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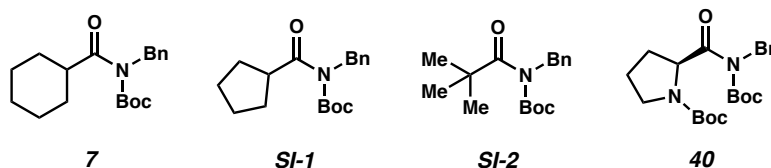
Materials and Methods

Unless stated otherwise, reactions were conducted in flame-dried glassware under an atmosphere of nitrogen and commercially obtained reagents were used as received. Reagent **SI-5** was purchased from Sigma-Aldrich. Reagents **SI-3**, **SI-7**, **SI-9**, **SI-18** and **rac-SI-18** were purchased from Combi-Blocks, Inc. Amines **SI-11**, **SI-15**, **SI-19**, **SI-20**, **SI-21**, **SI-22**, **SI-23**, **8**, **35**, **36** and **37** were purchased from Sigma-Aldrich. Amine **SI-24** was purchased from Spectrum Chemical. Benzylamine was purchased from Sigma-Aldrich. Amines were passed through a plug of basic Alumina, distilled over CaH₂, and stored in an inert atmosphere glovebox prior to use. EDC and HOBt were purchased from Chem-Impex International. DMAP and Boc₂O were purchased from Oakwood Products, Inc. LiHMDS was purchased from Sigma-Aldrich and stored in an inert atmosphere glovebox. **SI-13** was obtained from Sigma-Aldrich and distilled over CaH₂ prior to use. Toluene was purified by distillation and taken through five freeze-pump-thaw cycles prior to use. CH₂Cl₂, NEt₃, THF, DMF, and CH₃CN were pass through activated alumina columns before use. Ni(cod)₂, 1,3-dicyclohexylbenzimidazolium chloride (Benz-ICy•HCl) and 1,3-Bis(2,6-di-*i*-propylphenyl)-4,5-dihydroimidazol-2-ylidene (SIPr) were obtained from Strem Chemicals. Terpyridine and 1,3-dicyclohexylimidazolium chloride (ICy•HCl) were obtained from Sigma Aldrich. 1,3,5-trimethoxybenzene (TMB), hexamethylbenzene (HMB) and NaOtBu were obtained from Alfa Aesar. Reaction temperatures were controlled using an IKAmag temperature modulator, and unless stated otherwise, reactions were performed at room temperature (approximately 23 °C). Thin-layer chromatography (TLC) was conducted with EMD gel 60 F254 pre-coated plates (0.25 mm for analytical chromatography and 0.50 mm for preparative chromatography) and visualized using a combination of UV, anisaldehyde, ceric ammonium molybdate, iodine, vanillin, and potassium permanganate staining techniques. Silicycle Siliaflash P60 (particle size 0.040–0.063 mm) was used for flash column chromatography. ¹H NMR spectra were recorded on Bruker spectrometers (at 500 MHz) and are reported relative to residual solvent signals. Data for ¹H NMR spectra are reported as follows: chemical shift (δ ppm), multiplicity, coupling constant (Hz), and integration. Data for ¹³C NMR are reported in terms of chemical shift (at 125 MHz). IR spectra were recorded on a Perkin-Elmer 100 spectrometer and are reported in terms of frequency absorption (cm⁻¹). High-resolution mass spectra were obtained on Thermo Scientific™ Exactive Mass Spectrometer with DART ID-CUBE. DART-MS spectra were collected on a Thermo Exactive Plus MSD (Thermo Scientific) equipped with an ID-CUBE ion source and a Vapor Interface (IonSense Inc.). Both the source and MSD were controlled by Excalibur software v. 3.0. The analyte was spotted onto OpenSpot sampling cards (IonSense Inc.) using CHCl₃ as the solvent. Ionization was accomplished using UHP He (Airgas Inc.) plasma with no additional ionization agents. The mass calibration was carried out using Pierce LTQ Velos ESI (+) and (-) Ion calibration solutions (Thermo Fisher Scientific). Optical rotations were measured with a Rudolf Autopol III Automatic Polarimeter. Determination of enantiopurity was carried out on an Agilent 1260 HPLC (high performance liquid chromatography) and a Mettler Toledo SFC (supercritical fluid chromatography) using a Daicel ChiralPak OJ-H columns and Daicel ChiralPak IC-H.

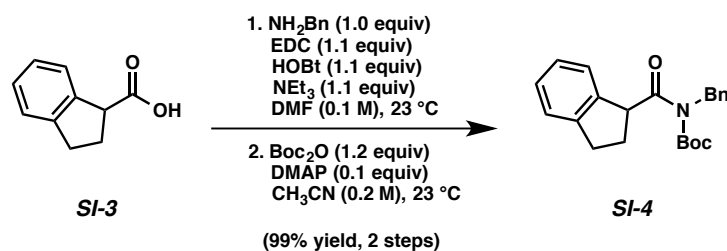
Experimental Procedure

A. Syntheses of Starting Materials

The following amides were synthesized following known protocols: cyclohexylamide **7**,¹ cyclopentylamide **SI-1**,¹ *tert*-butylamide **SI-2**,¹ and **40**.¹



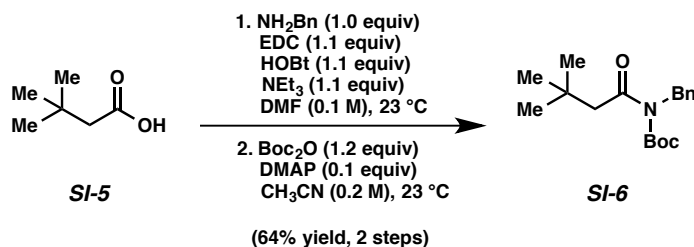
Syntheses for the remaining substrates shown in Figures 2, 3, 5, and 6 are as follows:



Amide SI-4: To a mixture of carboxylic acid **SI-3** (1.0 g, 6.17 mmol, 1.0 equiv), EDC (1.30 g, 6.79 mmol, 1.1 equiv), HOBt (917 mg, 6.79 mmol, 1.1 equiv), triethylamine (0.94 mL, 6.79 mmol, 1.1 equiv), and DMF (61.7 mL, 0.1 M) was added benzylamine (0.74 mL, 6.79 mmol, 1.1 equiv). The resulting mixture was stirred at 23 °C for 12 h, and then diluted with deionized water (50 mL) and EtOAc (50 mL). The layers were separated and the organic layer was washed successively with 1.0 M HCl (50 mL), saturated aqueous NaHCO₃ (50 mL), and brine (50 mL). The organic layer was dried over Na₂SO₄ and concentrated under reduced pressure. The resulting crude solid material was used in the subsequent step without further purification.

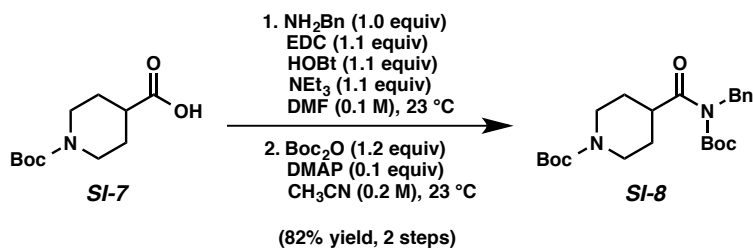
To a flask containing the crude material from the previous step was added DMAP (75 mg, 0.62 mmol, 0.1 equiv) followed by acetonitrile (31 mL, 0.2 M). Boc₂O (1.55 g, 7.40 mmol, 1.2 equiv) was added in one portion and the reaction vessel was flushed with N₂. The reaction mixture was allowed to stir at 23 °C for 16 h. The reaction mixture was diluted with EtOAc (50 mL) and then washed with saturated aqueous NaHCO₃ (2 x 50 mL) and brine (50 mL). The organic layer was dried over Na₂SO₄ and concentrated under reduced pressure. The resulting crude residue was purified by flash chromatography (29:1 Hexanes:EtOAc) to yield amide **SI-4** (3.0 g, 99% yield, over two steps) as a white solid. Amide **SI-4**: mp: 52.8–54.5 °C; R_f 0.56 (5:1 Hexanes:EtOAc); ¹H NMR (500 MHz, CDCl₃): δ 7.33–7.27 (m, 2H), 7.26–7.21 (m, 3H), 7.21–

7.17 (m, 2H), 7.16–7.12 (m, 2H), 4.91 (s, 2H), 4.39 (quint, $J = 8.3$, 1H), 3.34–3.23 (m, 4H), 1.42 (s, 9H); ^{13}C NMR (125 MHz, CDCl_3): δ 178.3, 153.1, 142.0, 138.5, 128.5, 127.6, 127.3, 126.6, 124.4, 83.4, 48.0, 45.8, 37.2, 28.0; IR (film): 3022, 2979, 1732, 1693, 1368 cm^{-1} ; HRMS-APCI (m/z) $[\text{M} + \text{H}]^+$ calcd for $\text{C}_{22}\text{H}_{26}\text{NO}_3$, 352.1913; found 352.1886.



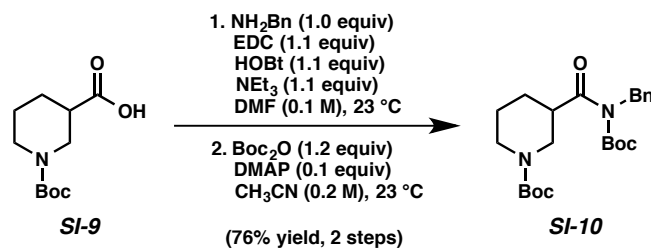
Amide SI-6: To a mixture of carboxylic acid **SI-5** (1.0 g, 8.61 mmol, 1.0 equiv), EDC (1.82 g, 9.47 mmol, 1.1 equiv), HOBt (1.28 g, 9.47 mmol, 1.1 equiv), triethylamine (1.31 mL, 9.47 mmol, 1.1 equiv), and DMF (86.1 mL, 0.1 M) was added benzylamine (1.03 mL, 9.47 mmol, 1.1 equiv). The resulting mixture was stirred at 23 °C for 12 h, and then diluted with deionized water (50 mL) and EtOAc (50 mL). The layers were separated and the organic layer was washed successively with 1.0 M HCl (50 mL), saturated aqueous NaHCO_3 (50 mL), and brine (50 mL). The organic layer was dried over Na_2SO_4 and concentrated under reduced pressure. The resulting crude solid material was used in the subsequent step without further purification.

To a flask containing the crude material from the previous step was added DMAP (105 mg, 0.86 mmol, 0.1 equiv) followed by acetonitrile (43 mL, 0.2 M). Boc_2O (2.30 g, 10.3 mmol, 1.2 equiv) was added in one portion and the reaction vessel was flushed with N_2 . The reaction mixture was allowed to stir at 23 °C for 24 h. The reaction mixture was diluted with EtOAc (50 mL) and then washed with saturated aqueous NaHCO_3 (2 x 50 mL) and brine (50 mL). The combined organic layers were dried over Na_2SO_4 and concentrated under reduced pressure. The resulting crude residue was purified by flash chromatography (49:1 Hexanes:EtOAc) to yield amide **SI-6** (675 mg, 64% yield, over two steps) as a clear oil. Amide **SI-6**: R_f 0.70 (5:1 Hexanes:EtOAc); ^1H NMR (500 MHz, CDCl_3): δ 7.31–7.26 (m, 2H), 7.26–7.19 (m, 3H), 4.87 (s, 2H), 2.91 (s, 2H), 1.39 (s, 9H), 1.03 (s, 9H); ^{13}C NMR (125 MHz, CDCl_3): δ 175.0, 153.6, 138.6, 128.4, 127.7, 127.1, 83.1, 49.3, 47.5, 31.7, 29.9, 28.0; IR (film): 2955, 2869, 1731, 1689, 1355 cm^{-1} ; HRMS-APCI (m/z) $[\text{M} + \text{H}]^+$ calcd for $\text{C}_{18}\text{H}_{28}\text{NO}_3$, 306.2069; found 306.2047.



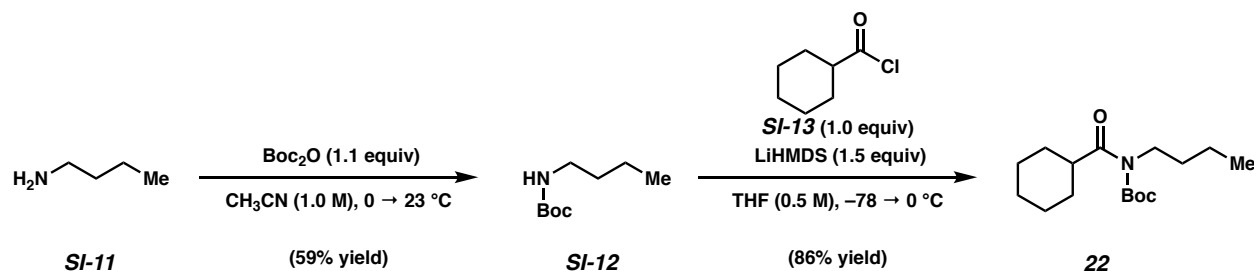
Amide SI-8: To a mixture of carboxylic acid **SI-7** (3.0 g, 13.1 mmol, 1.0 equiv), EDC (2.76 g, 14.4 mmol, 1.1 equiv), HOBt (1.94 g, 14.4 mmol, 1.1 equiv), triethylamine (1.99 mL, 14.4 mmol, 1.1 equiv), and DMF (131 mL, 0.1 M) was added benzylamine (1.57 mL, 14.4 mmol, 1.1 equiv). The resulting mixture was stirred at 23 °C for 17 h, and then diluted with deionized water (250 mL) and EtOAc (150 mL). The aqueous layer was extracted with EtOAc (3 x 150 mL). The organic layer was back-extracted with deionized water (3 x 60 mL). The organic layer was then dried over Na_2SO_4 and concentrated under reduced pressure. The resulting crude solid material was used in the subsequent step without further purification.

To a flask containing the crude material from the previous step was added DMAP (148 mg, 1.21 mmol, 0.1 equiv) followed by acetonitrile (60 mL, 0.2 M). Boc_2O (3.86 g, 15.7 mmol, 1.2 equiv) was added in one portion and the reaction vessel was flushed with N_2 . The reaction mixture was allowed to stir at 23 °C for 43 h. The reaction mixture was diluted with saturated aqueous NaHCO_3 (200 mL), EtOAc (200 mL), and deionized water (200 mL). The aqueous layer was extracted with EtOAc (3 x 150 mL). The combined organic layers were then dried over Na_2SO_4 and concentrated under reduced pressure. The resulting crude residue was purified by flash chromatography (9:1 Hexanes:EtOAc) and then recrystallized from heptanes to yield amide **SI-8** (3.6 g, 82% yield, over two steps) as a white solid. Amide **SI-8**: mp: 84.2–85.3 °C; R_f 0.32 (5:1 Hexanes:EtOAc); ^1H NMR (500 MHz, CDCl_3 , 14 of 15 carbons observed): δ 7.31–7.26 (m, 2H), 7.25–7.18 (m, 3H), 4.87 (s, 2H), 4.13 (br s, 2H), 3.60 (tt, $J = 11.3, 3.3$, 1H), 2.80 (br s, 2H), 1.93–1.77 (m, 2H), 1.72–1.60 (m, 2H), 1.46 (s, 9H), 1.40 (s, 9H); ^{13}C NMR (125 MHz, CDCl_3): δ 178.3, 154.9, 153.1, 138.4, 128.5, 127.5, 127.3, 83.5, 79.6, 47.8, 43.1, 29.0, 28.6, 28.0; IR (film): 2977, 2927, 2864, 1732, 1693 cm^{-1} ; HRMS-APCI (m/z) $[\text{M} + \text{H}]^+$ calcd for $\text{C}_{23}\text{H}_{35}\text{N}_2\text{O}_5$, 419.2546; found 419.2546.



Amide SI-10: To a mixture of carboxylic acid **SI-9** (3.0 g, 13.1 mmol, 1.0 equiv), EDC (2.76 g, 14.4 mmol, 1.1 equiv), HOBT (1.94 g, 14.4 mmol, 1.1 equiv), triethylamine (1.99 mL, 14.4 mmol, 1.1 equiv), and DMF (131 mL, 0.1 M) was added benzylamine (1.57 mL, 14.4 mmol, 1.1 equiv). The resulting mixture was stirred at 23 °C for 17 h, and then diluted with deionized water (250 mL) and EtOAc (150 mL). The aqueous layer was extracted with EtOAc (3 x 150 mL). The organic layer was back-extracted with deionized water (3 x 30 mL). The combined organic layers were dried over Na_2SO_4 and concentrated under reduced pressure. The resulting crude solid material was used in the subsequent step without further purification.

To a flask containing the crude material from the previous step was added DMAP (160 mg, 1.31 mmol, 0.1 equiv) followed by acetonitrile (60 mL, 0.2 M). Boc_2O (3.72 g, 17.0 mmol, 1.2 equiv) was added in one portion and the reaction vessel was flushed with N_2 . The reaction mixture was allowed to stir at 23 °C for 43 h. The reaction mixture was diluted with saturated aqueous NaHCO_3 (200 mL), EtOAc (200 mL) and deionized water (200 mL). The aqueous layer was extracted with EtOAc (3 x 150 mL). The combined organic layers were dried over Na_2SO_4 and concentrated under reduced pressure. The resulting crude residue was purified by flash chromatography (9:1 Hexanes:EtOAc) to yield amide **SI-10** (2.8 g, 76% yield, over two steps) as a white solid. Amide **SI-10**: mp: 75.1–79.1 °C; R_f 0.62 (5:1 Hexanes:EtOAc); ^1H NMR (500 MHz, CDCl_3): δ 7.32–7.26 (m, 2H), 7.26–7.17 (m, 3H), 4.94–4.77 (m, 2H), 4.33–3.87 (m, 2H), 3.56–3.46 (m, 1H), 2.99 (app t, $J = 12.2$, 1H), 2.75 (br s, 1H), 2.11 (br s, 1H), 1.76–1.67 (m, 1H), 1.63–1.48 (m, 2H), 1.45 (s, 9H), 1.41 (s, 9H); ^{13}C NMR (125 MHz, CDCl_3 , 15 of 17 carbons observed): δ 177.2, 154.9, 152.9, 138.3, 128.5, 127.5, 127.3, 83.6, 79.7, 47.7, 43.5, 28.7, 28.6, 28.0, 24.8; IR (film): 2977, 2935, 1732, 1689, 1367 cm^{-1} ; HRMS-APCI (m/z) $[\text{M} + \text{H}]^+$ calcd for $\text{C}_{23}\text{H}_{35}\text{N}_2\text{O}_5$, 419.2546; found 419.2516.

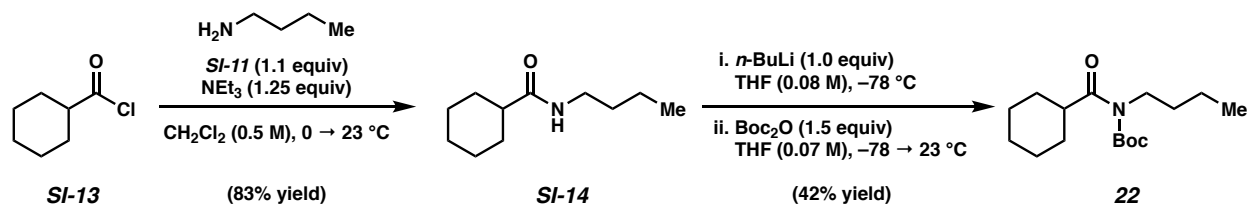


Amide 22: To a solution of *n*-BuNH₂ (**SI-11**, 1.0 g, 13.67 mmol, 1.0 equiv) in CH₃CN (8.7 mL) maintained at 0 °C was added Boc₂O (3.28 g, 15.05 mmol, 1.1 equiv) dropwise (1 drop/sec) as a solution in CH₃CN (5 mL). The ice bath was removed and the resulting mixture was warmed to 23 °C and stirred an additional 0.5 h. The reaction was concentrated under reduced pressure, then subsequently re-suspended in CH₂Cl₂ (50 mL), and transferred to a separatory funnel with deionized water (30 mL). The layers were separated and the organic layer was washed with deionized water (3 x 30 mL). The organic layer was dried over Na₂SO₄ and concentrated under reduced pressure to yield **SI-12** (1.45 g, 59% yield) as a white solid. The resulting crude solid material was used in the subsequent step without further purification.

To a flask containing crude **SI-12** (1.4 g, 8.08 mmol, 1.0 equiv) under N₂ from the previous step, THF (6 mL) was added. The resultant solution was cooled to –78 °C. A solution of LiHMDS (2.03 g, 12.12 mmol, 1.5 equiv) in THF (6 mL) was then added dropwise (1 drop/sec) at –78 °C with vigorous stirring. The resulting mixture was stirred at –78 °C for 1 h. Acid chloride **SI-13** (1.08 mL, 8.08 mmol, 1.0 equiv) was then added dropwise (1 drop/sec) at –78 °C and stirred for an additional 1 h. This mixture was then warmed to 0 °C and stirred for an additional 1 h. The reaction was warmed to 23 °C before quenching with saturated aqueous NaHCO₃ (30 mL). This biphasic solution was transferred to a separatory funnel with brine (10 mL) and EtOAc (30 mL). The layers were separated and the aqueous layer was extracted with EtOAc (3 x 30 mL). The combined organic layers were dried over Na₂SO₄ and concentrated under reduced pressure. The resulting crude residue was purified by flash chromatography (29:1 Hexanes:Et₂O) to yield amide **22** (1.99 g, 86% yield, over two steps) as a colorless oil. Amide **22**: R_f 0.37 (19:1 Hexanes: Et₂O); ¹H NMR (500 MHz, CDCl₃): δ 3.65–3.60 (m, 2H), 3.29 (tt, *J* = 11.3, 3.2, 1H), 1.88–1.80 (m, 2H), 1.80–1.73 (m, 2H), 1.70–1.73 (m, 1H), 1.53 (s, 9H), 1.50–1.38 (m, 4H), 1.35–1.20 (m, 5H), 0.91 (t, *J* = 7.3, 3H); ¹³C NMR (125 MHz, CDCl₃): δ 179.7, 153.5, 82.6, 45.0, 44.8, 31.1, 30.0, 28.2, 26.1, 26.0, 20.2, 14.0; IR (film): 2931, 1855, 1729,

1693, 1369, 1147 cm^{-1} ; HRMS-APCI (m/z) $[\text{M} + \text{H}]^+$ calcd for $\text{C}_{23}\text{H}_{35}\text{N}_2\text{O}_5$, 284.2226; found 284.2208.

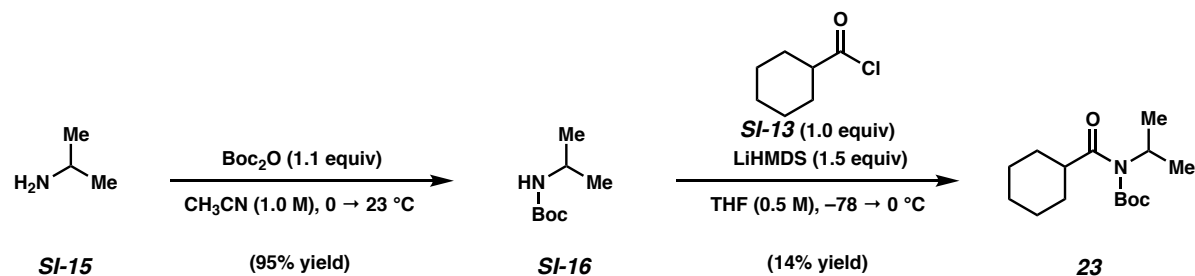
Note: Amide 22 can be prepared from the corresponding N-Bu,H secondary amide using the procedure outlined below. The procedure described above was used for preparative scale synthesis of 22 as it was higher yielding and operationally simpler.



Amide 22: To a solution of **SI-13** (1.0 g, 6.80 mmol, 1.0 equiv) and NEt_3 (1.20 mL, 8.50 mmol, 1.25 equiv) in CH_2Cl_2 (13.6 mL) maintained at $0 \text{ }^\circ\text{C}$ was added **SI-11** (738 μL , 7.48 mmol, 1.1 equiv) dropwise (1 drop/sec). The ice bath was removed and the resulting mixture was warmed to $23 \text{ }^\circ\text{C}$ and stirred an additional 2.5 h. The reaction was quenched with deionized water (20 mL) and 1 N HCl (4 mL), and then transferred to a separatory funnel with EtOAc (20 mL). The layers were separated and the aqueous layer was extracted with EtOAc (3 x 20 mL). The combined organic layers were dried over Na_2SO_4 and concentrated under reduced pressure to yield **SI-14** (1.04 g, 83% yield) as a white solid. The resulting crude solid material was used in the subsequent step without further purification.

To a flask containing crude **SI-14** (250 mg, 1.36 mmol, 1.0 equiv) under N_2 from the previous step, THF (17 mL, 0.08 M) was added. The resultant solution was cooled to $-78 \text{ }^\circ\text{C}$. A solution of $n\text{-BuLi}$ (2.20 M in hexanes, 618 μL , 1.36 mmol, 1.0 equiv) was then added dropwise (1 drop/sec) at $-78 \text{ }^\circ\text{C}$ with vigorous stirring. The resulting mixture was stirred at $-78 \text{ }^\circ\text{C}$ for 15 min. A solution of Boc_2O (445 mg, 2.04 mmol, 1.50 equiv) in THF (4.1 mL, 0.5 M) was then added dropwise (1 drop/sec) at $-78 \text{ }^\circ\text{C}$ and stirred for an additional 1 h. This mixture was then warmed to $0 \text{ }^\circ\text{C}$ and stirred for an additional 1 h. The reaction was warmed to $23 \text{ }^\circ\text{C}$ before quenching with saturated aqueous NH_4Cl (20 mL). This biphasic solution was transferred to a separatory funnel with deionized water (10 mL) and EtOAc (20 mL). The layers were separated and the aqueous layer was extracted with EtOAc (3 x 20 mL). The combined organic layers were

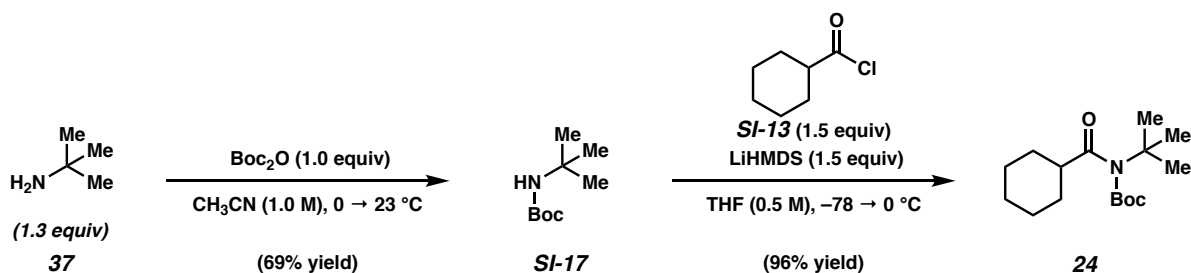
dried over Na_2SO_4 and concentrated under reduced pressure. The resulting crude residue was purified by flash chromatography (49:1 Hexanes:Et₂O) and the remaining Boc_2O was removed by evaporation at 70 °C under high vacuum to yield amide **22** (161 mg, 42% yield) as a colorless oil. Amide **22**: R_f 0.37 (19:1 Hexanes: Et₂O); Spectral data match those previously reported for amide **22** (see page S7).



Amide 23: To a solution of *i*-PrNH₂ (**SI-15**, 1.0 g, 16.95 mmol, 1.0 equiv) in CH₃CN (10 mL) maintained at 0 °C was added Boc_2O (4.07 g, 18.65 mmol, 1.1 equiv) dropwise (1 drop/sec) as a solution in CH₃CN (7 mL). The ice bath was removed and the resulting mixture was warmed to 23 °C and stirred an additional 0.5 h. The reaction was concentrated under reduced pressure, then subsequently re-suspended in CH₂Cl₂ (50 mL), and transferred to a separatory funnel with deionized water (30 mL). The layers were separated and the organic layer was washed with deionized water (3 x 30 mL). The organic layer was dried over Na_2SO_4 and concentrated under reduced pressure to yield **SI-16** (2.56 g, 95% yield) as a white solid. The resulting crude solid material was used in the subsequent step without further purification.

To a flask containing crude **SI-16** (2.25 g, 14.2 mmol, 1.0 equiv) under N₂ from the previous step, THF (14.2 mL) was added. The resultant solution was cooled to -78 °C. A solution of LiHMDS (3.36 g, 21.2 mmol, 1.5 equiv) in THF (14.2 mL) was then added dropwise (1 drop/sec) at -78 °C with vigorous stirring. The resulting mixture was stirred at -78 °C for 1 h. Acid chloride **SI-13** (1.89 mL, 14.2 mmol, 1.0 equiv) was then added dropwise (1 drop/sec) at -78 °C and stirred for an additional 1 h. This mixture was then warmed to 0 °C and stirred for an additional 1 h. The reaction was warmed to 23 °C before quenching with saturated aqueous NaHCO₃ (30 mL). This biphasic solution was transferred to a separatory funnel with brine (10 mL) and EtOAc (30 mL). The layers were separated and the aqueous layer was extracted with EtOAc (3 x 30 mL). The combined organic layers were dried over Na_2SO_4 and concentrated under reduced pressure. The resulting crude residue was purified by flash chromatography (49:1

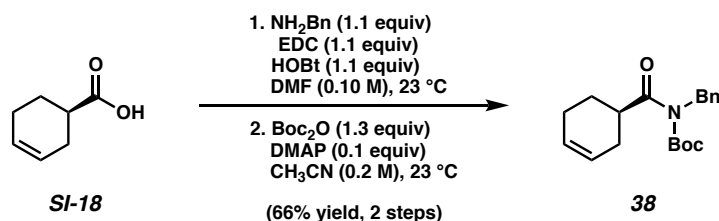
Hexanes:Et₂O) to yield amide **23** (537 mg, 14% yield) as a colorless oil. Amide **23**: R_f 0.35 (19:1 Hexanes: Et₂O); ¹H NMR (500 MHz, CDCl₃): δ 4.68 (septet, *J* = 6.8, 1H), 2.95 (tt, *J* = 11.4, 3.2, 1H), 1.87–1.81 (m, 2H), 1.80–1.73 (m, 2H), 1.69–1.63 (m, 1H), 1.54 (s, 9H), 1.48–1.37 (m, 3H), 1.27–1.22 (m, 8H); ¹³C NMR (125 MHz, CDCl₃): δ 179.7, 154.0, 82.9, 47.1, 45.8, 30.0, 28.2, 26.0, 25.95, 20.6; IR (film): 2974, 2932, 2855, 1727, 1687, 1368 cm⁻¹; HRMS-APCI (*m/z*) [M + H]⁺ calcd for C₂₃H₃₅N₂O₅, 270.2069; found 270.2051.



Amide 24: To a solution of *t*-BuNH₂ (**37**, 1.42 g, 19.5 mmol, 1.3 equiv) in CH₃CN (10 mL) maintained at 0 °C was added Boc₂O (3.27 g, 15.0 mmol, 1.0 equiv) dropwise (1 drop/sec) as a solution in CH₃CN (5 mL). The ice bath was removed and the resulting mixture was warmed to 23 °C and stirred an additional 0.5 h. The reaction was concentrated under reduced pressure, subsequently resuspended in CH₂Cl₂ (50 mL), and transferred to a separatory funnel with deionized water (30 mL). The layers were separated and the organic layer was washed with deionized water (3 x 30 mL). The organic layer was dried over Na₂SO₄ and concentrated under reduced pressure to yield **SI-17** (1.80 g, 69% yield) as a white solid. The resulting crude solid material was used in the subsequent step without further purification.

To a flask containing crude **SI-17** (1.0g, 5.78 mmol, 1.0 equiv) under N₂ from the previous step, THF (6 mL) was added. The resultant solution was cooled to -78 °C. A solution of LiHMDS (1.45 g, 8.67 mmol, 1.5 equiv) in THF (6 mL) was then added dropwise (1 drop/sec) at -78 °C with vigorous stirring. The resulting mixture was stirred at -78 °C for 1 h. Acid chloride **SI-13** (1.16 mL, 8.67 mmol, 1.5 equiv) was then added dropwise (1 drop/sec) at -78 °C and stirred for an additional 1 h. This mixture was then warmed to 0 °C and stirred for an additional 1 h. The reaction was warmed to 23 °C before quenching with saturated aqueous NaHCO₃ (30 mL). This biphasic solution was transferred to a separatory funnel with brine (10 mL) and EtOAc (30 mL). The layers were separated and the aqueous layer was extracted with EtOAc (3 x 30 mL). The combined organic layers were dried over Na₂SO₄ and concentrated

under reduced pressure. The resulting crude residue was purified by flash chromatography (49:1 Hexanes:EtOAc) to yield amide **24** (1.57 g, 96% yield) as a white solid. Amide **24**: R_f 0.19 (19:1 Hexanes: Et₂O); ¹H NMR (500 MHz, CDCl₃): δ 2.26 (tt, J = 11.3, 3.1, 1H), 1.87–1.74 (m, 4H), 1.69–1.63 (m, 1H), 1.53 (s, 9H), 1.50–1.40 (m, 11H), 1.27–1.12 (m, 3H); ¹³C NMR (125 MHz, CDCl₃): δ 176.2, 155.0, 83.6, 57.6, 46.4, 29.7, 28.5, 27.7, 25.9, 25.87; IR (film): 2977, 2932, 2855, 1739, 1703, 1677 cm⁻¹; HRMS-APCI (m/z) [M + H]⁺ calcd for C₁₆H₃₁NO₃, 284.2226; found 284.2210.



Amide 38. To a mixture of carboxylic acid **SI-18** (1.0 g, 7.9 mmol, 1.0 equiv), EDC (1.67 g, 8.7 mmol, 1.1 equiv), HOBt (1.2 g, 8.7 mmol, 1.1 equiv), and DMF (79 mL, 0.1 M) was added benzylamine (0.95 mL, 8.7 mmol, 1.1 equiv). The resulting mixture was stirred at 23 °C for 22 h, and then diluted with deionized water (50 mL) and EtOAc (50 mL). The aqueous layer was extracted with EtOAc (3 x 30 mL). The organic layer was back-extracted with deionized water (3 x 30 mL). The organic layer was then dried over Na₂SO₄ and concentrated under reduced pressure. The resulting crude solid material was used in the subsequent step without further purification.

To a flask containing the crude material from the previous step was added DMAP (97 mg, 0.79 mmol, 0.1 equiv) followed by acetonitrile (40 mL, 0.2 M). Boc₂O (2.25 g, 10.3 mmol, 1.3 equiv) was added in one portion and the reaction vessel was flushed with N₂. The reaction mixture was allowed to stir at 23 °C for 20 h. The reaction mixture was diluted with saturated aqueous NaHCO₃ (40 mL), EtOAc (50 mL) and deionized water (40 mL). The aqueous layer was extracted with EtOAc (3 x 50 mL). The combined organic layers were then dried over Na₂SO₄ and concentrated under reduced pressure. The resulting crude residue was purified by flash chromatography (19:1 Hexanes:EtOAc) to yield amide **38** (5.3 g, 66% yield, over two steps) as a clear oil. Amide **38**: R_f 0.63 (5:1 Hexanes:EtOAc); ¹H NMR (500 MHz, CDCl₃): δ 7.32–7.26 (m, 2H), 7.25–7.20 (m, 3H), 5.74–5.64 (m, 2H), 4.88 (dd, J = 18.1, 14.9, 2H), 3.64 (m, 1H), 2.33–2.21 (m, 2H), 2.19–2.06 (m, 2H), 2.00–1.93 (m, 1H), 1.78–1.65 (m, 1H), 1.46–1.36 (s, 9H);

^{13}C NMR (125 MHz, CDCl_3): δ 179.6, 153.2, 138.6, 128.4, 127.6, 127.2, 126.7, 125.8, 83.3, 47.8, 41.1, 28.6, 28.0, 26.3, 25.1; IR (film): 3028, 2978, 1732, 1693, 1369 cm^{-1} ; HRMS-APCI (m/z) $[\text{M} + \text{H}]^+$ calcd for $\text{C}_{19}\text{H}_{26}\text{NO}_3$, 316.1913; found 316.1888; $[\alpha]^{23.4}_{\text{D}} -20.40^\circ$ ($c = 1.00$, CHCl_3).

B. Reaction Discovery, Optimization, and Relevant Control Experiments

Representative procedure for ligand screening (coupling of amide 7 and cyclohexylamine (8) is used as an example). Amide 9 (Table S1, entry 3): A 1-dram vial containing a magnetic stir bar was flame-dried under reduced pressure, and then allowed to cool under N_2 . The vial was charged with amide substrate 7 (63.4 mg, 0.2 mmol, 1.0 equiv), 1,3,5-trimethoxybenzene (TMB) (10.1 mg, 0.06 mmol, 0.3 equiv), and the vial was flushed with N_2 . The vial was then taken into a glove box and charged with 1,3-dicyclohexylbenzimidazolium chloride (**12**, 0.04 mmol, 20 mol%), $\text{Ni}(\text{cod})_2$ (5.5 mg, 0.02 mmol, 10 mol%), and $\text{NaO}t\text{Bu}$ (4.2 mg, 0.044 mmol, 22 mol%). Subsequently, cyclohexylamine (**8**) (46 mL, 0.4 mmol, 2.0 equiv) and then toluene (0.2 mL, 1.0 M) were added. The vial was sealed with a Teflon-lined screw cap, removed from the glove box, and stirred at 60 $^\circ\text{C}$ for 24 h. After cooling to 23 $^\circ\text{C}$, the mixture was diluted with hexanes (0.5 mL) and filtered over a plug of silica gel (10 mL of EtOAc eluent). The volatiles were evaporated under reduced pressure, and the yield was determined by ^1H NMR analysis with 1,3,5-trimethoxybenzene as an internal standard.

Optimization efforts that deviate from the above conditions are indicated below.

Table S1. Optimization of Reaction Conditions.^a

Entry	mol% of Ni(cod) ₂	Ligand (mol%)	mol% of NaOtBu	Equivs of 8	Conc.	Time	Yield of 9
1	10	10 (20 mol%)	—	2.0	1.0	24 h	15%
2	10	11 (20 mol%)	—	2.0	1.0	24 h	0%
3	10	12 (20 mol%)	22	2.0	1.0	24 h	Quant. Yield
4	5	12 (10 mol%)	11	2.0	1.0	24 h	Quant. Yield
5	5	12 (10 mol%)	11	1.5	1.0	24 h	88%
6	5	12 (10 mol%)	11	1.5	1.5	18 h	90%
7	—	12 (10 mol%)	11	1.5	1.5	18 h	0%
8	—	—	—	1.5	1.5	18 h	0%

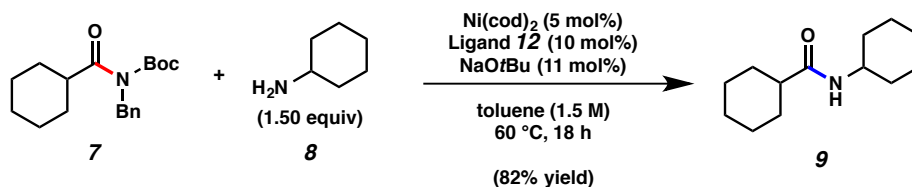
SIPr (10)

terpyridine (11)

**1,3-dichlorohexyl-
benzimidazolium chloride (12)**

^a Yields were determined using ¹H NMR analysis with 1,3,5-trimethoxybenzene (TMB) as an internal standard.

C. Scope of Amide Substrates

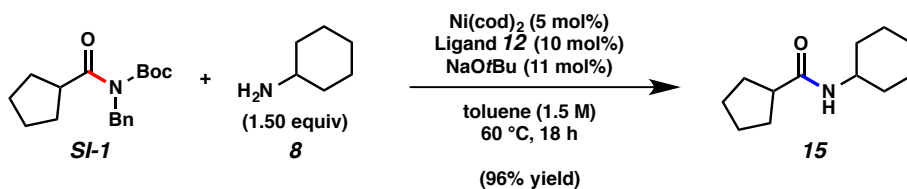


Representative Procedure (coupling of amide 7 and cyclohexylamine (8) is used as an example). Amide 9 (Figure 2): A 1-dram vial containing a magnetic stir bar was flame-dried under reduced pressure, and then allowed to cool under N_2 . The vial was charged with amide substrate **7** (63.4 mg, 0.200 mmol, 1.0 equiv) and the vial was flushed with N_2 . The vial was then taken into a glove box and charged with 1,3-dicyclohexylbenzimidazolium chloride (**12**, 6.4 mg, 0.020 mmol, 10 mol%), $\text{Ni}(\text{cod})_2$ (2.8 mg, 0.010 mmol, 5 mol%), and NaOtBu (2.1 mg, 0.022 mmol, 11 mol%). Subsequently, cyclohexylamine (**8**, 34 μL , 0.30 mmol, 1.5 equiv) and toluene (0.133 mL, 1.5 M) were added. The vial was sealed with a Teflon-lined screw cap, removed from the glove box, and stirred at 60 °C for 18 h. After cooling to 23 °C, the mixture was diluted with hexanes (0.5 mL) and filtered over a plug of silica gel (10 mL of EtOAc eluent). The volatiles were removed under reduced pressure and the crude residue was purified by flash chromatography (9:1 \rightarrow 3:1 Hexanes:EtOAc) to generate amide **9** (82% yield, average of two experiments) as a white solid. Amide **9**: mp: 167.5–168.3 °C; R_f 0.42 (2:1 Hexanes:EtOAc); ^1H NMR (500 MHz, CDCl_3): δ 5.24 (br s, 1H), 3.81–3.69 (m, 1H), 2.00 (tt, $J = 11.7, 3.4$, 1H), 1.92–1.81 (m, 4H), 1.81–1.74 (m, 2H), 1.72–1.64 (m, 3H), 1.63–1.58 (m, 1H), 1.46–1.31 (m, 4H), 1.30–1.03 (m, 6H); ^{13}C NMR (125 MHz, CDCl_3): δ 175.2, 47.8, 45.9, 33.4, 29.9, 25.9, 25.7, 25.0 (8 of 9 carbons observed); IR (film): 3293, 2929, 2853, 1638, 1549 cm^{-1} ; HRMS-APCI (m/z) [$\text{M} + \text{H}$] $^+$ calcd for $\text{C}_{13}\text{H}_{24}\text{NO}$, 210.1858; found 210.1842.

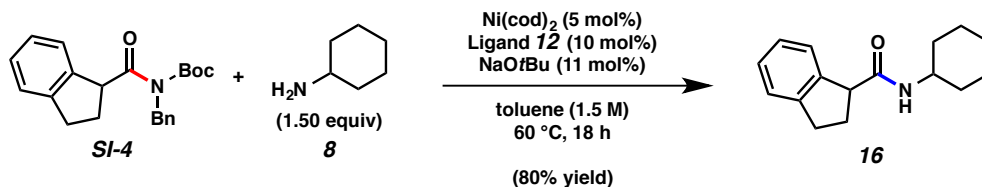
Note: It was found that the purity of both coupling partners had a significant effect on the yield of a given coupling. Additionally, maintaining a moderate stir rate (500–900 rpm) and ensuring all NaOtBu enters the reaction mixture are essential for the success of these couplings. Increased amounts of NaOtBu are not detrimental to the reaction and can help alleviate the latter of the aforementioned scenarios.

Any modifications of the conditions shown in the representative procedure above are specified in the following schemes, which depict all of the results shown in Figures 2 and 3.

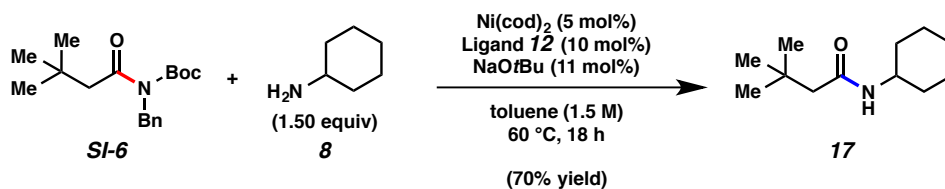
For each of the nickel-catalyzed reactions described herein, control experiments were performed concurrently where $\text{Ni}(\text{cod})_2$ and both $\text{Ni}(\text{cod})_2$ and ligand **12**/ NaOtBu were omitted from the reactions. In all cases, these control experiments led to the recovery of the amide substrates with minimal (<5%) conversion to the corresponding amides.



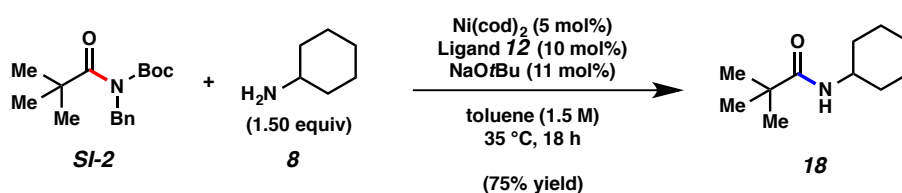
Amide 15 (Figure 2): Purification by flash chromatography (9:1 → 3:1 Hexanes:EtOAc) generated amide **15** (96% yield, average of two experiments) as a white solid. Amide **15**: mp: 157.1–159.3 °C; R_f 0.41 (2:1 Hexanes:EtOAc); ^1H NMR (500 MHz, CDCl_3): δ 5.25 (br s, 1H), 3.81–3.71 (m, 1H), 2.45 (app quintet, $J = 7.8$, 1H), 1.95–1.87 (m, 2H), 1.87–1.80 (m, 2H), 1.80–1.65 (m, 6H), 1.65–1.55 (m, 2H), 1.42–1.30 (m, 2H), 1.21–1.05 (m, 3H); ^{13}C NMR (125 MHz, CDCl_3): δ 175.3, 48.1, 46.2, 33.5, 30.6, 26.1, 25.7, 25.0; IR (film): 3298, 2934, 2854, 1640, 1545 cm^{-1} ; HRMS-APCI (m/z) [$\text{M} + \text{H}$] $^+$ calcd for $\text{C}_{12}\text{H}_{22}\text{NO}$, 196.1701; found 196.1685.



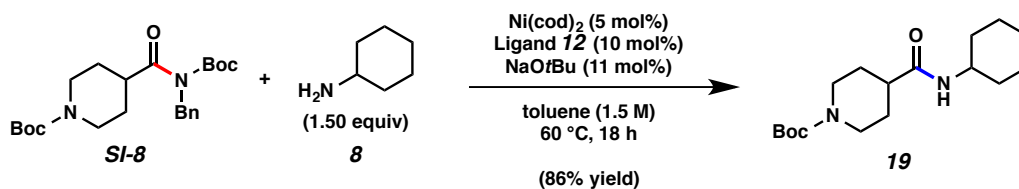
Amide 16 (Figure 2): Purification by flash chromatography (9:1 → 3:1 Hexanes:EtOAc) generated amide **16** (80% yield, average of two experiments) as a white solid. Amide **16**: mp: 175.2–178.5 °C; R_f 0.47 (2:1 Hexanes:EtOAc); ^1H NMR (500 MHz, CDCl_3): δ 7.23–7.18 (m, 2H), 7.17–7.12 (m, 2H), 5.36 (br s, 1H), 3.86–3.76 (m, 1H), 3.29–3.18 (m, 2H), 3.18–3.07 (m, 3H), 1.97–1.89 (m, 2H), 1.74–1.65 (m, 2H), 1.65–1.58 (m, 1H), 1.43–1.32 (m, 2H), 1.21–1.07 (m, 3H); ^{13}C NMR (125 MHz, CDCl_3): δ 173.8, 142.0, 126.7, 124.5, 48.3, 46.2, 37.1, 33.4, 25.7, 25.0; IR (film): 3296, 2933, 2854, 1633, 1541 cm^{-1} ; HRMS-APCI (m/z) [$\text{M} + \text{H}$] $^+$ calcd for $\text{C}_{16}\text{H}_{22}\text{NO}$, 244.1701; found 244.1683.



Amide 17 (Figure 2): Purification by flash chromatography (9:1 → 3:1 Hexanes:EtOAc) generated amide **17** (70% yield, average of two experiments) as a white solid. Amide **17**: mp: 146.5–148.8 °C; R_f 0.43 (2:1 Hexanes:EtOAc); $^1\text{H NMR}$ (500 MHz, CDCl_3): δ 5.18 (br s, 1H), 3.84–3.71 (m, 1H), 2.00 (s, 2H), 1.95–1.88 (m, 2H), 1.74–1.65 (m, 2H), 1.65–1.54 (m, 2H), 1.42–1.31 (m, 2H), 1.21–1.06 (m, 2H), 1.03 (s, 9H); $^{13}\text{C NMR}$ (125 MHz, CDCl_3): δ 170.8, 51.1, 48.1, 33.5, 31.0, 30.0, 25.7, 25.0; IR (film): 3284, 2931, 2853, 1634, 1550 cm^{-1} ; HRMS-APCI (m/z) $[\text{M} + \text{H}]^+$ calcd for $\text{C}_{12}\text{H}_{24}\text{NO}$, 198.1858; found 198.1843.

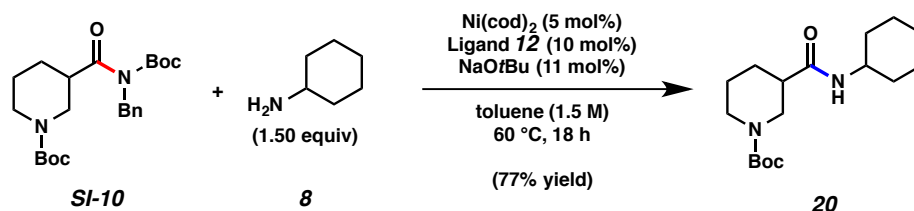


Amide 18 (Figure 2): Purification by flash chromatography (9:1 → 3:1 Hexanes:EtOAc) generated amide **18** (75% yield, average of two experiments) as a white solid. Amide **18**: mp: 121.8–123.1 °C; R_f 0.48 (2:1 Hexanes:EtOAc); $^1\text{H NMR}$ (500 MHz, CDCl_3): δ 5.43 (br s, 0.5H), 3.79–3.69 (m, 1H), 1.94–1.86 (m, 2H), 1.74–1.65 (m, 2H), 1.65–1.58 (m, 1H), 1.42–1.32 (m, 2H), 1.18 (s, 9H), 1.17–1.04 (m, 3H); $^{13}\text{C NMR}$ (125 MHz, CDCl_3): δ 177.6, 48.1, 38.7, 33.3, 27.8, 25.8, 25.0; IR (film): 3332, 2935, 2854, 1627, 1535 cm^{-1} ; HRMS-APCI (m/z) $[\text{M} + \text{H}]^+$ calcd for $\text{C}_{11}\text{H}_{22}\text{NO}$, 184.1701; found 184.1687.

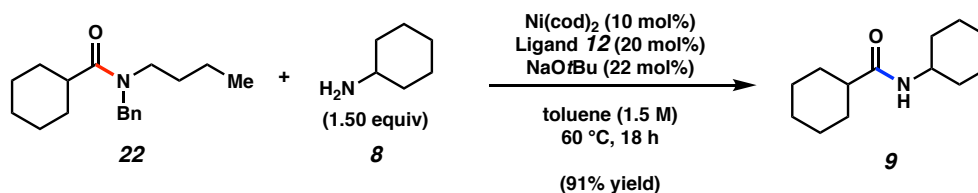


Amide 19 (Figure 2): Purification by flash chromatography (9:1 → 3:1 Hexanes:EtOAc) generated amide **19** (86% yield, average of two experiments) as a white solid. Amide **19**: mp: 148.9–150.2 °C; R_f 0.70 (100% EtOAc); $^1\text{H NMR}$ (500 MHz, CDCl_3): δ 5.30–5.23 (m, 1H), 4.14

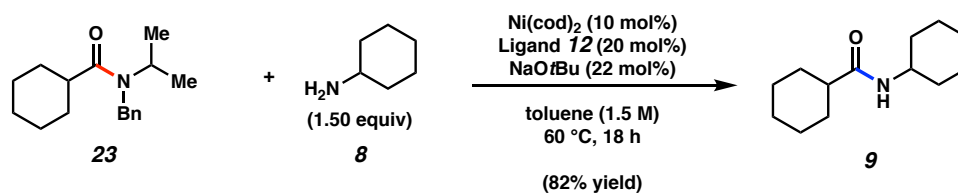
(br s, 2H), 3.81–3.70 (m, 1H), 2.73 (m, 2H), 2.16 (tt, $J = 11.6, 3.7$, 1H), 1.94–1.86 (m, 2H), 1.82–1.75 (m, 2H), 1.73–1.66 (m, 2H), 1.66–1.58 (m, 3H), 1.45 (s, 9H), 1.42–1.31 (m, 2H), 1.21–1.03 (m, 3H); ^{13}C NMR (125 MHz, CDCl_3 , (10 of 11 carbons observed): δ 173.5, 154.8, 79.7, 48.1, 43.7, 33.4, 28.9, 28.6, 25.7, 25.0; IR (film): 3300, 2931, 2855, 1697, 1642 cm^{-1} ; HRMS-APCI (m/z) $[\text{M} + \text{H}]^+$ calcd for $\text{C}_{17}\text{H}_{31}\text{N}_2\text{O}_3$, 311.2335; found 311.2310.



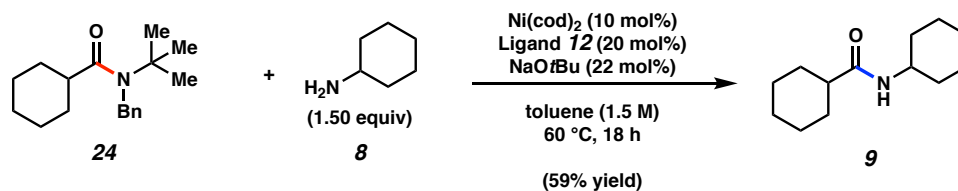
Amide 20 (Figure 2): Purification by flash chromatography (9:1 \rightarrow 3:1 Hexanes:EtOAc) generated amide **20** (77% yield, average of two experiments) as a white solid. Amide **20**: mp: 136.2–138.9 $^\circ\text{C}$; R_f 0.48 (1:1 Hexanes:EtOAc); ^1H NMR (500 MHz, CDCl_3 , 60 $^\circ\text{C}$): δ 5.63 (br s, 1H), 3.91–3.66 (m, 3H), 3.33–3.21 (m, 1H), 3.15–3.02 (m, 1H), 2.28–2.20 (m, 1H), 1.96–1.79 (m, 4H), 1.75–1.67 (m, 2H), 1.67–1.59 (m, 2H), 1.48 (s, 9H), 1.44–1.33 (m, 3H), 1.25–1.09 (m, 3H); ^{13}C NMR (125 MHz, CDCl_3 , 60 $^\circ\text{C}$): δ 172.1, 155.2, 80.0, 48.4, 46.2, 44.7, 43.3, 33.4, 33.3, 28.7, 27.9, 25.8, 25.04, 25.02, 24.3; IR (film): 3303, 2855, 1696, 1642, 1544 cm^{-1} ; HRMS-APCI (m/z) $[\text{M} + \text{H}]^+$ calcd for $\text{C}_{17}\text{H}_{31}\text{N}_2\text{O}_3$, 311.2335; found 311.2301.



Amide 9 (Figure 3): Purification by flash chromatography (9:1 \rightarrow 3:1 Hexanes:EtOAc) generated amide **9** (91% yield, average of two experiments) as a white solid. Amide **9**: R_f 0.42 (2:1 Hexanes:EtOAc). Spectral data match those previously reported for amide **9** (see page S14).

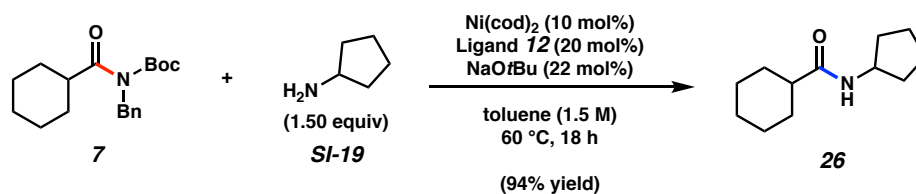


Amide 9 (Figure 3): Purification by flash chromatography (9:1 → 3:1 Hexanes:EtOAc) generated amide **9** (82% yield, average of two experiments) as a white solid. Amide **9**: R_f 0.42 (2:1 Hexanes:EtOAc). Spectral data match those previously reported for amide **9** (see page S14).



Amide 9 (Figure 3): Purification by flash chromatography (9:1 → 3:1 Hexanes:EtOAc) generated amide **9** (59% yield, average of two experiments) as a white solid. Amide **9**: R_f 0.42 (2:1 Hexanes:EtOAc). Spectral data match those previously reported for amide **9** (see page S14).

D. Scope of Amine Nucleophiles



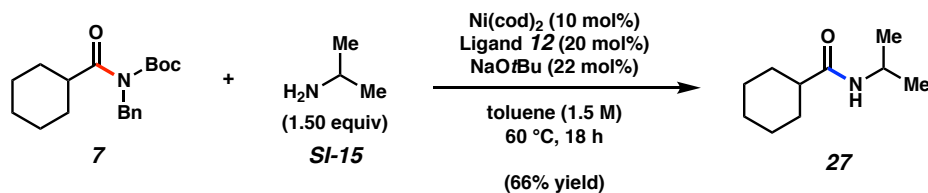
Representative Procedure (coupling of amide 7 and cyclopentylamine (SI-19) is used as an example). Amide **22 (Figure 4)**: A 1-dram vial containing a magnetic stir bar was flame-dried under reduced pressure, and then allowed to cool under N_2 . The vial was charged with amide substrate **7** (63.4 mg, 0.200 mmol, 1.0 equiv) and the vial was flushed with N_2 . The vial was then taken into a glove box and charged with 1,3-dicyclohexylbenzimidazolium chloride (**12**, 12.8 mg, 0.040 mmol, 20 mol%), $\text{Ni}(\text{cod})_2$ (5.5 mg, 0.010 mmol, 10 mol%) and NaOtBu (4.2 mg, 0.044 mmol, 22 mol%). Subsequently, cyclopentylamine (**SI-19**, 34 μL , 0.30 mmol, 1.5 equiv) and toluene (0.133 mL, 1.5 M) were added. The vial was sealed with a Teflon-lined screw cap, removed from the glove box, and stirred at 60 °C for 18 h. After cooling to 23 °C, the mixture was diluted with hexanes (0.5 mL) and filtered over a plug of silica gel (10 mL of EtOAc eluent). The volatiles were removed under reduced pressure and the crude residue was purified by flash chromatography (9:1 → 3:1 Hexanes:EtOAc) to generate amide **26** (94% yield, average of two experiments) as a white solid. Amide **26**: mp: 174.6–176.6 °C; R_f 0.39 (2:1 Hexanes:EtOAc); ^1H

NMR (500 MHz, CDCl₃): δ 5.33 (br s, 1H), 4.20 (sextet, *J* = 7.0, 1H), 2.04–1.95 (m, 3H), 1.85–1.76 (m, 4H), 1.67–1.57 (m, 5H), 1.45–1.37 (m, 2H), 1.36–1.29 (m, 2H), 1.27–1.22 (m, 3H); ¹³C NMR (125 MHz, CDCl₃): δ 175.8, 51.0, 45.8, 33.4, 29.9, 25.92, 23.9; IR (film): 3265, 3074, 2929, 2852, 1704, 1635, 1552, 1453 cm⁻¹; HRMS-APCI (*m/z*) [M + H]⁺ calcd for C₁₂H₂₂NO₂, 196.1701; found 196.1702.

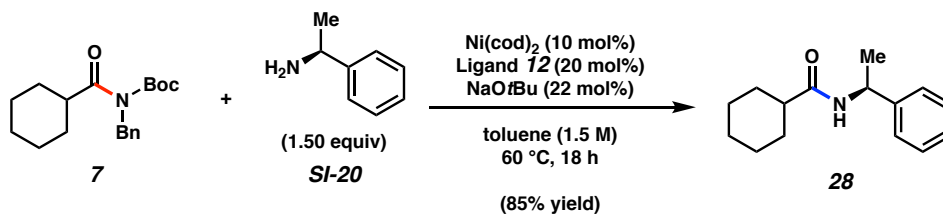
Note: It was found that the purity of both coupling partners had a significant effect on the yield of a given coupling. Additionally, maintaining a moderate stir rate (500–900 rpm) and ensuring all NaOtBu enters the reaction mixture are essential for the success of these couplings. Increased amounts of NaOtBu are not detrimental to the reaction and can help alleviate the latter of the aforementioned scenarios.

Any modifications of the conditions shown in the representative procedure above are specified in the following schemes, which depict all of the results shown in Figure 4.

*For each of the nickel-catalyzed reactions described herein, control experiments were performed concurrently where Ni(cod)₂ and both Ni(cod)₂ and **12**/NaOtBu were omitted from the reactions. In all cases, these control experiments led to the recovery of the amide substrates with minimal (< 10%) detectable conversion to the corresponding amides.*

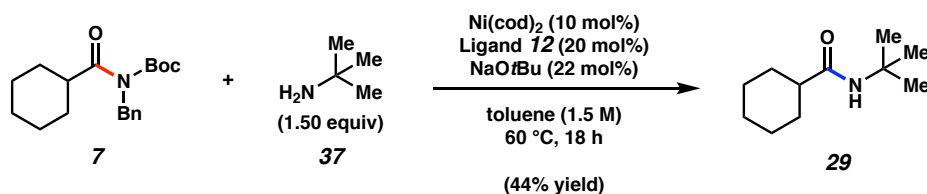


Amide 27 (Figure 4): Purification by flash chromatography (9:1 → 3:1 Hexanes:EtOAc) generated amide **27** (66% yield, average of two experiments) as a white solid. Amide **27**: *R_f* 0.29 (2:1 Hexanes:EtOAc). Spectral data match those previously reported.²

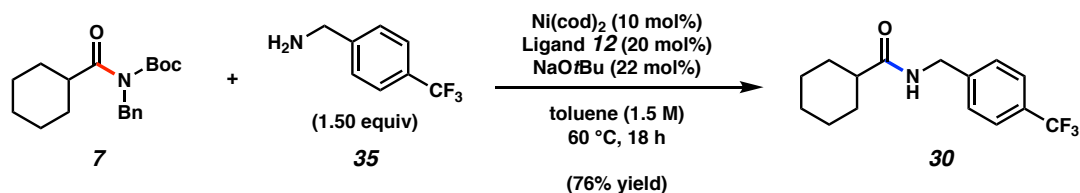


Amide 28 (Figure 4): Purification by flash chromatography (100% Hexanes → 9:1 Hexanes:EtOAc → 100% EtOAc) generated amide **28** (85% yield, average of two experiments) as a yellow solid Amide **28**: mp: 131.1–134.6 °C; *R_f* 0.46 (2:1 Hexanes:EtOAc); ¹H NMR (500

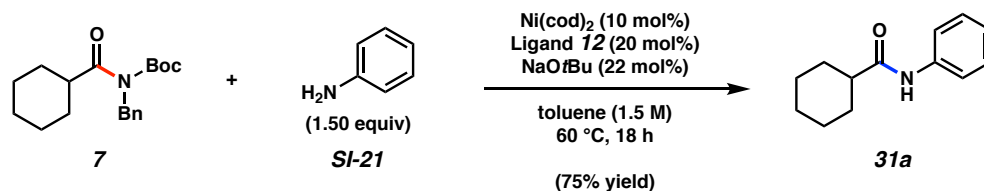
MHz, CDCl₃): δ 7.35–7.23 (m, 5H), 5.73–5.60 (m, 1H), 5.13 (quint, $J = 7.2$, 1H), 2.06 (tt, $J = 11.7, 3.3$, 1H), 1.88–1.77 (m, 4H), 1.67–1.64 (m, 1H), 1.48–1.38 (m, 5H), 1.31–1.15 (m, 3H); ¹³C NMR (125 MHz, CDCl₃): δ 175.2, 143.6, 128.8, 127.4, 126.2, 48.4, 45.7, 29.83, 29.77, 25.9, 21.9; IR (film): 3346, 2926, 2855, 1643, 1520, 1450 cm⁻¹; HRMS-APCI (m/z) [$M + H$]⁺ calcd for C₁₅H₂₂NO, 232.1701; found 232.1690; $[\alpha]^{20.1}_D -85.90^\circ$ ($c = 1.00$, CHCl₃).



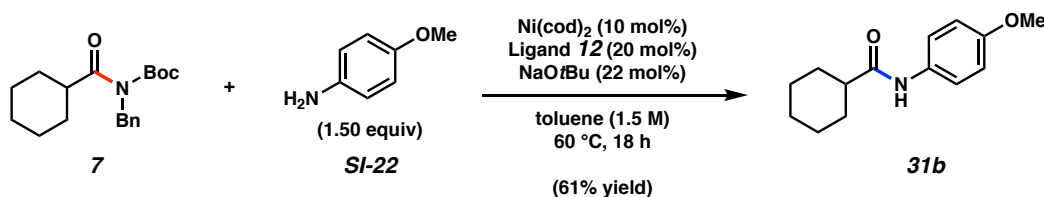
Amide 29 (Figure 4): Purification by preparative thin layer chromatography (5:1 Hexanes:EtOAc) generated amide **29** (44% yield, average of two experiments) as a white solid. Amide **29**: R_f 0.26 (5:1 Hexanes:EtOAc). Spectral data match those previously reported.³



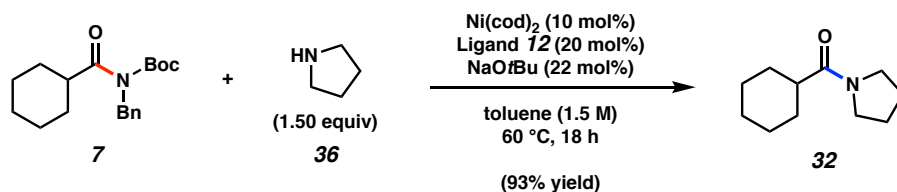
Amide 30 (Figure 4): Purification by flash chromatography (9:1 → 3:1 Hexanes:EtOAc) generated amide **30** (76% yield, average of two experiments) as a white solid. Amide **30**: mp: 135.9–137.4 °C; R_f 0.33 (2:1 Hexanes:EtOAc); ¹H NMR (500 MHz, CDCl₃): δ 7.58 (d, $J = 8.1$, 2H), 7.38 (d, $J = 8.0$, 2H), 5.78 (br s, 1H), 4.50 (d, $J = 6.1$, 2H), 2.13 (tt, $J = 11.7, 3.5$, 1H), 1.91–1.88 (m, 2H), 1.83–1.79 (m, 2H), 1.70–1.67 (m, 1H), 1.52–1.43 (m, 2H), 1.33–1.17 (m, 3H); ¹³C NMR (125 MHz, CDCl₃, 10 of 11 carbons observed): δ 176.2, 142.9, 130.0, 129.7, 128.0, 125.8 (quartet, $J_{C-F} = 3.8$), 45.7, 43.0, 29.9, 25.8; ¹⁹F NMR (282 MHz, CDCl₃): δ -62.5; IR (film): 3291, 2931, 2856, 1643, 1549, 1328 cm⁻¹; HRMS-APCI (m/z) [$M + H$]⁺ calcd for C₁₅H₁₉F₃NO, 286.1419; found 286.1405.



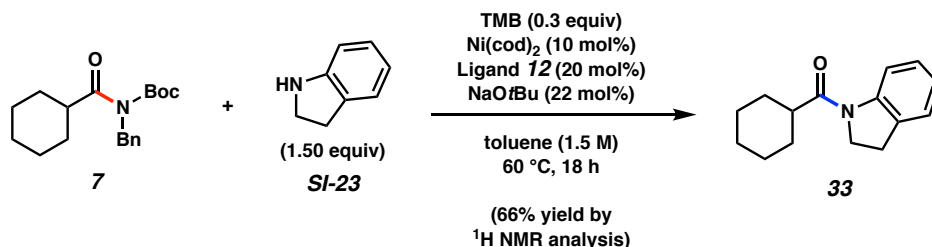
Amide 31a (Figure 4): Purification by flash chromatography (9:1 → 3:1 Hexanes:EtOAc) generated amide **31a** (75% yield, average of two experiments) as an off-white solid. Amide **31a**: R_f 0.25 (5:1 Hexanes:EtOAc). Spectral data match those previously reported.⁴



Amide 31b (Figure 4): Purification by flash chromatography (9:1 → 3:1 Hexanes:EtOAc) generated amide **31b** (61% yield, average of two experiments) as an off-white solid. Amide **31b**: R_f 0.23 (5:1 Hexanes:EtOAc). Spectral data match those previously reported.⁵

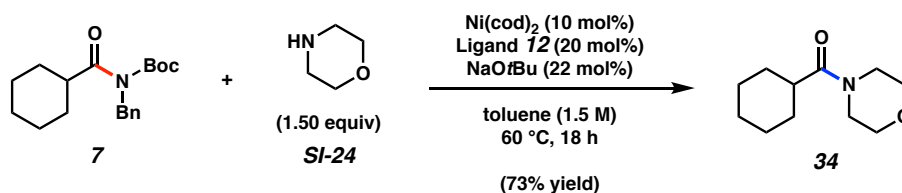


Amide 32 (Figure 4): Purification by preparative thin layer chromatography (2:1 Hexanes:EtOAc) generated amide **32** (93% yield, average of two experiments) as a white solid. Amide **32**: R_f 0.26 (5:1 Hexanes:EtOAc). Spectral data match those previously reported.⁶



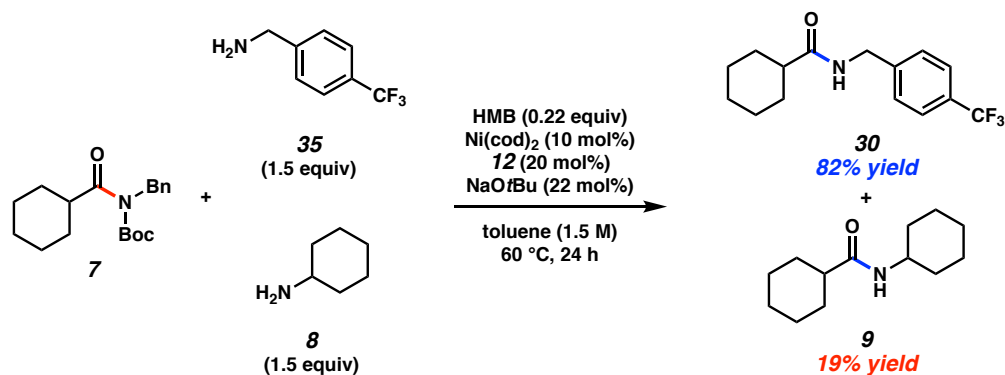
Amide 33 (Figure 4): Purification by preparative thin layer chromatography (2:1 Hexanes:EtOAc) generated amide **33** as an inseparable mixture with the HNBnBoc byproduct. To obtain an authentic sample of the product, to a flame dried scintillation vial containing the

mixture was added a stir bar and 0.100 mL TFA. The vial was sealed with a Teflon-lined screw cap and stirred at 23 °C for 3 h. The reaction was quenched by the slow addition of solid NaHCO₃ until bubbling ceased. The reaction mixture was diluted with EtOAc (25 mL) and deionized water (20 mL). The aqueous layer was extracted with EtOAc (3 x 25 mL). The combined organic layers were then dried over Na₂SO₄, filtered, and then concentrated under reduced pressure to yield amide **33** (66% crude ¹H NMR yield using TMB as an internal standard, average of two experiments) as a white solid. Amide **33**: mp: 133.6–135.2 °C; R_f 0.68 (2:1 Hexanes:EtOAc); ¹H NMR (500 MHz, CDCl₃): δ 8.26 (d, *J* = 8.0, 1H), 7.20–7.17 (m, 2H), 7.00 (dt, *J* = 7.3, 0.8 1H), 4.13 (t, *J* = 8.6, 2H), 3.19 (app t, *J* = 8.2, 2H), 2.46 (app t, *J* = 11.5, 1H), 1.92–1.80 (m, 4H), 1.77–1.68 (m, 1H), 1.67–1.55 (m, 2H), 1.42–1.23 (m, 3H); ¹³C NMR (125 MHz, CDCl₃): δ 174.9, 143.4, 131.3, 127.7, 124.6, 123.6, 117.5, 47.9, 44.1, 29.2, 28.2, 26.0, 25.9; IR (film): 3075, 2920, 2851, 1649, 1598, 1482 cm⁻¹; HRMS-APCI (*m/z*) [M + H]⁺ calcd for C₁₅H₂₀NO, 230.1545; found 230.1544.

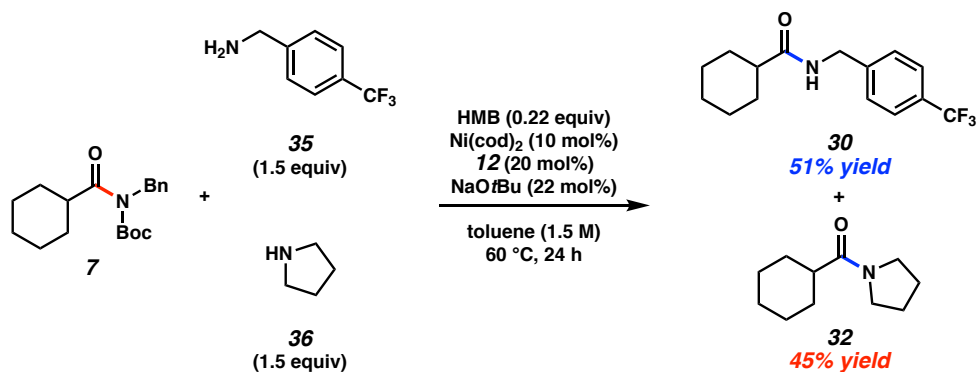


Amide 34 (Figure 4): Purification by preparative thin layer chromatography (9:1 → 3:1 → 1:1 Hexanes:EtOAc) generated amide **34** (73% yield, average of two experiments) as a white solid. Amide **34**: R_f 0.38 (2:1 Hexanes:EtOAc). Spectral data match those previously reported.⁷

E. Amine Nucleophile Competition Experiments

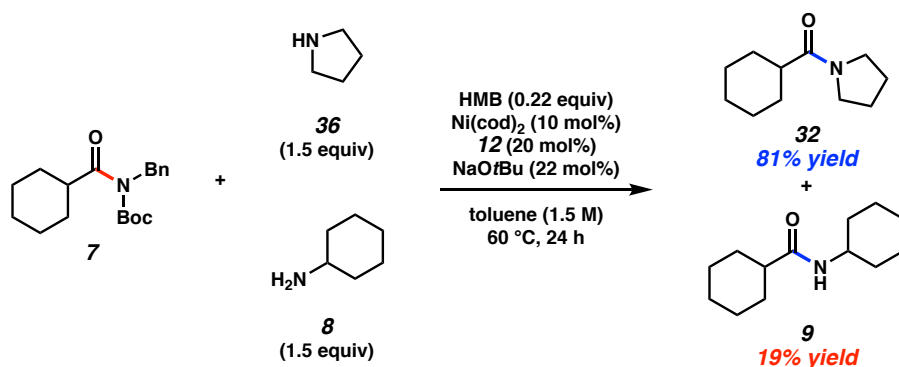


Unbranched vs α -Branched Primary Amine (Figure 5). A 1-dram vial containing a magnetic stir bar was flame-dried under reduced pressure, and then allowed to cool under N₂. The vial was charged with amide substrate **7** (63.4 mg, 0.200 mmol, 1.0 equiv) and the vial was flushed with N₂. The vial was then taken into a glove box and charged with 1,3-dicyclohexylbenzimidazolium chloride (**12**, 12.8 mg, 0.040 mmol, 20 mol%), Ni(cod)₂ (5.5 mg, 0.010 mmol, 10 mol%) and NaOtBu (4.2 mg, 0.044 mmol, 22 mol%). Subsequently, cyclohexylamine (**8**, 31.4 μ L, 0.30 mmol, 1.5 equiv), 4-(trifluoromethyl)benzylamine (**35**, 34.0 μ L, 0.30 mmol, 1.5 equiv) and then toluene (0.133 mL, 1.5 M) were added. The vial was sealed with a Teflon-lined screw cap, removed from the glove box, and stirred at 60 °C for 24 h. After cooling to 23 °C, the mixture was diluted with hexanes (0.5 mL) and filtered over a plug of silica gel (10 mL of EtOAc eluent). The volatiles were removed under reduced pressure. Yields were determined by ¹H NMR analysis with hexamethylbenzene (HMB). Spectral data match those previously reported for amides **30** and **9** (see pages S20 and S14, respectively).



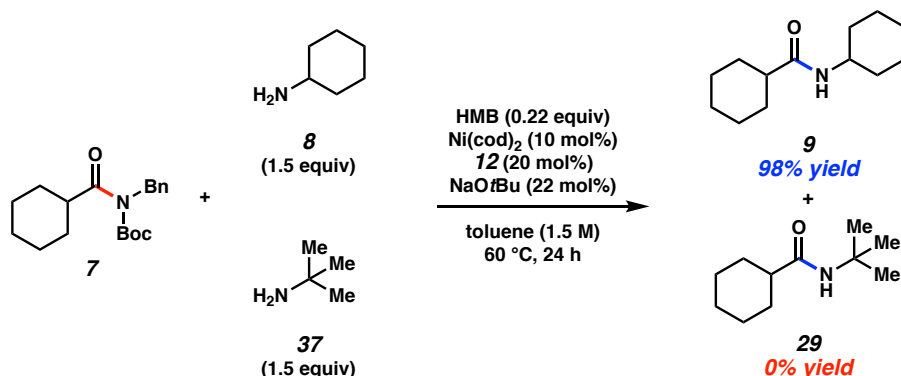
Unbranched Primary vs Secondary Amine (Figure 5). A 1-dram vial containing a magnetic stir bar was flame-dried under reduced pressure, and then allowed to cool under N₂. The vial was

charged with amide substrate **7** (63.4 mg, 0.200 mmol, 1.0 equiv) and the vial was flushed with N₂. The vial was then taken into a glove box and charged with 1,3-dicyclohexylbenzimidazolium chloride (**12**, 12.8 mg, 0.040 mmol, 20 mol%), Ni(cod)₂ (5.5 mg, 0.010 mmol, 10 mol%) and NaOtBu (4.2 mg, 0.044 mmol, 22 mol%). Subsequently, 4-(trifluoromethyl)benzylamine (**35**, 34.0 μL, 0.30 mmol, 1.5 equiv), pyrrolidine (**36**, 25.0 μL, 0.30 mmol, 1.5 equiv) and then toluene (0.133 mL, 1.5 M) were added. The vial was sealed with a Teflon-lined screw cap, removed from the glove box, and stirred at 60 °C for 24 h. After cooling to 23 °C, the mixture was diluted with hexanes (0.5 mL) and filtered over a plug of silica gel (10 mL of EtOAc eluent). The volatiles were removed under reduced pressure. Yields were determined by ¹H NMR analysis with hexamethylbenzene (HMB). Spectral data match those previously reported for amides **30** and **32** (see pages S20 and S21 respectively).

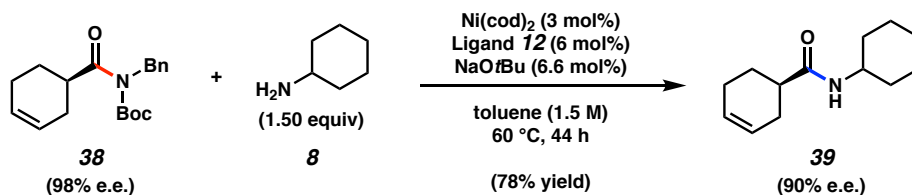


Secondary vs Primary α -Branched Amine (Figure 5). A 1-dram vial containing a magnetic stir bar was flame-dried under reduced pressure, and then allowed to cool under N₂. The vial was charged with amide substrate **7** (63.4 mg, 0.200 mmol, 1.0 equiv) and the vial was flushed with N₂. The vial was then taken into a glove box and charged with 1,3-dicyclohexylbenzimidazolium chloride (**12**, 12.8 mg, 0.040 mmol, 20 mol%), Ni(cod)₂ (5.5 mg, 0.010 mmol, 10 mol%) and NaOtBu (4.2 mg, 0.044 mmol, 22 mol%). Subsequently, pyrrolidine (**36**, 25.0 μL, 0.30 mmol, 1.5 equiv), cyclohexylamine (**8**, 34.0 μL, 0.30 mmol, 1.5 equiv), and then toluene (0.133 mL, 1.5 M) were added. The vial was sealed with a Teflon-lined screw cap, removed from the glove box, and stirred at 60 °C for 24 h. After cooling to 23 °C, the mixture was diluted with hexanes (0.5 mL) and filtered over a plug of silica gel (10 mL of EtOAc eluent). The volatiles were removed under reduced pressure. Yields were determined by ¹H NMR analysis with hexamethylbenzene

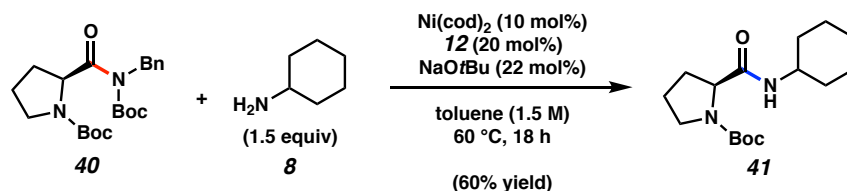
(HMB). Spectral data match those previously reported for amides **32** and **9** (see pages S21 and S14 respectively).



Cyclohexyl vs *t*-Butyl Amine (Figure 5). A 1-dram vial containing a magnetic stir bar was flame-dried under reduced pressure, and then allowed to cool under N₂. The vial was charged with amide substrate **7** (63.4 mg, 0.200 mmol, 1.0 equiv) and the vial was flushed with N₂. The vial was then taken into a glove box and charged with 1,3-dicyclohexylbenzimidazolium chloride (**12**, 12.8 mg, 0.040 mmol, 20 mol%), Ni(cod)₂ (5.5 mg, 0.010 mmol, 10 mol%) and NaOtBu (4.2 mg, 0.044 mmol, 22 mol%). Subsequently, cyclohexylamine (**8**, 34.0 μL, 0.30 mmol, 1.5 equiv), *tert*-butylamine (**37**, 32.0 μL, 0.30 mmol, 1.5 equiv), and then toluene (0.133 mL, 1.5 M) were added. The vial was sealed with a Teflon-lined screw cap, removed from the glove box, and stirred at 60 °C for 24 h. After cooling to 23 °C, the mixture was diluted with hexanes (0.5 mL) and filtered over a plug of silica gel (10 mL of EtOAc eluent). The volatiles were removed under reduced pressure. Yields were determined by ¹H NMR analysis with hexamethylbenzene (HMB). Spectral data match those previously reported for amide **9** (see page S14).

F. Gram Scale Transamidation of Enantioenriched Aliphatic Amide **38**

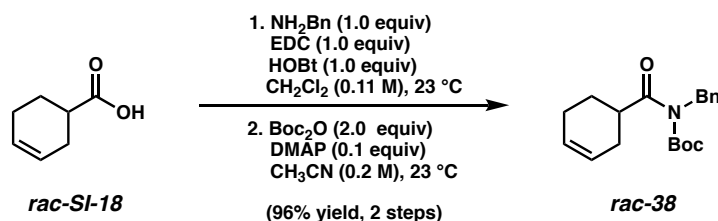
Amide 39 (Figure 6): A scintillation vial containing a magnetic stir bar was flame-dried under reduced pressure, and then allowed to cool under N₂. The vial was charged with amide substrate **38** (1.00 g, 3.18 mmol, 1.0 equiv) and the vial was flushed with N₂. The vial was then taken into a glove box and charged with 1,3-dicyclohexylbenzimidazolium chloride (**12**, 60.9 mg, 0.191 mmol, 6 mol%), Ni(cod)₂ (26.3 mg, 0.095 mmol, 3 mol%) and NaOtBu (20.2 mg, 0.210 mmol, 6.6 mol%). Subsequently, cyclohexylamine (**8**, 547 μL, 4.77 mmol, 1.5 equiv) and then toluene (2.12 mL, 1.5 M) were added. The vial was sealed with a Teflon-lined screw cap, removed from the glove box, and stirred at 60 °C for 44 h. After cooling to 23 °C, the mixture was diluted with hexanes (0.50 mL) and filtered over a plug of silica gel (20 mL of EtOAc eluent). The volatiles were removed under reduced pressure and the crude residue was purified by flash chromatography (9:1 Hexanes:EtOAc) to generate amide **39** (78% yield) as a white solid. Amide **39**: mp: 160.5–162.3 °C; R_f 0.31 (2:1 Hexanes:EtOAc); ¹H NMR (500 MHz, CDCl₃): δ 5.74–5.65 (m, 2H), 5.35 (s, 1H), 3.78 (m, 1H), 2.35–2.02 (m, 5H), 1.96–1.86 (m, 3H), 1.77–1.65 (m, 3H), 1.65–1.58 (m, 1H), 1.42–1.32 (m, 2H), 1.22–1.06 (m, 3H); ¹³C NMR (125 MHz, CDCl₃): δ 174.9, 127.0, 125.6, 48.0, 41.6, 33.4, 28.3, 26.0, 25.7, 25.0, 24.8; IR (film): 3294, 2932, 1637, 1548, 1234 cm⁻¹; HRMS-APCI (*m/z*) [M + H]⁺ calcd for C₁₃H₂₂NO, 208.1701; found 208.1686; [α]_D^{20.4} –42.40 ° (*c* = 1.00, CHCl₃).

G. Procedure for the Transamidation of **40** using Pre-Formed Catalyst Solution

Amide 41 (Figure 6): Two 1-dram vials containing magnetic stir bars were flame-dried under reduced pressure, and then allowed to cool under N_2 . One vial was charged with amide substrate **40** (80.9 mg, 0.200 mmol, 1.0 equiv) and then flushed with N_2 . Both vials were taken into a glove box. In one of the vials, a stock solution of active catalyst was made by charging the empty 1-dram vial with 1,3-dicyclohexylbenzimidazolium chloride (**12**, 38.4 mg, 0.120 mmol, 60 mol%), $\text{Ni}(\text{cod})_2$ (16.5 mg, 0.060 mmol, 30 mol%), NaOtBu (12.6 mg, 0.132 mmol, 66 mol%), and toluene (0.399 mL, 0.5 M). The vial was sealed with a Teflon-lined screw cap, and stirred at ambient temperature in the glove box for 1 h. After 1 h, a portion of the catalyst stock solution (0.133 mL) and cyclohexylamine (**8**, 34.1 μL , 0.30 mmol, 1.5 equiv) were added to the vial containing substrate **40**. This vial was sealed with a Teflon-lined screw cap, removed from the glove box, and stirred at 60 °C for 18 h. After cooling to 23 °C, the mixture was diluted with hexanes (0.5 mL) and filtered over a plug of silica gel (10 mL of EtOAc eluent). The volatiles were removed under reduced pressure and the crude residue was purified by flash chromatography (10:1 \rightarrow 3:1 Hexanes:EtOAc \rightarrow 100% EtOAc) to generate amide **41** (60% yield, average of two experiments) as a white solid. Amide **41**: R_f 0.17 (2:1 Hexanes:EtOAc). Spectral data match those previously reported.⁸

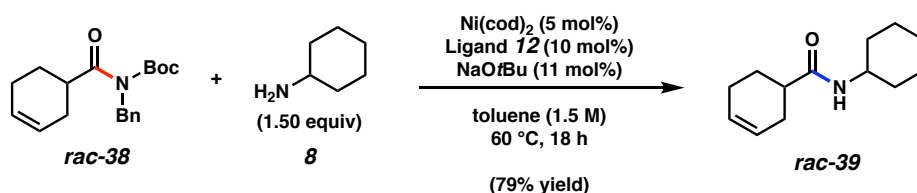
H. Verification of Enantiopurity

a) Synthesis of Racemic Compound



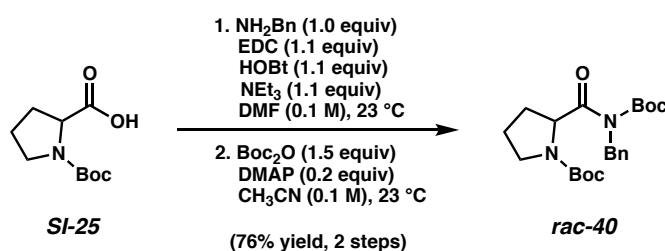
Rac-38 Amide. To a mixture of carboxylic acid **rac-SI-18** (1.0 g, 7.9 mmol, 1.0 equiv), EDC (1.50 g, 7.9 mmol, 1.0 equiv), HOBT (1.1 g, 7.9 mmol, 1.0 equiv), and CH_2Cl_2 (79 mL, 0.1 M) was added benzylamine (0.86 mL, 7.9 mmol, 1.0 equiv). The resulting mixture was stirred at 23 °C for 16 h, and then diluted with CH_2Cl_2 (30 mL). The mixture was washed with 1 M HCl (30 mL), saturated aqueous NaHCO_3 (30 mL), and brine (30 mL). The combined organic layer was dried over Na_2SO_4 , filtered, and then concentrated under reduced pressure. The resulting crude material was used in the subsequent step without further purification.

To a flask containing the crude material from the previous step was added DMAP (56.7 mg, 0.46 mmol, 0.1 equiv), followed by acetonitrile (23 mL, 0.2 M). Boc_2O (2.03 g, 9.28 mmol, 2.0 equiv) was added in one portion and the reaction vessel was flushed with N_2 . The reaction mixture was allowed to stir at 23 °C for 12 h. The mixture was washed with 1.0 M HCl (5 mL) and brine (5 mL). After drying over Na_2SO_4 , the organic layers were filtered and concentrated under reduced pressure. The resulting crude residue was purified by flash chromatography (10:1 Hexanes:EtOAc) to yield **rac-38** (1.40 g, 96% yield, over two steps) as a clear oil. Spectral data matched those previously reported for amide **38** (see page S11).



Amide rac-39. A 1-dram vial containing a magnetic stir bar was flame-dried under reduced pressure, and then allowed to cool under N_2 . The vial was charged with amide substrate **rac-38** (63.1 mg, 0.200 mmol, 1.0 equiv) and the vial was flushed with N_2 . The vial was then taken into a glove box and charged with 1,3-dicyclohexylbenzimidazolium chloride (**12**, 6.4 mg, 0.020

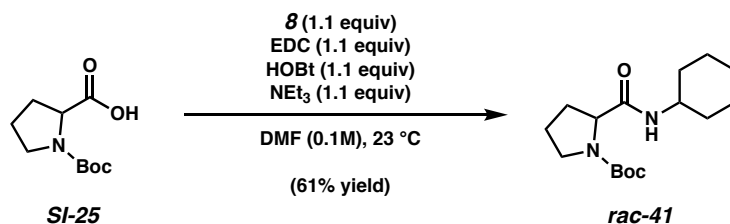
mmol, 10 mol%), Ni(cod)₂ (2.8 mg, 0.010 mmol, 5 mol%) and NaOtBu (2.1 mg, 0.022 mmol, 11 mol%). Subsequently, cyclohexylamine (**8**, 34.0 μL, 0.30 mmol, 1.5 equiv) and then toluene (0.133 mL, 1.5 M) were added. The vial was sealed with a Teflon-lined screw cap, removed from the glove box, and stirred at 60 °C for 18 h. After cooling to 23 °C, the mixture was diluted with hexanes (0.5 mL) and filtered over a plug of silica gel (10 mL of EtOAc eluent). The volatiles were removed under reduced pressure and the crude residue was purified by flash chromatography (9:1 → 3:1 Hexanes:EtOAc) to generate amide **rac-39** (79% yield, average of two experiments) as a white solid. Spectral data matched those previously reported for amide **39** (page S24).



Amide rac-40 (Figure 6). **rac-40** was prepared using the known procedure described for (–)-**40**,¹ but using racemic carboxylic acid **SI-25**. To a mixture of carboxylic acid **SI-25** (500 mg, 2.32 mmol, 1.0 equiv), EDC (490 mg, 2.55 mmol, 1.1 equiv), HOBt (344 mg, 2.55 mmol, 1.1 equiv), triethylamine (0.356 mL, 2.55 mmol, 1.1 equiv), and DMF (23 mL, 0.1 M) was added benzylamine (0.279 mL, 2.55 mmol, 1.1 equiv). The resulting mixture was stirred at 23 °C for 4 h, and then diluted with deionized water (30 mL) and EtOAc (30 mL). The layers were separated and the organic layer was washed successively with 1.0 M HCl (30 mL), saturated aqueous NaHCO₃ (30 mL), and brine (30 mL). The organic layer was dried over Na₂SO₄ and concentrated under reduced pressure. The resulting crude solid material was used in the subsequent step without further purification.

To a flask containing the crude material from the previous step was added DMAP (28 mg, 0.232 mmol, 0.2 equiv), followed by acetonitrile (23 mL, 0.1 M). Boc₂O (0.759 mg, 3.50 mmol, 1.5 equiv) was added in one portion and the reaction vessel was flushed with N₂. The reaction mixture was allowed to stir at 23 °C for 15 h. The reaction mixture was diluted with EtOAc (30 mL) and then washed sequentially with saturated aqueous NaHCO₃ (2 x 30 mL) and brine (30 mL). The organic layer was dried over Na₂SO₄ and concentrated under reduced pressure. The resulting crude residue was purified by flash chromatography (9:1 → 3:1

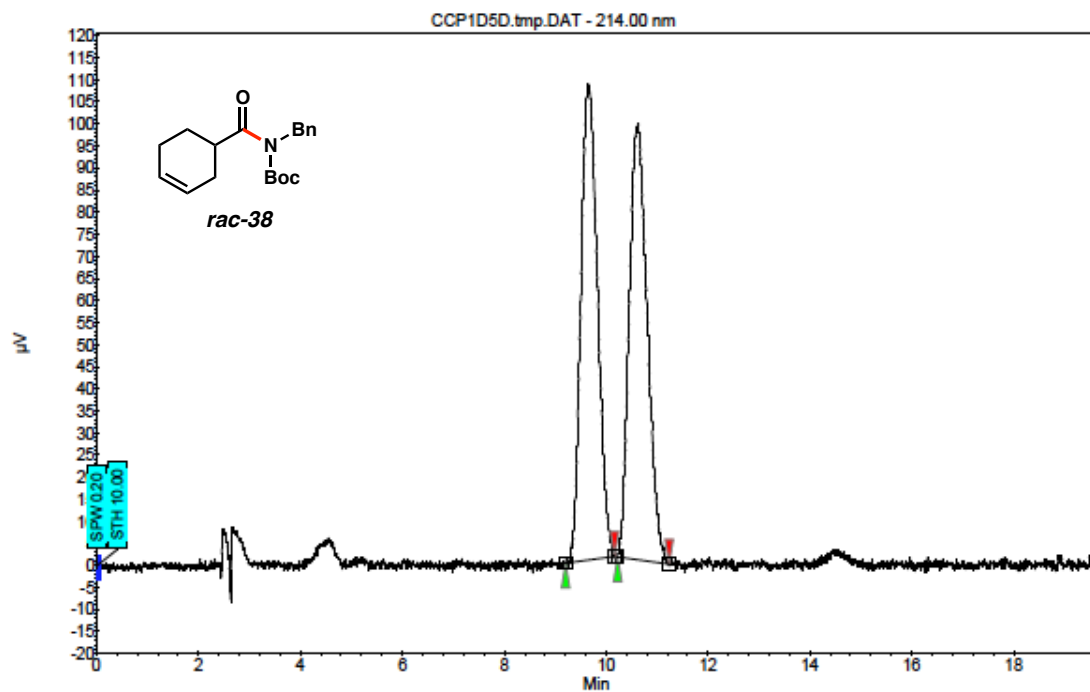
Hexanes:EtOAc) to yield amide **rac-40** (484 mg, 76% yield, over two steps) as a yellow oil. Spectral data matched those previously reported.¹



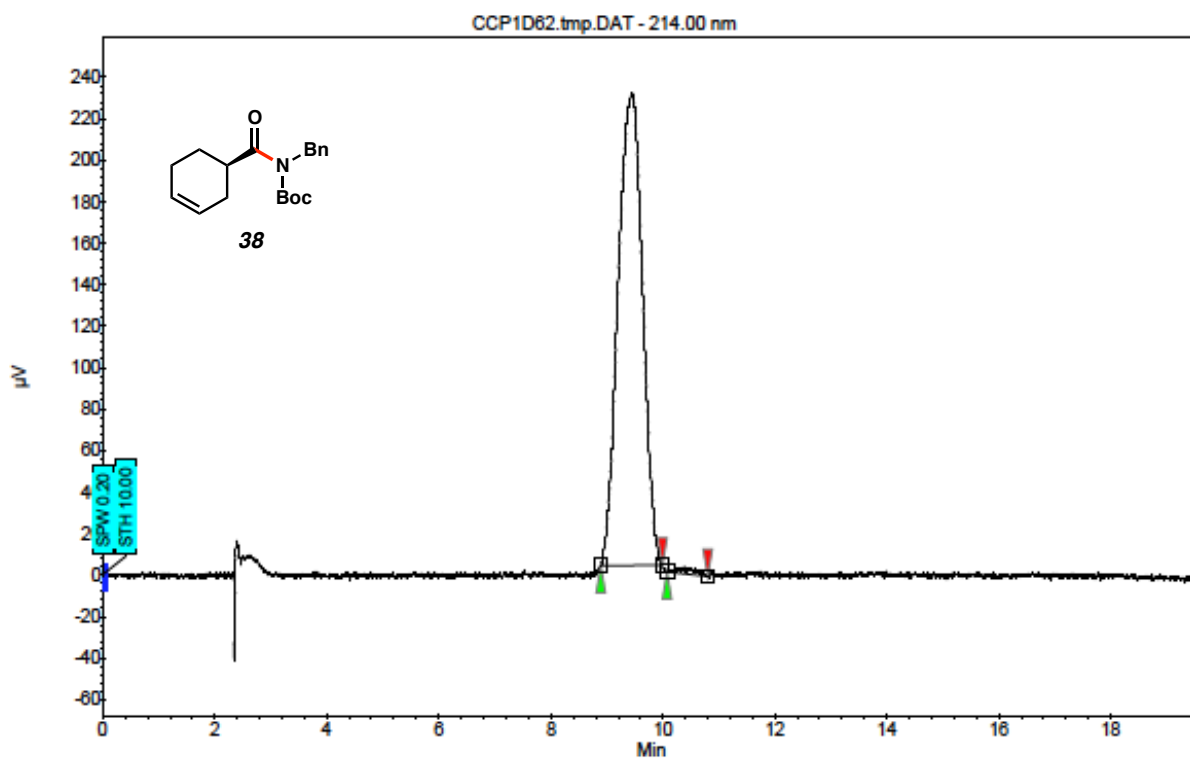
Amide rac-41. To a mixture of racemic carboxylic acid **SI-25** (250 mg, 1.16 mmol, 1.0 equiv), EDC (246 mg, 1.28 mmol, 1.1 equiv), HOBt (173 mg, 1.28 mmol, 1.1 equiv), triethylamine (0.178 mL, 1.28 mmol, 1.1 equiv), and DMF (12 mL, 0.1 M) was added cyclohexylamine (**8**) (0.147 mL, 1.28 mmol, 1.1 equiv). The resulting mixture was stirred at 23 °C for 3 h, and then diluted with deionized water (20 mL) and EtOAc (20 mL). The layers were separated and the organic layer was washed successively with 1.0 M HCl (20 mL), saturated aqueous NaHCO₃ (20 mL), and brine (20 mL). The organics were dried over Na₂SO₄ and concentrated under reduced pressure. The resulting crude residue was purified by flash chromatography (9:1 → 4:1 Hexanes:EtOAc → 100% EtOAc) to yield amide **rac-41** (206 mg, 61% yield) as a white solid. Spectral data matched those previously reported.⁸

b) Chiral SFC/HPLC Assays

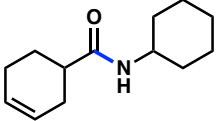
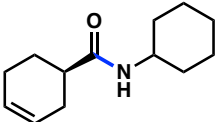
Compound	Method Column/Temp.	Solvent	Method Flow Rate	Retention Times (min)	Enantiomeric Ratio (er)
 rac-38	Daicel ChiralPak OJ-H/23 °C	1% isopropanol in CO ₂	1 mL/min	9.36/10.35	50:50
 38	Daicel ChiralPak OJ-H/23 °C	1% isopropanol in CO ₂	1 mL/min	9.16/10.33	99:1

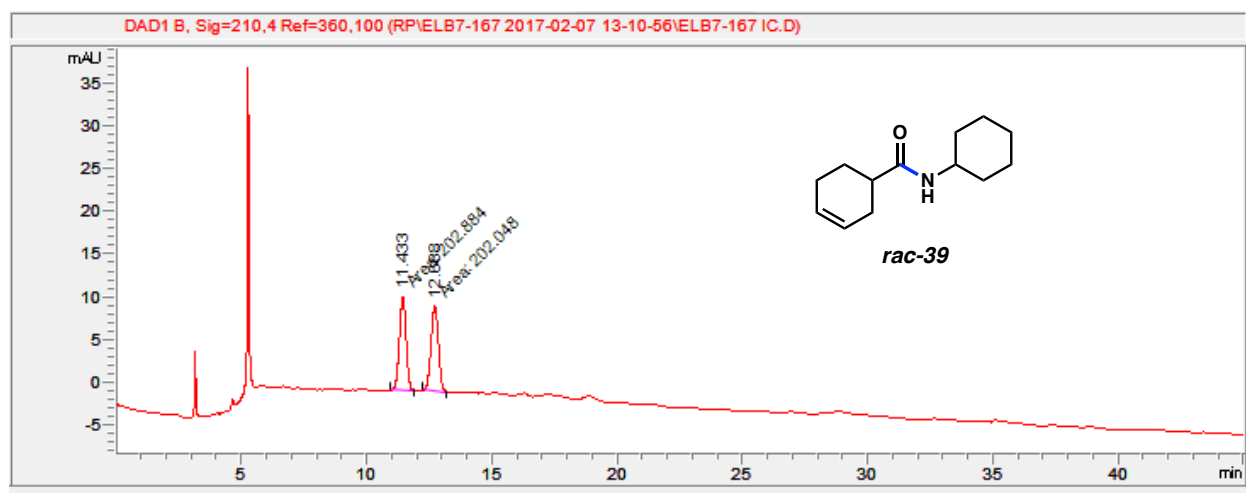


Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[μV]	[μV.Min]	[%]
1	UNKNOWN	9.21	9.64	10.16	0.00	50.12	107.8	40.6	50.117
2	UNKNOWN	10.22	10.63	11.24	0.00	49.88	98.8	40.4	49.883
Total						100.00	206.6	81.0	100.000

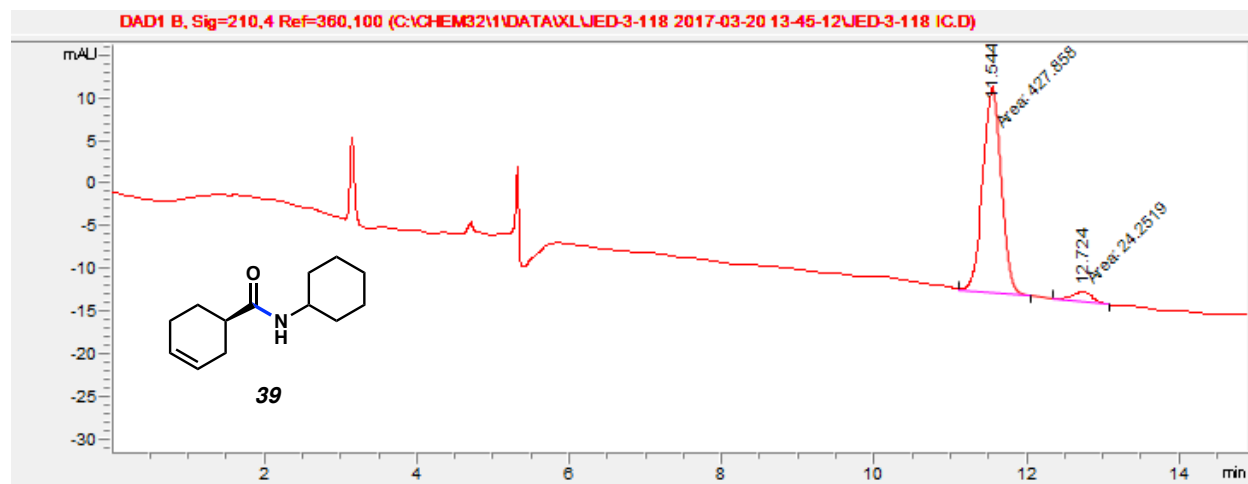


Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[μ V]	[μ V.Min]	[%]
1	UNKNOWN	8.89	9.46	9.99	0.00	99.02	227.6	115.1	99.024
2	UNKNOWN	10.07	10.39	10.80	0.00	0.98	3.5	1.1	0.978
Total						100.00	231.2	116.2	100.000

Compound	Method Column/Temp.	Solvent	Method Flow Rate	Retention Times (min)	Enantiomeric Ratio (er)
 <i>rac-39</i>	Daicel ChiralPak IC-H/23 °C	10% isopropanol in hexanes	1 mL/min	11.4/12.7	50:50
 39	Daicel ChiralPak IC-H/23 °C	10% isopropanol in hexanes	1 mL/min	11.5/12.7	95:5

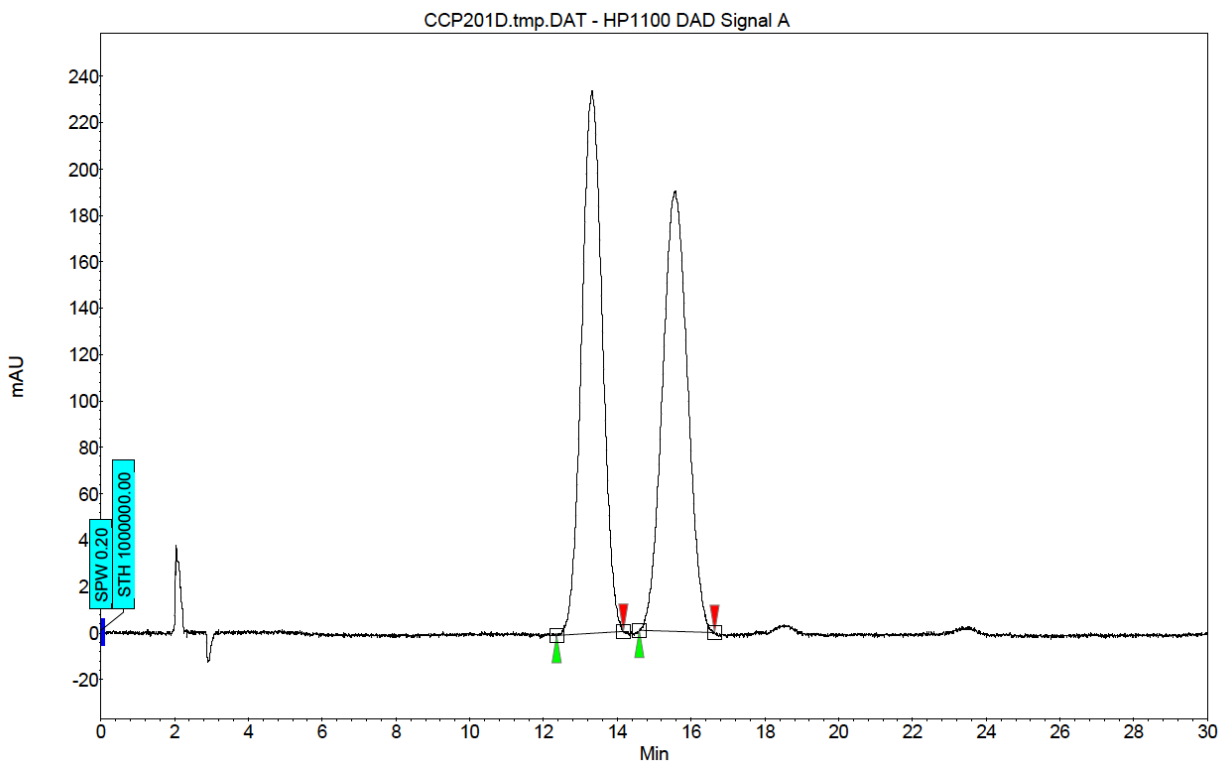


#	Time	Area	Height	Width	Area%	Symmetry
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2	12.688	202	10	0.3383	49.897	1.032

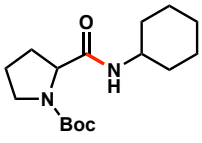
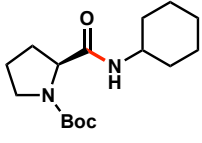


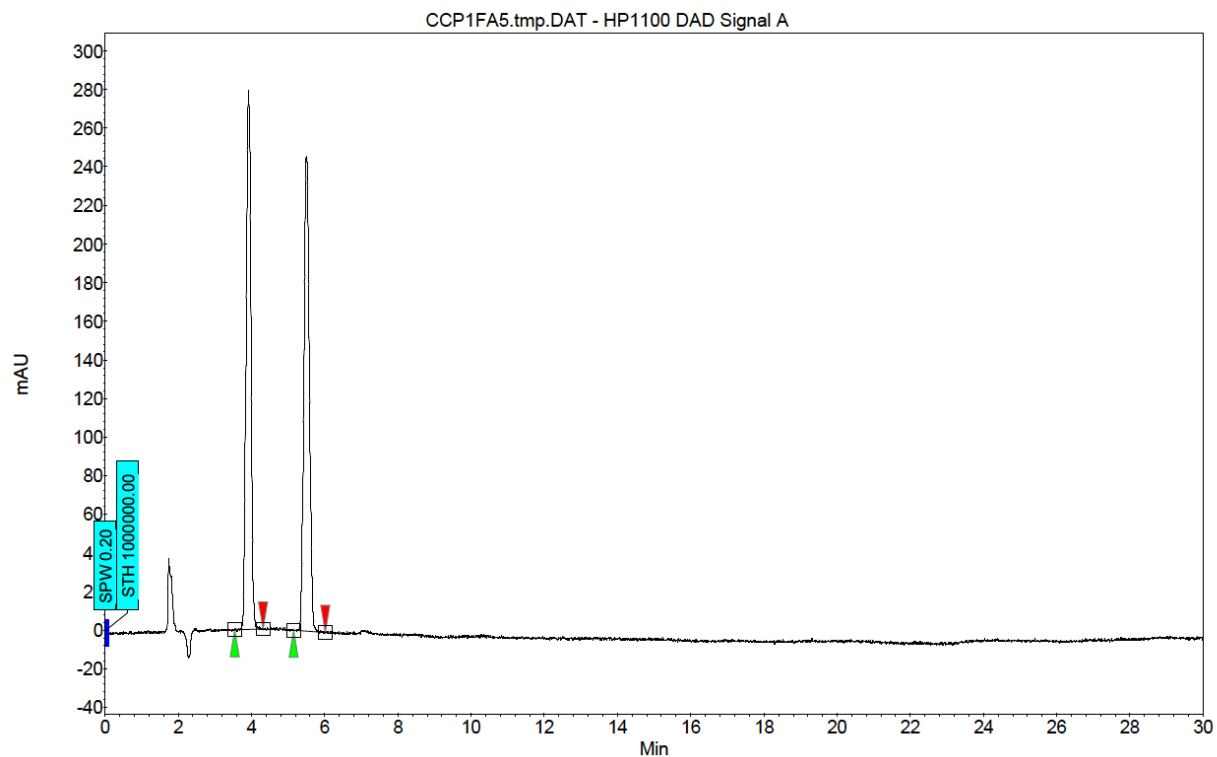
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1	11.544	427.9	24.1	0.2957	94.636	0.997
2	12.724	24.3	1.2	0.3383	5.364	0.902

Compound	Method Column/Temp.	Solvent	Method Flow Rate	Retention Times (min)	Enantiomeric Ratio (er)
 <i>rac-40</i>	Daicel ChiralPak IC-H/23 °C	10% isopropanol in hexanes	1 mL/min	13.3/15.6	50:50
 40	Daicel ChiralPak IC-H/23 °C	10% isopropanol in hexanes	1 mL/min	14.5	>99:1

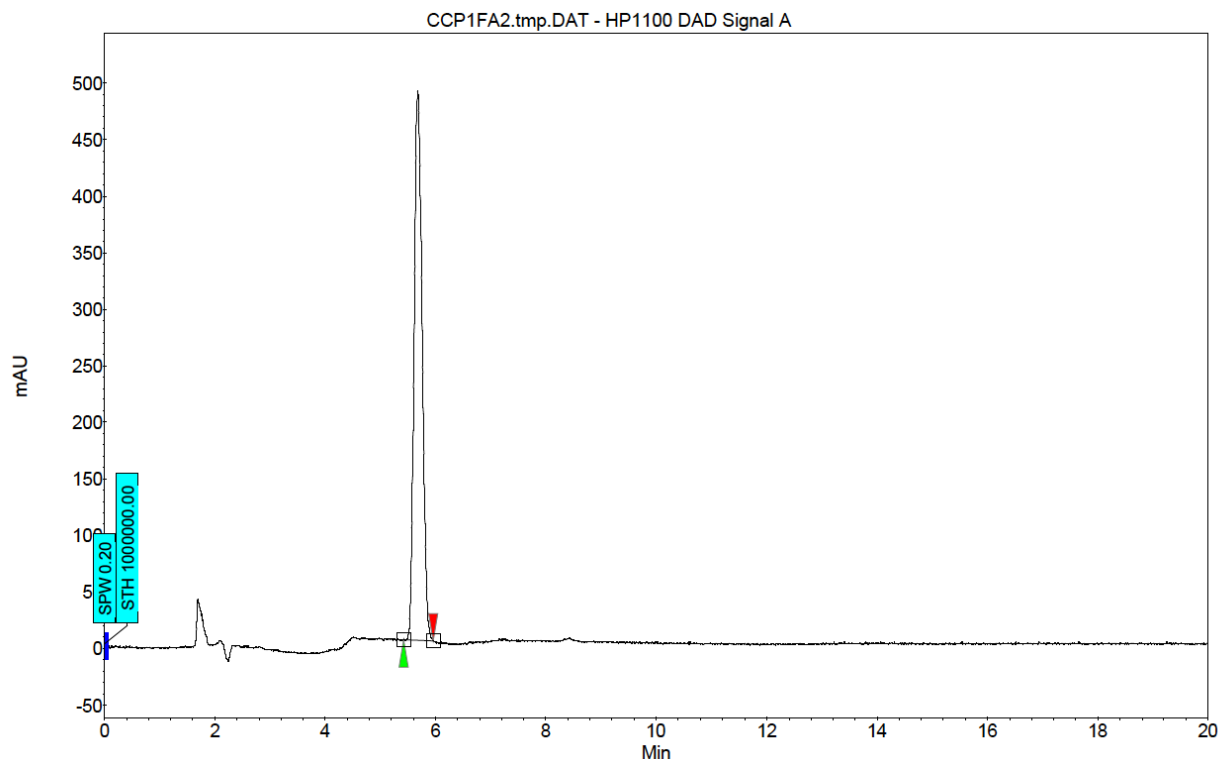


Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[μ V]	[μ V.Min]	[%]
1	UNKNOWN	12.35	13.31	14.16	0.00	50.27	233.8	151.6	50.268
2	UNKNOWN	14.59	15.57	16.63	0.00	49.73	190.0	149.9	49.732
Total						100.00	423.8	301.5	100.000

Compound	Method Column/Temp.	Solvent	Method Flow Rate	Retention Times (min)	Enantiomeric Ratio (er)
 <i>rac-41</i>	Daicel ChiralPak AD-H/23 °C	10% isopropanol in hexanes	1 mL/min	3.9/5.5	50:50
 41	Daicel ChiralPak AD-H/23 °C	10% isopropanol in hexanes	1 mL/min	5.7	>99:1



Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[μ V]	[μ V.Min]	[%]
1	UNKNOWN	3.54	3.92	4.31	0.00	50.05	279.3	42.5	50.049
2	UNKNOWN	5.15	5.50	6.02	0.00	49.95	246.1	42.4	49.951
Total						100.00	525.3	85.0	100.000



Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[μ V]	[μ V.Min]	[%]
1	UNKNOWN	5.42	5.68	5.96	0.00	100.00	486.2	82.3	100.000
Total						100.00	486.2	82.3	100.000

I. Lewis Base-Catalyzed Transamidation Control Experiments

a) Representative procedure for Lewis base-catalyzed transamidation experiments (coupling of amide **38 and cyclohexylamine (**8**) is used as an example).** A 1-dram vial containing a magnetic stir bar was flame-dried under reduced pressure, and then allowed to cool under N_2 . The vial was charged with amide substrate **38** (63.0 mg, 0.2 mmol, 1.0 equiv) and the vial was flushed with N_2 . To the vial were added dichloromethane (200 μ L, 1.0 M), NEt_3 (84 μ L, 0.6 mmol, 3.0 equiv), and cyclohexylamine (**8**, 69 μ L, 0.6 mmol, 3.0 equiv) sequentially at 23 $^{\circ}C$ with vigorous stirring. The vial was then sealed with a Teflon-lined screw cap under a positive stream of N_2 and allowed to stir at 23 $^{\circ}C$ for 15 h. After this time, the reaction was diluted with CH_2Cl_2 (2 mL) and filtered over a celite plug. The mixture was then washed with 1 N HCl (1 mL) and brine (1 mL) sequentially. The organic layer was then dried over Na_2SO_4 , subsequently

filtered, and the volatiles were evaporated under reduced pressure. The yield was determined by ^1H NMR analysis with hexamethylbenzene (HMB) as an external standard.

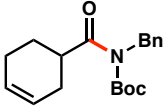
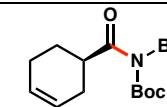
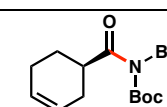
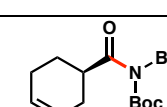
Any modifications of the conditions shown in the representative procedure above are specified in Table S2 below.

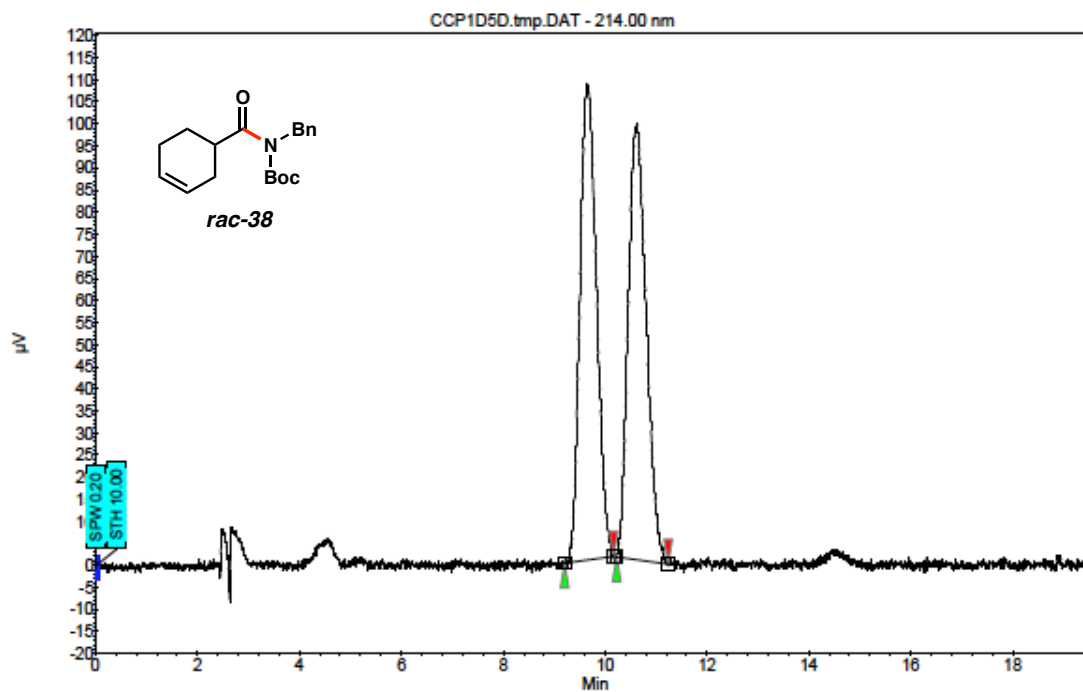
Table S2. Lewis Base-Catalyzed Transamidations of Aliphatic Amides.^a

Entry	Amide	Amine	Temp	Recovery of SM	Amide Product
1			23 °C	97% (98% e.e.)	0%
2			60 °C	93% (99% e.e.)	trace
3			23 °C	95%	0%
4			60 °C	97%	0%
5			23 °C	Quant.	0%
6			60 °C	Quant.	0%

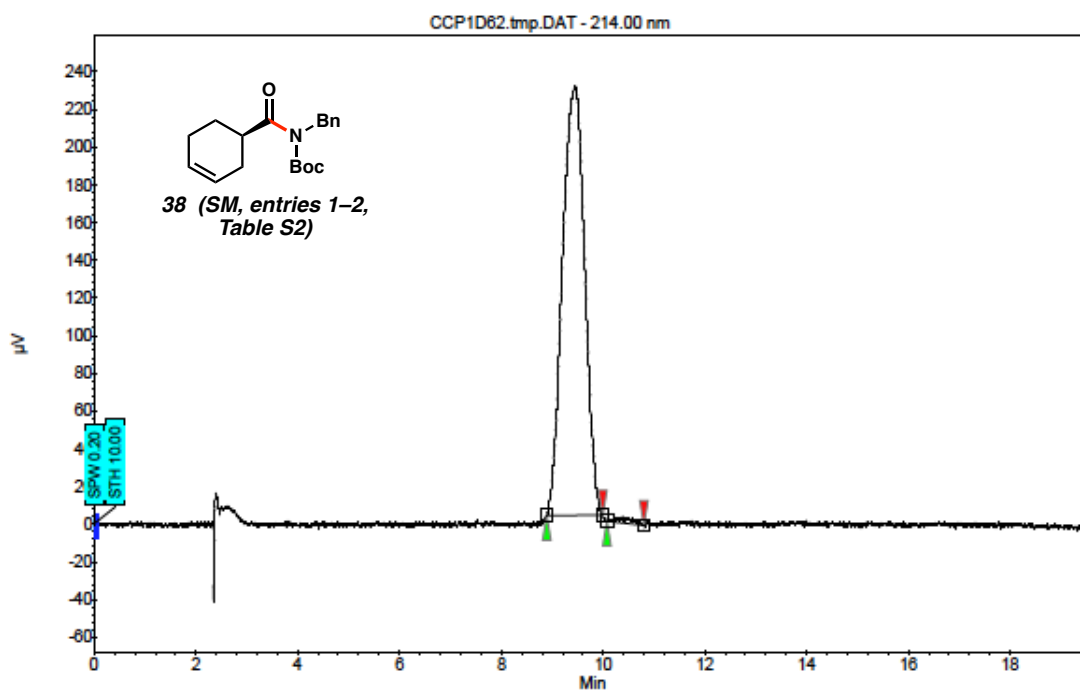
^a Yields were determined using ^1H NMR analysis with hexamethylbenzene (HMB) as an external standard.

b) Verification of enantiopurity for entries 1 and 2 in Table S2 (Chiral SFC/HPLC Assays)

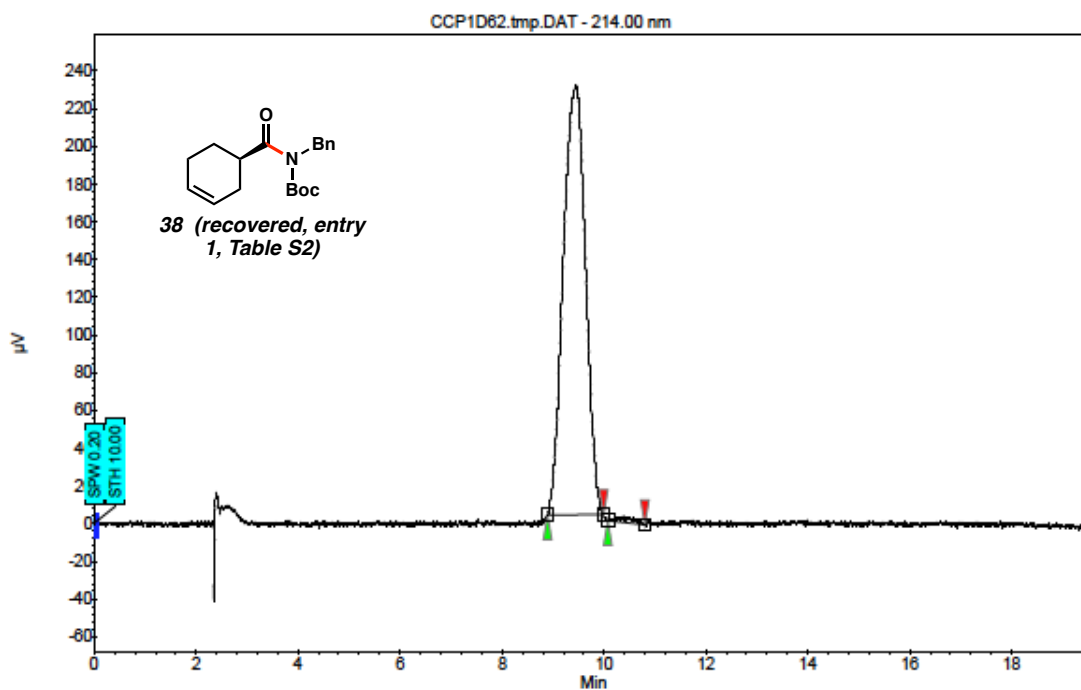
Compound	Method Column/Temp.	Solvent	Method Flow Rate	Retention Times (min)	Enantiomeric Ratio (er)
 <i>rac-38</i>	Daicel ChiralPak OJ-H/23 °C	1% isopropanol in CO ₂	1 mL/min	9.4/10.4	50:50
 <i>38 (SM, entries 1–2, Table S2)</i>	Daicel ChiralPak OJ-H/23 °C	1% isopropanol in CO ₂	1 mL/min	9.2/10.3	99:1
 <i>38 (recovered, entry 1, Table S2)</i>	Daicel ChiralPak OJ-H/23 °C	1% isopropanol in CO ₂	1 mL/min	9.2/10.3	99:1
 <i>38 (recovered, entry 2, Table S2)</i>	Daicel ChiralPak OJ-H/23 °C	1% isopropanol in CO ₂	1 mL/min	9.2/10.3	>99:1



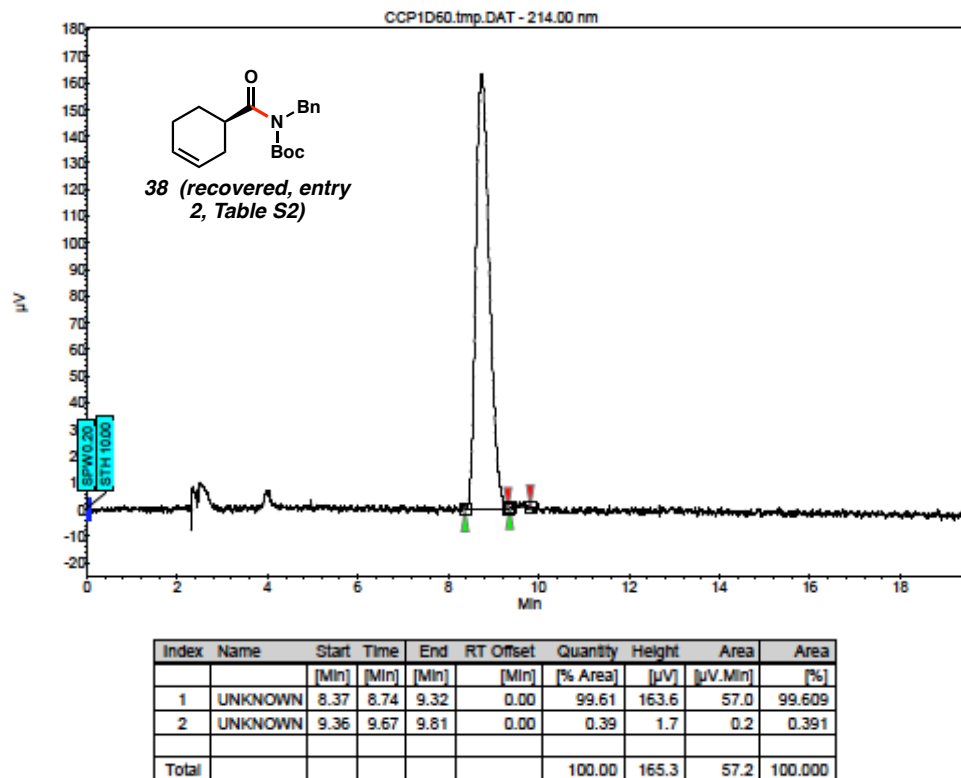
Index	Name	Start [Min]	Time [Min]	End [Min]	RT Offset [Min]	Quantity [% Area]	Height [μV]	Area [μV.Min]	Area [%]
1	UNKNOWN	9.21	9.64	10.16	0.00	50.12	107.8	40.6	50.117
2	UNKNOWN	10.22	10.63	11.24	0.00	49.88	98.8	40.4	49.883
Total						100.00	206.6	81.0	100.000



Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[μ V]	[μ V.Min]	[%]
1	UNKNOWN	8.89	9.46	9.99	0.00	99.02	227.6	115.1	99.024
2	UNKNOWN	10.07	10.39	10.80	0.00	0.98	3.5	1.1	0.976
Total						100.00	231.2	116.2	100.000



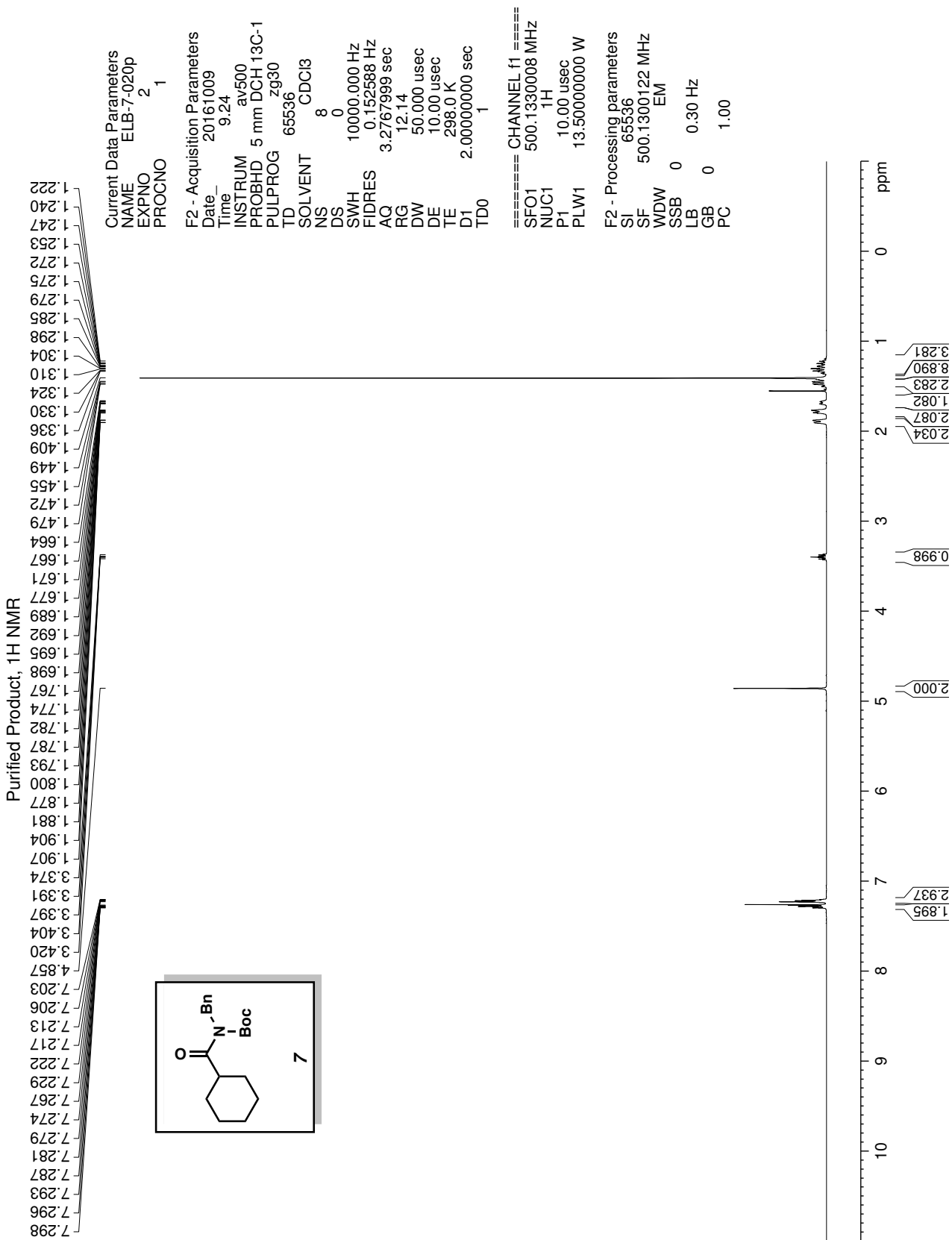
Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[μ V]	[μ V.Min]	[%]
1	UNKNOWN	8.89	9.46	9.99	0.00	99.02	227.6	115.1	99.024
2	UNKNOWN	10.07	10.39	10.80	0.00	0.98	3.5	1.1	0.976
Total						100.00	231.2	116.2	100.000

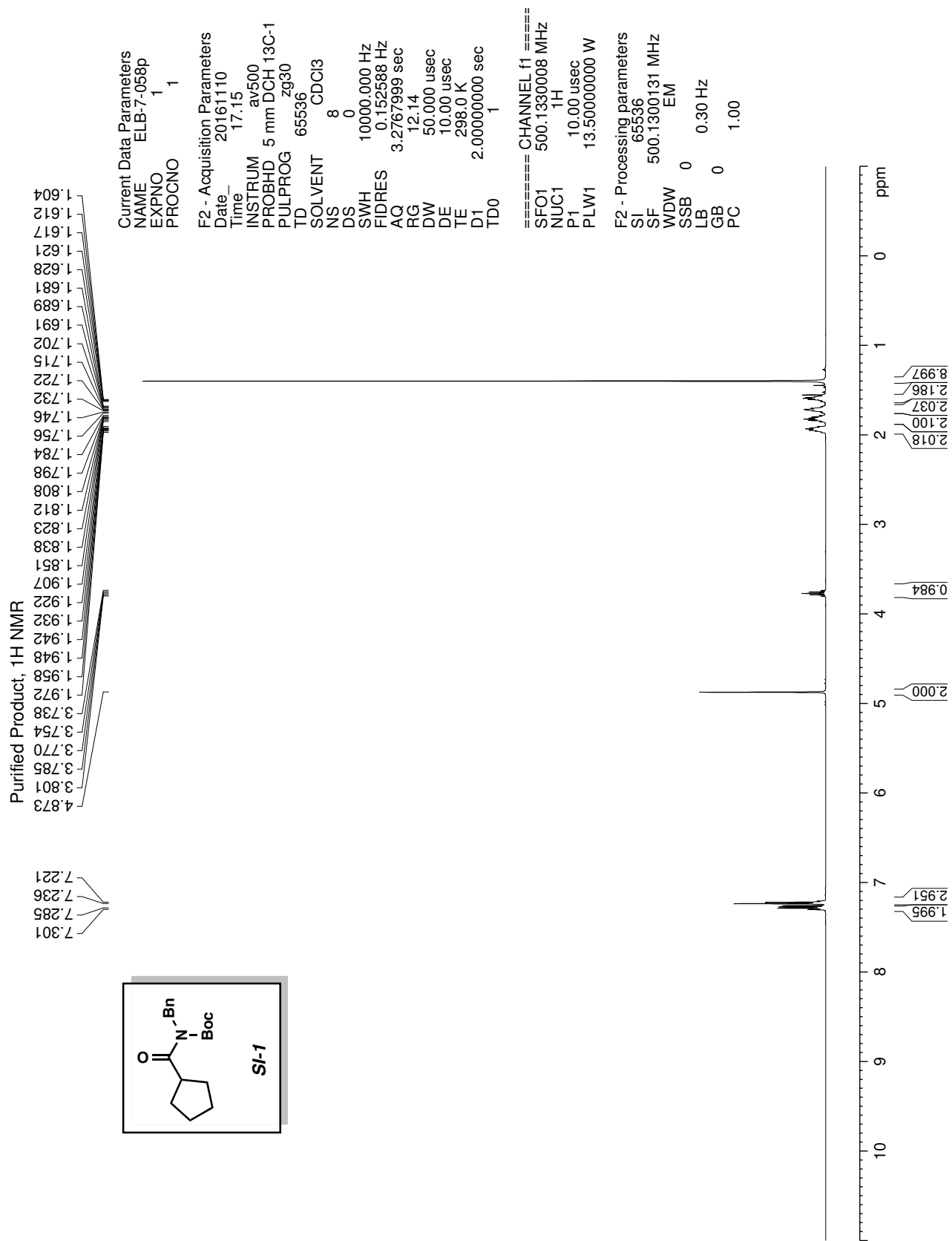


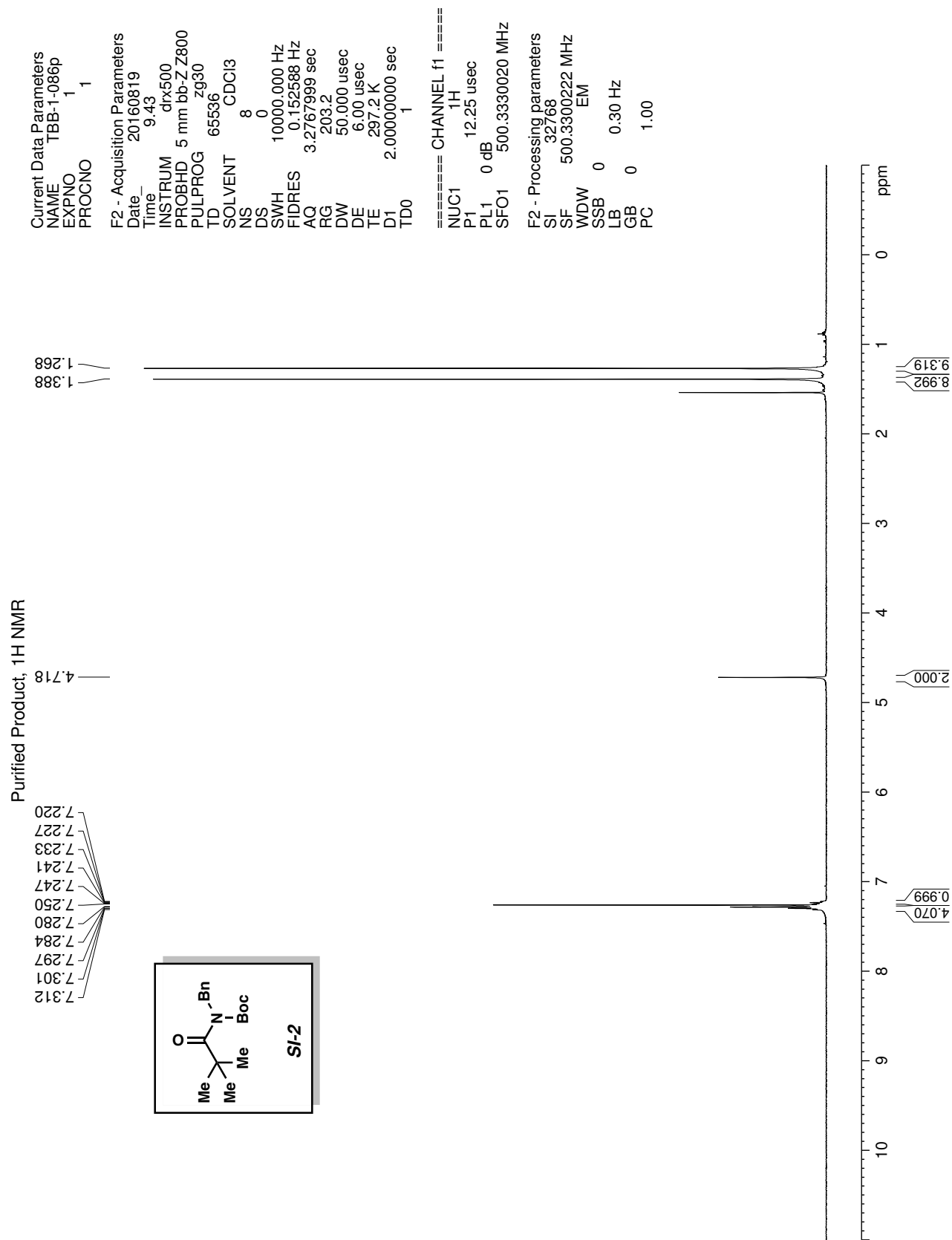
References

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- ⁷ Miyamura, H.; Min, H.; Soulé, J.-F.; Kobayashi, S. *Angew. Chem., Int. Ed.* **2015**, *54*, 7564–7567.
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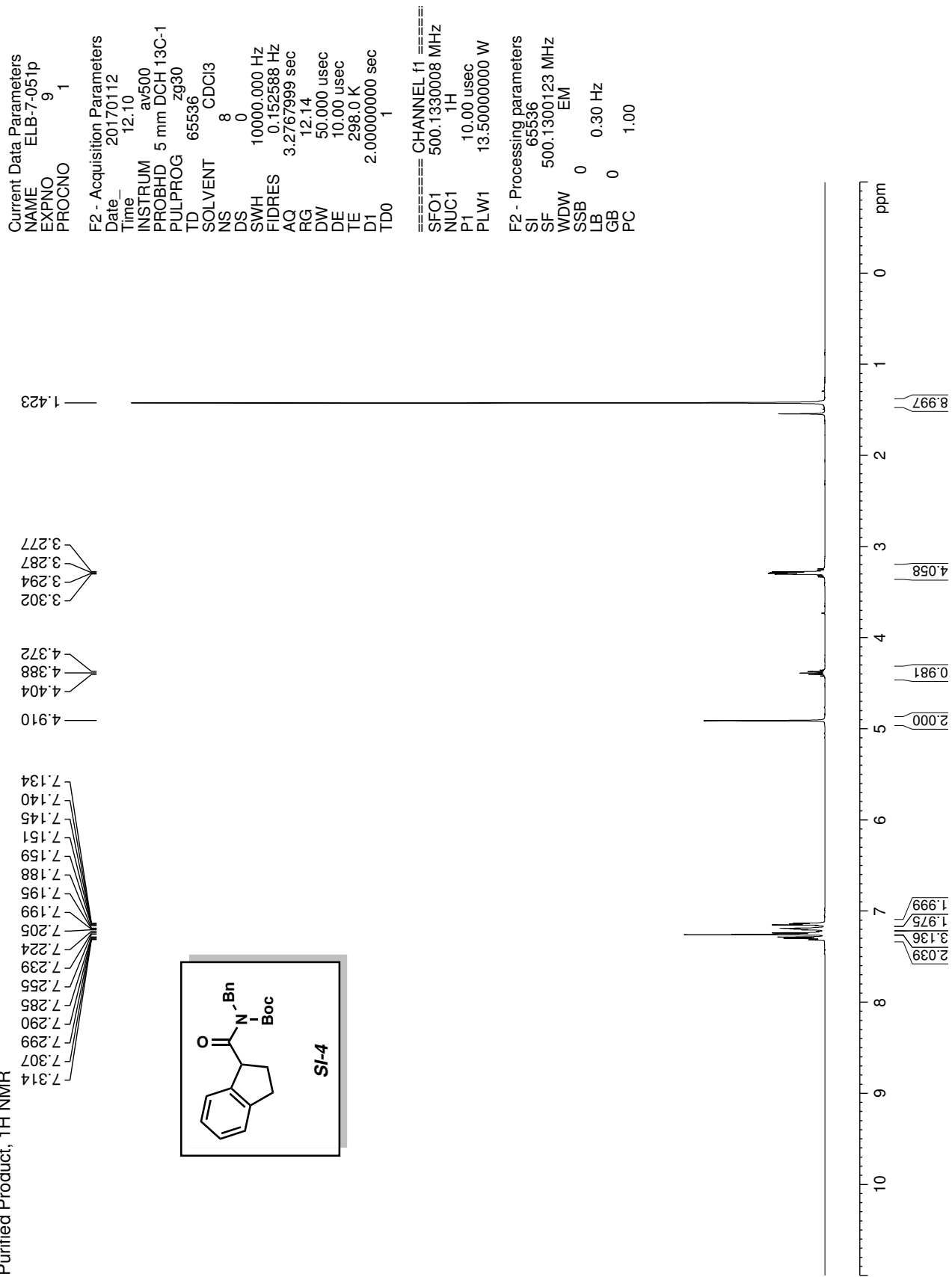
^1H NMR Spectra

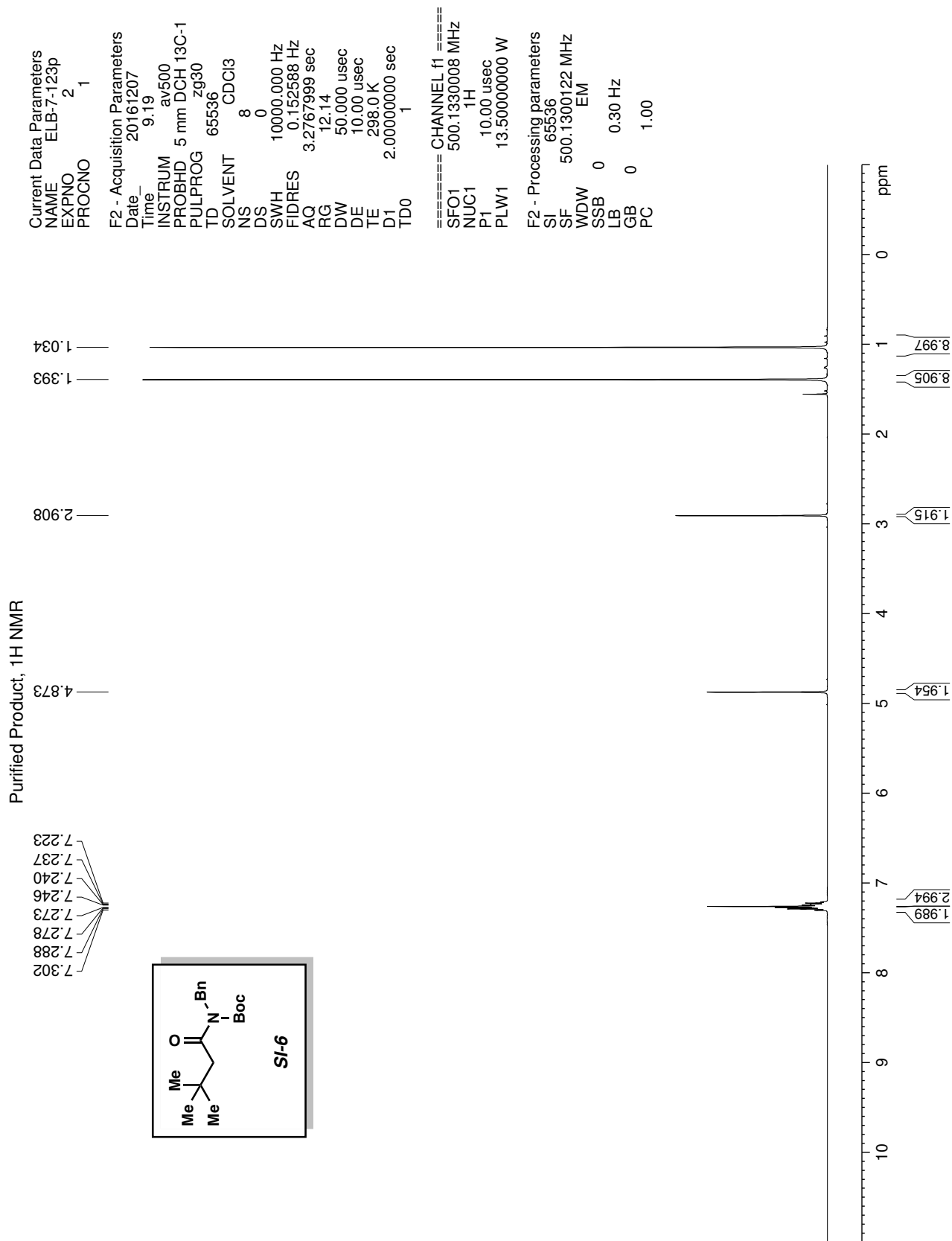


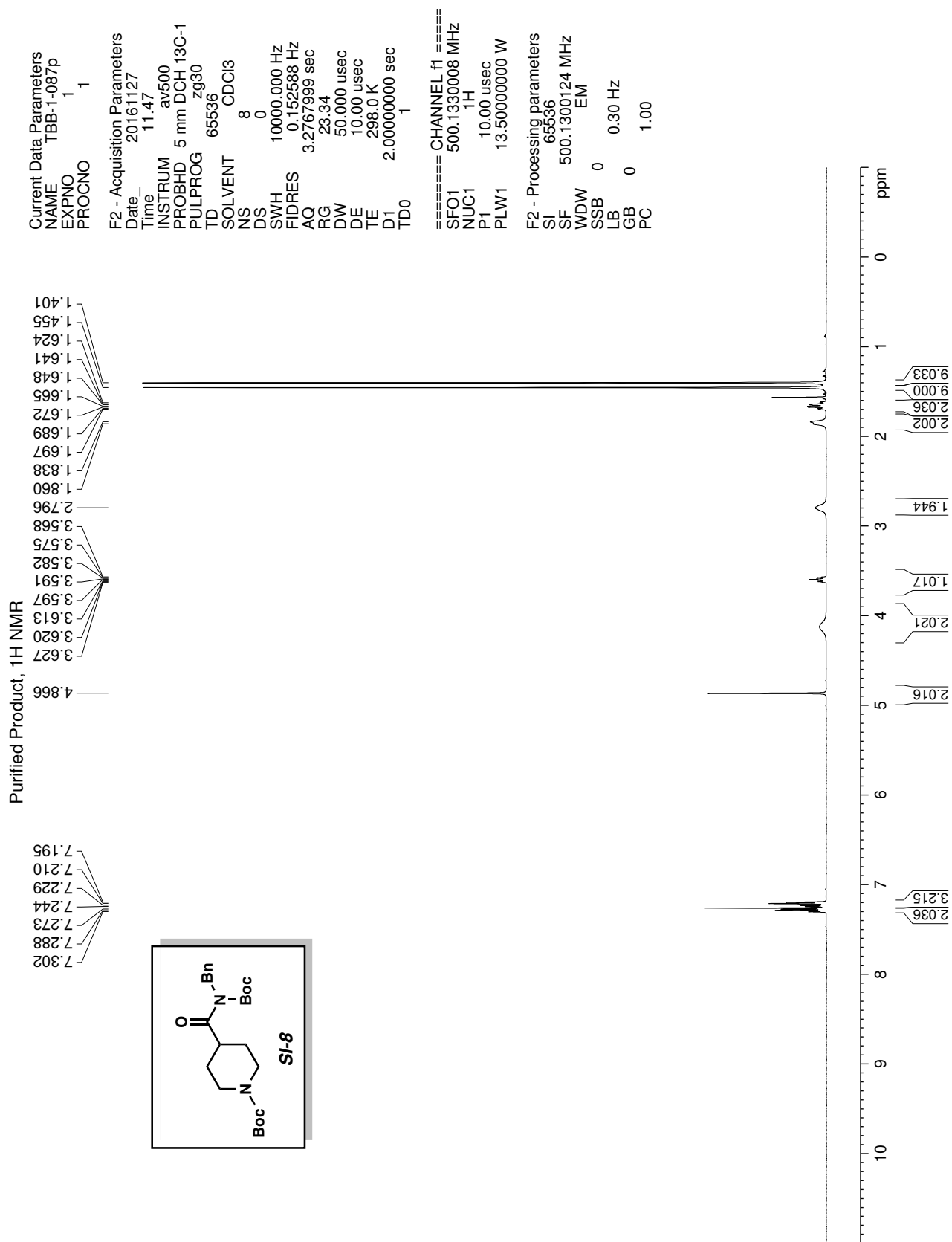


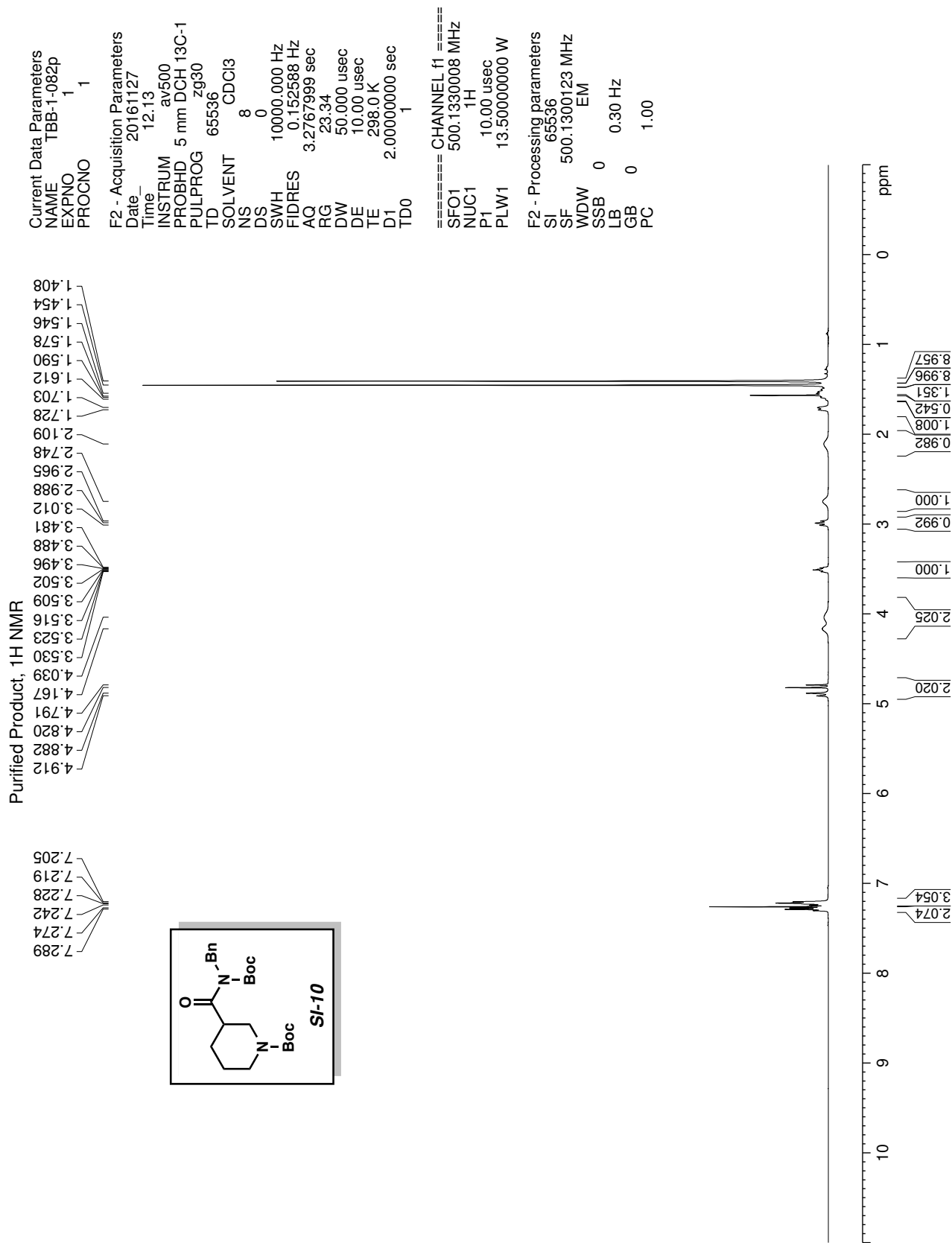


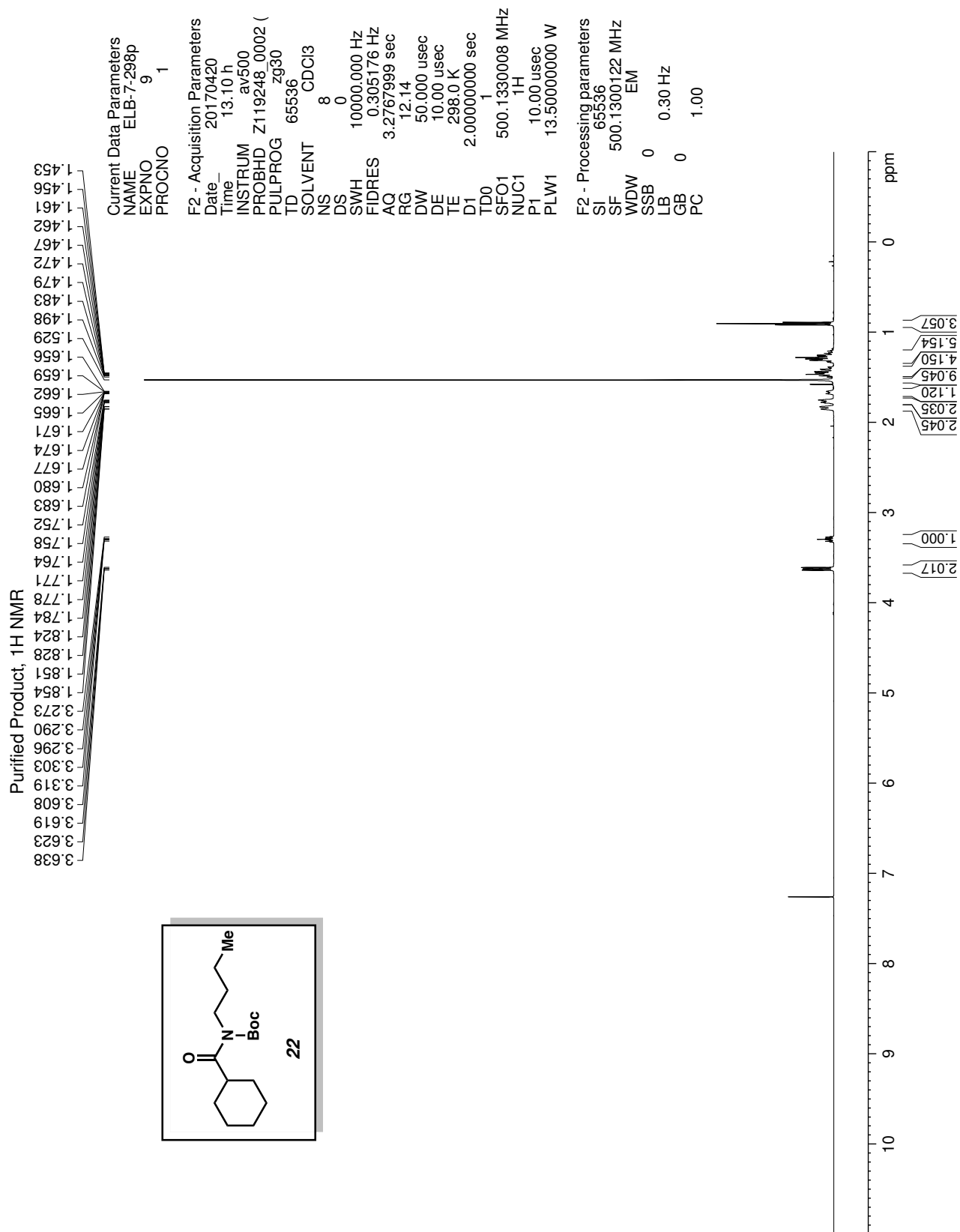
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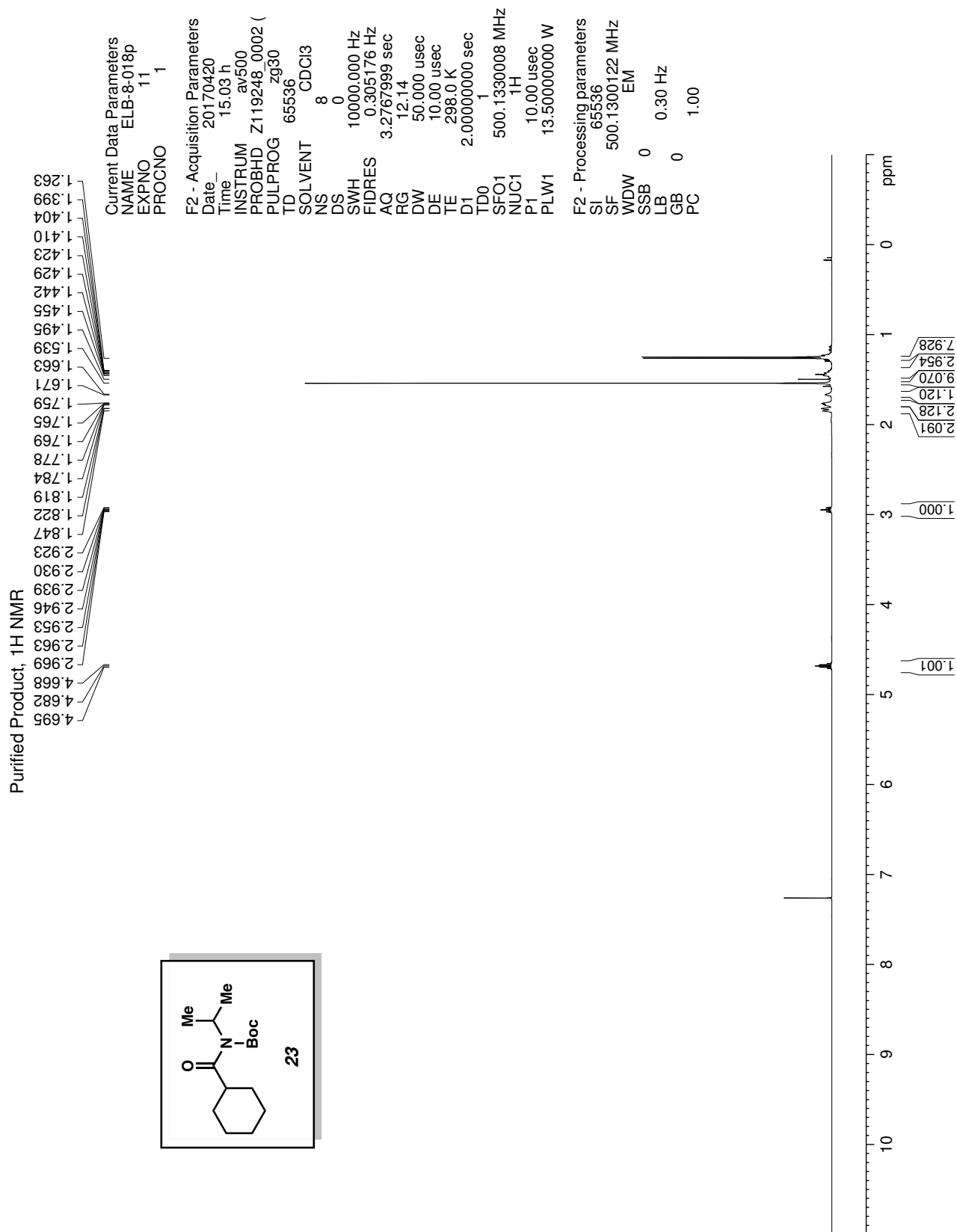




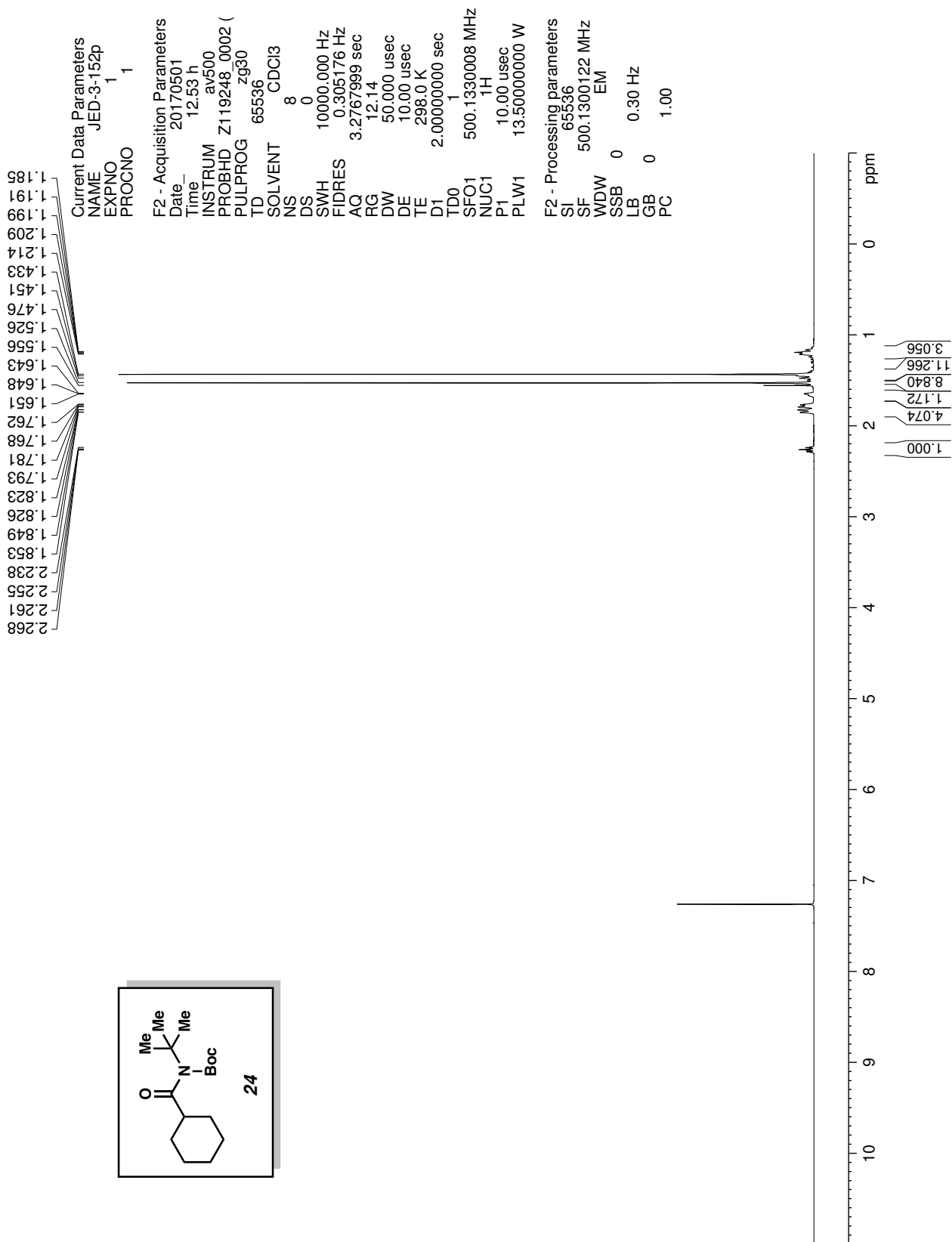


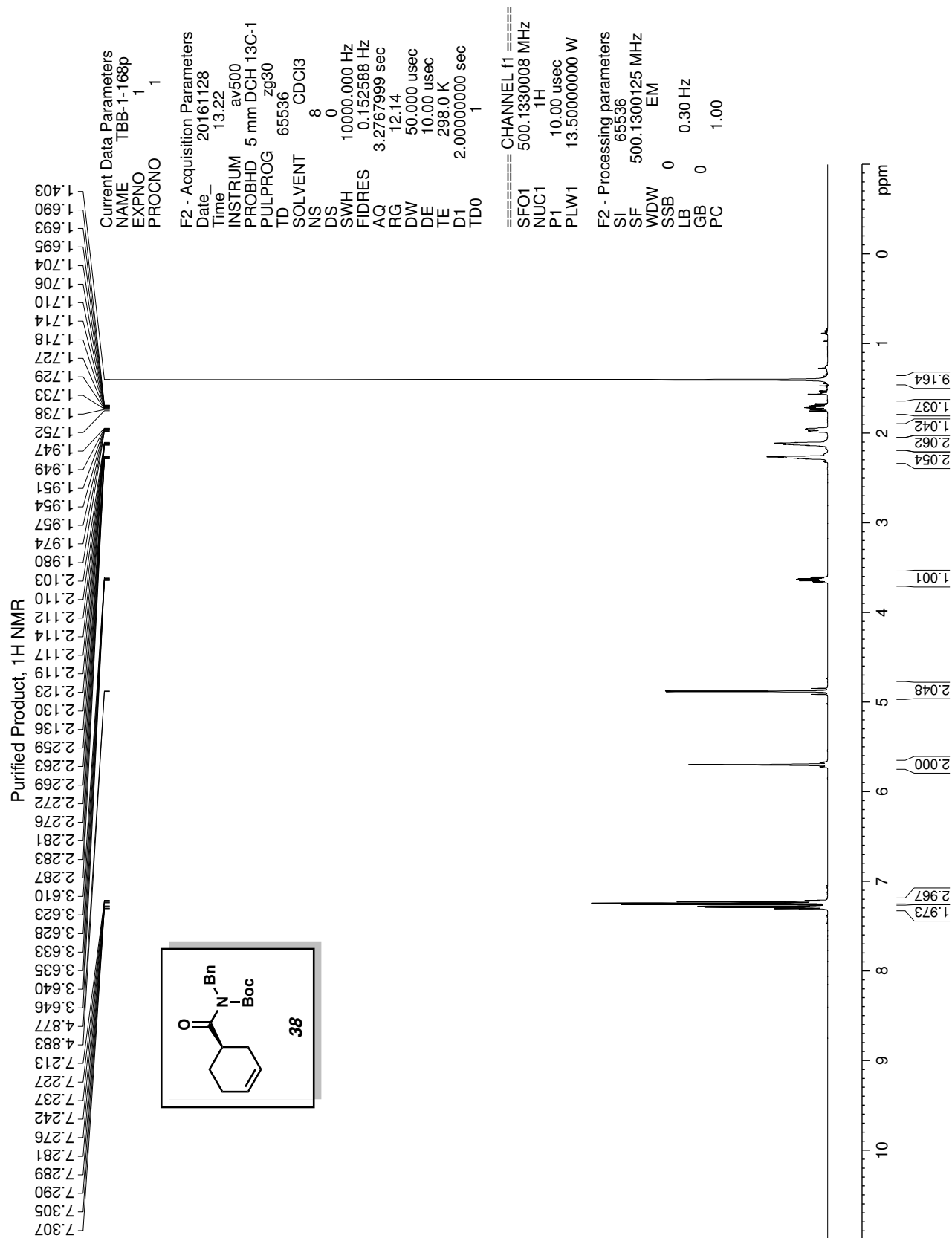


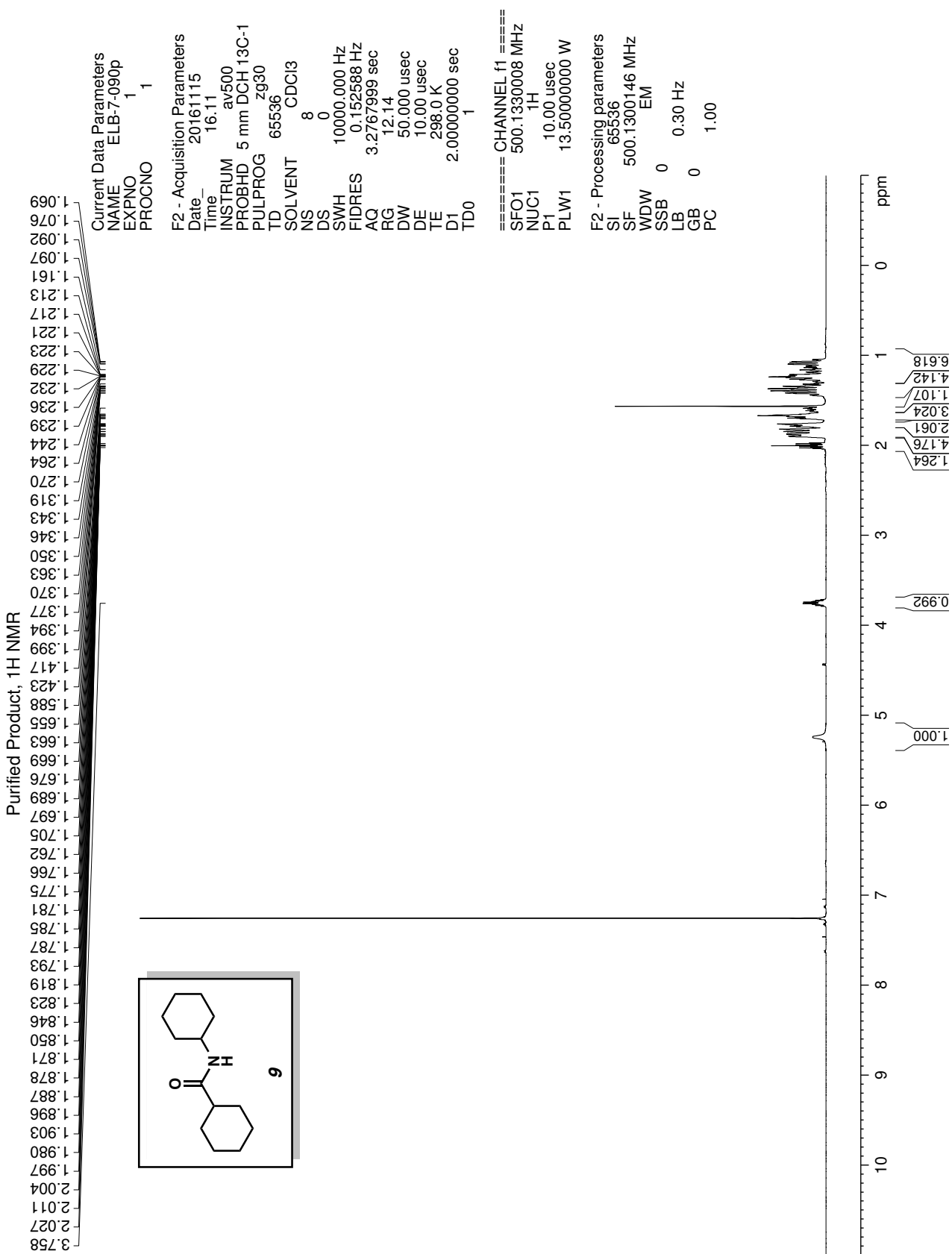


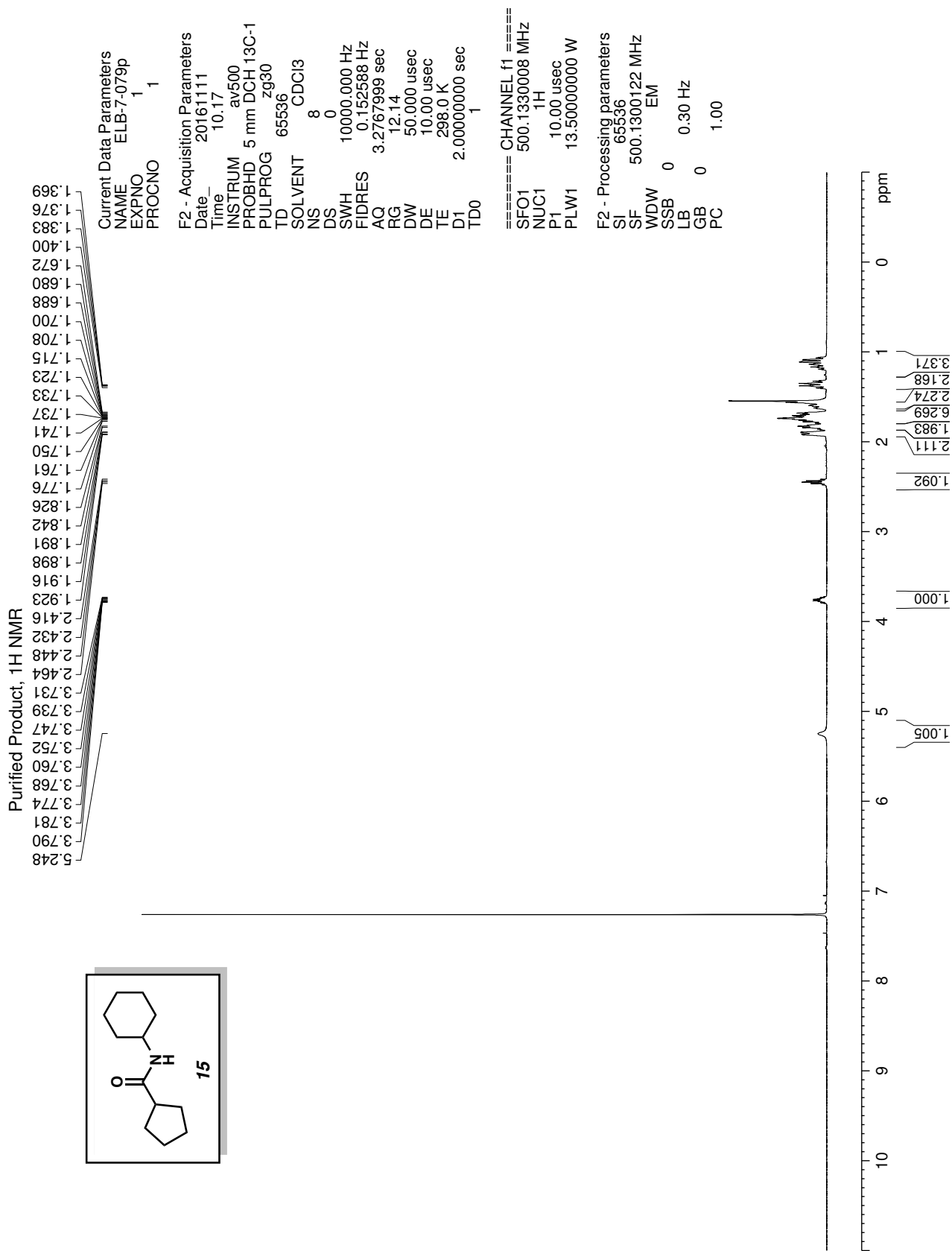


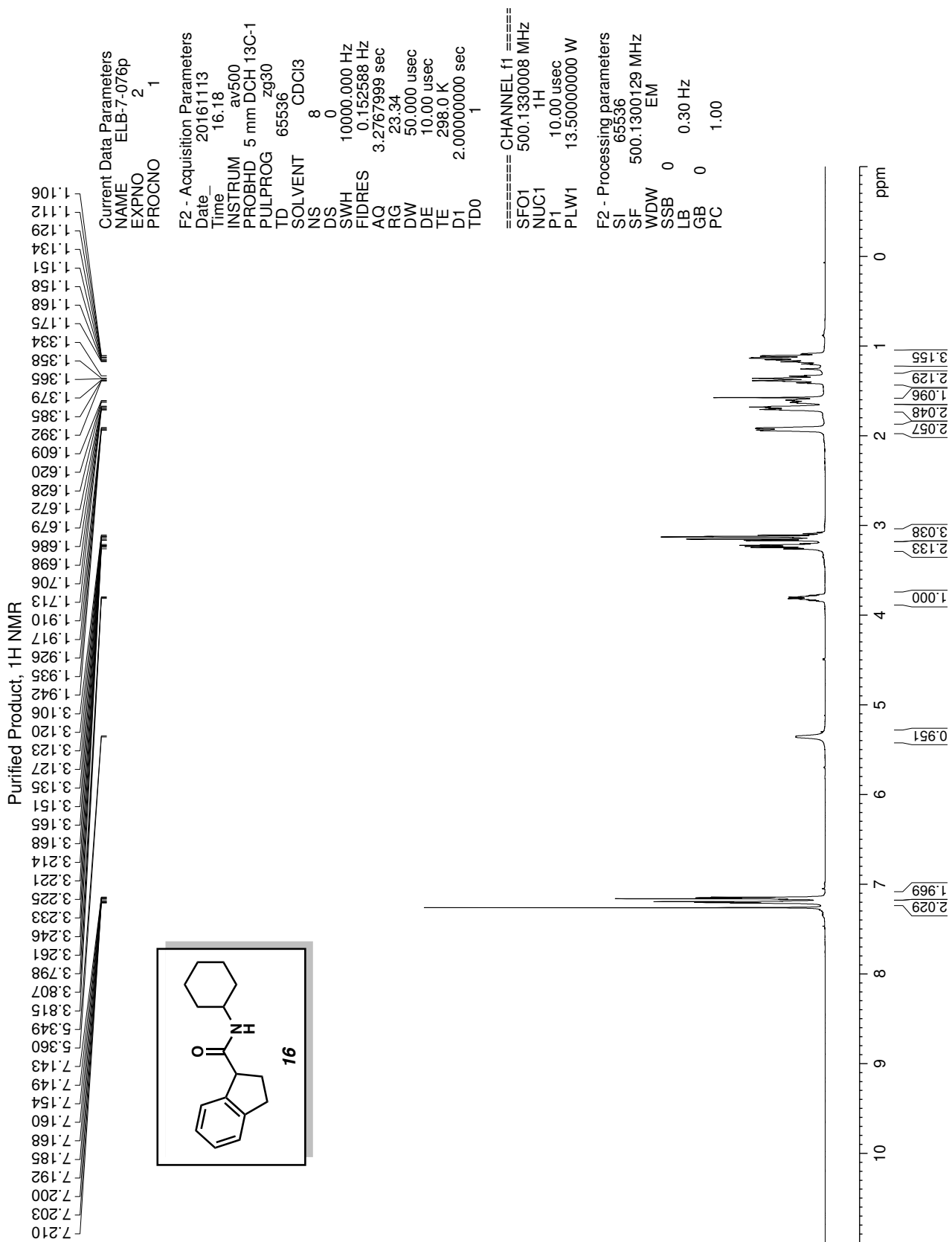
Purified Product, ¹H NMR

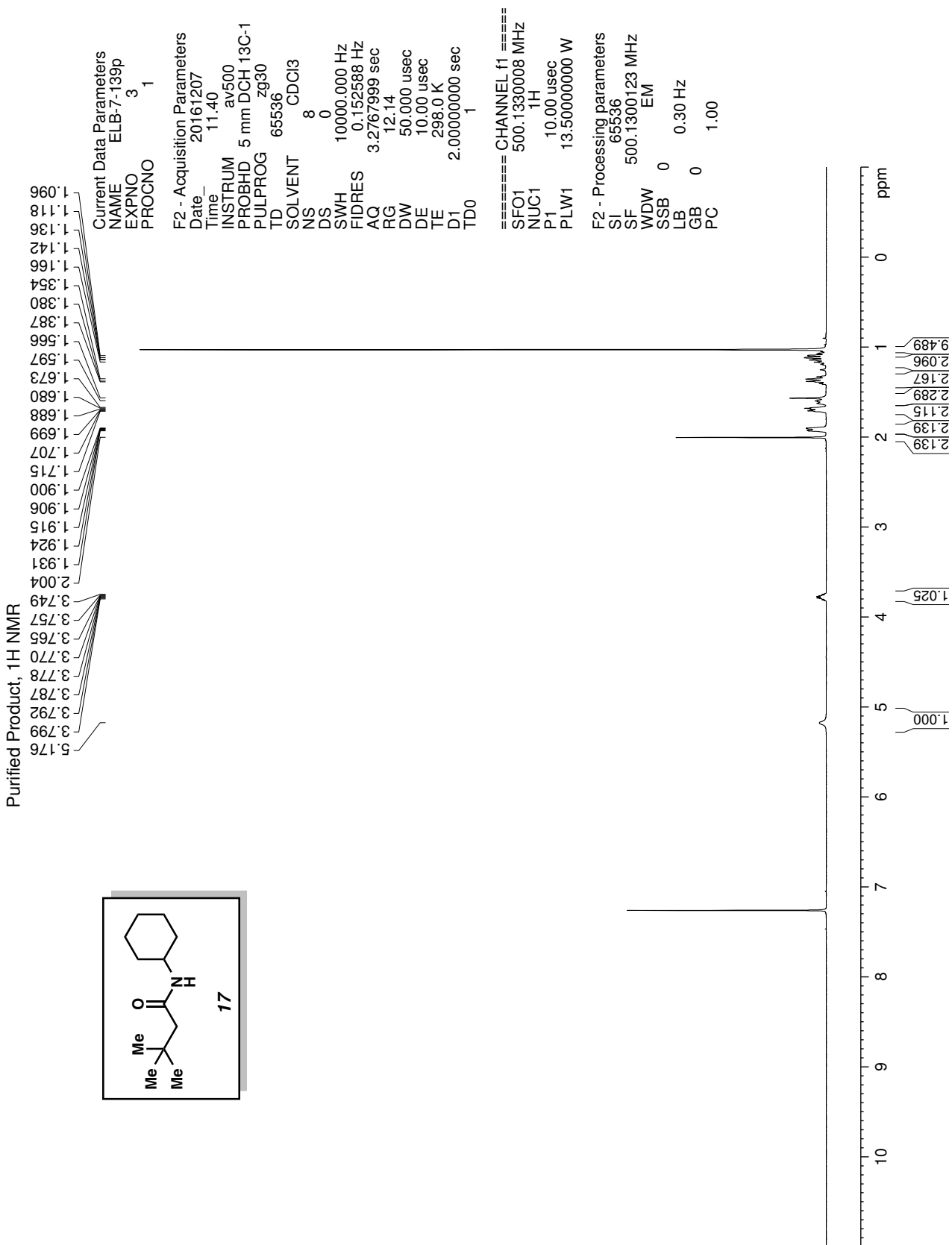


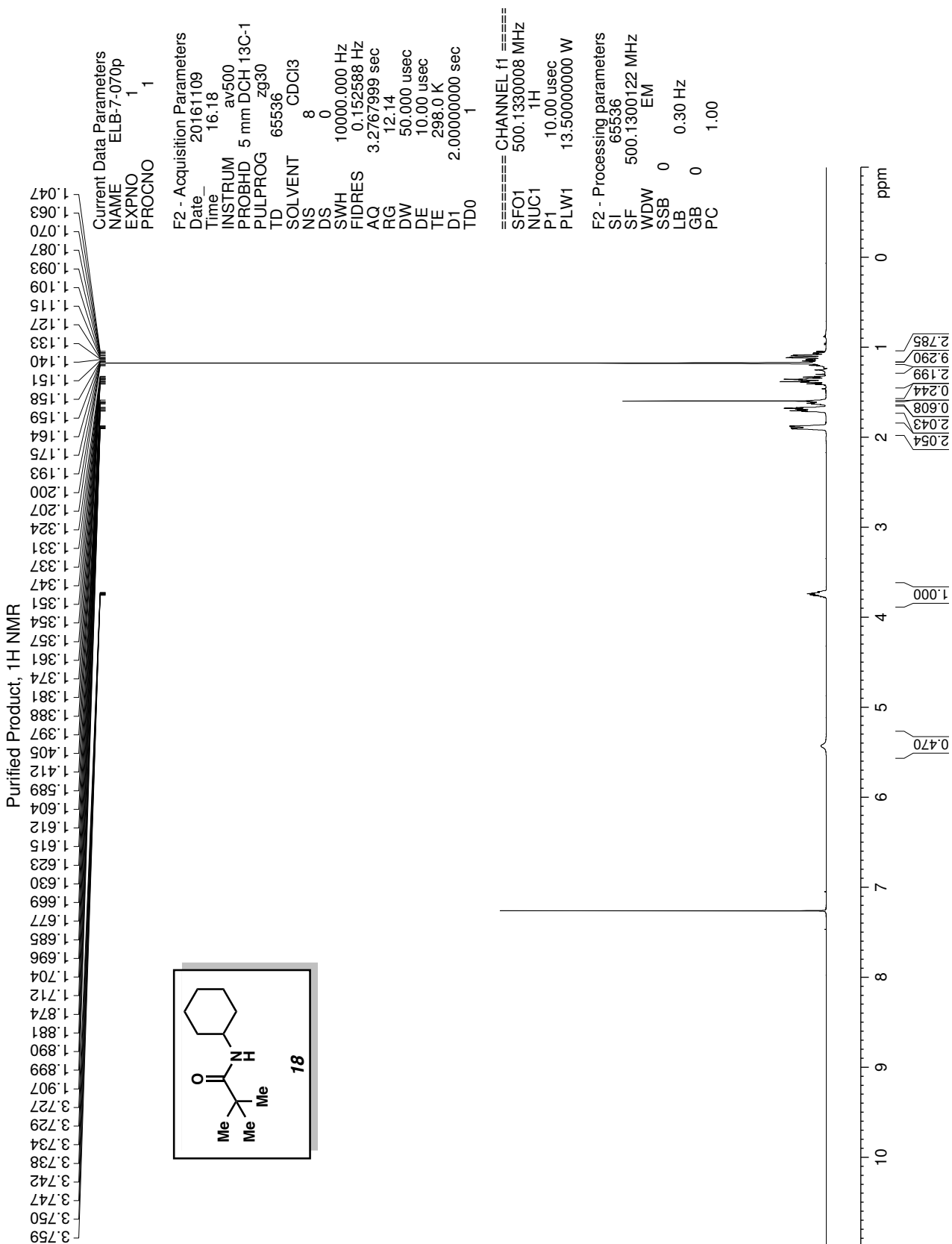


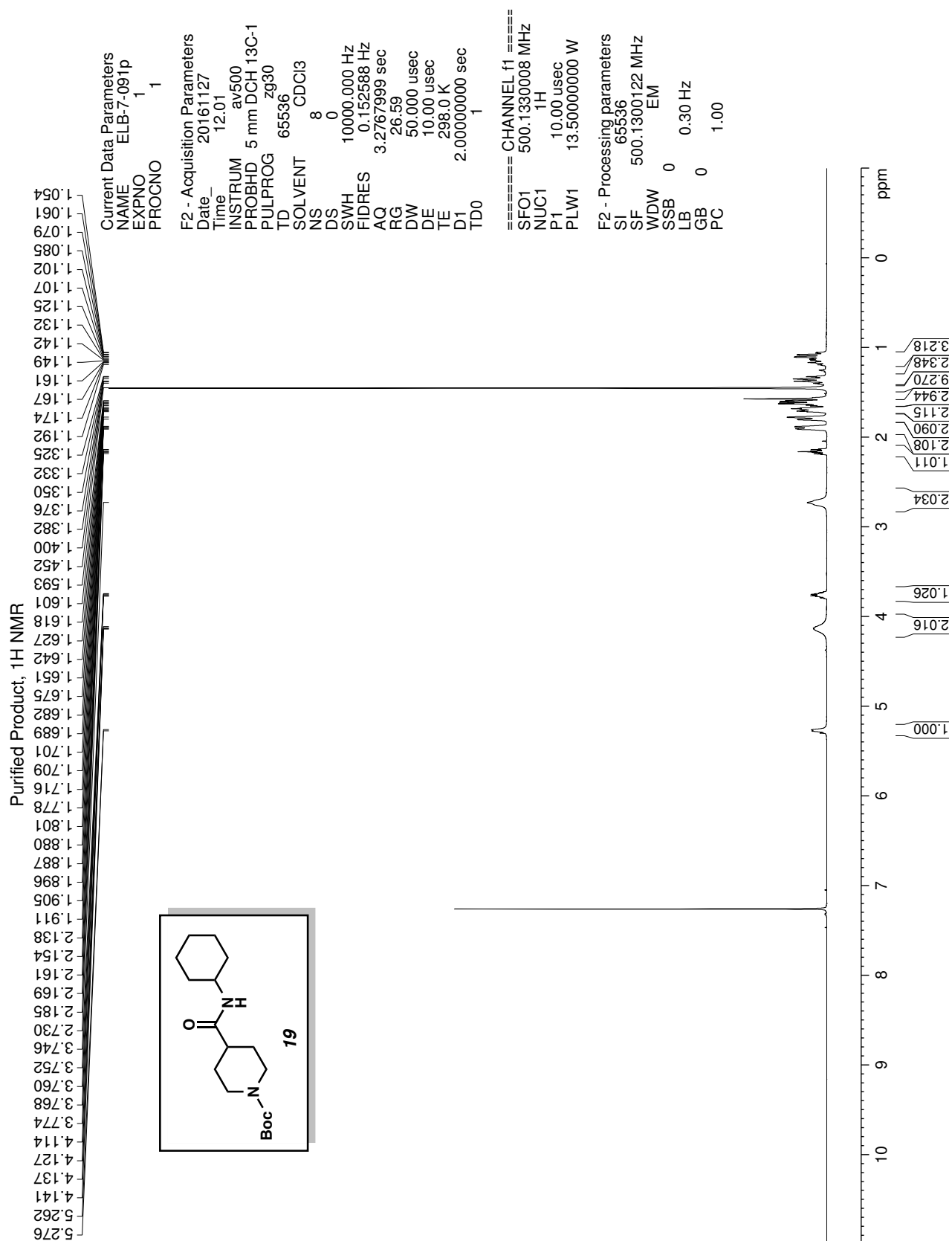


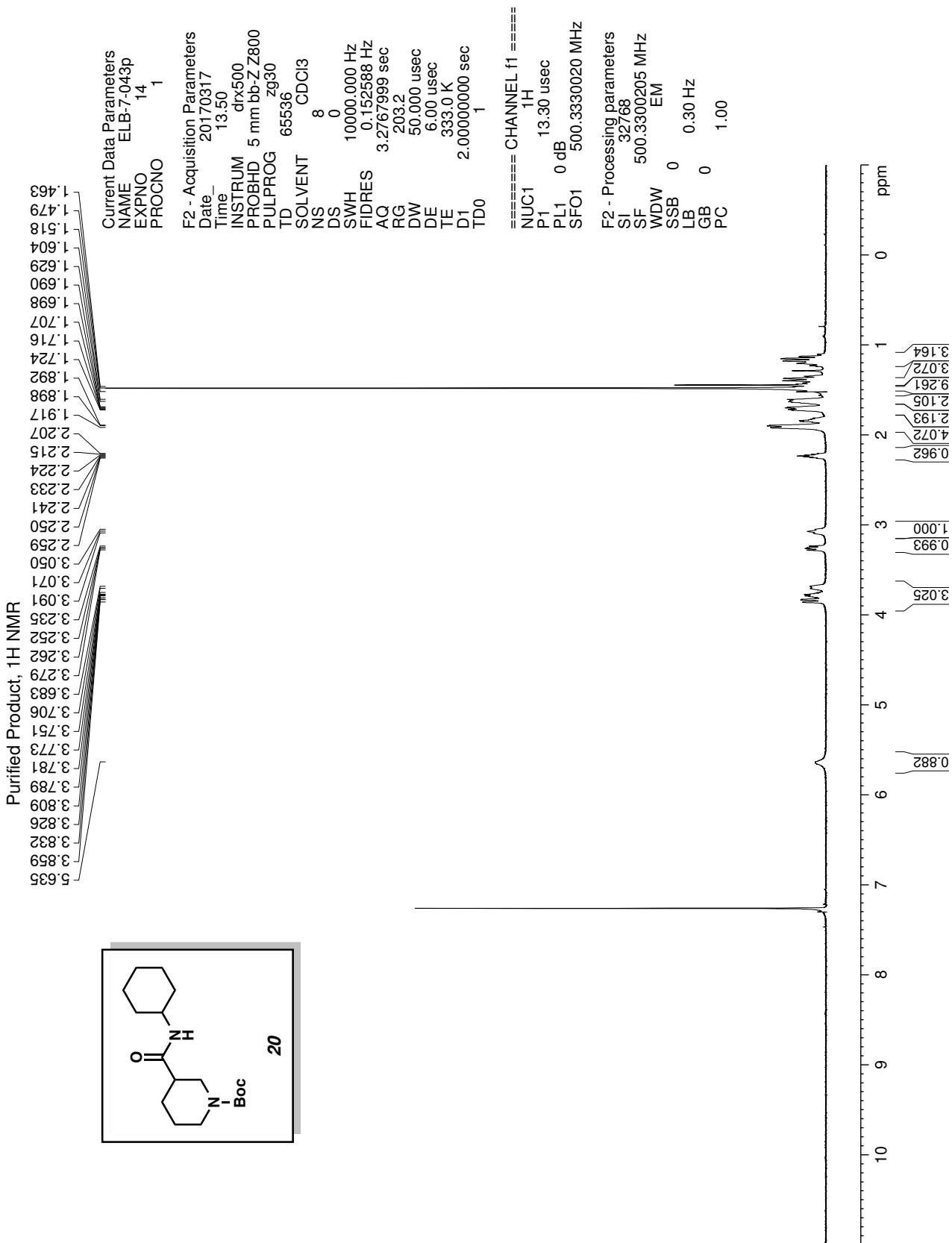


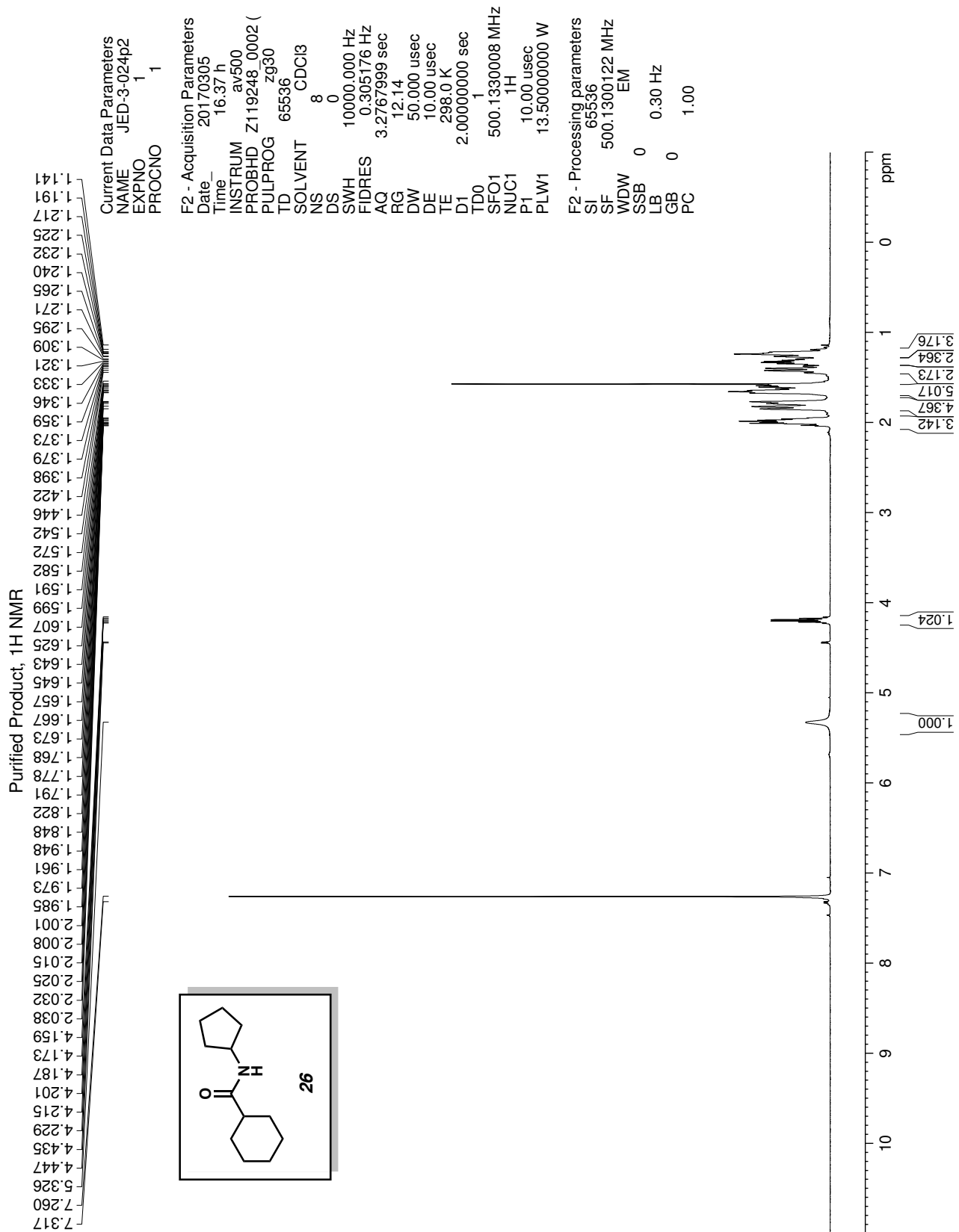


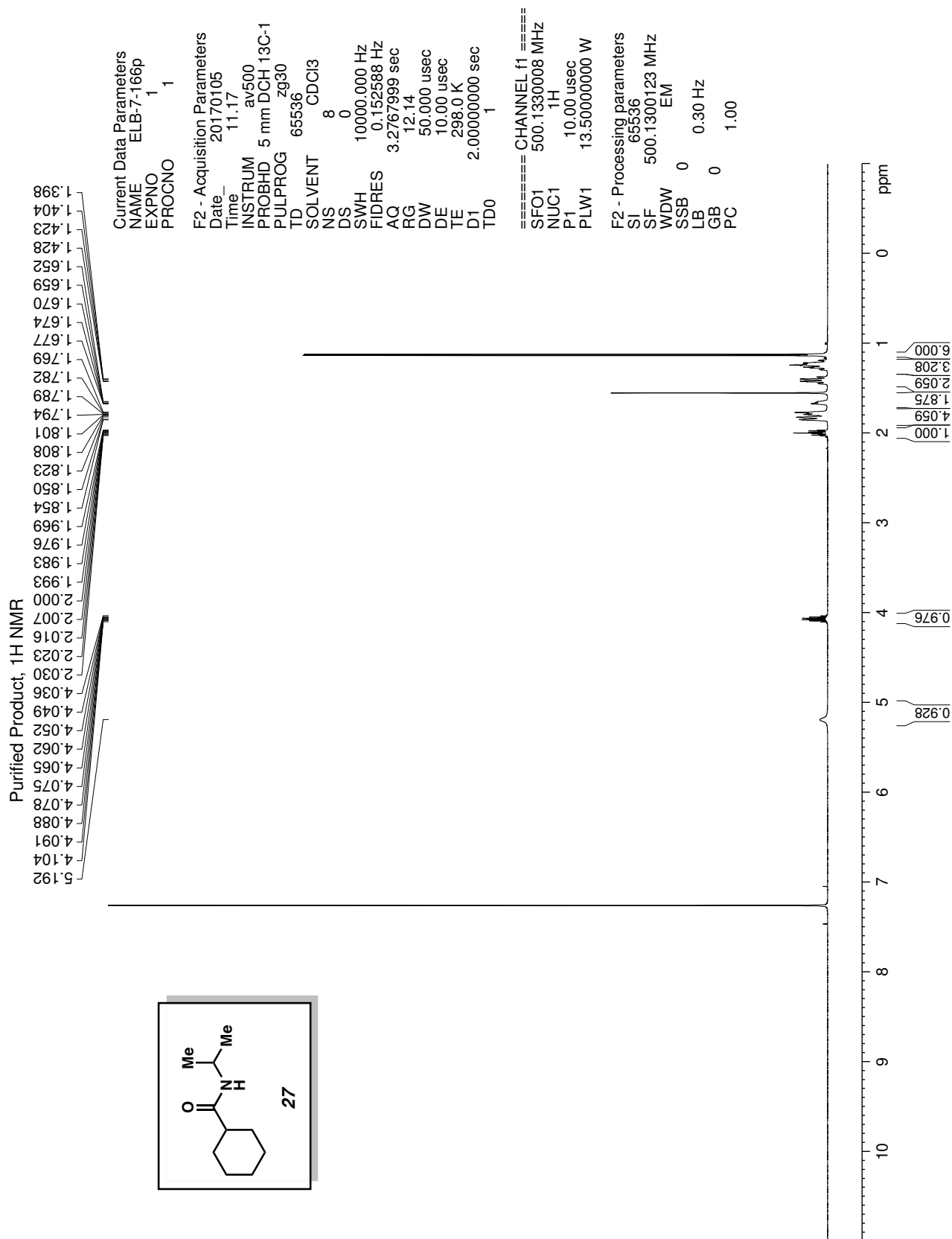


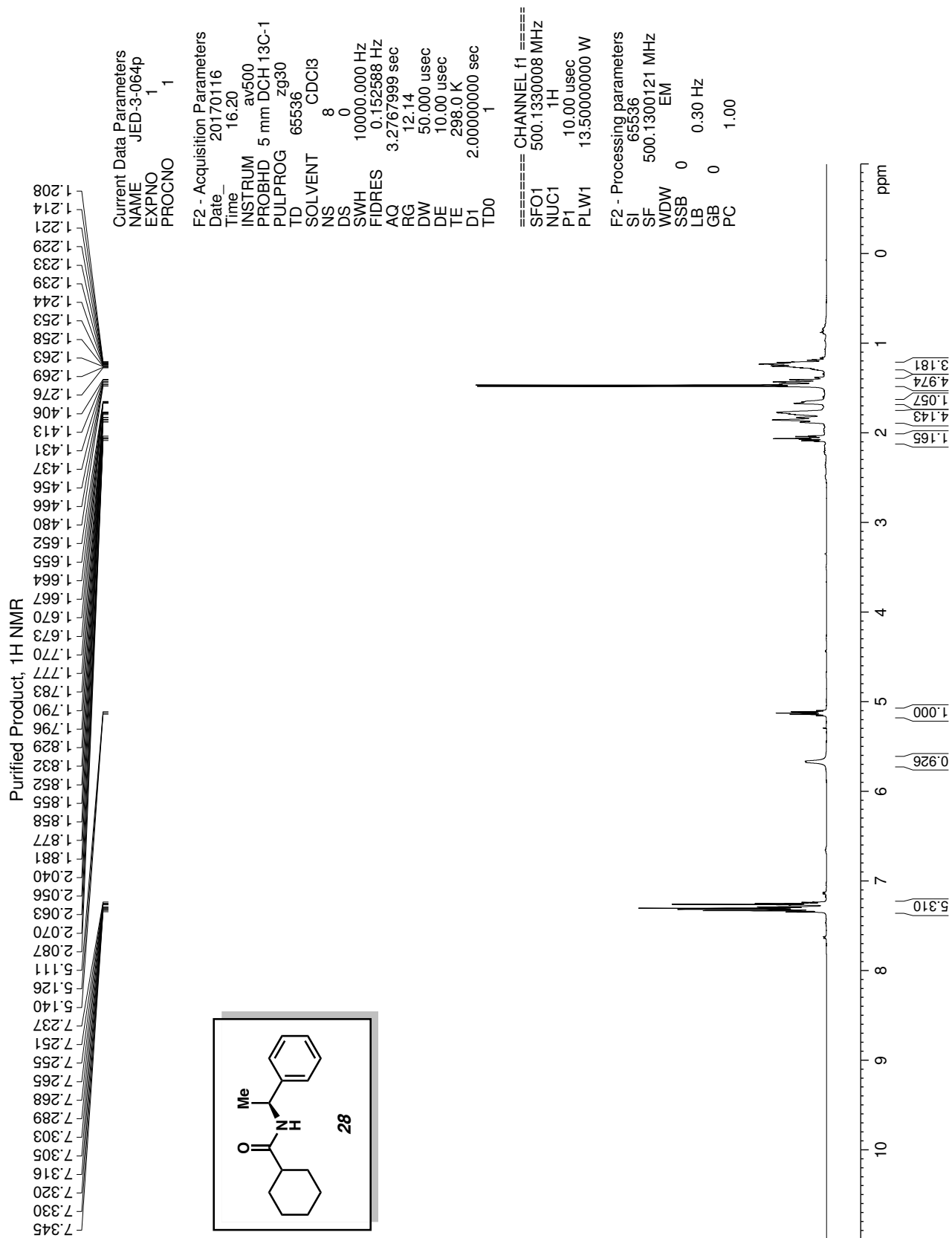


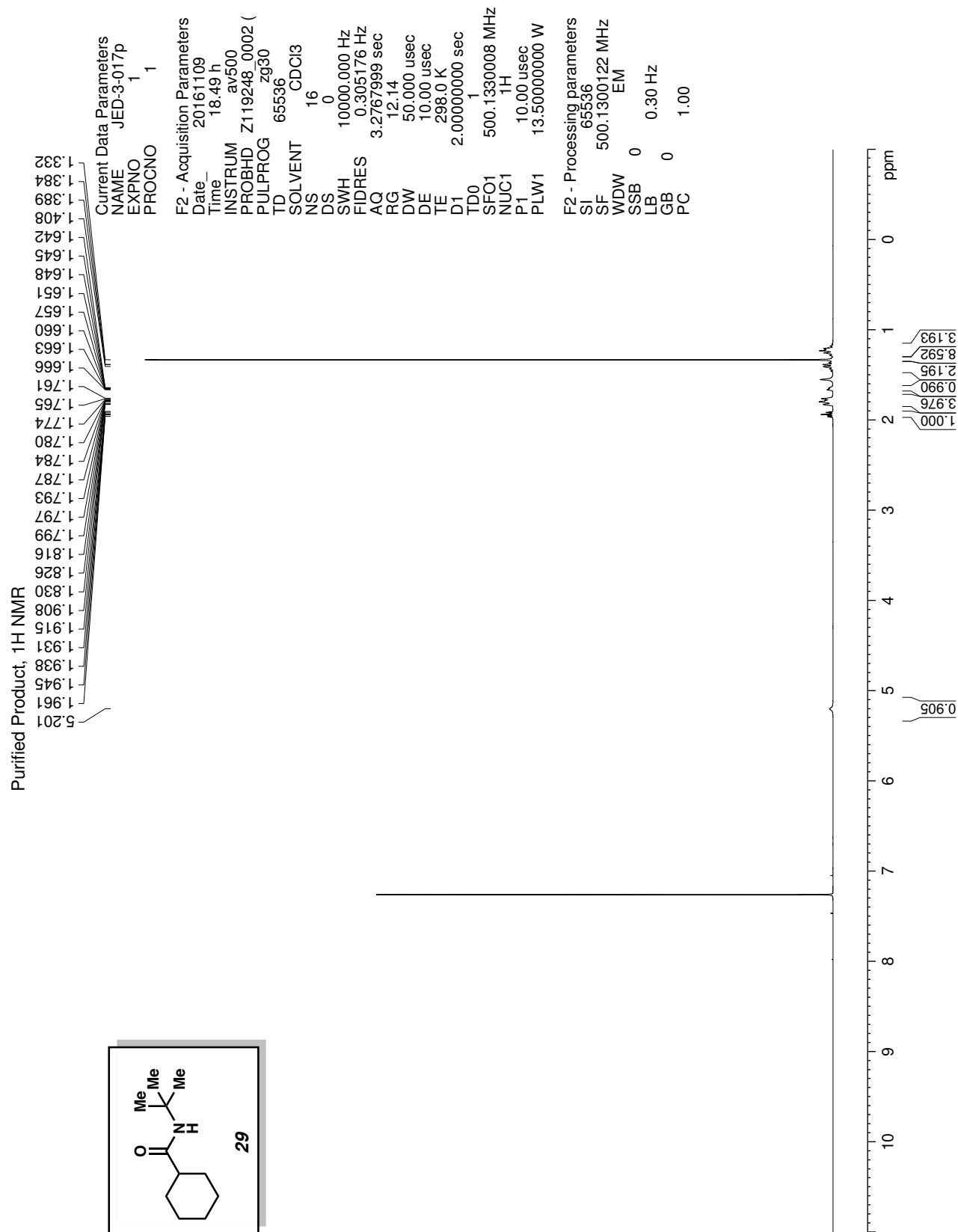


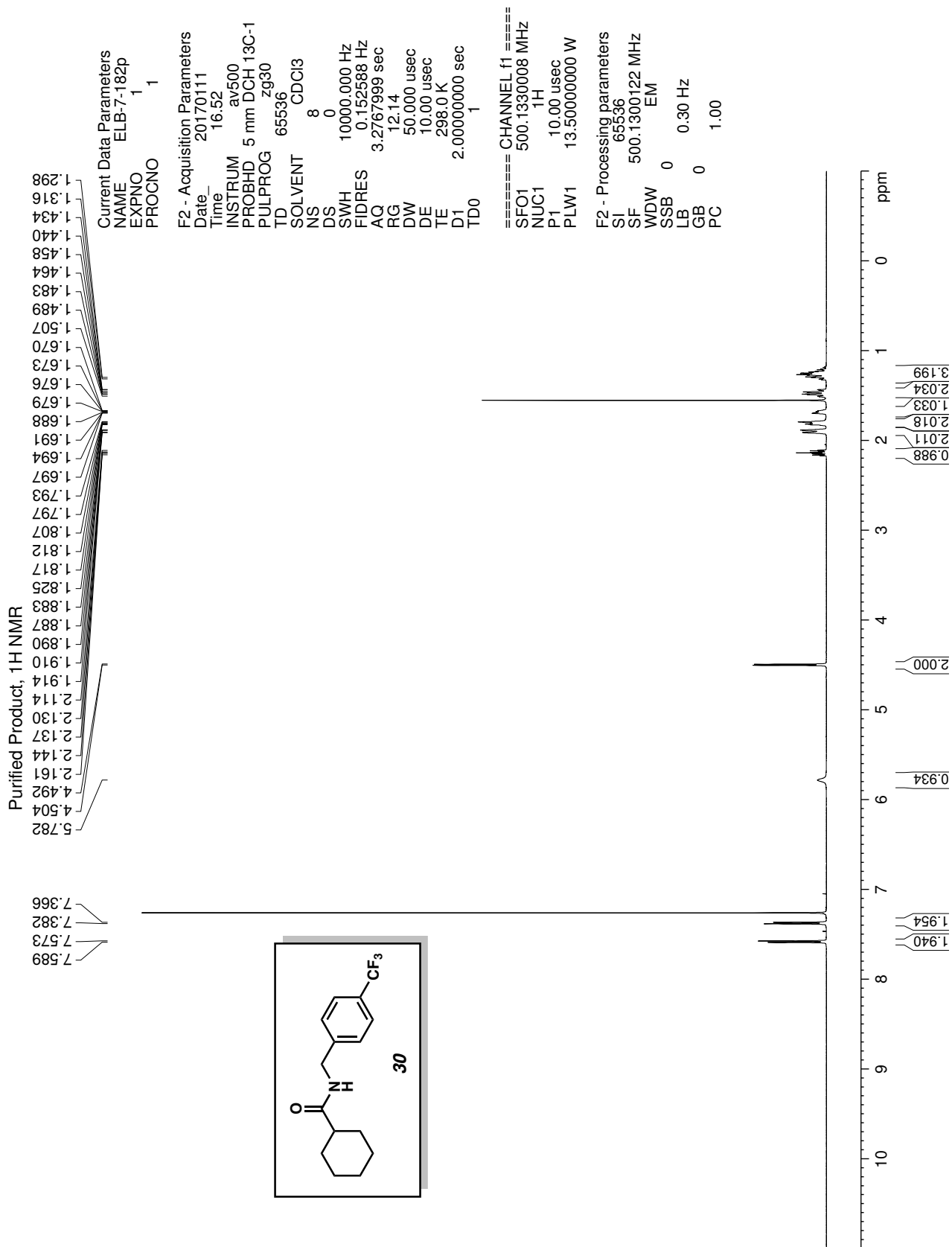


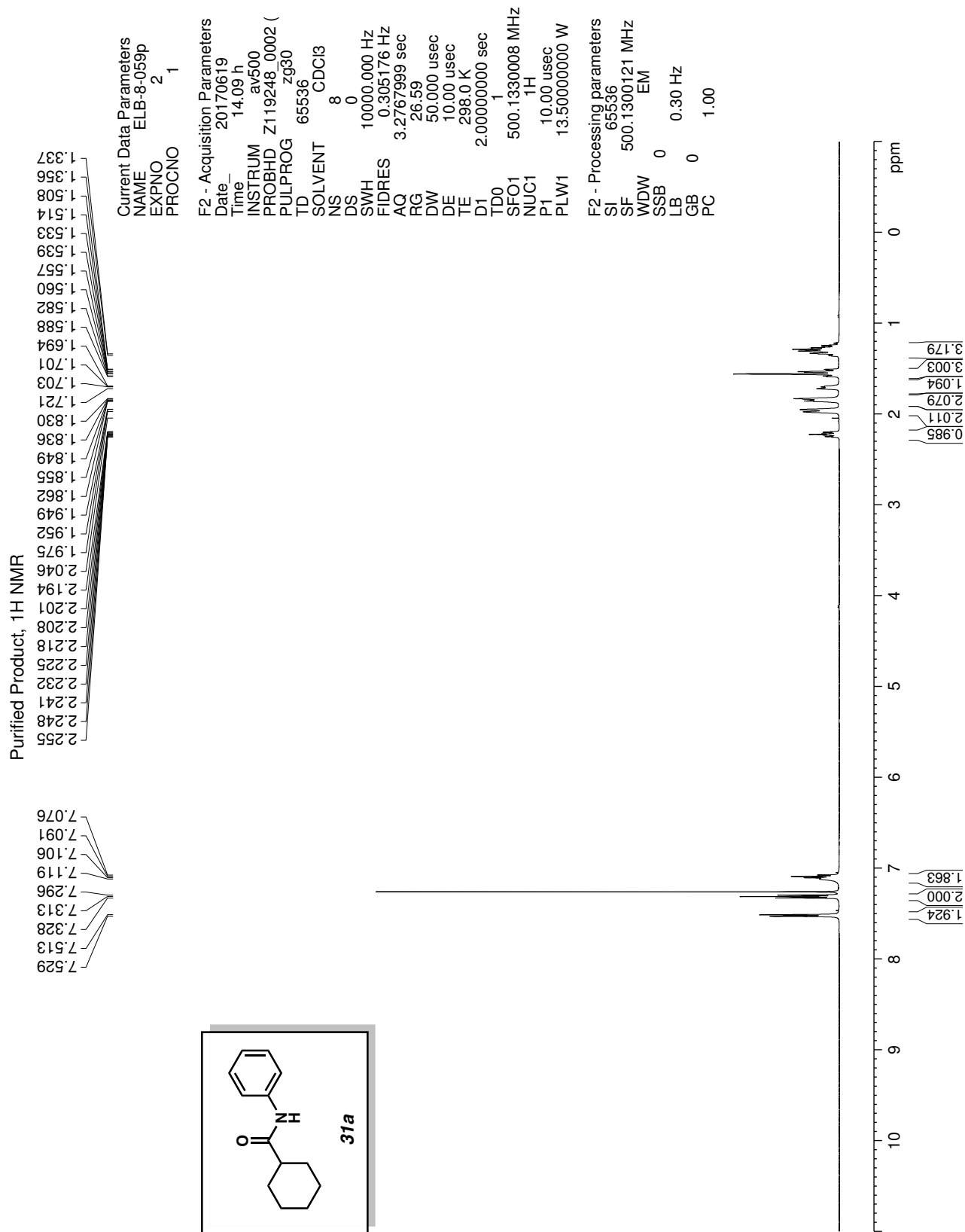


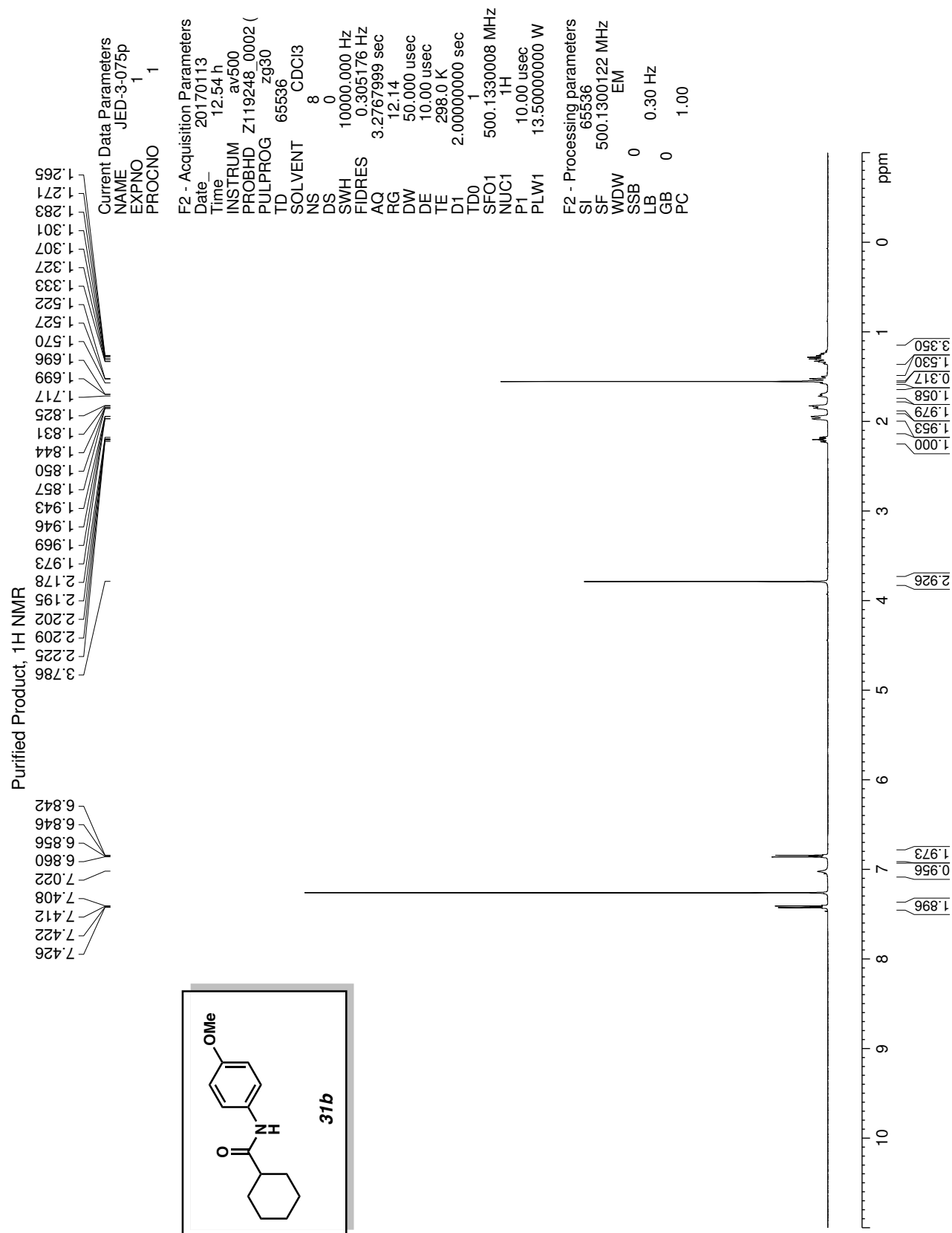


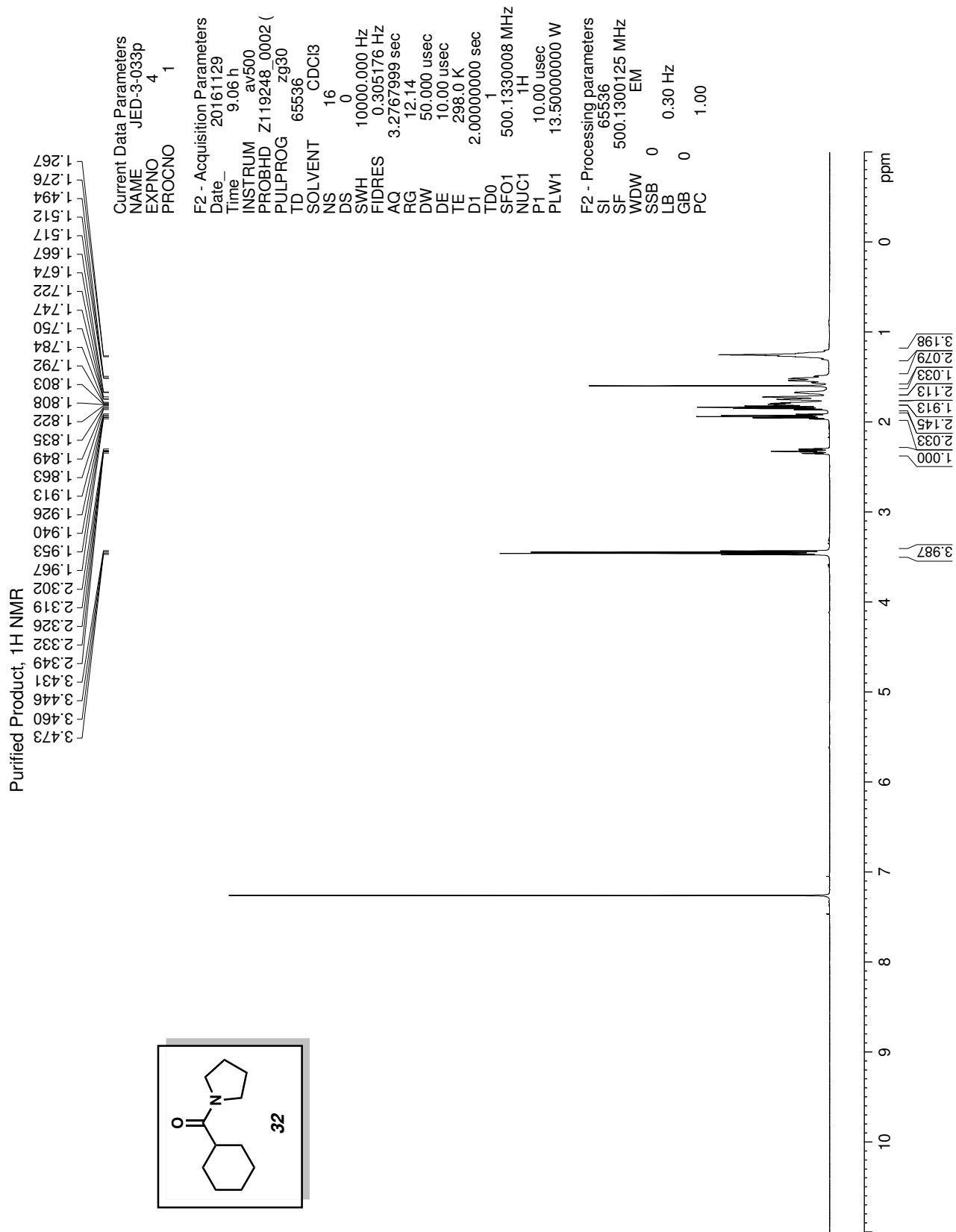


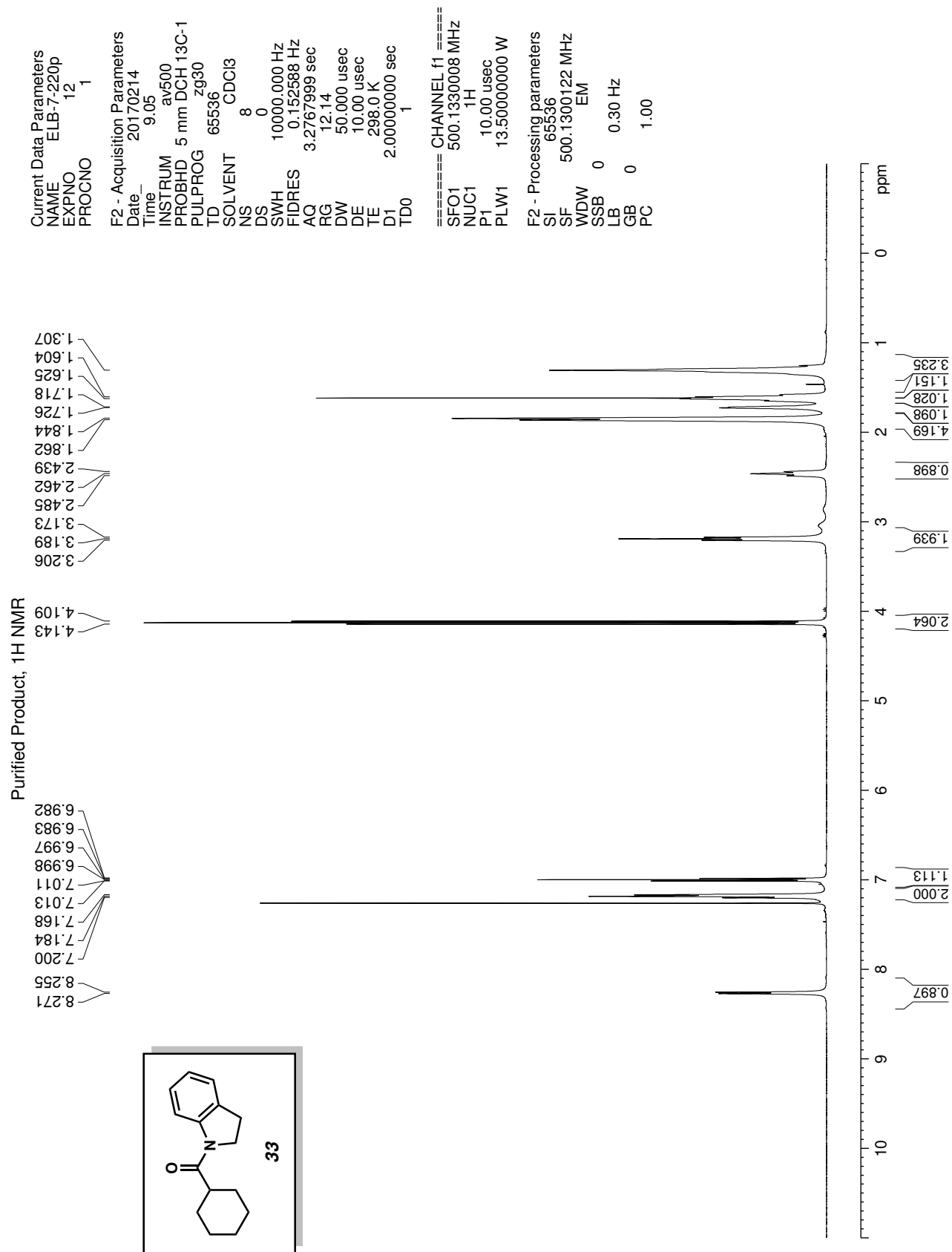




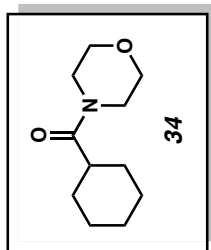








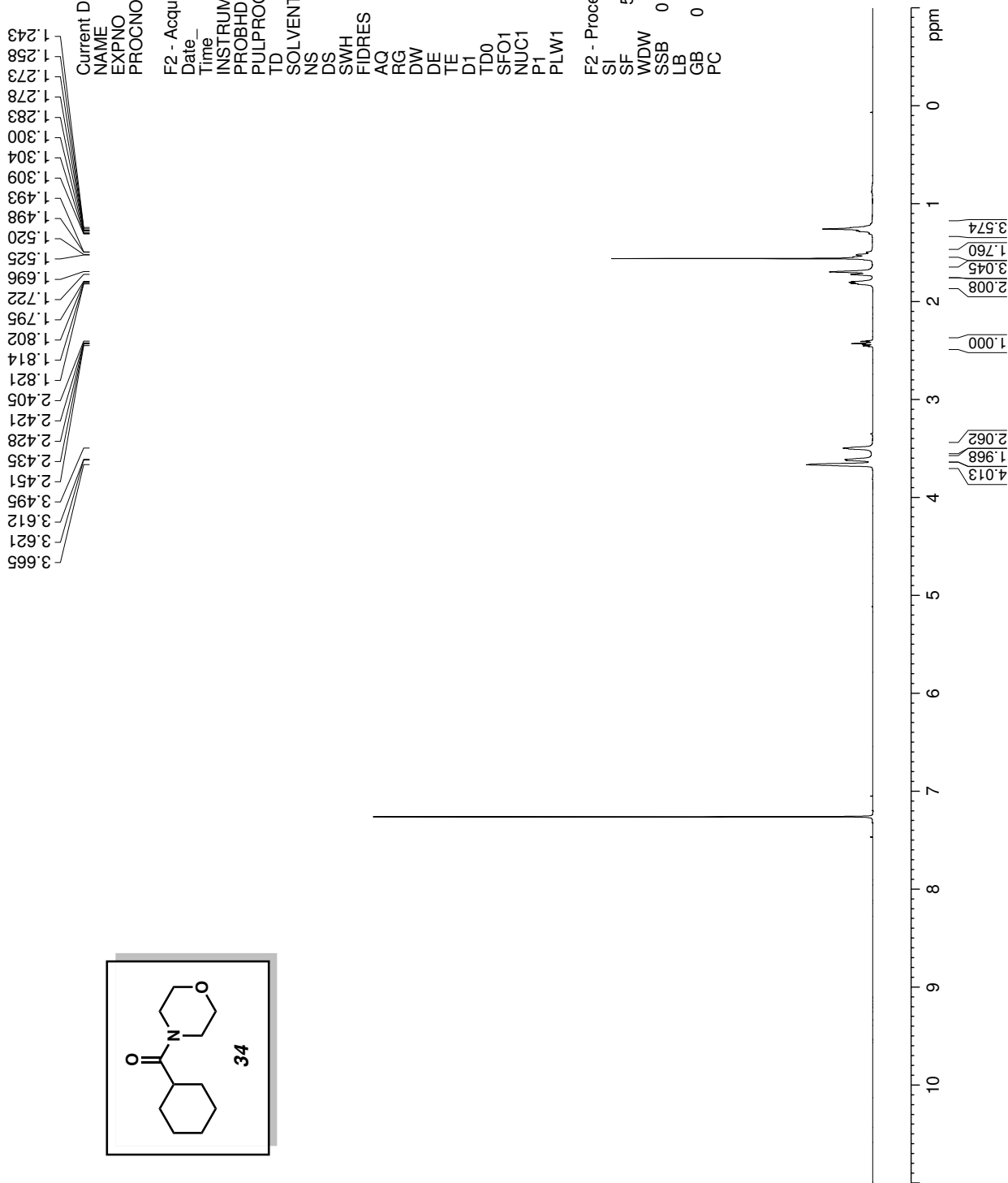
Purified Product, ¹H NMR

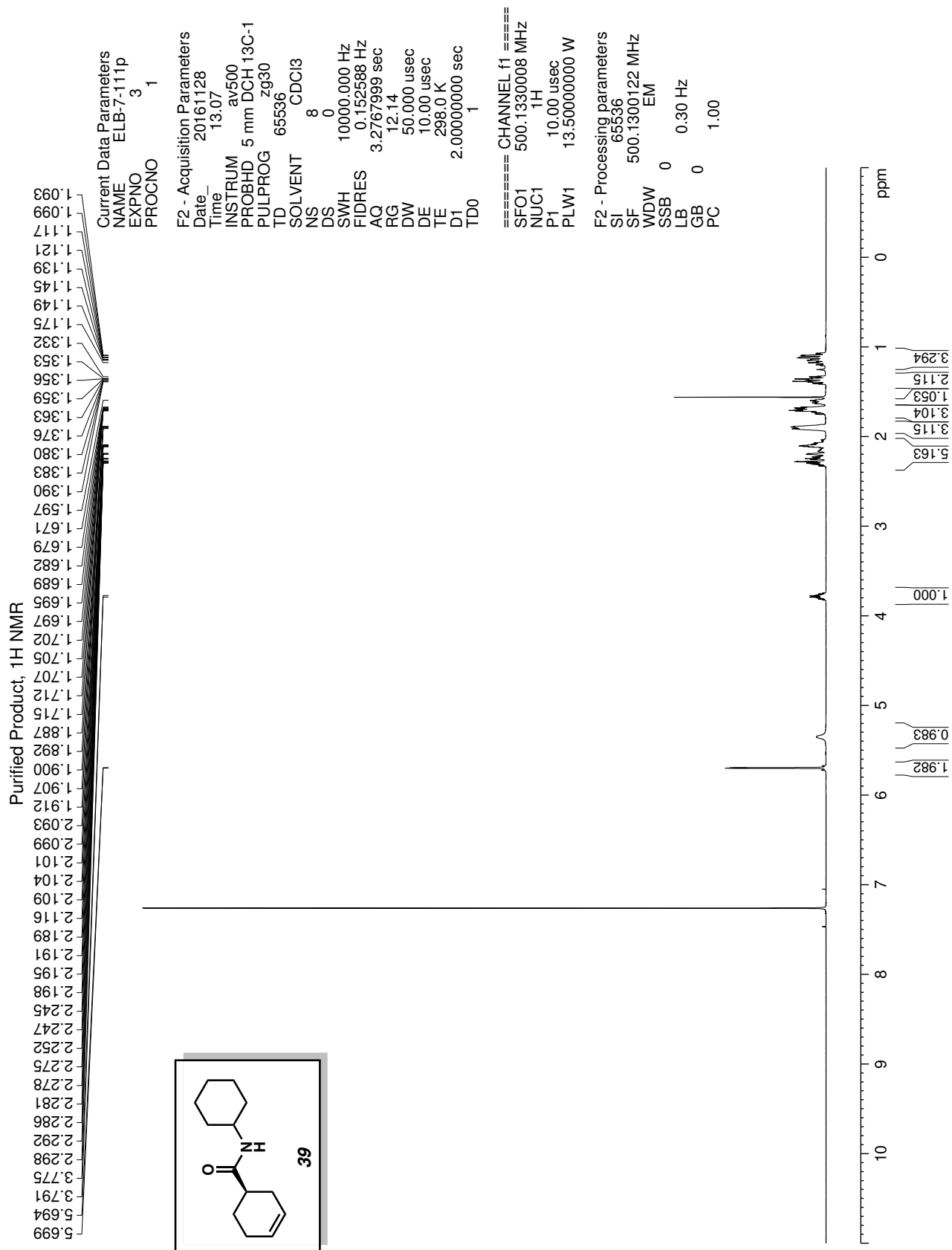


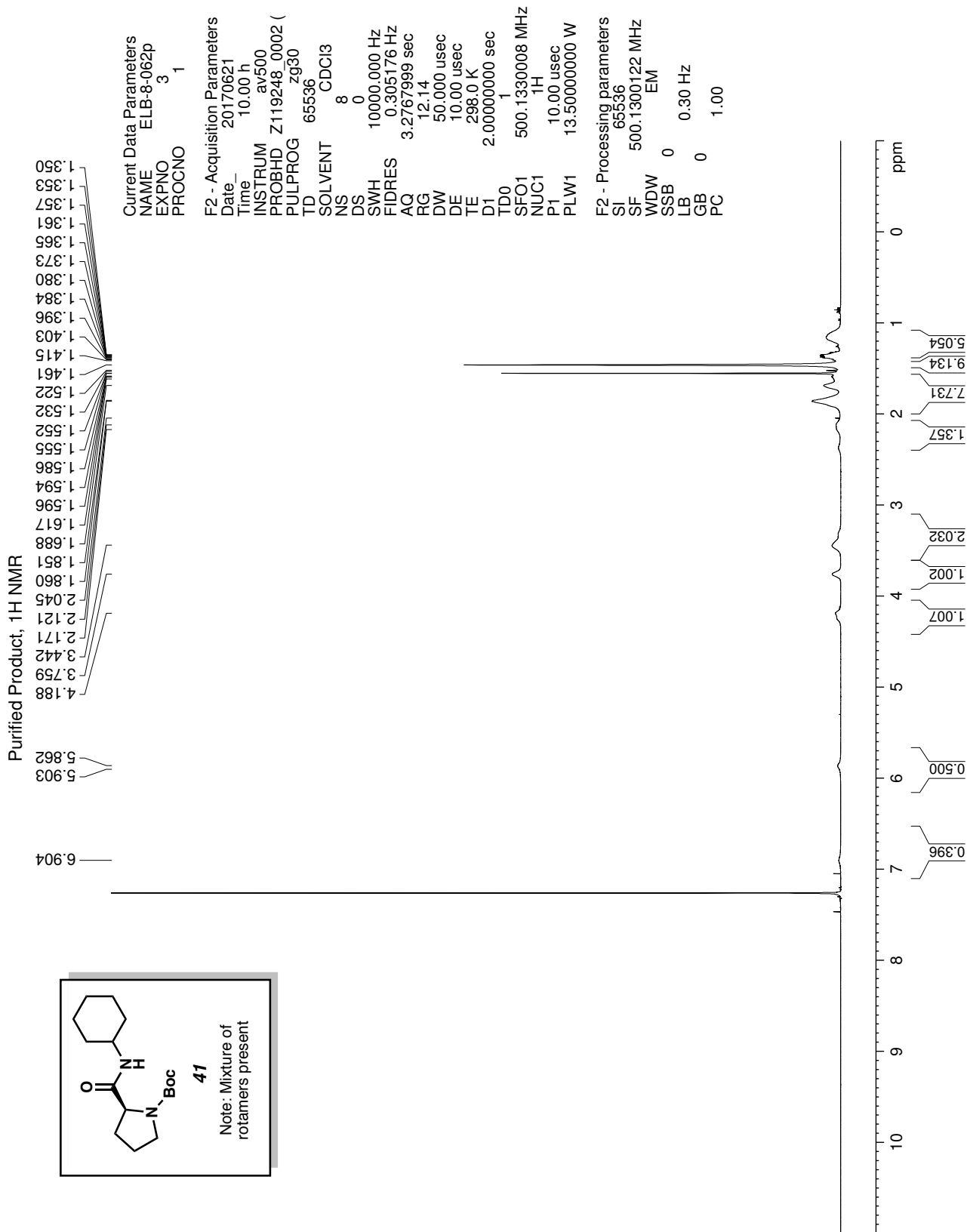
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 PLW1 13.50000000 W

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^{13}C NMR Spectra

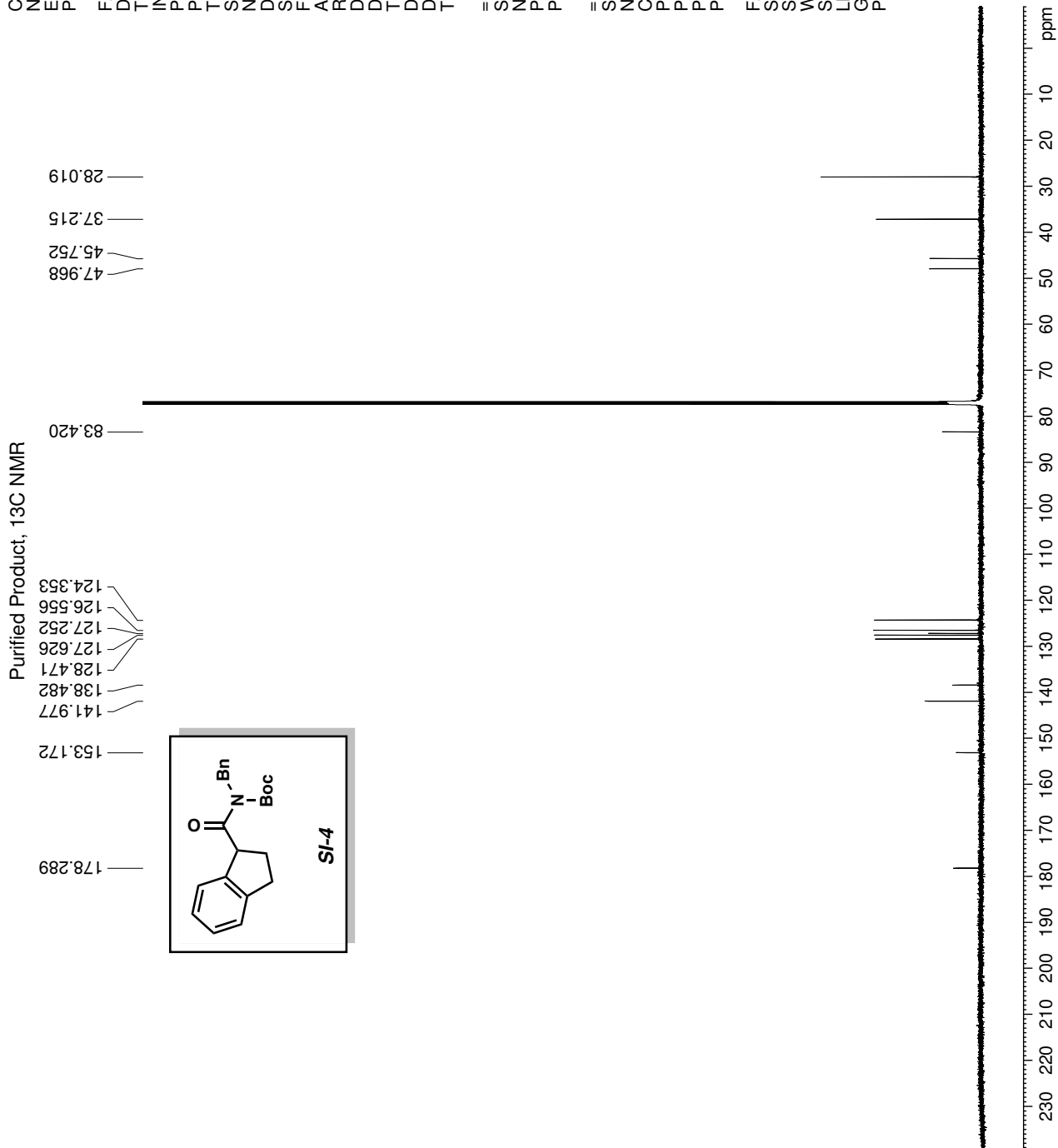
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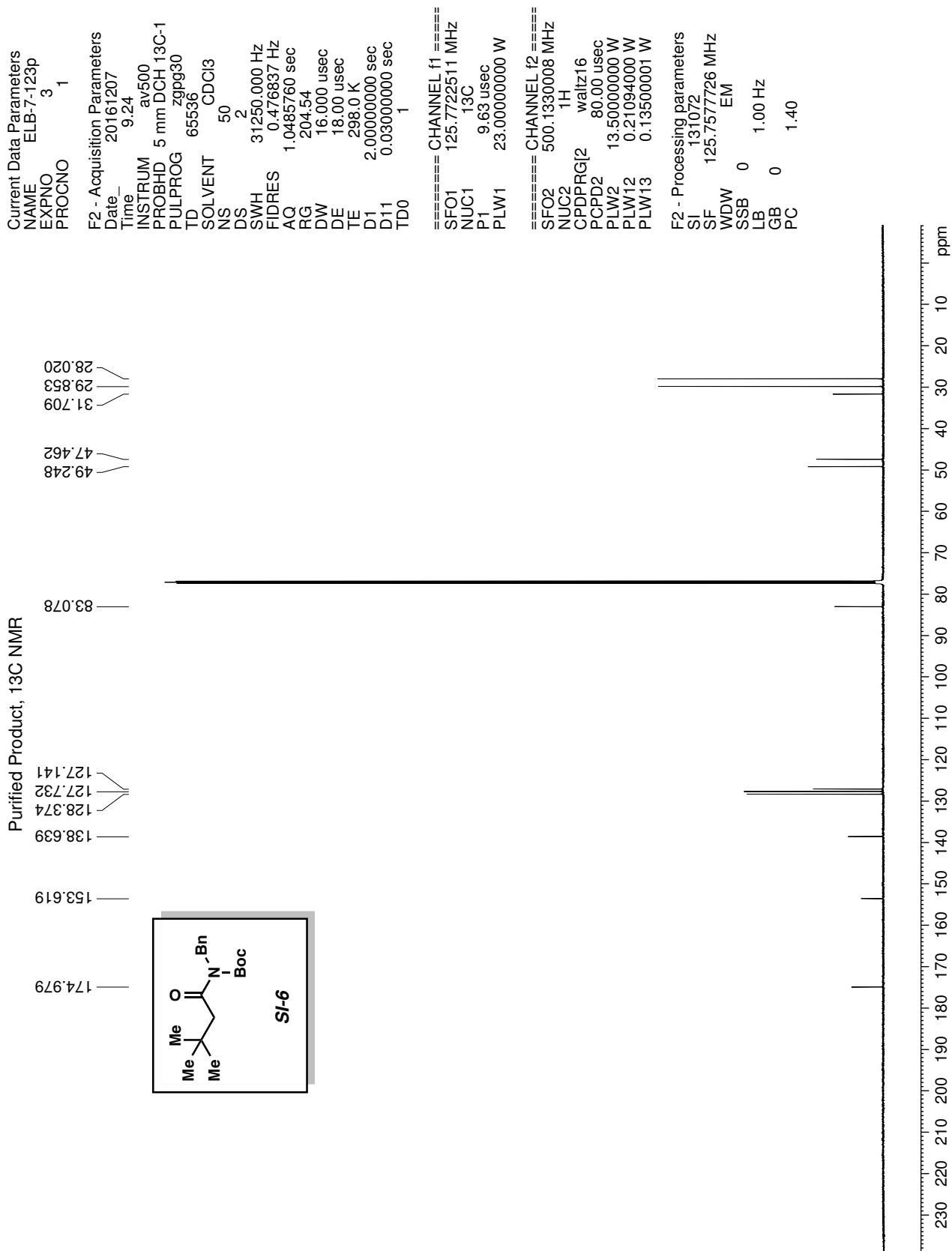
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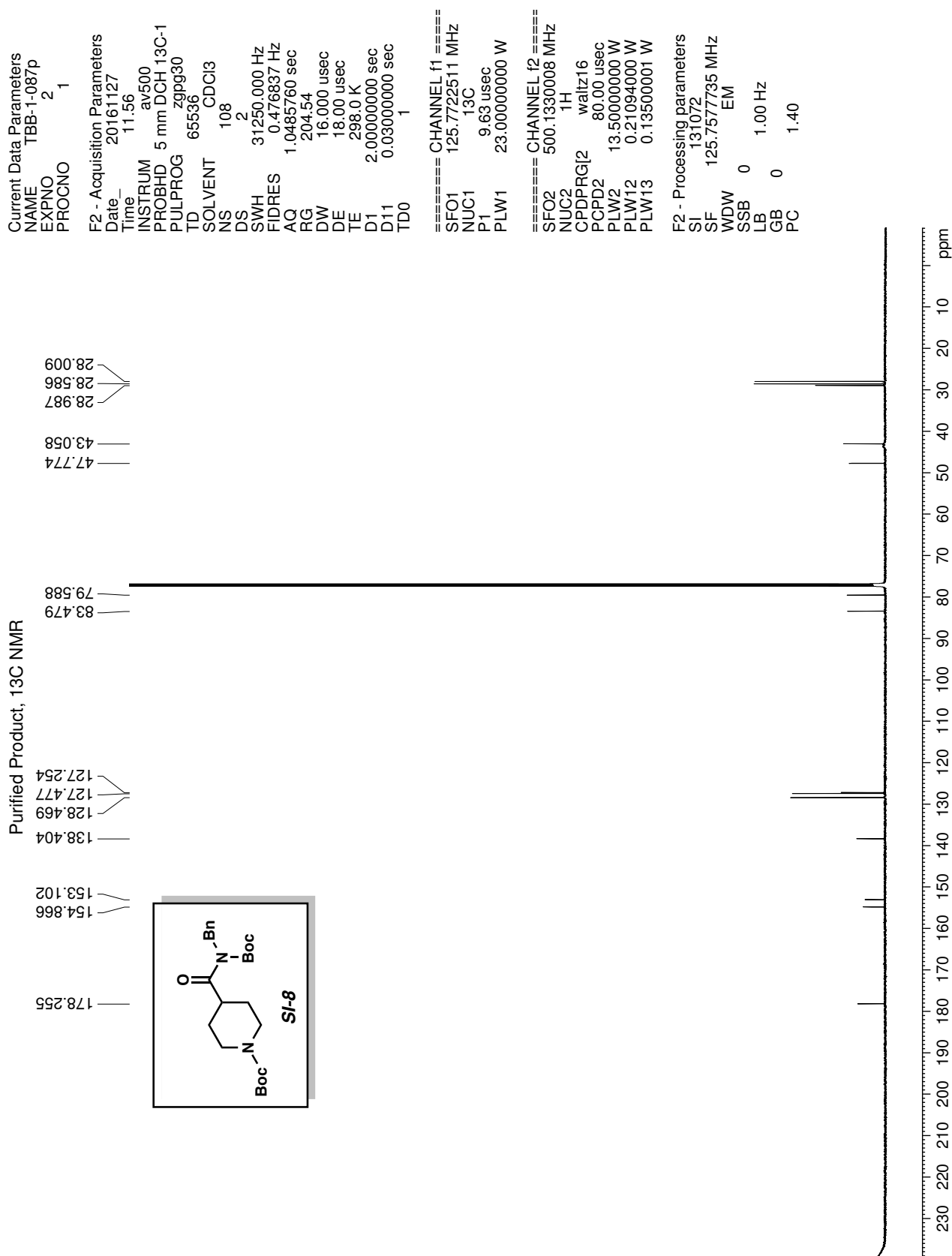
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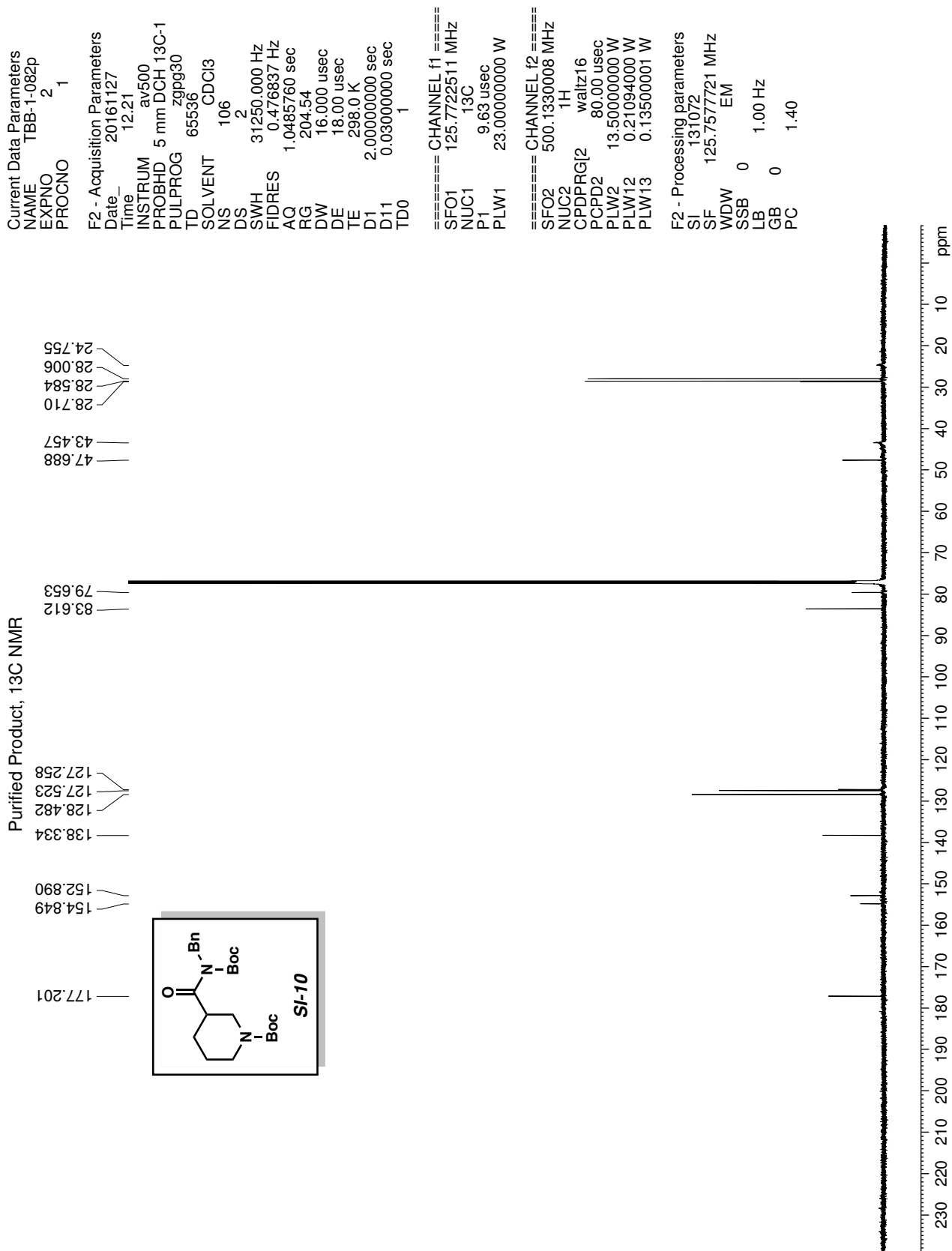
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 GB 0
 PC 1.40







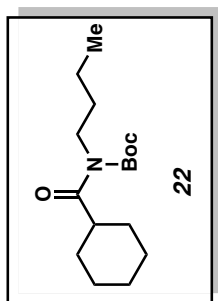
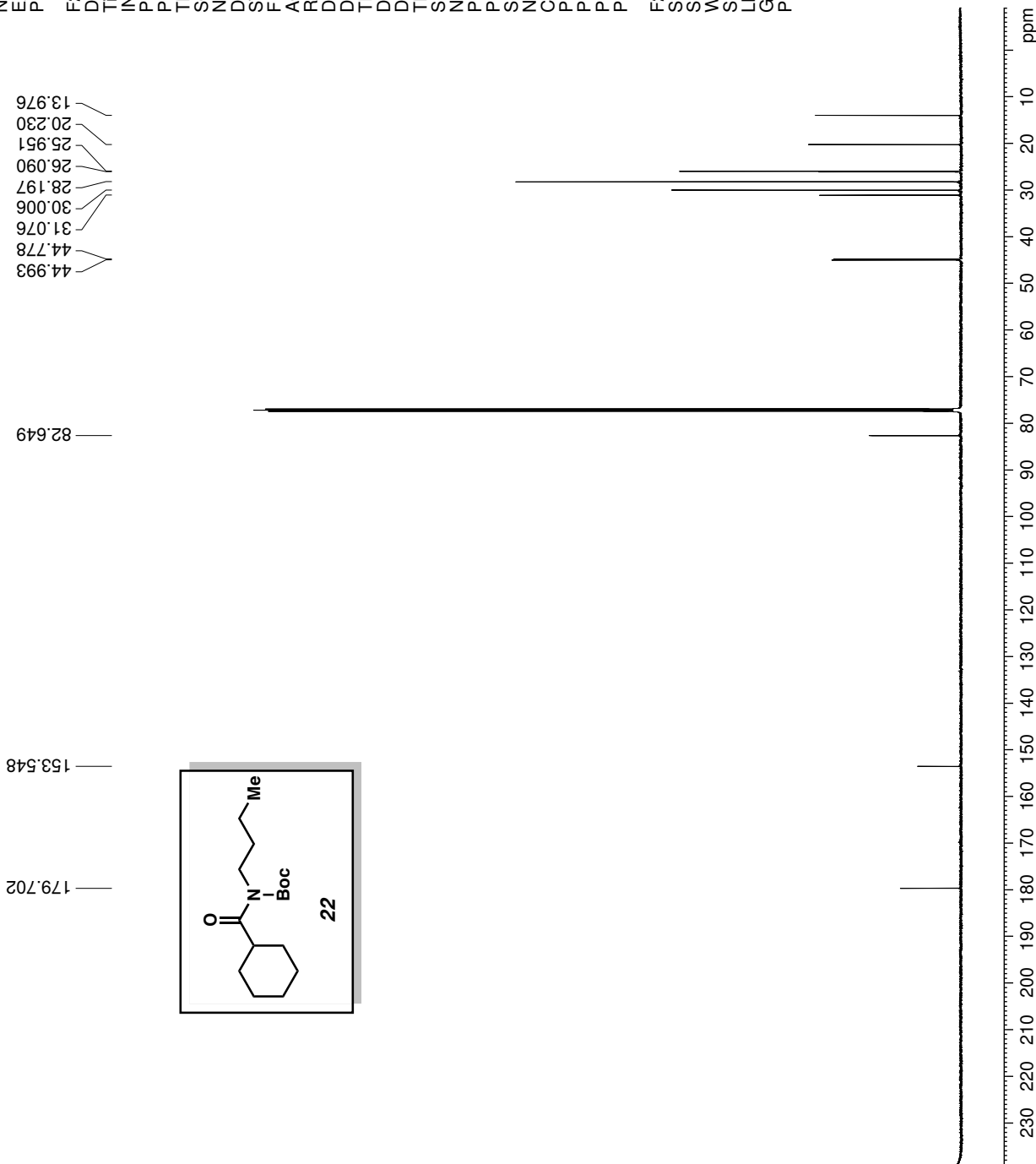


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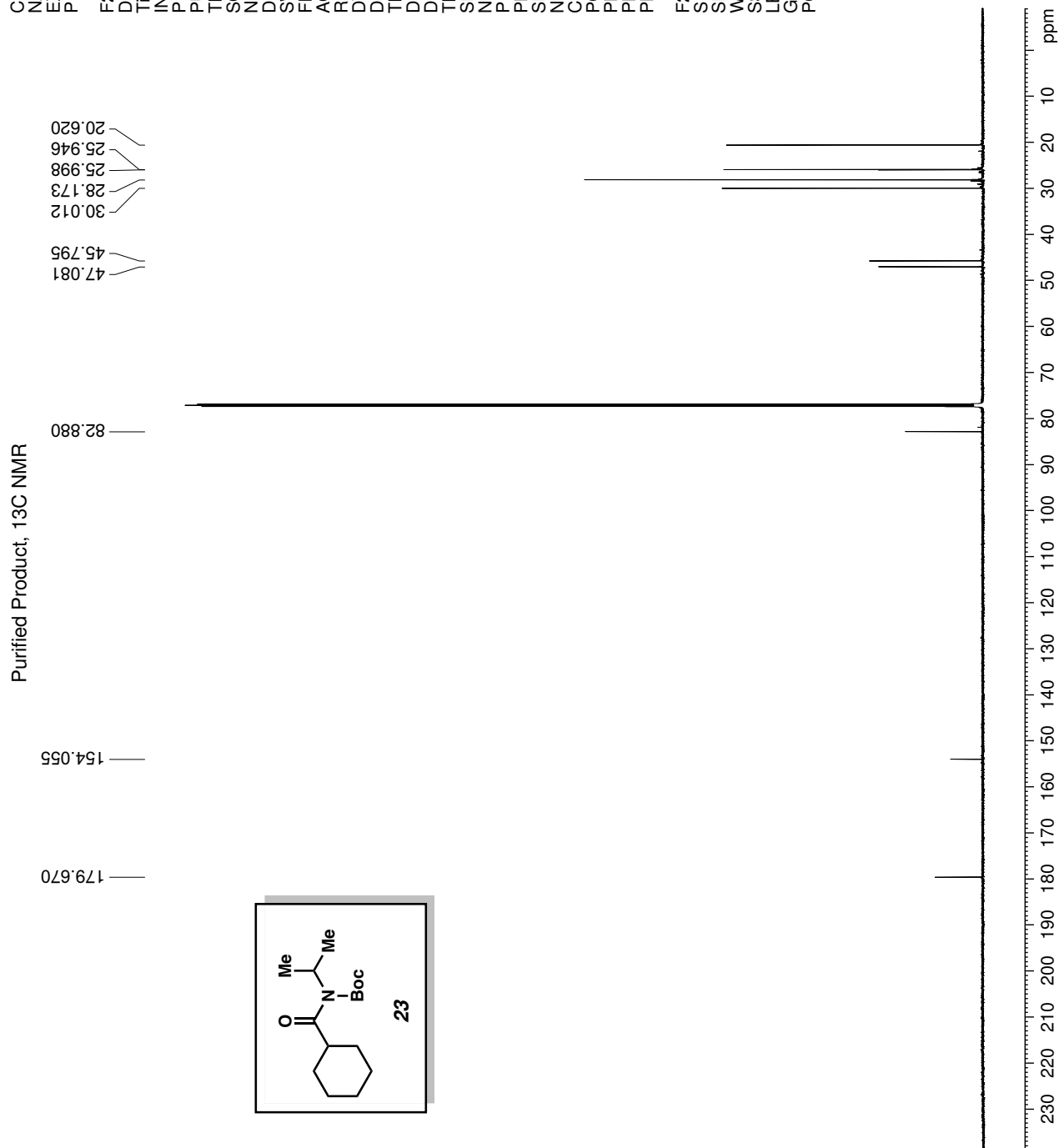
Purified Product, ¹³C NMR



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 DW 16.000 usec
 DE 18.00 usec
 TE 298.0 K
 D1 2.00000000 sec
 D11 0.03000000 sec
 TD0 1
 SFO1 125.7722511 MHz
 NUC1 13C
 P1 10.50 usec
 PLW1 23.0000000 W
 SFO2 500.1330008 MHz
 NUC2 1H
 CPDPRG2 waltz16
 PCPD2 80.00 usec
 PLW2 13.5000000 W
 PLW12 0.21094000 W
 PLW13 0.10610000 W

F2 - Processing parameters
 SI 131072
 SF 125.7577725 MHz
 WDW EM
 SSB 0
 LB 1.00 Hz
 GB 0
 PC 1.40

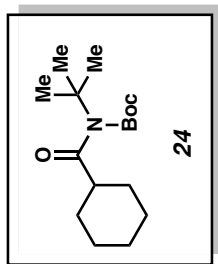
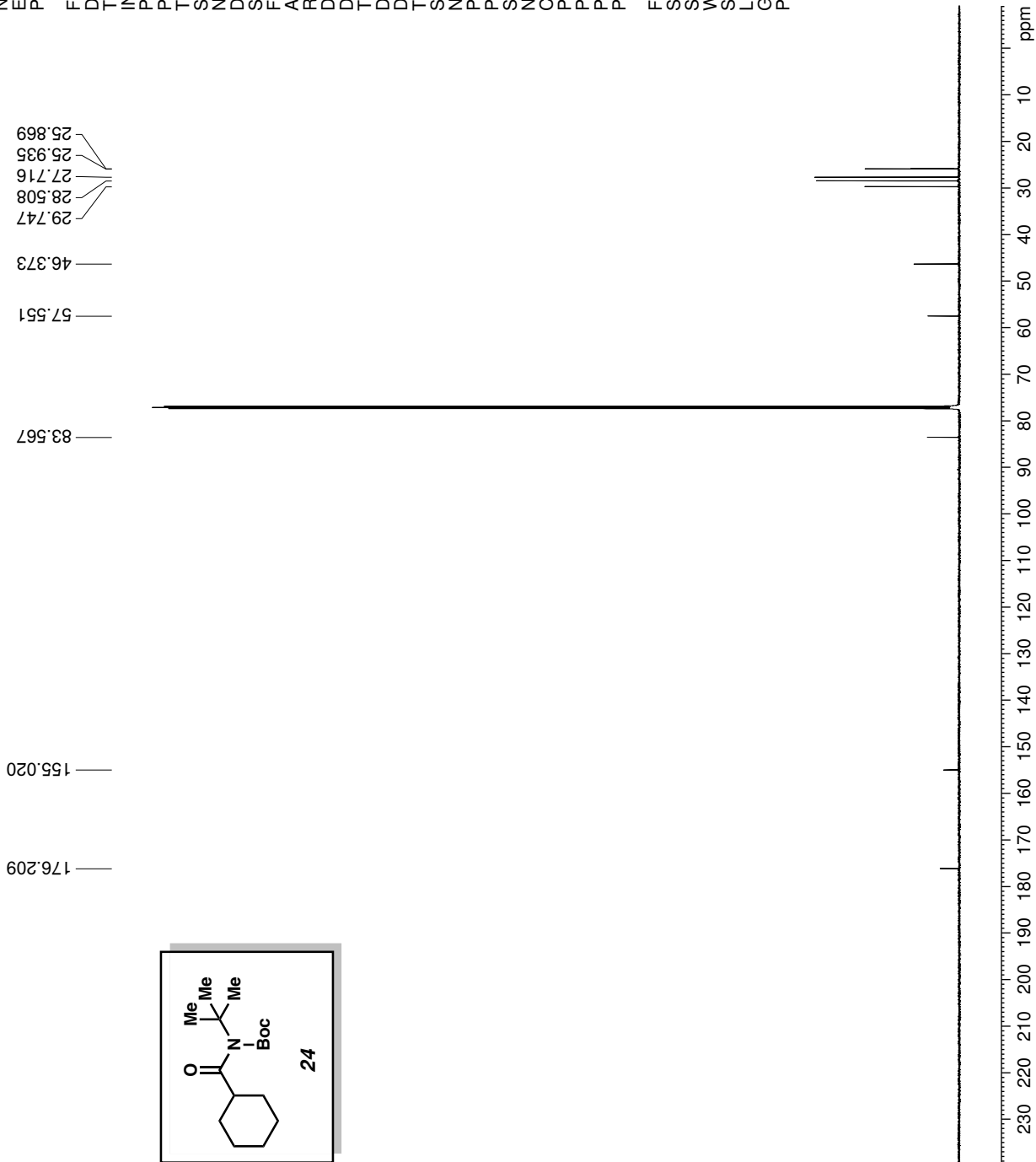


Current Data Parameters
 NAME JED-3-152p
 EXPNO 2
 PROCNO 1

F2 - Acquisition Parameters
 Date_ 20170501
 Time 13.01 h
 INSTRUM av500
 PROBHD Z119248_0002 (zpgp30)
 PULPROG zgpg30
 TD 65536
 SOLVENT CDCl3
 NS 108
 DS 2
 SWH 31250.000 Hz
 FIDRES 0.953674 Hz
 AQ 1.0485760 sec
 RG 204.54
 DW 16.000 usec
 DE 18.00 usec
 TE 298.0 K
 D1 2.00000000 sec
 D11 0.03000000 sec
 TD0 1
 SFO1 125.7722511 MHz
 NUC1 13C
 P1 10.50 usec
 PLW1 23.00000000 W
 SFO2 500.1330008 MHz
 NUC2 1H
 CPDPRG2 waltz16
 PCPD2 80.00 usec
 PLW2 13.50000000 W
 PLW12 0.21094000 W
 PLW13 0.10610000 W

F2 - Processing parameters
 SI 131072
 SF 125.7577711 MHz
 WDW EM
 SSB 0
 LB 1.00 Hz
 GB 0
 PC 1.40

Purified Product, ¹³C NMR



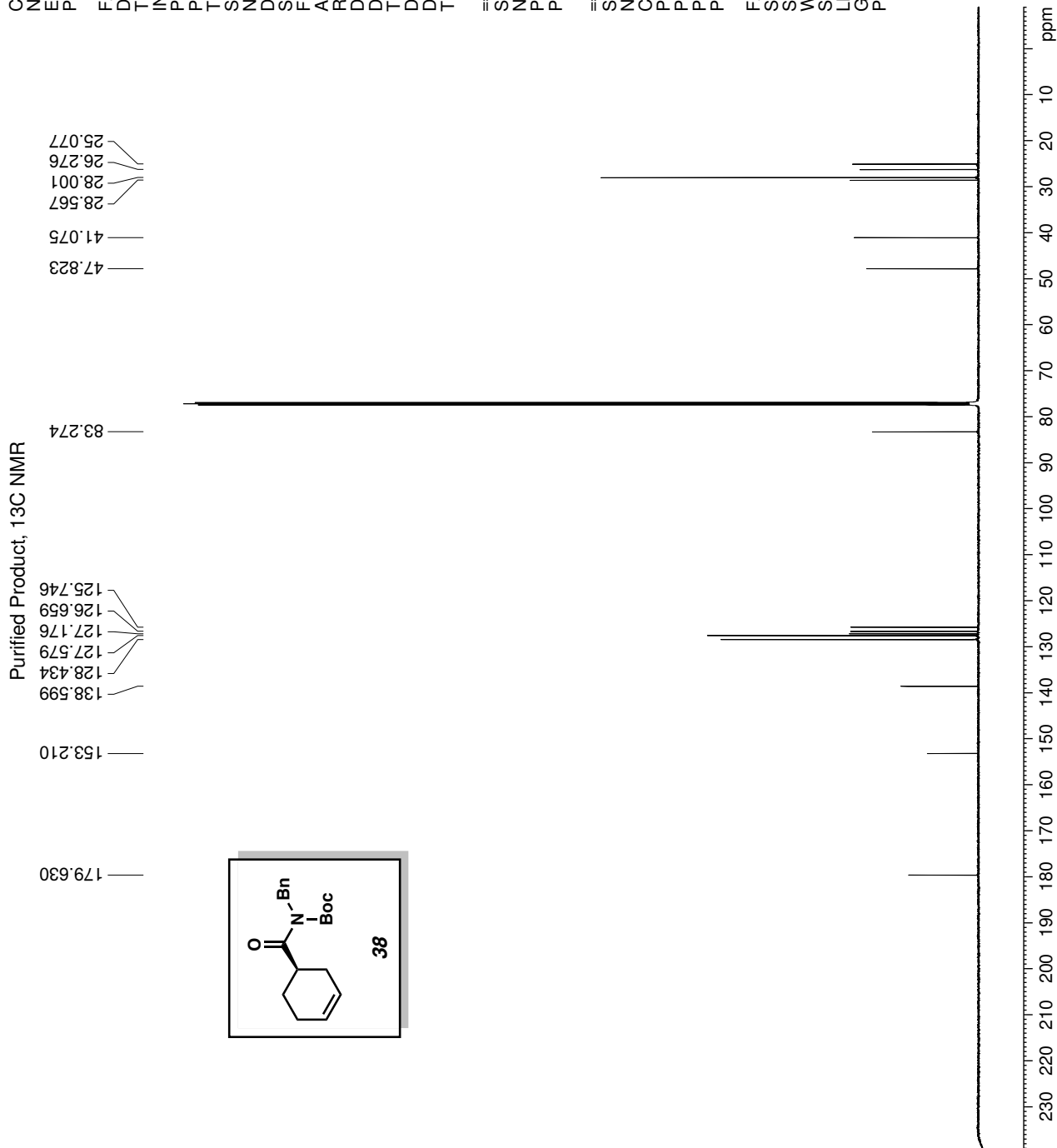
Current Data Parameters
 NAME TBB-1-168p
 EXPNO 2
 PROCNO 1

F2 - Acquisition Parameters
 Date_ 20161128
 Time_ 15.22
 INSTRUM av500
 PROBHD 5 mm DCH 13C-1
 PULPROG zgpg30
 TD 65536
 SOLVENT CDCI3
 NS 108
 DS 2
 SWH 31250.000 Hz
 FIDRES 0.476837 Hz
 AQ 1.0485760 sec
 RG 204.54
 DW 16.000 usec
 DE 18.00 usec
 TE 298.0 K
 D1 2.00000000 sec
 D11 0.03000000 sec
 TD0 1

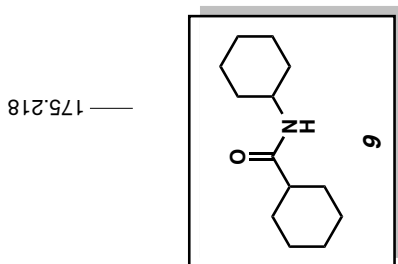
==== CHANNEL f1 =====
 SFO1 125.7722511 MHz
 NUC1 13C
 P1 9.63 usec
 PLW1 23.00000000 W

==== CHANNEL f2 =====
 SFO2 500.1330008 MHz
 NUC2 1H
 CPDPRG2 waltz16
 PCPD2 80.00 usec
 PLW2 13.50000000 W
 PLW12 0.21094000 W
 PLW13 0.13500001 W

F2 - Processing parameters
 SI 131072
 SF 125.7577730 MHz
 WDW EM
 SSB 0
 LB 1.00 Hz
 GB 0
 PC 1.40



Purified Product, ¹³C NMR



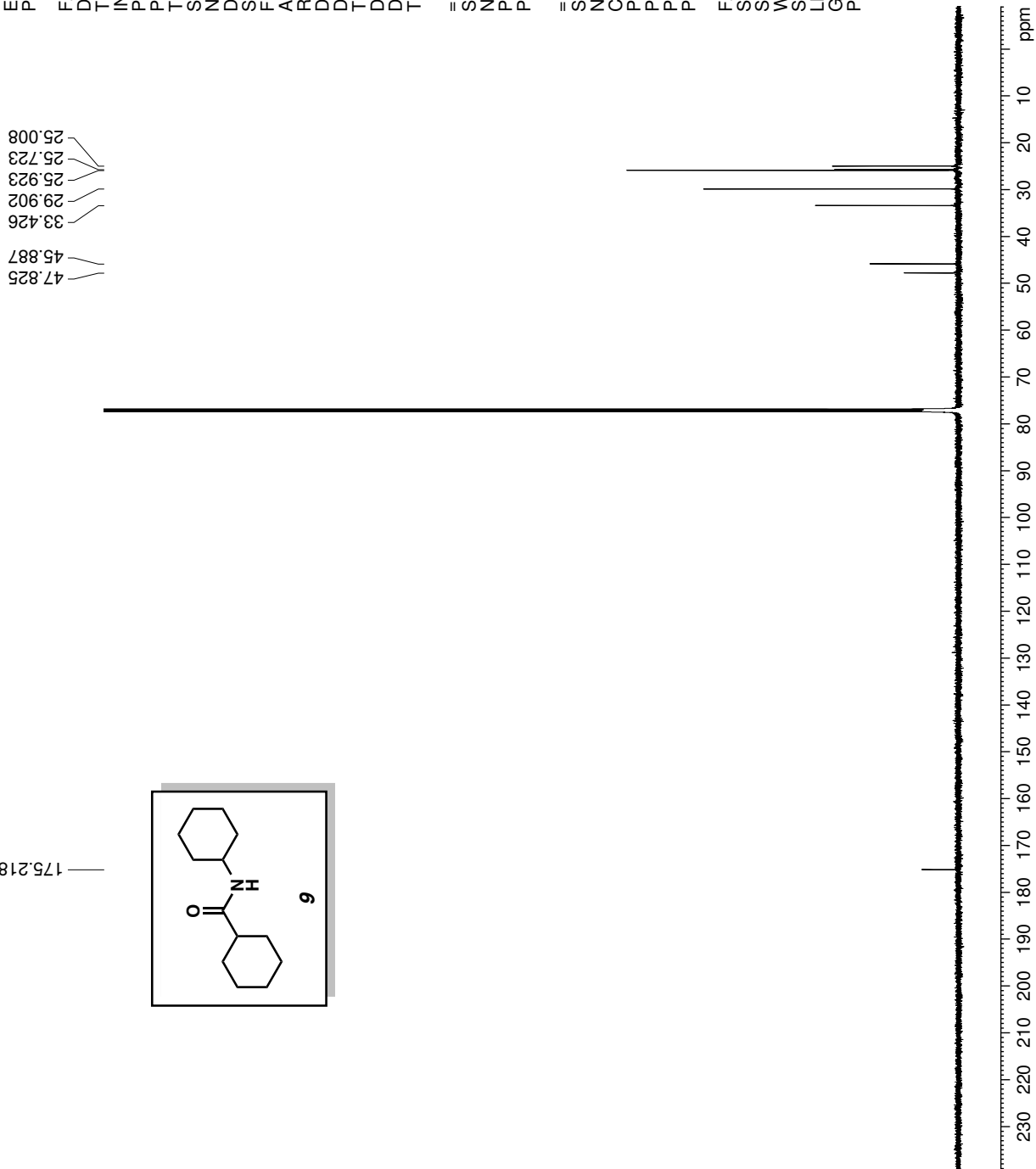
Current Data Parameters
 NAME ELB-7-090p
 EXPNO 2
 PROCNO 1

F2 - Acquisition Parameters
 Date_ 20161128
 Time_ 10.18
 INSTRUM av500
 PROBHD 5 mm DCH 13C-1
 PULPROG zgpg30
 TD 65536
 SOLVENT CDCl3
 NS 108
 DS 2
 SWH 31250.000 Hz
 FIDRES 0.476837 Hz
 AQ 1.0485760 sec
 RG 204.54
 DW 16.000 usec
 DE 18.00 usec
 TE 298.0 K
 D1 2.00000000 sec
 D11 0.03000000 sec
 TD0 1

==== CHANNEL f1 =====
 SFO1 125.7722511 MHz
 NUC1 13C
 P1 9.63 usec
 PLW1 23.00000000 W

==== CHANNEL f2 =====
 SFO2 500.1330008 MHz
 NUC2 1H
 CPDPRG2 waltz16
 PCPD2 80.00 usec
 PLW2 13.50000000 W
 PLW12 0.21094000 W
 PLW13 0.13500001 W

F2 - Processing parameters
 SI 131072
 SF 125.7577722 MHz
 WDW EM
 SSB 0
 LB 1.00 Hz
 GB 0
 PC 1.40



Purified Product, ¹³C NMR

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Current Data Parameters
NAME      ELB-7-079p
EXPNO    3
PROCNO   1

F2 - Acquisition Parameters
Date_    20161111
Time     13.41
INSTRUM  av500
PROBHD   5 mm DCH 13C-1
PULPROG  zgpg30
TD       65536
SOLVENT  CDCl3
NS       108
DS       2
SWH      31250.000 Hz
FIDRES   0.476837 Hz
AQ       1.0485760 sec
RG       204.54
DW       16.000 usec
DE       18.00 usec
TE       298.0 K
D1       2.00000000 sec
D11      0.03000000 sec
TD0      1

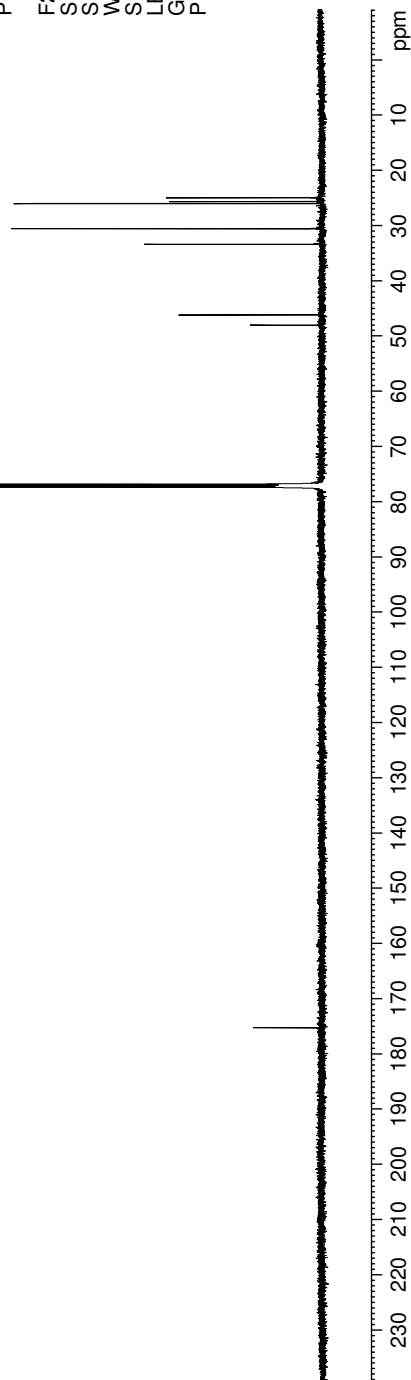
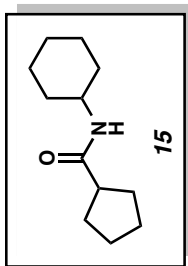
===== CHANNEL f1 =====
SFO1    125.7722511 MHz
NUC1     13C
P1       9.63 usec
PLW1    23.00000000 W

===== CHANNEL f2 =====
SFO2    500.1330008 MHz
NUC2     1H
CPDPRG2  waltz16
PCPD2    80.00 usec
PLW2    13.50000000 W
PLW12   0.21094000 W
PLW13   0.13500001 W

F2 - Processing parameters
SI       131072
SF       125.7577724 MHz
WDW      EM
SSB      0
LB       1.00 Hz
GB       0
PC       1.40
    
```

48.087
46.235
33.447
30.613
26.064
25.727
25.031

175.316



Current Data Parameters
 NAME ELB-7-076p
 EXPNO 3
 PROCNO 1

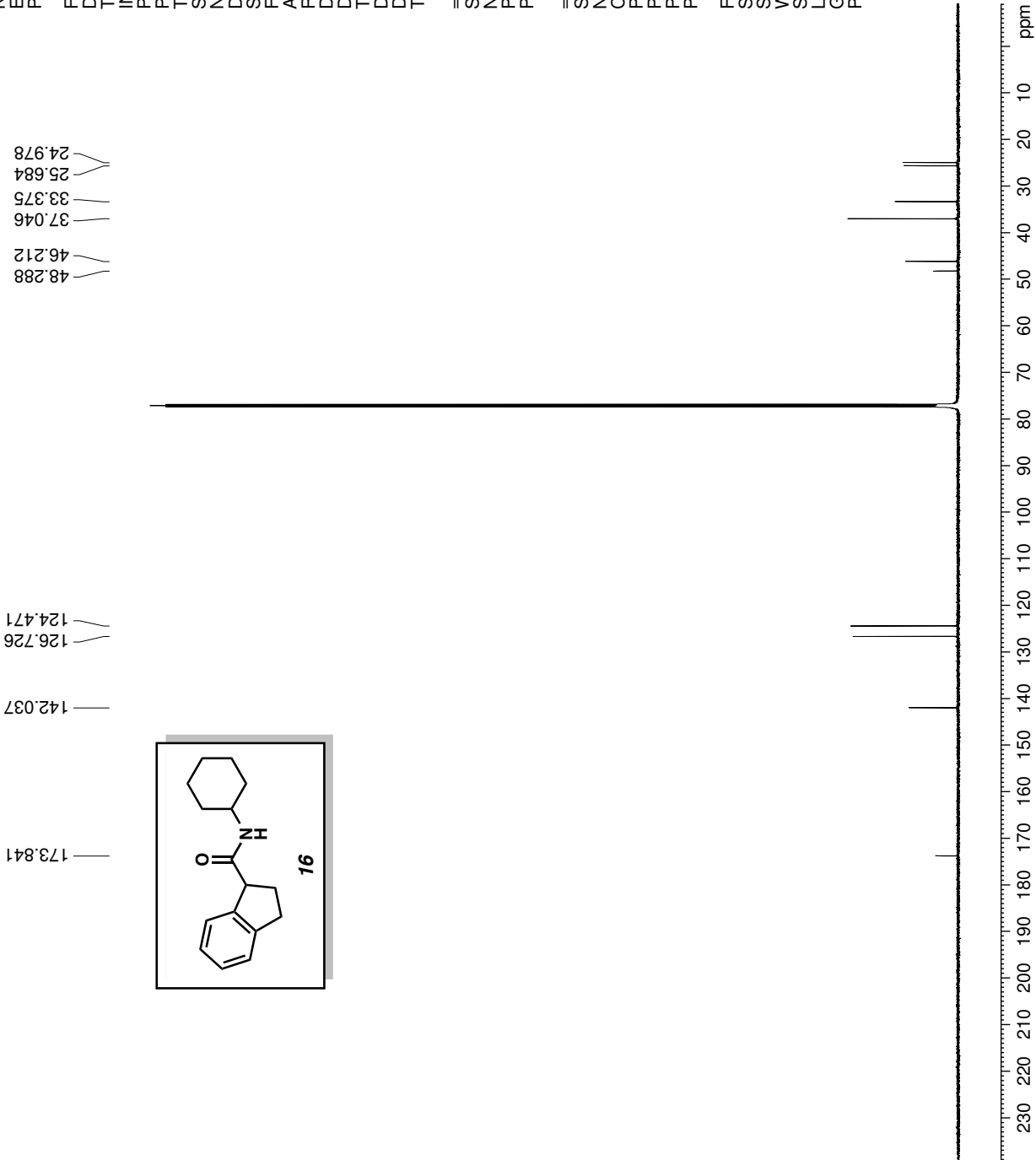
F2 - Acquisition Parameters
 Date_ 20161113
 Time_ 16.26
 INSTRUM av500
 PROBHD 5 mm DCH 13C-1
 PULPROG zgpg30
 TD 65536
 SOLVENT CDCI3
 NS 72
 DS 2
 SWH 31250.000 Hz
 FIDRES 0.476837 Hz
 AQ 1.0485760 sec
 RG 204.54
 DW 16.000 usec
 DE 18.00 usec
 TE 298.0 K
 D1 2.00000000 sec
 D11 0.03000000 sec
 TD0 1

==== CHANNEL f1 =====
 SFO1 125.7722511 MHz
 NUC1 13C
 P1 9.63 usec
 PLW1 23.00000000 W

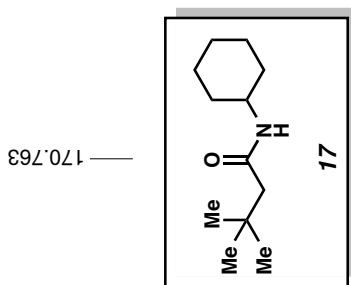
==== CHANNEL f2 =====
 SFO2 500.1330008 MHz
 NUC2 1H
 CPDPRG2 waltz16
 PCPD2 80.00 usec
 PLW2 13.50000000 W
 PLW12 0.21094000 W
 PLW13 0.13500001 W

F2 - Processing parameters
 SI 131072
 SF 125.7577725 MHz
 WDW EM
 SSB 0
 LB 1.00 Hz
 GB 0
 PC 1.40

Purified Product, ¹³C NMR



Purified Product, ¹³C NMR



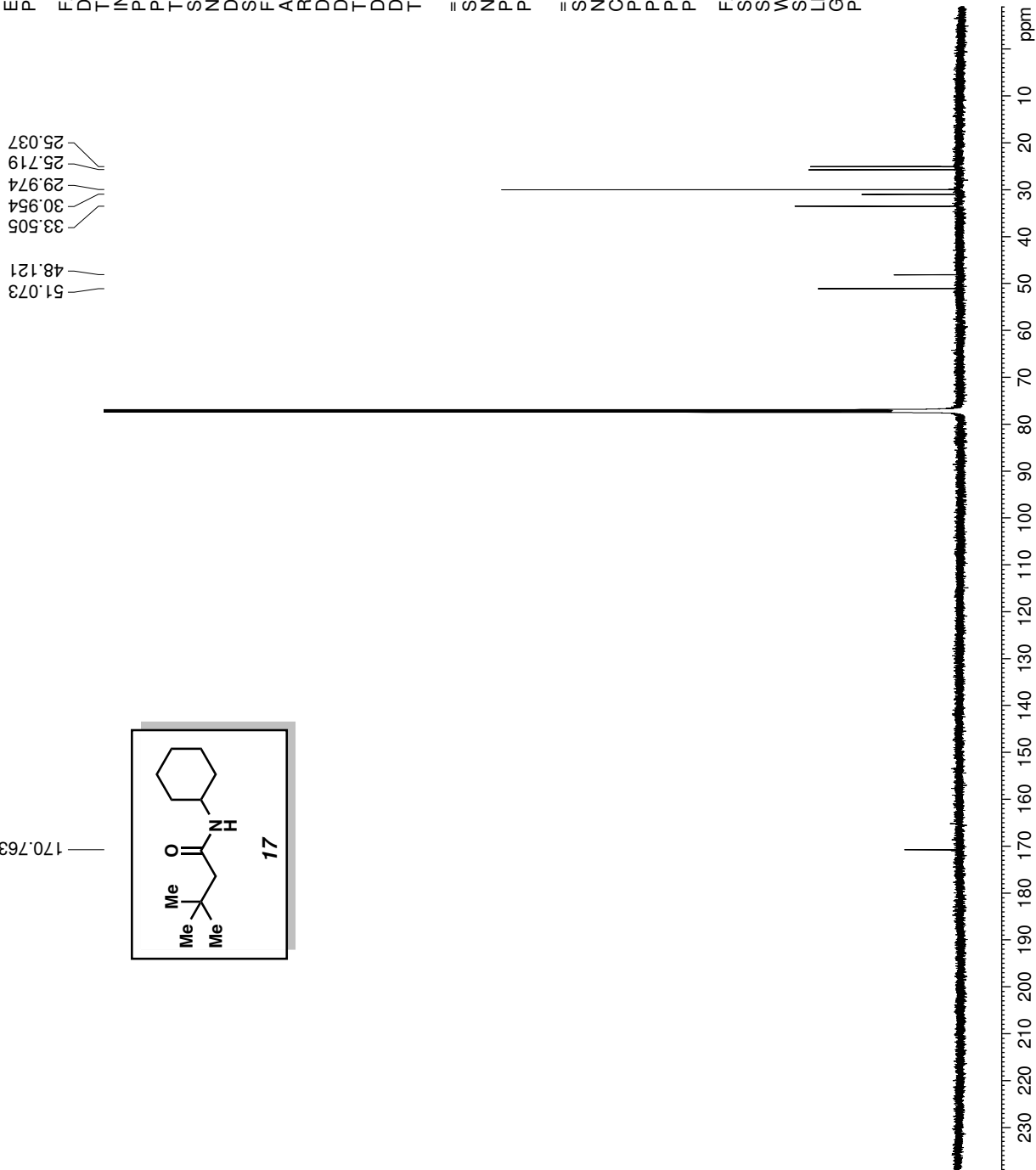
Current Data Parameters
 NAME ELB-7-139p
 EXPNO 4
 PROCNO 1

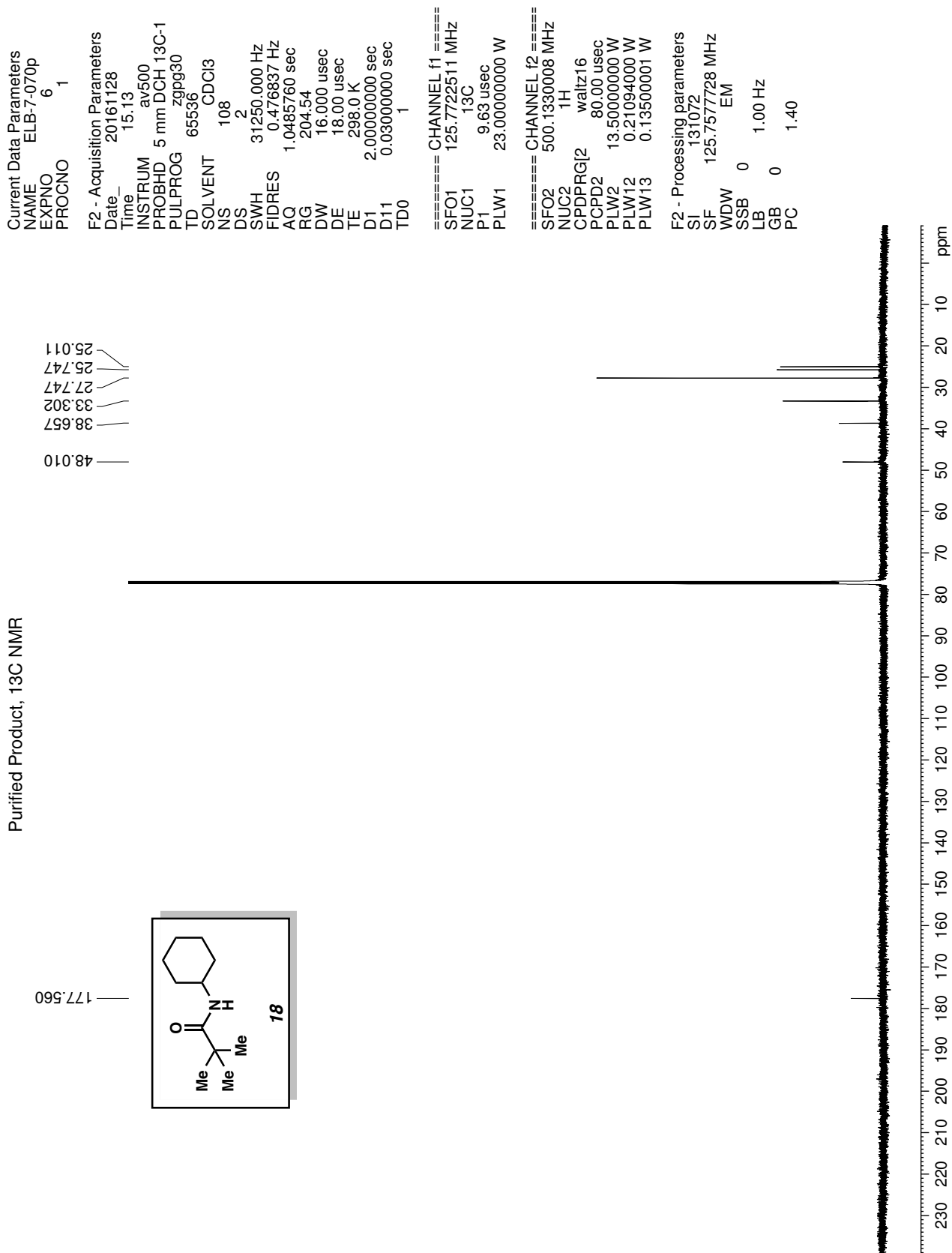
F2 - Acquisition Parameters
 Date_ 20161207
 Time_ 11.48
 INSTRUM av500
 PROBHD 5 mm DCH 13C-1
 PULPROG zgpg30
 TD 65536
 SOLVENT CDCl3
 NS 108
 DS 2
 SWH 31250.000 Hz
 FIDRES 0.476837 Hz
 AQ 1.0485760 sec
 RG 204.54
 DW 16.000 usec
 DE 18.00 usec
 TE 298.0 K
 D1 2.00000000 sec
 D11 0.03000000 sec
 TD0 1

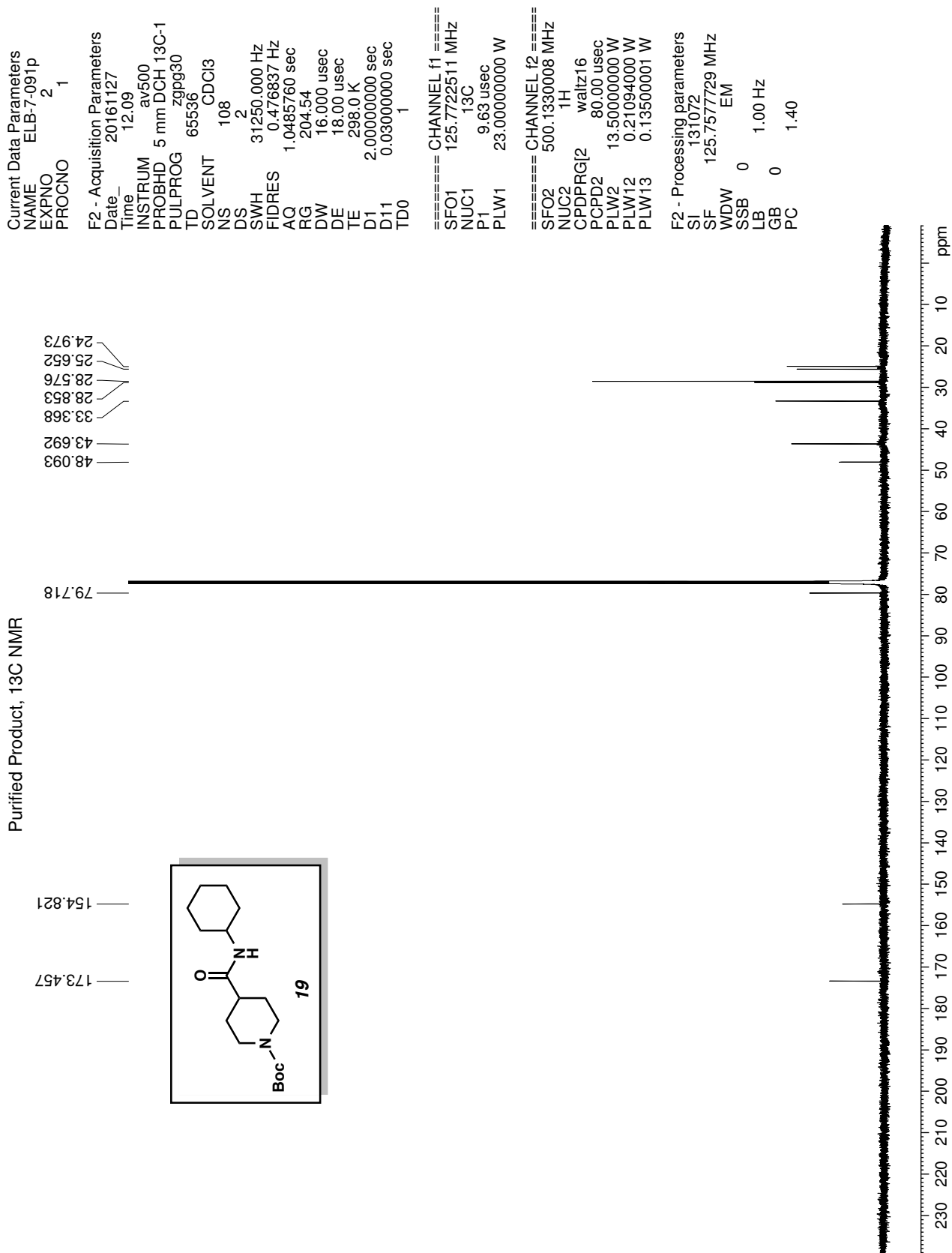
==== CHANNEL f1 =====
 SFO1 125.7722511 MHz
 NUC1 13C
 P1 9.63 usec
 PLW1 23.00000000 W

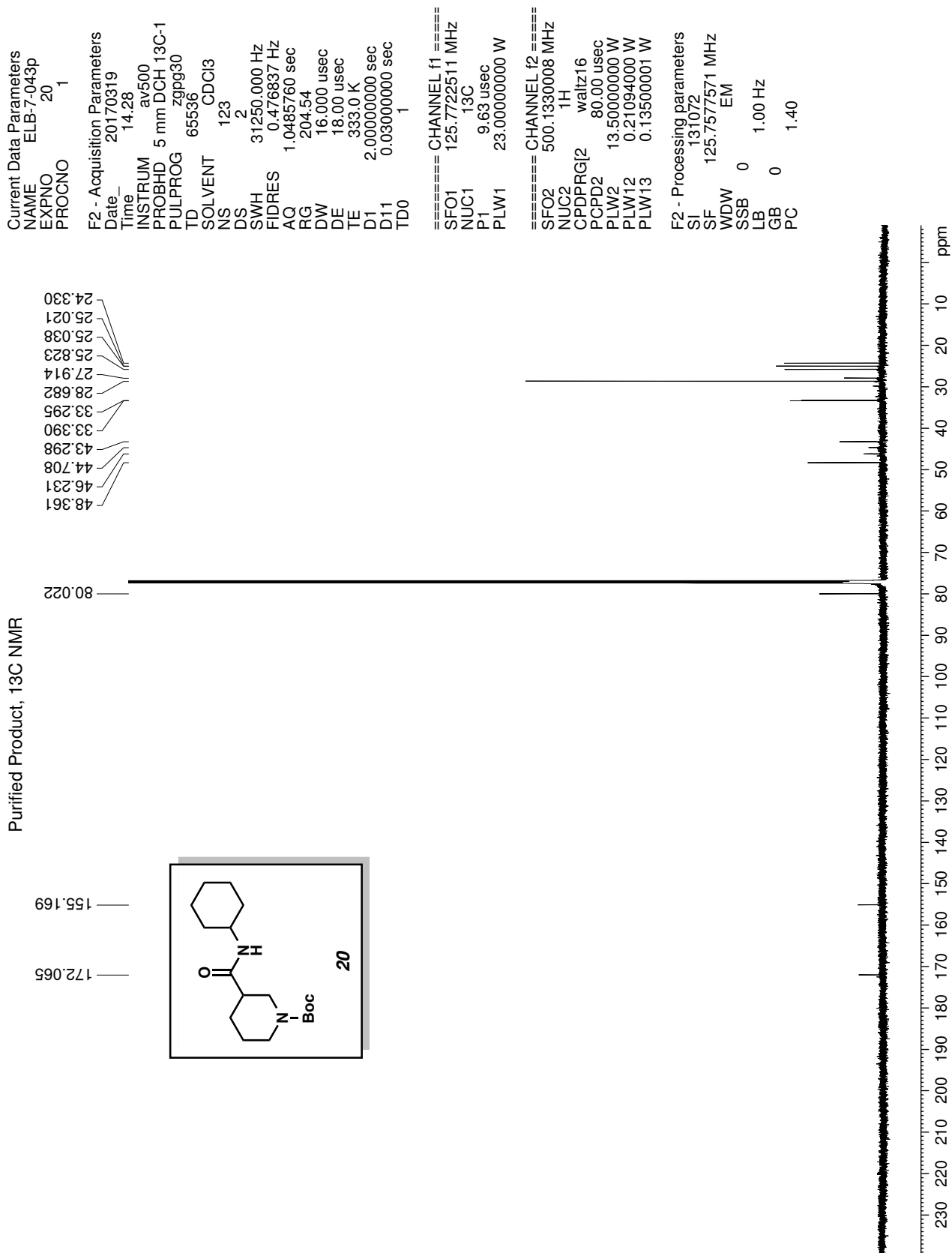
==== CHANNEL f2 =====
 SFO2 500.1330008 MHz
 NUC2 1H
 CPDPRG2 waltz16
 PCPD2 80.00 usec
 PLW2 13.50000000 W
 PLW12 0.21094000 W
 PLW13 0.13500001 W

F2 - Processing parameters
 SI 131072
 SF 125.7577719 MHz
 WDW EM
 SSB 0
 LB 0 1.00 Hz
 GB 0
 PC 1.40







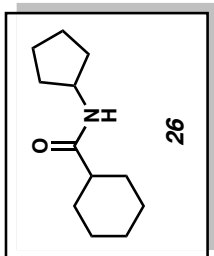
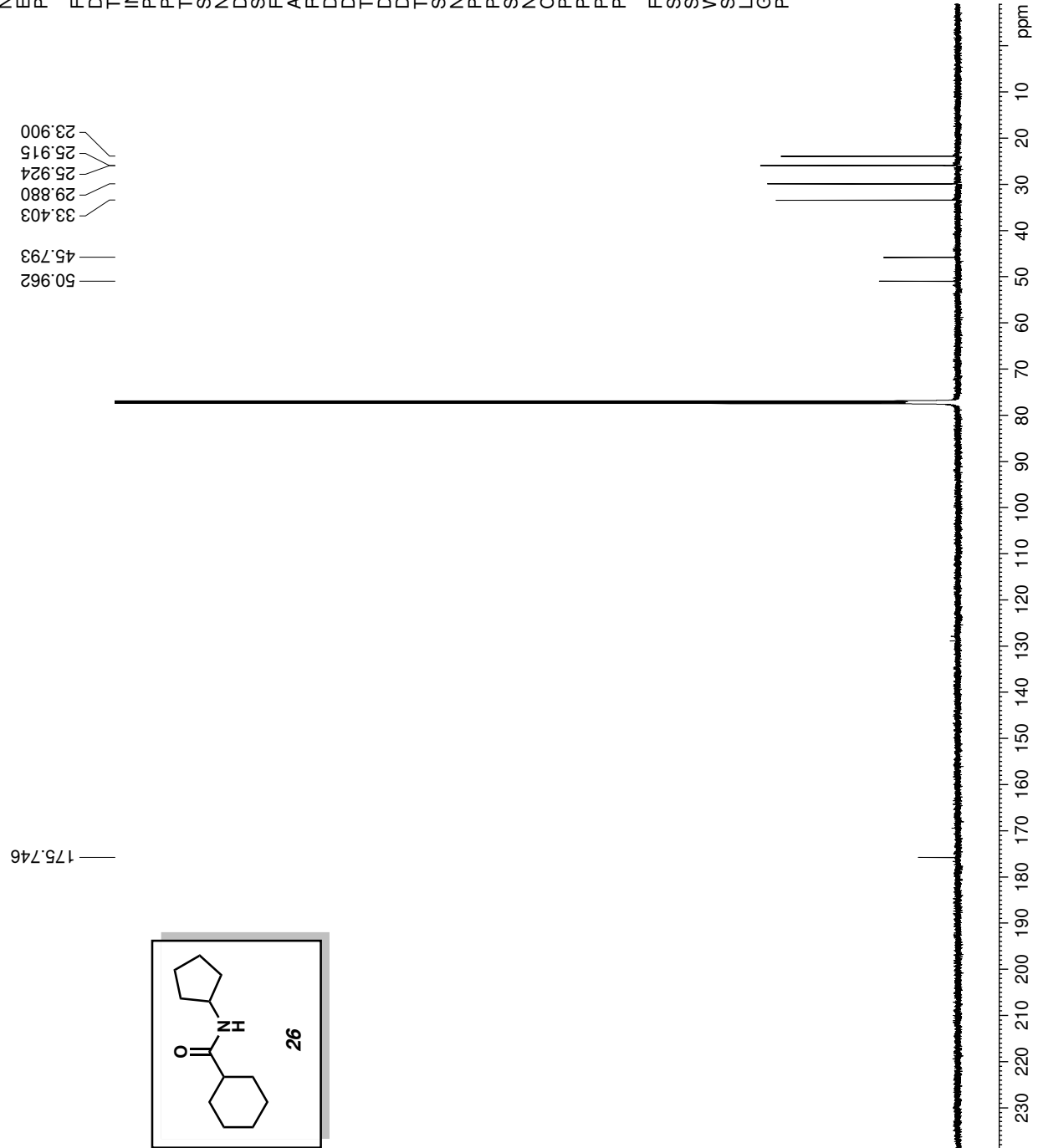


Purified Product, ¹³C NMR

Current Data Parameters
 NAME JED-3-024p2
 EXPNO 2
 PROCNO 1

F2 - Acquisition Parameters
 Date_ 20170305
 Time_ 16.51 h
 INSTRUM av500
 PROBHD Z119248_0002 (
 PULPROG zgpg30
 TD 65536
 SOLVENT CDCI3
 NS 200
 DS 2
 SWH 31250.000 Hz
 FIDRES 0.953674 Hz
 AQ 1.0485760 sec
 RG 103.52
 DW 16.000 usec
 DE 18.00 usec
 TE 298.0 K
 D1 2.00000000 sec
 D11 0.03000000 sec
 TD0 1
 SFO1 125.7722511 MHz
 NUC1 ¹³C
 P1 10.50 usec
 PLW1 23.00000000 W
 SFO2 500.1330008 MHz
 NUC2 ¹H
 CPDPRG[2] waltz16
 PCPD2 80.00 usec
 PLW2 13.50000000 W
 PLW12 0.21094000 W
 PLW13 0.10610000 W

F2 - Processing parameters
 SI 131072
 SF 125.7577719 MHz
 WDW EM
 SSB 0
 LB 1.00 Hz
 GB 0
 PC 1.40



Current Data Parameters
 NAME JED-3-064p
 EXPNO 2
 PROCNO 1

F2 - Acquisition Parameters
 Date_ 20170116
 Time_ 16.25
 INSTRUM av500
 PROBHD 5 mm DCH 13C-1
 PULPROG zgpg30
 TD 65536
 SOLVENT CDCI3
 NS 62
 DS 2
 SWH 31250.000 Hz
 FIDRES 0.476837 Hz
 AQ 1.0485760 sec
 RG 204.54
 DW 16.000 usec
 DE 18.00 usec
 TE 298.0 K
 D1 2.00000000 sec
 D11 0.03000000 sec
 TD0 1

==== CHANNEL f1 =====
 SFO1 125.7722511 MHz
 NUC1 13C
 P1 9.63 usec
 PLW1 23.00000000 W

==== CHANNEL f2 =====
 SFO2 500.1330008 MHz
 NUC2 1H
 CPDPRG2 waltz16
 PCPD2 80.00 usec
 PLW2 13.50000000 W
 PLW12 0.21094000 W
 PLW13 0.13500001 W

F2 - Processing parameters
 SI 131072
 SF 125.7577745 MHz
 WDW EM
 SSB 0
 LB 0 1.00 Hz
 GB 0
 PC 1.40

Purified Product, 13C NMR

