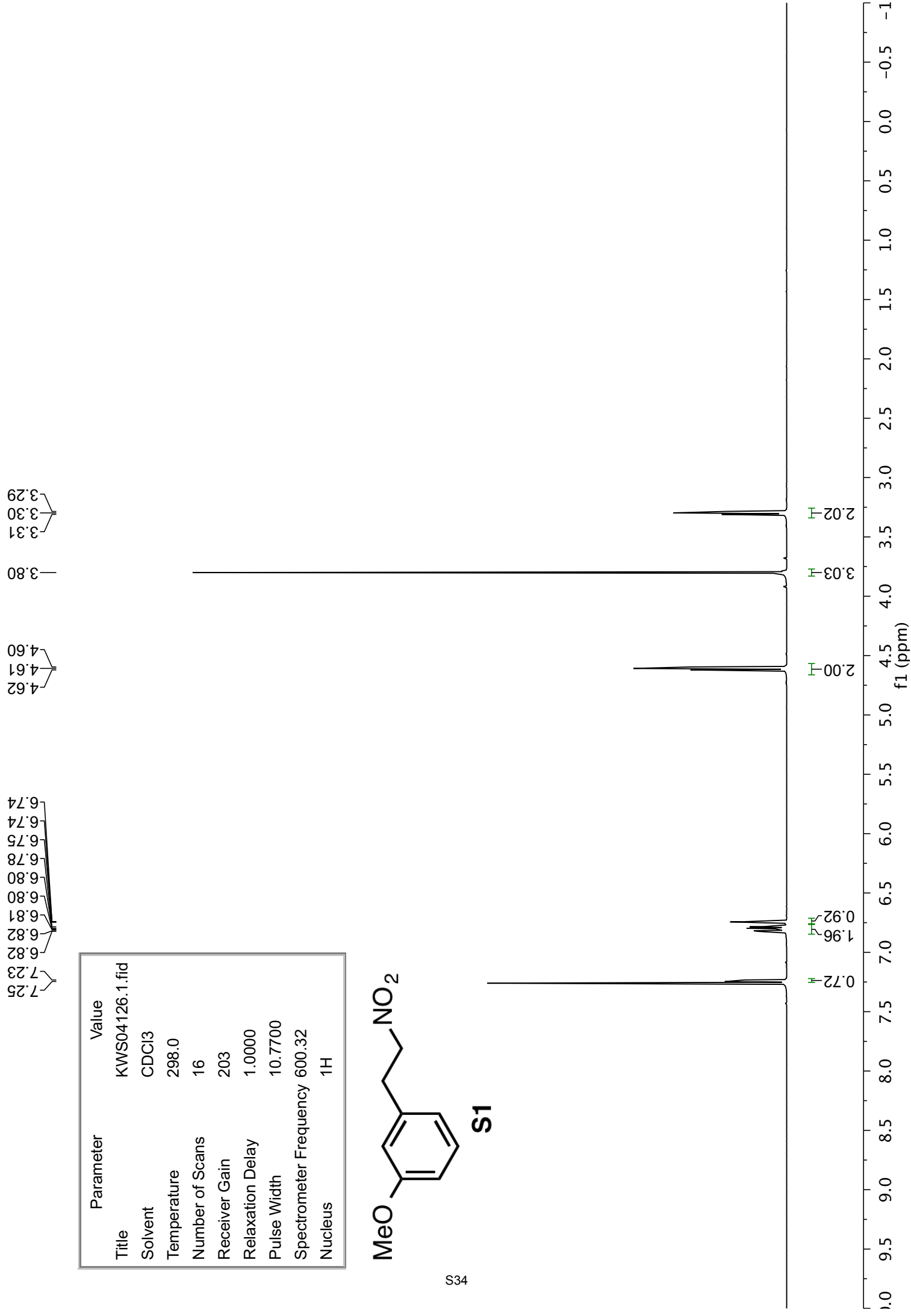
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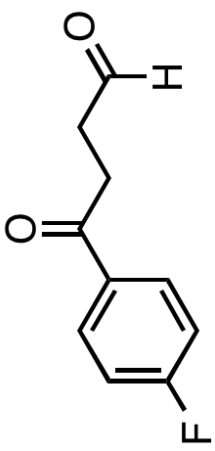


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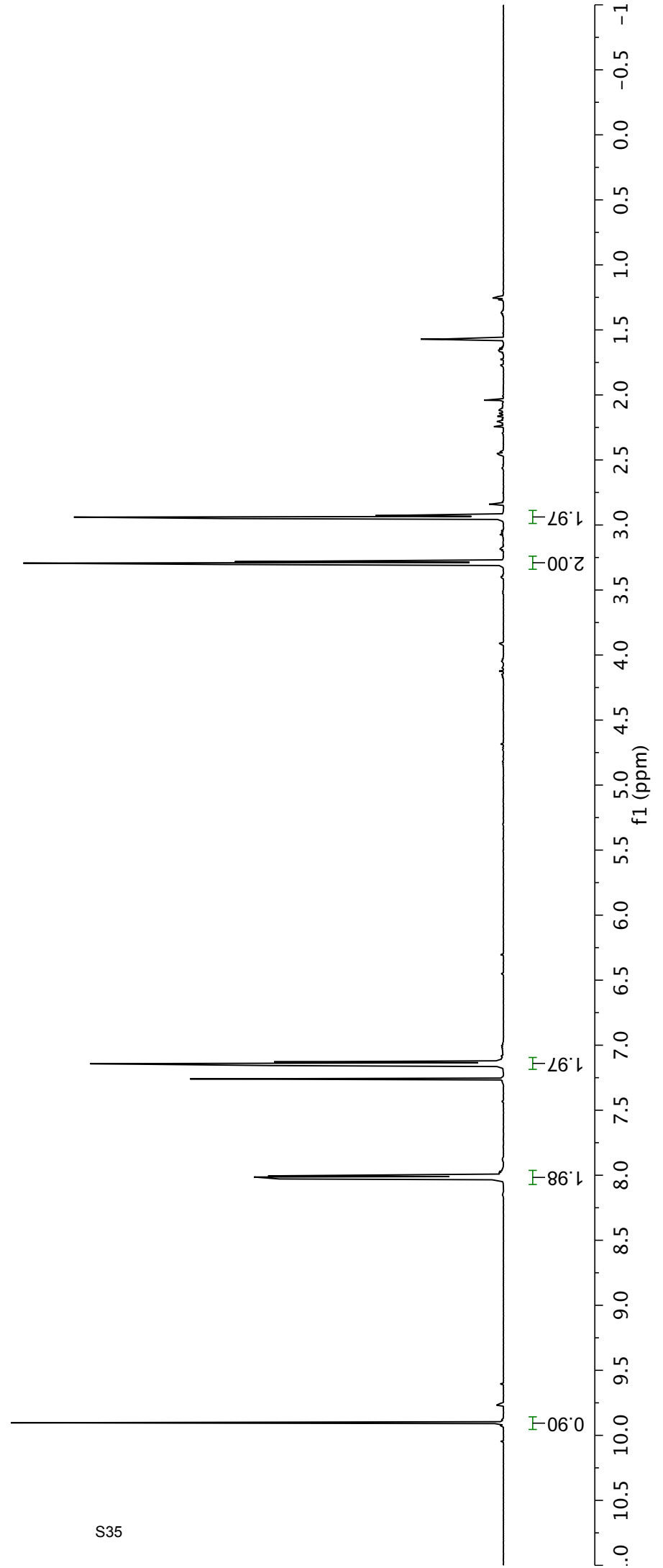
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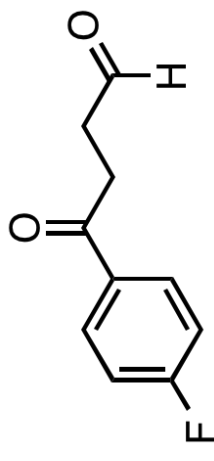


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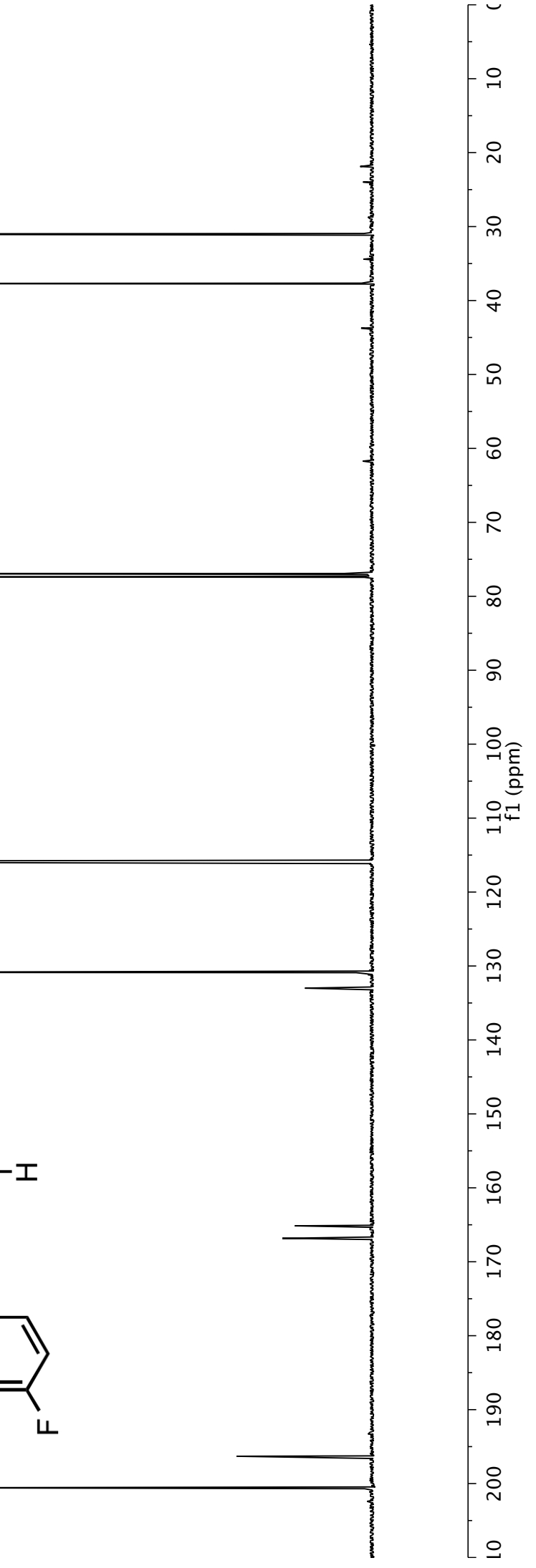


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Nucleus	13C

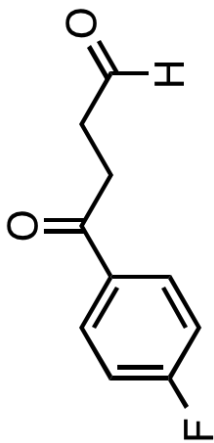


965



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S37

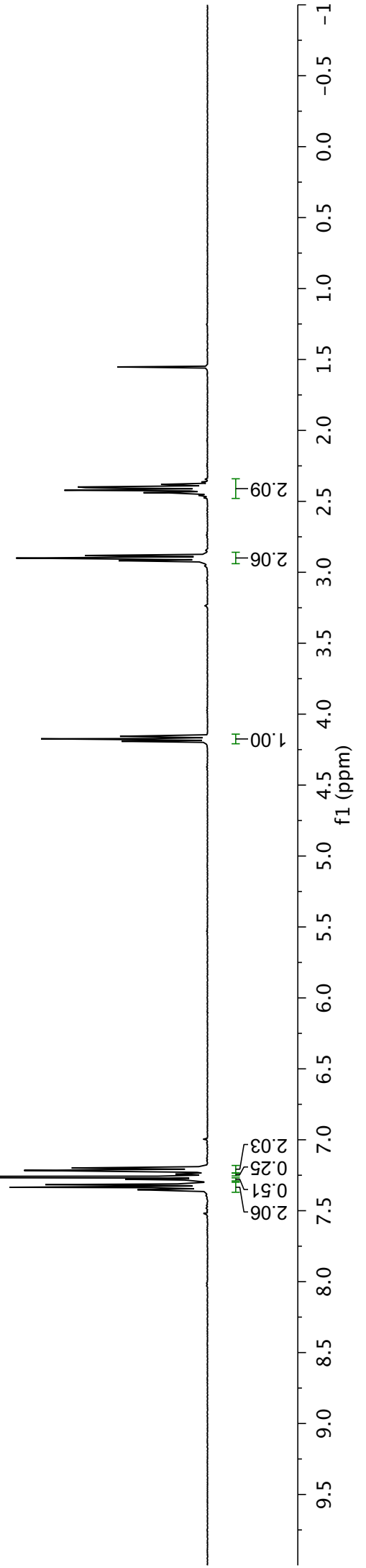
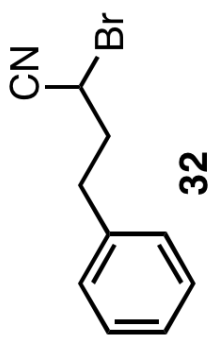
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f1 (ppm)

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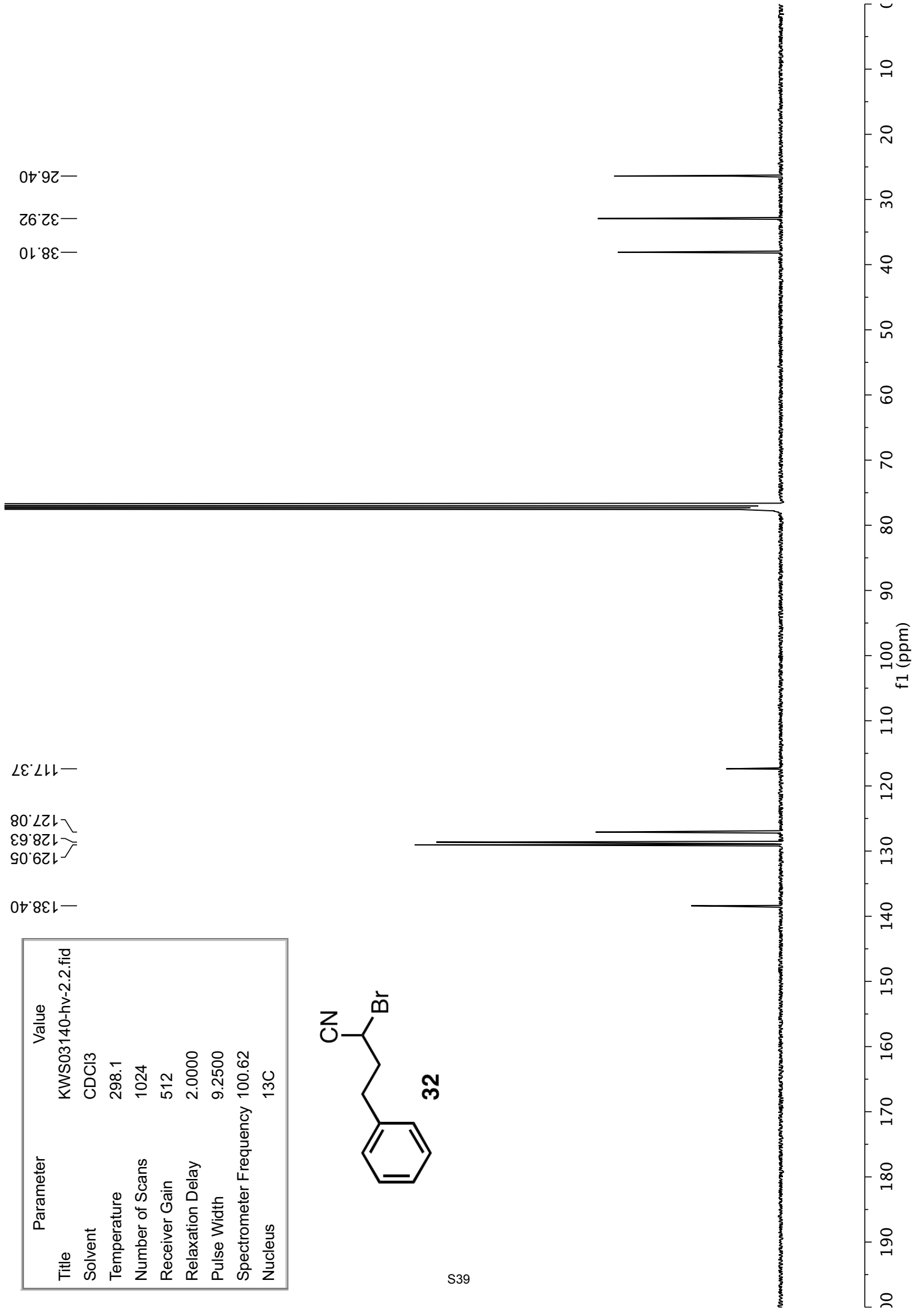
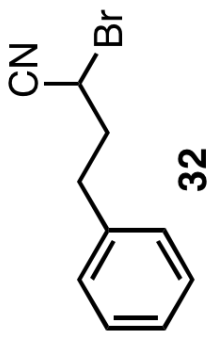
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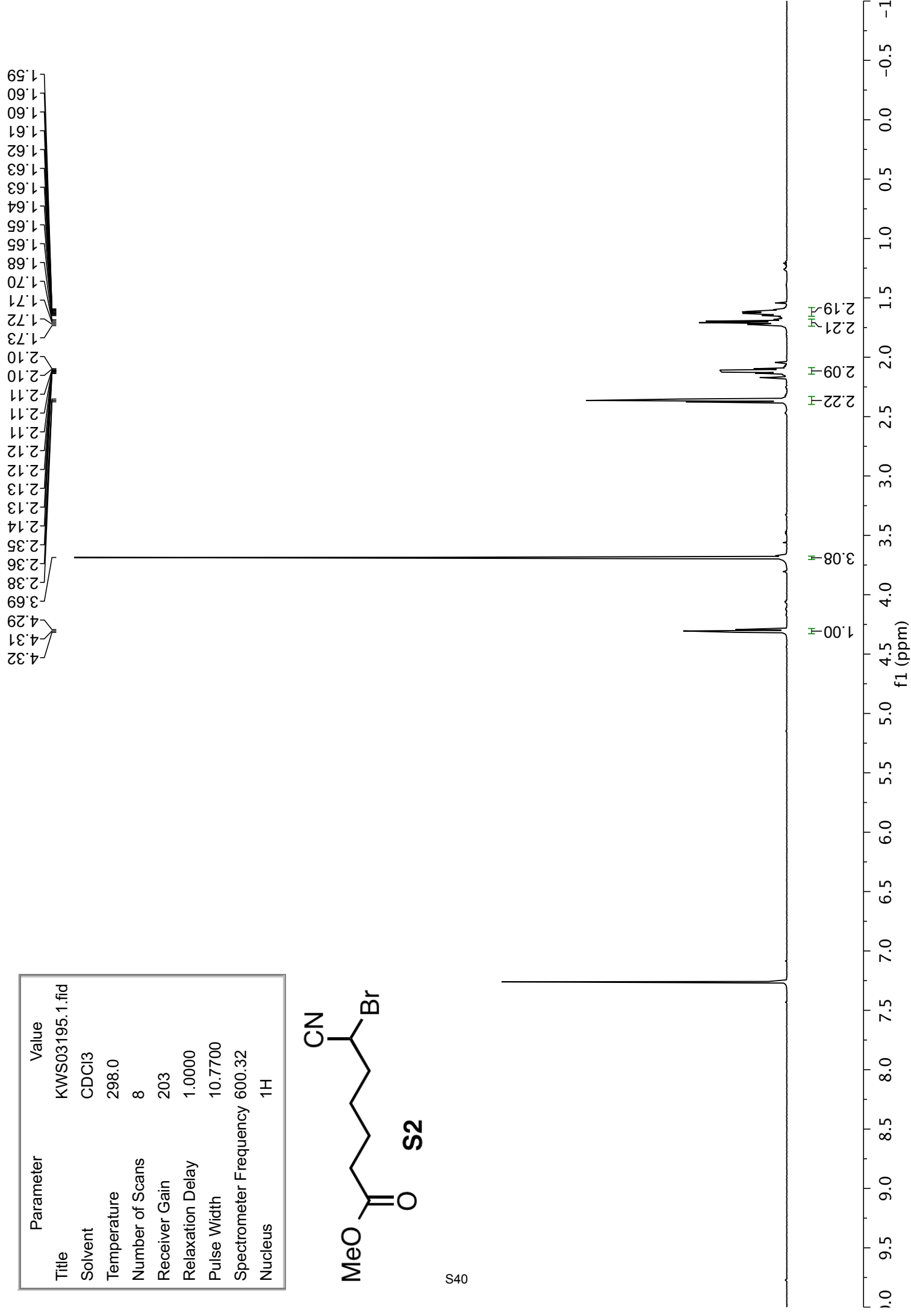
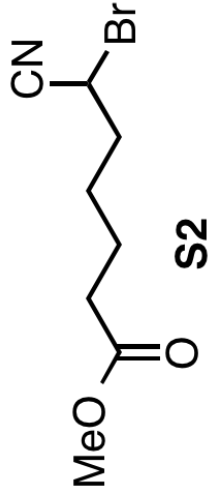
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Nucleus	13C

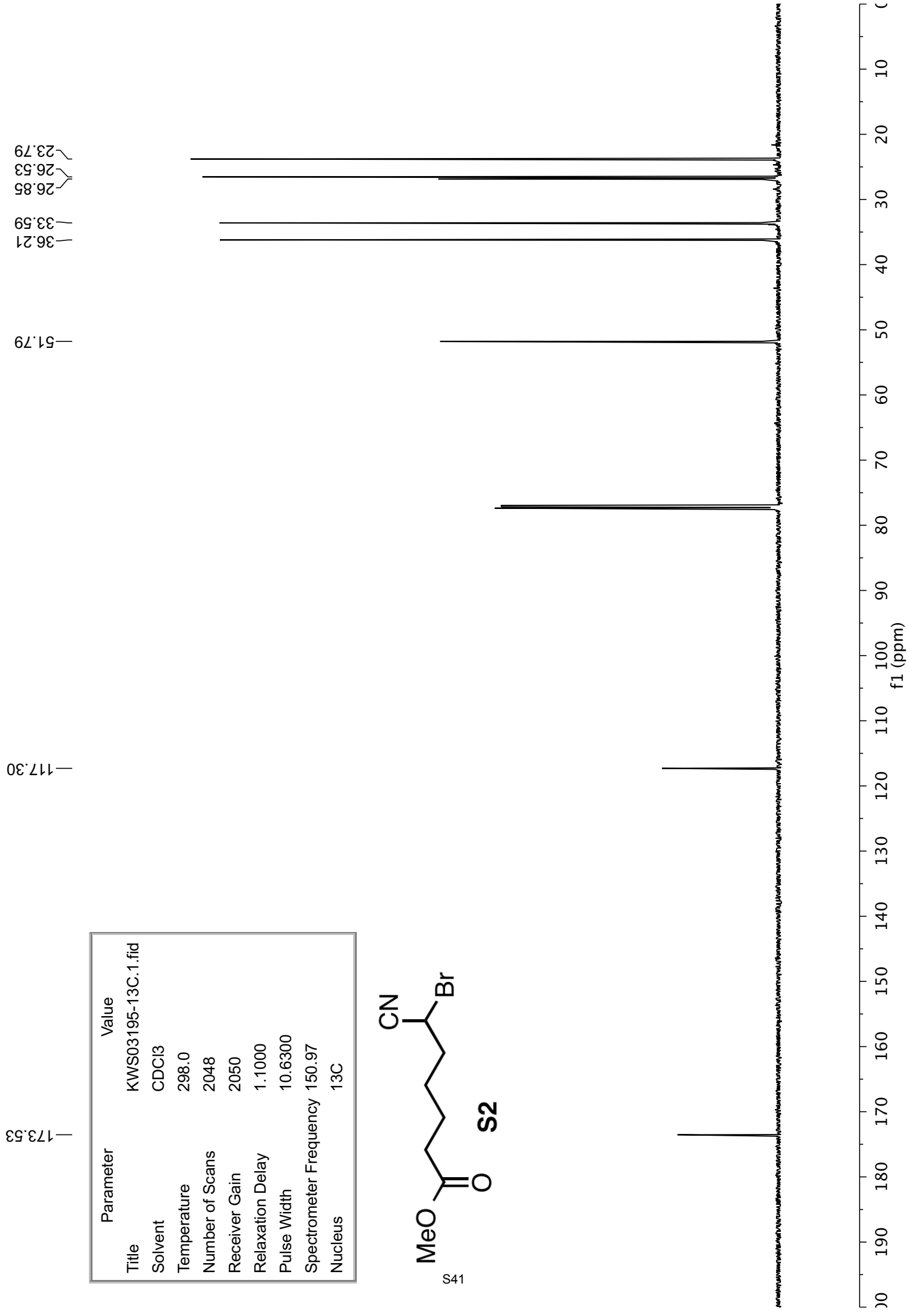
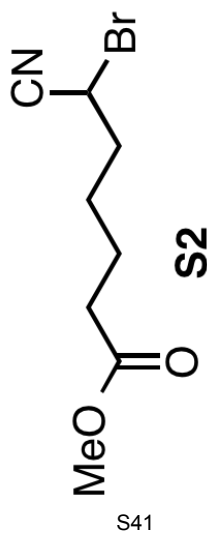


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Nucleus	<sup>1</sup> H

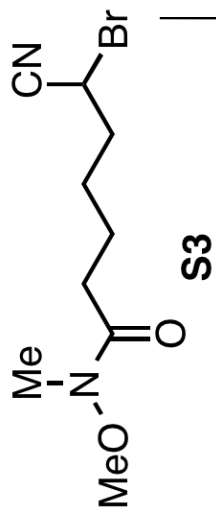




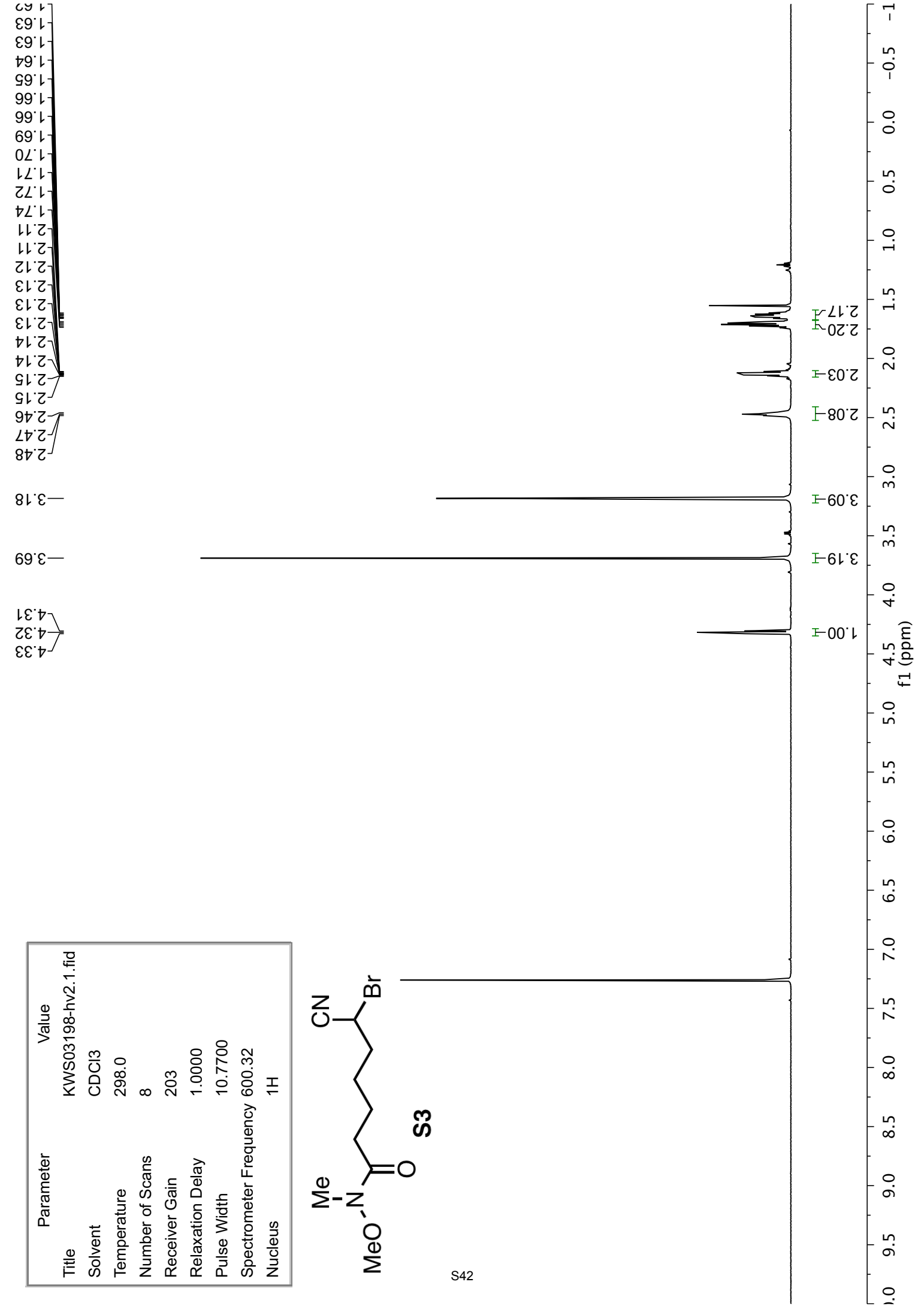
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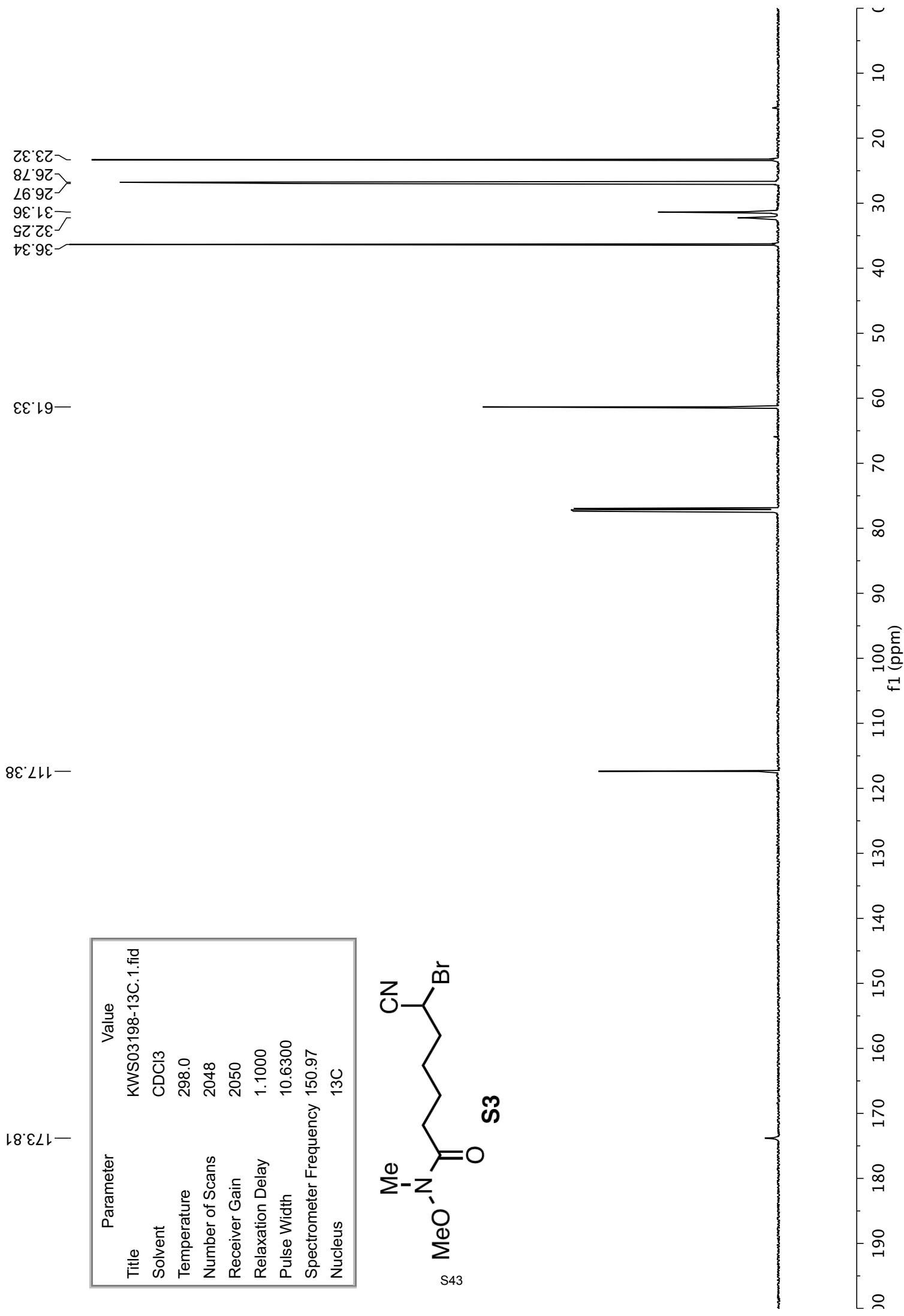
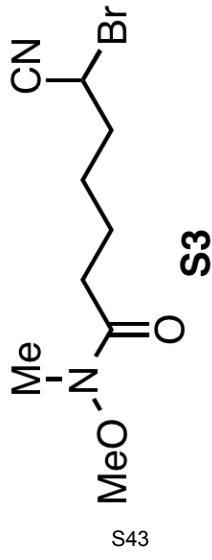
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Pulse Width	10.7700
Spectrometer Frequency	600.32
Nucleus	<sup>1</sup> H



25



Parameter	Value
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Solvent	CDCl3
Temperature	298.0
Number of Scans	2048
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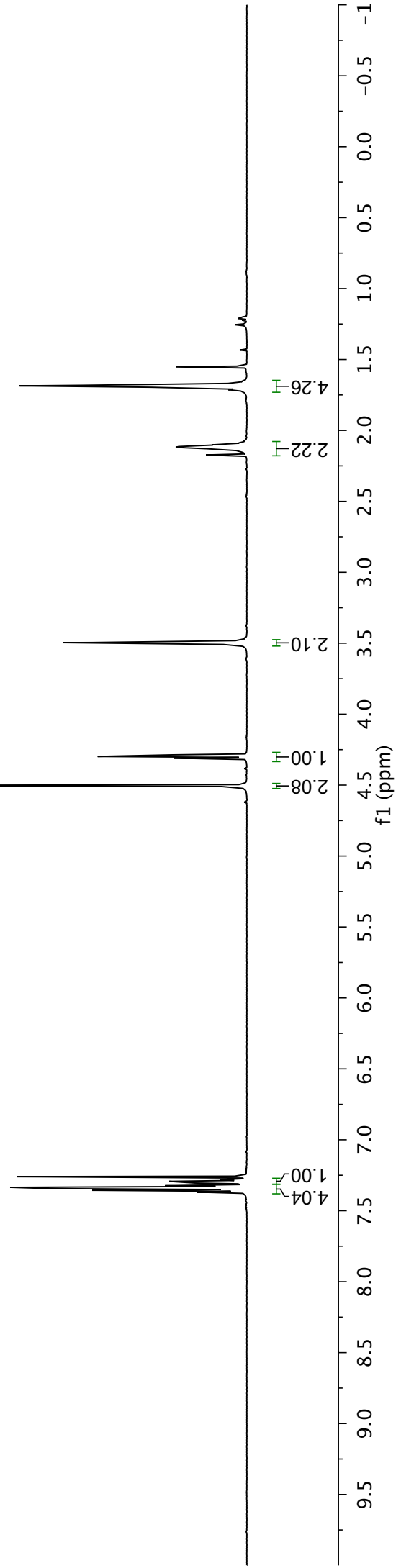
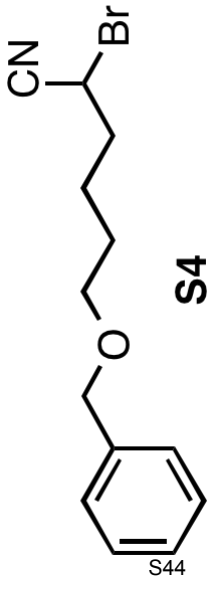
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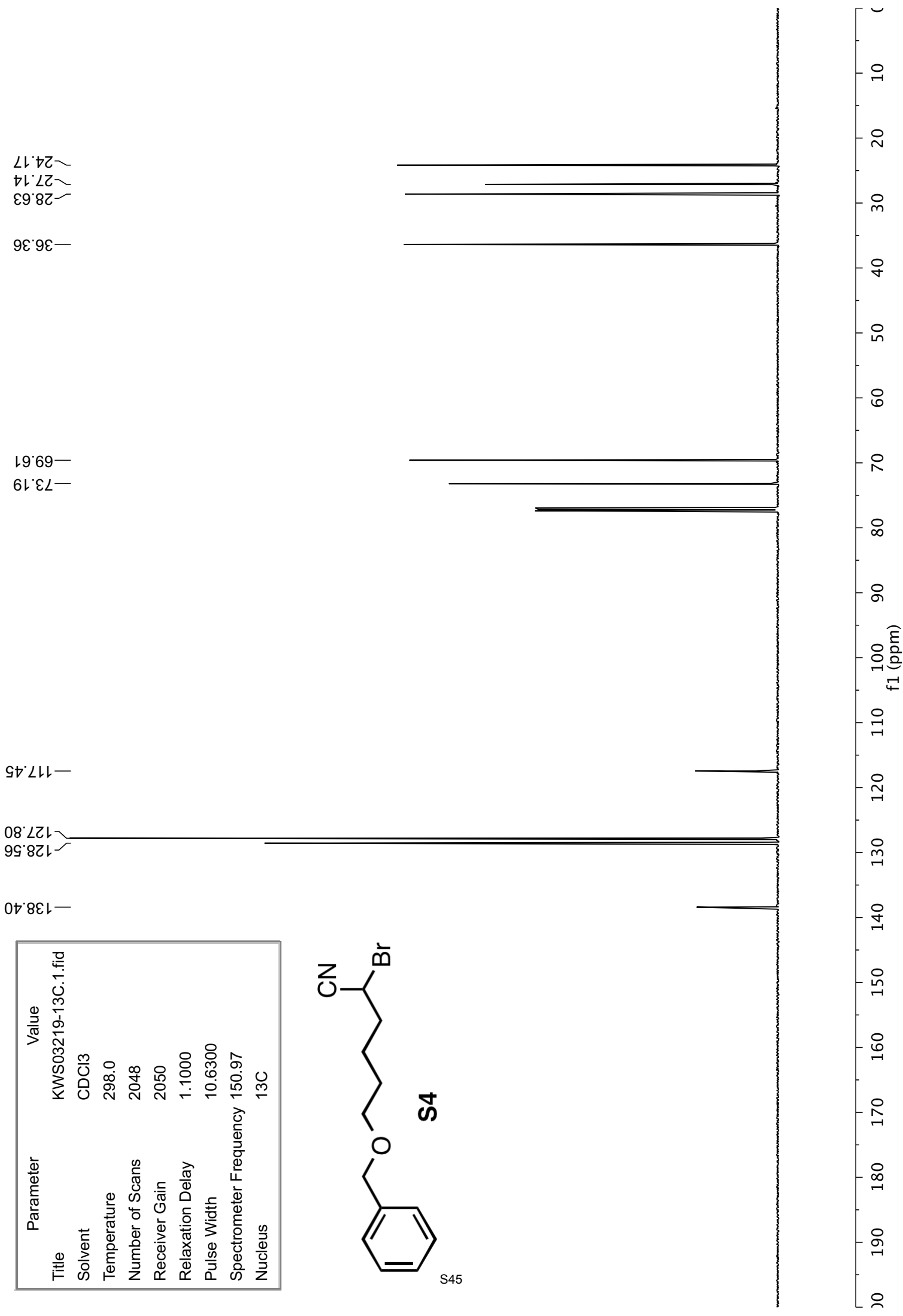
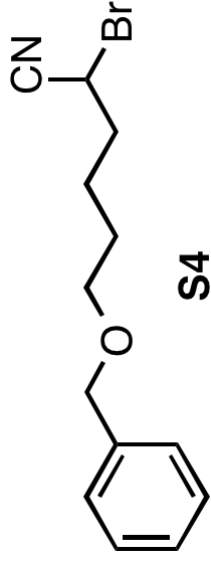
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Temperature	298.0
Number of Scans	8
Receiver Gain	181
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Pulse Width	10.7700
Spectrometer Frequency	600.32
Nucleus	<sup>1</sup> H



Parameter	Value
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Nucleus	13C

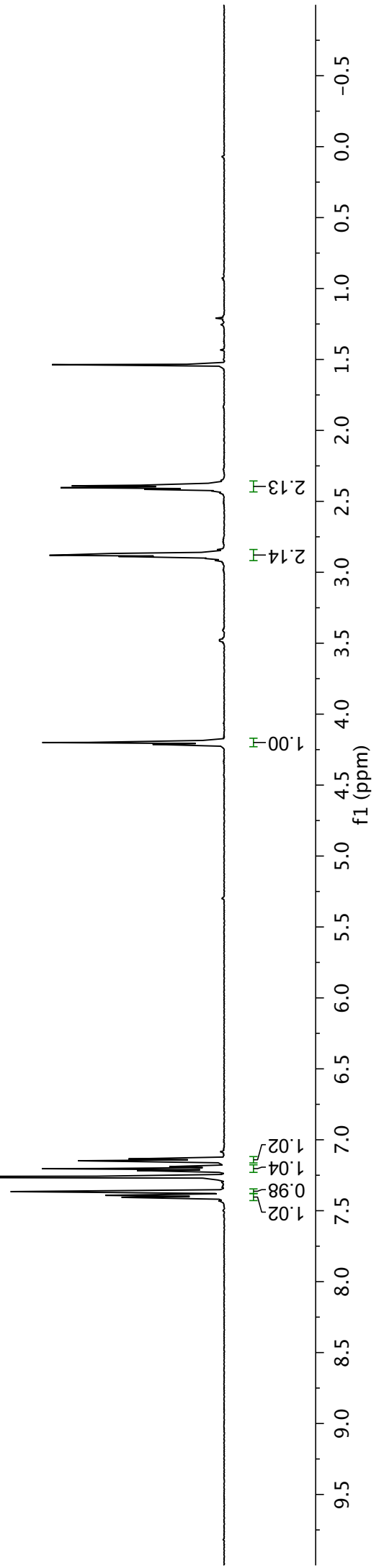
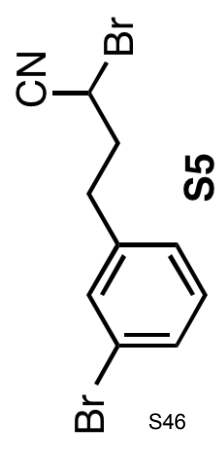


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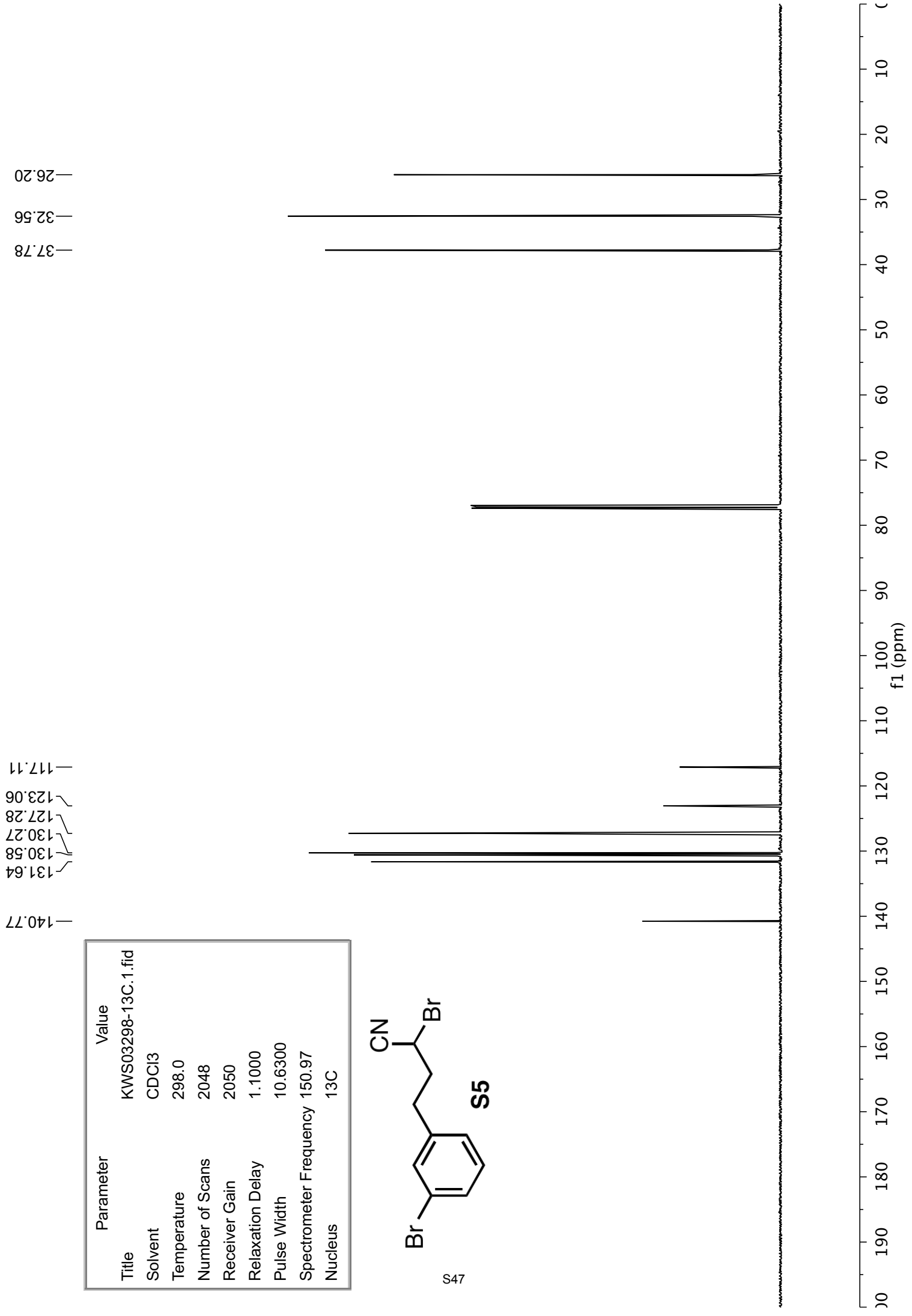
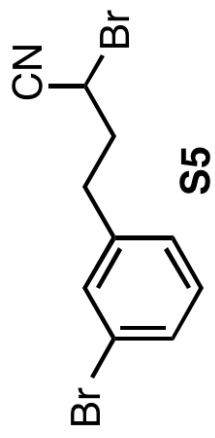
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Spectrometer Frequency	600.32
Nucleus	<sup>1</sup> H



Parameter	Value
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Temperature	298.0
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Relaxation Delay	1.1000
Pulse Width	10.6300
Spectrometer Frequency	150.97
Nucleus	<sup>13</sup> C

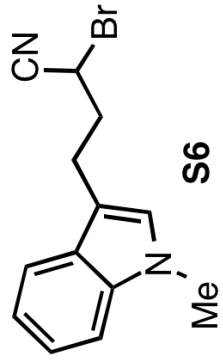


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3.07

3.77  
4.17  
4.19  
4.20

6.93  
7.12  
7.14  
7.16  
7.24  
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7.32  
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Pulse Width	15.0000
Spectrometer Frequency	400.13
Nucleus	<sup>1</sup> H



85

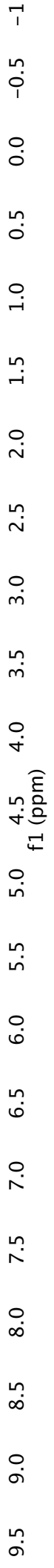
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1.04  
1.03  
1.01

2.05

2.08

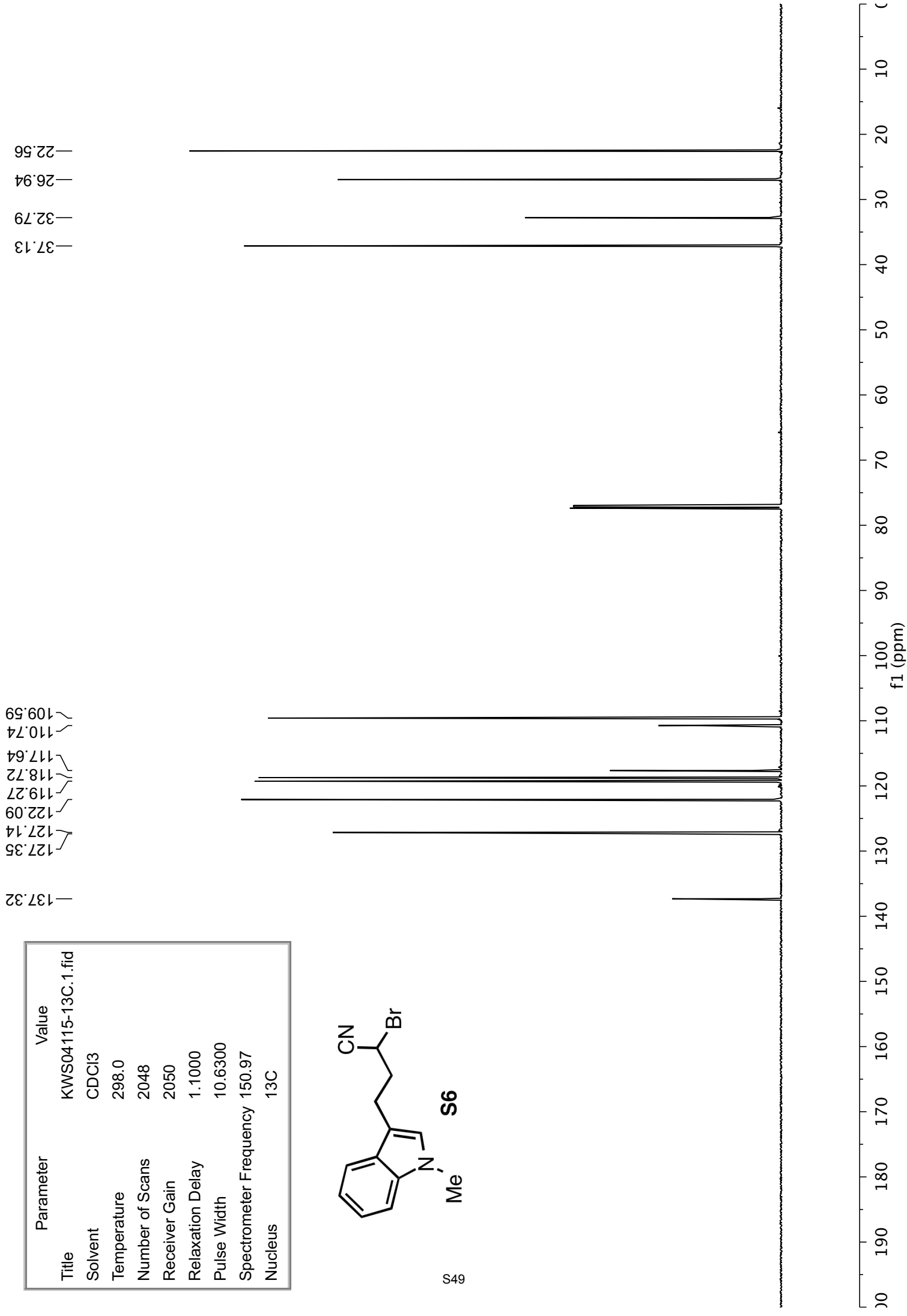
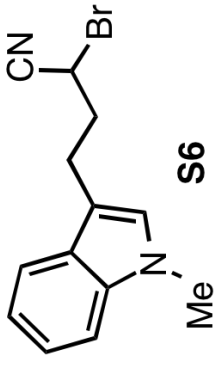
3.09

1.00



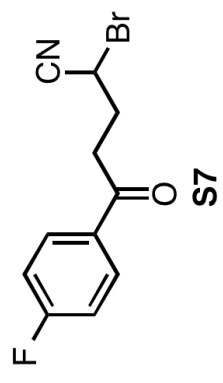


Parameter	Value
Title	KWS04115-13C:1.fid
Solvent	CDCl3
Temperature	298.0
Number of Scans	2048
Receiver Gain	2050
Relaxation Delay	1.1000
Pulse Width	10.6300
Spectrometer Frequency	150.97
Nucleus	13C

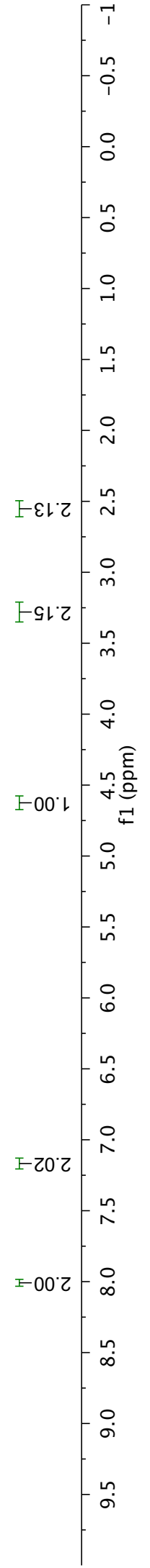


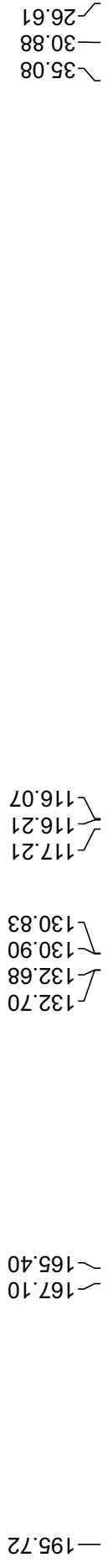
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8.01  
8.01  
8.01  
8.01  
8.00  
8.00  
7.99  
7.18  
7.17  
7.15

Parameter	Value
Title	KWS04062.1.fid
Solvent	CDCl3
Temperature	298.0
Number of Scans	16
Receiver Gain	228
Relaxation Delay	1.0000
Pulse Width	10.7700
Spectrometer Frequency	600.32
Nucleus	<sup>1</sup> H

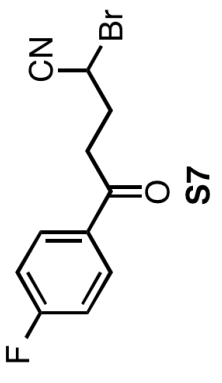


4.64  
4.63  
4.61  
3.34  
3.33  
3.32  
3.31  
3.30  
3.29  
3.28  
3.27  
3.25  
3.25  
3.24  
3.22  
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2.59  
2.58  
2.56  
2.55  
2.54  
2.53  
2.52  
2.51

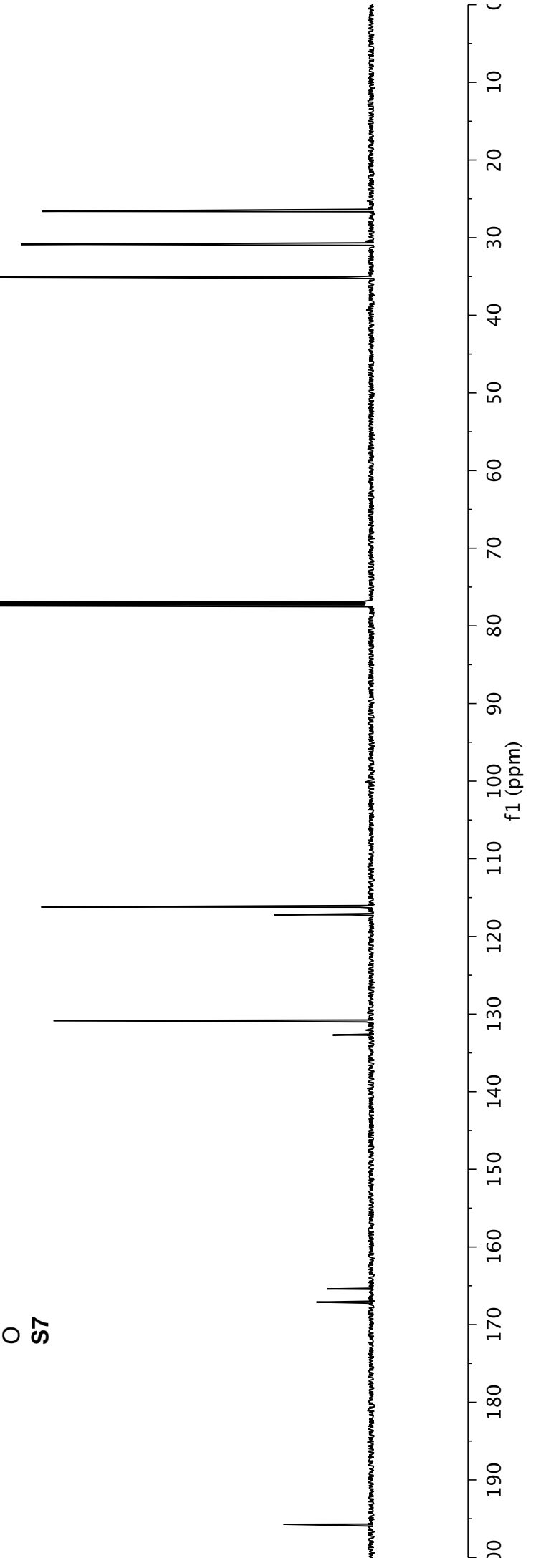




Parameter	Value
Title	KWS04062-13C:1.fid
Solvent	CDCl3
Temperature	298.0
Number of Scans	2048
Receiver Gain	2050
Relaxation Delay	1.1000
Pulse Width	10.6300
Spectrometer Frequency	150.97
Nucleus	13C

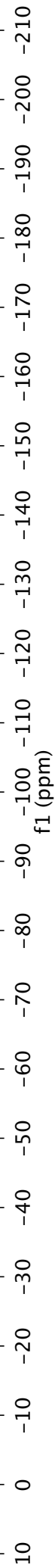
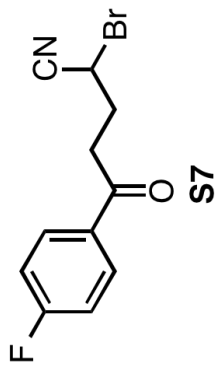


S7



Parameter	Value
Title	KWS04062.2.fid
Solvent	CDCl3
Temperature	298.0
Number of Scans	16
Receiver Gain	406
Relaxation Delay	3.0000
Pulse Width	11.6200
Spectrometer Frequency	564.81
Nucleus	19F

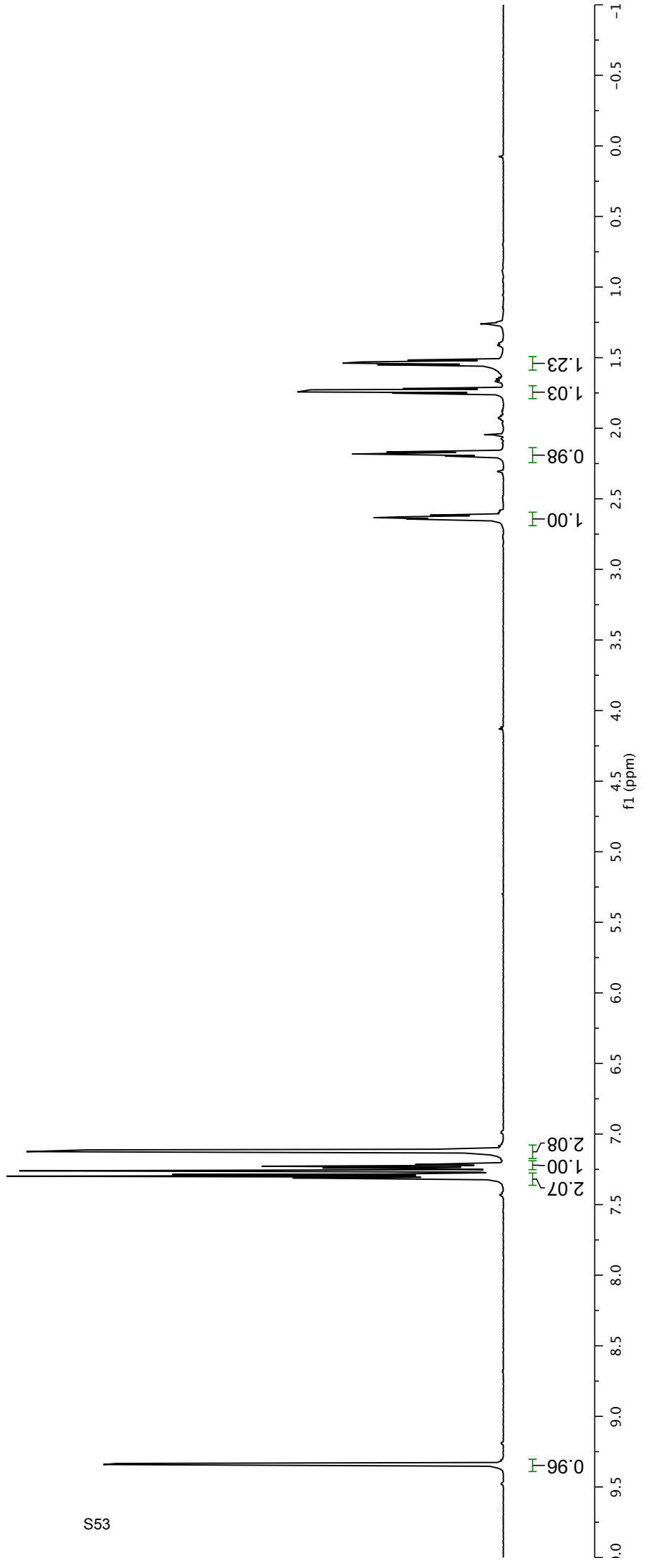
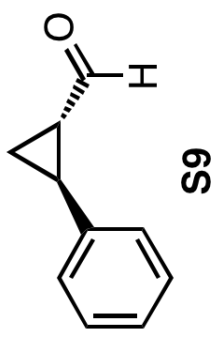
—103.85



2.65  
2.64  
2.64  
2.63  
2.62  
2.62  
2.20  
2.19  
2.18  
2.18  
2.17  
2.16  
1.75  
1.74  
1.74  
1.73  
1.72  
1.55  
1.54  
1.54  
1.54  
1.52

9.34  
9.33  
7.31  
7.30  
7.29  
7.24  
7.24  
7.23  
7.22  
7.12  
7.11

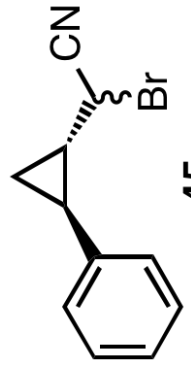
Parameter	Value
Title	KWS05045.1.fid
Solvent	CDCl3
Temperature	300.0
Number of Scans	16
Receiver Gain	181
Relaxation Delay	1.0000
Pulse Width	10.7700
Spectrometer Frequency	600.32
Nucleus	<sup>1</sup> H



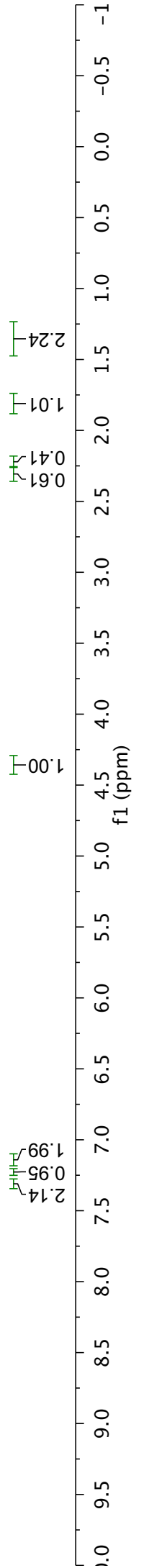
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1.29  
1.30  
1.32  
1.33  
1.34  
1.35  
1.36  
1.38  
1.40  
1.41  
1.42  
1.43  
1.77  
1.79  
1.80  
1.83  
2.20  
2.21  
2.22  
2.22  
2.23  
2.28  
2.28  
2.29  
2.30  
2.31

4.33  
4.33  
4.34  
4.35

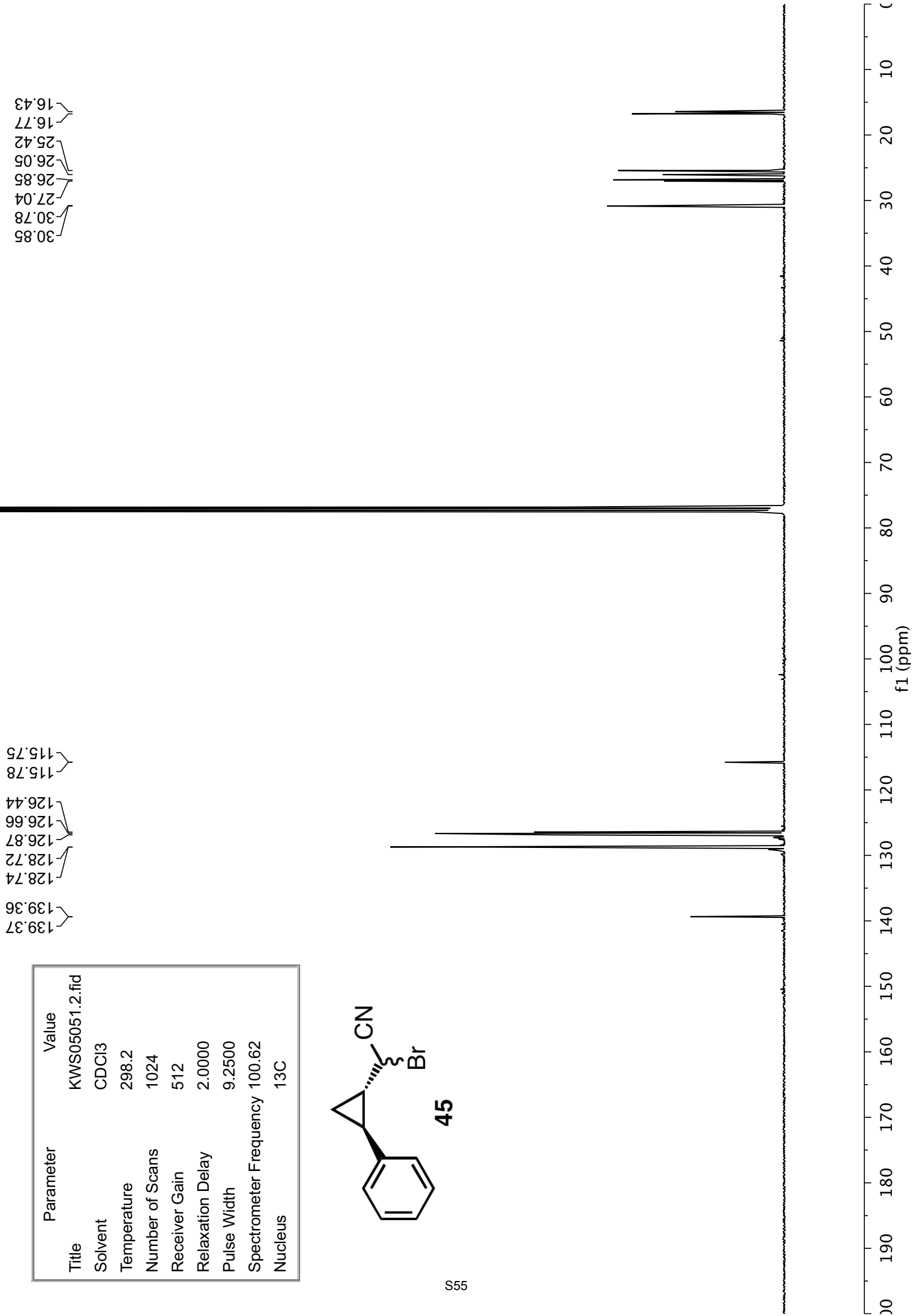
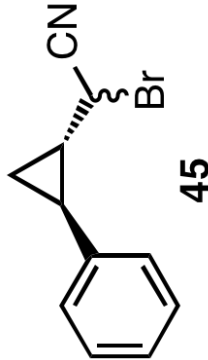
Parameter	Value
Title	KWS05051cf12-19.1.fid
Solvent	CDCl3
Temperature	300.0
Number of Scans	16
Receiver Gain	203
Relaxation Delay	1.0000
Pulse Width	10.7700
Spectrometer Frequency	600.32
Nucleus	<sup>1</sup> H



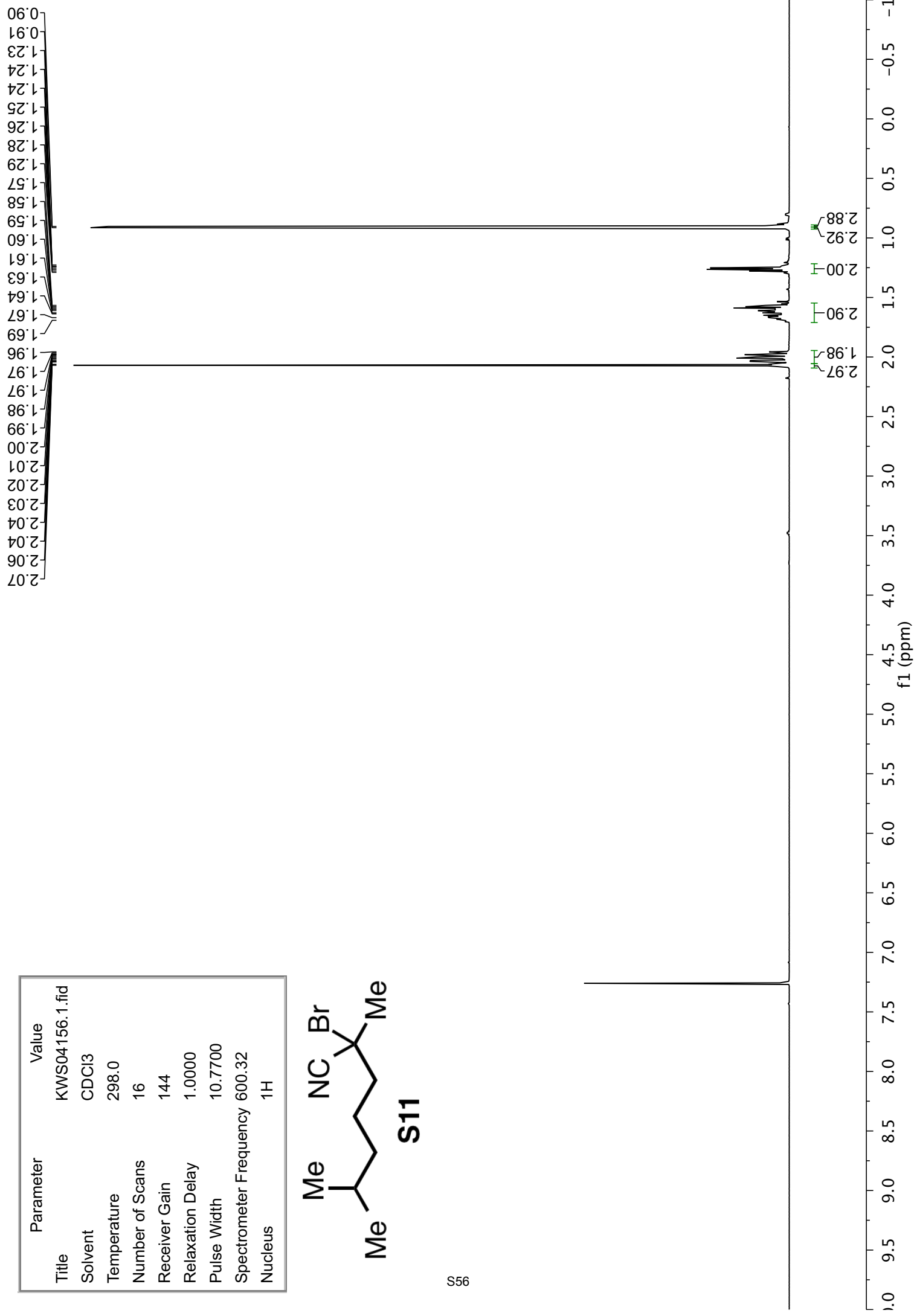
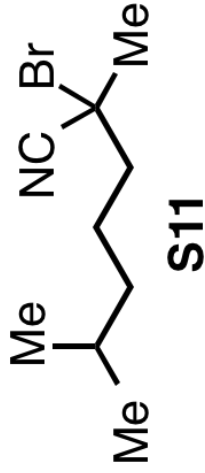
S54



Parameter	Value
Title	KWS05051.2.fid
Solvent	CDCl3
Temperature	298.2
Number of Scans	1024
Receiver Gain	512
Relaxation Delay	2.0000
Pulse Width	9.2500
Spectrometer Frequency	100.62
Nucleus	13C

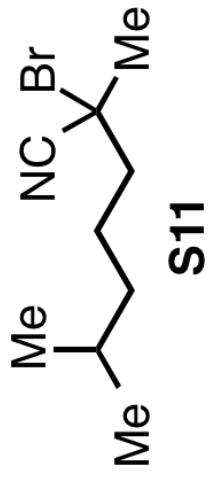


Parameter	Value
Title	KWS04156.1.fid
Solvent	CDCl3
Temperature	298.0
Number of Scans	16
Receiver Gain	144
Relaxation Delay	1.0000
Pulse Width	10.7700
Spectrometer Frequency	600.32
Nucleus	<sup>1</sup> H



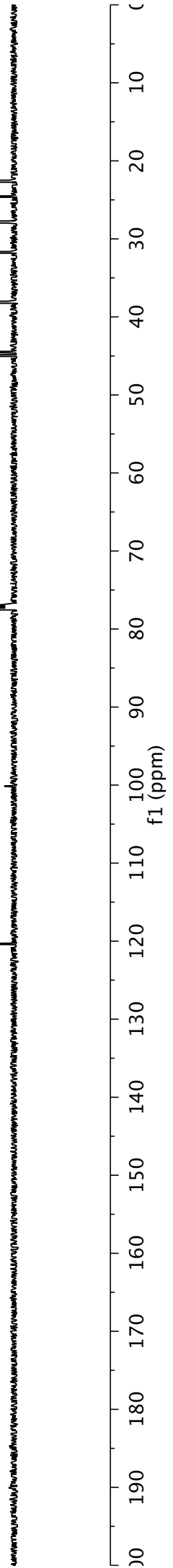


Parameter	Value
Title	KWS04156.2.fid
Solvent	CDCI3
Temperature	298.0
Number of Scans	2048
Receiver Gain	2050
Relaxation Delay	1.1000
Pulse Width	10.6300
Spectrometer Frequency	150.97
Nucleus	<sup>13</sup> C



—120.37  
 —38.11  
 —31.76  
 —27.88  
 —24.61  
 —22.62  
 —22.60  
 —44.91  
 —44.46

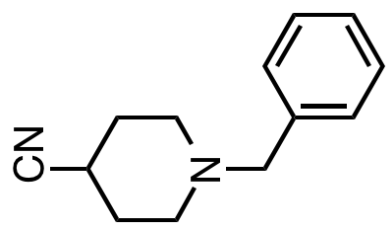
57



1.84  
1.85  
1.86  
1.87  
1.88  
1.88  
1.89  
1.91  
1.92  
1.92  
1.93  
1.96  
-2.31  
-2.66  
-3.50

7.25  
7.27  
7.29  
7.30  
7.31  
7.32  
7.33

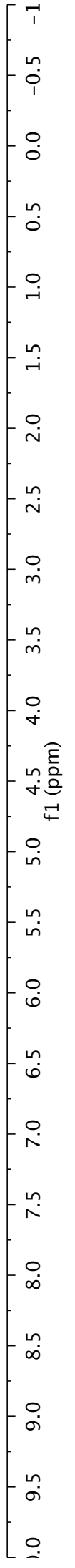
Parameter	Value
Title	KWS04221.1.fid
Solvent	CDCl3
Temperature	298.0
Number of Scans	16
Receiver Gain	161
Relaxation Delay	1.0000
Pulse Width	10.7700
Spectrometer Frequency	600.32
Nucleus	<sup>1</sup> H



89

2.02  
2.00  
1.72  
2.80  
2.00

0.18  
0.37  
3.78



7.34  
7.33  
7.32  
7.30  
7.29  
7.27

Parameter	Value
Title	KWS04224-13C.1.fid
Solvent	CDCl3
Temperature	298.0
Number of Scans	16
Receiver Gain	101
Relaxation Delay	1.0000
Pulse Width	10.7700
Spectrometer Frequency	600.32
Nucleus	<sup>1</sup> H

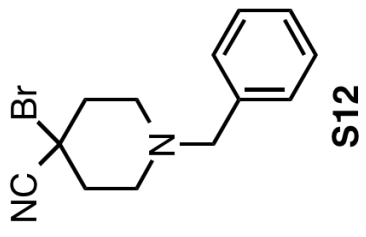
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2.39  
2.37  
2.34  
2.33  
2.32  
2.32  
2.30  
2.29

3.54

4.60

1.88  
1.88  
1.99  
2.08

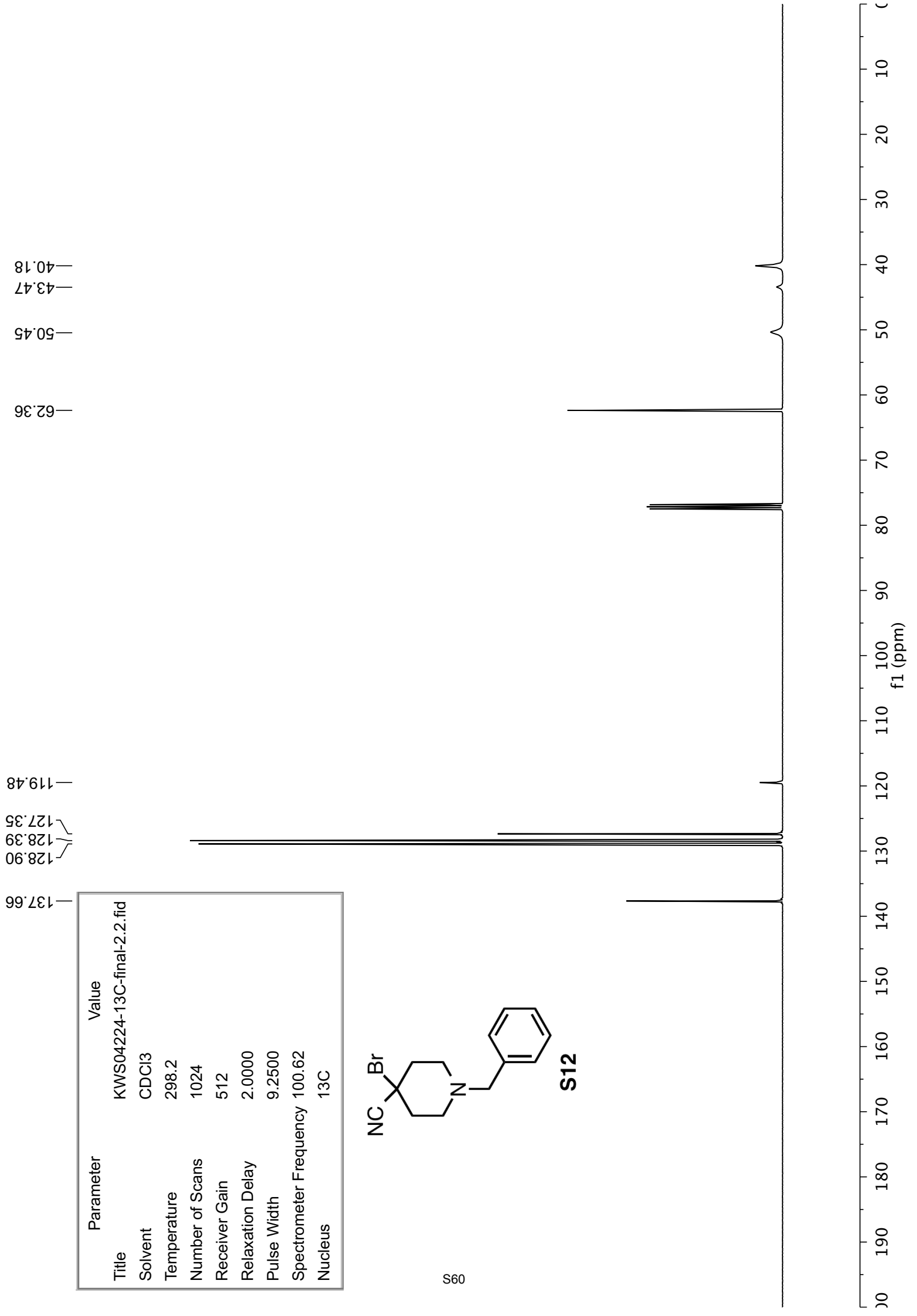
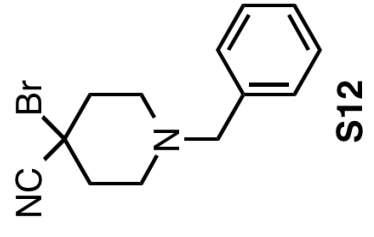
2.00



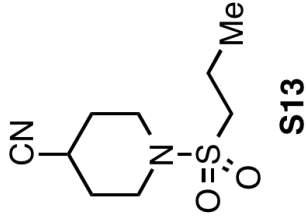
69



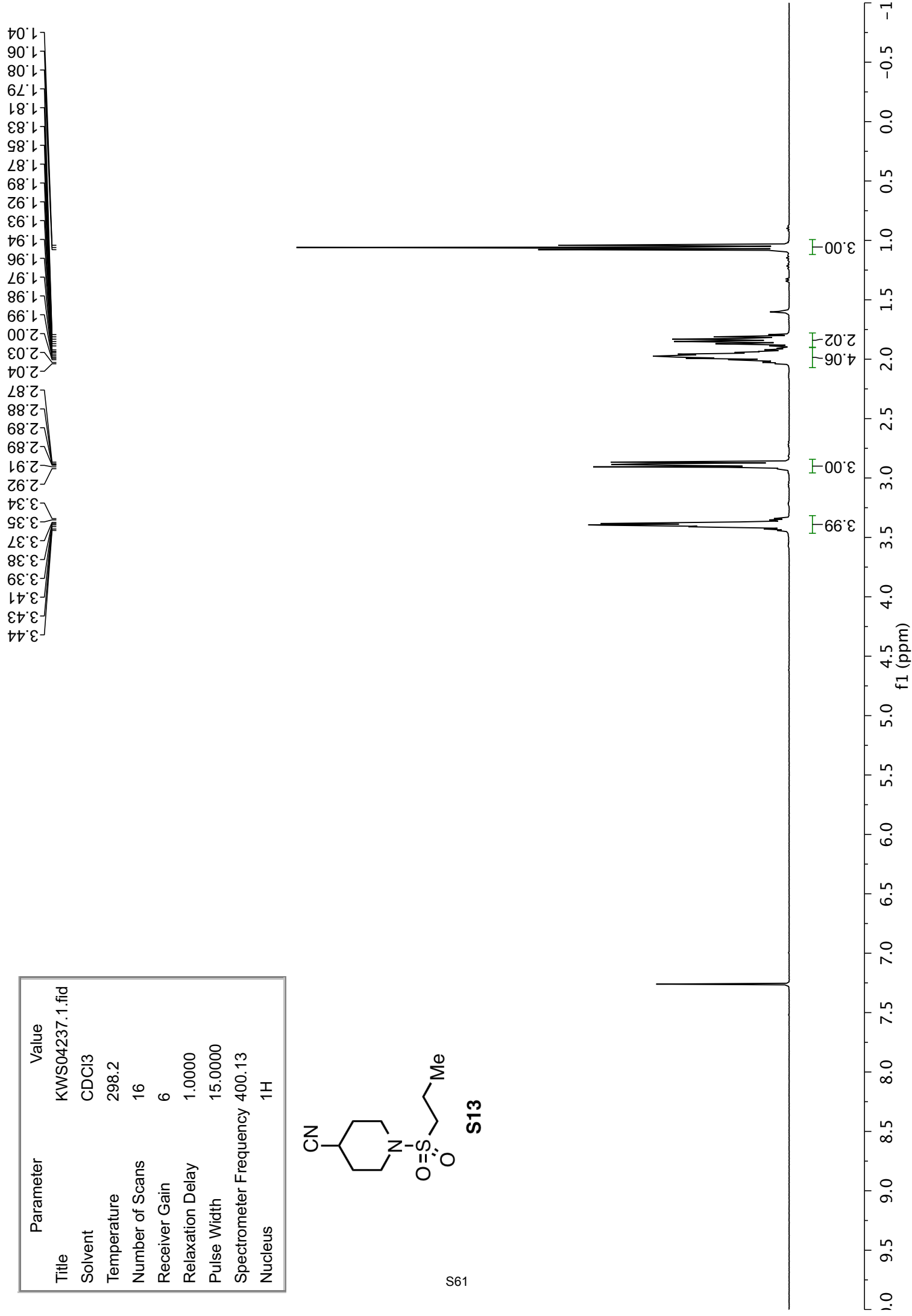
Parameter	Value
Title	KWS04224-13C-final-2.2.fid
Solvent	CDCl3
Temperature	298.2
Number of Scans	1024
Receiver Gain	512
Relaxation Delay	2.0000
Pulse Width	9.2500
Spectrometer Frequency	100.62
Nucleus	13C



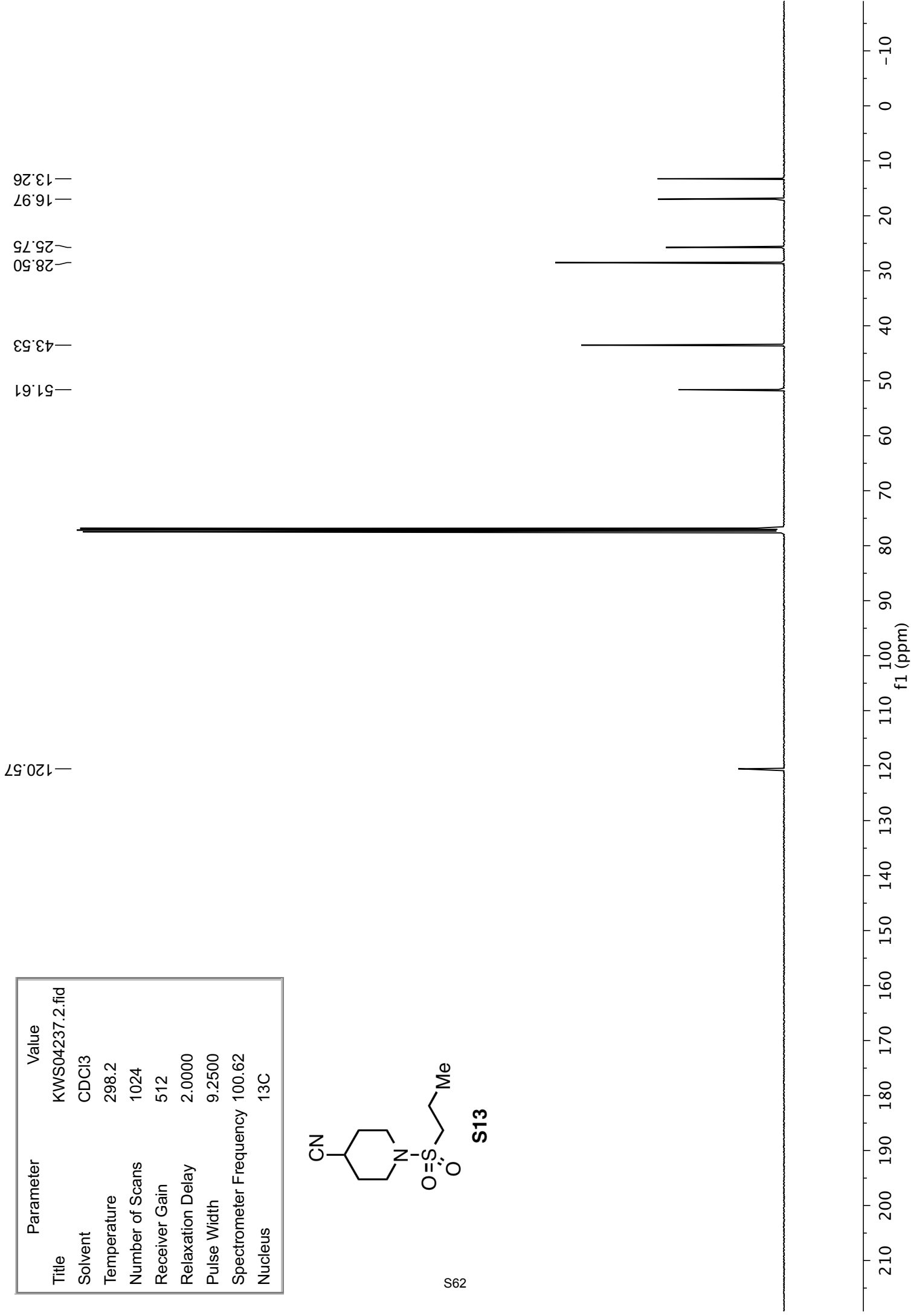
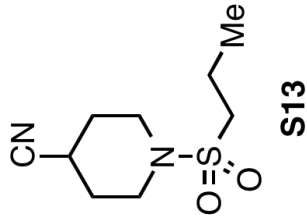
Parameter	Value
Title	KWS04237.1.fid
Solvent	CDCl <sub>3</sub>
Temperature	298.2
Number of Scans	16
Receiver Gain	6
Relaxation Delay	1.0000
Pulse Width	15.0000
Spectrometer Frequency	400.13
Nucleus	<sup>1</sup> H



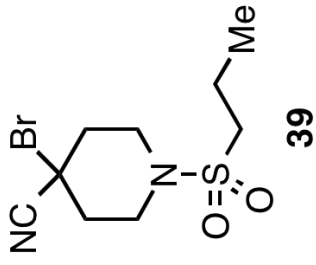
189



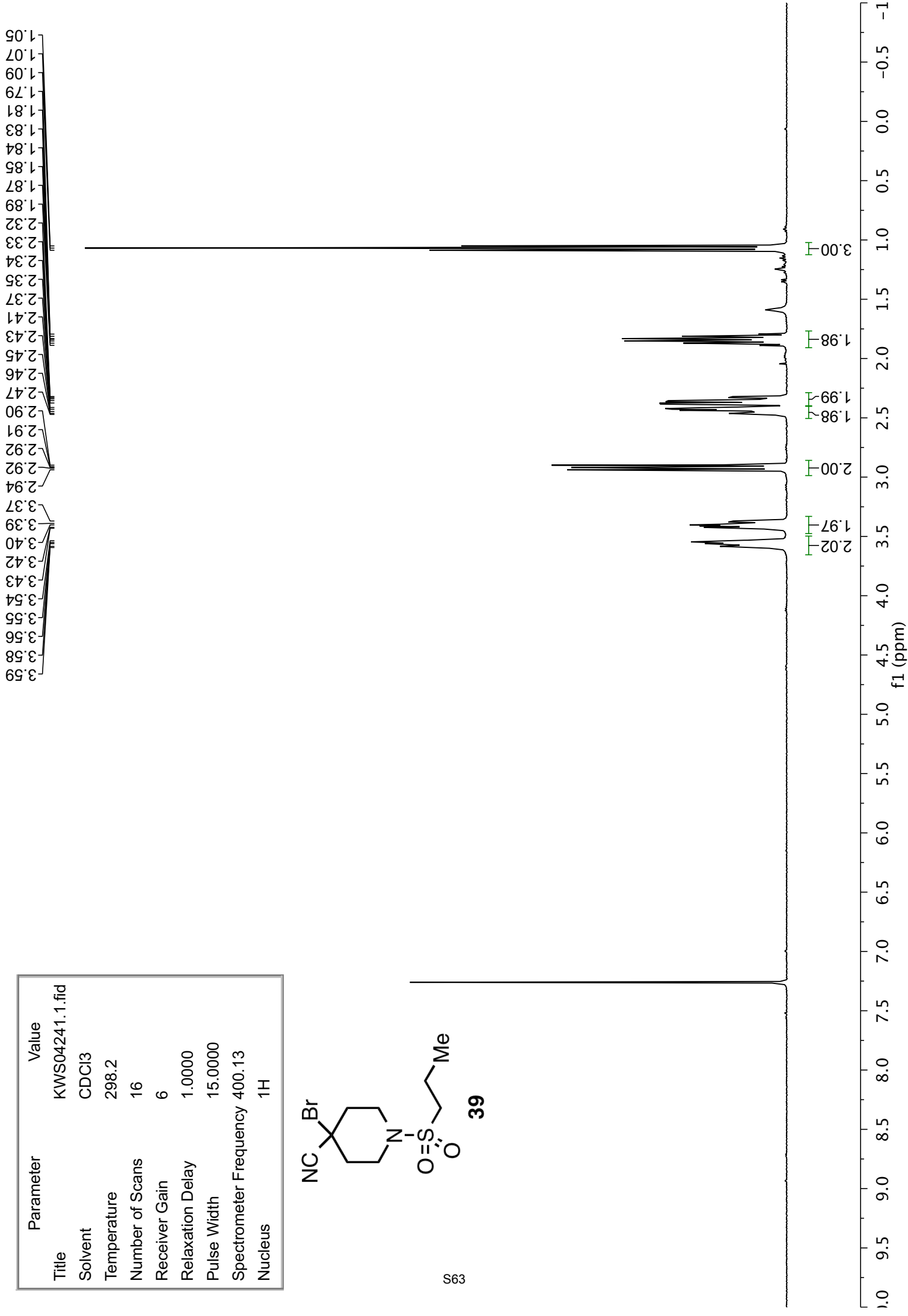
Parameter	Value
Title	KWS04237.2.fid
Solvent	CDCl3
Temperature	298.2
Number of Scans	1024
Receiver Gain	512
Relaxation Delay	2.0000
Pulse Width	9.2500
Spectrometer Frequency	100.62
Nucleus	13C



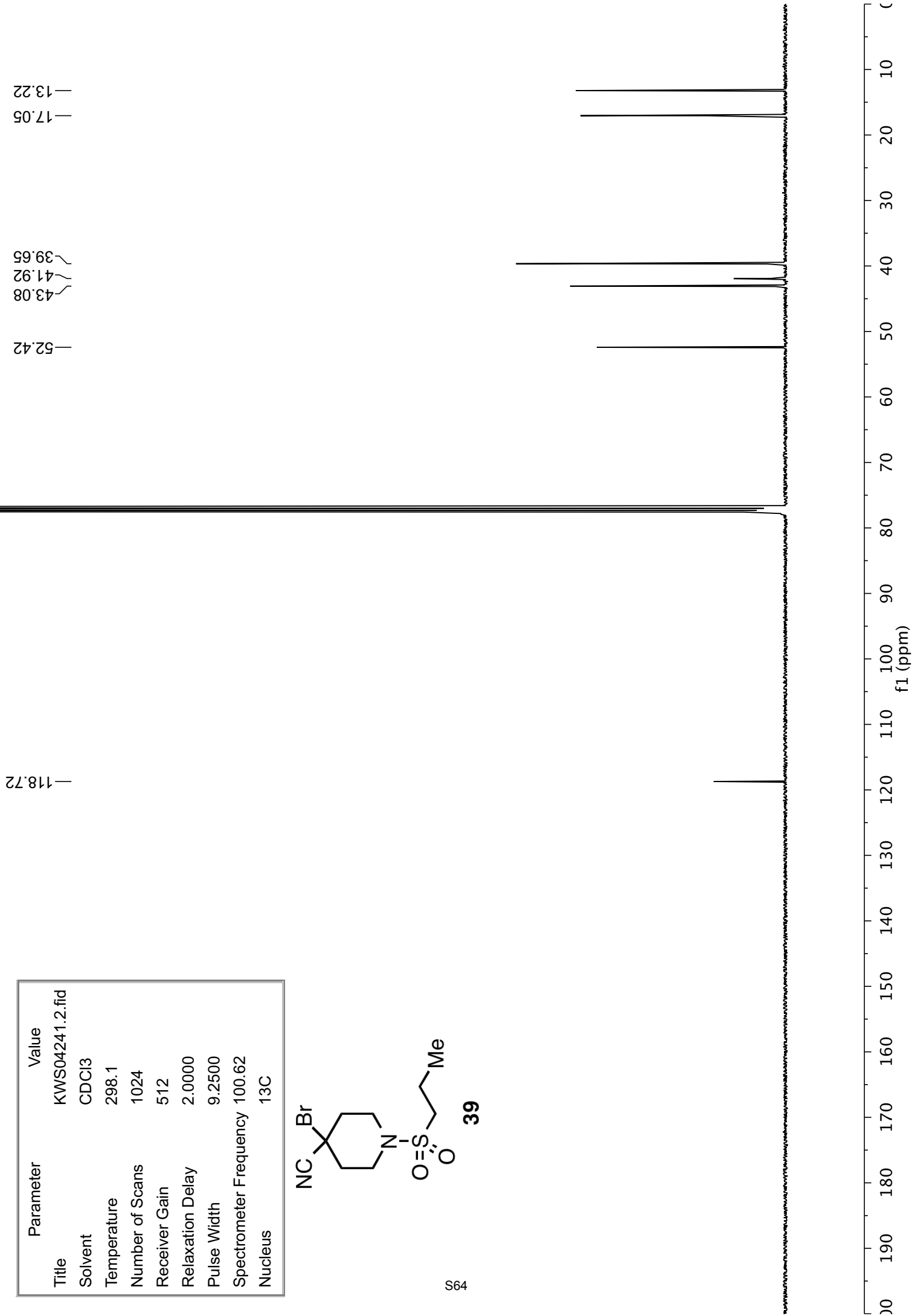
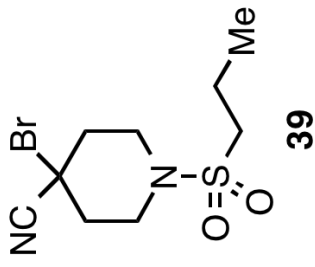
Parameter	Value
Title	KWS04241.1.fid
Solvent	CDCl3
Temperature	298.2
Number of Scans	16
Receiver Gain	6
Relaxation Delay	1.0000
Pulse Width	15.0000
Spectrometer Frequency	400.13
Nucleus	<sup>1</sup> H



863



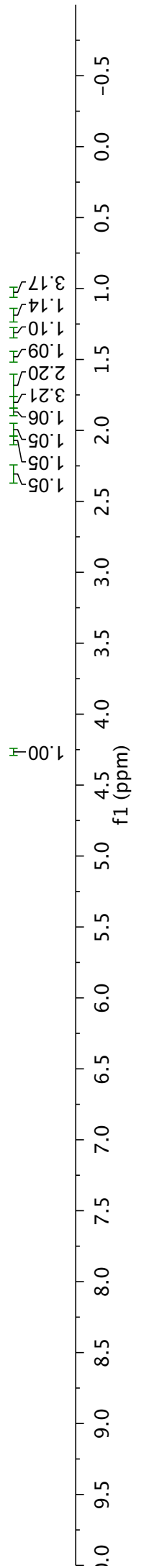
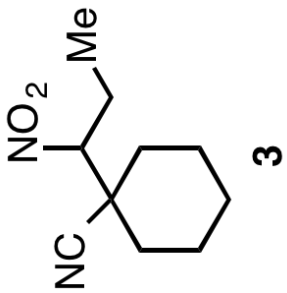
Parameter	Value
Title	KWS04241.2.fid
Solvent	CDCl <sub>3</sub>
Temperature	298.1
Number of Scans	1024
Receiver Gain	512
Relaxation Delay	2.0000
Pulse Width	9.2500
Spectrometer Frequency	100.62
Nucleus	<sup>13</sup> C



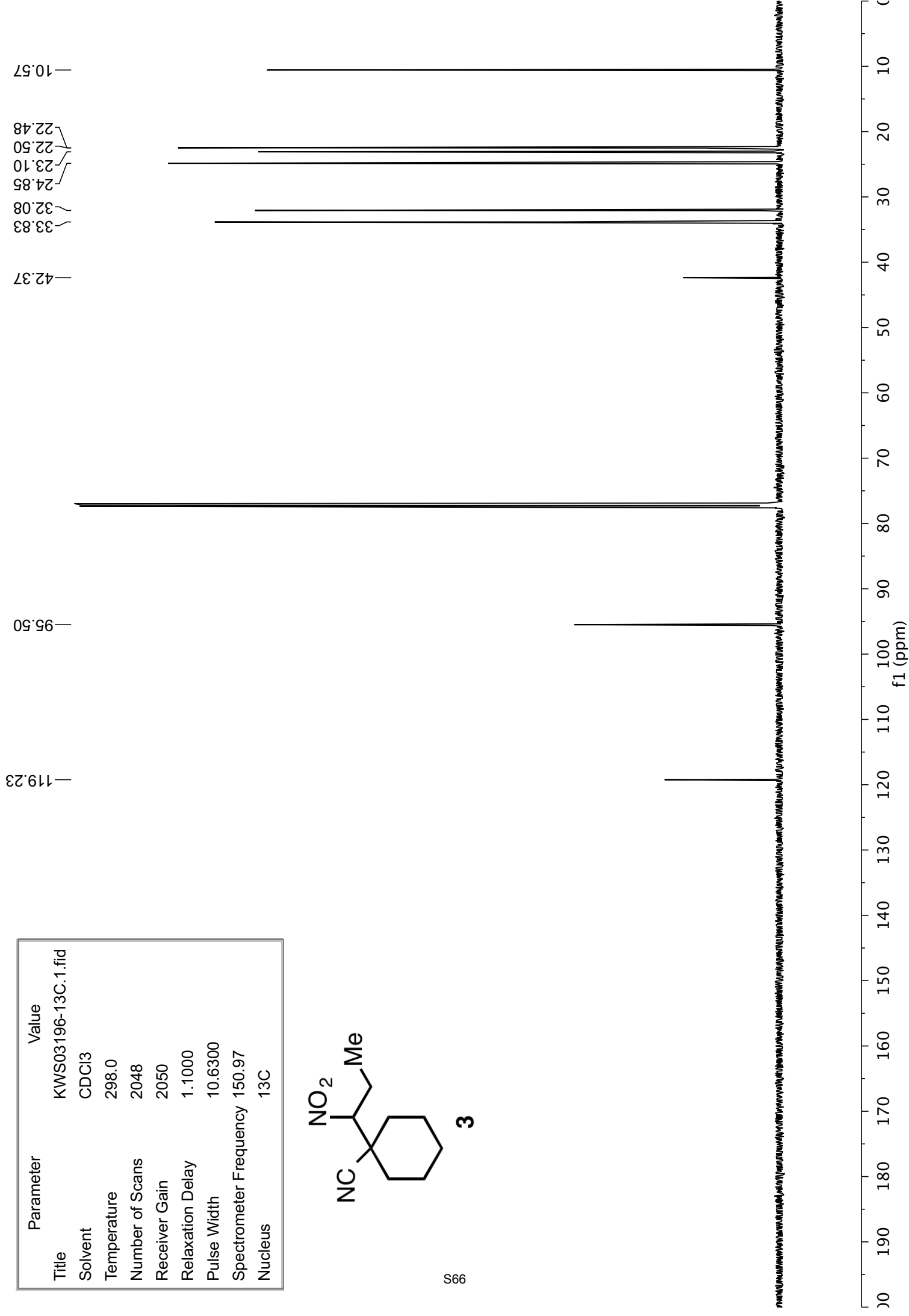
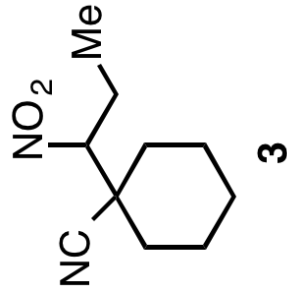


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4.27  
4.26  
4.25  
2.33  
2.32  
2.31  
2.31  
2.30  
2.30  
2.29  
2.28  
2.08  
2.08  
2.06  
2.06  
2.01  
2.01  
2.00  
1.99  
1.98  
1.98  
1.97  
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1.88  
1.88  
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1.85  
1.83  
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1.80  
1.79  
1.78  
1.77  
1.75  
1.73  
1.73  
1.72  
1.71  
1.70  
1.70  
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1.64  
1.64  
1.50  
1.50  
1.50  
1.48  
1.48  
1.46  
1.45  
1.33  
1.33  
1.31  
1.31  
1.29  
1.28  
1.20  
1.20  
1.19  
1.18  
1.18  
1.04  
1.03  
1.01

Parameter	Value
Title	KWS03196cf14-36.1.fid
Solvent	CDCl3
Temperature	298.0
Number of Scans	8
Receiver Gain	256
Relaxation Delay	1.0000
Pulse Width	10.7700
Spectrometer Frequency	600.32
Nucleus	1H

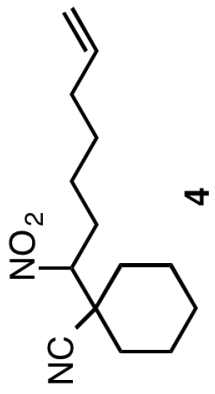


Parameter	Value
Title	KWS03196-13C.1.fid
Solvent	CDCl3
Temperature	298.0
Number of Scans	2048
Receiver Gain	2050
Relaxation Delay	1.1000
Pulse Width	10.6300
Spectrometer Frequency	150.97
Nucleus	13C

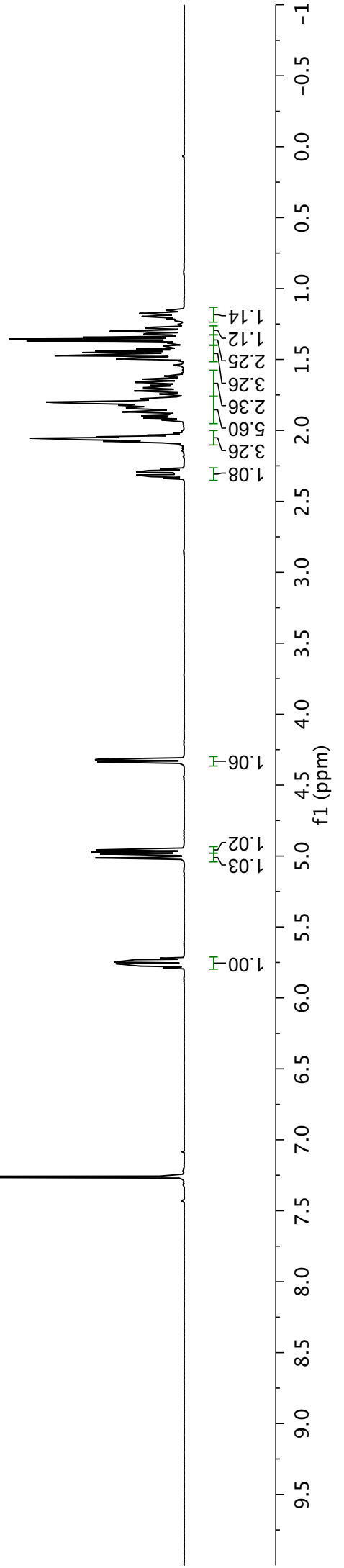


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1.32  
1.34  
1.36  
1.37  
1.38  
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2.04  
2.06  
2.07  
2.08  
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2.29  
2.30  
2.31  
2.31  
2.33  
4.32  
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4.34  
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5.76  
5.78

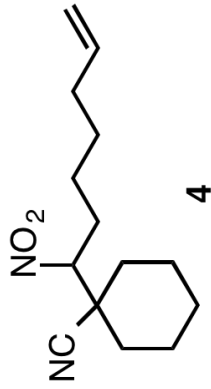
Parameter	Value
Title	KWS04011B.1.fid
Solvent	CDCl3
Temperature	298.0
Number of Scans	16
Receiver Gain	144
Relaxation Delay	1.0000
Pulse Width	10.7700
Spectrometer Frequency	600.32
Nucleus	<sup>1</sup> H

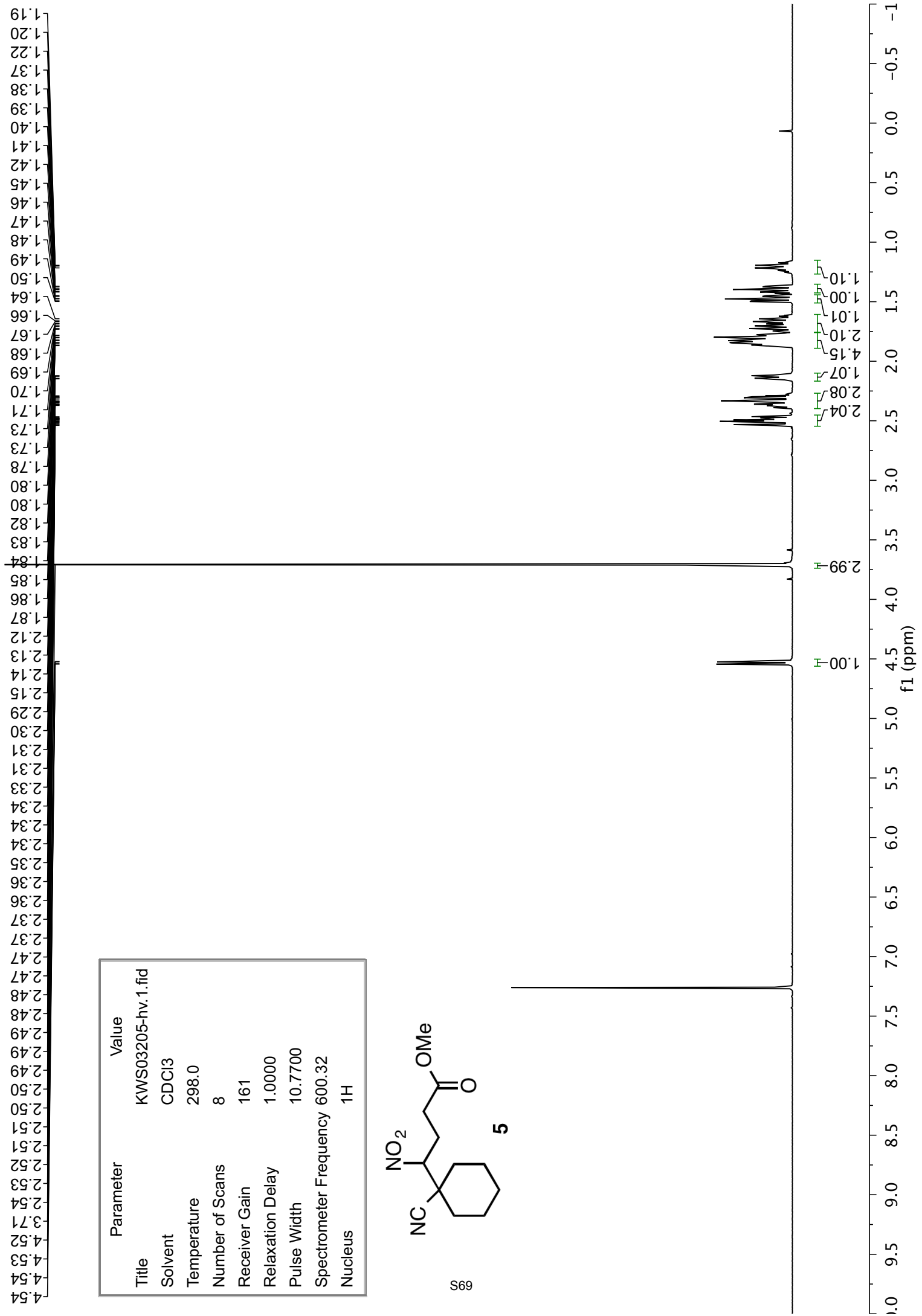


799

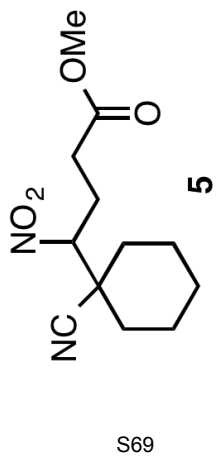


Parameter	Value
Title	KWS04011-C13.1.fid
Solvent	CDCl <sub>3</sub>
Temperature	298.0
Number of Scans	2048
Receiver Gain	2050
Relaxation Delay	1.1000
Pulse Width	10.6300
Spectrometer Frequency	150.97
Nucleus	<sup>13</sup> C

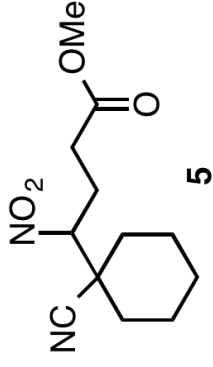




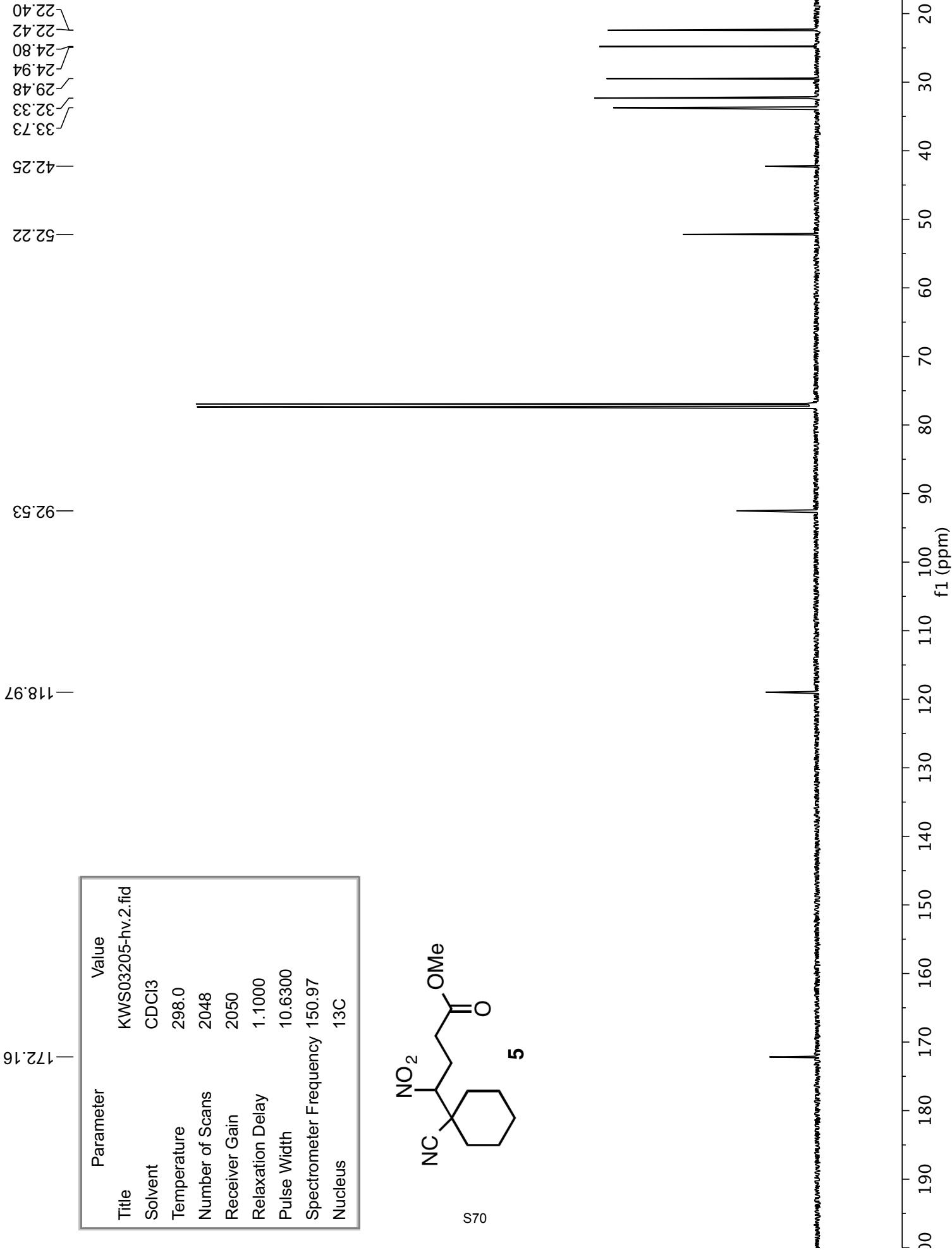
Parameter	Value
Title	KWS03205-hv.1.fid
Solvent	CDCl3
Temperature	298.0
Number of Scans	8
Receiver Gain	161
Relaxation Delay	1.0000
Pulse Width	10.7700
Spectrometer Frequency	600.32
Nucleus	<sup>1</sup> H



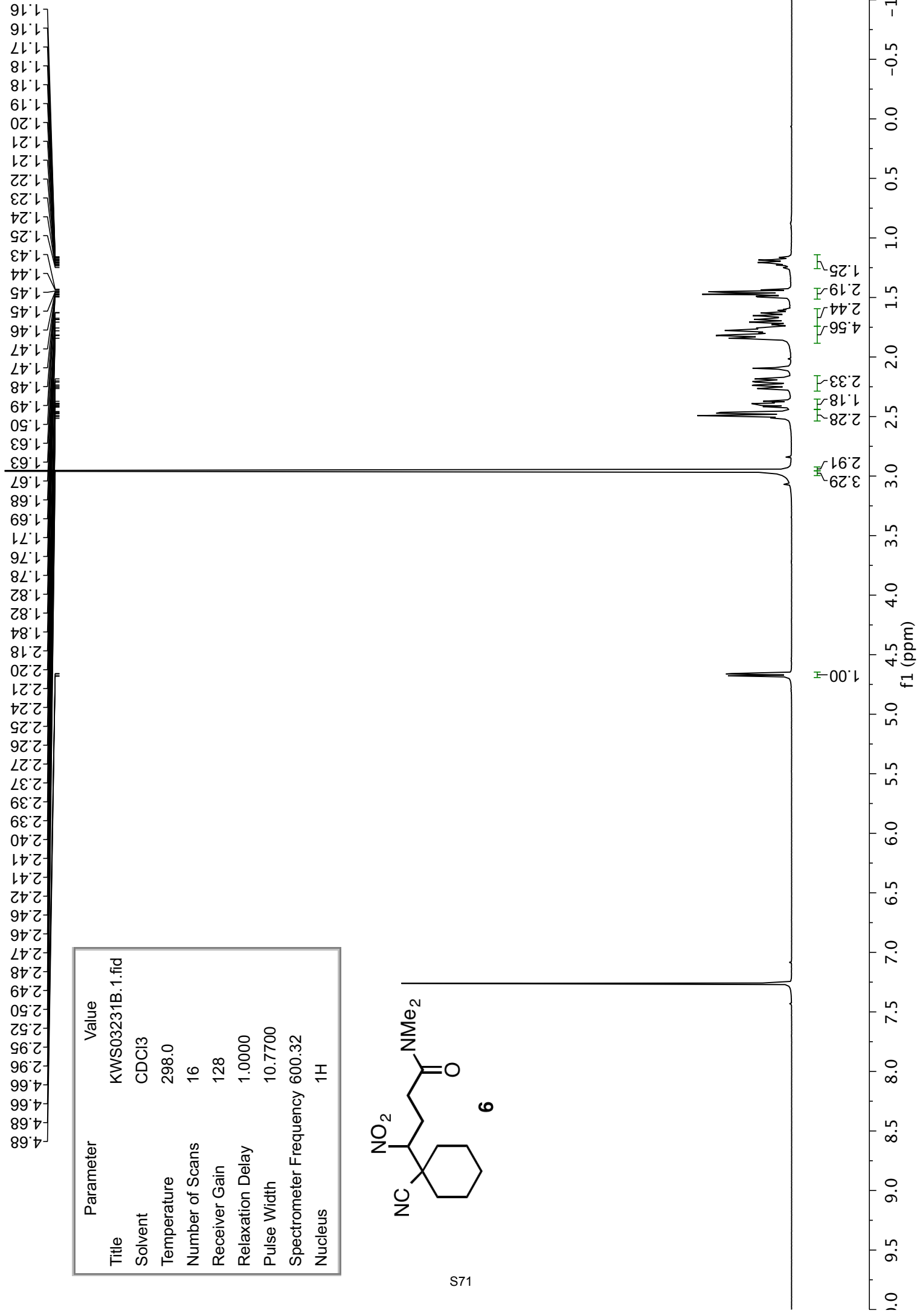
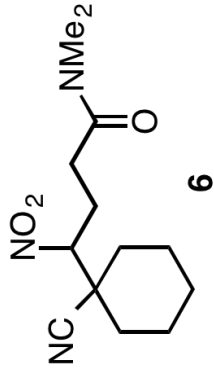
Parameter	Value
Title	KWS03205-hv.2.fid
Solvent	CDCl3
Temperature	298.0
Number of Scans	2048
Receiver Gain	2050
Relaxation Delay	1.1000
Pulse Width	10.6300
Spectrometer Frequency	150.97
Nucleus	<sup>13</sup> C



05



Parameter	Value
Title	KWS03231B.1.fid
Solvent	CDCl3
Temperature	298.0
Number of Scans	16
Receiver Gain	128
Relaxation Delay	1.0000
Pulse Width	10.7700
Spectrometer Frequency	600.32
Nucleus	<sup>1</sup> H



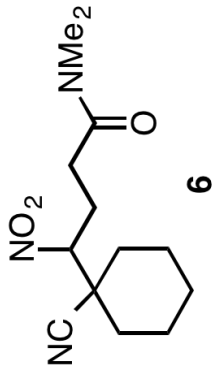
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35.67  
33.71  
32.62  
28.27  
25.25  
24.86  
22.43  
22.38

93.01

119.27

170.39

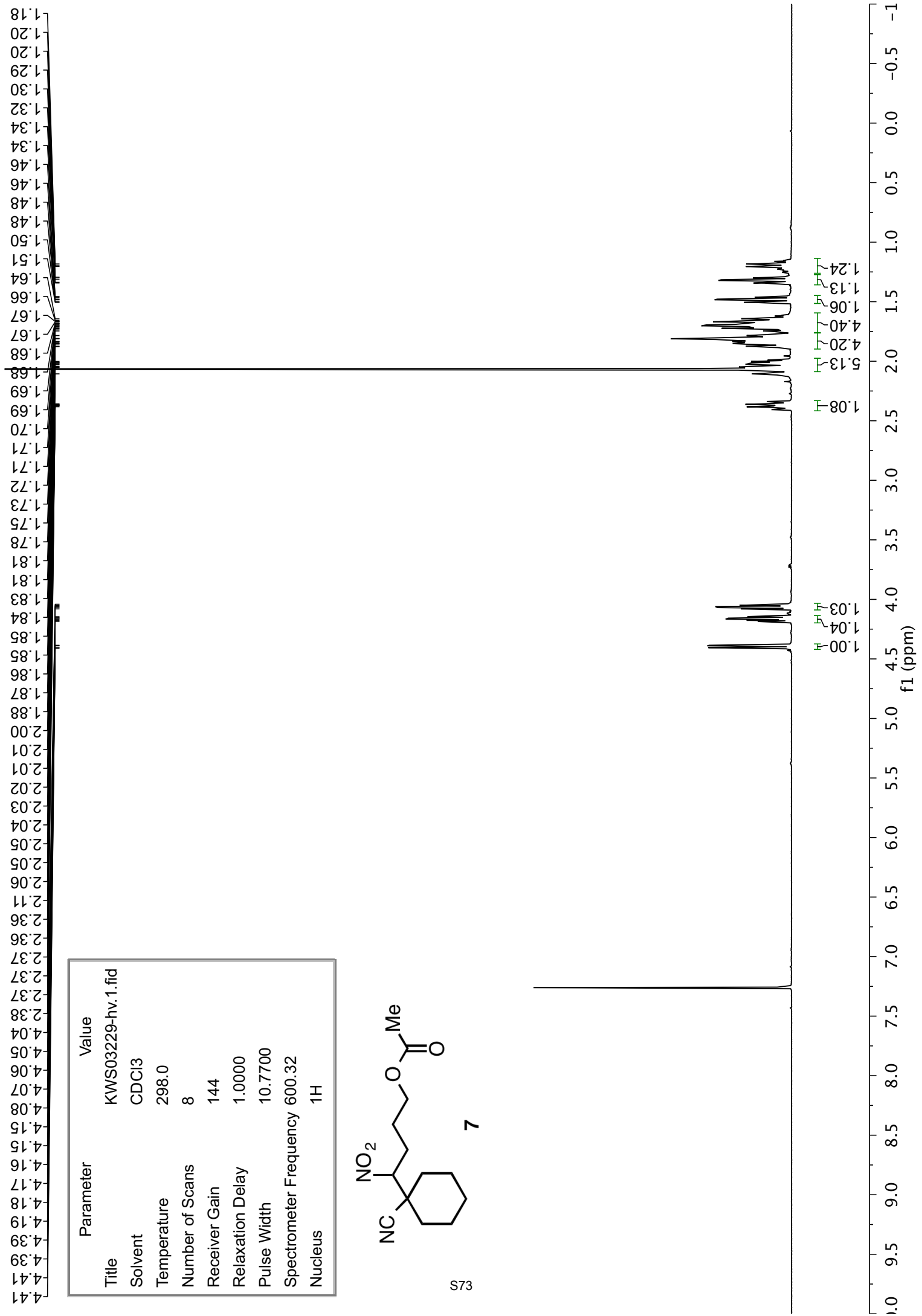
Parameter	Value
Title	KWS03231-13C.1.fid
Solvent	CDCl <sub>3</sub>
Temperature	298.0
Number of Scans	2048
Receiver Gain	2050
Relaxation Delay	1.1000
Pulse Width	10.6300
Spectrometer Frequency	150.97
Nucleus	<sup>13</sup> C



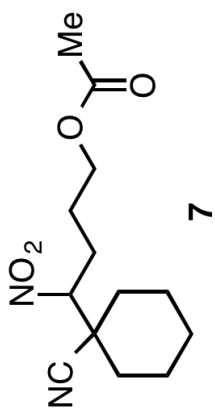
S72



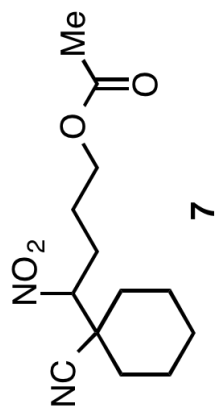




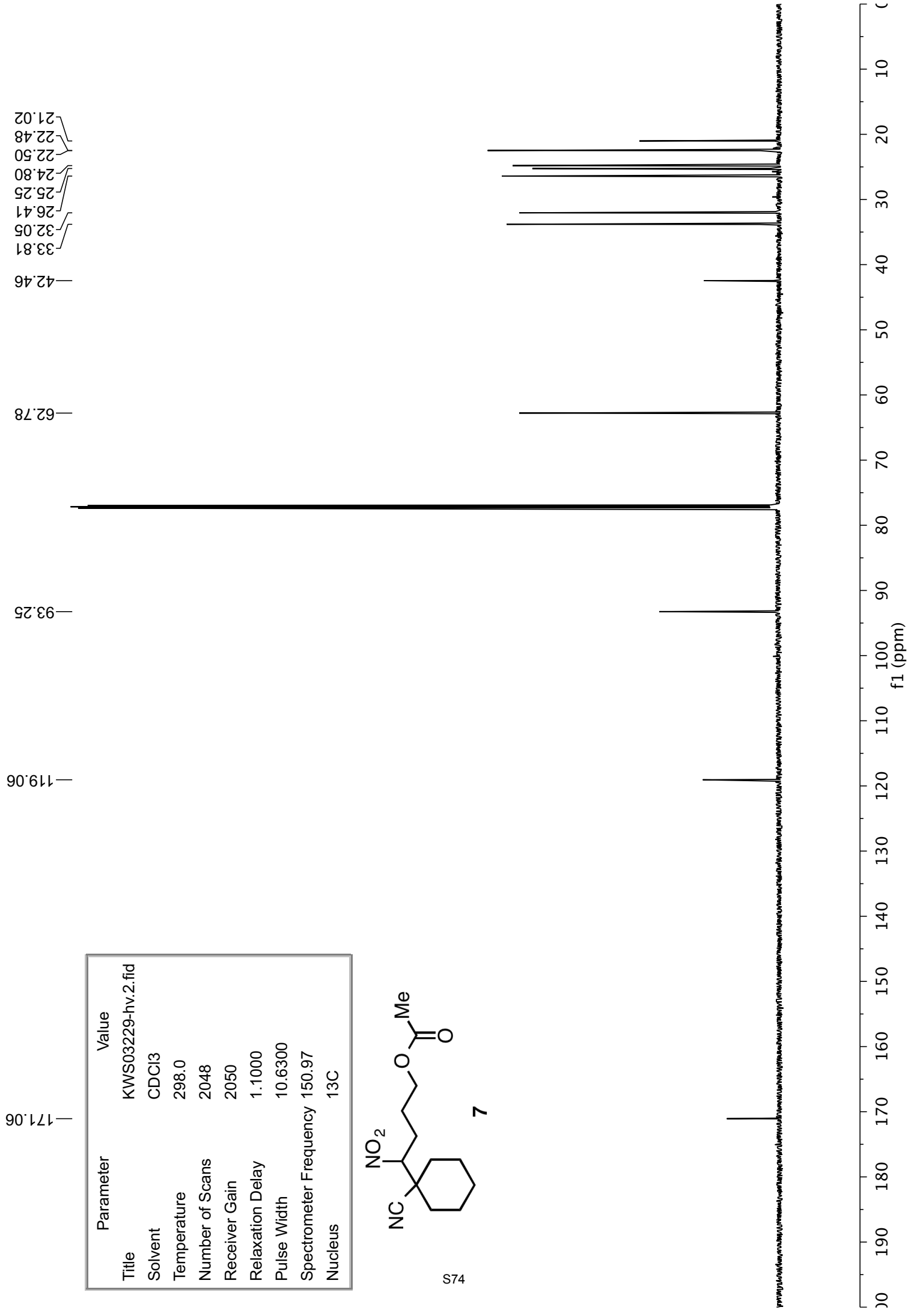
Parameter	Value
Title	KWS03229-hv.1.fid
Solvent	CDCl3
Temperature	298.0
Number of Scans	8
Receiver Gain	144
Relaxation Delay	1.0000
Pulse Width	10.7700
Spectrometer Frequency	600.32
Nucleus	<sup>1</sup> H



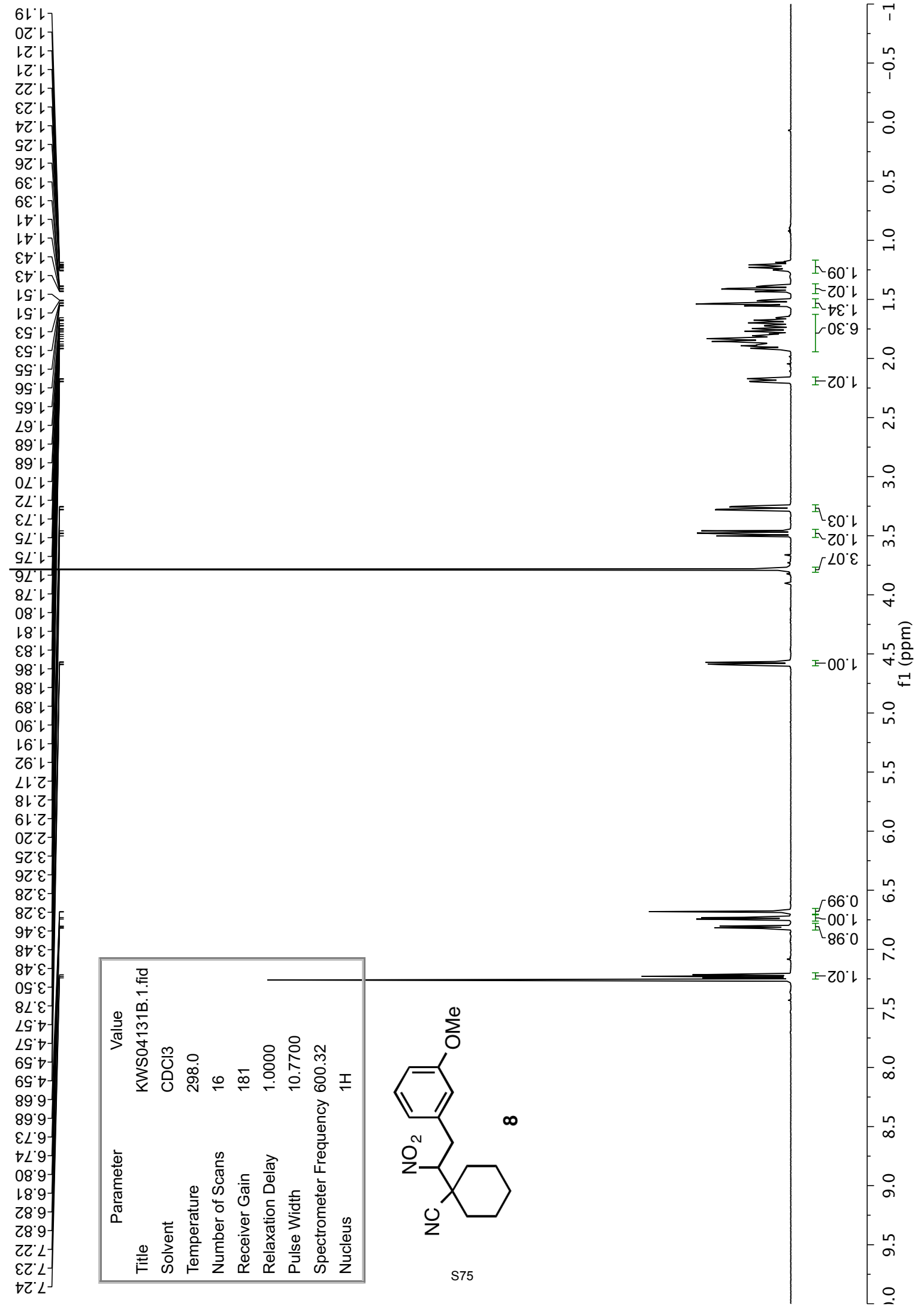
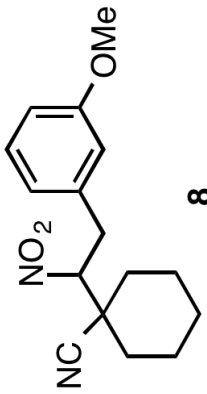
Parameter	Value
Title	KWS03229-hv.2.fid
Solvent	CDCl3
Temperature	298.0
Number of Scans	2048
Receiver Gain	2050
Relaxation Delay	1.1000
Pulse Width	10.6300
Spectrometer Frequency	150.97
Nucleus	<sup>13</sup> C



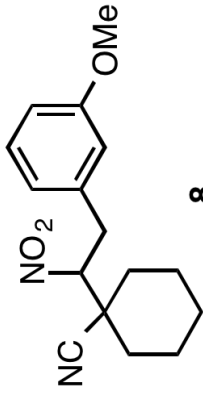
S74



Parameter	Value
Title	KWS04131B.1.fid
Solvent	CDCl3
Temperature	298.0
Number of Scans	16
Receiver Gain	181
Relaxation Delay	1.0000
Pulse Width	10.7700
Spectrometer Frequency	600.32
Nucleus	<sup>1</sup> H

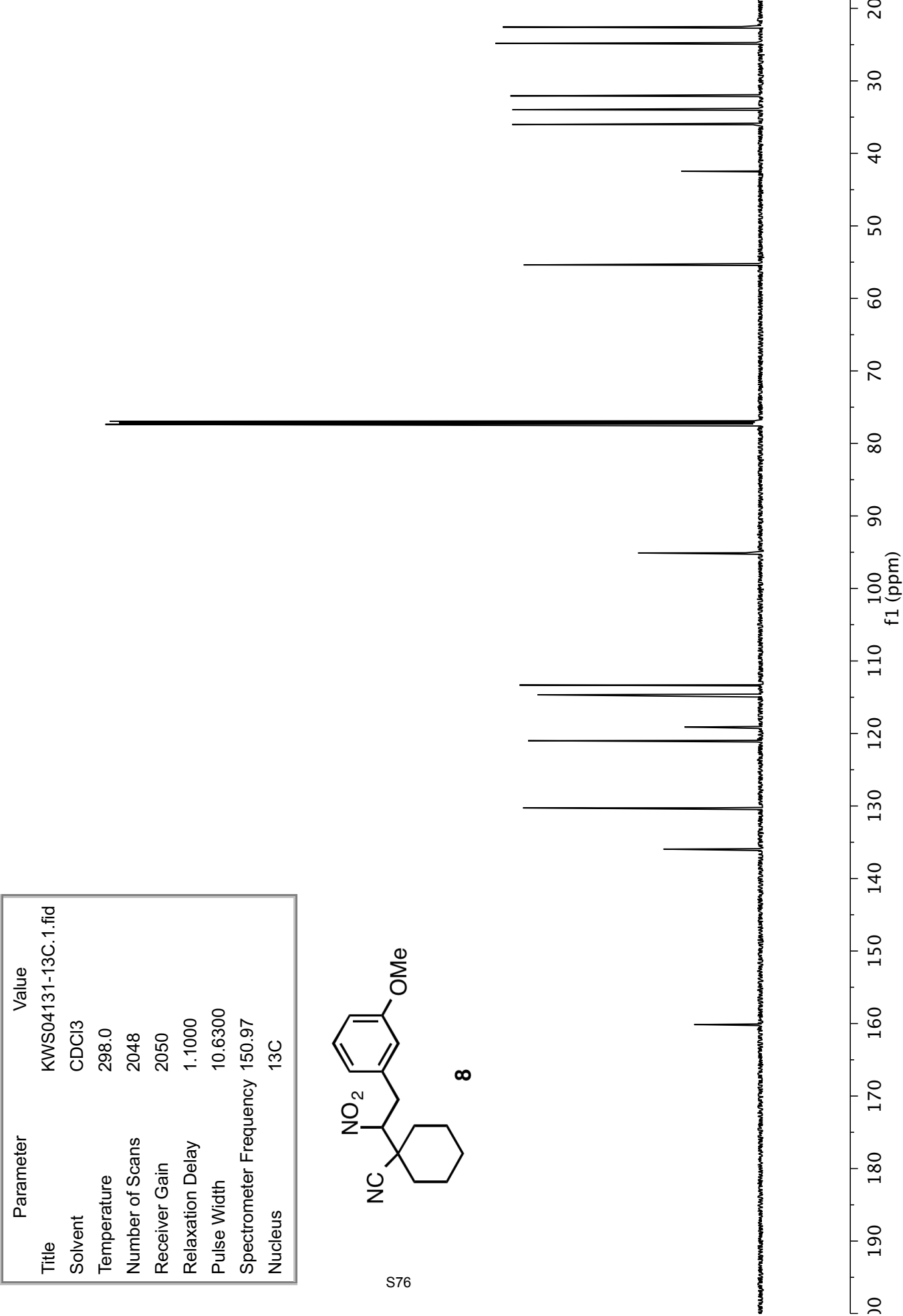


Parameter	Value
Title	KWS04131-13C.1.fid
Solvent	CDCl3
Temperature	298.0
Number of Scans	2048
Receiver Gain	2050
Relaxation Delay	1.1000
Pulse Width	10.6300
Spectrometer Frequency	150.97
Nucleus	<sup>13</sup> C

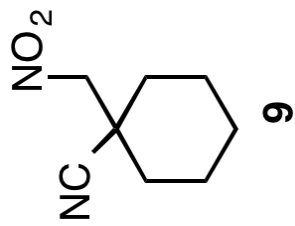


8

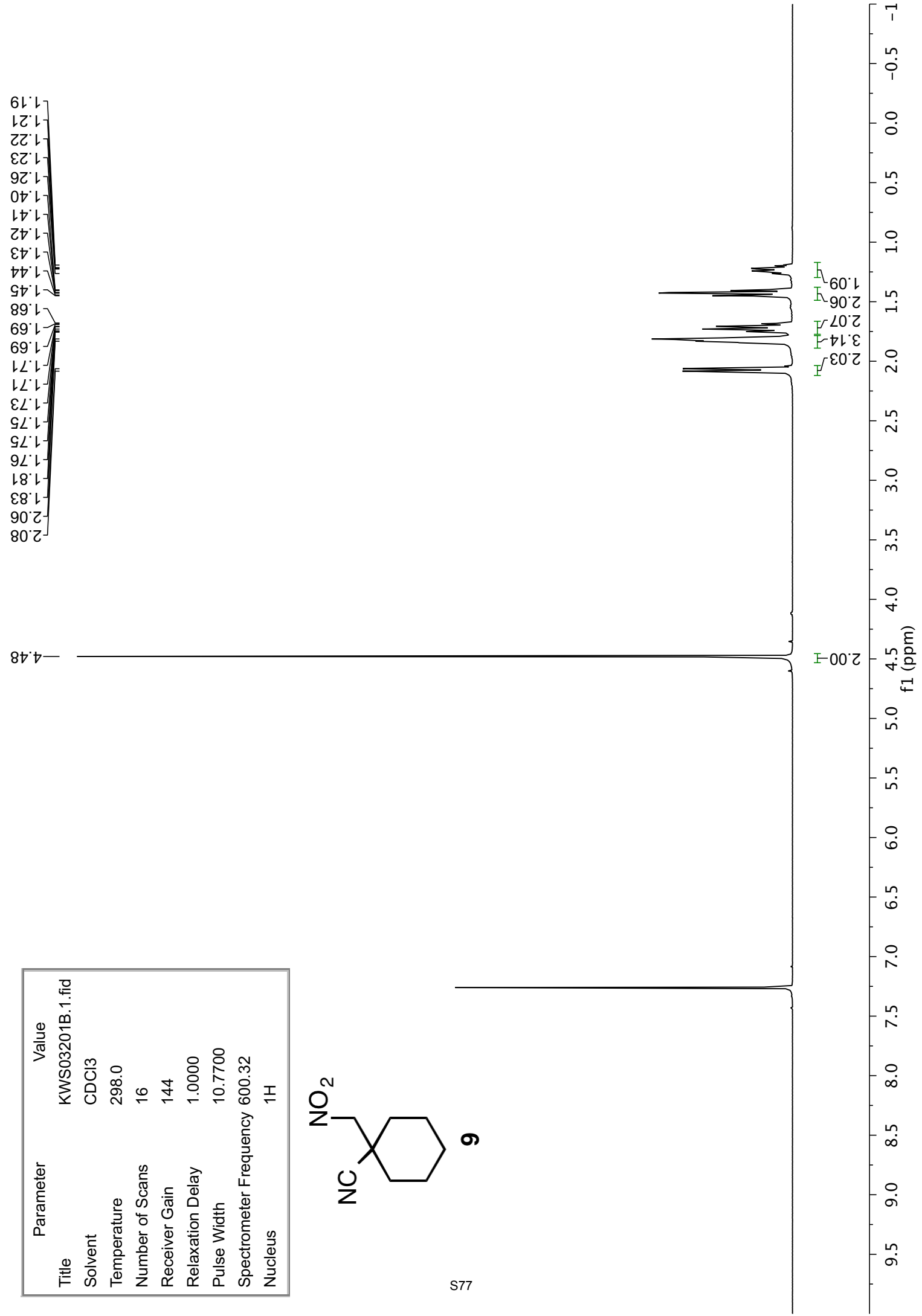
95



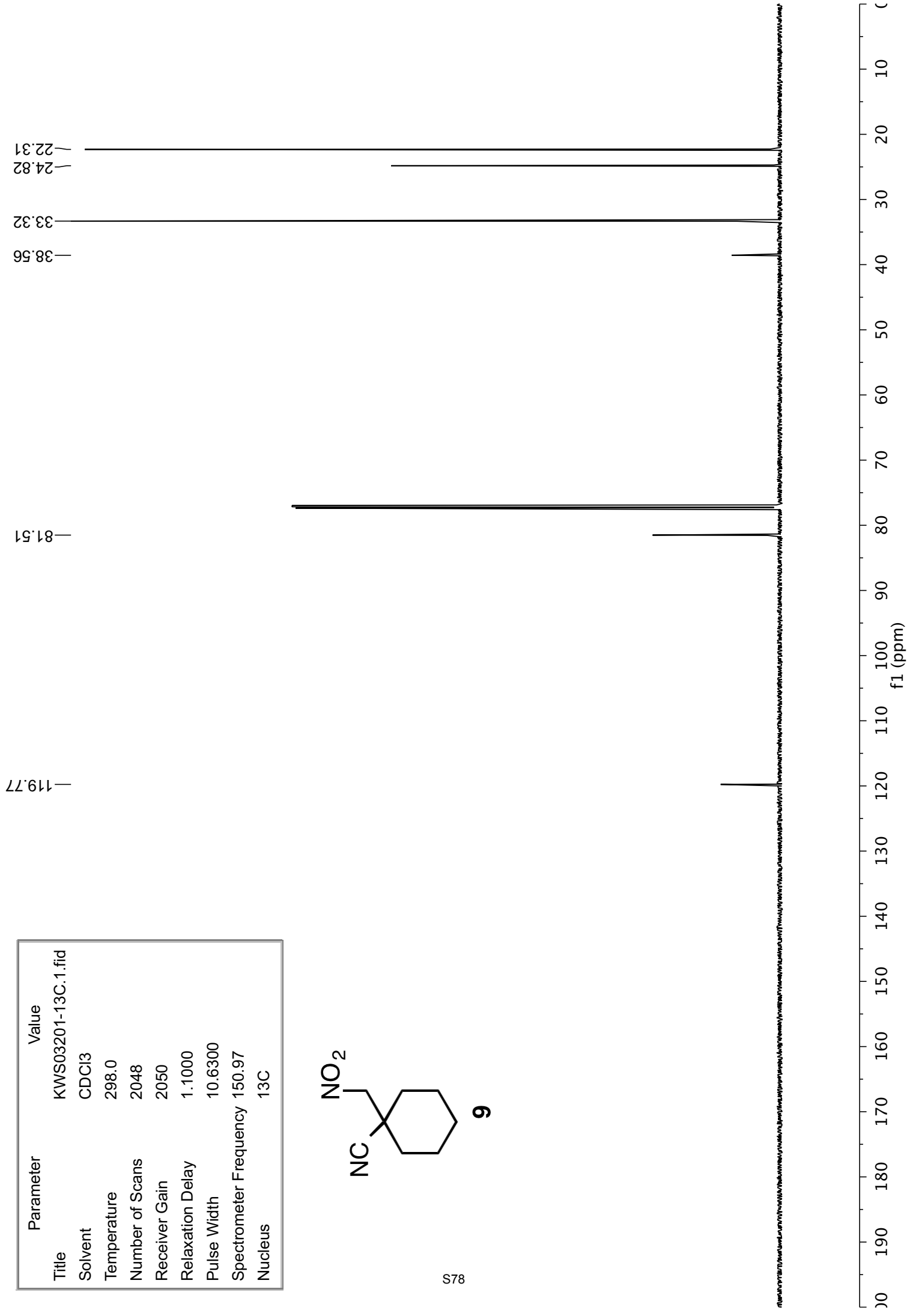
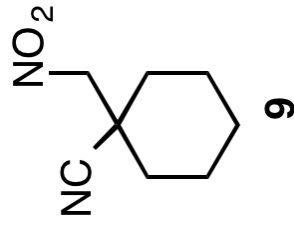
Parameter	Value
Title	KWS03201B.1.fid
Solvent	CDCl3
Temperature	298.0
Number of Scans	16
Receiver Gain	144
Relaxation Delay	1.0000
Pulse Width	10.7700
Spectrometer Frequency	600.32
Nucleus	<sup>1</sup> H



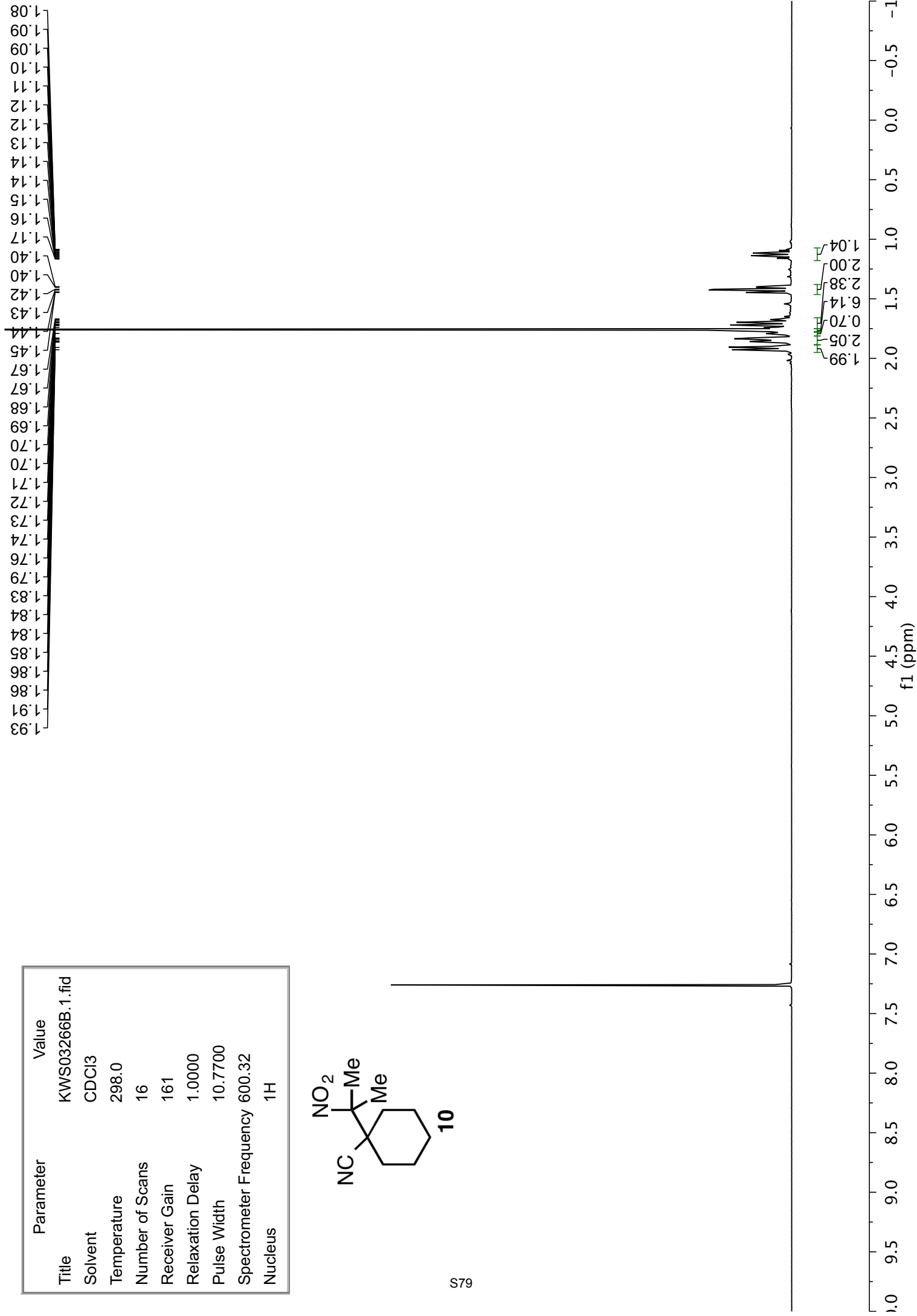
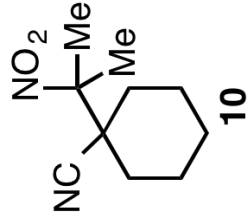
S77



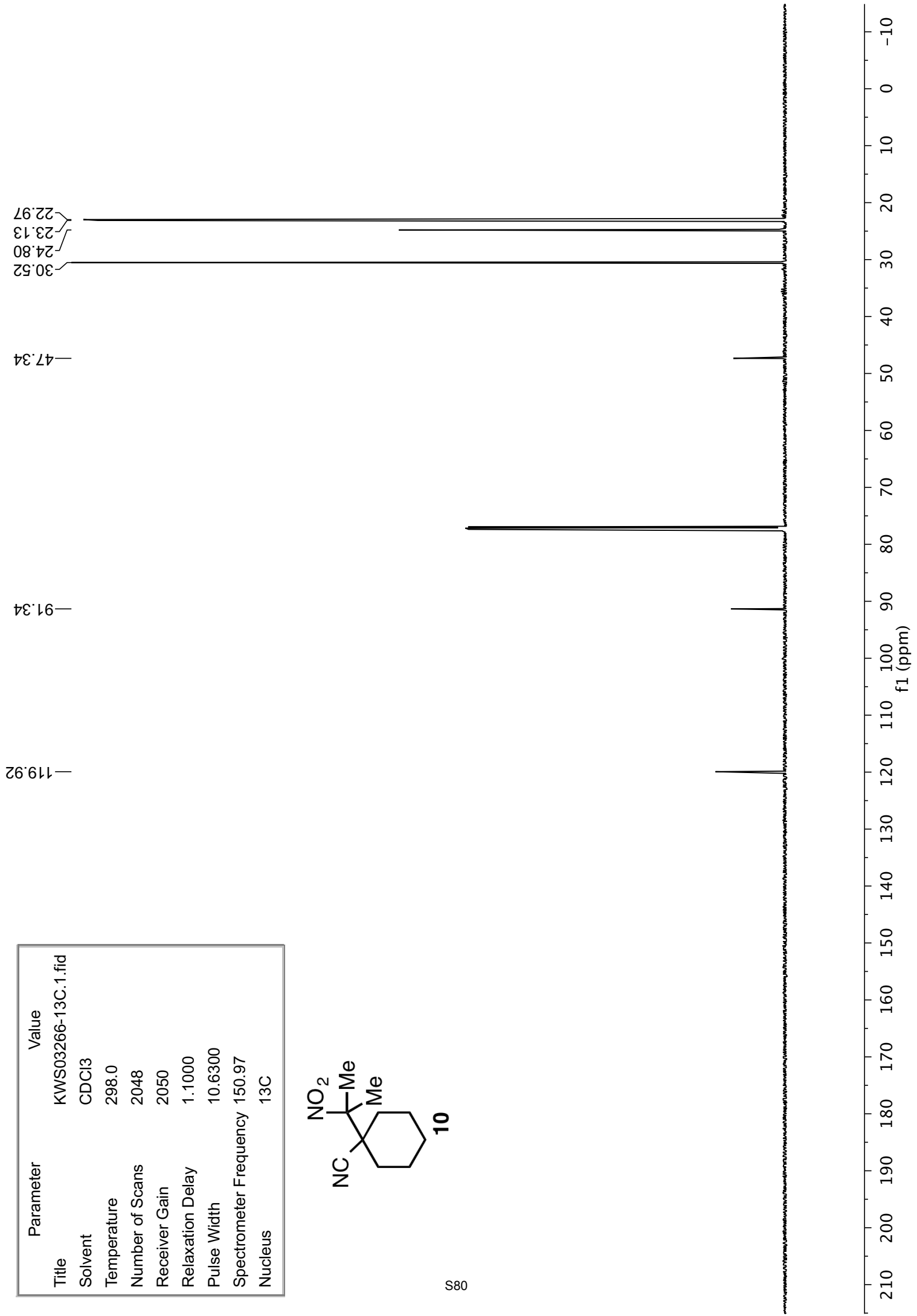
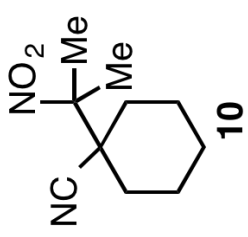
Parameter	Value
Title	KWS03201-13C.1.fid
Solvent	CDCl3
Temperature	298.0
Number of Scans	2048
Receiver Gain	2050
Relaxation Delay	1.1000
Pulse Width	10.6300
Spectrometer Frequency	150.97
Nucleus	13C



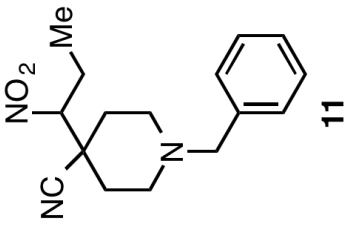
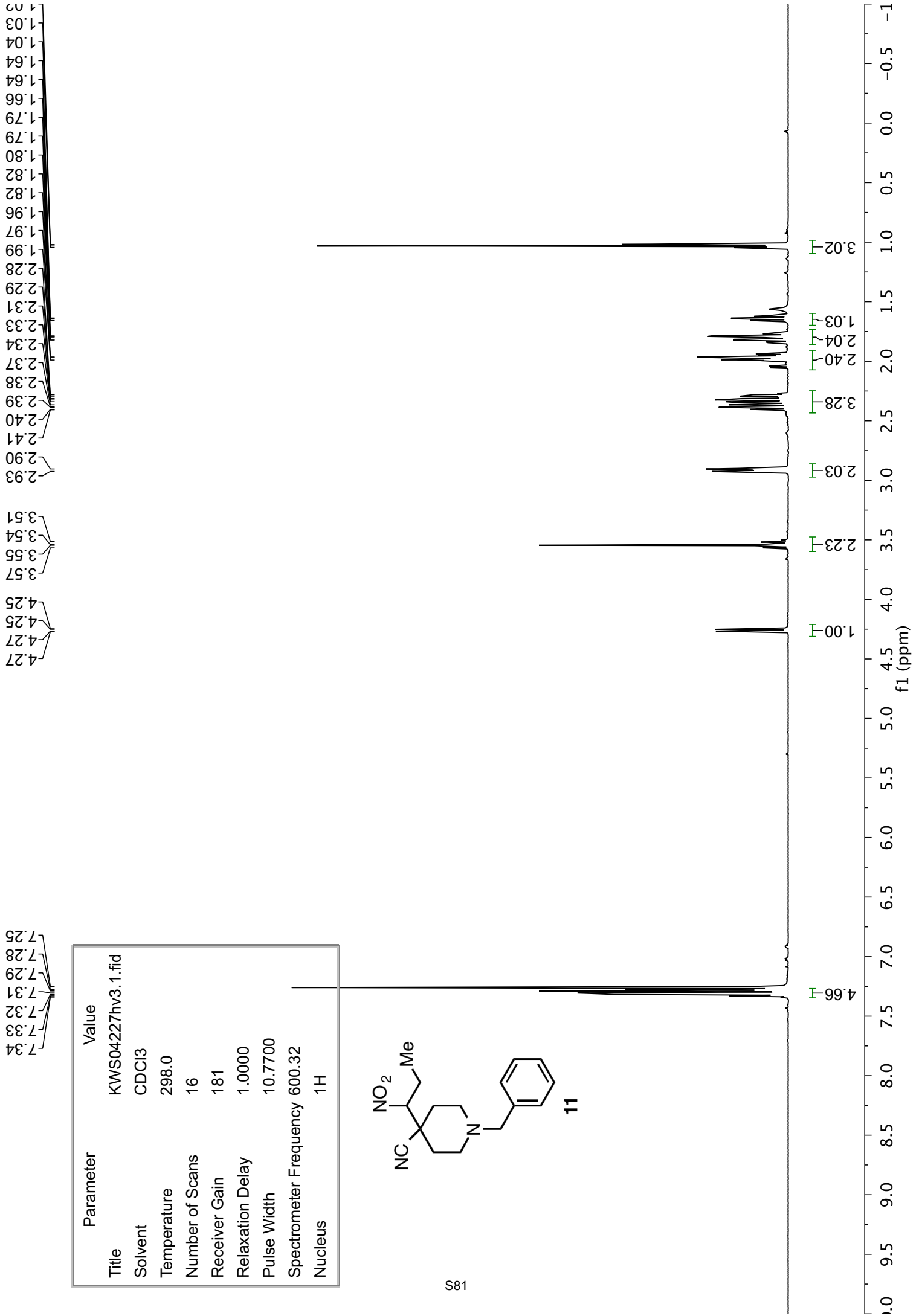
Parameter	Value
Title	KWS03266B.1.fid
Solvent	CDCl <sub>3</sub>
Temperature	298.0
Number of Scans	16
Receiver Gain	161
Relaxation Delay	1.0000
Pulse Width	10.7700
Spectrometer Frequency	600.32
Nucleus	<sup>1</sup> H



Parameter	Value
Title	KWS03266-13C.1.fid
Solvent	CDCl3
Temperature	298.0
Number of Scans	2048
Receiver Gain	2050
Relaxation Delay	1.1000
Pulse Width	10.6300
Spectrometer Frequency	150.97
Nucleus	13C





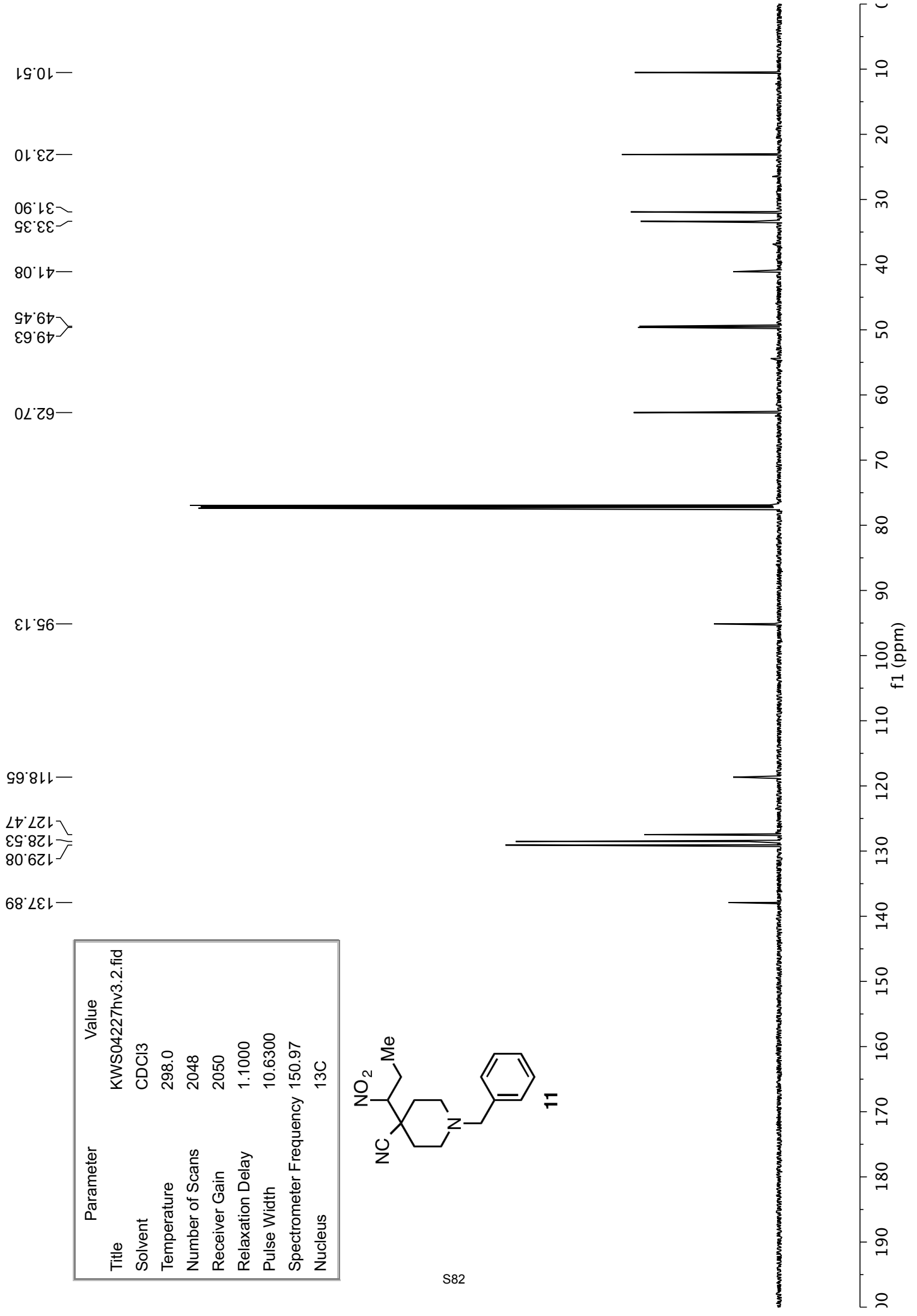
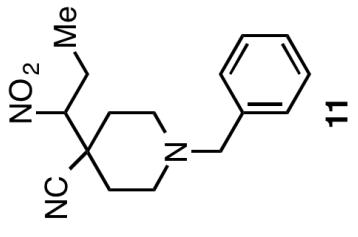


Parameter	Value
Title	KWS04227hv3.1.fid
Solvent	CDCl3
Temperature	298.0
Number of Scans	16
Receiver Gain	181
Relaxation Delay	1.0000
Pulse Width	10.7700
Spectrometer Frequency	600.32
Nucleus	1H

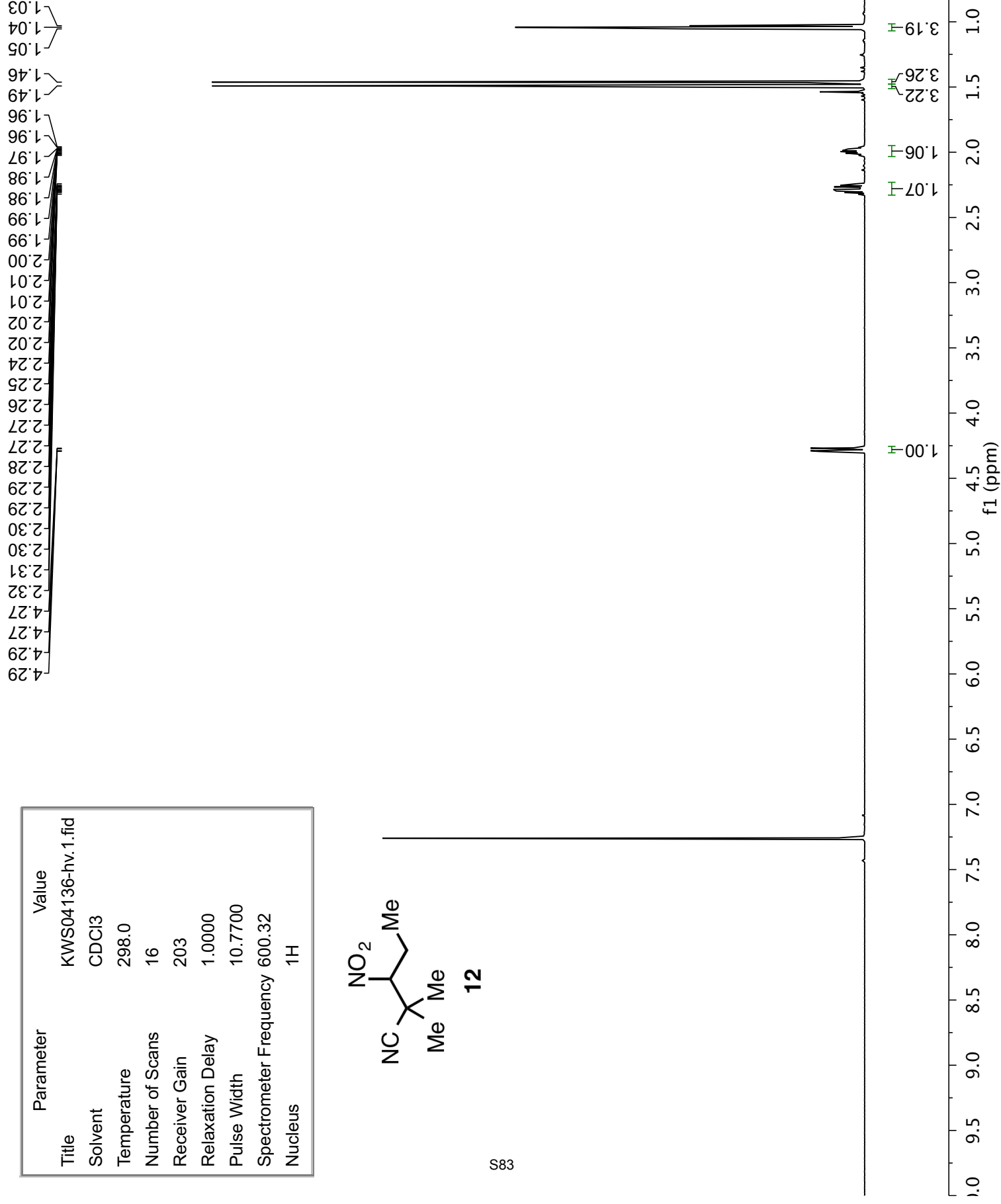
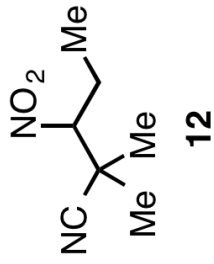
7.34  
7.33  
7.32  
7.31  
7.29  
7.28  
7.25

4.27  
4.27  
4.25  
3.57  
3.57  
3.55  
3.54  
3.51  
2.93  
2.90  
2.41  
2.40  
2.39  
2.38  
2.37  
2.34  
2.33  
2.31  
2.29  
2.28  
1.99  
1.97  
1.96  
1.82  
1.82  
1.80  
1.79  
1.79  
1.66  
1.64  
1.64  
1.04  
1.03

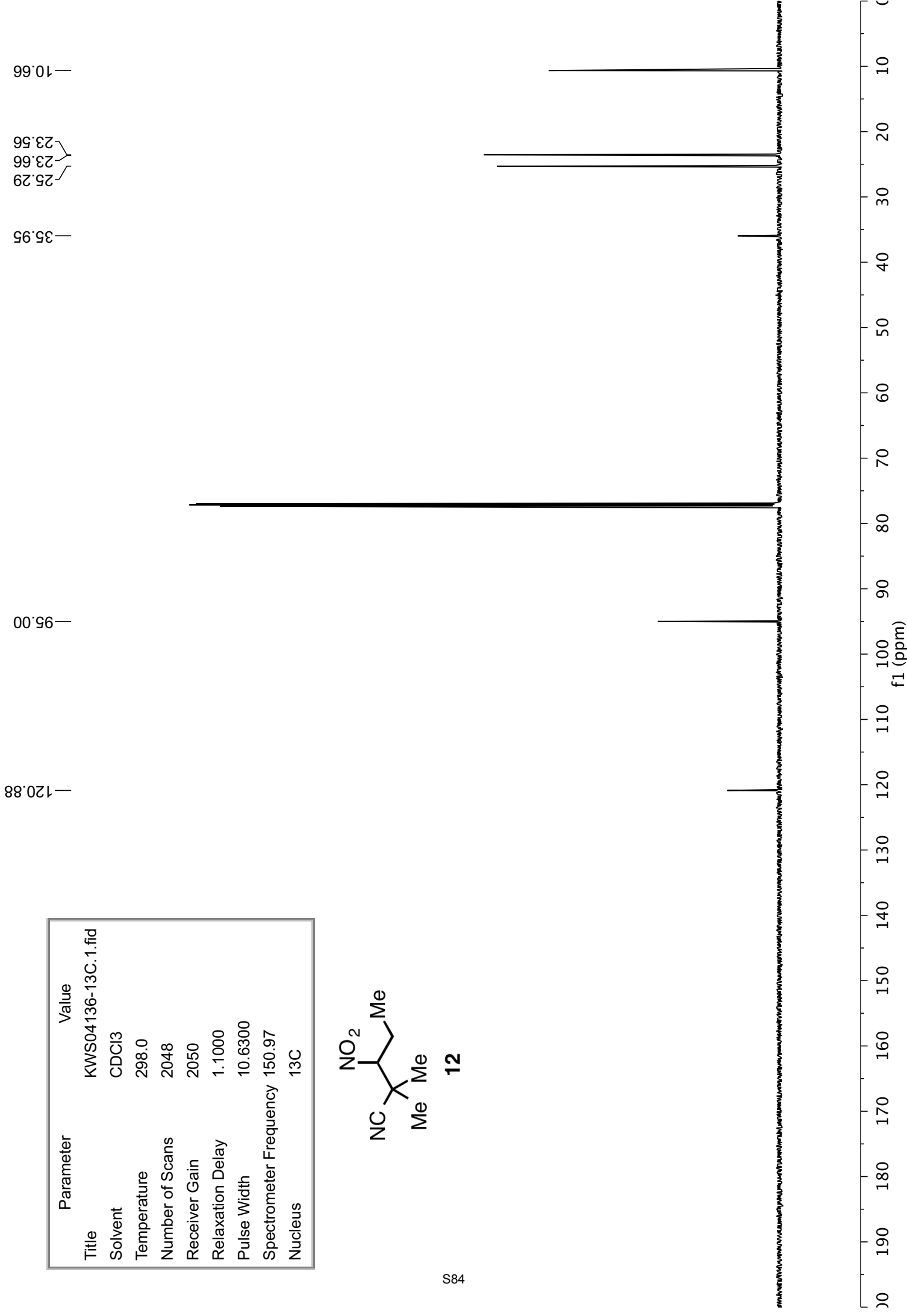
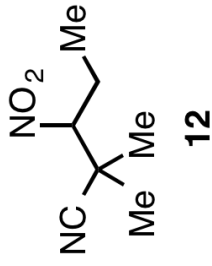
Parameter	Value
Title	KWS04227hv3.2.fid
Solvent	CDCl3
Temperature	298.0
Number of Scans	2048
Receiver Gain	2050
Relaxation Delay	1.1000
Pulse Width	10.6300
Spectrometer F Frequency	150.97
Nucleus	<sup>13</sup> C



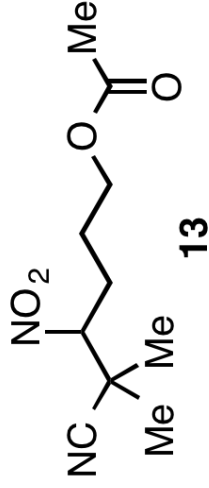
Parameter	Value
Title	KWS04136-hv.1.fid
Solvent	CDCl3
Temperature	298.0
Number of Scans	16
Receiver Gain	203
Relaxation Delay	1.0000
Pulse Width	10.7700
Spectrometer Frequency	600.32
Nucleus	<sup>1</sup> H



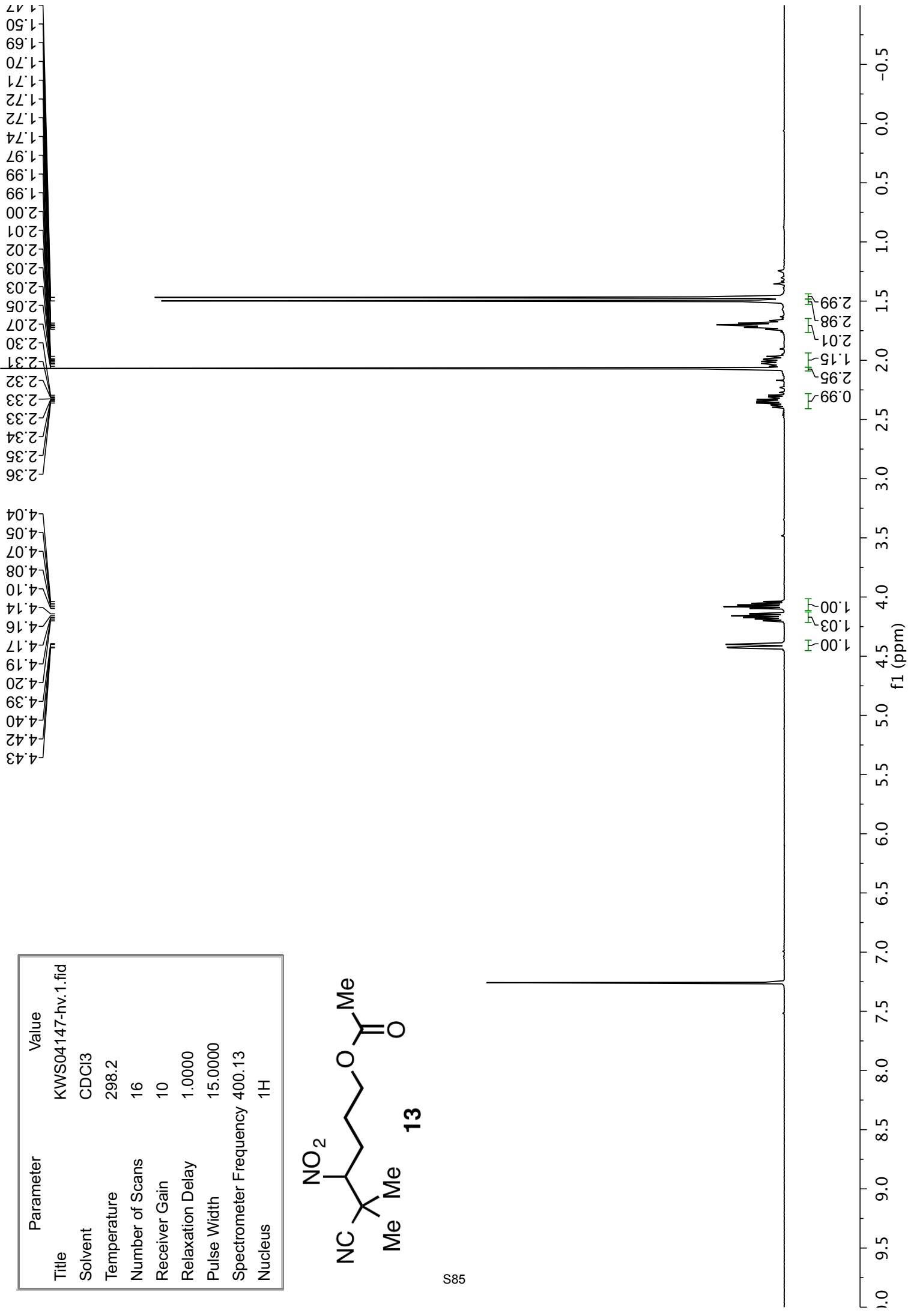
Parameter	Value
Title	KWS04136-13C.1.fid
Solvent	CDCl3
Temperature	298.0
Number of Scans	2048
Receiver Gain	2050
Relaxation Delay	1.1000
Pulse Width	10.6300
Spectrometer Frequency	150.97
Nucleus	13C



Parameter	Value
Title	KWS04147-hv.1.fid
Solvent	CDCl3
Temperature	298.2
Number of Scans	16
Receiver Gain	10
Relaxation Delay	1.0000
Pulse Width	15.0000
Spectrometer Frequency	400.13
Nucleus	<sup>1</sup> H

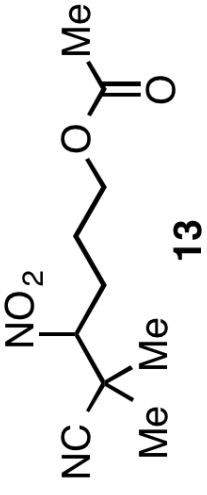


885

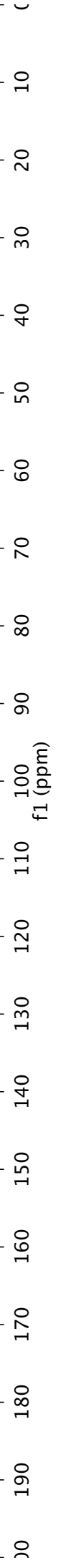


-171.02  
 -120.68  
 -92.74  
 -62.70  
 -36.02  
 26.92  
 25.30  
 25.24  
 23.51  
 20.99

Parameter	Value
Title	KWS04147-13C.1.fid
Solvent	CDCl3
Temperature	298.0
Number of Scans	2048
Receiver Gain	2050
Relaxation Delay	1.1000
Pulse Width	10.6300
Spectrometer Frequency	150.97
Nucleus	13C



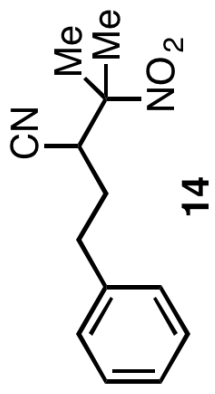
98



3.32  
3.30  
3.30  
3.32  
3.30  
3.30  
3.03  
3.03  
3.02  
3.01  
3.00  
3.00  
2.75  
2.74  
2.73  
2.73  
2.72  
2.70  
1.98  
1.97  
1.97  
1.96  
1.95  
1.95  
1.94  
1.94  
1.93  
1.92  
1.92  
1.75  
1.74  
1.73  
1.72  
1.72  
1.71  
1.70

7.34  
7.33  
7.32  
7.27  
7.25  
7.24  
7.19  
7.18

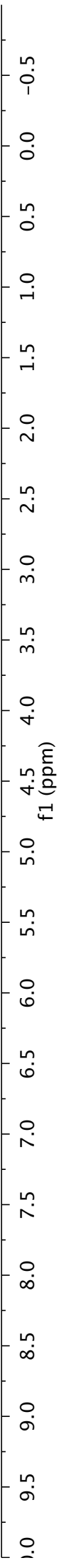
Parameter	Value
Title	KWS03245-hv.1.fid
Solvent	CDCl3
Temperature	298.0
Number of Scans	8
Receiver Gain	228
Relaxation Delay	1.0000
Pulse Width	10.7700
Spectrometer Frequency	600.32
Nucleus	<sup>1</sup> H



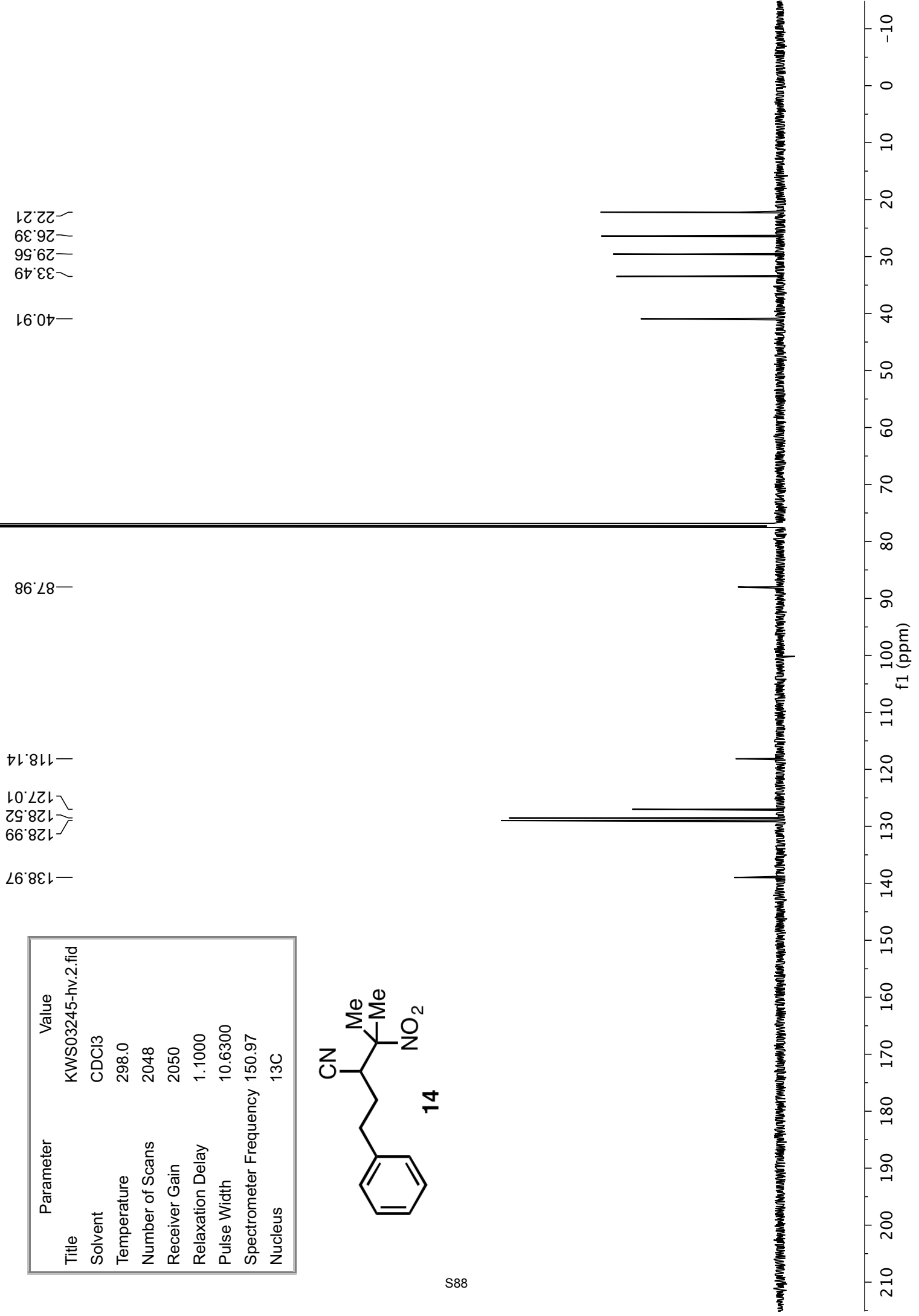
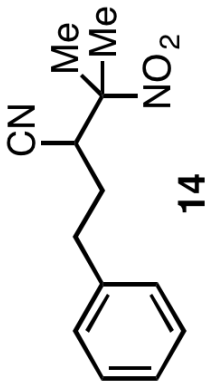
789

1.07  
3.26  
0.94  
3.22

1.97  
0.29  
0.66  
2.01



Parameter	Value
Title	KWS03245-hv.2.fid
Solvent	CDCl <sub>3</sub>
Temperature	298.0
Number of Scans	2048
Receiver Gain	2050
Relaxation Delay	1.1000
Pulse Width	10.6300
Spectrometer Frequency	150.97
Nucleus	<sup>13</sup> C



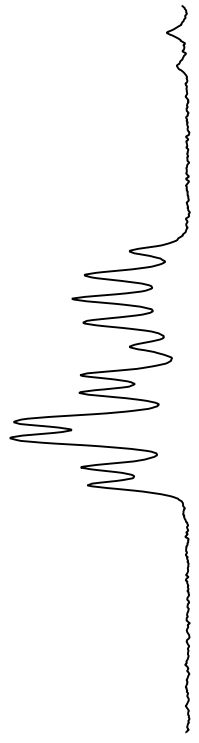


Parameter	Value
Title	KWS04017crd.1.fid
Solvent	CDCl3
Temperature	298.0
Number of Scans	8
Receiver Gain	228
Relaxation Delay	1.0000
Pulse Width	10.7700
Spectrometer Frequency	600.32
Nucleus	<sup>1</sup> H



4.51  
4.51  
4.50  
4.49  
4.48  
4.47  
4.46  
4.45  
4.44  
4.43

4.51  
4.51  
4.50  
4.49  
4.48  
4.46  
4.45  
4.44  
4.43

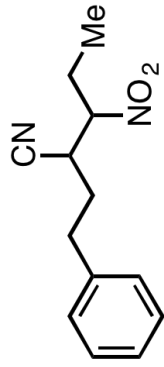


4.55 4.50 4.45 4.40 4.35  
f1 (ppm)

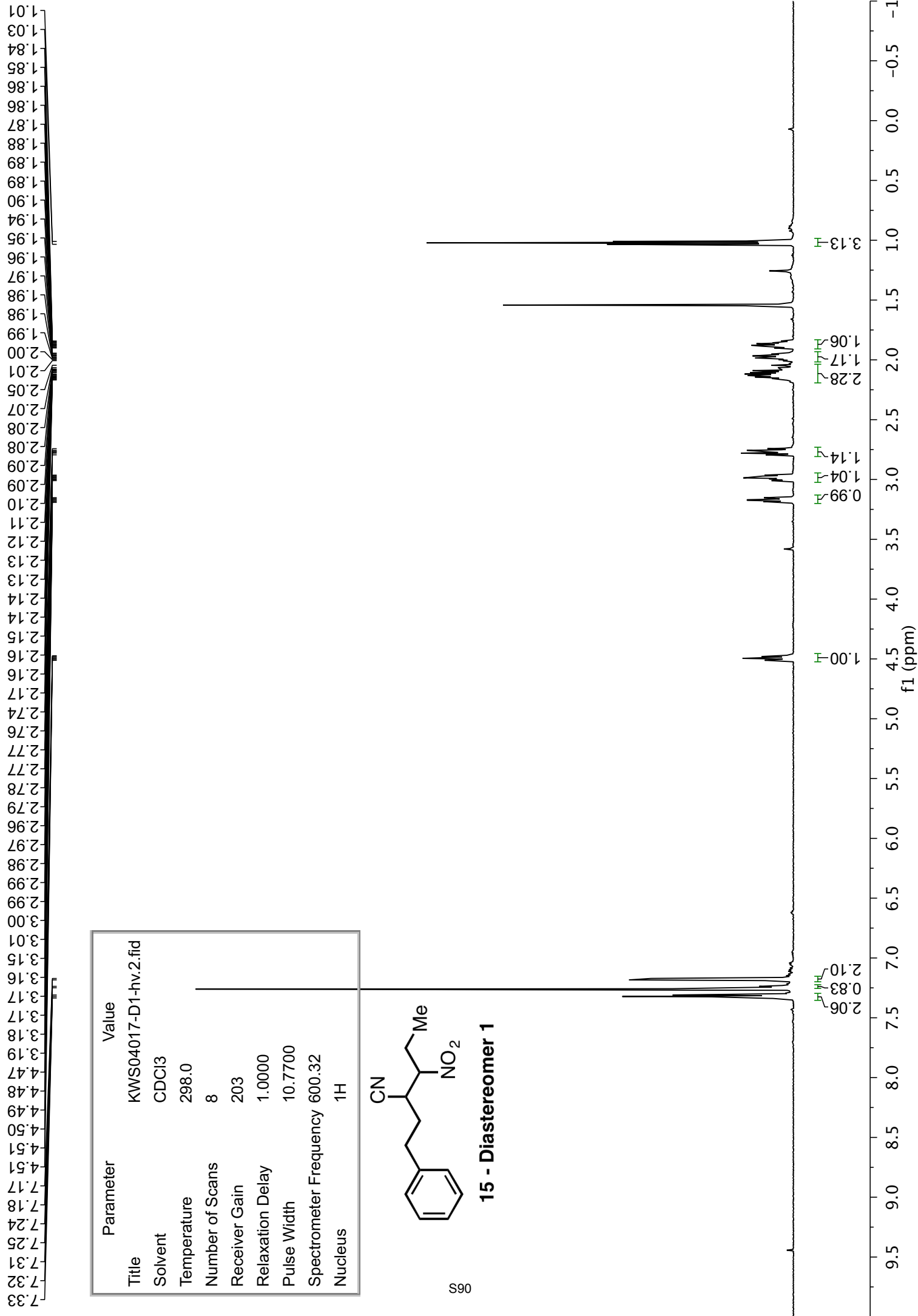
0.64  
0.36

1.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1

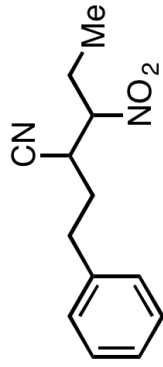
Parameter	Value
Title	KWS04017-D11-hv.2.fid
Solvent	CDCl3
Temperature	298.0
Number of Scans	8
Receiver Gain	203
Relaxation Delay	1.0000
Pulse Width	10.7700
Spectrometer Frequency	600.32
Nucleus	<sup>1</sup> H



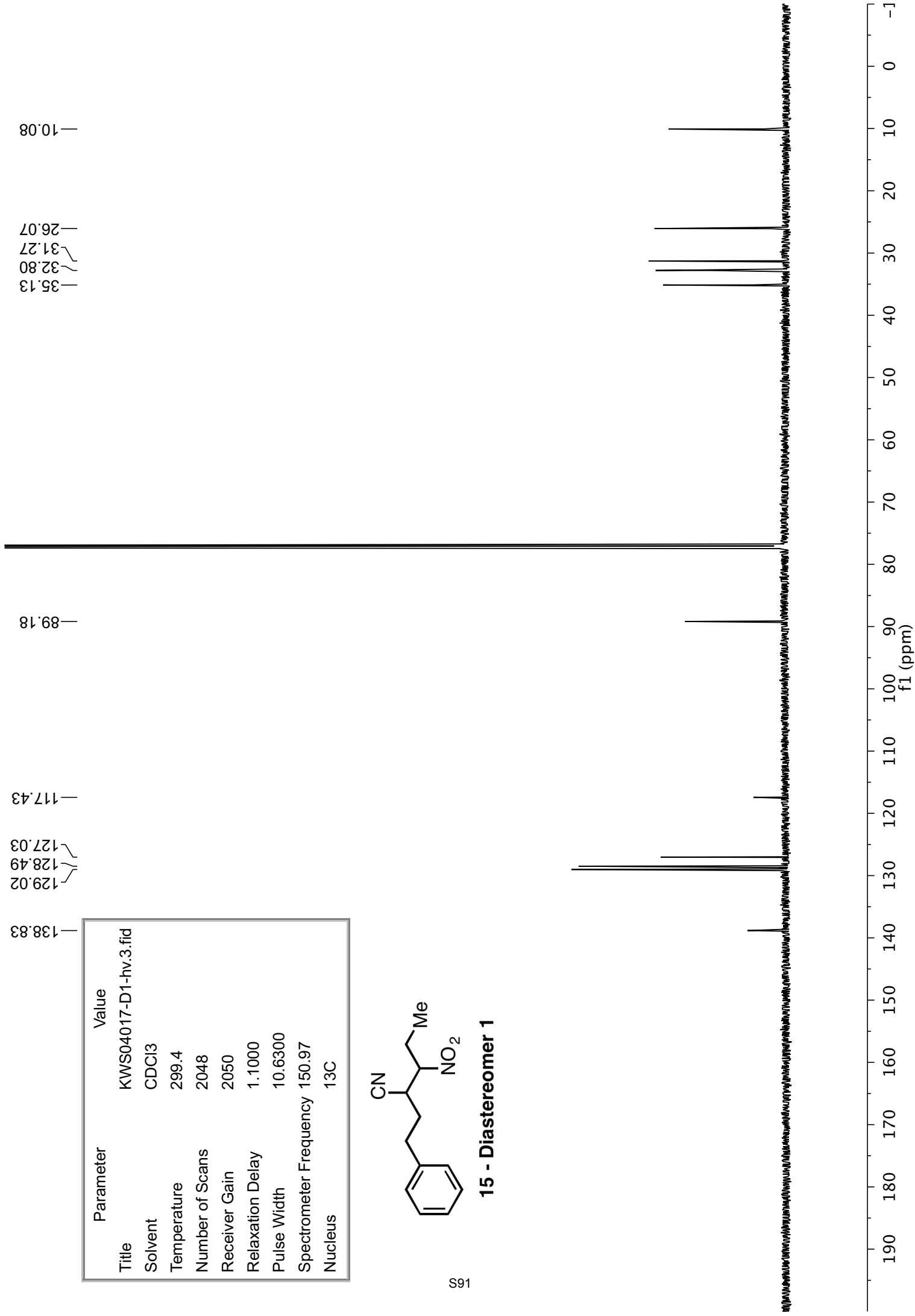
15 - Diastereomer 1



Parameter	Value
Title	KWS04017-D1-hv.3.fid
Solvent	CDCl3
Temperature	299.4
Number of Scans	2048
Receiver Gain	2050
Relaxation Delay	1.1000
Pulse Width	10.6300
Spectrometer Frequency	150.97
Nucleus	<sup>13</sup> C



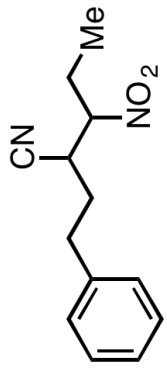
15 - Diastereomer 1



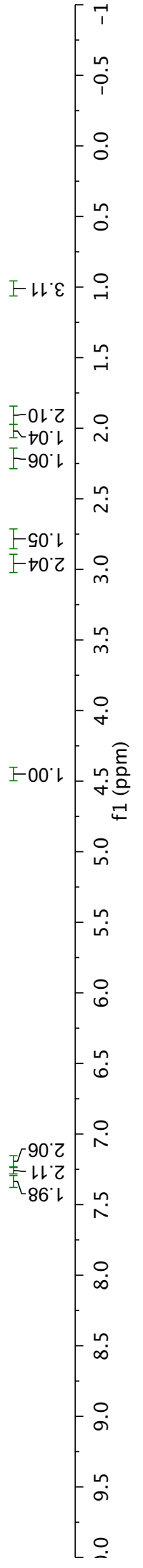
4.46  
4.46  
4.45  
4.44  
4.43  
3.00  
2.99  
2.98  
2.97  
2.96  
2.96  
2.95  
2.94  
2.93  
2.92  
2.91  
2.81  
2.80  
2.79  
2.79  
2.78  
2.76  
2.24  
2.23  
2.23  
2.22  
2.21  
2.20  
2.02  
2.01  
2.00  
1.99  
1.95  
1.94  
1.94  
1.93  
1.92  
1.92  
1.91  
1.90  
1.01  
1.00  
0.88

7.34  
7.33  
7.32  
7.27  
7.24  
7.20  
7.19

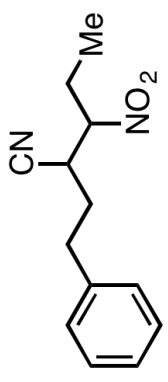
Parameter	Value
Title	KWS04017-D2-hv.2.fid
Solvent	CDCl3
Temperature	298.0
Number of Scans	8
Receiver Gain	181
Relaxation Delay	1.0000
Pulse Width	10.7700
Spectrometer Frequency	600.32
Nucleus	<sup>1</sup> H



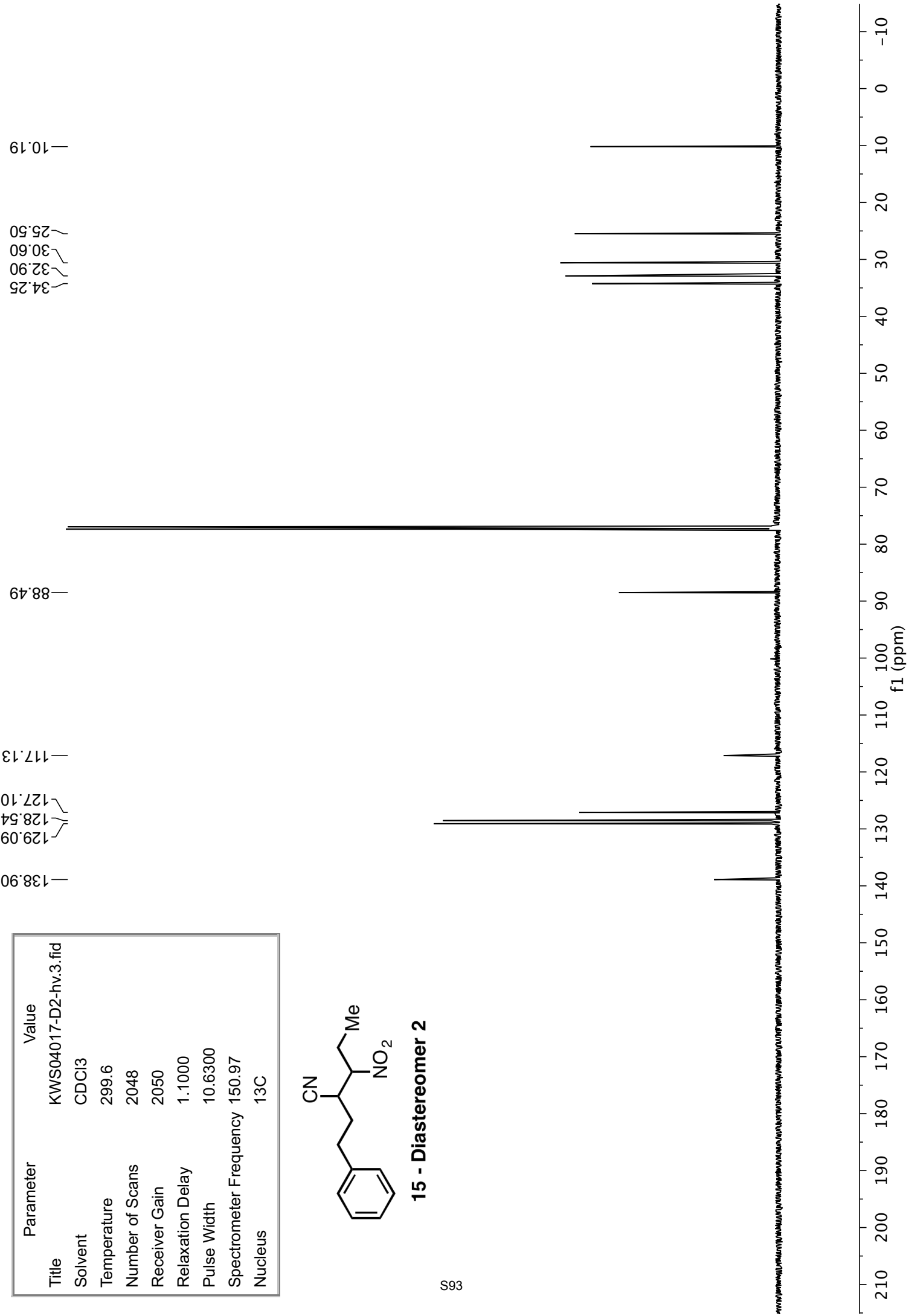
15 - Diastereomer 2



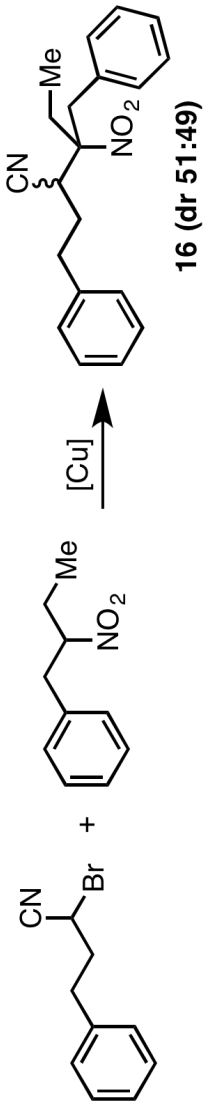
Parameter	Value
Title	KWS04017-D2-hv.3.fid
Solvent	CDCl3
Temperature	299.6
Number of Scans	2048
Receiver Gain	2050
Relaxation Delay	1.1000
Pulse Width	10.6300
Spectrometer Frequency	150.97
Nucleus	13C



15 - Diastereomer 2

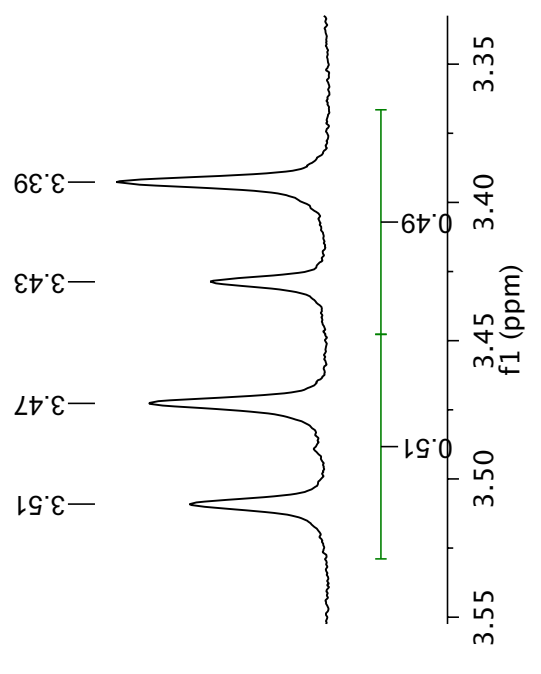


Parameter	Value
Title	KWS04163crd.1.fid
Solvent	CDCI3
Temperature	298.2
Number of Scans	16
Receiver Gain	4
Relaxation Delay	1.0000
Pulse Width	15.0000
Spectrometer Frequency	400.13
Nucleus	<sup>1</sup> H



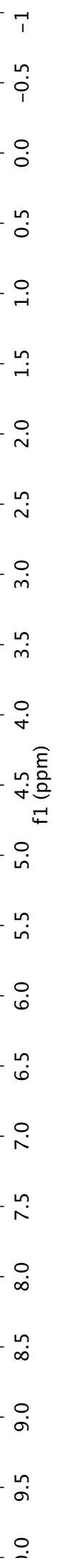
0.86  
 0.88  
 0.90  
 1.11  
 1.13  
 1.14

3.39  
 3.43  
 3.47  
 3.51

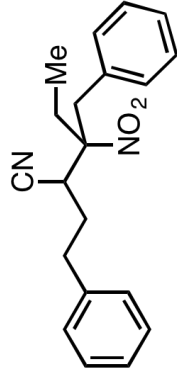


1.48  
 1.56

0.51  
 0.49

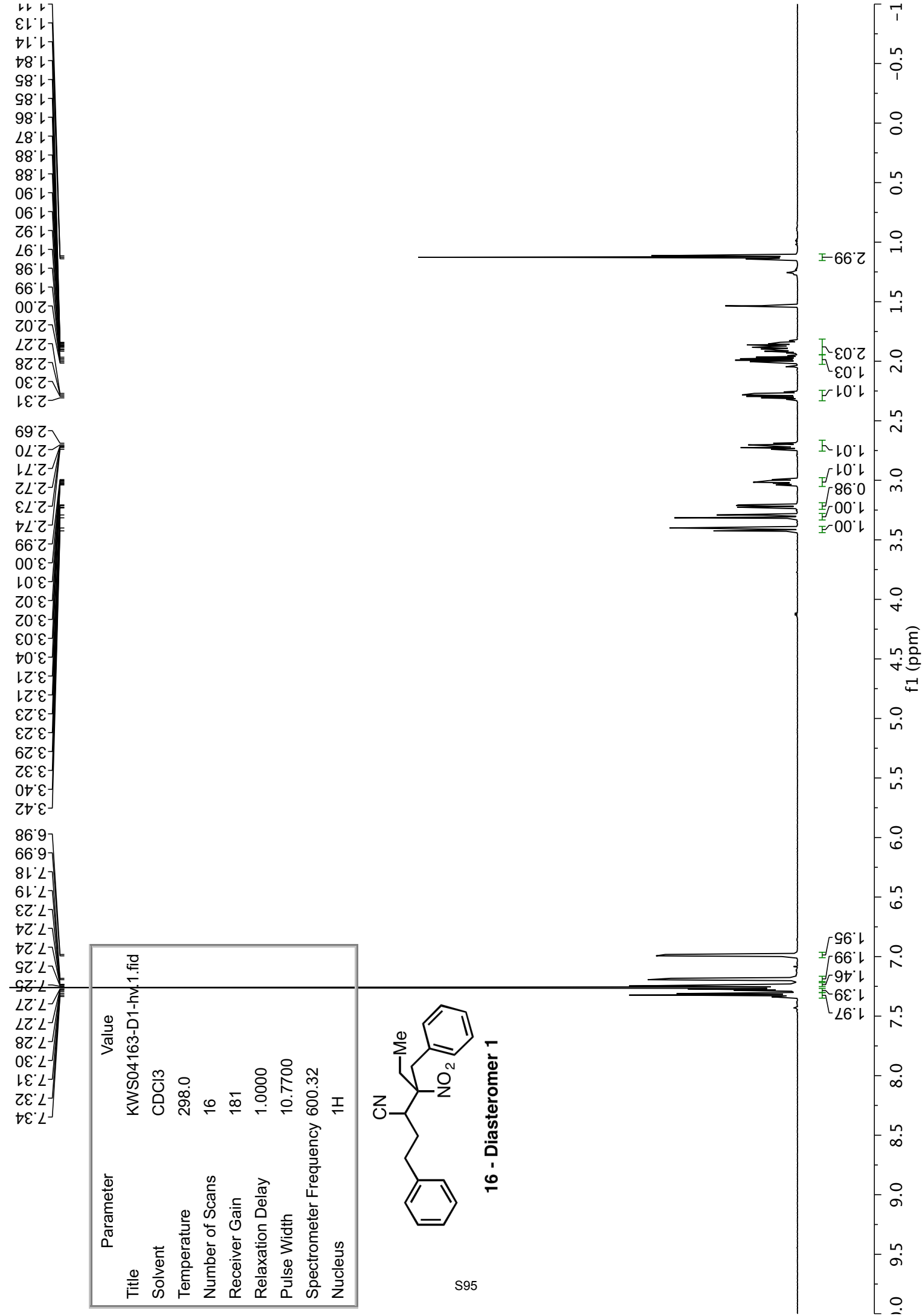


Parameter	Value
Title	KWS04163-D1-hv.1.fid
Solvent	CDCl3
Temperature	298.0
Number of Scans	16
Receiver Gain	181
Relaxation Delay	1.0000
Pulse Width	10.7700
Spectrometer Frequency	600.32
Nucleus	<sup>1</sup> H

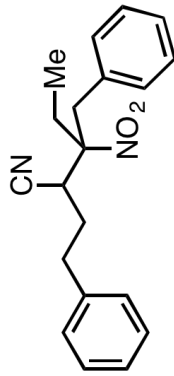


16 - Diastomer 1

96



Parameter	Value
Title	KWS04163-D1-13C.1.fid
Solvent	CDCl3
Temperature	298.0
Number of Scans	2048
Receiver Gain	2050
Relaxation Delay	1.1000
Pulse Width	10.6300
Spectrometer Frequency	150.97
Nucleus	<sup>13</sup> C



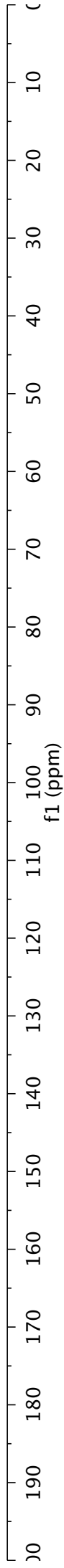
16 - Diastomer 1

139.20  
133.13  
129.94  
129.08  
129.00  
128.65  
128.24  
127.00  
118.58

94.43

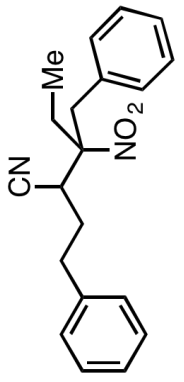
40.04  
37.34  
33.52  
29.68  
27.58

8.88

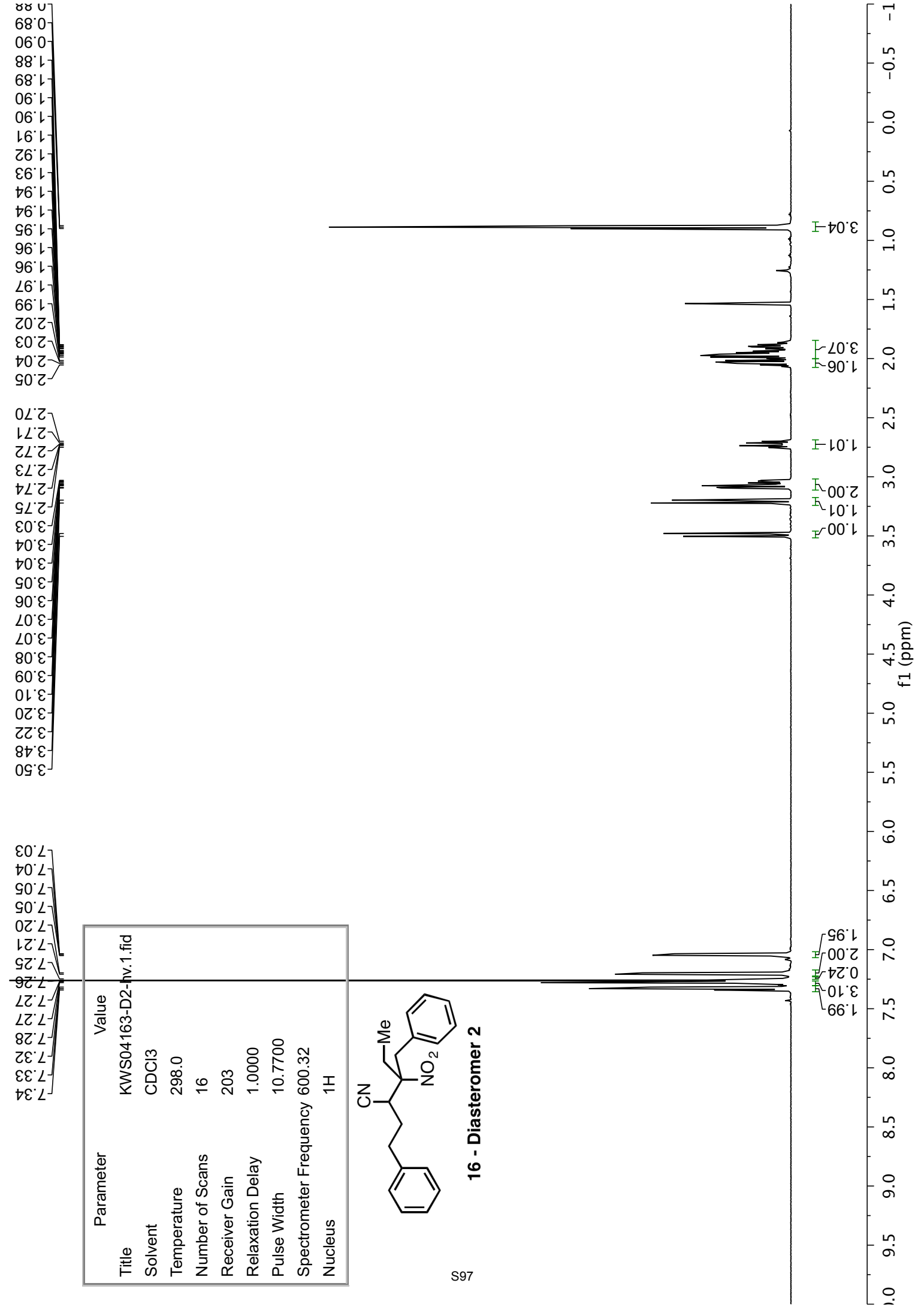




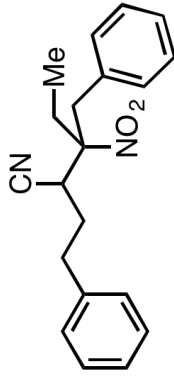
Parameter	Value
Title	KWS04163-D2-hv.1.fid
Solvent	CDCl3
Temperature	298.0
Number of Scans	16
Receiver Gain	203
Relaxation Delay	1.0000
Pulse Width	10.7700
Spectrometer Frequency	600.32
Nucleus	<sup>1</sup> H



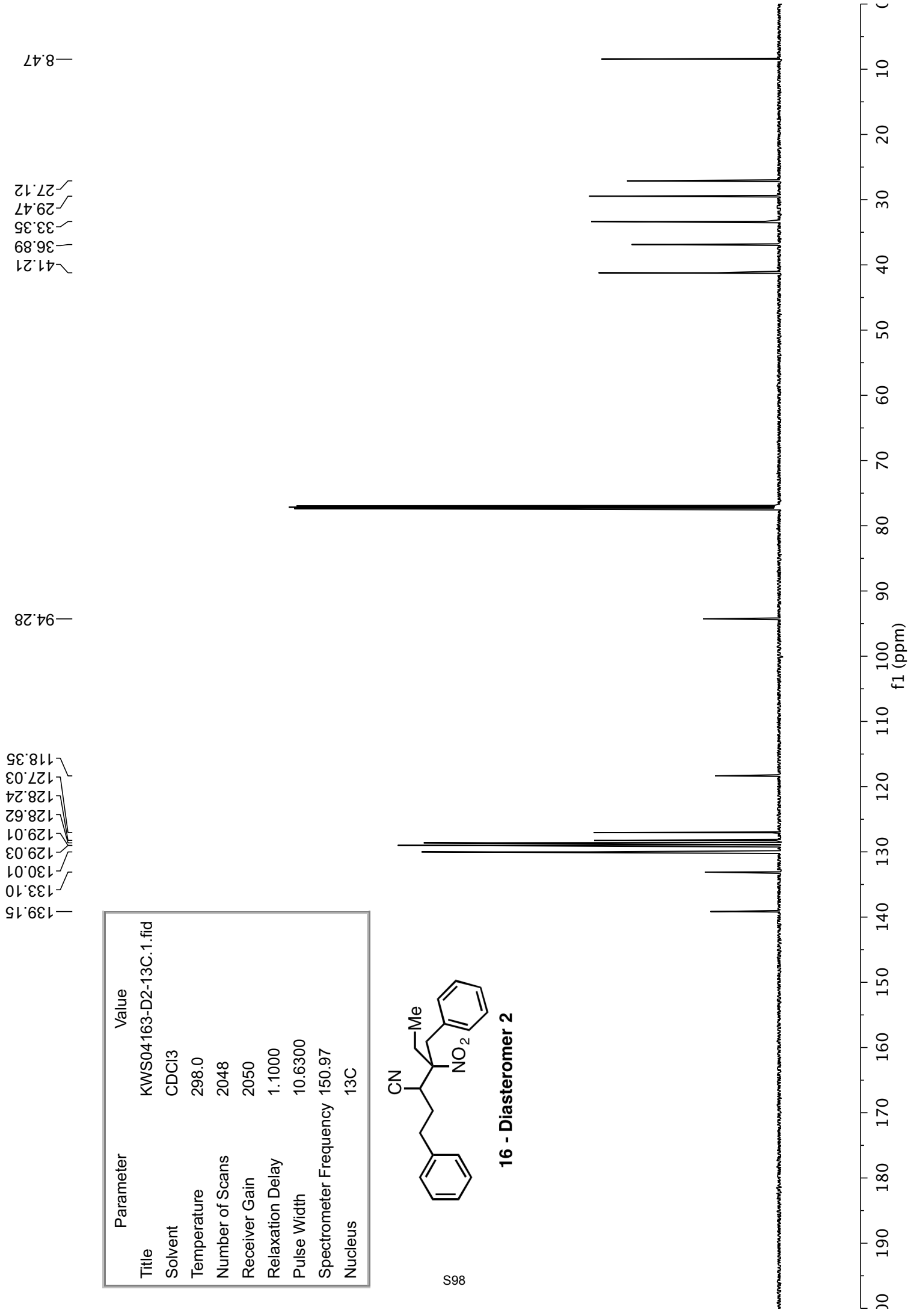
16 - Diastomer 2



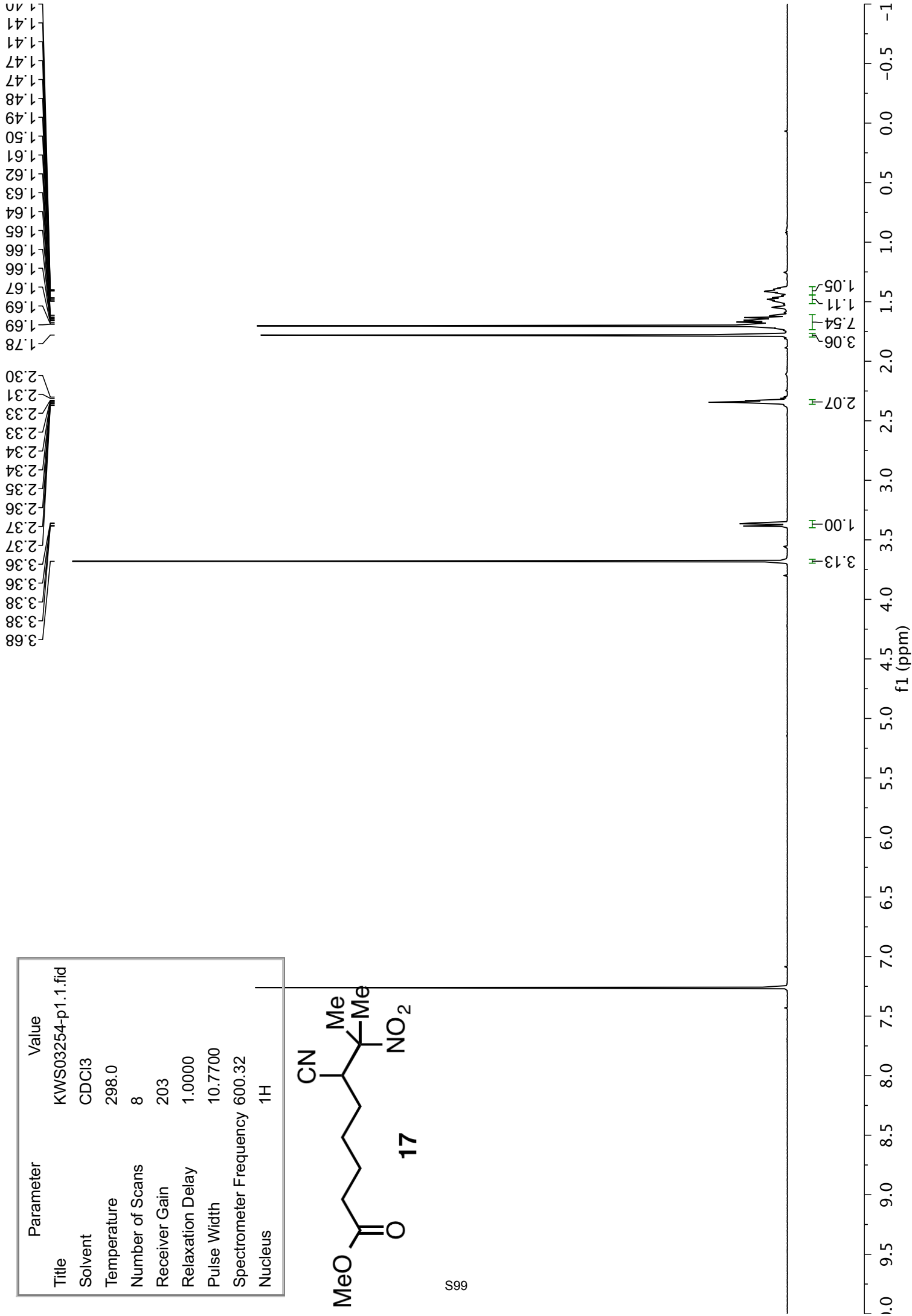
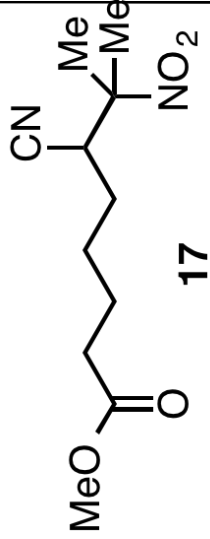
Parameter	Value
Title	KWS04163-D2-13C.1.fid
Solvent	CDCl <sub>3</sub>
Temperature	298.0
Number of Scans	2048
Receiver Gain	2050
Relaxation Delay	1.1000
Pulse Width	10.6300
Spectrometer Frequency	150.97
Nucleus	<sup>13</sup> C



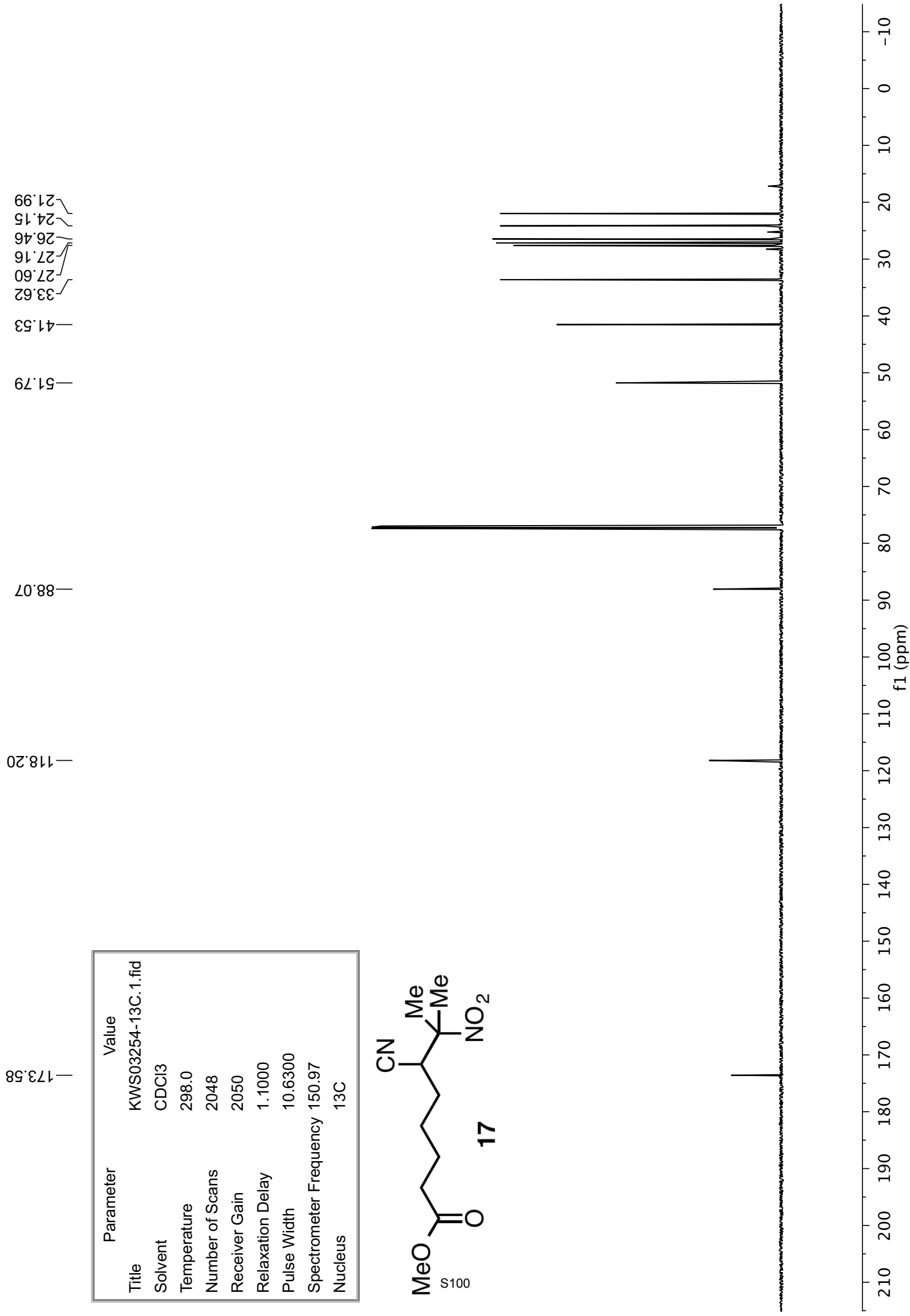
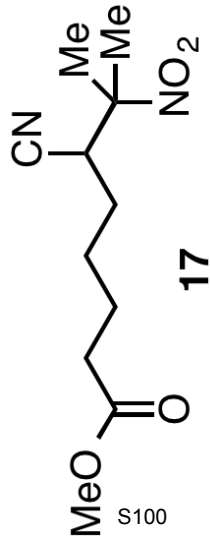
86



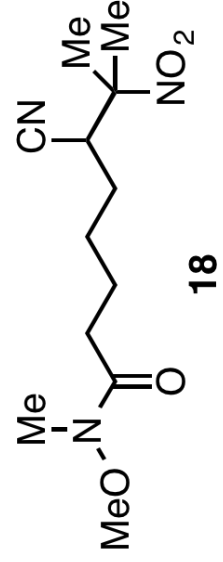
Parameter	Value
Title	KWS03254-p1.1.fid
Solvent	CDCl3
Temperature	298.0
Number of Scans	8
Receiver Gain	203
Relaxation Delay	1.0000
Pulse Width	10.7700
Spectrometer Frequency	600.32
Nucleus	<sup>1</sup> H



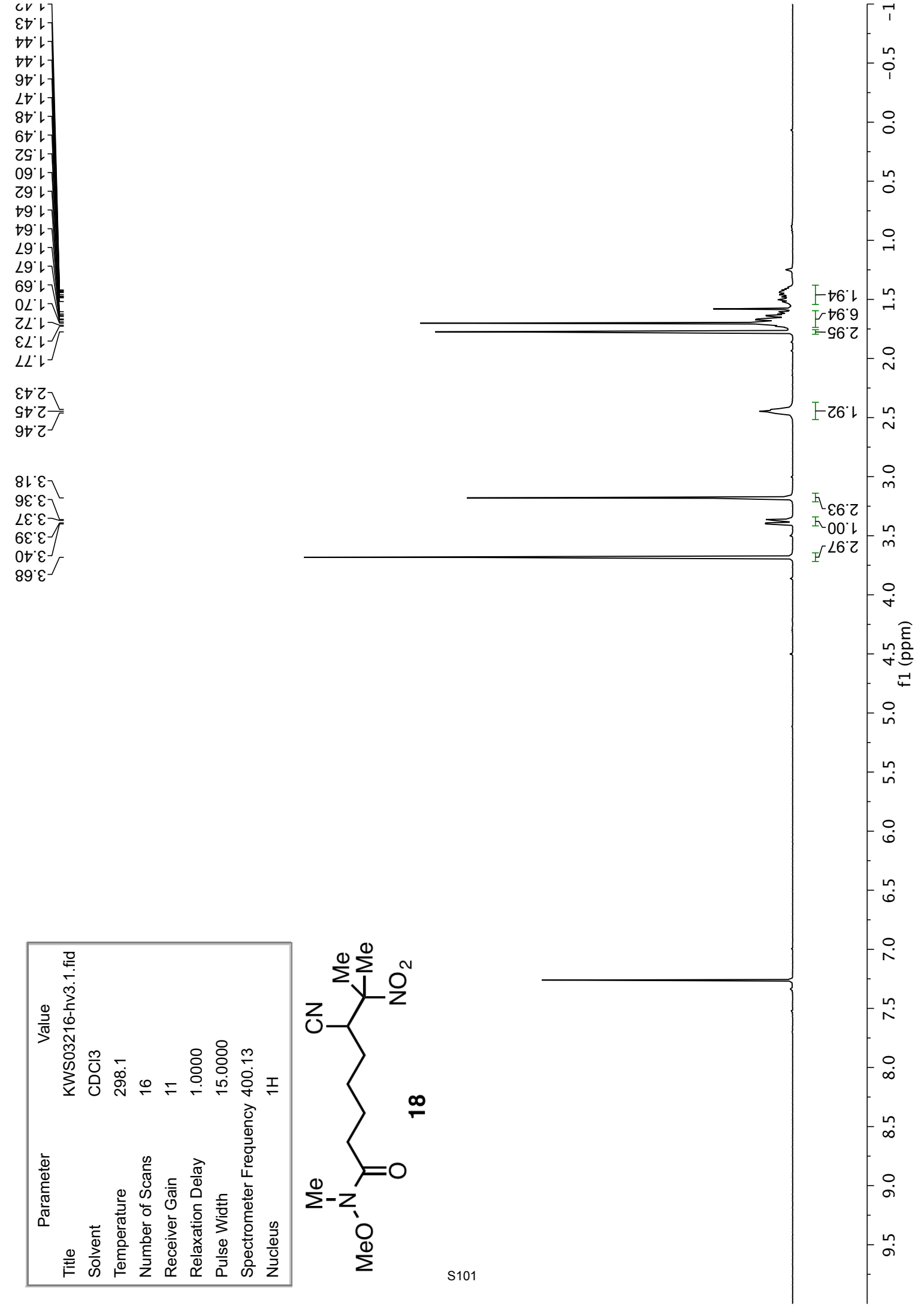
Parameter	Value
Title	KWS03254-13C.1.fid
Solvent	CDCl3
Temperature	298.0
Number of Scans	2048
Receiver Gain	2050
Relaxation Delay	1.1000
Pulse Width	10.6300
Spectrometer Frequency	150.97
Nucleus	<sup>13</sup> C



Parameter	Value
Title	KWS03216-hv3.1.fid
Solvent	CDCl3
Temperature	298.1
Number of Scans	16
Receiver Gain	11
Relaxation Delay	1.0000
Pulse Width	15.0000
Spectrometer Frequency	400.13
Nucleus	<sup>1</sup> H

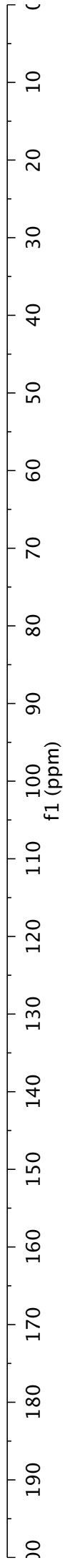
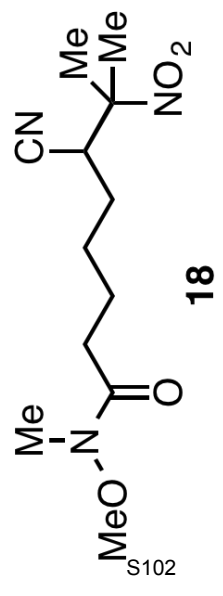


S101



173.95  
 118.25  
 88.05  
 61.35  
 41.48  
 32.24  
 31.34  
 27.62  
 27.33  
 26.15  
 23.70  
 22.20

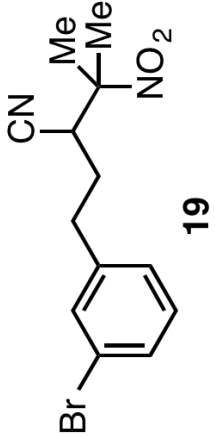
Parameter	Value
Title	KWS03216-13C.1.fid
Solvent	CDCl3
Temperature	298.0
Number of Scans	2048
Receiver Gain	2050
Relaxation Delay	1.1000
Pulse Width	10.6300
Spectrometer Frequency	150.97
Nucleus	13C



1.68  
1.68  
1.69  
1.70  
1.71  
1.73  
1.73  
1.77  
1.90  
1.91  
1.91  
1.92  
1.93  
1.93  
1.94  
1.95  
1.96  
1.96  
2.67  
2.69  
2.70  
2.70  
2.71  
2.73  
2.96  
2.97  
2.98  
2.98  
2.99  
3.00  
3.01  
3.31  
3.31  
3.33  
3.33

7.40  
7.39  
7.34  
7.21  
7.20  
7.19  
7.12  
7.11

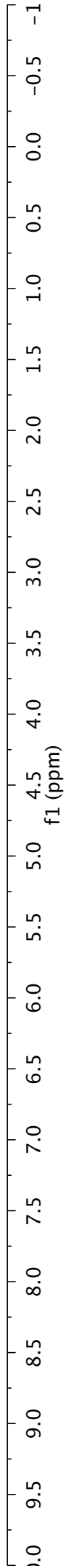
Parameter	Value
Title	KWS04013-hv2.1.fid
Solvent	CDCl3
Temperature	298.0
Number of Scans	8
Receiver Gain	256
Relaxation Delay	1.0000
Pulse Width	10.7700
Spectrometer Frequency	600.32
Nucleus	<sup>1</sup> H



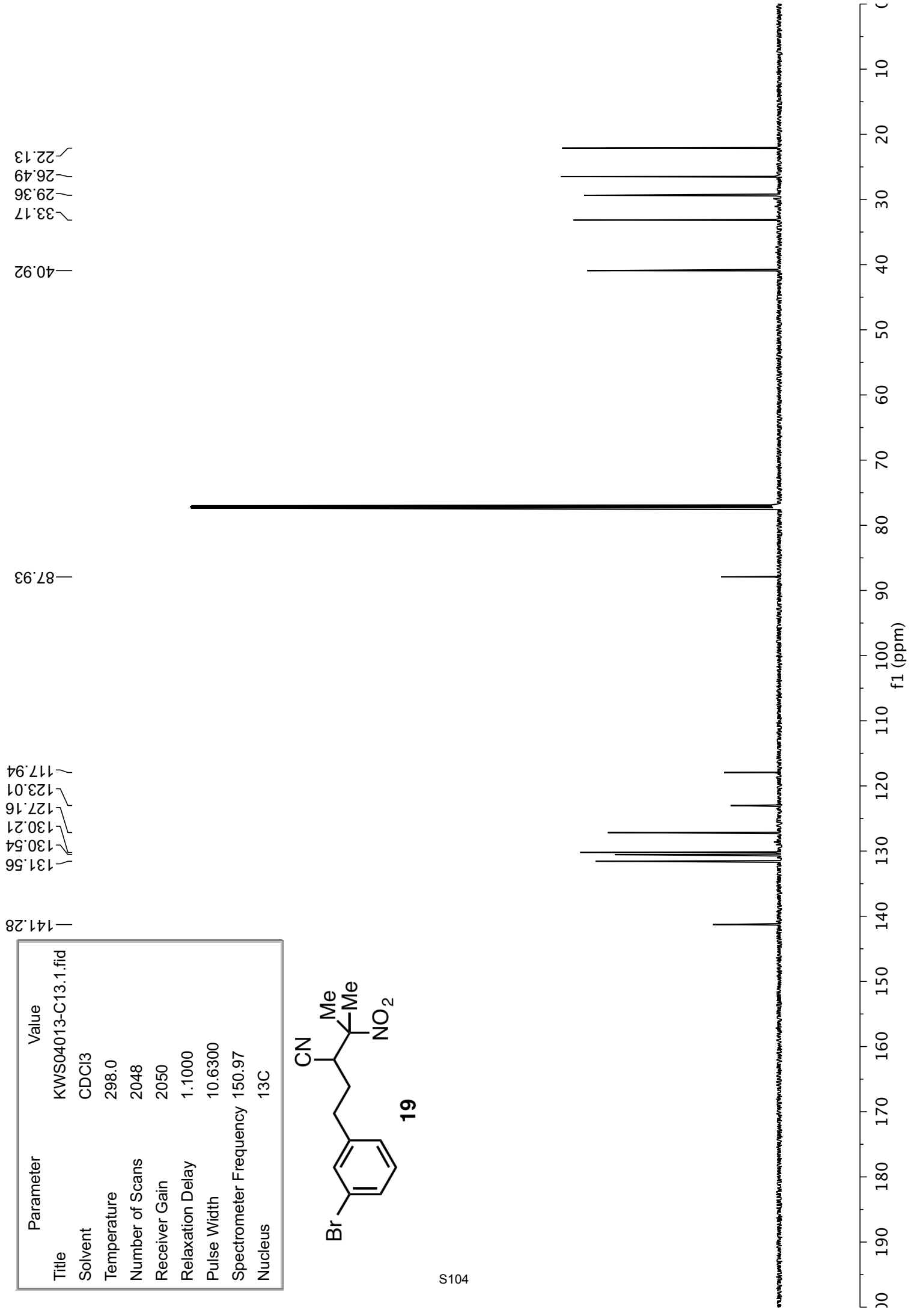
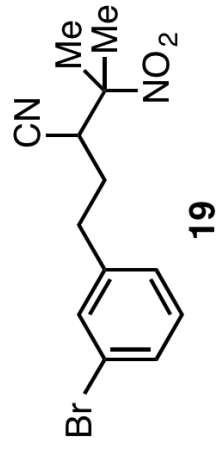
S103

4.20  
3.08  
1.02  
1.02  
1.00

0.99  
1.03  
0.98  
0.93

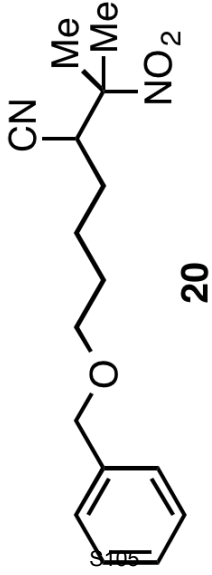


Parameter	Value
Title	KWS04013-C13.1.fid
Solvent	CDCI3
Temperature	298.0
Number of Scans	2048
Receiver Gain	2050
Relaxation Delay	1.1000
Pulse Width	10.6300
Spectrometer Frequency	150.97
Nucleus	<sup>13</sup> C





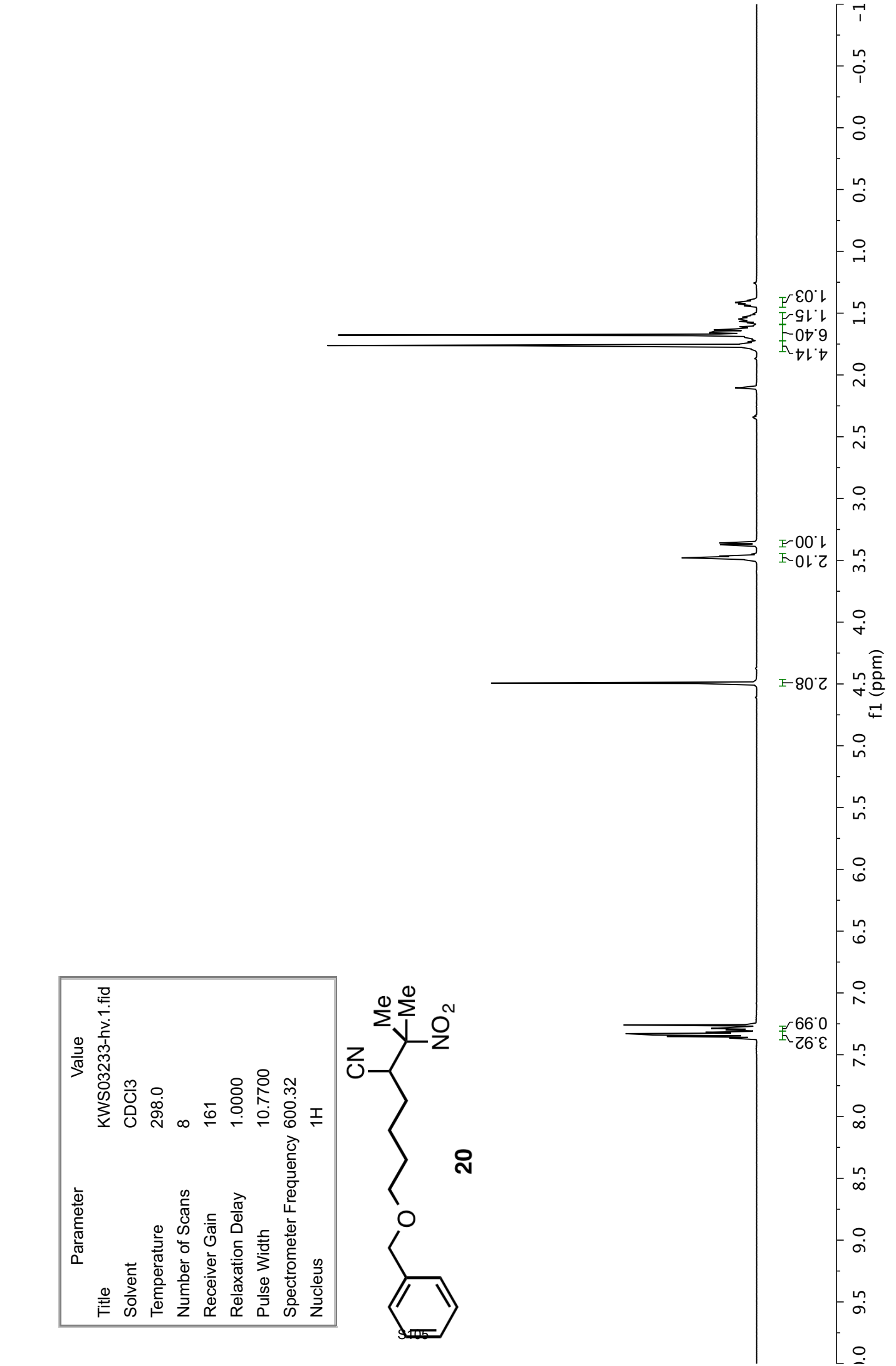
Parameter	Value
Title	KWS03233-hv.1.fid
Solvent	CDCl3
Temperature	298.0
Number of Scans	8
Receiver Gain	161
Relaxation Delay	1.0000
Pulse Width	10.7700
Spectrometer Frequency	600.32
Nucleus	<sup>1</sup> H



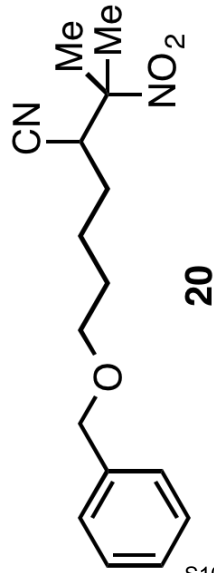
7.36  
7.35  
7.34  
7.33  
7.32  
7.30  
7.29

3.51  
3.49  
3.49  
3.48  
3.48  
3.47  
3.47  
3.46  
3.45  
3.38  
3.37  
3.36  
3.35

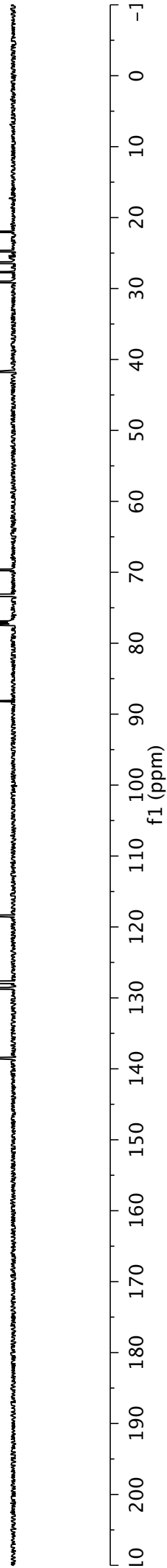
1.78  
1.78  
1.76  
1.74  
1.69  
1.68  
1.66  
1.65  
1.65  
1.64  
1.62  
1.61  
1.57  
1.55  
1.55  
1.53  
1.44  
1.44  
1.43  
1.42  
1.42  
1.41  
1.41  
1.40



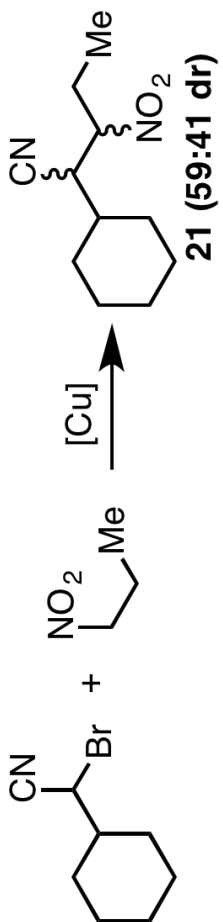
Parameter	Value
Title	KWS032333-hv.2.fid
Solvent	CDCl3
Temperature	298.0
Number of Scans	2048
Receiver Gain	2050
Relaxation Delay	1.1000
Pulse Width	10.6300
Spectrometer Frequency	150.97
Nucleus	<sup>13</sup> C



138.46  
 128.57  
 127.83  
 127.78  
 118.36  
 88.13  
 73.20  
 69.68  
 41.69  
 29.03  
 27.73  
 26.40  
 24.73  
 22.04



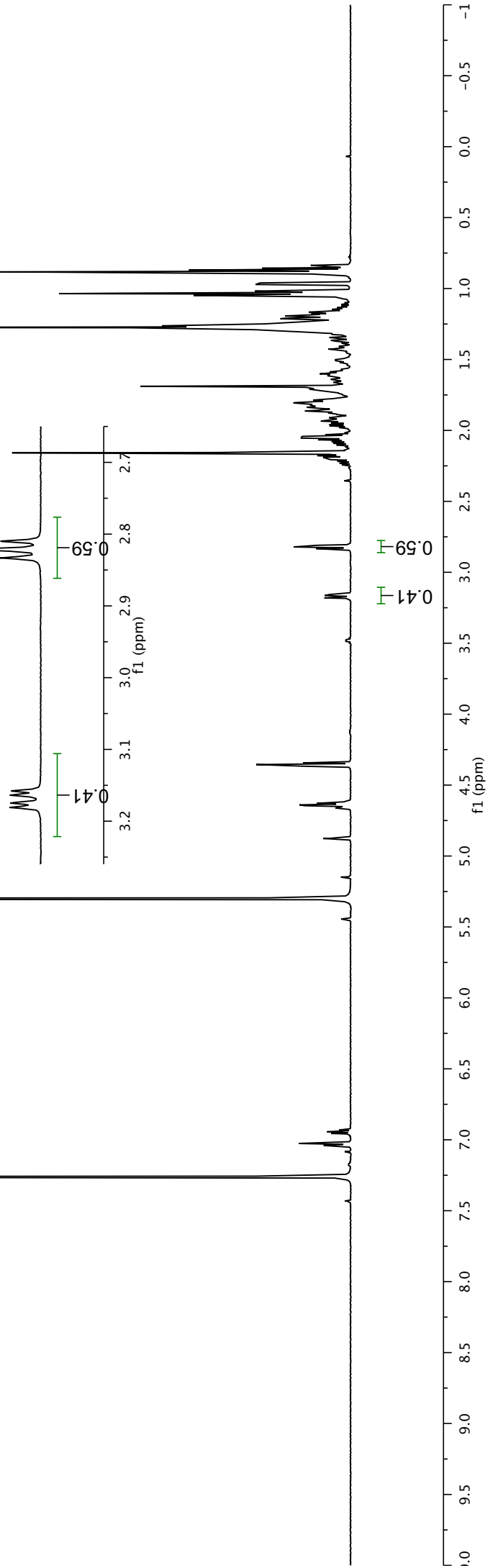
Parameter	Value
Title	KWS03269crd.1.fid
Solvent	CDCl <sub>3</sub>
Temperature	298.0
Number of Scans	8
Receiver Gain	161
Relaxation Delay	1.0000
Pulse Width	10.7700
Spectrometer Frequency	600.32
Nucleus	<sup>1</sup> H



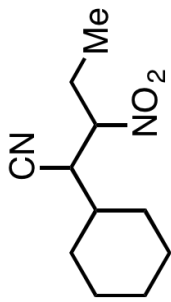
3.18  
 3.17  
 3.16  
 3.16  
 2.83  
 2.82  
 2.81

3.18  
 3.17  
 3.16  
 3.16

2.83  
 2.82  
 2.81

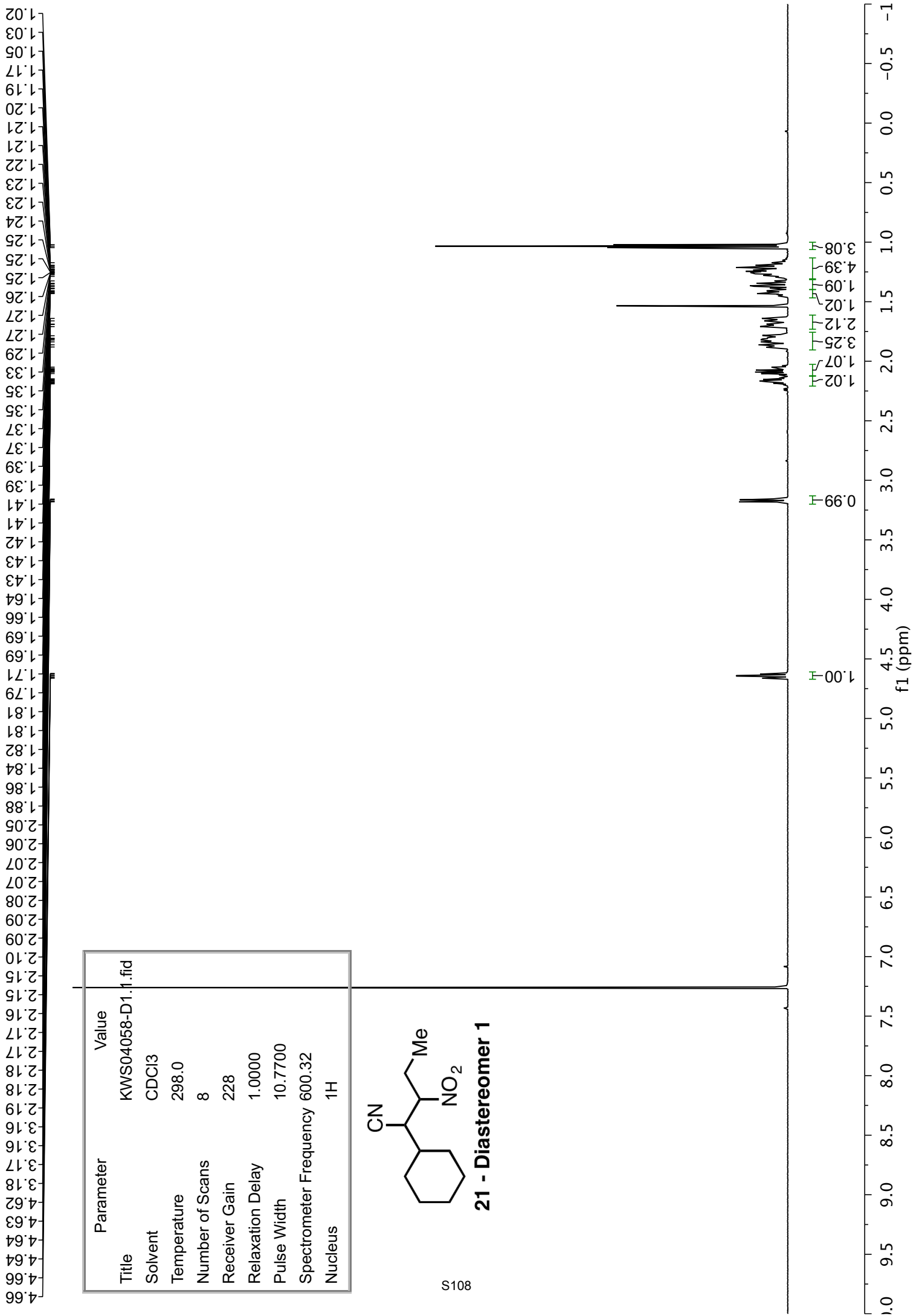


Parameter	Value
Title	KWS04058-D1.1.fid
Solvent	CDCl <sub>3</sub>
Temperature	298.0
Number of Scans	8
Receiver Gain	228
Relaxation Delay	1.0000
Pulse Width	10.7700
Spectrometer Frequency	600.32
Nucleus	<sup>1</sup> H

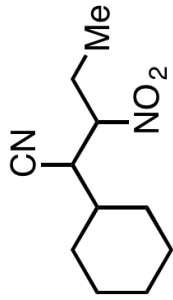


21 - Diastereomer 1

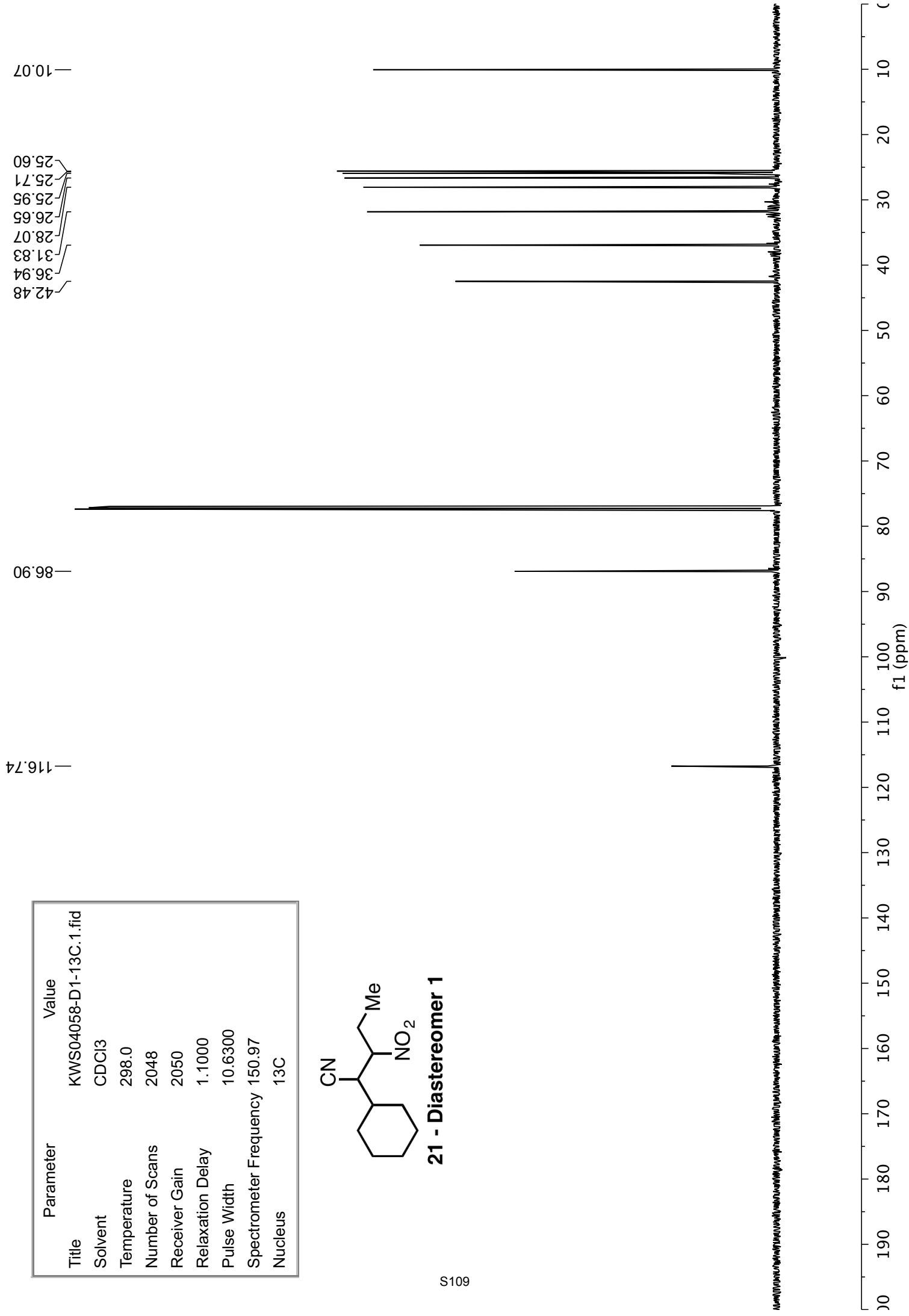
S108



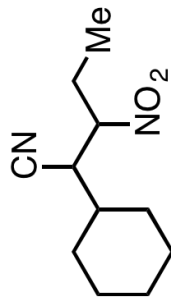
Parameter	Value
Title	KWS04058-D1-13C.1.fid
Solvent	CDCl3
Temperature	298.0
Number of Scans	2048
Receiver Gain	2050
Relaxation Delay	1.1000
Pulse Width	10.6300
Spectrometer Frequency	150.97
Nucleus	13C



21 - Diastereomer 1

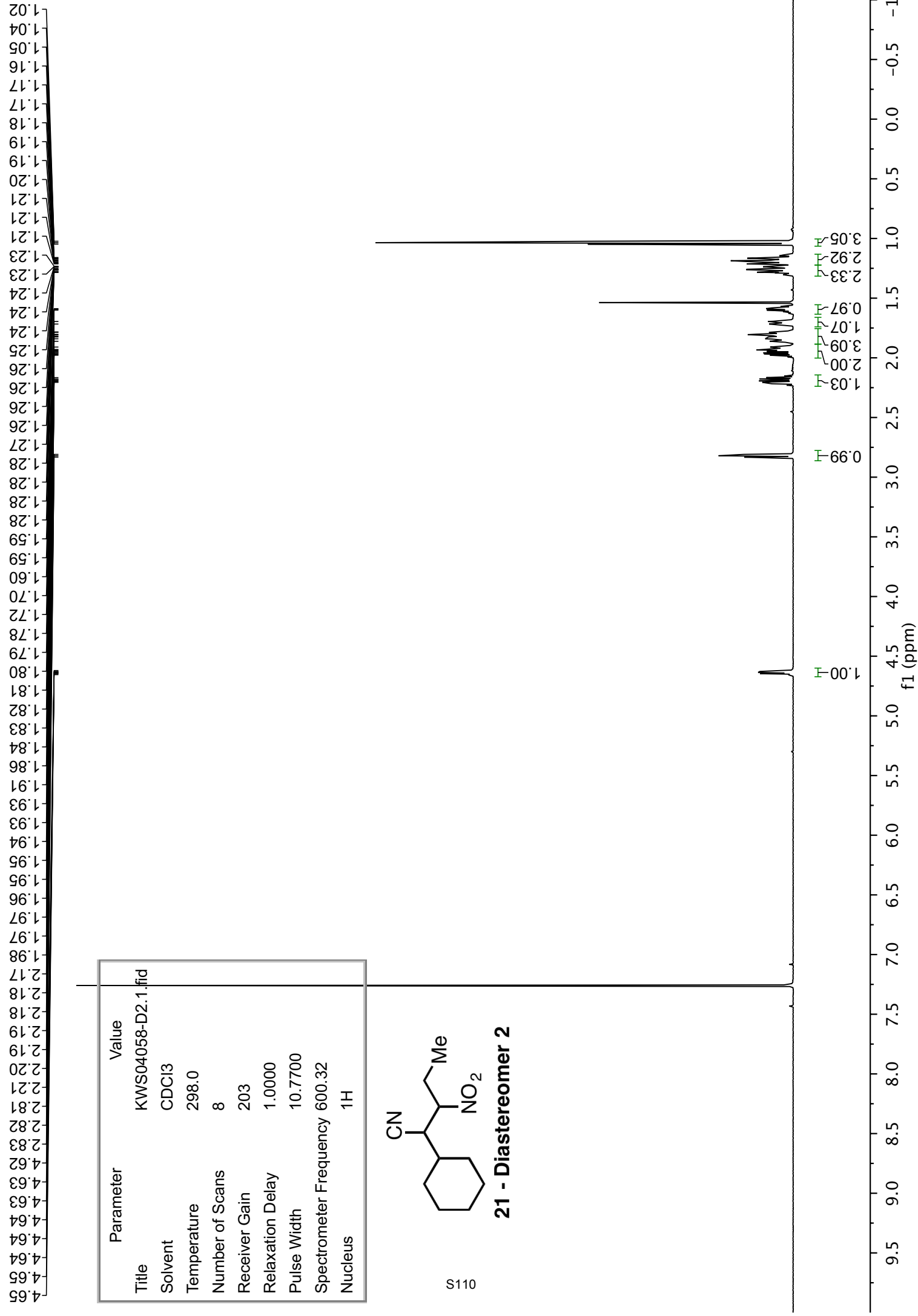


Parameter	Value
Title	KWS04058-D2.1.fid
Solvent	CDCl3
Temperature	298.0
Number of Scans	8
Receiver Gain	203
Relaxation Delay	1.0000
Pulse Width	10.7700
Spectrometer Frequency	600.32
Nucleus	<sup>1</sup> H

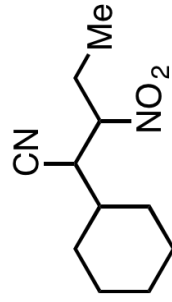


21 - Diastereomer 2

S110

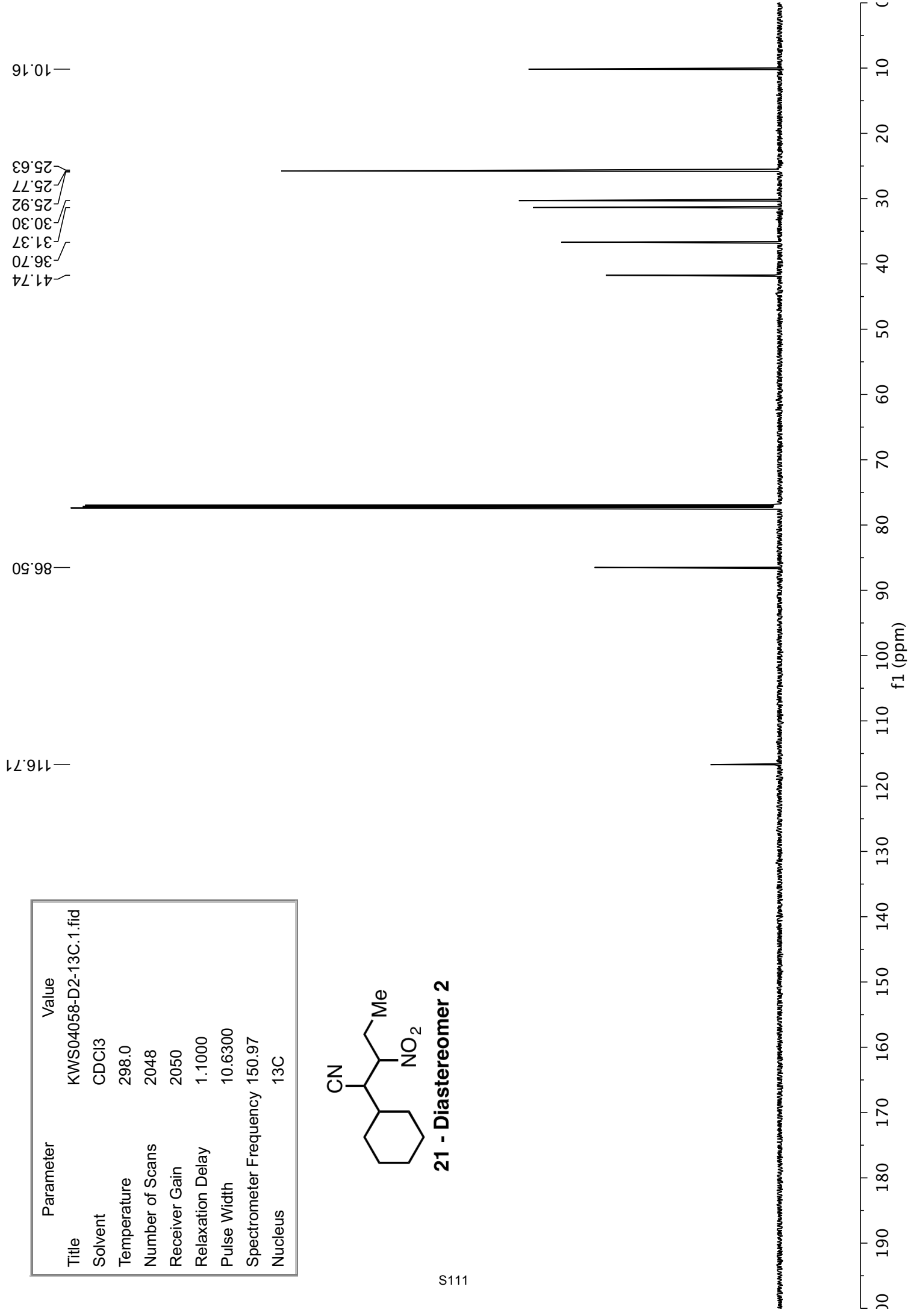


Parameter	Value
Title	KWS04058-D2-13C.1.fid
Solvent	CDCI3
Temperature	298.0
Number of Scans	2048
Receiver Gain	2050
Relaxation Delay	1.1000
Pulse Width	10.6300
Spectrometer Frequency	150.97
Nucleus	13C

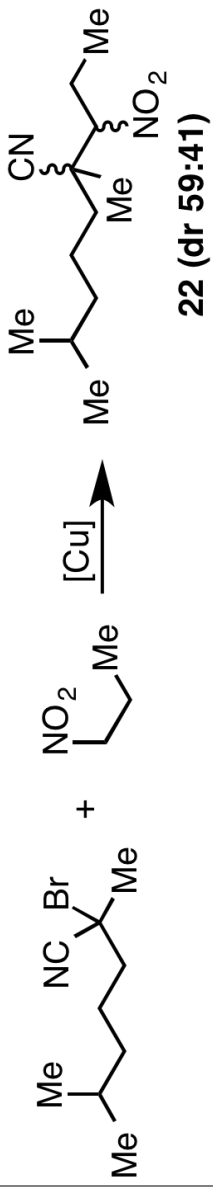


21 - Diastereomer 2

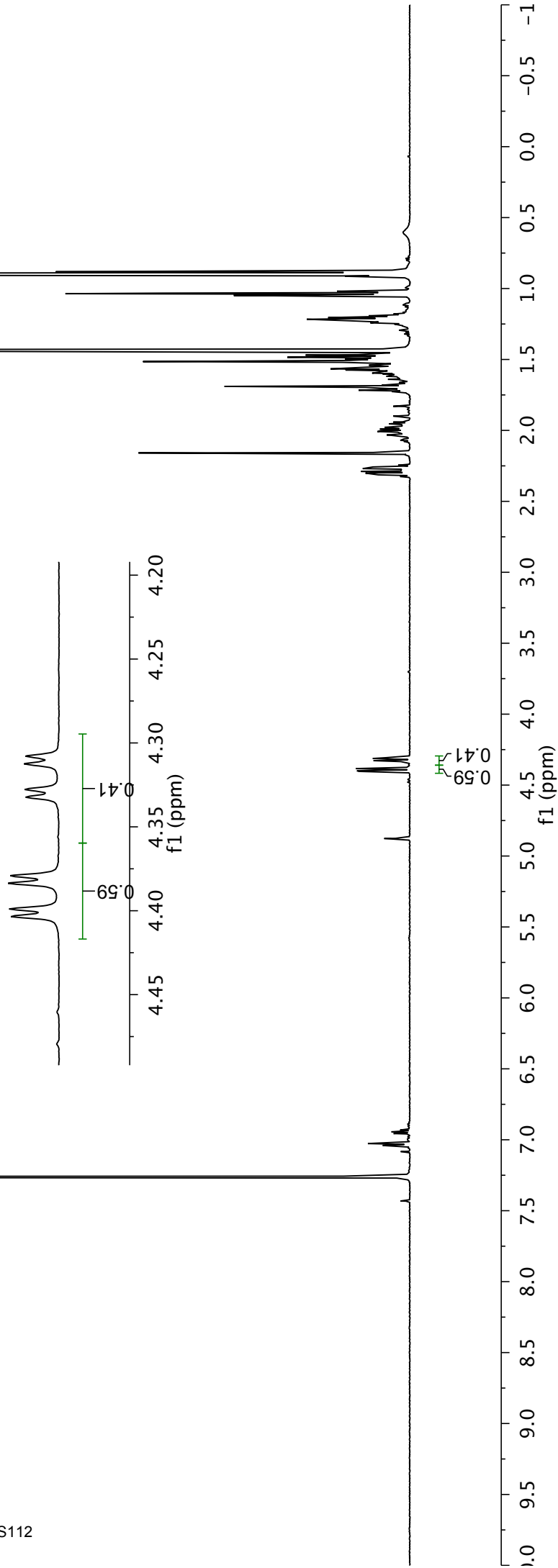
S111



Parameter	Value
Title	KWS04157crd.1.fid
Solvent	CDCI3
Temperature	298.0
Number of Scans	16
Receiver Gain	203
Relaxation Delay	1.0000
Pulse Width	10.7700
Spectrometer Frequency	600.32
Nucleus	<sup>1</sup> H



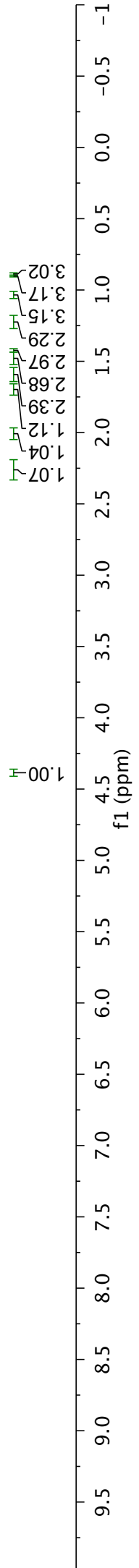
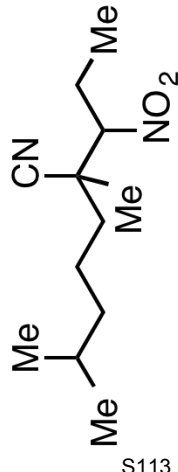
4.40  
 4.40  
 4.38  
 4.38  
 4.33  
 4.33  
 4.31  
 4.31



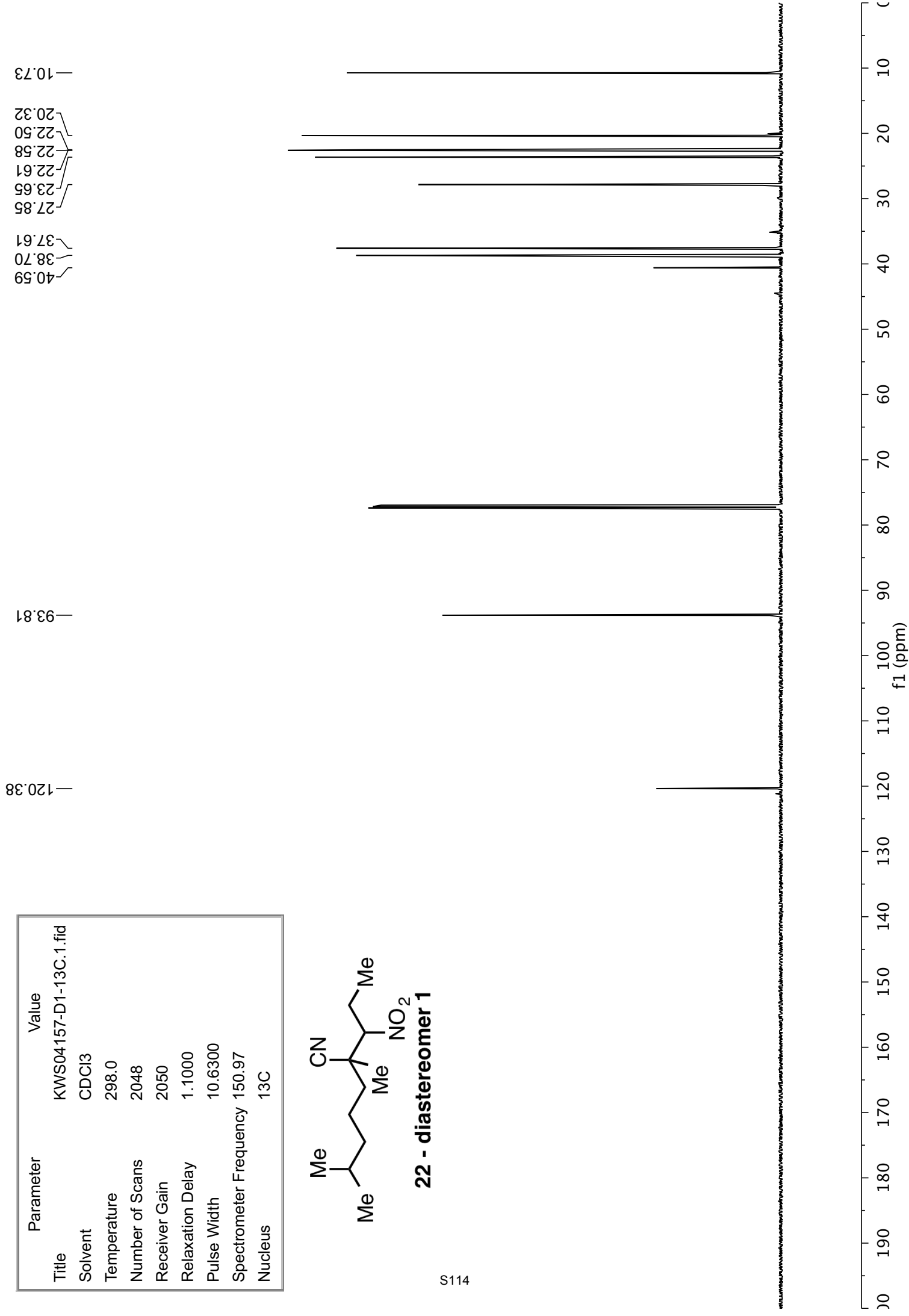
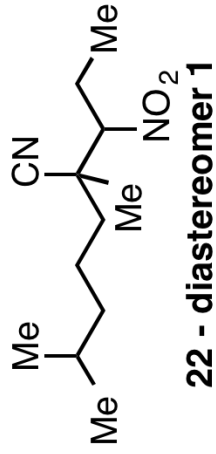


4.40  
4.38  
4.38  
2.32  
2.31  
2.30  
2.30  
2.29  
2.29  
2.28  
2.27  
2.27  
2.26  
2.25  
2.24  
2.04  
2.04  
2.03  
2.02  
2.02  
2.01  
2.00  
2.00  
1.99  
1.99  
1.98  
1.72  
1.71  
1.70  
1.69  
1.68  
1.67  
1.64  
1.63  
1.62  
1.62  
1.61  
1.60  
1.59  
1.58  
1.57  
1.56  
1.55  
1.53  
1.49  
1.48  
1.47  
1.47  
1.46  
1.45  
1.44  
1.43  
1.25  
1.24  
1.23  
1.23  
1.22  
1.22  
1.21  
1.21  
1.20  
1.19  
1.05  
1.03  
1.02  
0.90  
0.89

Parameter	Value
Title	KWS04157-D1_1.fid
Solvent	CDCl3
Temperature	298.0
Number of Scans	16
Receiver Gain	203
Relaxation Delay	1.0000
Pulse Width	10.7700
Spectrometer Frequency	600.32
Nucleus	1H

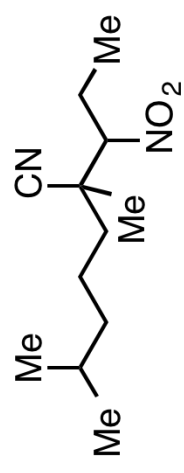


Parameter	Value
Title	KWS04157-D1-13C.1.fid
Solvent	CDCI3
Temperature	298.0
Number of Scans	2048
Receiver Gain	2050
Relaxation Delay	1.1000
Pulse Width	10.6300
Spectrometer Frequency	150.97
Nucleus	<sup>13</sup> C



4.33  
4.33  
4.31  
2.32  
2.31  
2.30  
2.30  
2.29  
2.29  
2.28  
2.28  
2.27  
2.26  
2.26  
2.24  
2.00  
2.00  
1.99  
1.99  
1.98  
1.97  
1.97  
1.96  
1.95  
1.95  
1.94  
1.66  
1.65  
1.65  
1.64  
1.63  
1.63  
1.62  
1.61  
1.58  
1.57  
1.56  
1.54  
1.54  
1.53  
1.51  
1.50  
1.50  
1.49  
1.48  
1.48  
1.47  
1.47  
1.46  
1.44  
1.24  
1.23  
1.22  
1.20  
1.19  
1.18  
1.17  
1.04  
1.03  
1.02  
0.88  
0.88

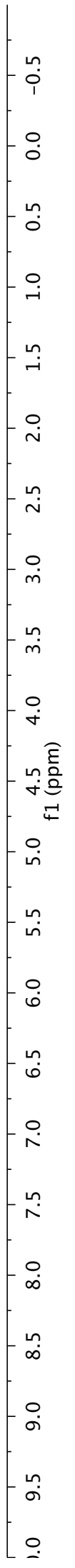
Parameter	Value
Title	KWS04157-D2.1.fid
Solvent	CDCl3
Temperature	298.0
Number of Scans	16
Receiver Gain	203
Relaxation Delay	1.0000
Pulse Width	10.7700
Spectrometer Frequency	600.32
Nucleus	<sup>1</sup> H



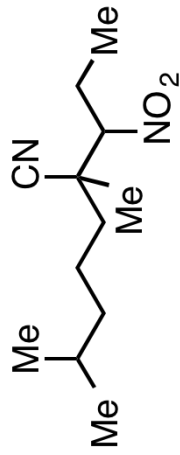
**22 - diastereomer 2**

S115

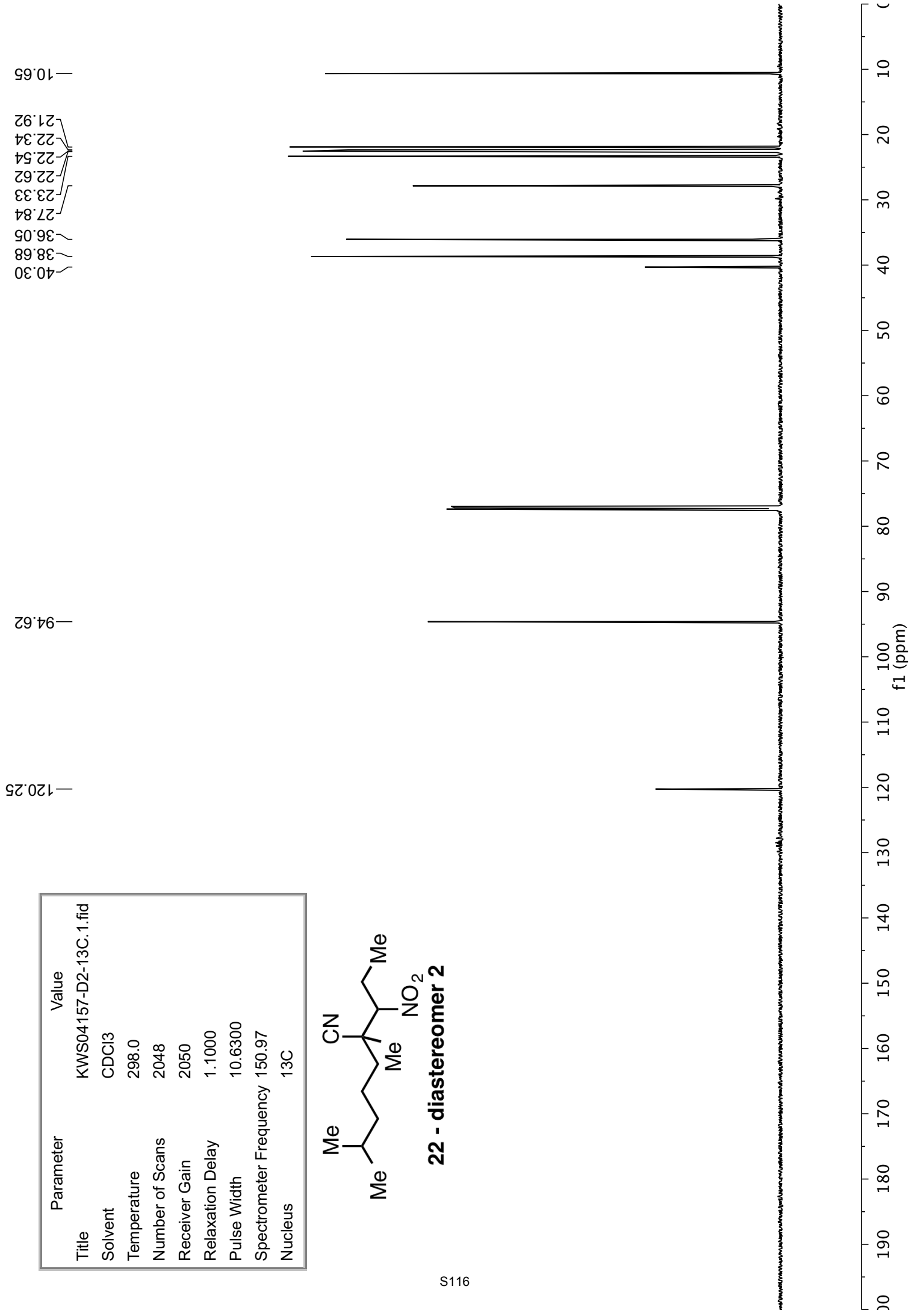
1.00  
1.07  
1.11  
1.06  
5.11  
3.12  
2.12  
3.10  
3.21  
2.98



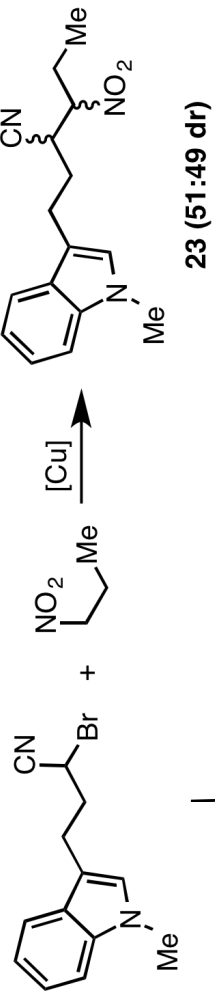
Parameter	Value
Title	KWS04157-D2-13C.1.fid
Solvent	CDCl3
Temperature	298.0
Number of Scans	2048
Receiver Gain	2050
Relaxation Delay	1.1000
Pulse Width	10.6300
Spectrometer Frequency	150.97
Nucleus	<sup>13</sup> C



**22 - diastereomer 2**



Parameter	Value
Title	KWS04120crd.1.fid
Solvent	CDCl3
Temperature	298.2
Number of Scans	16
Receiver Gain	13
Relaxation Delay	1.0000
Pulse Width	15.0000
Spectrometer Frequency	400.13
Nucleus	<sup>1</sup> H



23 (51:49 dr)

4.52  
4.51  
4.50  
4.48  
4.47  
4.46  
3.26  
3.25  
3.23  
3.22  
3.22  
3.21  
3.20  
3.17  
3.16  
3.13  
3.12  
3.10  
3.09

3.26  
3.25  
3.23  
3.22  
3.22  
3.21  
3.20  
3.17  
3.16  
3.13  
3.12  
3.10  
3.09

4.52  
4.51  
4.50  
4.48  
4.47  
4.46

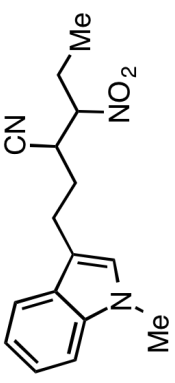
4.50  
4.45  
f1 (ppm)

3.30  
3.25  
3.20  
3.15  
3.10  
3.05  
3.00  
f1 (ppm)

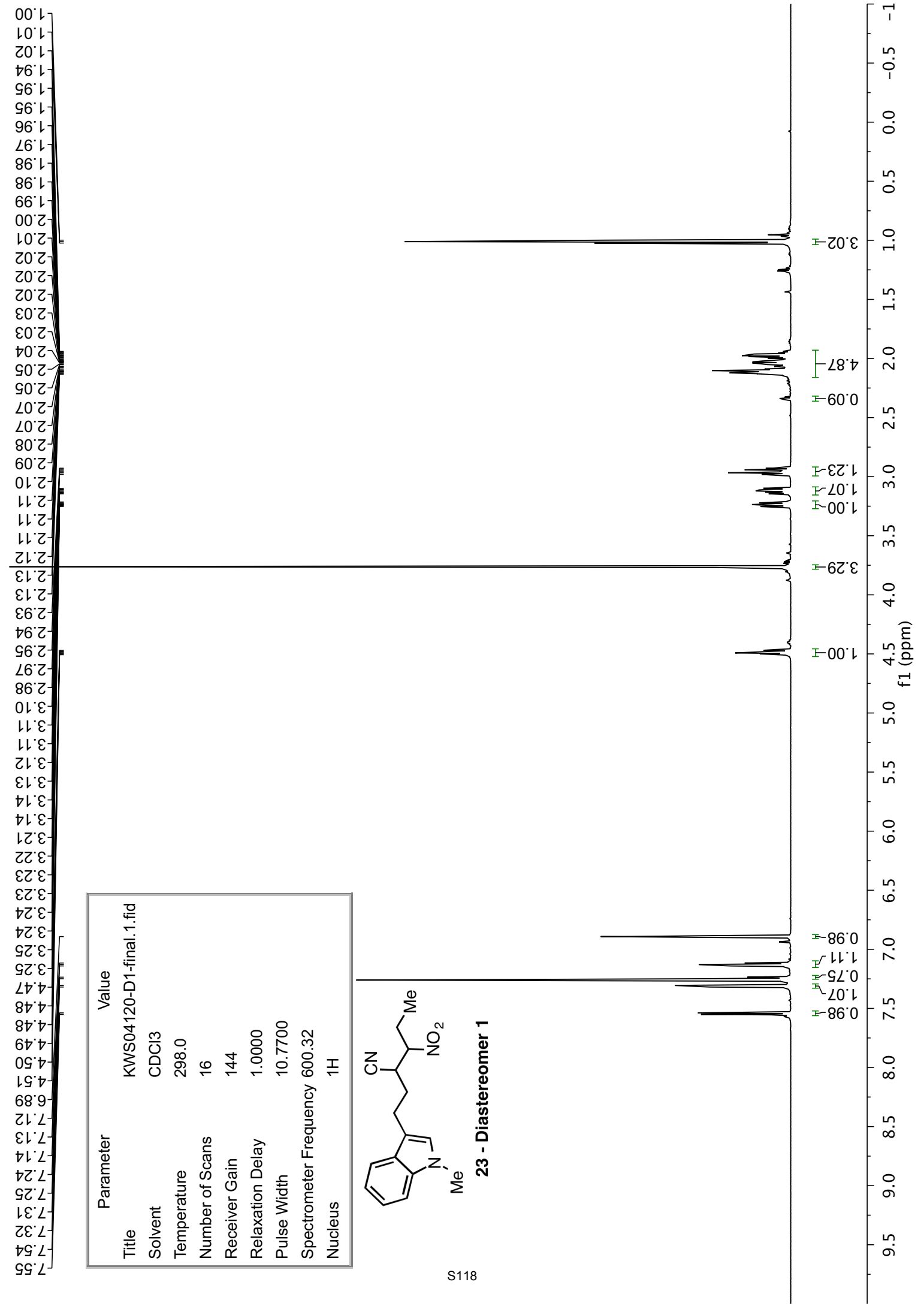
0.49  
1.00  
5.14

1.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1

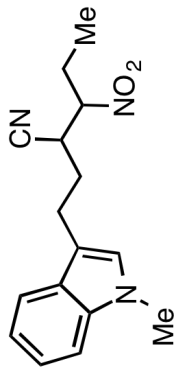
Parameter	Value
Title	KWS04120-D1-final.1.fid
Solvent	CDCl3
Temperature	298.0
Number of Scans	16
Receiver Gain	144
Relaxation Delay	1.0000
Pulse Width	10.7700
Spectrometer Frequency	600.32
Nucleus	<sup>1</sup> H



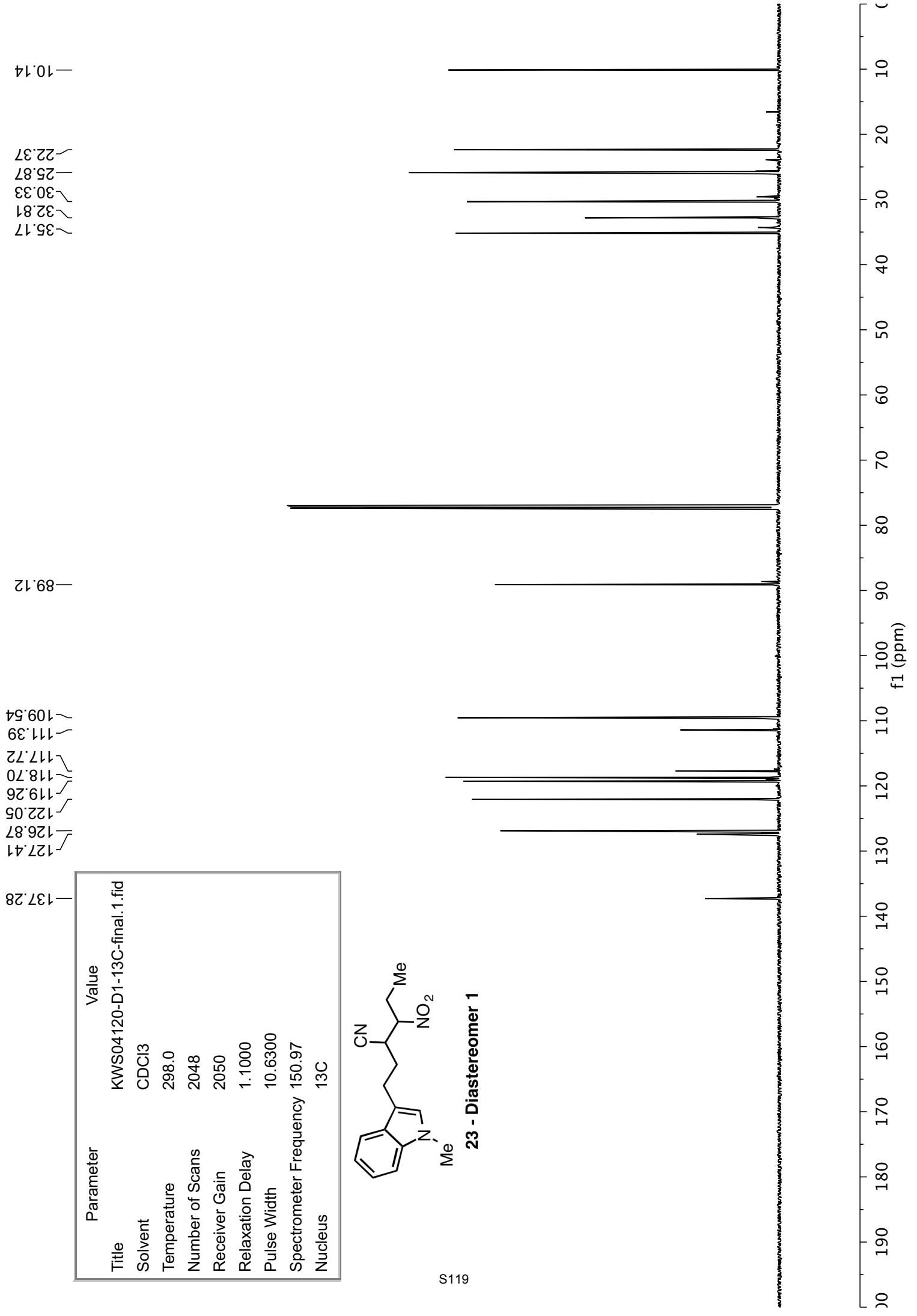
23 - Diastereomer 1



Parameter	Value
Title	KWS04120-D1-13C-final.1.fid
Solvent	CDCl3
Temperature	298.0
Number of Scans	2048
Receiver Gain	2050
Relaxation Delay	1.1000
Pulse Width	10.6300
Spectrometer Frequency	150.97
Nucleus	<sup>13</sup> C

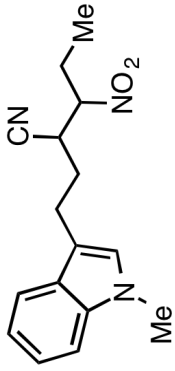


23 - Diastereomer 1

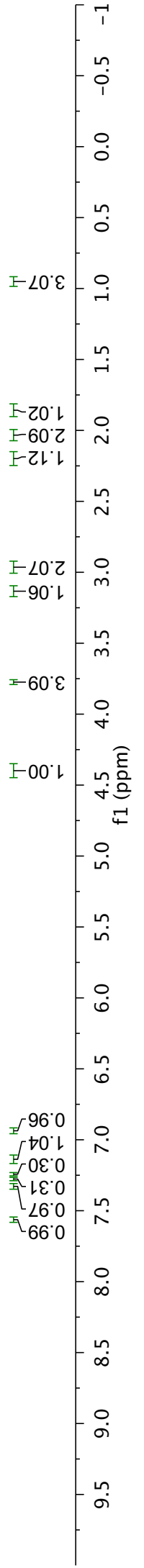


7.57  
7.55  
7.33  
7.32  
7.27  
7.25  
7.15  
7.13  
7.12  
6.94  
4.42  
4.41  
4.40  
4.38  
3.77  
3.16  
3.15  
3.14  
3.13  
3.12  
3.11  
2.99  
2.98  
2.97  
2.96  
2.95  
2.24  
2.23  
2.21  
2.21  
2.20  
2.20  
2.19  
2.18  
2.18  
2.17  
2.16  
2.05  
2.04  
2.02  
2.02  
2.01  
1.89  
1.88  
1.88  
1.87  
1.87  
1.86  
1.86  
1.85  
1.84  
1.84  
1.83  
1.82  
0.96  
0.95  
0.94

Parameter	Value
Title	KWS04120-D2-hvA.1.fid
Solvent	CDCl3
Temperature	298.0
Number of Scans	16
Receiver Gain	161
Relaxation Delay	1.0000
Pulse Width	10.7700
Spectrometer Frequency	600.32
Nucleus	<sup>1</sup> H



23 - Diastereomer 2





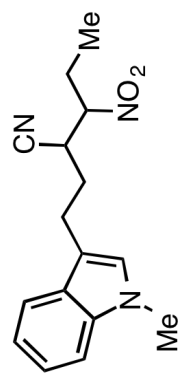
— 10.19  
— 22.41  
— 25.66  
— 29.60  
— 32.85  
— 34.32

— 88.66

— 109.65  
— 111.26  
— 117.39  
— 118.72  
— 119.33  
— 122.14  
— 127.28  
— 127.34

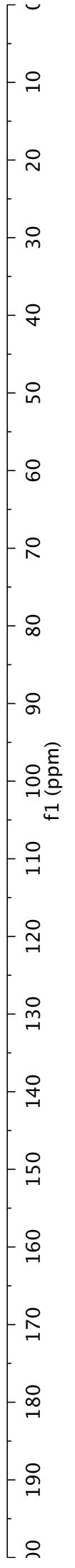
— 137.40

Parameter	Value
Title	KWS04120-d2-13C.1.fid
Solvent	CDCl3
Temperature	298.0
Number of Scans	2048
Receiver Gain	2050
Relaxation Delay	1.1000
Pulse Width	10.6300
Spectrometer Frequency	150.97
Nucleus	13C

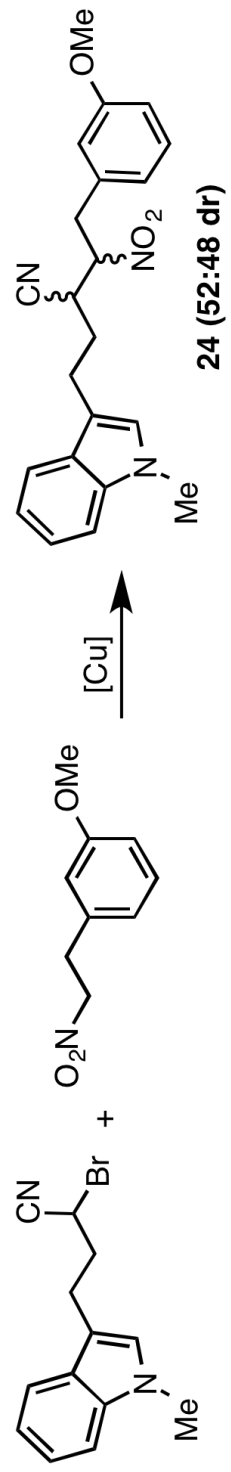


23 - Diastereomer 2

S121

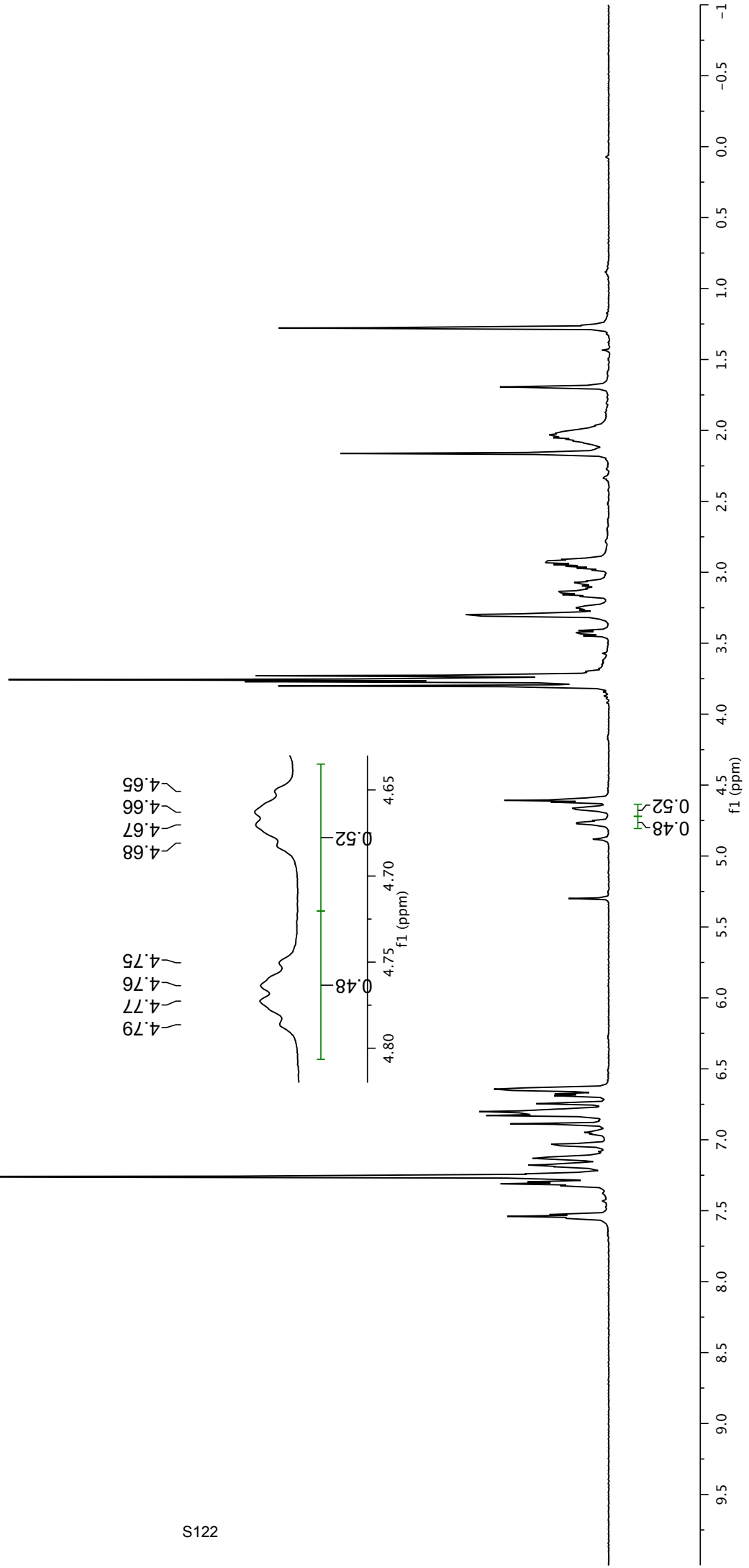


Parameter	Value
Title	KWS04144crd.1.fid
Solvent	CDCl3
Temperature	298.0
Number of Scans	16
Receiver Gain	161
Relaxation Delay	1.0000
Pulse Width	10.7700
Spectrometer Frequency	600.32
Nucleus	<sup>1</sup> H

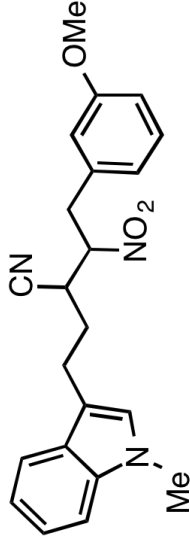


4.79  
4.77  
4.76  
4.75  
4.68  
4.67  
4.66  
4.65

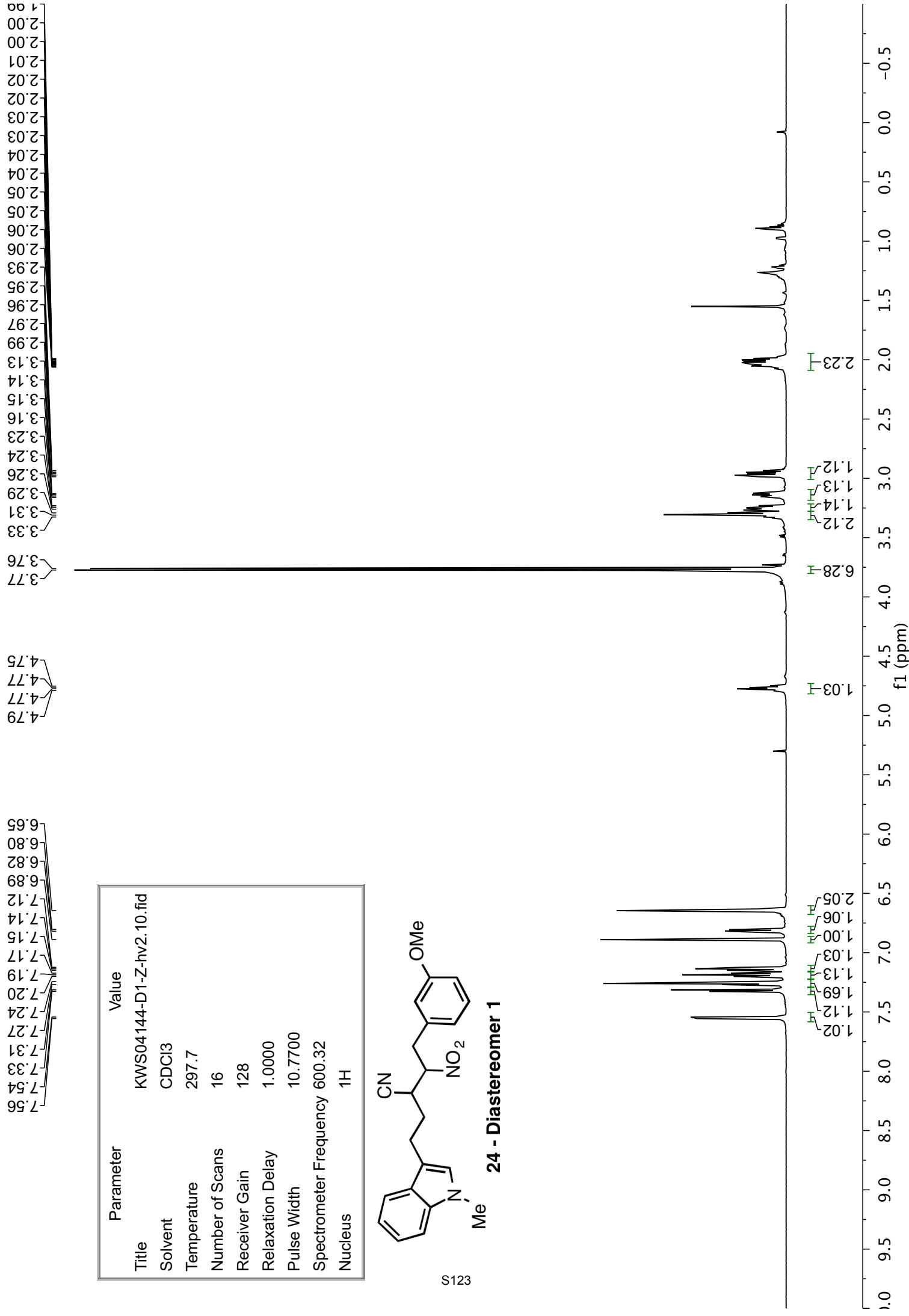
4.79  
4.77  
4.76  
4.75  
4.68  
4.67  
4.66  
4.65



Parameter	Value
Title	KWS04144-D1-Z-hv2.10.fid
Solvent	CDCl3
Temperature	297.7
Number of Scans	16
Receiver Gain	128
Relaxation Delay	1.0000
Pulse Width	10.7700
Spectrometer Frequency	600.32
Nucleus	<sup>1</sup> H

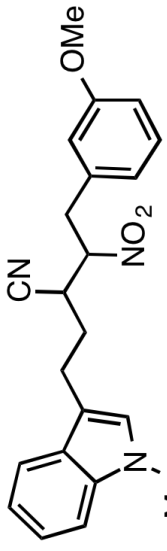


S123



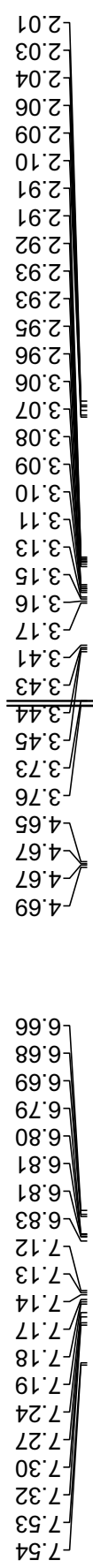
160.12  
 137.32  
 135.30  
 130.23  
 127.39  
 126.97  
 122.11  
 121.08  
 119.33  
 118.70  
 117.77  
 114.63  
 113.50  
 111.25  
 109.59  
 88.72  
 55.36  
 38.18  
 35.03  
 32.82  
 30.04  
 22.39

Parameter	Value
Title	KWS04144-D1-Z-hv2.11.fid
Solvent	CDCl3
Temperature	298.6
Number of Scans	2048
Receiver Gain	2050
Relaxation Delay	1.1000
Pulse Width	10.6300
Spectrometer Frequency	150.97
Nucleus	<sup>13</sup> C

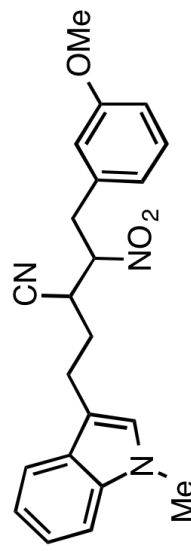


24 - Diastereomer 1

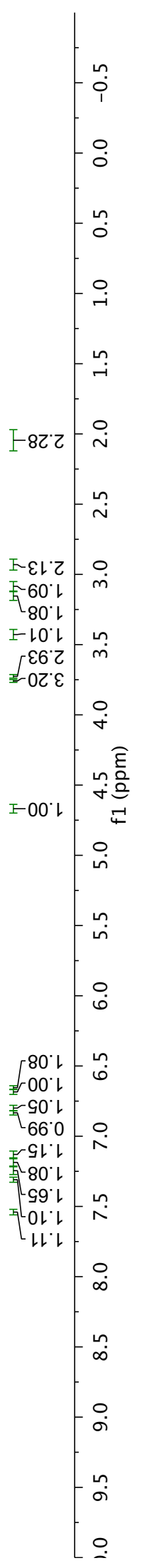
f1 (ppm)



Parameter	Value
Title	KWS04144-D2-Z-hv2.11.fid
Solvent	CDCl3
Temperature	297.8
Number of Scans	16
Receiver Gain	114
Relaxation Delay	1.0000
Pulse Width	10.7700
Spectrometer Frequency	600.32
Nucleus	<sup>1</sup> H

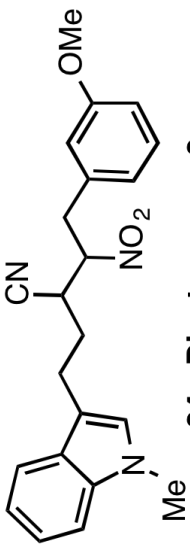


**24 - Diastereomer 2**



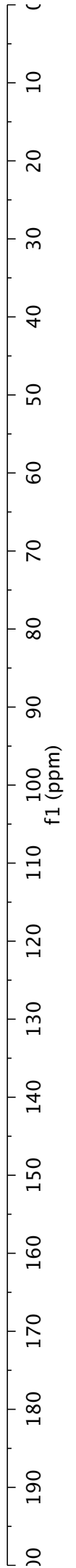
137.33  
135.19  
130.30  
127.28  
122.12  
122.12  
121.08  
119.33  
118.67  
117.28  
114.53  
113.61  
111.17  
109.61

Parameter	Value
Title	KWS04144-D2-Z-hv2.12.fid
Solvent	CDCl3
Temperature	298.6
Number of Scans	2048
Receiver Gain	2050
Relaxation Delay	1.1000
Pulse Width	10.6300
Spectrometer Frequency	150.97
Nucleus	<sup>13</sup> C

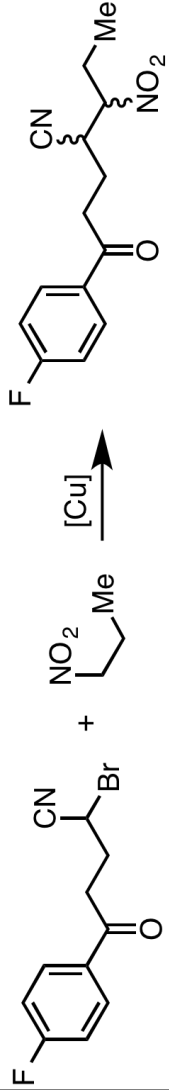


24 - Diastereomer 2

87.77  
55.36  
38.31  
38.31  
33.81  
32.77  
29.84  
22.28



Parameter	Value
Title	KWS04089crd-2.1.fid
Solvent	CDCl3
Temperature	298.0
Number of Scans	8
Receiver Gain	181
Relaxation Delay	1.0000
Pulse Width	10.7700
Spectrometer Frequency	600.32
Nucleus	<sup>1</sup> H

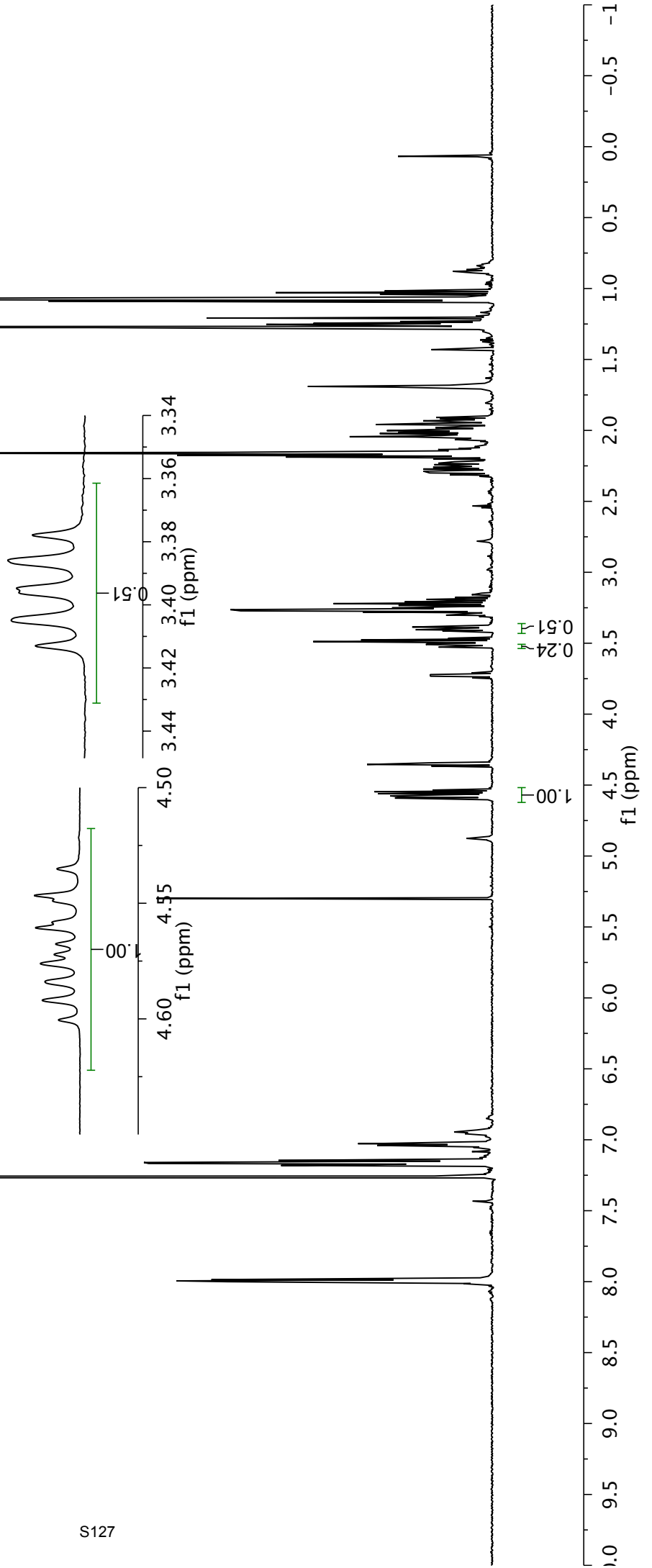


25 (51:49 dr)

4.60  
4.59  
4.58  
4.58  
4.57  
4.57  
4.56  
4.56  
4.55  
4.55  
4.54  
3.41  
3.40  
3.40  
3.39  
3.39  
3.38

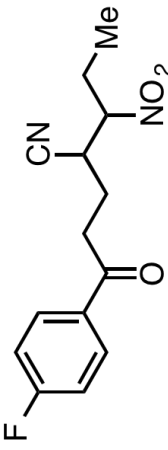
4.60  
4.59  
4.58  
4.58  
4.57  
4.57  
4.56  
4.56  
4.55  
4.55  
4.54

3.41  
3.40  
3.40  
3.39  
3.39  
3.38



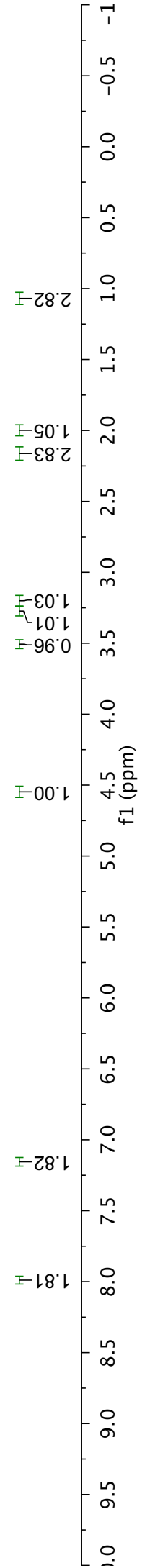
8.00  
7.99  
7.99  
7.98  
7.98  
7.17  
7.17  
7.16  
7.15  
7.14  
4.57  
4.56  
4.55  
4.54  
4.54  
4.53  
3.52  
3.52  
3.51  
3.50  
3.50  
3.49  
3.49  
3.29  
3.29  
3.28  
3.27  
3.26  
3.26  
3.25  
3.23  
3.22  
3.21  
3.20  
3.19  
3.18  
2.20  
2.19  
2.17  
2.16  
2.16  
2.15  
2.15  
2.14  
2.13  
2.02  
2.02  
2.01  
2.01  
2.01  
2.00  
2.00  
2.00  
1.99  
1.99  
1.98  
1.98  
1.97  
1.09  
1.07  
1.06

Parameter	Value
Title	KWS04089-D1-hv.1.fid
Solvent	CDCl3
Temperature	298.0
Number of Scans	8
Receiver Gain	228
Relaxation Delay	1.0000
Pulse Width	10.7700
Spectrometer Frequency	600.32
Nucleus	<sup>1</sup> H



25 - Diastereomer 1

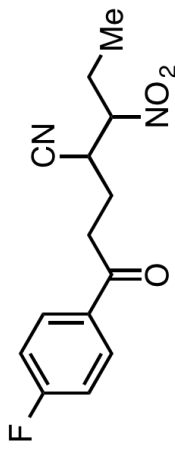
S128







Parameter	Value
Title	KWS04089-D1-13C.1.fid
Solvent	CDCI3
Temperature	298.0
Number of Scans	2048
Receiver Gain	2050
Relaxation Delay	1.1000
Pulse Width	10.6300
Spectrometer Frequency	150.97
Nucleus	13C

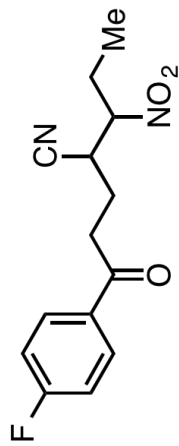


25 - Diastereomer 1

6129

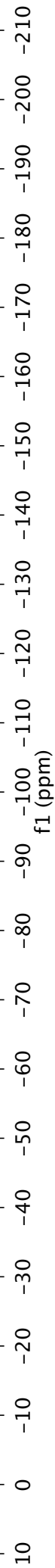
—103.95

Parameter	Value
Title	KWS04089-D1-hv.2.fid
Solvent	CDCl <sub>3</sub>
Temperature	298.0
Number of Scans	16
Receiver Gain	406
Relaxation Delay	3.0000
Pulse Width	11.6200
Spectrometer Frequency	564.81
Nucleus	<sup>19</sup> F

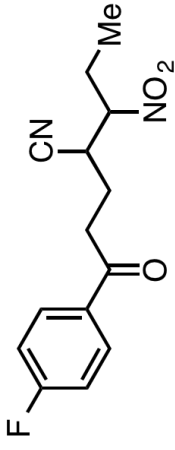


25 - Diastereomer 1

S130

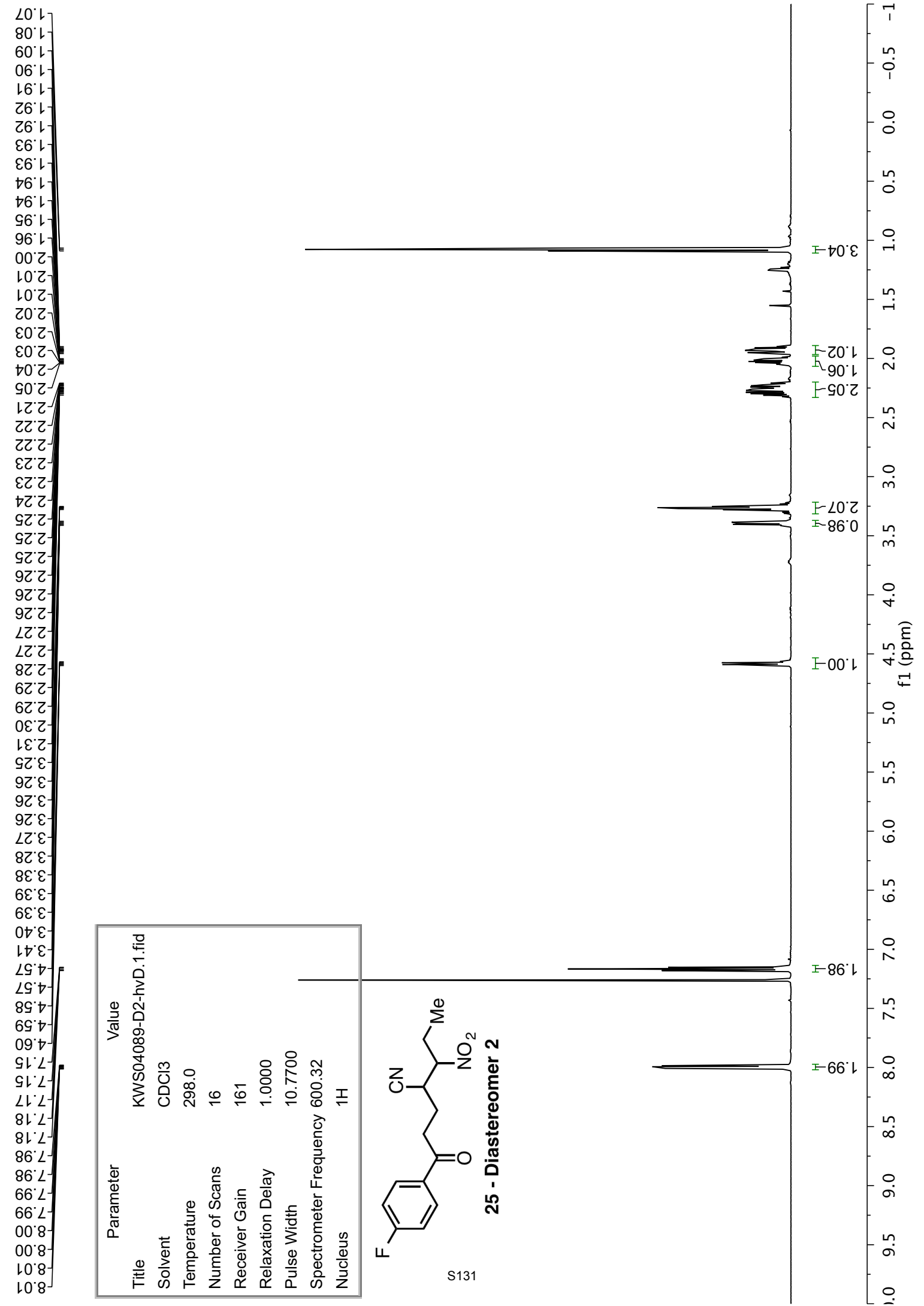


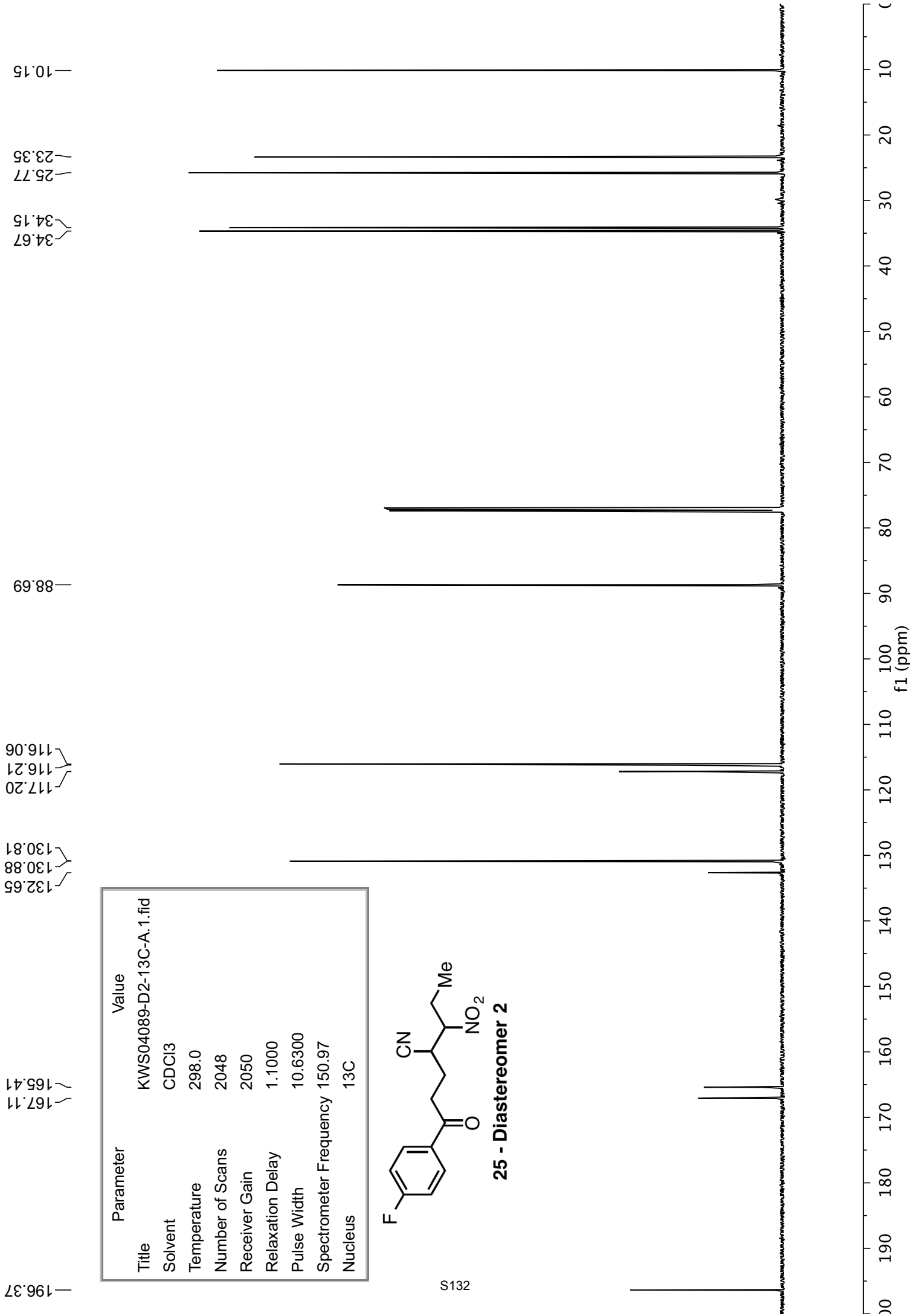
Parameter	Value
Title	KWS04089-D2-hvD.1.fid
Solvent	CDCl3
Temperature	298.0
Number of Scans	16
Receiver Gain	161
Relaxation Delay	1.0000
Pulse Width	10.7700
Spectrometer Frequency	600.32
Nucleus	<sup>1</sup> H



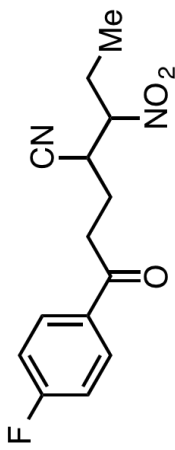
25 - Diastereomer 2

S131





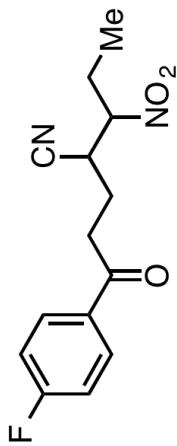
Parameter	Value
Title	KWS04089-D2-13C-A.1.fid
Solvent	CDCl3
Temperature	298.0
Number of Scans	2048
Receiver Gain	2050
Relaxation Delay	1.1000
Pulse Width	10.6300
Spectrometer Frequency	150.97
Nucleus	13C



25 - Diastereomer 2

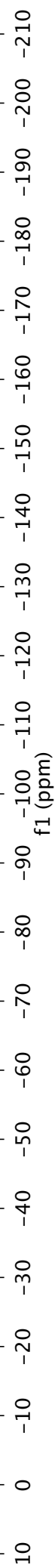
-103.68

Parameter	Value
Title	KWS-04089-D2-hvD.1.fid
Solvent	CDCl <sub>3</sub>
Temperature	298.0
Number of Scans	16
Receiver Gain	406
Relaxation Delay	3.0000
Pulse Width	11.6200
Spectrometer Frequency	564.81
Nucleus	<sup>19</sup> F

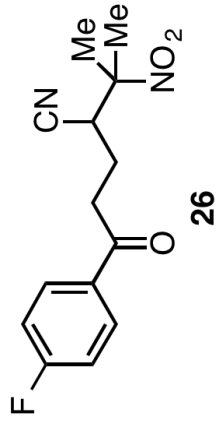


25 - Diastereomer 2

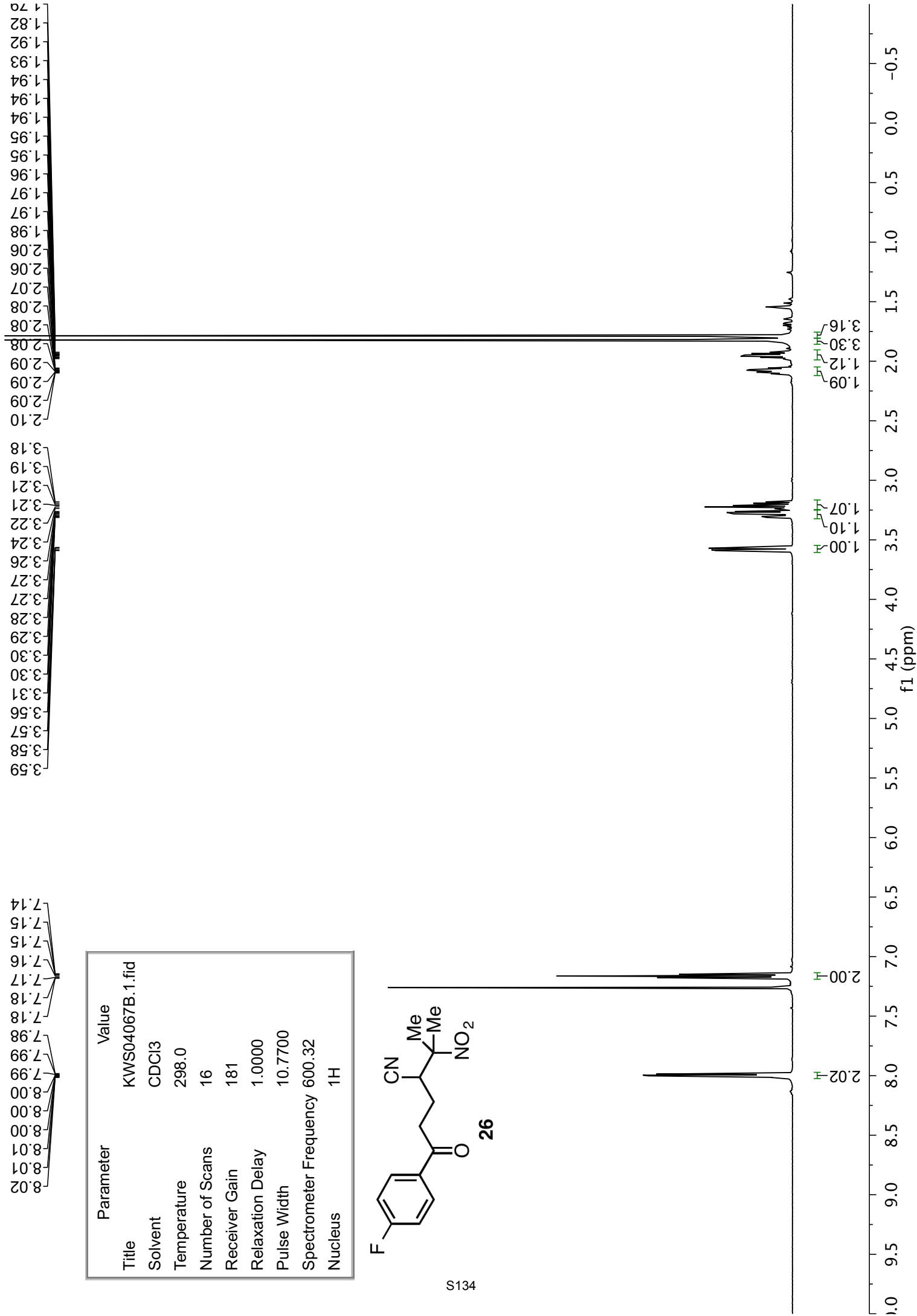
S133



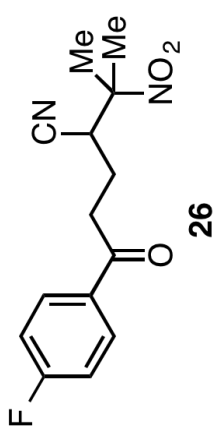
Parameter	Value
Title	KWS04067B.1.fid
Solvent	CDCl3
Temperature	298.0
Number of Scans	16
Receiver Gain	181
Relaxation Delay	1.0000
Pulse Width	10.7700
Spectrometer Frequency	600.32
Nucleus	<sup>1</sup> H



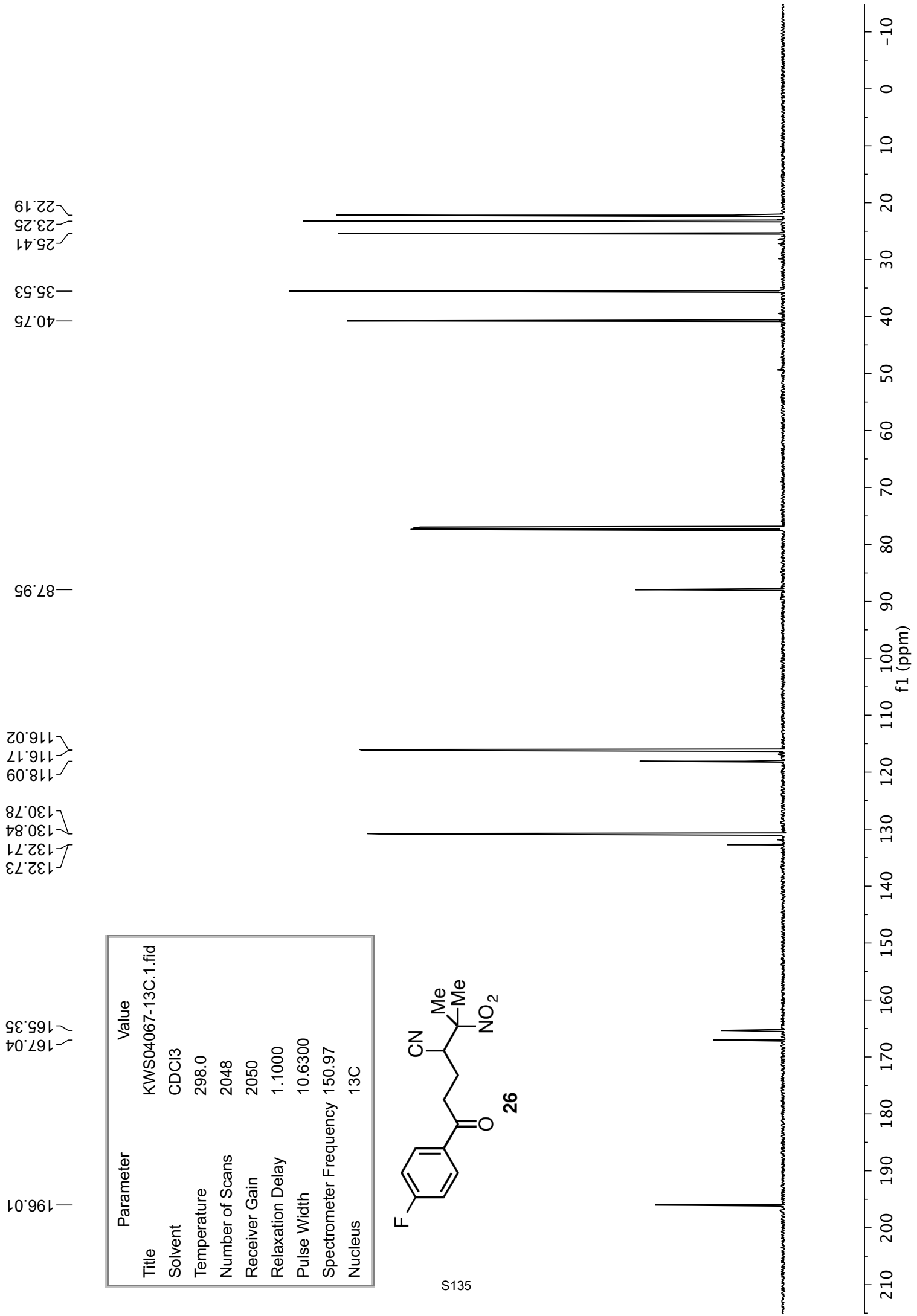
S134



Parameter	Value
Title	KWS04067-13C.1.fid
Solvent	CDCI3
Temperature	298.0
Number of Scans	2048
Receiver Gain	2050
Relaxation Delay	1.1000
Pulse Width	10.6300
Spectrometer Frequency	150.97
Nucleus	<sup>13</sup> C

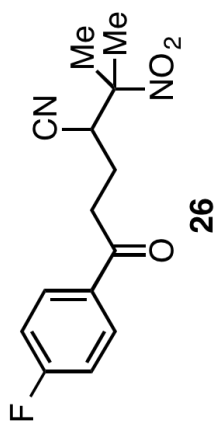


S135

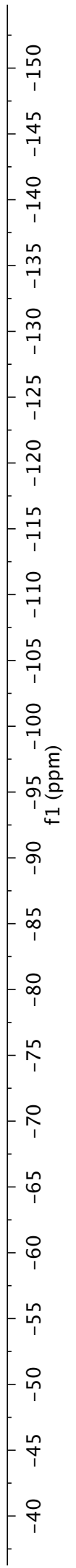


—103.95

Parameter	Value
Title	KWS04067-hv.2.fid
Solvent	CDCl3
Temperature	298.0
Number of Scans	16
Receiver Gain	406
Relaxation Delay	3.0000
Pulse Width	11.6200
Spectrometer Frequency	564.81
Nucleus	<sup>19</sup> F

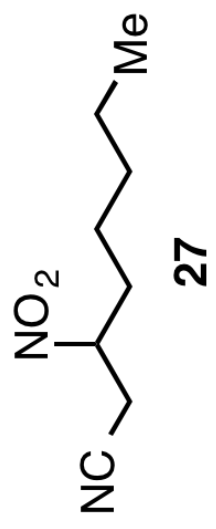


S136

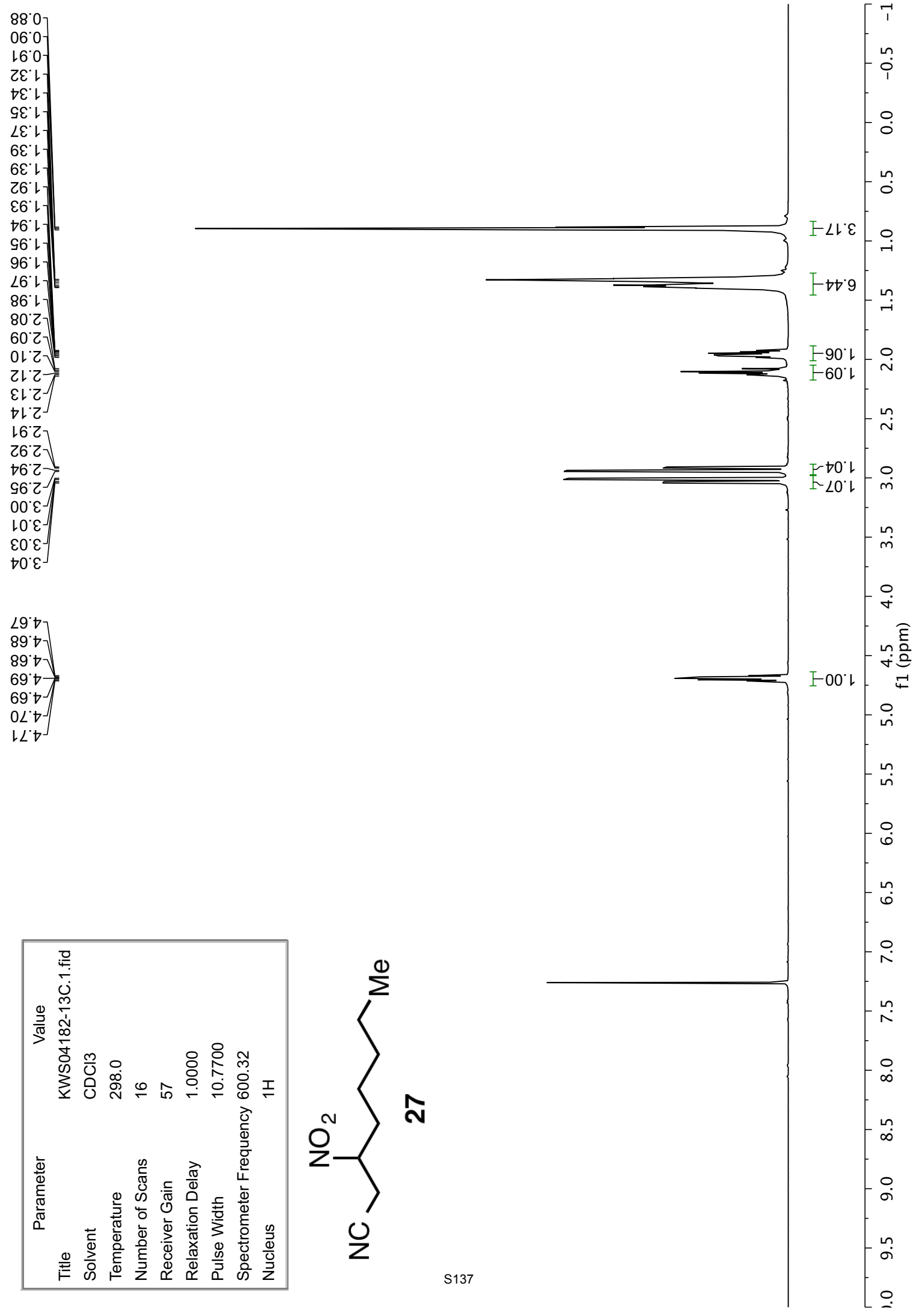




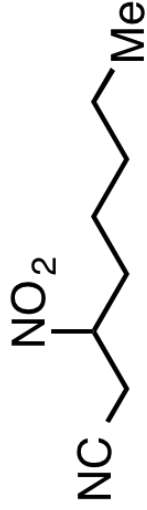
Parameter	Value
Title	KWS04182-13C.1.fid
Solvent	CDCl3
Temperature	298.0
Number of Scans	16
Receiver Gain	57
Relaxation Delay	1.0000
Pulse Width	10.7700
Spectrometer Frequency	600.32
Nucleus	<sup>1</sup> H



S137

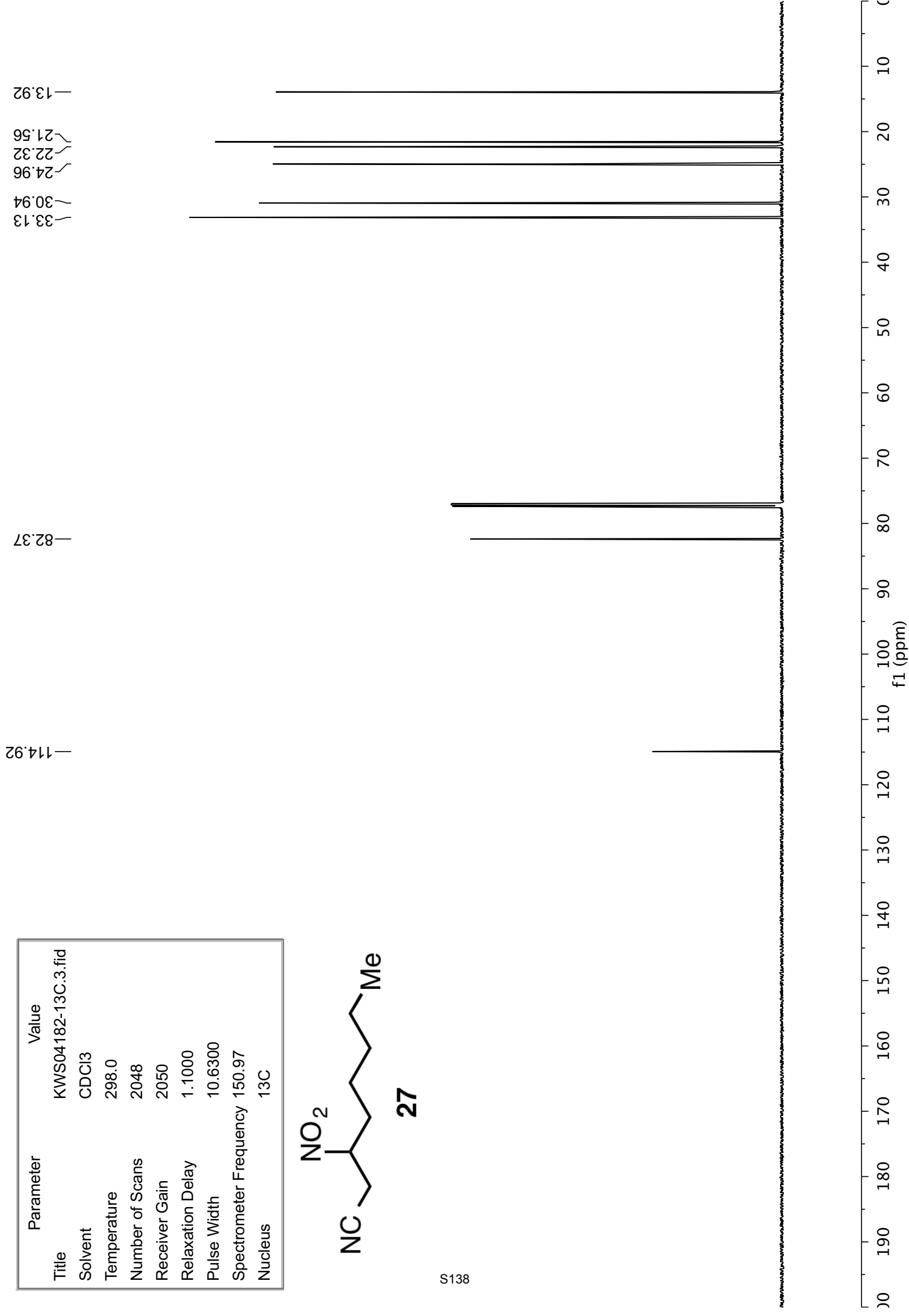


Parameter	Value
Title	KWS04182-13C.3.fid
Solvent	CDCl <sub>3</sub>
Temperature	298.0
Number of Scans	2048
Receiver Gain	2050
Relaxation Delay	1.1000
Pulse Width	10.6300
Spectrometer Frequency	150.97
Nucleus	<sup>13</sup> C



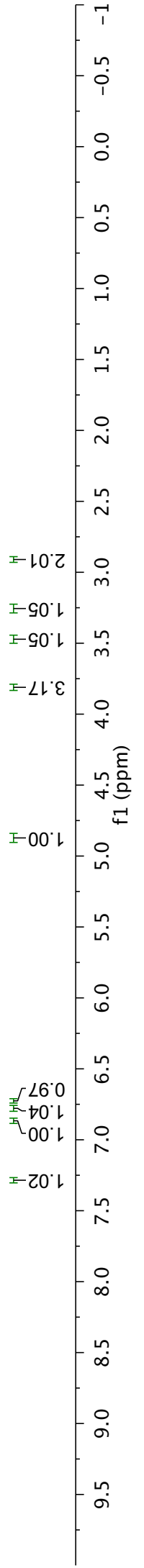
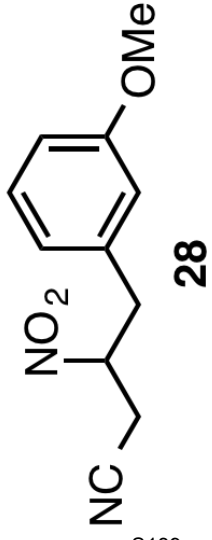
27

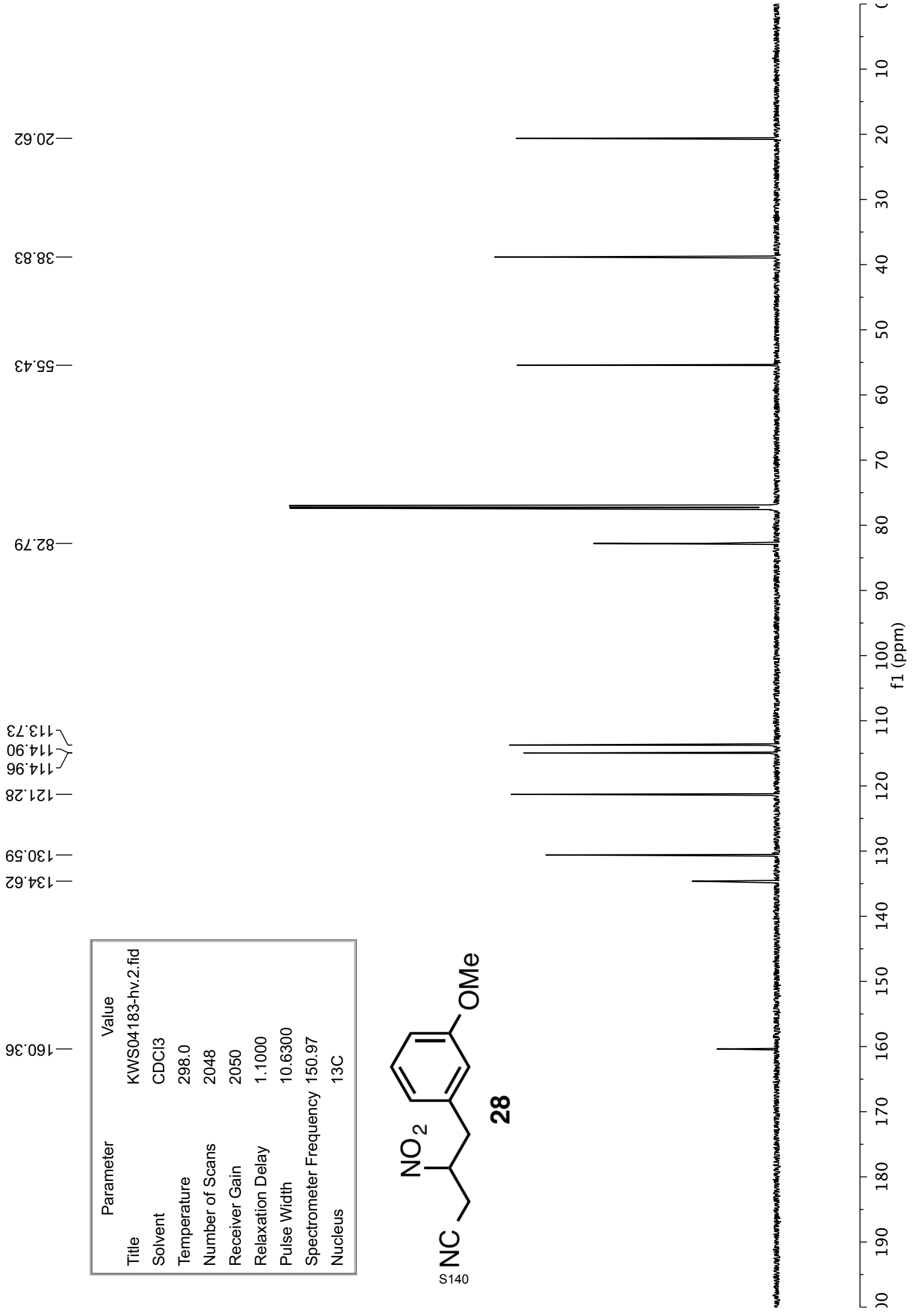
815



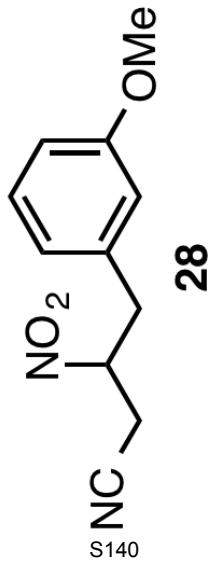
7.29  
7.28  
7.27  
6.87  
6.87  
6.86  
6.86  
6.86  
6.78  
6.77  
6.73  
6.72  
4.89  
4.88  
4.88  
4.87  
4.87  
4.86  
4.86  
4.85  
3.81  
3.48  
3.47  
3.46  
3.45  
3.27  
3.26  
3.25  
3.24  
2.91  
2.90

Parameter	Value
Title	KWS04183-hv.1.fid
Solvent	CDCl3
Temperature	298.0
Number of Scans	16
Receiver Gain	161
Relaxation Delay	1.0000
Pulse Width	10.7700
Spectrometer Frequency	600.32
Nucleus	<sup>1</sup> H



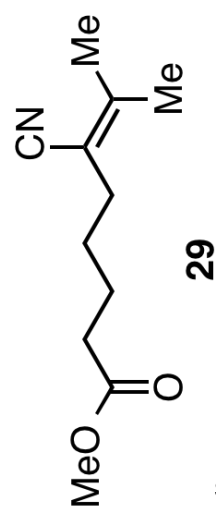


Parameter	Value
Title	KWS04183-hv.2.fid
Solvent	CDCl3
Temperature	298.0
Number of Scans	2048
Receiver Gain	2050
Relaxation Delay	1.1000
Pulse Width	10.6300
Spectrometer Frequency	150.97
Nucleus	13C

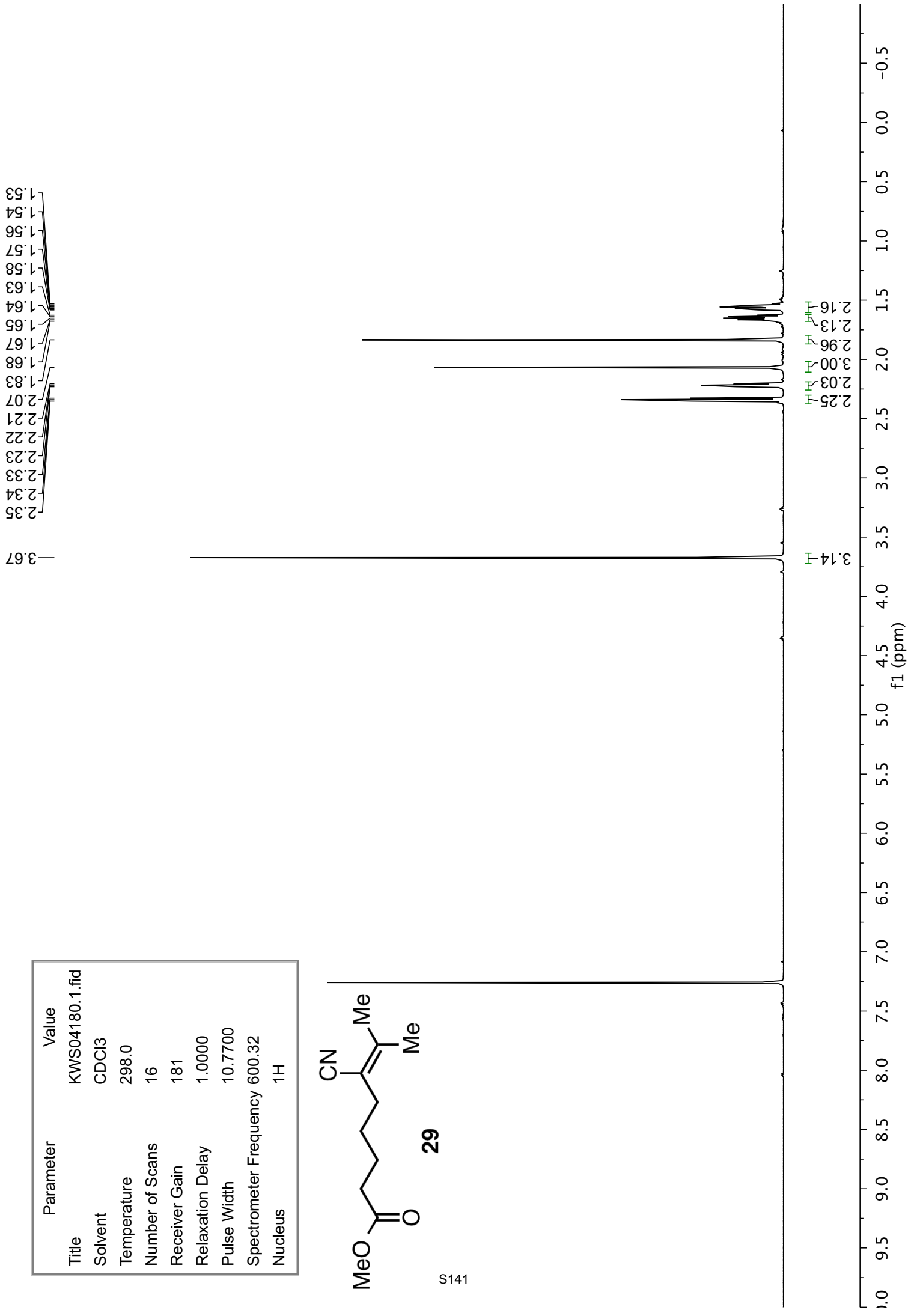


0149

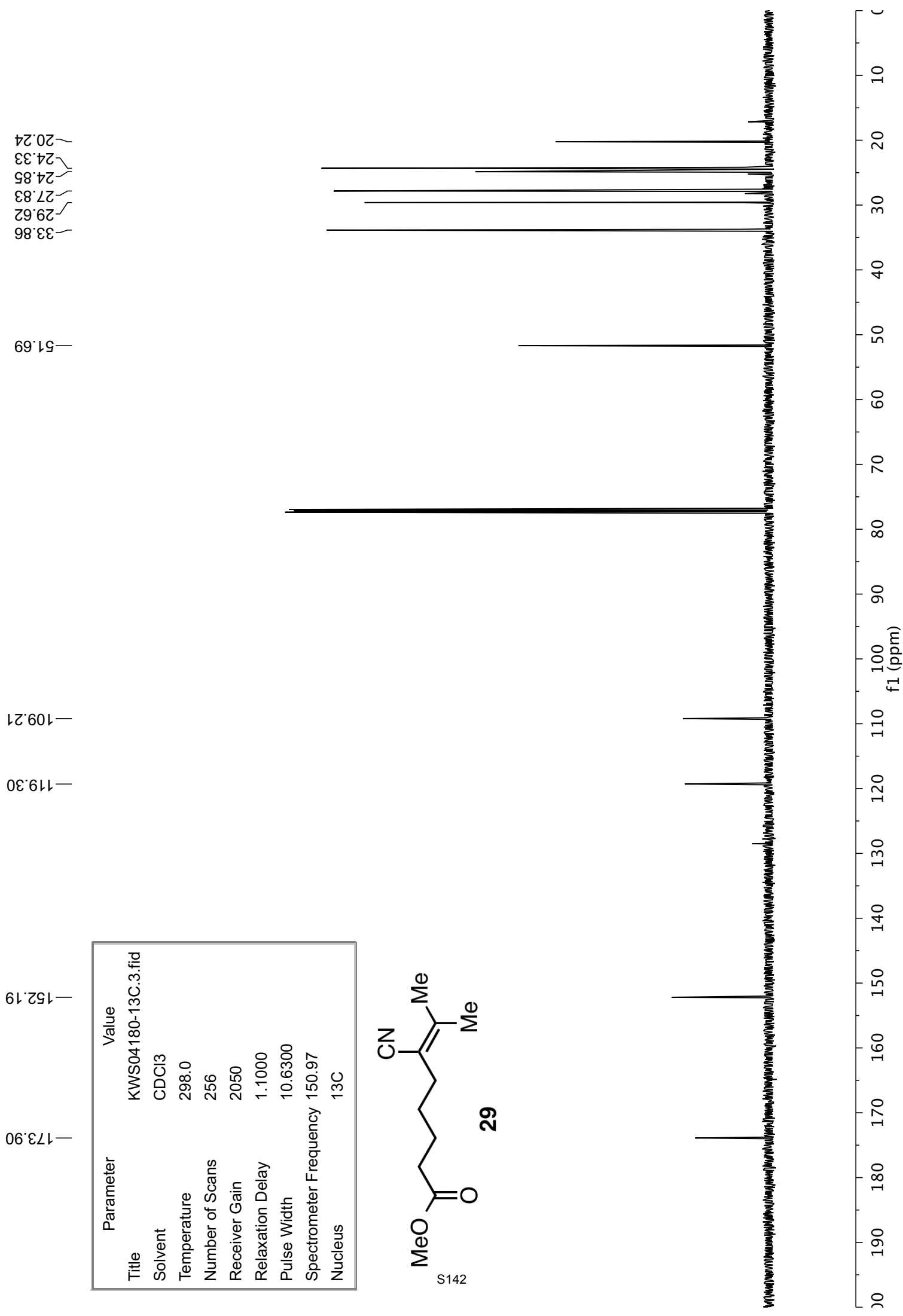
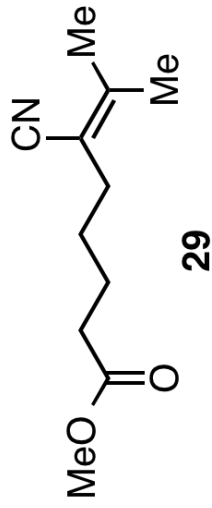
Parameter	Value
Title	KWS04180.1.fid
Solvent	CDCl3
Temperature	298.0
Number of Scans	16
Receiver Gain	181
Relaxation Delay	1.0000
Pulse Width	10.7700
Spectrometer Frequency	600.32
Nucleus	<sup>1</sup> H



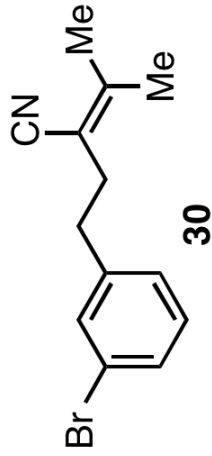
S141



Parameter	Value
Title	KWS04180-13C.3.fid
Solvent	CDCl3
Temperature	298.0
Number of Scans	256
Receiver Gain	2050
Relaxation Delay	1.1000
Pulse Width	10.6300
Spectrometer Frequency	150.97
Nucleus	13C



Parameter	Value
Title	KWS04181-13C.1.fid
Solvent	CDCl3
Temperature	298.0
Number of Scans	16
Receiver Gain	161
Relaxation Delay	1.0000
Pulse Width	10.7700
Spectrometer Frequency	600.32
Nucleus	<sup>1</sup> H

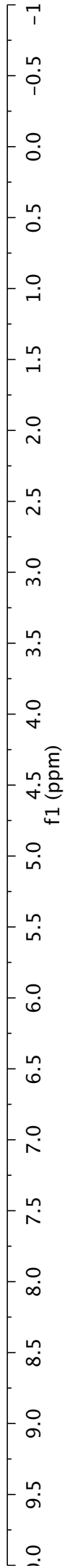


7.35  
7.34  
7.17  
7.16  
7.14  
7.12  
7.11

2.81  
2.80  
2.78  
2.49  
2.48  
2.47  
2.05  
1.66

1.93  
0.99  
1.03

2.01  
2.00  
2.97  
2.94

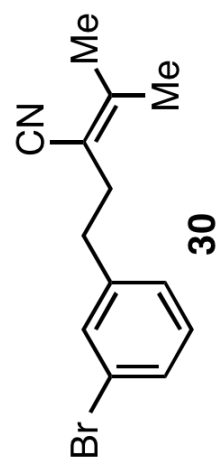


34.12  
31.85  
24.87  
20.12

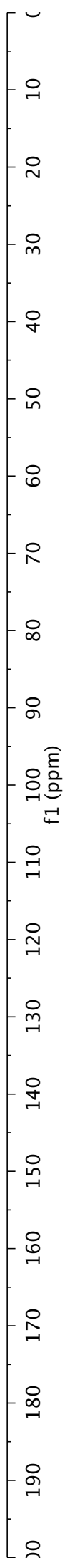
131.68  
130.18  
129.59  
127.36  
122.61  
119.18  
108.30

153.24  
142.79

Parameter	Value
Title	KWS04181-13C.3.fid
Solvent	CDCl3
Temperature	298.0
Number of Scans	2048
Receiver Gain	2050
Relaxation Delay	1.1000
Pulse Width	10.6300
Spectrometer Frequency	150.97
Nucleus	13C



4144



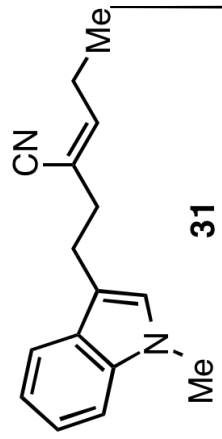


0.80  
0.81  
0.82  
0.96  
0.97  
0.99  
1.97  
1.98  
1.99  
2.01  
2.02  
2.30  
2.31  
2.33  
2.34  
2.35  
2.55  
2.56  
2.57  
2.98  
2.99  
3.00

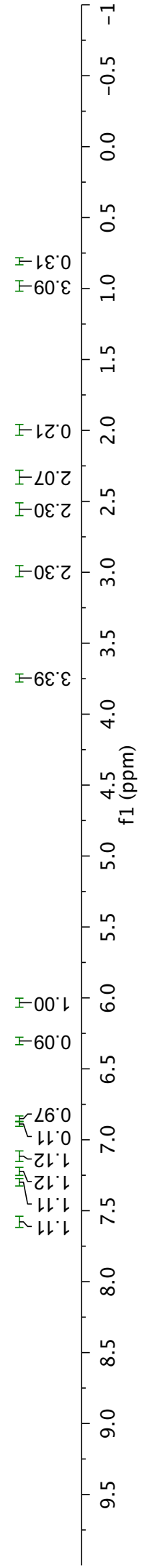
3.74

6.02  
6.03  
6.05  
6.30  
6.31  
6.32  
6.85  
6.89  
7.10  
7.11  
7.13  
7.22  
7.23  
7.24  
7.29  
7.30  
7.57  
7.59  
7.60

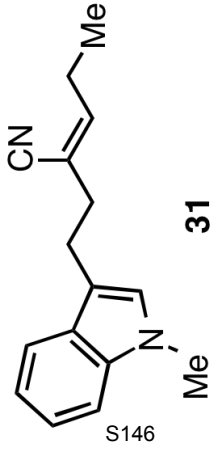
Parameter	Value
Title	KWS04193-hv.1.fid
Solvent	CDCl3
Temperature	298.0
Number of Scans	16
Receiver Gain	161
Relaxation Delay	1.0000
Pulse Width	10.7700
Spectrometer Frequency	600.32
Nucleus	<sup>1</sup> H



S145

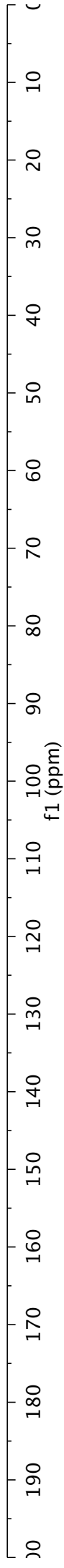


Parameter	Value
Title	KWS04193-13C.1.fid
Solvent	CDCl3
Temperature	298.0
Number of Scans	2048
Receiver Gain	2050
Relaxation Delay	1.1000
Pulse Width	10.6300
Spectrometer Frequency	150.97
Nucleus	13C



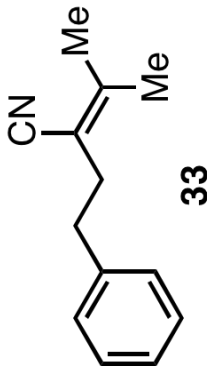
12.88  
13.25  
21.94  
23.84  
24.09  
25.06  
29.71  
32.72  
35.26

109.36  
112.95  
113.66  
117.87  
118.74  
118.88  
121.73  
126.76  
127.68  
137.17  
149.87  
150.29



7.30  
7.29  
7.27  
7.22  
7.21  
7.19  
7.18

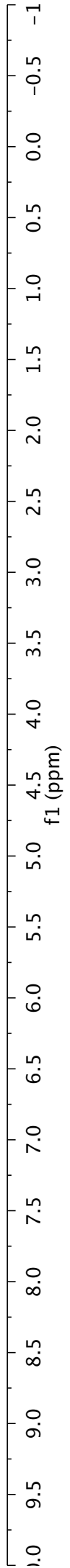
Parameter	Value
Title	KWS04162.1.fid
Solvent	CDCl3
Temperature	298.0
Number of Scans	16
Receiver Gain	203
Relaxation Delay	1.0000
Pulse Width	10.7700
Spectrometer Frequency	600.32
Nucleus	<sup>1</sup> H



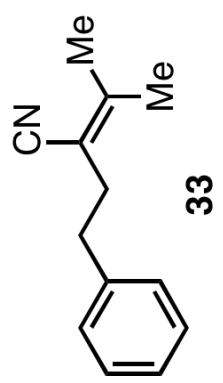
2.84  
2.82  
2.81  
2.51  
2.49  
2.48  
2.04  
1.64

1.92  
2.87

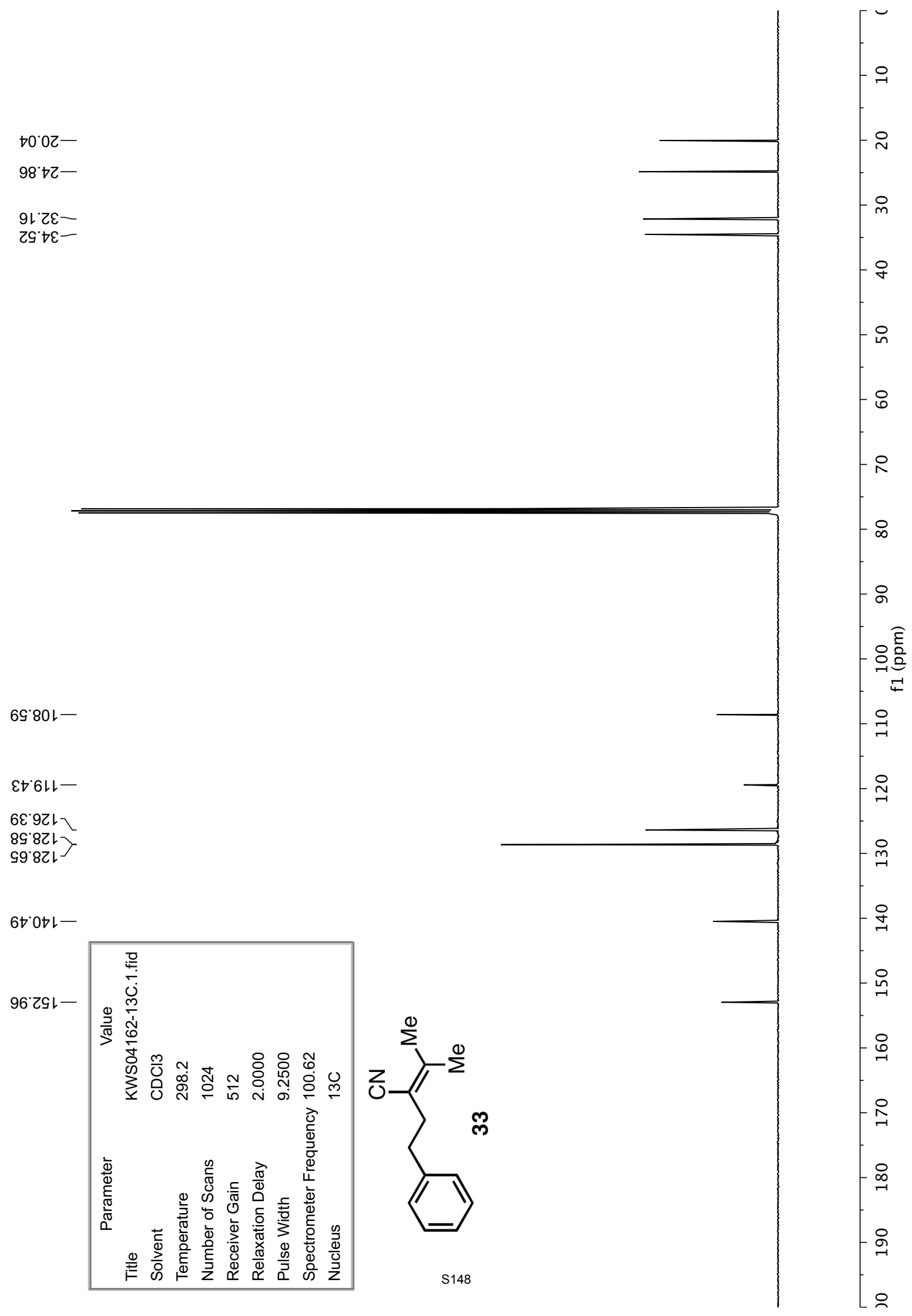
2.00  
2.01  
3.02  
2.93



Parameter	Value
Title	KWS04162-13C.1.fid
Solvent	CDCl3
Temperature	298.2
Number of Scans	1024
Receiver Gain	512
Relaxation Delay	2.0000
Pulse Width	9.2500
Spectrometer Frequency	100.62
Nucleus	<sup>13</sup> C

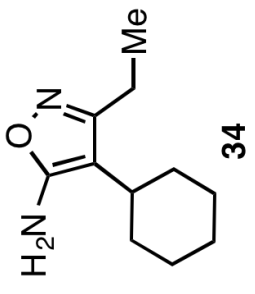


S148

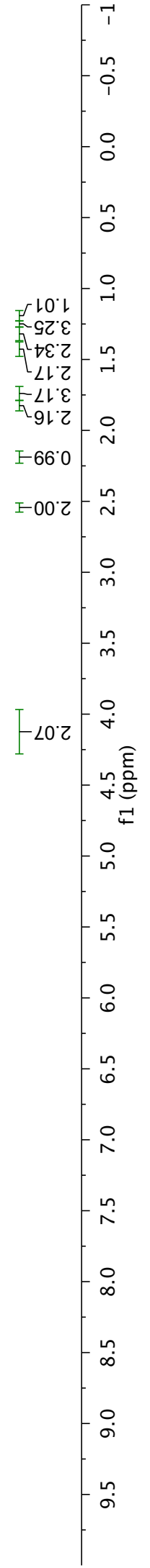


4.12  
2.57  
2.55  
2.54  
2.53  
2.21  
2.21  
2.20  
2.19  
2.19  
2.18  
2.17  
2.17  
2.16  
1.83  
1.81  
1.77  
1.75  
1.72  
1.46  
1.46  
1.44  
1.43  
1.42  
1.41  
1.40  
1.39  
1.36  
1.35  
1.35  
1.33  
1.33  
1.32  
1.31  
1.31  
1.30  
1.29  
1.29  
1.28  
1.26  
1.25  
1.23  
1.22  
1.21  
1.21  
1.20  
1.19  
1.19  
1.18  
1.17  
1.17  
1.16

Parameter	Value
Title	KWS04137-A.1.fid
Solvent	CDCl3
Temperature	298.0
Number of Scans	16
Receiver Gain	128
Relaxation Delay	1.0000
Pulse Width	10.7700
Spectrometer Frequency	600.32
Nucleus	1H

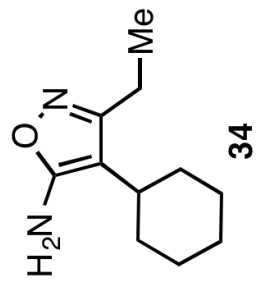


S149



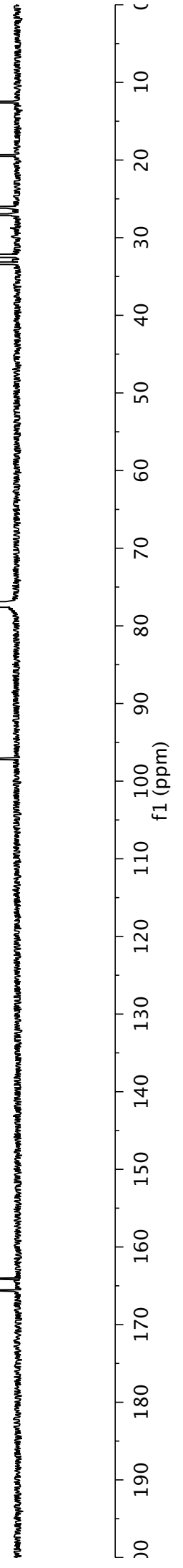
165.55  
 164.06

Parameter	Value
Title	KWS04137-A.2.fid
Solvent	CDCl3
Temperature	298.0
Number of Scans	2048
Receiver Gain	2050
Relaxation Delay	1.1000
Pulse Width	10.6300
Spectrometer Frequency	150.97
Nucleus	13C

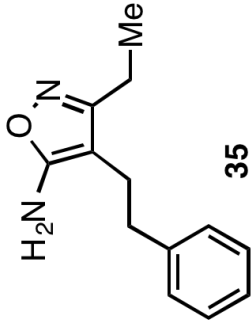


S150

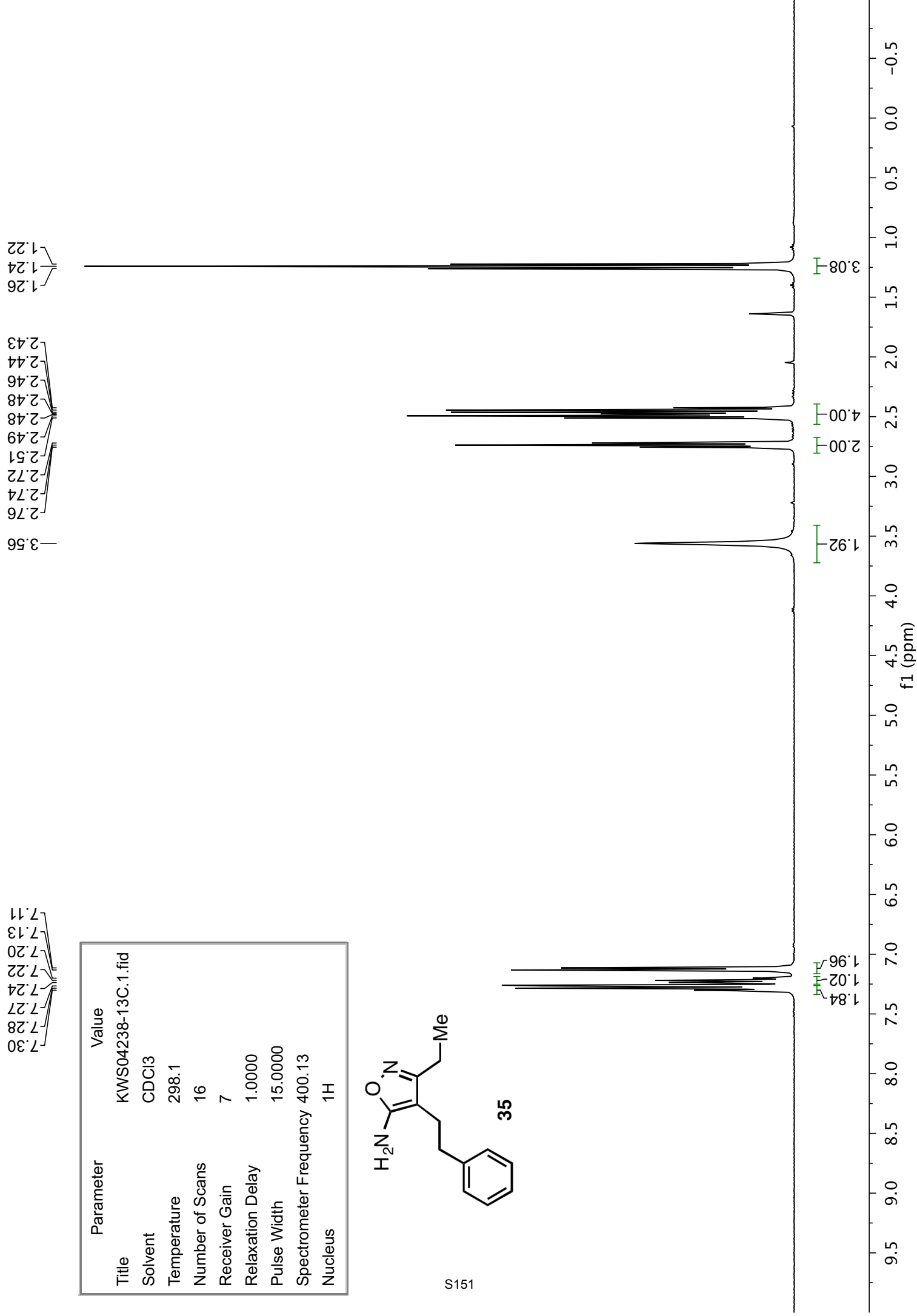
97.15  
 33.28  
 32.36  
 27.05  
 26.16  
 19.44  
 12.52



Parameter	Value
Title	KWS04238-13C.1.fid
Solvent	CDCl3
Temperature	298.1
Number of Scans	16
Receiver Gain	7
Relaxation Delay	1.0000
Pulse Width	15.0000
Spectrometer Frequency	400.13
Nucleus	<sup>1</sup> H



S151



165.86  
165.55

141.49

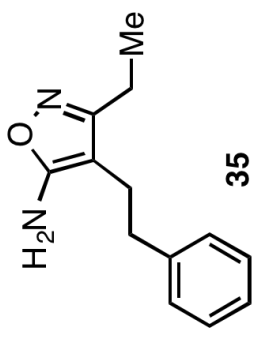
128.91  
128.79  
126.47

91.27

36.17

24.17  
19.01  
12.26

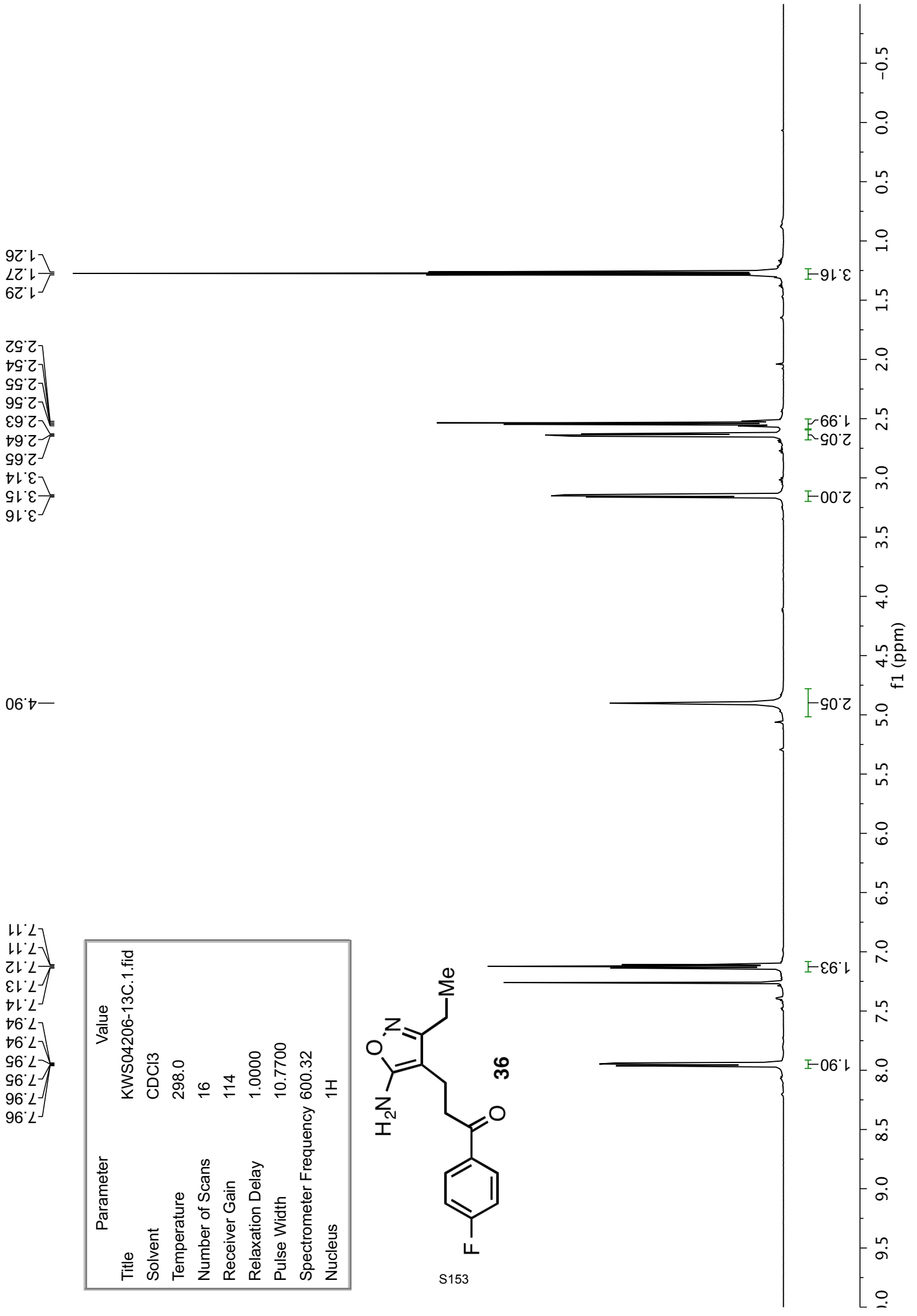
Parameter	Value
Title	KWS04238-13C.2.fid
Solvent	CDCl3
Temperature	298.1
Number of Scans	1024
Receiver Gain	512
Relaxation Delay	2.0000
Pulse Width	9.2500
Spectrometer Frequency	100.62
Nucleus	13C



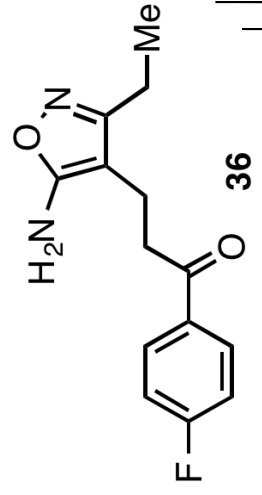
S152







Parameter	Value
Title	KWS04206-13C.1.fid
Solvent	CDCl3
Temperature	298.0
Number of Scans	16
Receiver Gain	114
Relaxation Delay	1.0000
Pulse Width	10.7700
Spectrometer Frequency	600.32
Nucleus	<sup>1</sup> H



S153

198.86  
166.91  
166.36  
165.49  
165.21

133.23  
133.21  
130.81  
130.75

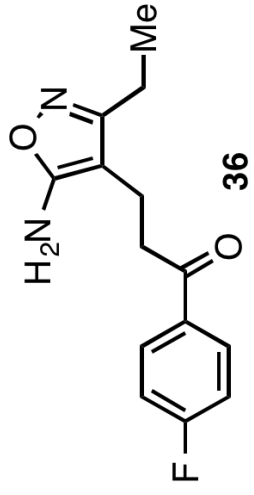
116.02  
115.87

90.93

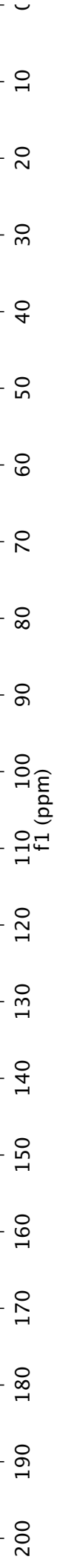
38.66

19.13  
15.08  
12.23

Parameter	Value
Title	KWS04206-13C.3.fid
Solvent	CDCl3
Temperature	298.0
Number of Scans	2048
Receiver Gain	2050
Relaxation Delay	1.1000
Pulse Width	10.6300
Spectrometer Frequency	150.97
Nucleus	13C

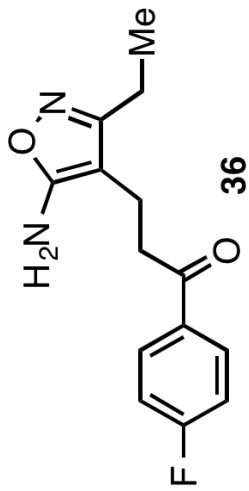


S154

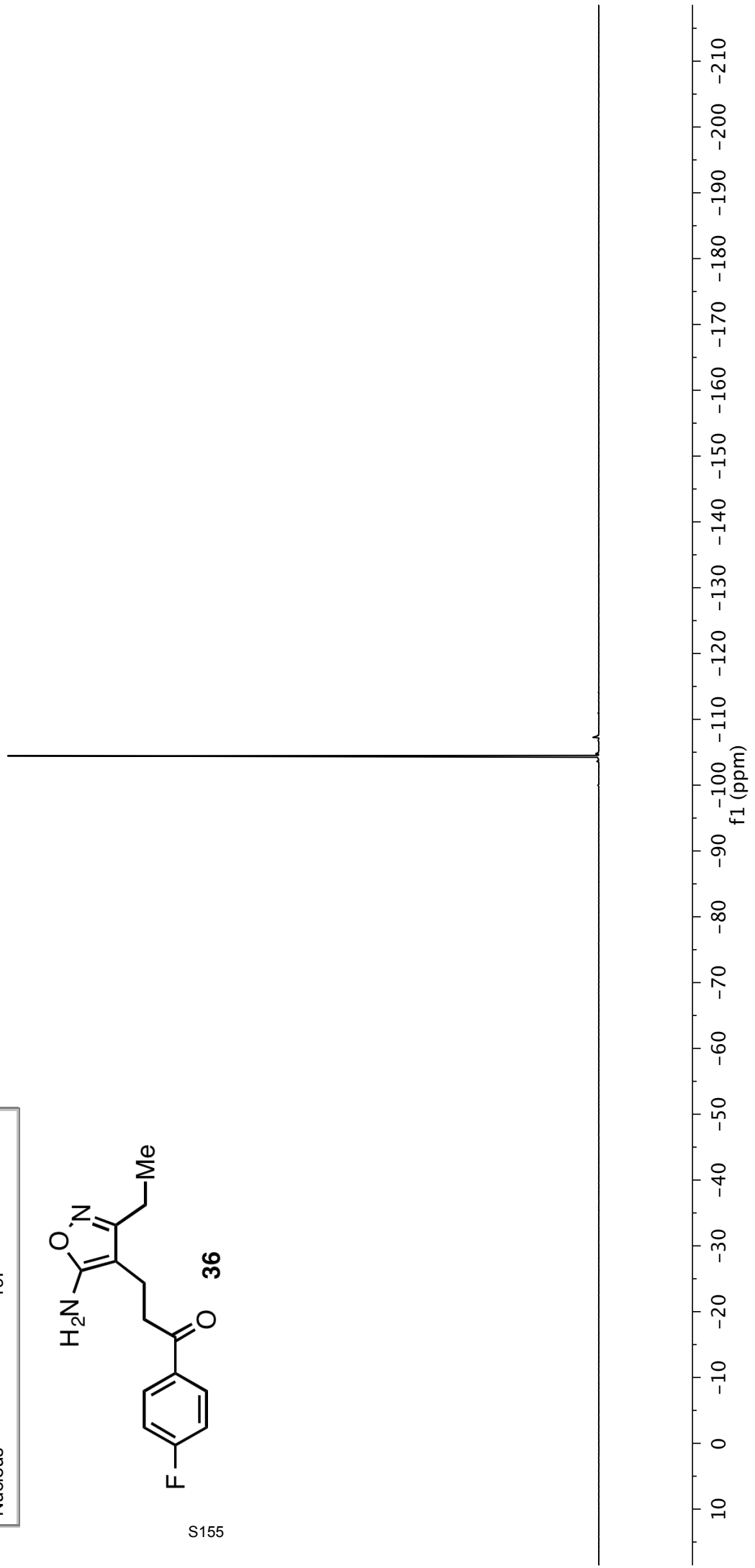


—104.45

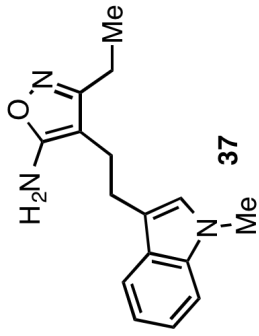
Parameter	Value
Title	KWS04206-13C.2.fid
Solvent	CDCl3
Temperature	298.0
Number of Scans	16
Receiver Gain	456
Relaxation Delay	3.0000
Pulse Width	11.6200
Spectrometer Frequency	564.81
Nucleus	19F



S155



Parameter	Value
Title	KWS04195-hv.1.fid
Solvent	CDCl3
Temperature	298.0
Number of Scans	16
Receiver Gain	228
Relaxation Delay	1.0000
Pulse Width	10.7700
Spectrometer Frequency	600.32
Nucleus	<sup>1</sup> H



S156

1.27  
1.26  
1.24

3.73  
3.55  
2.90  
2.89  
2.88  
2.60  
2.59  
2.57  
2.52  
2.51  
2.50  
2.49

7.59  
7.58  
7.30  
7.29  
7.24  
7.23  
7.22  
7.13  
7.12  
7.11  
6.75

3.10

1.97

2.00

1.87

2.92

0.92

0.97

1.06

0.93

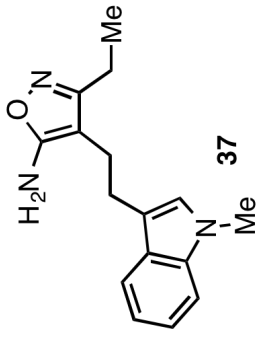
0.94

f1 (ppm)

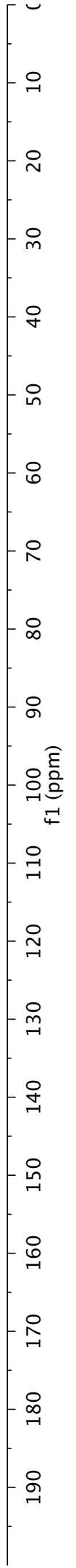
1.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5

165.88  
 165.62  
 137.21  
 127.45  
 127.03  
 121.91  
 119.13  
 118.77  
 113.81  
 109.53  
 92.05  
 32.75  
 25.59  
 22.73  
 19.10  
 12.32

Parameter	Value
Title	KWS04195-13C.3.fid
Solvent	CDCl3
Temperature	298.0
Number of Scans	2048
Receiver Gain	2050
Relaxation Delay	1.1000
Pulse Width	10.6300
Spectrometer Frequency	150.97
Nucleus	13C



S157

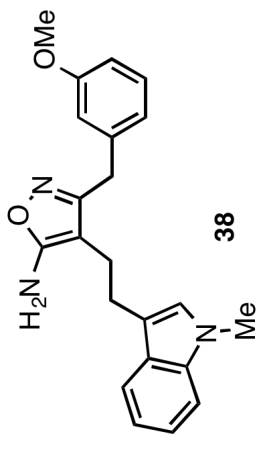


2.57  
2.56  
2.55  
2.44  
2.43  
2.42

3.78  
3.77  
3.71  
3.54

7.46  
7.45  
7.28  
7.27  
7.23  
7.22  
7.21  
7.21  
7.20  
7.10  
7.08  
7.07  
6.84  
6.83  
6.80  
6.79  
6.77  
6.77  
6.57

Parameter	Value
Title	KWS04200-hv.1.fid
Solvent	CDCl3
Temperature	298.0
Number of Scans	16
Receiver Gain	203
Relaxation Delay	1.0000
Pulse Width	10.7700
Spectrometer Frequency	600.32
Nucleus	<sup>1</sup> H

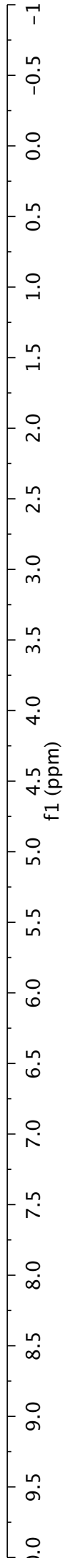


S158

1.95  
2.00

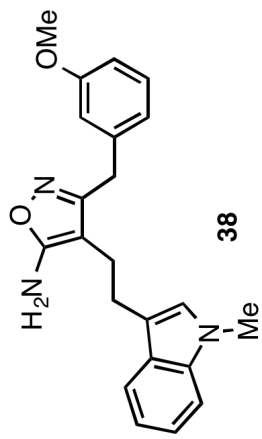
1.91  
2.86  
1.96  
2.98

0.91  
1.83  
0.96  
0.95  
1.90  
0.74  
0.93

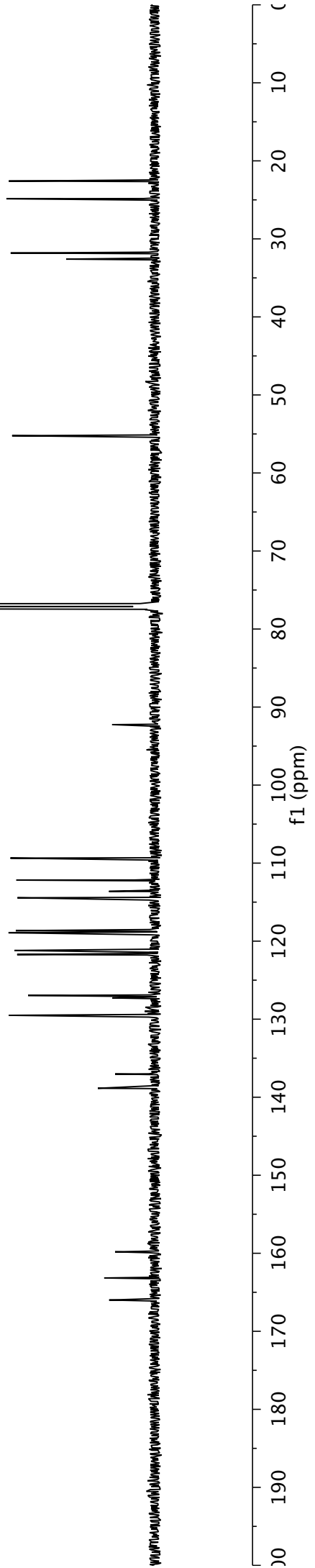


165.99  
 163.17  
 159.82  
 138.86  
 137.03  
 129.50  
 127.28  
 126.96  
 121.72  
 121.19  
 118.92  
 118.65  
 114.44  
 113.62  
 112.17  
 109.36  
 92.25  
 55.23  
 32.60  
 31.81  
 24.85  
 22.59

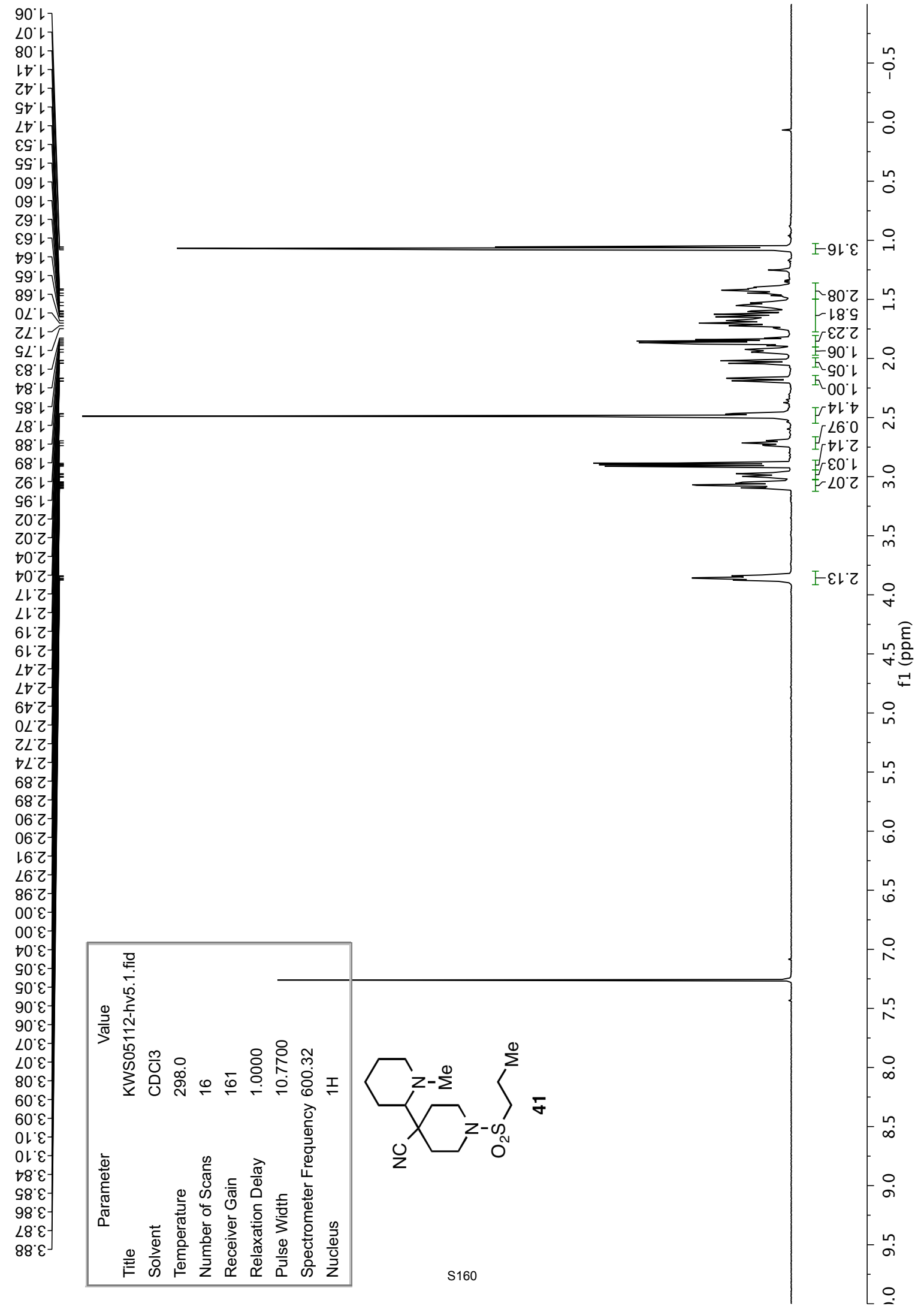
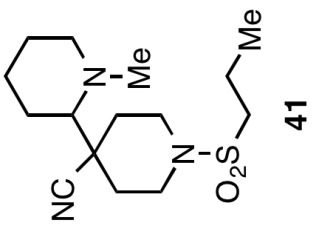
Parameter	Value
Title	KWS04200-hv.2.fid
Solvent	CDCl3
Temperature	298.0
Number of Scans	2048
Receiver Gain	2050
Relaxation Delay	1.1000
Pulse Width	10.6300
Spectrometer Frequency	150.97
Nucleus	13C



S159

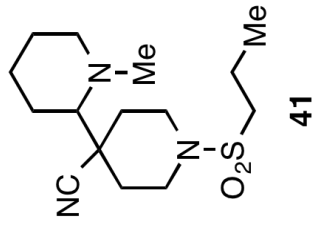


Parameter	Value
Title	KWS05112-hv5.1.fid
Solvent	CDCl3
Temperature	298.0
Number of Scans	16
Receiver Gain	161
Relaxation Delay	1.0000
Pulse Width	10.7700
Spectrometer Frequency	600.32
Nucleus	<sup>1</sup> H

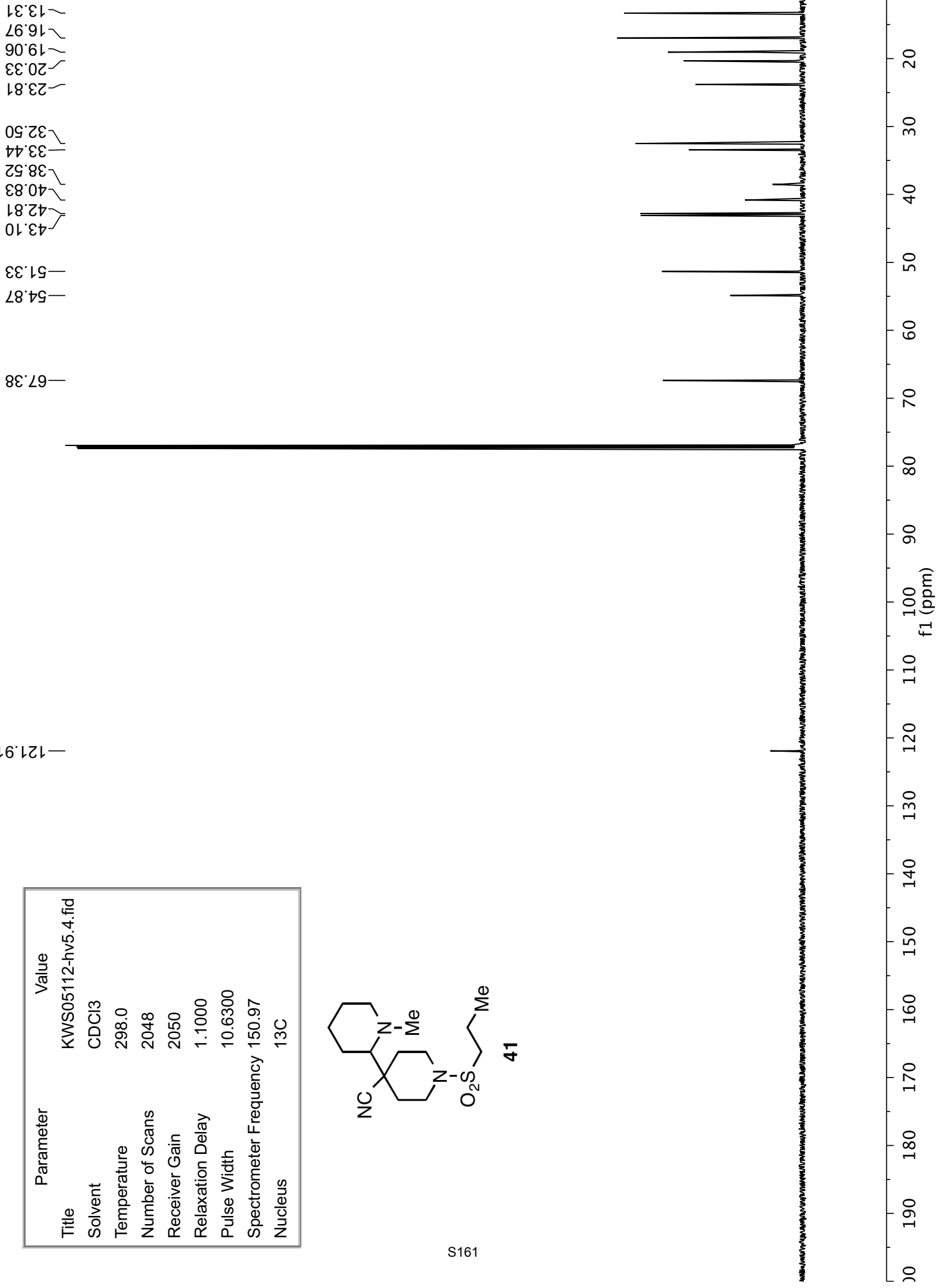




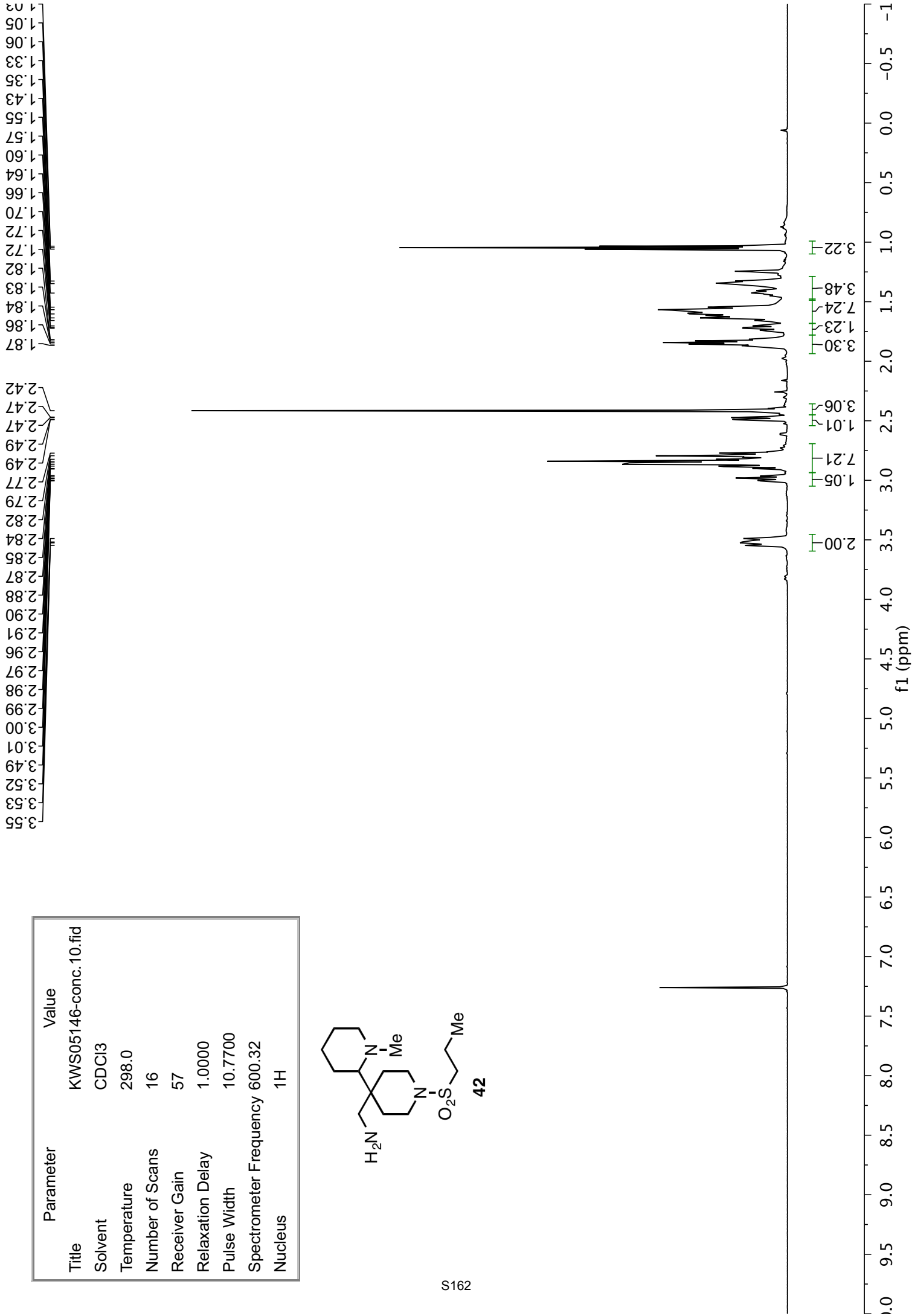
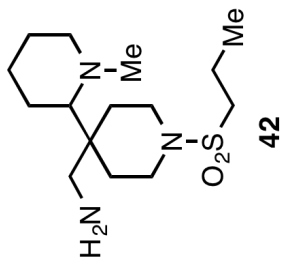
Parameter	Value
Title	KWS05112-hv5.4.fid
Solvent	CDCl3
Temperature	298.0
Number of Scans	2048
Receiver Gain	2050
Relaxation Delay	1.1000
Pulse Width	10.6300
Spectrometer Frequency	150.97
Nucleus	13C



1919



Parameter	Value
Title	KWS05146-conc. 10.fid
Solvent	CDCl3
Temperature	298.0
Number of Scans	16
Receiver Gain	57
Relaxation Delay	1.0000
Pulse Width	10.7700
Spectrometer Frequency	600.32
Nucleus	<sup>1</sup> H

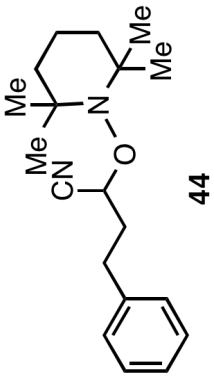




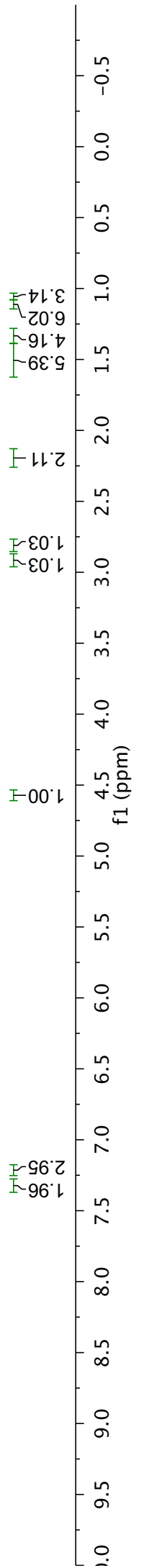
1.06  
1.09  
1.11  
1.32  
1.34  
1.35  
1.41  
1.44  
1.48  
1.49  
1.54  
1.56  
2.15  
2.16  
2.18  
2.19  
2.21  
2.22  
2.24  
2.79  
2.80  
2.81  
2.82  
2.83  
2.84  
2.89  
2.90  
2.91  
2.92  
2.92  
2.93  
2.94  
4.56  
4.57  
4.58  
4.59

7.22  
7.22  
7.23  
7.30  
7.31  
7.32

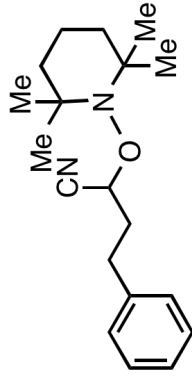
Parameter	Value
Title	KWS05179-hv.10.fid
Solvent	CDCl3
Temperature	297.2
Number of Scans	16
Receiver Gain	57
Relaxation Delay	1.0000
Pulse Width	10.7700
Spectrometer Frequency	600.32
Nucleus	1H



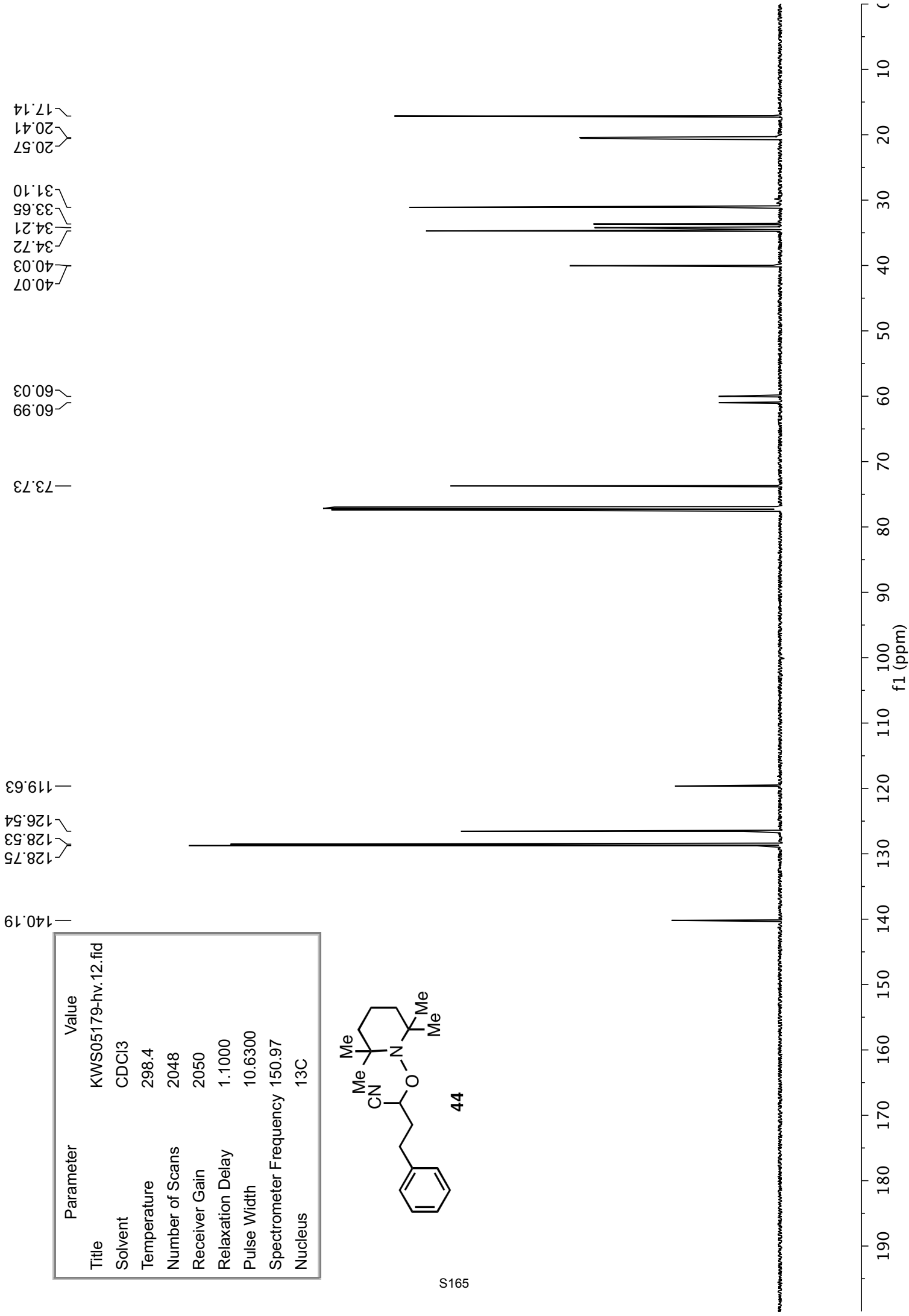
5164



Parameter	Value
Title	KWS05179-hv.12.fid
Solvent	CDCl3
Temperature	298.4
Number of Scans	2048
Receiver Gain	2050
Relaxation Delay	1.1000
Pulse Width	10.6300
Spectrometer Frequency	150.97
Nucleus	<sup>13</sup> C

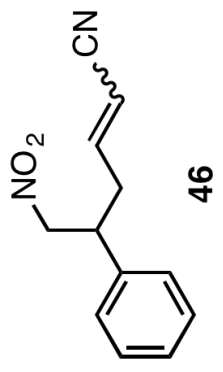


S165

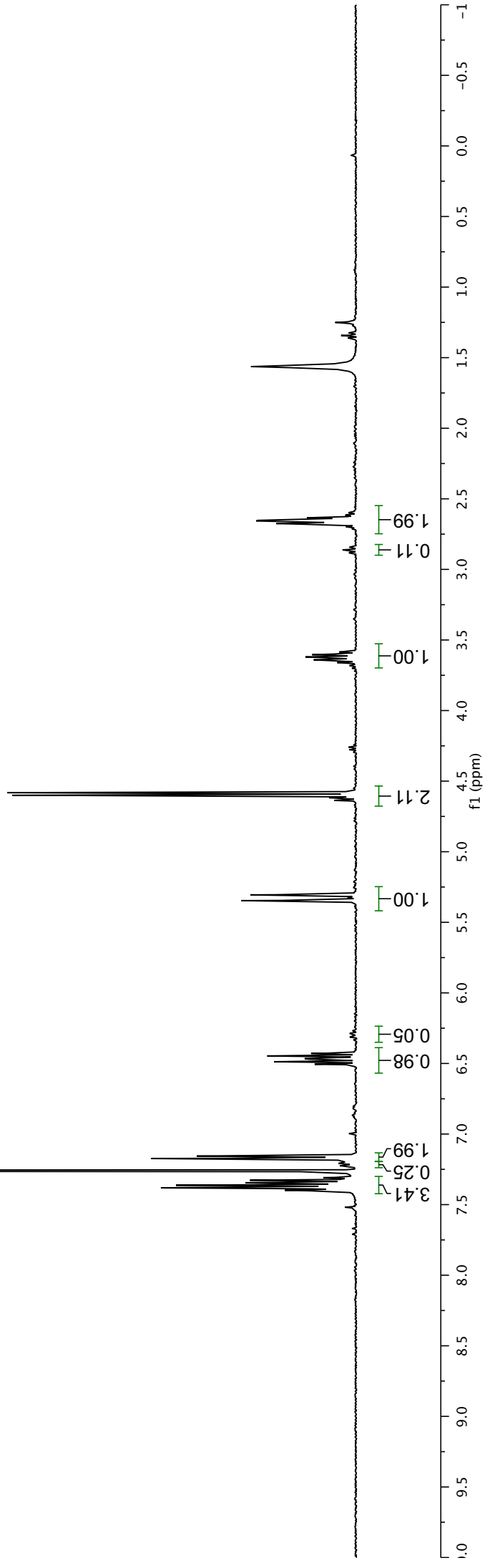


7.40 7.38 7.38 7.36 7.34 7.33 7.18 7.17 7.16 6.51 6.49 6.47 6.47 6.45 6.43 5.35 5.35 5.34 5.31 5.31 5.30 4.64 4.62 4.60 4.58 3.66 3.64 3.62 3.60 3.59 2.68 2.67 2.66 2.66 2.65 2.65 2.64 2.63

Parameter	Value
Title	KWS05055-hv.1.fid
Solvent	CDCl3
Temperature	298.2
Number of Scans	16
Receiver Gain	11
Relaxation Delay	1.0000
Pulse Width	15.0000
Spectrometer Frequency	400.13
Nucleus	<sup>1</sup> H



S166



Parameter	Value
Title	KWS05055cf30-36.2.fid
Solvent	CDCl3
Temperature	300.0
Number of Scans	2048
Receiver Gain	2050
Relaxation Delay	1.1000
Pulse Width	10.6300
Spectrometer Frequency	150.97
Nucleus	<sup>13</sup> C

