

Supporting Information

**Arynes and Cyclic Alkynes as Synthetic Building Blocks
for Stereodefined Quaternary Centers**

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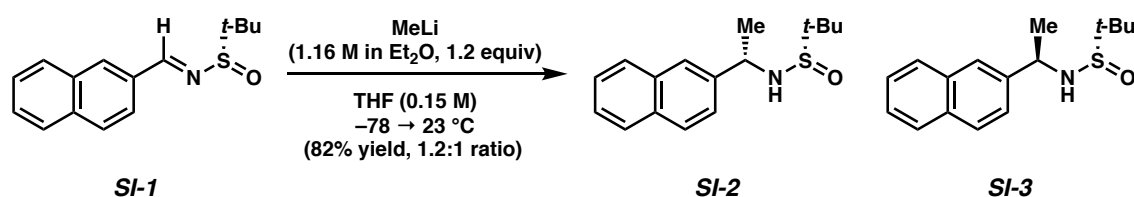
Part I: Experimental Section

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. Anhydrous solvents were either freshly distilled or passed through activated alumina columns, unless otherwise stated. Non-commercially available reagents and substrates were synthesized following protocols specified in Section A, Section B, and Section C in the Experimental Procedures. Benzylamine, ethyl magnesium bromide, isopropyl magnesium chloride, methyllithium, (*R*)-1-(naphthalen-1-yl)ethan-1-amine (**20**), ethyl 2-methyl-3-oxobutanoate, sodium sulfate, and 2-(trimethylsilyl)phenyl trifluoromethanesulfonate (**11**) were obtained from Millipore Sigma. 2-Naphthaldehyde, titanium tetraethoxide, 4 M HCl in dioxane, ethyl 2-oxocyclohexane-1-carboxylate (**9**), concentrated HCl, and 4-(dimethylamino)pyridine (DMAP) were purchased from Oakwood. (*S*)-2-Methylpropane-2-sulfinamide, anthracene-9-carbaldehyde, 1-(*tert*-butyl) 3-ethyl 4-oxopiperidine-1,3-dicarboxylate, and methyl 2-oxocycloheptane-1-carboxylate (**39**) were obtained from Combi-Blocks. CsF was purchased and used as received from Strem Chemicals. 3-(Trimethylsilyl)-2-naphthyl trifluoromethanesulfonate, 2-methyl-6-(trimethylsilyl)phenyl trifluoromethanesulfonate, and 2-nitrobenzenesulfonyl chloride (NsCl) were purchased from TCI. (*R*)-1-Phenylethan-1-amine (**18**) was purchased from Honeywell Fluka. (*R*)-1-Cyclohexylethan-1-amine (**19**) was purchased from Alfa Aesar. The silyltriflate precursors to bromobenzynes,¹ cyclohexynes,² 3,4-piperidynes,³ and 3,4-oxocyclohexynes⁴ were prepared following literature procedures. Ketoesters benzyl 2-oxocyclohexane-1-carboxylate,⁵ ethyl 4-oxotetrahydro-2*H*-pyran-3-carboxylate,⁶ and ethyl 5-oxooxepane-4-carboxylate⁷ were prepared following literature procedures. 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, phosphomolybdic acid, anisaldehyde, iodine, and potassium permanganate staining techniques. Silicycle Siliaflash P60 (particle size 40–63 μm) or aluminum oxide, activated, neutral, Brockman I (particle size 58 angstroms) were used for flash column chromatography. ¹H NMR spectra were recorded on Bruker spectrometers (at 300, 400, 500, and

600 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), integration. Data for ^{13}C NMR are reported in terms of chemical shift (125 MHz). IR spectra were recorded on a Perkin-Elmer UATR Two FT-IR spectrometer and are reported in terms of frequency absorption (cm^{-1}). 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 CHCl_3 as the solvent. Ionization was accomplished using UHP He 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 Daicel ChiralPak OD-H, Daicel ChiralPak IA-3, Daicel ChiralPak IC-3, Daicel ChiralPak AD-3, and Daicel ChiralPak OJ-H columns. Data for SFC spectra are reported in enantiomeric excess (ee).

Experimental Procedures

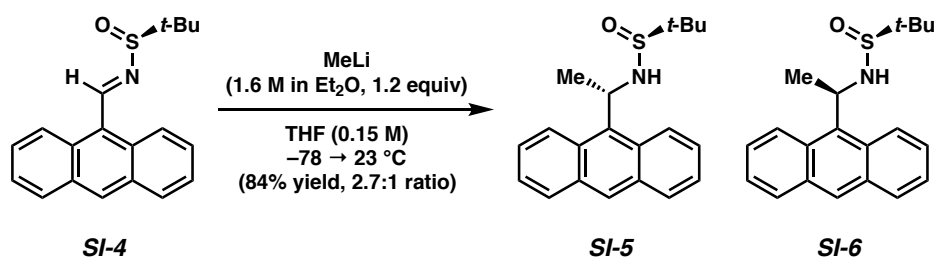
A. Syntheses of Sulfinamides



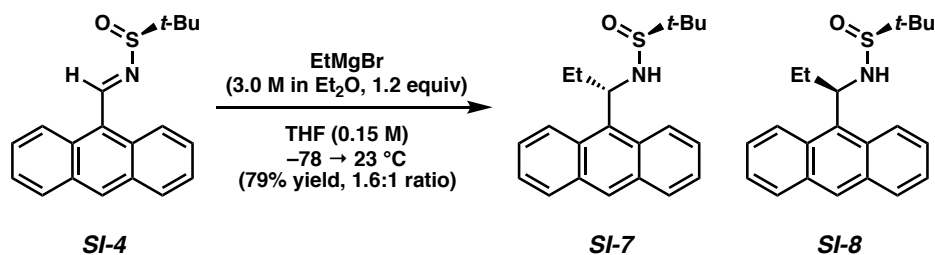
Representative Procedure for Sulfinamide Synthesis (synthesis of sulfonamides SI-2 and SI-3 is used as an example).

To a mixture of known sulfenyl imine **SI-1**⁸ (1.0 g, 3.85 mmol, 1.0 equiv) in THF (25 mL) at -78 $^\circ\text{C}$, was added 1.16 M MeLi in Et_2O (4.0 mL, 4.63 mmol, 1.2 equiv). The resulting mixture was allowed to warm up to 23 $^\circ\text{C}$, then stirred for 16 h. The reaction was diluted with saturated aqueous NH_4Cl (10 mL) and the mixture was poured onto $\text{H}_2\text{O}/\text{EtOAc}$ 1:1 (50 mL). The layers were separated and the aqueous phase was extracted with EtOAc (3 x 50 mL). The combined organic layers were dried over Na_2SO_4 , filtered, and

evaporated under reduced pressure. The resulting crude residue was purified by flash chromatography (SiO_2 ; 9:1 \rightarrow 1:1 hexanes:EtOAc) to yield sulfinamides **SI-2** and **SI-3** (871 mg, 82% yield, 1.2:1 ratio) as off-white solids. **Sulfinamide SI-2**: $[\alpha]_{\text{D}}^{21.3} = + 52.10$ ($c = 0.81$, CHCl_3); R_f 0.38 (1:1 hexanes:EtOAc). The spectral data match those previously reported in the literature.⁹ **Sulfinamide SI-3**: $[\alpha]_{\text{D}}^{21.5} = + 31.70$ ($c = 0.68$, CHCl_3); R_f 0.23 (1:1 hexanes:EtOAc). The spectral data match those previously reported in the literature.⁹



Sulfinamides SI-5 and SI-6. Purification by flash chromatography (SiO_2 ; 9:1 \rightarrow 1:2 hexanes:EtOAc) generated sulfinamides **SI-5** and **SI-6** (84% yield, 2.7:1 ratio) as light yellow foams. **Sulfinamide SI-5**: $[\alpha]_{\text{D}}^{20.2} = + 52.40$ ($c = 0.81$, CHCl_3); R_f 0.45 (1:1 hexanes:EtOAc). The spectral data match those previously reported in the literature.¹⁰ **Sulfinamide SI-6**: $[\alpha]_{\text{D}}^{20} = + 31.70$ ($c = 0.68$, CHCl_3); R_f 0.19 (1:1 hexanes:EtOAc). The spectral data match those previously reported in the literature.¹⁰



Sulfinamides SI-7 and SI-8. Purification by flash chromatography (SiO_2 ; 9:1 \rightarrow 1:1 hexanes:EtOAc) generated sulfinamides **SI-7** and **SI-8** (79% yield, 1.6:1 ratio) as light yellow solids. Crystals suitable for X-ray diffraction studies (CCDC 1817465) were obtained by slow evaporation of MeOH. **Sulfinamide SI-7**: $[\alpha]_{\text{D}}^{21.6} = + 78.75$ ($c = 0.64$, CHCl_3); mp: 130–132 °C; R_f 0.40 (1:1 hexanes:EtOAc); $^1\text{H NMR}$ (500 MHz, CDCl_3): δ 8.76 (br s, 1H), 8.48 (br s, 1H),

8.44 (s, 1H), 8.02 (d, $J = 7.9$, 1H), 7.54–7.49 (m, 4H), 5.95–5.92 (m, 1H), 3.79 (s, 1H), 2.57–2.43 (m, 2H), 1.27 (s, 9H), 0.75 (t, $J = 7.3$, 3H); ^{13}C NMR (125 MHz, CDCl_3): (17 of 19 signals observed) δ 132.7, 132.3, 131.5, 129.9, 129.6, 128.7, 128.1, 126.8, 126.5, 125.7, 125.1, 123.8, 55.8, 54.6, 28.8, 22.9, 11.7; IR (film): 3210, 3051, 2966, 2972, 2872, 1623, 1524, 1448, 1363, 1062, 906, 837, 732, 601 cm^{-1} ; HRMS-APCI (m/z) $[\text{M} + \text{H}]^+$ calcd for $\text{C}_{21}\text{H}_{26}\text{NOS}^+$, 340.1729; found 340.1728. Sulfonamide **SI-8**: $[\alpha]_{\text{D}}^{21.9} = +72.67$ ($c = 0.60$, CHCl_3); mp: 153–156 $^{\circ}\text{C}$; R_f 0.13 (1:1 hexanes:EtOAc); ^1H NMR (500 MHz, CDCl_3): δ 8.80 (br d, $J = 7.8$, 1H), 8.51 (br d, $J = 8.4$, 1H), 8.43 (s, 1H), 8.01 (br s, 2H), 7.54–7.43 (m, 4H), 5.91 (br t, $J = 7.4$, 1H), 3.82 (s, 1H), 2.53–2.44 (m, 1H), 2.31–2.23 (m, 1H), 1.09 (s, 9H), 0.77 (t, $J = 7.6$, 3H); ^{13}C NMR (125 MHz, CDCl_3): (18 of 19 signals observed) δ 132.2, 131.9, 131.5, 131.1, 129.7, 129.4, 128.7, 127.0, 126.8, 125.0, 124.7, 124.6, 123.6, 55.20, 55.16, 30.4, 22.6, 11.7; IR (film): 3200, 3049, 2965, 2927, 2873, 1623, 1454, 1364, 1054, 887, 731 cm^{-1} ; HRMS-APCI (m/z) $[\text{M} + \text{H}]^+$ calcd for $\text{C}_{21}\text{H}_{26}\text{NOS}^+$, 340.1729; found 340.1729.

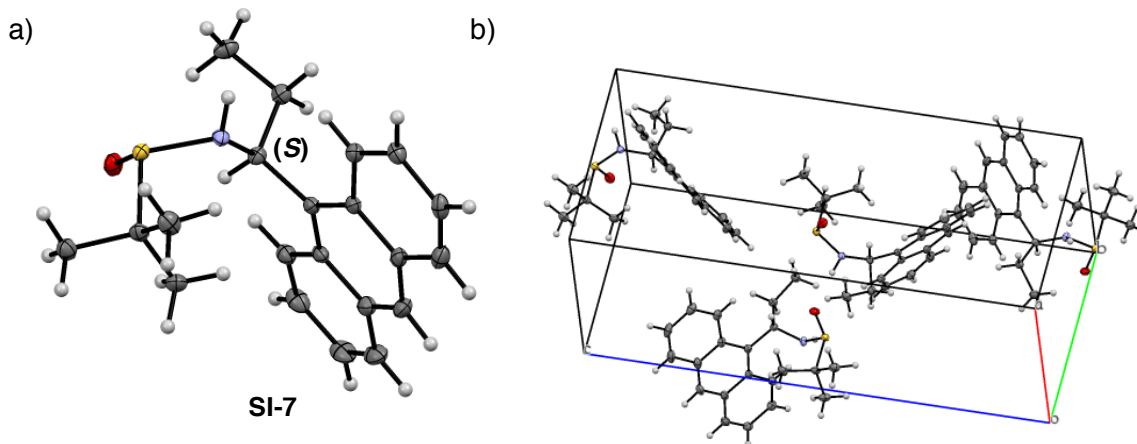
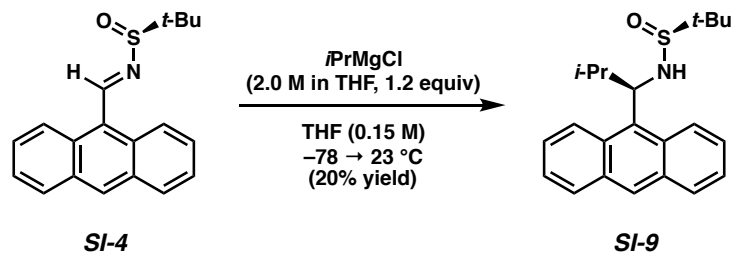
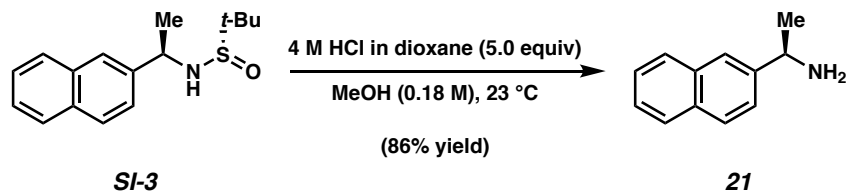


Figure S1. a) ORTEP plot of **SI-7** (CCDC 1817465) at 100 K with ellipsoids shown at 50% probability level. The stereocenter was assigned to be (S). b) Crystal packing of **SI-7**. Color code: C gray, H light gray, O red, N blue, S yellow.



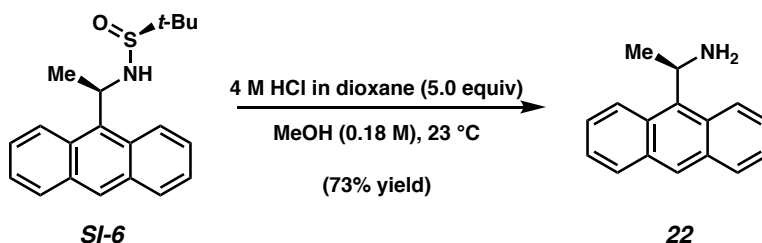
Sulfinamide SI-9. Purification by flash chromatography (SiO_2 ; 9:1 \rightarrow 1:1 hexanes:EtOAc) generated sulfinamide **SI-9** (20% yield) as a light yellow foam. Sulfinamide **SI-9**: $[\alpha]_{\text{D}}^{22.5} = +36.11$ ($c = 0.36$, CHCl_3); R_f 0.39 (1:1 hexanes:EtOAc); $^1\text{H NMR}$ (500 MHz, CDCl_3): δ 8.73 (d, $J = 9.4$, 1H), 8.51 (d, $J = 9.2$, 1H), 8.42 (s, 1H), 8.02–7.02 (m, 2H), 7.55–7.51 (m, 1H), 7.47–7.39 (m, 3H), 5.51 (dd, $J = 10.4$, 2.3, 1H), 4.01 (d, $J = 2.2$, 1H), 2.92–2.85 (m, 1H), 2.37 (d, $J = 6.3$, 3H), 1.06 (s, 9H), 0.46 (d, $J = 6.7$, 3H); $^{13}\text{C NMR}$ (125 MHz, CDCl_3): δ 132.2, 132.1, 131.52, 131.45, 129.7, 129.6, 129.4, 128.6, 127.1, 126.8, 125.0, 124.7, 124.6, 123.9, 60.2, 55.2, 33.9, 22.6, 21.2, 20.7; IR (film): 3246, 3051, 2859, 1455, 1390, 1055, 731 cm^{-1} ; HRMS-APCI (m/z) $[\text{M} + \text{H}]^+$ calcd for $\text{C}_{22}\text{H}_{28}\text{NOS}^+$, 354.1886; found 354.1871.

B. Syntheses of Amines

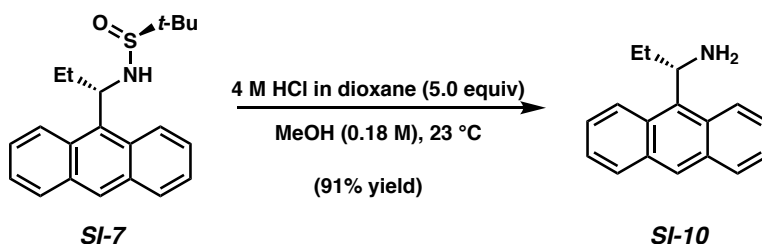


Representative Procedure for Amine Synthesis (synthesis of amine 21 is used as an example). To a mixture of sulfinamide **SI-3** (250 mg, 0.91 mmol, 1.0 equiv) in MeOH (5 mL), at 23 $^\circ\text{C}$, was added 4 M HCl in 1,4-dioxane (1.1 mL, 4.54 mmol, 5.0 equiv). The resulting mixture was stirred for 20 min at 23 $^\circ\text{C}$, before being diluted with a 1 M NaOH solution (5 mL) and CH_2Cl_2 (50 mL). The layers were separated and the aqueous layer was extracted with CH_2Cl_2 (3 x 50 mL). The combined organic layers were dried over Na_2SO_4 , filtered, and evaporated under reduced pressure. Purification by flash chromatography (SiO_2 ; 1:1 hexanes:EtOAc, 1% Et_3N) afforded amine **21** (133 mg, 86% yield) as a light yellow oil. Amine **21**. $[\alpha]_{\text{D}}^{20.9} = +24.53$ ($c =$

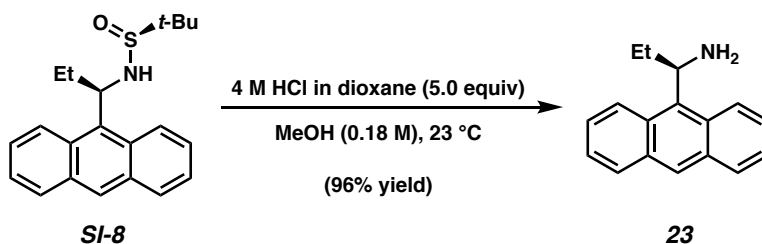
0.38, CHCl_3); R_f 0.03 (1:1 hexanes:EtOAc). The spectral data match those previously reported in the literature.¹¹



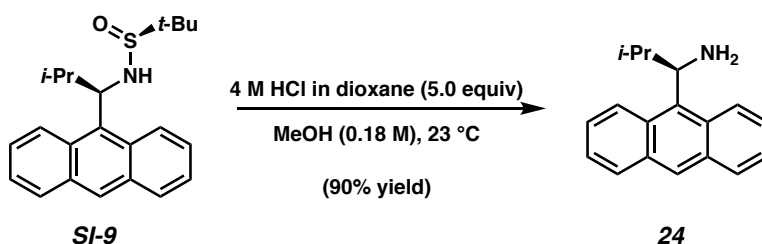
Amine 22. Purification by flash chromatography (SiO_2 ; 1:1 hexanes:EtOAc, 1% Et_3N) generated amine **22** (73% yield) as a light yellow solid. Amine **22**: $[\alpha]_D^{20} = +4.74$ ($c = 0.38$, CHCl_3); R_f 0.05 (1:1 hexanes:EtOAc). The spectral data match those previously reported in the literature.¹²



Amine SI-10. Purification by flash chromatography (SiO_2 ; 1:1 hexanes:EtOAc, 1% Et_3N) generated amine **SI-10** (91% yield) as a yellow solid. Amine **SI-10**: $[\alpha]_D^{26.5} = -380.00$ ($c = 0.10$, CHCl_3); mp: 74–76 °C; R_f 0.27 (1:1 hexanes:EtOAc, 1% Et_3N); $^1\text{H NMR}$ (500 MHz, CDCl_3): δ 9.01–8.37 (m, 3H), 8.00 (d, $J = 7.8$, 2H), 7.49–7.43 (m, 4H), 5.49 (t, $J = 7.5$, 1H), 2.34–2.25 (m, 2H), 1.93 (s, 2H), 0.94 (t, $J = 7.5$, 3H); $^{13}\text{C NMR}$ (125 MHz, CDCl_3): (10 of 17 signals observed) δ 137.0, 132.0, 129.8, 129.5, 127.5, 125.2, 124.8, 52.9, 31.4, 12.3; IR (film): 3371, 3047, 2953, 2931, 2861, 1623, 1448, 1158, 1019, 886, 848, 731, 635, 545 cm^{-1} ; HRMS-APCI (m/z) [$\text{M} - \text{NH}_2$] $^+$ calcd for $\text{C}_{17}\text{H}_{15}^+$, 219.1168; found 219.1168.

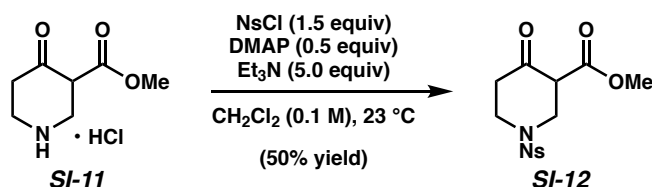


Amine 23. Purification by flash chromatography (SiO_2 ; 1:1 hexanes:EtOAc, 1% Et_3N) generated amine **23** (96% yield) as a yellow solid. Amine **23**: $[\alpha]_{\text{D}}^{25.2} = +360.00$ ($c = 0.10$, CHCl_3). NMR, mass, and IR spectral data match those of amine **SI-10**.



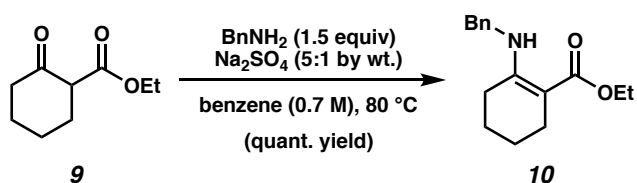
Amine 24. Purification by flash chromatography (SiO_2 ; 1:1 hexanes:EtOAc, 1% Et_3N) generated amine **24** (90% yield) as a yellow oil. Amine **24**: $[\alpha]_{\text{D}}^{21.7} = +80.00$ ($c = 0.10$, CHCl_3); R_f 0.15 (1:1 hexanes:EtOAc); ^1H NMR (500 MHz, CDCl_3): δ 9.08 (br s, 1H), 8.40–8.37 (m, 2H), 8.00 (d, $J = 9.6$, 2H), 7.47–7.43 (m, 4H), 5.11 (d, $J = 10.3$, 1H), 2.83–2.79 (m, 1H), 1.76 (br s, 2H), 1.36 (d, $J = 6.5$, 3H), 0.52 (d, $J = 6.3$, 3H); ^{13}C NMR (125 MHz, CDCl_3): (12 of 18 signals observed) δ 137.2, 129.5, 127.7, 127.5, 125.9, 124.9, 124.6, 124.0, 57.9, 35.0, 21.4, 21.0; IR (film): 3049, 2958, 2868, 1673, 1284, 885, 731 cm^{-1} ; HRMS-APCI (m/z) $[\text{M} + \text{H}]^+$ calcd for $\text{C}_{18}\text{H}_{20}\text{N}^+$, 250.1590; found 250.1587.

C. Synthesis of Ketoester SI-12



Ketoester SI-12. To ketoester hydrochloride salt **SI-11** (1.0 g, 5.16 mmol, 1.0 equiv) was added CH_2Cl_2 (51.0 mL), 2-nitrobenzenesulfonyl chloride (1.70 g, 7.75 mmol, 1.5 equiv), DMAP (315 mg, 2.58 mmol, 0.5 equiv), and triethylamine (3.6 mL, 25.8 mmol, 5.0 equiv), sequentially. The resultant mixture was stirred at 23 °C for 12 h. The reaction was then concentrated under reduced pressure and the crude residue was purified by flash chromatography (SiO_2 ; 9:1 \rightarrow 1:1 hexanes:EtOAc) to afford ketoester **SI-12** (946 mg, 50% yield) as a yellow foam. Ketoester **SI-12**: R_f 0.20 (7:3 hexanes:EtOAc); ^1H NMR (500 MHz, CDCl_3): δ 11.97 (s, 1H), 8.07–8.04 (m, 1H), 7.74–7.70 (m, 2H), 7.67–7.64 (m, 1H), 4.01 (t, $J = 1.5$, 2H), 3.79 (s, 3H), 3.56 (t, $J = 6.0$, 2H), 2.50 (tt, $J = 5.9$, 1.5, 2H); ^{13}C NMR (125 MHz, CDCl_3): δ 170.6, 169.7, 148.3, 134.0, 132.3, 131.9, 131.1, 124.5, 95.3, 51.9, 42.2, 42.1, 29.1; IR (film): 2955, 2920, 2863, 1669, 1542 cm^{-1} ; HRMS-APCI (m/z) $[\text{M} + \text{H}]^+$ calcd for $\text{C}_{13}\text{H}_{15}\text{N}_2\text{O}_7\text{S}^+$, 343.0595; found 343.0607.

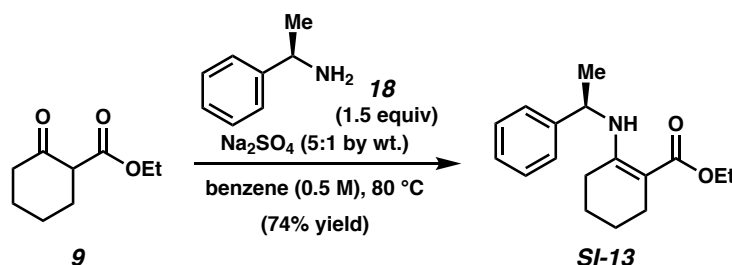
D. Syntheses of Enamine Substrates



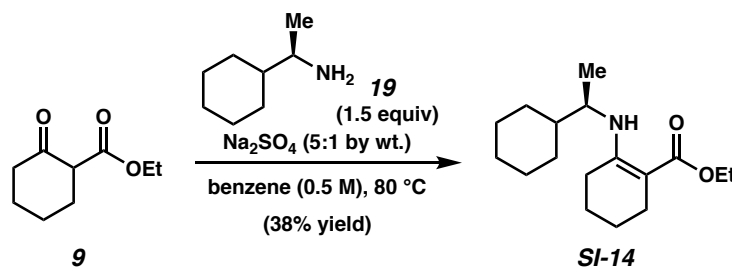
Representative Procedure for Amine Condensation Reaction (synthesis of enamine 10 is used as an example). To ketoester **9** (1.0 g, 5.8 mmol, 1.0 equiv) was added benzene (8.0 mL), benzylamine (0.96 mL, 8.8 mmol, 1.5 equiv), and Na_2SO_4 (5.0 g, 5:1 by weight), sequentially. The resulting mixture was stirred at 80 °C for 12 h. After cooling to 23 °C, the reaction mixture was filtered by passage through a plug of Na_2SO_4 (10 mL of benzene eluent). Evaporation under reduced pressure yielded the crude residue, which was purified via flash chromatography (neutral alumina; 20:1 hexanes:EtOAc) to afford enamine **10** (1.5 g, quant. yield).

Enamine 10. Purification by flash chromatography (neutral alumina; 20:1 hexanes:EtOAc) generated enamine **10** (quant. yield) as a clear oil. Enamine **10**: R_f 0.62 (5:1 hexanes:EtOAc). The spectral data match those previously reported in the literature.¹³

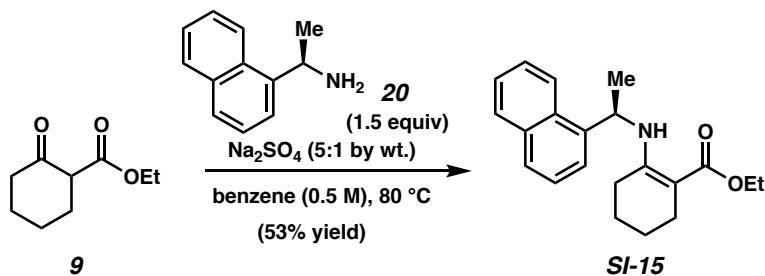
Note: Enamine compounds were not stable to silica. R_f values are representative of the corresponding enamine products, however, degradation to ketoester and amine starting materials were observed.



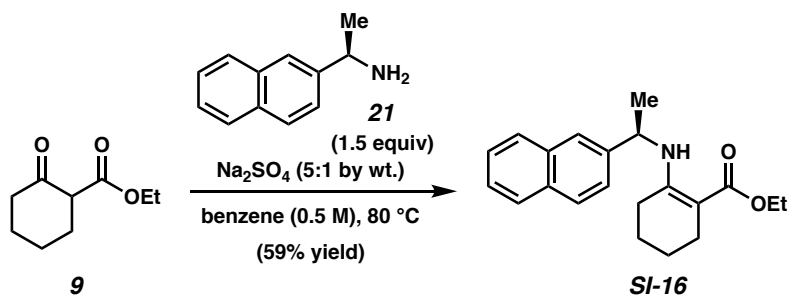
Enamine SI-13. Purification by flash chromatography (neutral alumina; benzene) generated enamine **SI-13** (74% yield) as a colorless oil. Enamine **SI-13**: $[\alpha]_D^{22.1} = -474.50$ ($c = 0.40$, CHCl₃); R_f 0.56 (benzene). Spectral data matched those previously reported in the literature.¹⁴



Enamine SI-14. Purification by flash chromatography (neutral alumina; benzene) generated enamine **SI-14** (38% yield) as a colorless oil. Enamine **SI-14**: $[\alpha]_D^{21.8} = -81.62$ ($c = 0.55$, CHCl₃); R_f 0.50 (benzene); ¹H NMR (500 MHz, CDCl₃): δ 9.04 (d, $J = 9.62$, 1H), 4.14–4.08 (m, 2H), 3.36–3.32 (m, 1H), 2.28 (q, $J = 6.8$, 4H), 1.80–1.52 (m, 9H), 1.34–1.12 (m, 7H), 1.09 (d, $J = 6.43$, 3H), 1.05–0.92 (m, 2H); ¹³C NMR (125 MHz, CDCl₃): (16 of 17 signals observed) δ 171.1, 159.2, 88.6, 58.6, 52.1, 44.5, 29.3, 26.60, 26.58, 26.50, 26.46, 24.1, 23.0, 22.6, 19.6, 14.9; IR (film): 2925, 2852, 1644, 1593, 1448, 1225, 1162, 1083, 1060, 1128, 775 cm⁻¹; HRMS-APCI (m/z) $[M + H]^+$ calcd for C₁₇H₃₀NO₂⁺, 280.2271; found 280.2274.

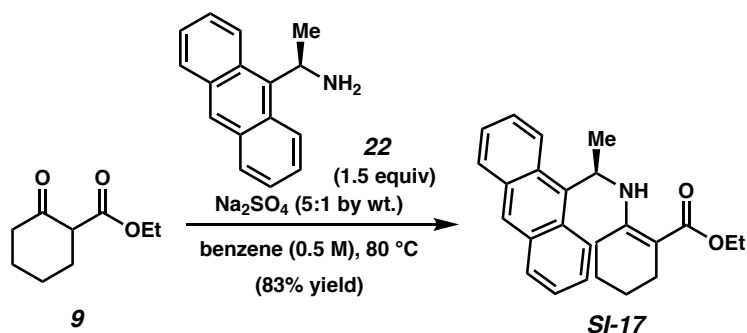


Enamine SI-15. Purification by flash chromatography (neutral alumina; benzene) generated enamine **SI-15** (53% yield) as a light yellow oil. Enamine **SI-15**: $[\alpha]_D^{23.1} = -383.20$ ($c = 0.87$, CHCl_3); R_f 0.50 (benzene); $^1\text{H NMR}$ (500 MHz, CDCl_3): δ 9.55 (d, $J = 7.2$, 1H), 8.04 (d, $J = 8.4$, 1H), 7.89 (d, $J = 8.1$, 1H), 7.75–7.72 (m, 1H), 7.56–7.44 (m, 4H), 5.47–5.41 (m, 1H), 4.24–4.17 (m, 2H), 2.35–2.26 (m, 3H), 1.84–1.78 (m, 1H), 1.61 (d, $J = 6.8$, 3H), 1.50–1.34 (m, 4H), 1.32 (t, $J = 7.1$, 3H); $^{13}\text{C NMR}$ (125 MHz, CDCl_3): δ 171.2, 159.3, 141.5, 133.9, 129.9, 129.1, 127.3, 126.2, 126.1, 125.5, 122.4, 122.2, 91.0, 58.8, 48.1, 26.4, 24.2, 23.9, 22.6, 22.1, 14.7; IR (film): 2975, 2931, 2855, 1644, 1593, 1445, 1238, 1225, 1053, 775 cm^{-1} ; HRMS-APCI (m/z) $[\text{M} + \text{H}]^+$ calcd for $\text{C}_{21}\text{H}_{26}\text{NO}_2^+$, 324.1958; found 324.1948.

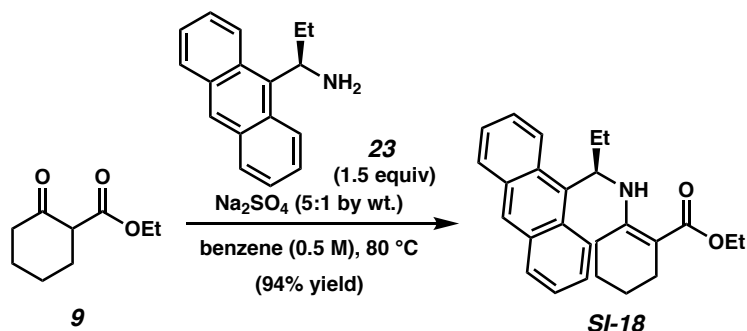


Enamine SI-16. Purification by flash chromatography (neutral alumina; benzene) generated enamine **SI-16** (59% yield) as a white solid. Enamine **SI-16**: $[\alpha]_D^{26.5} = -581.00$ ($c = 0.29$, CHCl_3); R_f 0.56 (benzene); mp: 66–69 $^\circ\text{C}$; $^1\text{H NMR}$ (500 MHz, CDCl_3): δ 9.48 (d, $J = 7.3$, 1H), 7.81 (br d, $J = 9.3$, 3H), 7.67 (s, 1H), 7.49–7.43 (m, 2H), 7.39 (dd, $J = 8.6$, 1.7, 1H), 4.81–4.76 (m, 1H), 4.23–4.16 (m, 2H), 2.35 (dt, $J = 17.2$, 5.7, 1H), 2.26 (t, $J = 5.9$, 2H), 1.97 (dt, $J = 18.1$, 6.2, 1H), 1.55 (br s, 3H), 1.53–1.46 (m, 2H), 1.46–1.36 (m, 2H), 1.32 (t, $J = 7.1$, 3H); $^{13}\text{C NMR}$

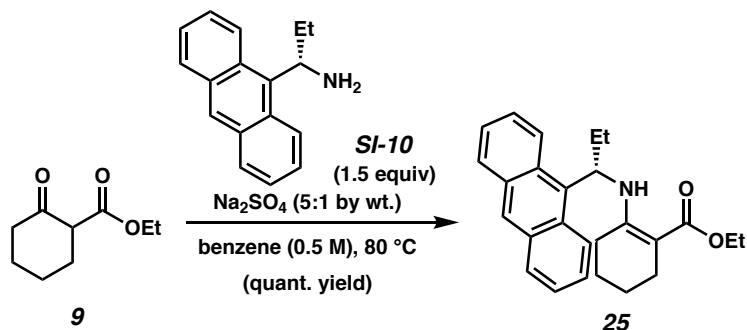
(125 MHz, CDCl₃): δ 171.2, 159.3, 143.6, 133.6, 132.7, 128.7, 128.0, 127.8, 126.3, 125.8, 124.2, 123.9, 90.8, 58.9, 52.4, 26.9, 25.4, 24.0, 22.7, 22.3, 14.9; IR (film): 2979, 2930, 2850, 1644, 1595, 1508, 1233, 1172, 1058, 818, 747, 478 cm⁻¹; HRMS-APCI (m/z) [M + H]⁺ calcd for C₂₁H₂₆NO₂⁺, 324.1958; found 324.1952.



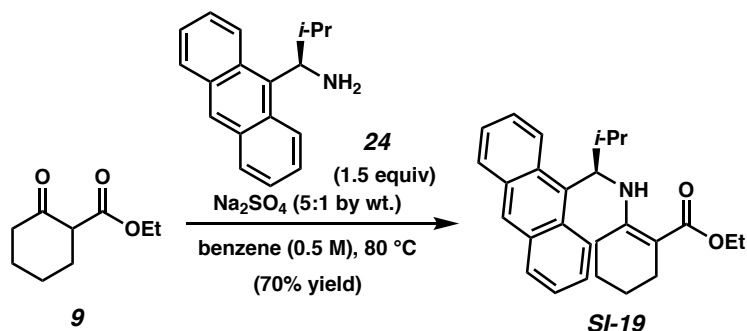
Enamine SI-17. Purification by flash chromatography (neutral alumina; benzene) generated enamine **SI-17** (83% yield) as a light yellow oil. Enamine **SI-17**: $[\alpha]_D^{25.2} = -595.00$ ($c = 0.42$, CHCl₃); R_f 0.63 (benzene); ¹H NMR (500 MHz, CDCl₃): δ 10.09 (d, $J = 5.46$, 1H), 8.54 (br s, 2H), 8.39 (s, 1H), 8.01 (d, $J = 8.4$, 2H), 7.52–7.43 (m, 4H), 6.16–6.10 (m, 1H), 4.19 (dd, $J = 14.6, 7.1$, 2H), 2.27 (dt, $J = 5.6, 17.3$, 1H), 2.22–2.08 (m, 2H), 1.95 (d, $J = 7.2$, 3H), 1.48–1.32 (m, 3H), 1.31 (t, $J = 7.11$, 3H), 1.23–1.14 (m, 2H); ¹³C NMR (125 MHz, CDCl₃): (21 of 25 signals observed) δ 171.4, 159.5, 135.3, 134.3, 131.9, 129.8, 128.7, 128.5, 128.0, 127.4, 126.1, 124.9, 89.8, 58.9, 48.2, 26.9, 23.8, 23.1, 22.5, 22.2, 14.9; IR (film): 2976, 2931, 2856, 1640, 1593, 1448, 1238, 1226, 1166, 1058, 885, 731 cm⁻¹; HRMS-APCI (m/z) [M + H]⁺ calcd for C₂₅H₂₈NO₂⁺, 374.2115; found 374.2120.



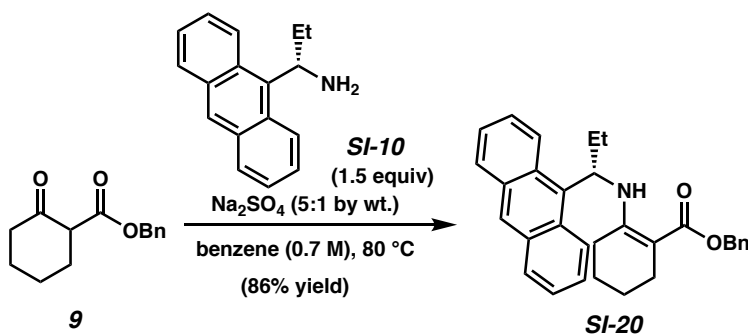
Enamine SI-18. Purification by flash chromatography (neutral alumina; benzene) generated enamine **SI-18** (94% yield) as a light yellow oil. Enamine **SI-18**: $[\alpha]_{\text{D}}^{23.8} = -408.00$ ($c = 0.20$, CHCl_3); R_f 0.62 (5:1 hexanes:EtOAc); ^1H NMR (500 MHz, CDCl_3): δ 10.16 (d, $J = 5.3$, 1H), 8.76 (s, 1H), 8.46–8.27 (m, 2H), 8.01 (d, $J = 7.0$, 2H), 7.61–7.40 (m, 4H), 5.89 (q, $J = 7.0$, 1H), 4.20 (q, $J = 7.0$, 2H), 2.47 (sept, $J = 7.4$, 1H), 2.38–2.24 (m, 2H), 2.23–2.10 (m, 2H), 1.53–1.28 (m, 6H), 1.25–1.15 (m, 2H), 1.08 (t, $J = 7.21$, 3H); ^{13}C NMR (125 MHz, CDCl_3): (21 of 26 signals observed) δ 171.2, 159.3, 141.6, 134.0, 130.1, 129.3, 127.4, 126.3, 126.2, 125.7, 122.5, 122.3, 91.1, 58.9, 48.2, 26.6, 24.4, 24.0, 22.7, 22.3, 14.9; IR (film): 2931, 1638, 1591, 1444, 1223 cm^{-1} ; HRMS-APCI (m/z) $[\text{M} + \text{H}]^+$ calcd for $\text{C}_{26}\text{H}_{30}\text{NO}_2^+$, 388.2271; found 388.2275.



Enamine 25. Purification by flash chromatography (neutral alumina; benzene) generated enamine **25** (quant. yield) as a yellow foam. Enamine **25**: $[\alpha]_{\text{D}}^{24.3} = +524.00$ ($c = 0.10$, CH_2Cl_2). NMR, mass, and IR spectral data match those of enamine **SI-18**.

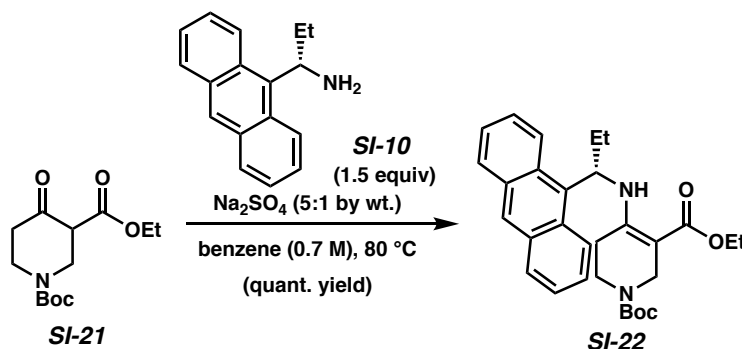


Enamine SI-19. Purification by flash chromatography (neutral alumina; benzene) generated enamine **SI-19** (70% yield) as a light yellow oil. Enamine **SI-19**: $[\alpha]_{\text{D}}^{24.9} = -582.00$ ($c = 0.62$, CHCl_3); R_f 0.67 (benzene); $^1\text{H NMR}$ (500 MHz, CDCl_3): δ 10.31 (d, $J = 6.6$, 1H), 8.70 (d, $J = 8.9$, 1H), 8.39 (s, 1H), 8.36 (d, $J = 9.1$, 1H), 8.01 (d, $J = 8.6$, 1H), 7.99 (d, $J = 8.9$, 1H), 7.55–7.42 (m, 4H), 5.63–5.59 (m, 1H), 4.18 (q, $J = 7.1$, 2H), 2.86–2.79 (m, 1H), 2.40–2.37 (m, 1H), 2.22–2.09 (m, 2H), 1.57–1.52 (m, 1H), 1.42–1.37 (m, 5H), 1.30 (t, $J = 7.1$, 3H), 1.26–1.19 (m, 2H), 0.66 (d, $J = 6.8$, 3H); $^{13}\text{C NMR}$ (125 MHz, CDCl_3): δ 171.38, 159.94, 134.37, 132.37, 131.31, 130.25, 129.93, 129.63, 129.36, 128.12, 126.37, 126.04, 125.58, 124.98, 124.60, 123.28, 89.40, 58.90, 58.82, 35.20, 27.15, 23.89, 22.55, 22.34, 21.62, 20.76, 14.86; IR (film): 2933, 1640, 1595, 1444, 1235, 1154, 1085, 1051, 731 cm^{-1} ; HRMS-APCI (m/z) $[\text{M} + \text{H}]^+$ calcd for $\text{C}_{27}\text{H}_{32}\text{NO}_2^+$, 402.2428; found 402.2434.

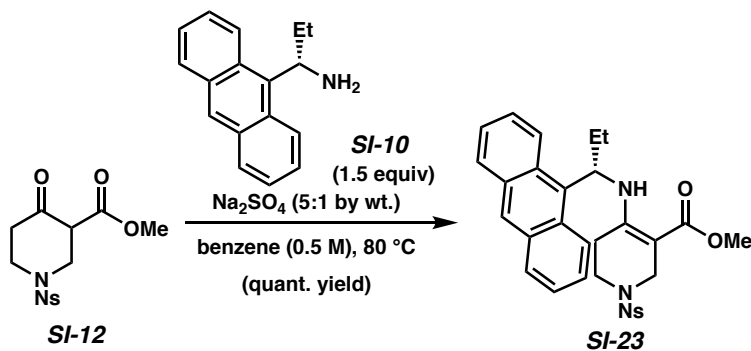


Enamine SI-20. Purification by flash chromatography (neutral alumina; 20:1 hexanes:EtOAc) generated enamine **SI-20** (86% yield) as a yellow oil. Enamine **SI-20**: $[\alpha]_{\text{D}}^{24.2} = +5520.00$ ($c = 0.10$, CHCl_3); R_f 0.59 (5:1 hexanes:EtOAc); $^1\text{H NMR}$ (500 MHz, CDCl_3): δ 10.17 (br d, $J = 5.6$, 1H), 8.78 (br s, 1H), 8.40 (br s, 1H), 8.38–8.29 (m, 1H), 8.07–7.96 (m, 2H), 7.60–7.33 (m, 8H),

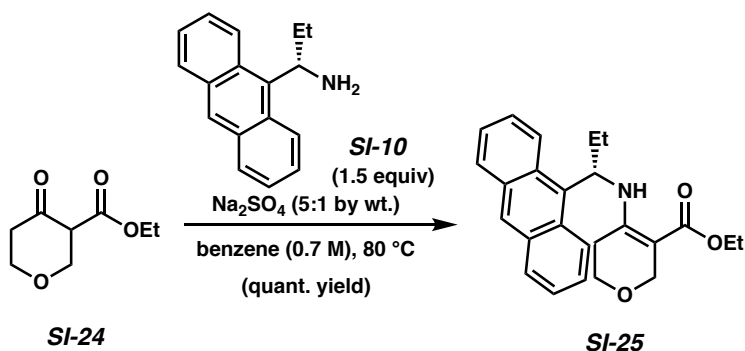
7.33–7.28 (m, 1H), 5.95–5.86 (m, 1H), 5.28–5.19 (m, 2H), 2.54–2.41 (m, 1H), 2.39–2.16 (m, 4H), 1.54–1.33 (m, 3H), 1.29–1.16 (m, 2H), 1.08 (t, $J = 7.4$, 3H); ^{13}C NMR (125 MHz, CDCl_3): (26 of 31 signals observed); δ 170.9, 160.4, 137.8, 134.4, 129.9, 129.7, 129.3, 128.54, 128.52, 128.1, 128.0, 127.6, 127.5, 126.6, 125.7, 124.9, 122.6, 89.5, 64.6, 54.4, 30.5, 27.1, 23.8, 22.5, 22.2, 12.2; IR (film): 2932, 1641, 1592, 1224, 1165 cm^{-1} ; HRMS-APCI (m/z) $[\text{M} + \text{H}]^+$ calcd for $\text{C}_{31}\text{H}_{32}\text{NO}_2^+$, 450.2428; found 450.2395.



Enamine SI-22. Purification by flash chromatography (neutral alumina; 20:1 hexanes:EtOAc) generated enamine **SI-22** (quant. yield) as a yellow oil. Enamine **SI-22**: $[\alpha]_{\text{D}}^{23.1} = +2260.00$ ($c = 0.10$, CH_2Cl_2); R_f 0.20 (5:1 hexanes:EtOAc); ^1H NMR (500 MHz, CDCl_3): δ 10.01 (d, $J = 5.4$, 1H), 8.67 (br s, 1H), 8.41 (s, 1H), 8.32–8.30 (m, 1H), 8.02 (s, 2H), 7.47 (br s, 4H), 5.85 (q, $J = 6.8$, 1H), 4.20 (q, $J = 7.1$, 2H), 4.08–3.97 (m, 1H), 3.93–3.83 (m, 1H), 3.28–3.17 (m, 1H), 3.02 (s, 1H), 2.47 (sept, $J = 6.9$, 1H), 2.41–2.23 (m, 2H), 1.51–1.41 (m, 1H), 1.41–1.27 (m, 12H), 1.08 (t, $J = 7.5$, 3H); ^{13}C NMR (125 MHz, CD_3OD): (19 of 28 signals observed) δ 170.6, 159.8, 156.2, 135.4, 134.6, 130.8, 129.4, 128.1, 125.9, 88.3, 81.2, 60.2, 55.4, 55.3, 31.14, 31.09, 28.5, 14.9, 11.9; IR (film): 2974, 1241, 1164, 730 cm^{-1} ; HRMS-APCI (m/z) $[\text{M} + \text{H}]^+$ calcd for $\text{C}_{30}\text{H}_{37}\text{N}_2\text{O}_4^+$, 489.2748; found 489.2730.

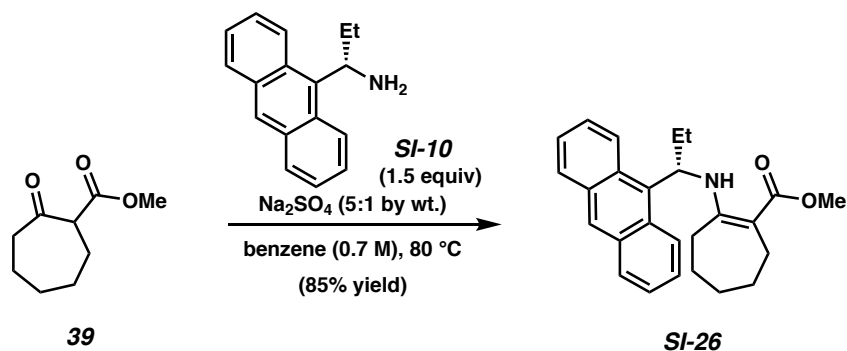


Enamine SI-23. Purification by flash chromatography (neutral alumina; benzene) over neutral alumina afforded enamine **SI-23** (quant. yield) as a yellow foam. Enamine **SI-23**: $[\alpha]_{\text{D}}^{26.7} = +234.70$ ($c = 0.10$, CH_2Cl_2); R_f 0.30 (7:3 hexanes:EtOAc); $^1\text{H NMR}$ (500 MHz, CDCl_3): δ 10.02 (d, $J = 5.7$, 1H), 8.57 (s, 1H), 8.41 (s, 1H), 8.27 (s, 1H), 8.02 (d, $J = 7.8$, 2H), 7.81 (dd, $J = 7.9$, 1.3, 1H), 7.57–7.39 (m, 7H), 5.81 (q, $J = 6.6$, 1H), 3.98 (d, $J = 14.7$, 1H), 3.84 (d, $J = 14.5$, 1H), 3.74 (s, 3H), 3.32–3.22 (m, 1H), 3.02–2.94 (m, 1H), 2.57–2.39 (m, 2H), 2.28 (sep, $J = 7.5$, 1H), 1.68 (dt, $J = 17.4$, 6.0, 1H), 1.05 (t, $J = 7.5$, 3H); $^{13}\text{C NMR}$ (125 MHz, CDCl_3): (24 of 30 signals observed) δ 169.2, 157.2, 148.2, 133.5, 133.1, 131.8, 131.4, 130.8, 130.0, 128.6, 127.1, 125.9, 125.3, 125.0, 124.0, 122.1, 86.1, 54.5, 50.8, 43.3, 42.0, 30.2, 26.7, 12.1; IR (film): 2965, 2923, 2853, 1654, 1248 cm^{-1} ; HRMS-APCI (m/z) $[\text{M} + \text{H}]^+$ calcd for $\text{C}_{30}\text{H}_{30}\text{N}_3\text{O}_6\text{S}^+$, 560.1850; found 560.1862.

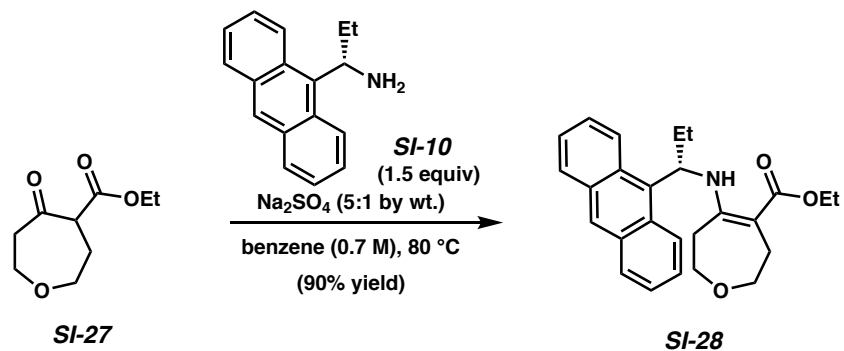


Enamine SI-25. Purification by flash chromatography (neutral alumina; benzene) generated enamine **SI-25** (quant. yield) as a yellow foam. Enamine **SI-25**: $[\alpha]_{\text{D}}^{29.1} = +640.00$ ($c = 0.10$, CH_2Cl_2); R_f 0.49 (5:1 hexanes:EtOAc); $^1\text{H NMR}$ (500 MHz, CDCl_3): δ 9.86 (d, $J = 5.0$, 1H), 8.67 (br s, 1H), 8.41 (s, 1H), 8.40–8.22 (m, 1H), 8.02 (d, $J = 8.0$, 2H), 7.64–7.39 (m, 4H), 5.87

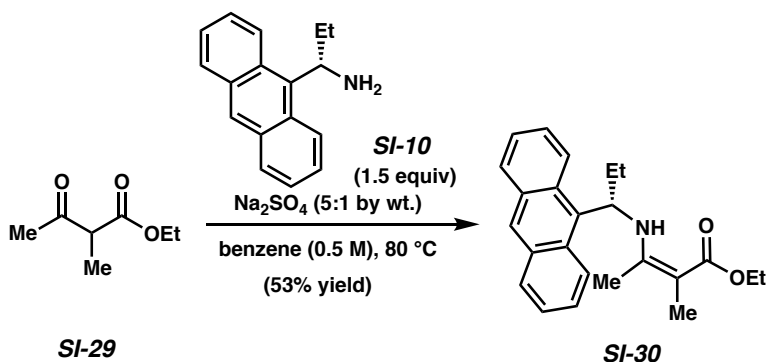
(q, $J = 6.5$, 1H), 4.27–4.11 (m, 4H), 3.57–3.46 (m, 1H), 3.38–3.29 (m, 1H), 2.56–2.44 (m, 1H), 2.39–2.24 (m, 2H), 1.56–1.49 (m, 1H), 1.28 (t, $J = 7.1$, 3H), 1.09 (t, $J = 7.3$, 3H); ^{13}C NMR (125 MHz, CDCl_3): (19 of 25 signals observed) δ 168.8, 156.6, 133.6, 129.8, 128.3, 127.3, 126.7, 125.7, 124.8, 122.2, 88.6, 64.6, 63.5, 58.8, 54.2, 30.2, 26.4, 14.6, 12.0; IR (film): 2927, 1729, 1676, 1285 cm^{-1} ; HRMS-APCI (m/z) $[\text{M} + \text{H}]^+$ calcd for $\text{C}_{25}\text{H}_{28}\text{NO}_3^+$, 390.2064; found 390.2037.



Enamine SI-26. Purification by flash chromatography (neutral alumina; 10:1 \rightarrow 5:1 hexanes:EtOAc) generated enamine **SI-26** (85% yield) as a yellow foam. Enamine **SI-26**: $[\alpha]_{\text{D}}^{30.4} = +4540.00$ ($c = 0.10$, CH_2Cl_2); R_f 0.61 (5:1 hexanes:EtOAc); ^1H NMR (300 MHz, CDCl_3): δ 10.39 (d, $J = 4.9$, 1H), 8.71 (br s, 1H), 8.48–8.24 (m, 2H), 8.07–7.92 (m, 2H), 7.64–7.39 (m, 4H), 5.99–5.87 (m, 1H), 3.75 (s, 3H), 2.65–2.46 (m, 1H), 2.46–2.00 (m, 5H), 1.44–1.19 (m, 3H), 1.17–1.07 (m, 4H), 0.81–0.65 (m, 1H), 0.32–0.13 (m, 1H); ^{13}C NMR (125 MHz, CDCl_3): (20 of 26 signals observed) δ 171.5, 167.6, 134.9, 129.3, 128.2, 127.9, 127.7, 125.7, 124.8, 122.4, 94.3, 55.3, 50.6, 31.4, 30.2, 30.0, 28.4, 25.8, 24.0, 12.2; IR (film): 2923, 1634, 1592, 1252, 1209 cm^{-1} ; HRMS-APCI (m/z) $[\text{M} + \text{H}]^+$ calcd for $\text{C}_{26}\text{H}_{30}\text{NO}_2^+$, 388.22711; found 388.2233.



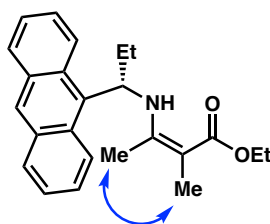
Enamine SI-28. Purification by flash chromatography (neutral alumina; 20:1 hexanes:EtOAc) generated enamine **SI-28** (90% yield) as a yellow oil. Enamine **SI-28**: $[\alpha]_{\text{D}}^{25.8} = +358.00$ ($c = 0.10$, CH_2Cl_2); R_f 0.93 (1:1 hexanes:EtOAc); $^1\text{H NMR}$ (500 MHz, CDCl_3): δ 10.35 (br d, $J = 4.6$, 1H), 8.65 (br s, 1H), 8.45–8.18 (m, 2H), 8.00 (br s, 2H), 7.65–7.39 (m, 4H), 5.93–5.84 (m, 1H), 4.20 (q, $J = 7.1$, 2H), 3.55–3.46 (m, 1H), 3.06–2.97 (m, 1H), 2.82–2.73 (m, 1H), 2.64–2.29 (m, 5H), 2.19–2.11 (m, 1H), 2.10–2.01 (m, 1H), 1.31 (t, $J = 7.1$, 3H), 1.14 (t, $J = 7.3$, 3H); $^{13}\text{C NMR}$ (125 MHz, CDCl_3): (20 of 26 signals observed) δ 170.9, 166.1, 134.4, 134.3, 128.5, 128.2, 128.0, 127.8, 127.4, 124.9, 94.4, 71.5, 65.5, 59.2, 55.6, 34.3, 30.1, 29.3, 14.8, 12.2; IR (film): 2971, 1634, 1591, 1249, 1114 cm^{-1} ; HRMS-APCI (m/z) $[\text{M} + \text{H}]^+$ calcd for $\text{C}_{26}\text{H}_{30}\text{NO}_3^+$, 404.2220; found 404.2209.



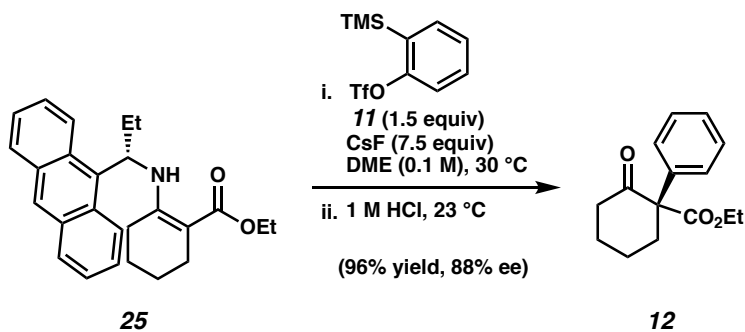
Enamine SI-30. Purification by flash chromatography (neutral alumina; benzene) afforded enamine **SI-30** (53% yield) as an orange oil. Enamine **SI-30**: $[\alpha]_{\text{D}}^{25.3} = +956.00$ ($c = 0.1$, CHCl_3); R_f 0.72 (benzene); $^1\text{H NMR}$ (500 MHz, CDCl_3): δ 10.42 (d, $J = 6.2$, 1H), 8.72 (br s, 1H), 8.39–8.35 (m, 2H), 8.00 (d, $J = 7.6$, 2H), 7.45 (m, 4H), 5.89 (q, $J = 8.3$, 1H), 4.19 (q, $J =$

7.5, 2H), 2.52–2.45 (m, 1H), 2.31–2.24 (m, 1H), 1.61 (s, 3H), 1.53 (s, 3H), 1.31 (t, $J = 7.3$, 3H), 1.09 (t, $J = 7.6$, 3H); ^{13}C NMR (125 MHz, CDCl_3): (23 of 24 signals observed) δ 171.6, 159.7, 134.5, 134.3, 133.7, 132.5, 131.4, 129.8, 129.4, 128.1, 127.4, 126.6, 125.8, 124.9, 122.6, 87.0, 58.9, 55.5, 30.4, 16.4, 14.8, 12.6, 12.2; IR (film): 3051, 2971, 2930, 2873, 1637, 1594, 1247, 1164, 1125, 1082, 731 cm^{-1} ; HRMS-APCI (m/z) $[\text{M} + \text{H}]^+$ calcd for $\text{C}_{24}\text{H}_{28}\text{NO}_2^+$, 362.2115; found 362.2114.

The configuration of **SI-30** was verified by 2D-NOESY (500 MHz, C_6D_6), as the following correlations were observed:



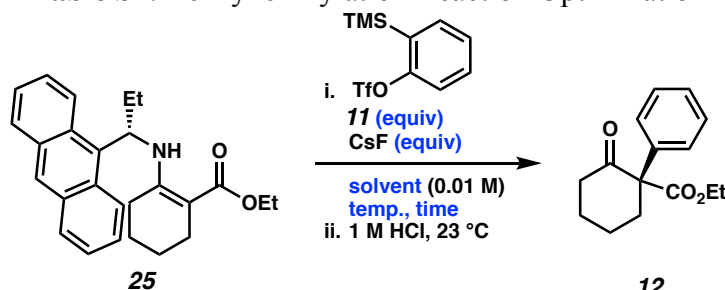
E. Benzyne Arylation Reaction Optimization



Representative Procedure for Benzyne Arylation Reaction (Entry 6, Table S1, is used as an example). To enamine **25** (32.0 mg, 0.08 mmol, 1.0 equiv), was added DME (0.8 mL), benzyne precursor **11** (37.0 mg, 0.12 mmol, 1.5 equiv), and CsF (94.0 mg, 0.62 mmol, 7.5 equiv), sequentially. This mixture was stirred vigorously (1000 rpm) at 30 °C for 6 h. After cooling to 23 °C, aqueous 1 M HCl (1.0 mL) was added and this mixture was stirred vigorously (1000 rpm) for 30 min. Subsequently, the layers were separated and the aqueous layer was extracted with EtOAc (3 x 5 mL). The organic layers were combined, dried over Na_2SO_4 , and removed under reduced

pressure. The crude residue was purified by flash chromatography (SiO₂; benzene eluent) to afford ketoester **12** (19 mg, 96% yield, 88% ee) as a clear oil. Ketoester **12**. $[\alpha]_D^{25.3} = -96.67$ ($c = 0.10$, CH₂Cl₂); R_f 0.18 (benzene). Chiral SFC: 250 mm CHIRALPAK AD–3, 2% *i*-PrOH, 2.0 mL/min, 210 nm, 35 °C, nozzle pressure = 100 bar CO₂, t_{R1} (major) = 21.5 min, t_{R2} (minor) = 26.8 min. The spectral data matched the racemic data previously made in the literature.¹⁵ The absolute stereochemistry was assigned as (*S*) by analogy to **SI-32**.

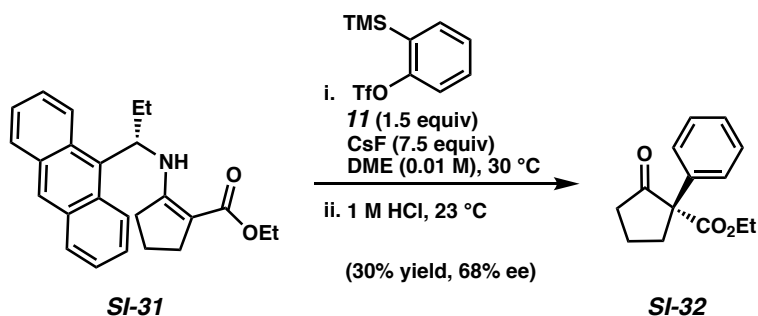
Table S1. Benzyne Arylation Reaction Optimization



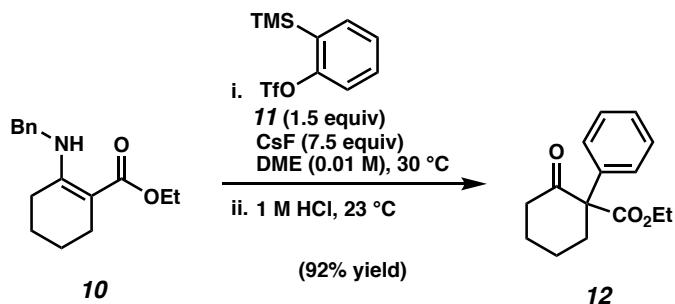
entry	solvent	11 (equiv)	CsF (equiv)	temp. (°C)	time (h)	yield (%) ^a	ee
1	MeCN	2.0	10.0	60	6	36%	62%
2	DME	2.0	10.0	30	6	59%	88%
3	DME	2.0	10.0	-41	6	3%	<i>n.d.</i>
4	DME	2.0	10.0	-20	6	36%	82%
5	DME	1.5	7.5	30	6	96%	88%
6	DME	1.5	7.5	30	3	95%	80%

(a) Reaction yields shown are NMR yields determined using 1,3,5-trimethoxybenzene as an external standard.

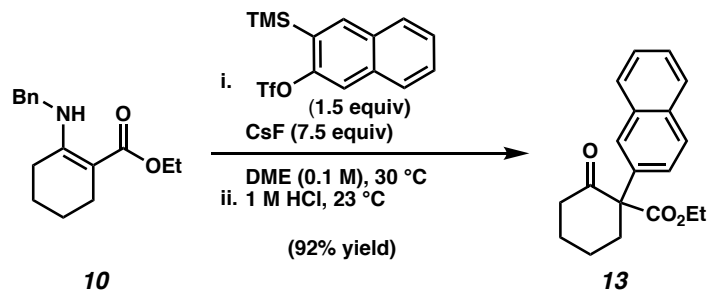
F. Arylation and Vinylation Reactions



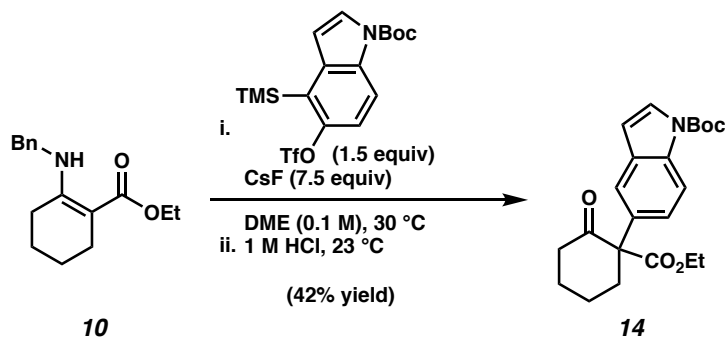
Ketoester SI-32. Purification by flash chromatography (SiO₂; benzene) generated ketoester **SI-32** (30% yield, 68% ee) as a colorless oil. Ketoester **SI-32**: $[\alpha]_D^{22} = -7.30$ ($c = 0.56$, CH₂Cl₂); R_f 0.40 (benzene). Chiral SFC: 250 mm CHIRALPAK IC-3, 10% *i*-PrOH, 2.0 mL/min, 228 nm, 35 °C, nozzle pressure = 100 bar CO₂, t_{R1} (major) = 6.2 min, t_{R2} (minor) = 8.1 min. The spectral data match those previously reported in the literature.¹⁶ The absolute stereochemistry was assigned as (*S*) by comparison to the sign of the specific rotation in the literature.¹⁶



Ketoester 12. Purification by flash chromatography (SiO₂; benzene) generated racemic ketoester **12** (92% yield) as a colorless oil.

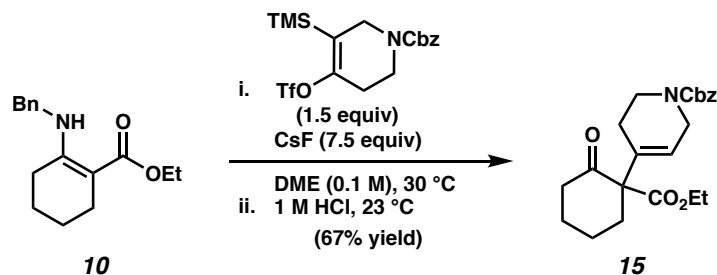


Ketoester 13. Purification by flash chromatography (SiO₂; benzene) generated ketoester **13** (92% yield) as a clear oil. Ketoester **13**: R_f 0.18 (benzene); ¹H NMR (500 MHz, CDCl₃): δ 7.85–7.79 (m, 3H), 7.68 (d, J = 1.8, 1H), 7.50–7.46 (m, 2H), 7.37 (dd, J = 8.7, 1.9, 1H), 4.29–4.19 (m, 2H), 2.90–2.83 (m, 1H), 2.67–2.48 (m, 3H), 2.07–1.99 (m, 1H), 1.93–1.79 (m, 3H), 1.24 (t, J = 7.1, 3H); ¹³C NMR (125 MHz, CDCl₃): δ 207.1, 171.4, 134.5, 133.3, 132.8, 128.3, 128.0, 127.6, 126.43, 126.35, 126.3, 126.2, 66.7, 61.9, 41.0, 35.4, 27.9, 22.3, 14.2; IR (film): 3054, 2935, 2863, 1716, 1237, 1130 cm⁻¹; HRMS-APCI (m/z) [$M + H$]⁺ calcd for C₁₉H₂₁O₃⁺, 297.1485; found 297.1490.



Ketoester 14. Purification by flash chromatography (SiO₂; 20:1 hexanes:EtOAc) generated ketoester **14** (42% yield) as a clear oil. Ketoester **14**: R_f 0.21 (5:1 hexanes:EtOAc); ¹H NMR (300 MHz, CDCl₃): δ 8.15–8.04 (br d, J = 8.6, 1H), 7.64–7.57 (m, 1H), 7.43 (d, J = 1.6, 1H), 7.19 (dd, J = 1.9, 8.8, 1H), 6.55 (d, J = 3.4, 1H), 4.26–4.18 (m, 2H), 2.85–2.77 (m, 1H), 2.62–2.55 (m, 2H), 2.51–2.44 (m, 1H), 2.02–1.95 (m, 1H), 1.91–1.75 (m, 3H), 1.67 (s, 9H), 1.21 (t, J = 7.2, 3H); ¹³C NMR (101 MHz, CDCl₃): δ 207.3, 171.8, 149.9, 131.2, 130.8, 126.5, 124.4, 120.8, 120.2, 115.2, 107.6, 83.9, 66.5, 61.7, 40.9, 35.5, 28.3, 27.9, 22.3, 14.2; IR (film): 2934,

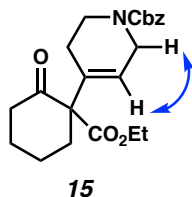
1730, 1469, 1370, 1141 cm^{-1} ; HRMS-APCI (m/z) $[\text{M} + \text{H}]^+$ calcd for $\text{C}_{22}\text{H}_{28}\text{NO}_5^+$, 386.1962; found 386.1966.

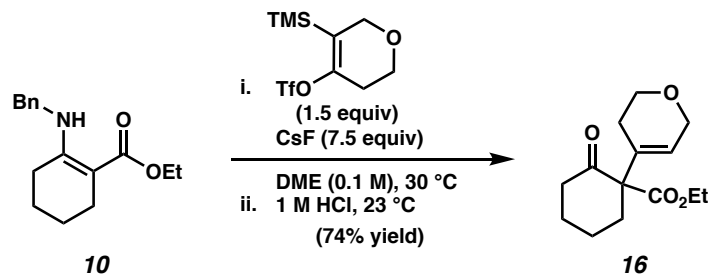


Ketoester 15. Purification by flash chromatography (SiO_2 ; 20:1 \rightarrow 7:3 hexanes:EtOAc) generated ketoester **15** (67% yield) as a colorless oil. Ketoester **15**: R_f 0.33 (7:3 hexanes:EtOAc); ^1H NMR (500 MHz, CDCl_3): δ 7.38–7.29 (m, 10H), 5.48 (s, 1H), 5.39 (s, 1H), 5.15 (s, 4H), 4.23 (q, $J = 7.1$, 4H), 4.11–3.97 (m, 4H), 3.66 (s, 2H), 3.58–3.49 (m, 2H), 2.57–2.51 (m, 2H), 2.49–2.41 (m, 4H), 2.13–1.91 (m, 8H), 1.80–1.72 (m, 4H), 1.67–1.62 (m, 2H), 1.27 (t, $J = 7.1$, 6H); ^{13}C NMR (125 MHz, CDCl_3): δ 207.1, 171.2, 155.5, 155.3, 136.9, 134.4, 133.9, 128.6, 128.14, 128.07, 122.3, 121.8, 67.5, 67.2, 61.7, 43.8, 43.6, 41.0, 40.9, 40.5, 33.7, 27.3, 27.2, 26.9, 22.2, 14.3, 1.2; IR (film): 2940, 2866, 1708, 1428, 1237, 1109 cm^{-1} ; HRMS-APCI (m/z) $[\text{M} + \text{H}]^+$ calcd for $\text{C}_{22}\text{H}_{28}\text{NO}_5^+$, 386.1962; found 386.1990.

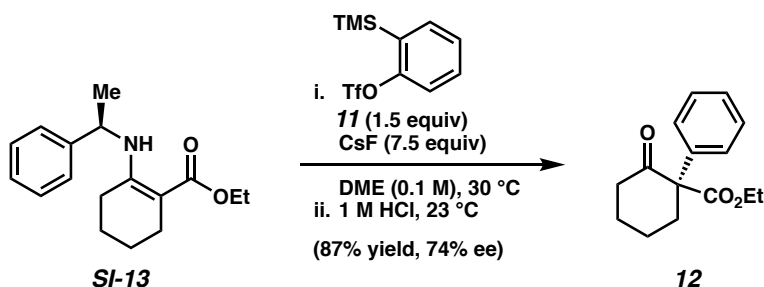
Note: Ketoester 15 was obtained as a mixture of rotamers. These data represent empirically observed chemical shifts and coupling constants from the ^1H and ^{13}C NMR spectra.

The regiochemical outcome was verified by performing a COSY experiment (500 MHz, CDCl_3), as the following correlations were observed:

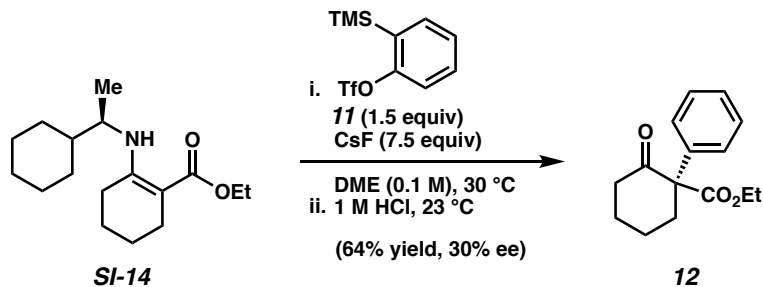




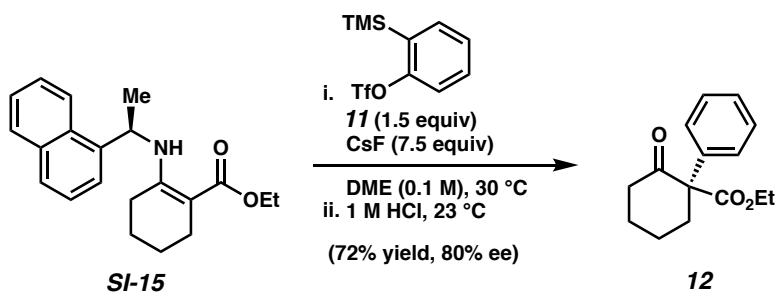
Ketoester 16. Purification by flash chromatography (SiO₂; 20:1 → 10:1 hexanes:EtOAc) generated ketoester **16** (74% yield) as a clear oil. Ketoester **16**: R_f 0.21 (5:1 hexanes:EtOAc); ¹H NMR (500 MHz, CDCl₃): δ 5.53–5.43 (m, 1H), 4.28–4.19 (m, 4H), 3.87–3.74 (m, 2H), 2.59–2.36 (m, 3H), 2.10–1.99 (m, 3H), 1.98–1.87 (m, 1H), 1.84–1.72 (m, 2H), 1.71–1.61 (m, 1H), 1.28 (t, *J* = 7.16, 3H); ¹³C NMR (125 MHz, CDCl₃): δ 207.2, 171.3, 132.9, 124.5, 67.4, 65.8, 64.4, 61.7, 41.0, 33.4, 27.3, 26.9, 22.1, 14.3; IR (film): 2936, 2862, 1712, 1236, 1236 cm⁻¹; HRMS-APCI (*m/z*) [M + H]⁺ calcd for C₁₄H₂₁O₄⁺, 253.1434; found 253.1422.



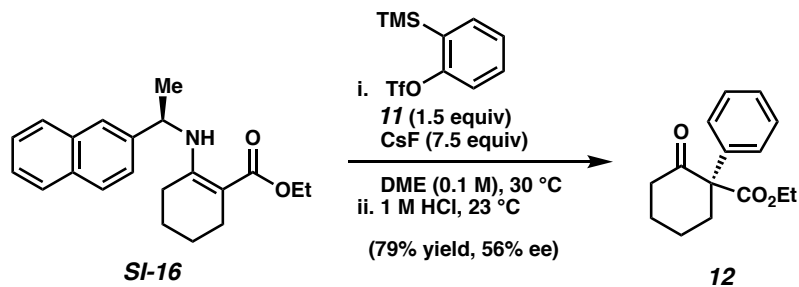
Ketoester 12. Purification by flash chromatography (SiO₂; benzene) generated ketoester **12** (87% yield, 74% ee) as a clear oil. Chiral SFC: 250 mm CHIRALPAK AD-3, 2% *i*-PrOH, 2.0 mL/min, λ = 210 nm, 35 °C, nozzle pressure = 100 bar CO₂, t_{R1} (major) = 23.0 min, t_{R2} (minor) = 29.0 min.



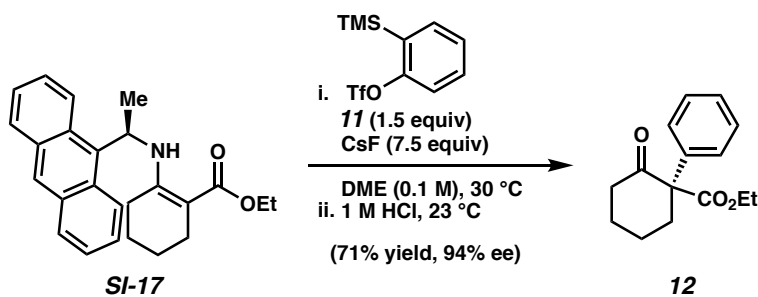
Ketoester 12. Purification by flash chromatography (SiO₂; benzene) generated ketoester **12** (64% yield, 30% ee) as a clear oil. Chiral SFC: 250 mm CHIRALPAK AD-3, 2% *i*-PrOH, 2.0 mL/min, λ = 210 nm, 35 °C, nozzle pressure = 100 bar CO₂, t_{R1} (major) = 22.9 min, t_{R2} (minor) = 28.9 min.



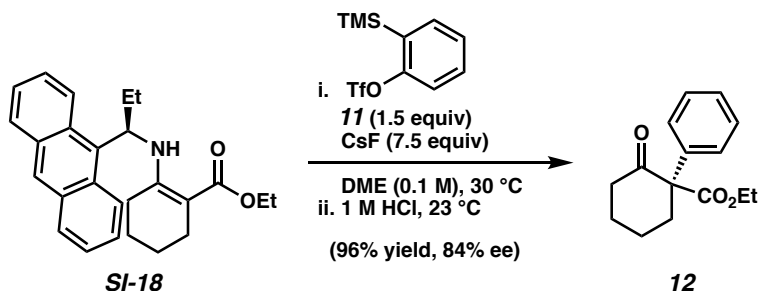
Ketoester 12. Purification by flash chromatography (SiO₂; benzene) generated ketoester **12** (72% yield, 80% ee) as a clear oil. Chiral SFC: 250 mm CHIRALPAK AD-3, 2% *i*-PrOH, 2.0 mL/min, λ = 210 nm, 35 °C, nozzle pressure = 100 bar CO₂, t_{R1} (major) = 21.4 min, t_{R2} (minor) = 26.8 min.



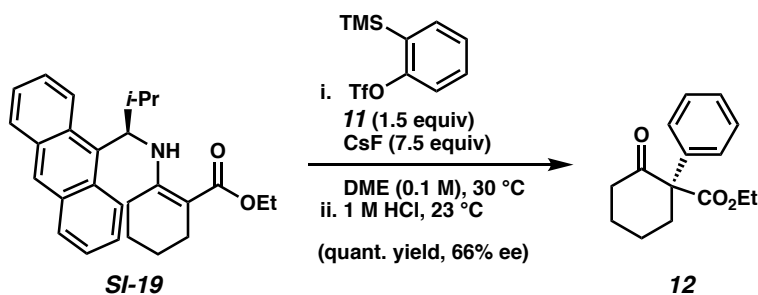
Ketoester 12. Purification by flash chromatography (SiO₂; benzene) generated ketoester **12** (79% yield, 56% ee) as a clear oil. Chiral SFC: 250 mm CHIRALPAK AD-3, 2% *i*-PrOH, 2.0 mL/min, λ = 210 nm, 35 °C, nozzle pressure = 100 bar CO₂, t_{R1} (major) = 22.2 min, t_{R2} (minor) = 27.7 min.



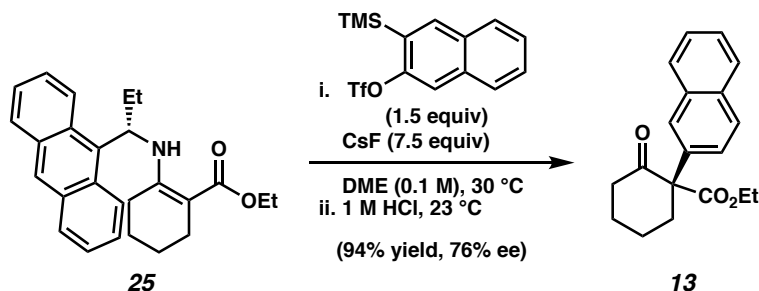
Ketoester 12. Purification by flash chromatography (SiO₂; benzene) generated ketoester **12** (71% yield, 94% ee) as a clear oil. Chiral SFC: 250 mm CHIRALPAK AD-3, 2% *i*-PrOH, 2.0 mL/min, λ = 210 nm, 35 °C, nozzle pressure = 100 bar CO₂, t_{R1} (major) = 22.5 min, t_{R2} (minor) = 28.4 min.



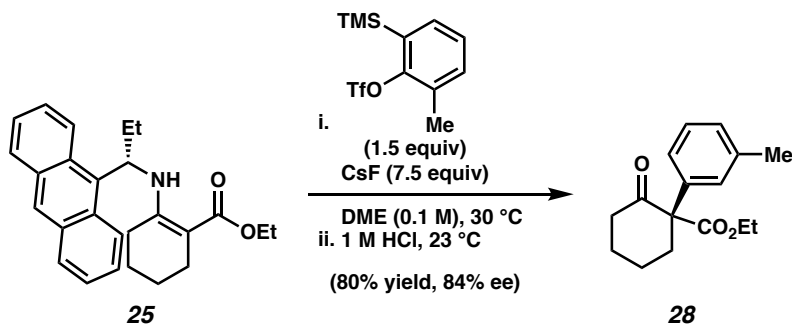
Ketoester 12. Purification by flash chromatography (SiO₂; benzene) generated ketoester **12** (96% yield, 84% ee) as a clear oil. Chiral SFC: 250 mm CHIRALPAK AD-3, 2% *i*-PrOH, 2.0 mL/min, λ = 210 nm, 35 °C, nozzle pressure = 100 bar CO₂, t_{R1} (major) = 19.3 min, t_{R2} (minor) = 24.6 min.



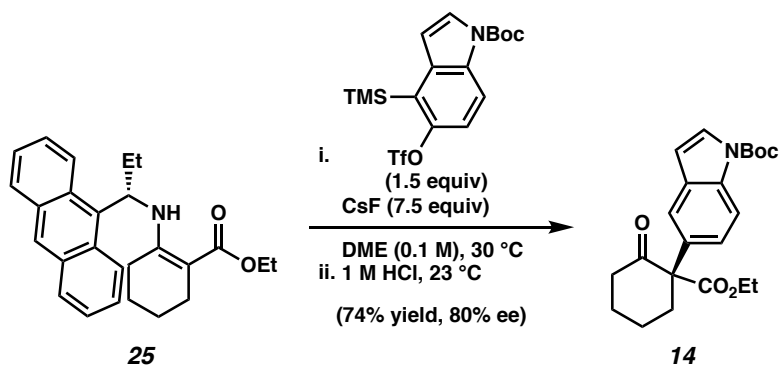
Ketoester 12. Purification by flash chromatography (SiO₂; benzene) generated ketoester **12** (quant. yield, 66% ee) as a clear oil. Chiral SFC: 250 mm CHIRALPAK AD-3, 2% *i*-PrOH, 2.0 mL/min, λ = 210 nm, 35 °C, nozzle pressure = 100 bar CO₂, t_{R1} (major) = 22.2 min, t_{R2} (minor) = 27.6 min.



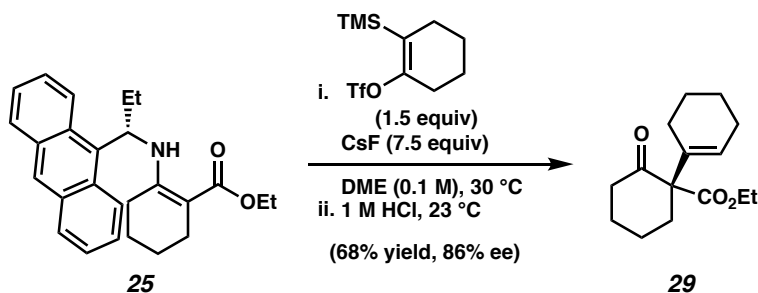
Ketoester 13. Purification by flash chromatography (SiO₂; benzene) generated ketoester **13** (94% yield, 76% ee) as a clear oil. Ketoester **13**: $[\alpha]_D^{26.5} = -24.00$ ($c = 0.10$, CH₂Cl₂); R_f 0.18 (benzene). Chiral SFC: 250 mm CHIRALPAK IA-3, 5% *i*-PrOH, 2.0 mL/min, $\lambda = 222$ nm, 35 °C, nozzle pressure = 100 bar CO₂, t_{R1} (minor) = 14.0 min, t_{R2} (major) = 14.8 min. The absolute stereochemistry was assigned as (*S*) by analogy to **SI-32**.



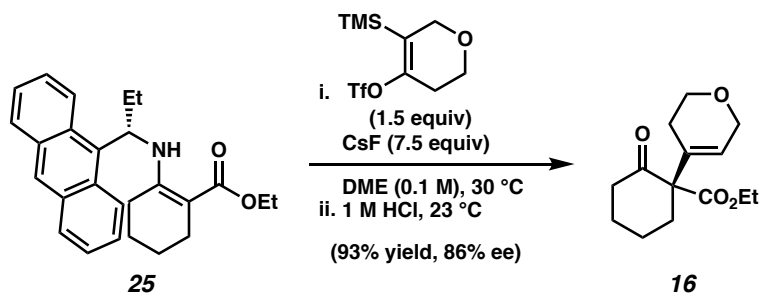
Ketoester 28. Purification by flash chromatography (SiO₂; benzene) generated ketoester **28** (80% yield, 84% ee) as a colorless oil. Ketoester **28**: $[\alpha]_D^{26.2} = -418.00$ ($c = 0.10$, CH₂Cl₂); R_f 0.18 (benzene); ¹H NMR (600 MHz, CD₂Cl₂): δ 7.24 (t, $J = 7.8$, 1H), 7.12 (dt, $J = 7.6$, 0.7, 1H), 7.00 (s, 1H), 6.98 (d, $J = 8.5$, 1H), 4.21 (q, $J = 7.1$, 2H), 2.73–2.68 (m, 1H), 2.60–2.54 (m, 1H), 2.52–2.47 (m, 1H), 2.34 (s, 3H), 2.33–2.27 (m, 1H), 2.03–1.96 (m, 1H), 1.86–1.76 (m, 2H), 1.76–1.70 (m, 1H), 1.24 (t, $J = 7.1$, 3H); ¹³C NMR (125 MHz, CDCl₃): δ 207.0, 171.5, 138.1, 136.8, 128.6, 128.5, 128.4, 125.0, 66.6, 61.8, 41.0, 35.5, 27.8, 22.3, 21.8, 14.2; IR (film): 2942, 2866, 1715, 1451, 1231 cm⁻¹; HRMS-APCI (m/z) $[M + H]^+$ calcd for C₁₆H₂₁O₃⁺, 261.1485; found 261.1490. Chiral SFC: 250 mm CHIRALPAK OJ-H, 1% *i*-PrOH, 2.0 mL/min, $\lambda = 210$ nm, 35 °C, nozzle pressure = 100 bar CO₂, t_{R1} (major) = 12.3 min, t_{R2} (minor) = 14.7 min. The absolute stereochemistry was assigned as (*S*) by analogy to **SI-32**.



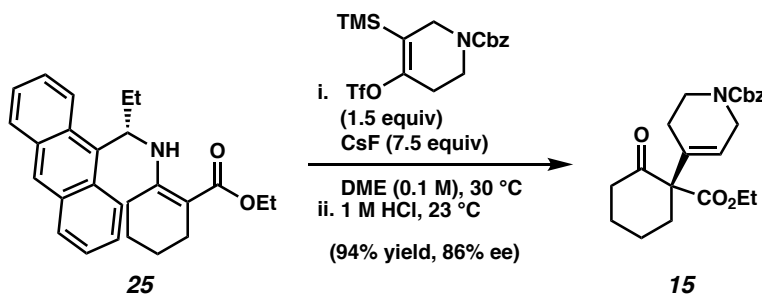
Ketoester 14. Purification by flash chromatography (SiO₂; 20:1 hexanes:EtOAc) generated ketoester **14** (74% yield, 80% ee) as a yellow oil. Ketoester **14**: $[\alpha]_D^{25.5} = -100.00$ ($c = 0.10$, CH₂Cl₂); R_f 0.21 (5:1 hexanes:EtOAc). Chiral SFC: 250 mm CHIRALPAK AD-3, 10% *i*-PrOH, 2.0 mL/min, $\lambda = 210$ nm, 35 °C, nozzle pressure = 100 bar CO₂, t_{R1} (major) = 11.1 min, t_{R2} (minor) = 15.2 min. The absolute stereochemistry was assigned as (*S*) by analogy to **SI-32**.



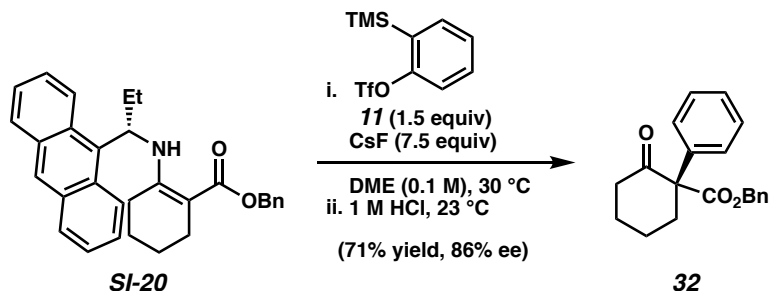
Ketoester 29. Purification by flash chromatography (SiO₂; benzene) generated ketoester **29** (68% yield, 86% ee) as a colorless oil. Ketoester **29**: $[\alpha]_D^{27.0} = -2.00$ ($c = 0.10$, CH₂Cl₂); R_f 0.18 (benzene); ¹H NMR (500 MHz, CDCl₃): δ 5.49–5.44 (m, 1H), 4.21 (q, $J = 7.1$, 2H), 2.52–2.46 (m, 2H), 2.39–2.31 (m, 1H), 2.13–2.04 (m, 3H), 1.93–1.84 (m, 3H), 1.81–1.71 (m, 2H), 1.68–1.56 (m, 5H), 1.26 (t, $J = 7.1$, 3H); ¹³C NMR (125 MHz, CDCl₃): δ 208.1, 171.9, 134.7, 126.1, 68.3, 61.3, 41.0, 33.6, 27.4, 26.8, 25.8, 23.0, 22.2, 22.1, 14.2; IR (film): 2938, 2861, 1714, 1448, 1232 cm⁻¹; HRMS-APCI (m/z) $[M + H]^+$ calcd for C₁₅H₂₃O₃⁺, 251.1642; found 251.1648. Chiral HPLC: 250 mm CHIRALPAK OJ-H, 10% *i*-PrOH:90% hexanes, 1.0 mL/min, $\lambda = 210$ nm, 23 °C, t_{R1} (major) = 4.5 min, t_{R2} (minor) = 4.8 min. The absolute stereochemistry was assigned as (*S*) by analogy to **SI-32**.



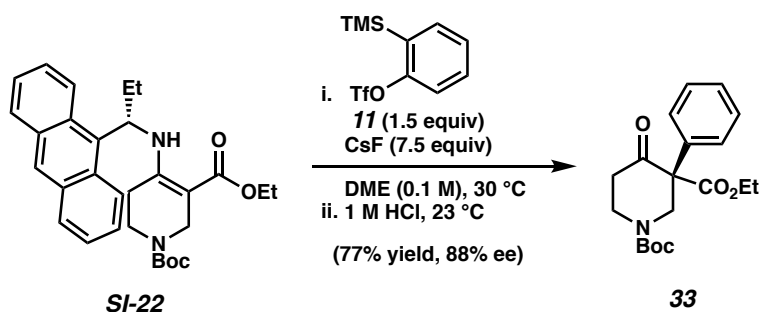
Ketoester 16. Purification by flash chromatography (SiO₂; 20:1 → 10:1 hexanes:EtOAc) generated ketoester **16** (93% yield, 86% ee) as a clear oil. Ketoester **16**: $[\alpha]_D^{23} = -24.00$ ($c = 0.10$, CH₂Cl₂); R_f 0.21 (5:1 hexanes:EtOAc). Chiral SFC: 250 mm CHIRALPAK IA-3, 10% *i*-PrOH, 2.0 mL/min, $\lambda = 210$ nm, 35 °C, nozzle pressure = 100 bar CO₂, t_{R1} (major) = 11.1 min, t_{R2} (minor) = 12.1 min. The absolute stereochemistry was assigned as (*S*) by analogy to **SI-32**.



Ketoester 15. Purification by flash chromatography (SiO₂; 20:1 → 7:3 hexanes:EtOAc) generated ketoester **15** (94% yield, 86% ee) as a colorless oil. Ketoester **15**: $[\alpha]_D^{26.8} = -27.30$ ($c = 0.1$, CH₂Cl₂); R_f 0.18 (benzene). Chiral HPLC: 250 mm CHIRALPAK AD-H, 5% *i*-PrOH : 95% hexanes, 1.0 mL/min, $\lambda = 210$ nm, 23 °C, t_{R1} (major) = 27.2 min, t_{R2} (minor) = 36.5 min. The absolute stereochemistry was assigned as (*S*) by analogy to **SI-32**.

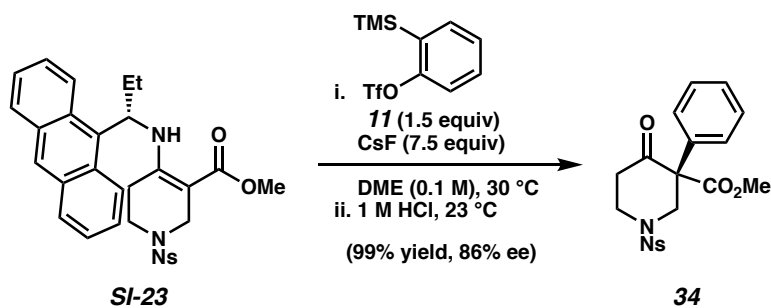


Ketoester 32. Purification by flash chromatography (SiO₂; 15:1 hexanes:EtOAc) generated ketoester **32** (71% yield, 86% ee) as a clear oil. Ketoester **32**: $[\alpha]_D^{25.5} = -80.00$ ($c = 0.10$, CH₂Cl₂); R_f 0.32 (5:1 hexanes:EtOAc); ¹H NMR (500 MHz, CDCl₃): δ 7.38–7.28 (m, 6H), 7.24–7.19 (m, 4H), 5.19 (q, $J = 8.2$, 2H), 2.81–2.72 (m, 1H), 2.59–2.49 (m, 2H), 2.46–2.38 (m, 1H), 2.00–1.89 (m, 1H), 1.88–1.68 (m, 3H); ¹³C NMR (125 MHz, CDCl₃): δ 206.8, 171.3, 136.7, 135.6, 128.61, 128.60, 128.3, 128.1, 128.0, 127.8, 67.3, 66.7, 40.8, 35.3, 27.8, 22.2; IR (film): 3033, 2942, 2866, 1711, 1214, 695 cm⁻¹; HRMS-APCI (m/z) $[M + H]^+$ calcd for C₂₀H₂₁O₃⁺, 309.1485; found 309.1465. Chiral SFC: 250 mm CHIRALPAK AD-3, 10% *i*-PrOH, 2.0 mL/min, $\lambda = 210$ nm, 35 °C, nozzle pressure = 100 bar CO₂, t_{R1} (minor) = 22.1 min, t_{R2} (major) = 23.2 min. The absolute stereochemistry was assigned as (*S*) by analogy to **SI-32**.

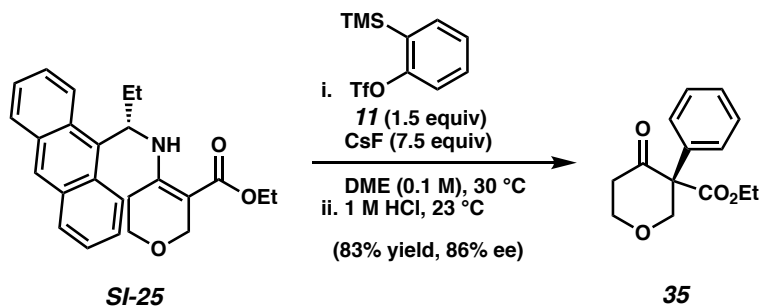


Ketoester 33. Purification by flash chromatography (SiO₂; 15:1 → 10:1 hexanes:EtOAc) generated ketoester **33** (77% yield, 88% ee) as a yellow oil. Ketoester **33**: $[\alpha]_D^{24.4} = +180.00$ ($c = 0.10$, CH₂Cl₂); R_f 0.37 (2:1 hexanes:EtOAc); ¹H NMR (500 MHz, CDCl₃): δ 7.39–7.26 (m, 4H), 7.25–7.18 (br s, 1H), 4.50–4.11 (m, 4H), 3.74 (br s, 2H), 2.63 (br s, 2H), 1.48 (br s, 9H), 1.22 (t, $J = 7.1$, 3H); ¹³C NMR (125 MHz, CDCl₃): (13 of 17 signals observed) δ 203.8, 169.4, 154.1, 128.6, 128.1, 127.9, 80.8, 66.8, 62.0, 50.0, 43.3, 28.3, 14.0; IR (film): 2928, 2977, 1719,

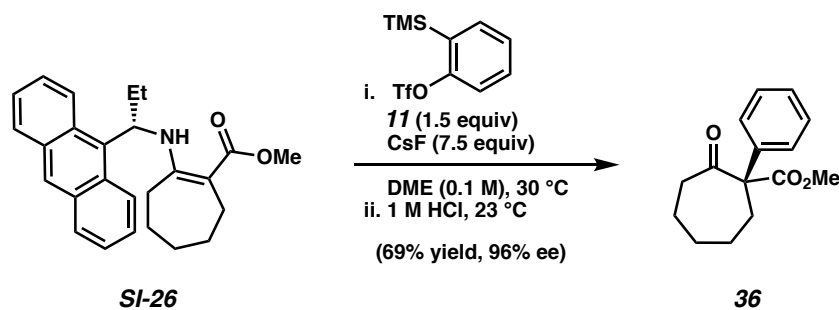
1696, 1163, 697 cm^{-1} ; HRMS-APCI (m/z) $[\text{M} + \text{H}]^+$ calcd for $\text{C}_{19}\text{H}_{26}\text{NO}_5^+$, 348.1806; found 348.1806. Chiral SFC: 250 mm CHIRALPAK IC-3, 10% *i*-PrOH, 2.0 mL/min, $\lambda = 210$ nm, 35 $^\circ\text{C}$, nozzle pressure = 100 bar CO_2 , $t_{\text{R}1}$ (minor) = 6.1 min, $t_{\text{R}2}$ (major) = 8.5 min. The absolute stereochemistry was assigned as (*R*) by analogy to **SI-32**.



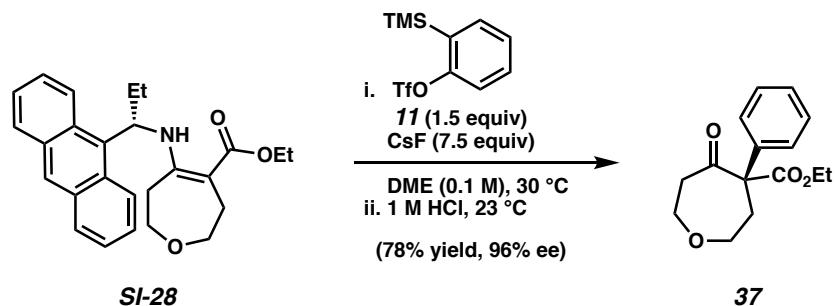
Ketoester 34. Purification by flash chromatography (SiO_2 ; 15:1 \rightarrow 7:3 hexanes:EtOAc) generated ketoester **34** (99% yield, 86% ee) as a yellow foam. Ketoester **34**: $[\alpha]_{\text{D}}^{27.1} = +10.00$ ($c = 0.10$, CH_2Cl_2); R_f 0.10 (7:3 hexanes:EtOAc); $^1\text{H NMR}$ (500 MHz, CDCl_3): δ 8.08 (dd, $J = 7.6$, 1.5, 1H), 7.80–7.68 (m, 3H), 7.38–7.32 (m, 3H), 7.18–7.14 (m, 2H), 4.47 (dd, $J = 13.1$, 2.1, 1H), 3.98–3.90 (m, 2H), 3.67 (s, 3H), 3.53–3.45 (m, 1H), 2.97 (ddd, $J = 15.5$, 9.7, 6.1, 1H), 2.74 (dt, $J = 14.6$, 4.5, 1H); $^{13}\text{C NMR}$ (125 MHz, CDCl_3): δ 201.5, 169.5, 148.4, 134.4, 133.4, 132.0, 131.8, 131.4, 128.9, 128.6, 127.8, 124.6, 66.1, 53.3, 52.8, 46.5, 39.6; IR (film): 2960, 2866, 1729, 1542, 1369, 1163, 581.6 cm^{-1} ; HRMS-APCI (m/z) $[\text{M} + \text{H}]^+$ calcd for $\text{C}_{19}\text{H}_{19}\text{N}_2\text{O}_7\text{S}^+$, 419.0908; found 419.0909. Chiral SFC: 250 mm CHIRALPAK AD-3, 7% MeOH, 2.0 mL/min, $\lambda = 211$ nm, 35 $^\circ\text{C}$, nozzle pressure = 100 bar CO_2 , $t_{\text{R}1}$ (major) = 13.6 min, $t_{\text{R}2}$ (minor) = 17.6 min. The absolute stereochemistry was assigned as (*R*) by analogy to **SI-32**.



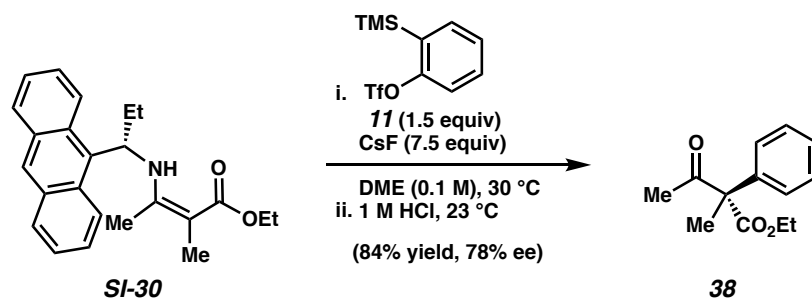
Ketoester 35. Purification by flash chromatography (SiO₂; 15:1 hexanes:EtOAc) generated ketoester **35** (83% yield, 86% ee) as a colorless oil. Ketoester **35**: $[\alpha]_D^{29.5} = -200.00$ ($c = 0.10$, CH₂Cl₂); R_f 0.20 (benzene); ¹H NMR (400 MHz, CDCl₃): δ 7.42–7.29 (m, 3H), 7.22–7.15 (m, 2H), 4.76 (dd, $J = 1.6, 11.8$, 1H), 4.35–4.25 (m, 2H), 4.24–4.16 (m, 2H), 3.97–3.88 (m, 1H), 2.90–2.79 (m, 1H), 2.64–2.56 (m, 1H), 1.27 (t, $J = 7.0$, 3H); ¹³C NMR (125 MHz, CDCl₃): δ 202.0, 169.6, 133.7, 128.7, 128.2, 127.9, 74.2, 68.9, 68.0, 62.3, 41.4, 14.1; IR (film): 2979, 2862, 1720, 1236, 1209 cm⁻¹; HRMS-APCI (m/z) $[M + H]^+$ calcd for C₁₄H₁₇O₄⁺, 249.1121; found 249.1108; Chiral SFC: 250 mm CHIRALPAK IA-3, 5% *i*-PrOH, 2.0 mL/min, $\lambda = 210$ nm, 35 °C, nozzle pressure = 100 bar CO₂, t_{R1} (major) = 8.7 min, t_{R2} (minor) = 9.7 min. The absolute stereochemistry was assigned as (*R*) by analogy to **SI-32**.



Ketoester 36. Purification by flash chromatography (SiO₂; 20:1 \rightarrow 15:1 hexanes:EtOAc) generated ketoester **36** (69% yield, 96% ee) as a colorless oil. Ketoester **36**: $[\alpha]_D^{24.4} = +1060.00$ ($c = 0.10$, CH₂Cl₂); R_f 0.47 (5:1 hexanes:EtOAc). Chiral SFC: 250 mm CHIRALPAK IC-3, 5% *i*-PrOH, 3.5 mL/min, $\lambda = 210$ nm, 40 °C, nozzle pressure = 100 bar CO₂, t_{R1} (minor) = 22.2 min, t_{R2} (major) = 22.7 min. The spectral data matched those previously reported in the literature.¹⁷ The absolute stereochemistry was assigned as (*S*) by analogy to **SI-32**.



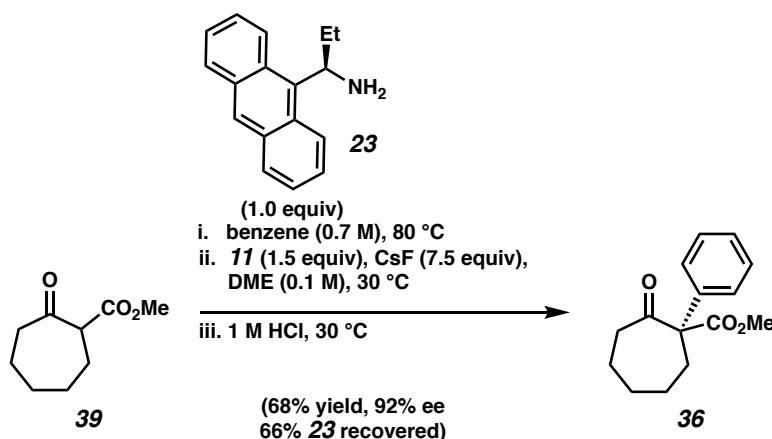
Ketoester 37. Purification by flash chromatography (SiO₂; 20:1 hexanes:EtOAc) generated ketoester **37** (78% yield, 96% ee) as a clear oil. Ketoester **37**: $[\alpha]_D^{23.0} = +48.00$ ($c = 0.1$ in CH₂Cl₂); R_f 0.73 (1:1 hexanes:EtOAc); ¹H NMR (600 MHz, CDCl₃): δ 7.40–7.33 (m, 2H), 7.34 (m, 1H), 7.21–7.17 (m, 2H), 4.26–4.14 (m, 2H), 4.12–4.06 (m, 1H), 3.88–3.78 (m, 2H), 3.70–3.62 (m, 1H), 2.91–2.84 (m, 1H), 2.82–2.73 (m, 2H), 2.47–2.40 (m, 1H), 1.22 (t, $J = 7.2$, 3H); ¹³C NMR (125 MHz, CDCl₃): δ 205.7, 171.4, 138.0, 128.7, 128.6, 128.3, 127.8, 127.5, 68.8, 67.5, 67.0, 61.8, 45.9, 34.8, 14.0; IR (film): 2927, 1726, 1233, 1142, 1100 cm⁻¹; HRMS-APCI (m/z) $[M + H]^+$ calcd for C₁₅H₁₈O₄, 263.1278; found 263.1270. Chiral SFC: 250 mm CHIRALPAK IA–3, 5% *i*-PrOH, 2.0 mL/min, $\lambda = 210$ nm, 35 °C, nozzle pressure = 100 bar CO₂, t_{R1} (minor) = 7.3 min, t_{R2} (major) = 8.1 min. The absolute stereochemistry was assigned as (*S*) by analogy to **SI-32**.



Ketoester 38. Purification by flash chromatography (SiO₂; benzene) generated ketoester **38** (84% yield, 78% ee) as a colorless oil. Ketoester **38**: $[\alpha]_D^{24.0} = -38.37$ ($c = 0.25$ in CHCl₃); R_f 0.22 (benzene). Chiral SFC: 250 mm CHIRALPAK OJ–H, 1% MeOH, 2.0 mL/min, $\lambda = 212$ nm, 35 °C, nozzle pressure = 100 bar CO₂, t_{R1} (major) = 9.7, t_{R2} (minor) = 12.9 min. The spectral

data match those previously reported in the literature.¹⁸ The absolute stereochemistry was assigned as (*S*) by analogy to **SI-32**.

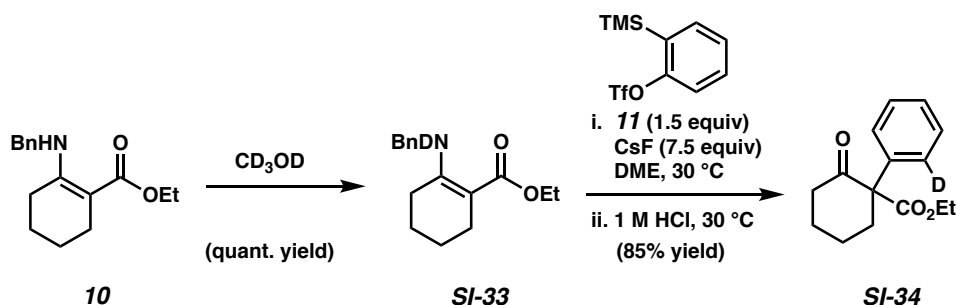
G. One-Pot, 1.0 mmol Scale Arylation Reaction



Procedure for One-Pot, mmol Scale Arylation Reaction. To amine **23** (250 mg, 1.06 mmol, 1.0 equiv) was added methyl 2-oxocycloheptane-1-carboxylate (181 mg, 1.06 mmol, 1.0 equiv) and benzene (4 mL), sequentially. The mixture was stirred for 15.5 h at 80 °C, before being cooled down to 23 °C. The volatiles were then evaporated under reduced pressure. The residue was dissolved in DME (15 mL), and silyl triflate **11** (387 μ L, 1.59 mmol, 1.5 equiv) and CsF (1.21 g, 7.97 mmol, 7.5 equiv) were added. The mixture was stirred for 6 h at 30 °C, and then quenched with 1 M aqueous HCl (10 mL). After stirring at 30 °C for 17 h, the mixture was diluted with EtOAc (50 mL). The layers were separated, and the aqueous phase was extracted with EtOAc (3 x 50 mL). The combined organic layers were dried over Na₂SO₄, and evaporated under reduced pressure to yield the crude product. Purification by flash chromatography (SiO₂; 20:1 hexanes:EtOAc \rightarrow 1:1 hexanes:EtOAc, 1% Et₃N) afforded ketoester **36** (178 mg, 68% yield, 92% ee) as a light yellow oil and amine **23** (166 mg, 66%) as a yellow solid. Ketoester **36**: $[\alpha]_D^{22.5} = -82.00$ ($c = 0.10$, CHCl₃); Chiral SFC: 250 mm CHIRALPAK IA-3, 2% *i*-PrOH, 3.5 mL/min, $\lambda = 210$ nm, 40 °C, nozzle pressure = 100 bar CO₂, t_{R1} (major) = 8.4 min, t_{R2} (minor) =

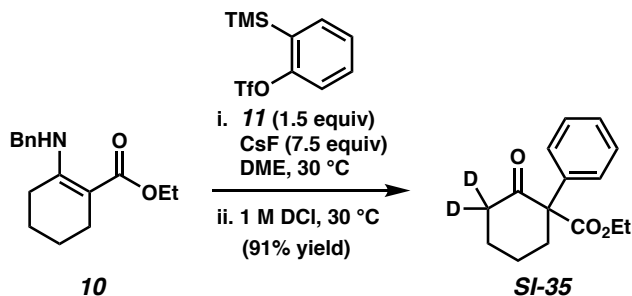
10.7 min. The spectral data matched those previously reported in the literature.¹⁷ The absolute stereochemistry was assigned as (*S*) by analogy to **SI-32**.

H. Deuterium Labeling Experiments



Ketoester SI-34. Enamine **10** (46 mg, 0.18 mmol, 1.0 equiv) was suspended in CD_3OD (0.8 mL) and the volatiles were removed under reduced pressure. This process was repeated two more times to afford enamine **SI-33** (47 mg, quant. yield), which was used without further purification.

To deuterated enamine **SI-33** (36 mg, 0.14 mmol, 1.0 equiv) was added DME (0.7 mL, 0.1 M), silyl triflate **11** (50 μL , 0.20 mmol, 1.5 equiv), and CsF (157.0 mg, 1.03 mmol, 7.5 equiv), sequentially. This mixture was stirred vigorously (1000 rpm) at 30 °C for 6 h. After cooling to 23 °C, aqueous 1 M HCl (1.0 mL) was added and this mixture was stirred vigorously (1000 rpm) for 30 min. The mixture was diluted with EtOAc (5 mL), the layers were separated, and the aqueous layer was extracted with EtOAc (3 x 10 mL). The combined organic layers were dried over Na_2SO_4 , and evaporated under reduced pressure. Purification by flash chromatography (SiO_2 ; benzene) gave **SI-34** (29 mg, 85% yield) as a light yellow oil. Deuterium incorporation onto the aromatic ring was deemed quantitative by ^1H NMR analysis (see page S82 for the spectrum).



Ketoester SI-35. To enamine **10** (25.0 mg, 0.96 mmol, 1.0 equiv) was added DME (0.74 mL, 0.1 M), silyl triflate **11** (35 μ L, 0.14 mmol, 1.5 equiv), and CsF (109 mg, 0.72 mmol, 7.5 equiv), sequentially. This mixture was stirred vigorously (1000 rpm) at 30 °C for 6 h. After cooling to 23 °C, aqueous 1 M DCl in D₂O (1 mL) was added and this mixture was stirred vigorously (1000 rpm) for 30 min. The mixture was diluted with EtOAc (5 mL), the layers were separated, and the aqueous layer was extracted with EtOAc (3 x 10 mL). The combined organic layers were dried over Na₂SO₄, and evaporated under reduced pressure. Purification by flash chromatography (SiO₂; benzene) gave **SI-35** (22 mg, 91% yield) as a light yellow oil. Deuterium incorporation onto the aromatic ring was not detected by ¹H NMR analysis, suggesting that quenching of the intermediate aryl anion occurs prior to workup. We do observe partial α deuteration, presumably via keto-enol tautomerization (see page S83 for the spectrum).

^1H NMR Spectra

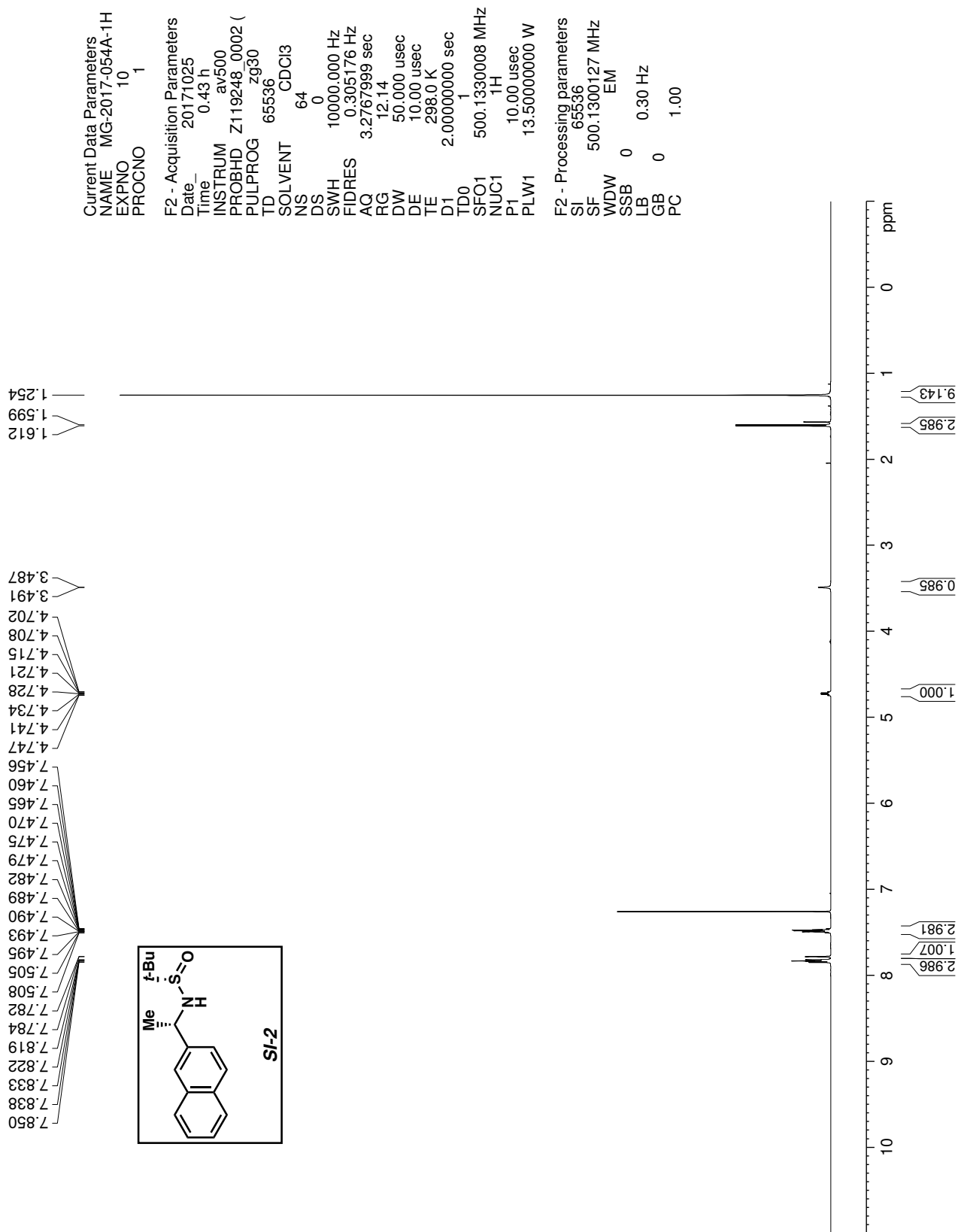


Figure S2 ^1H NMR (500 MHz, CDCl_3) of compound SI-2.

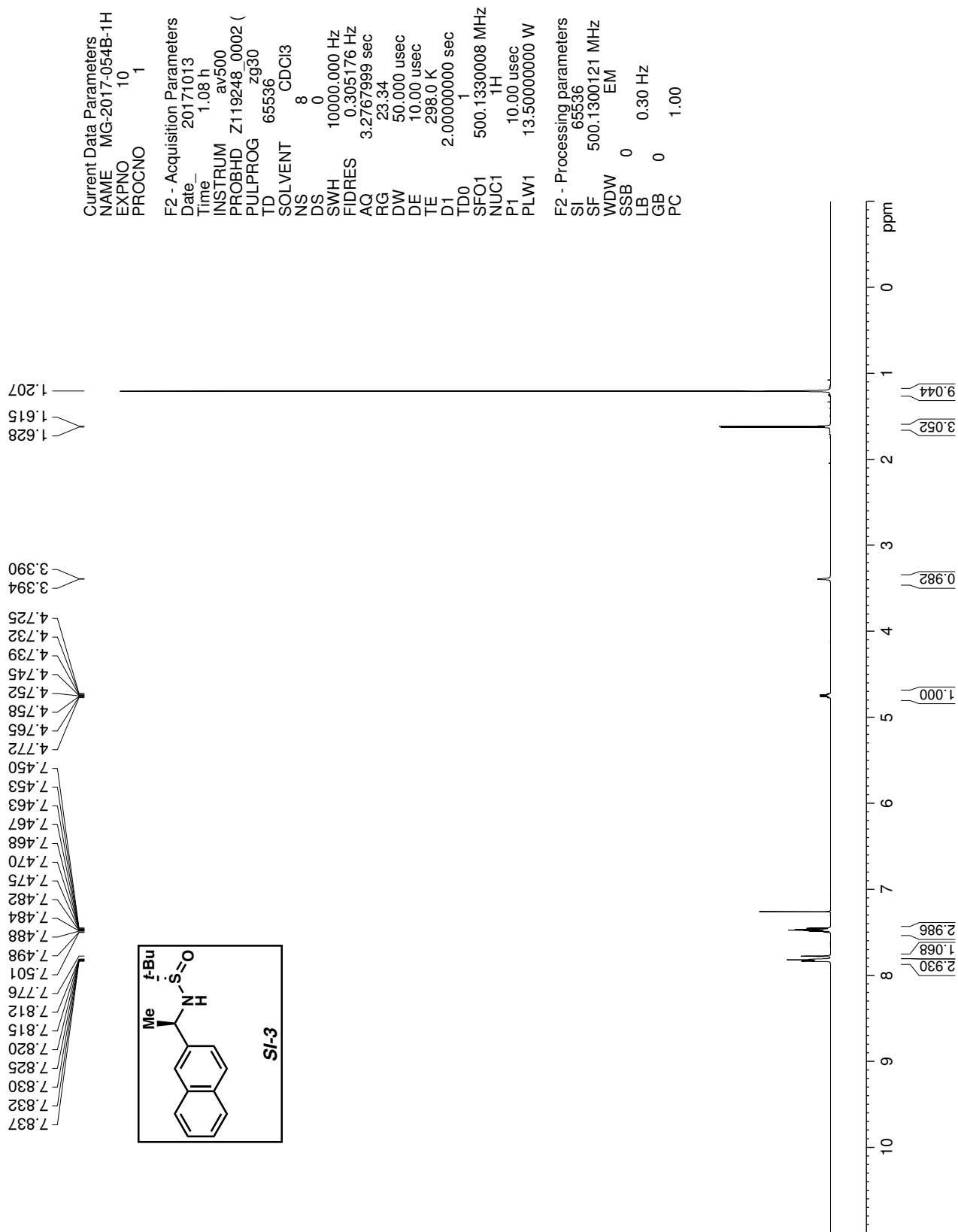


Figure S3 ^1H NMR (500 MHz, CDCl_3) of compound SI-3.

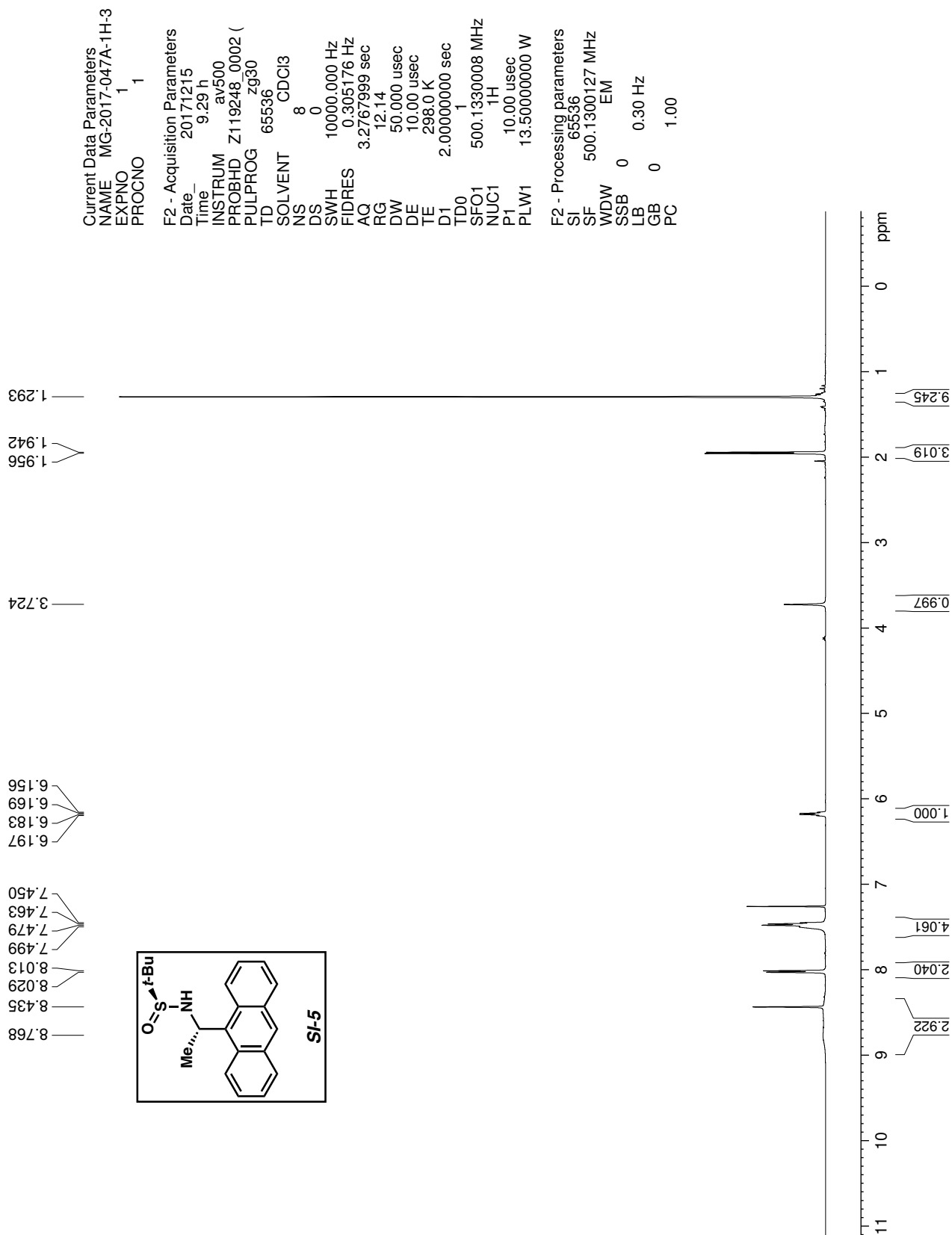


Figure S4 ^1H NMR (500 MHz, CDCl_3) of compound SI-5.

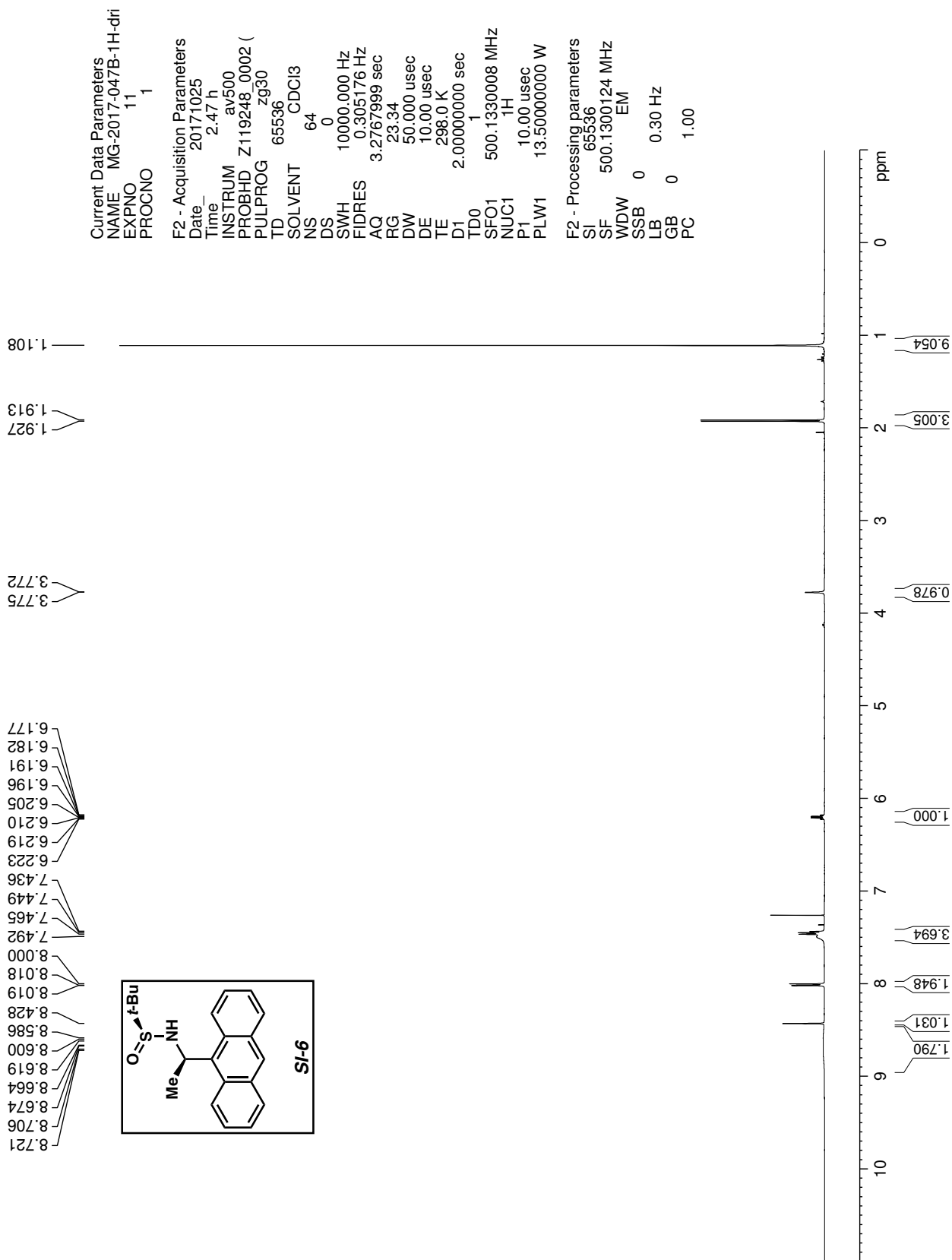


Figure S5 ^1H NMR (500 MHz, CDCl_3) of compound SI-6.

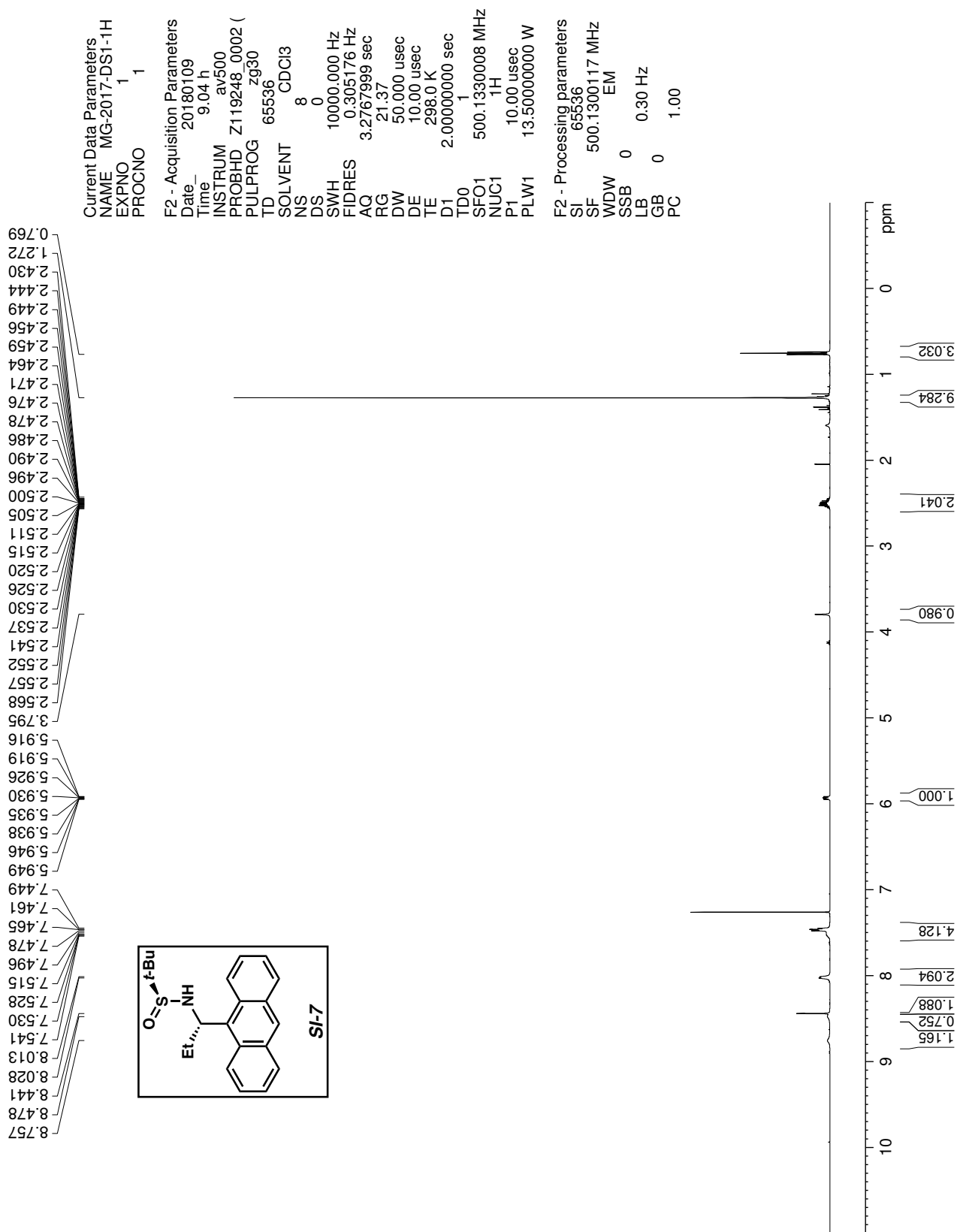


Figure S6 ¹H NMR (500 MHz, CDCl₃) of compound SI-7.

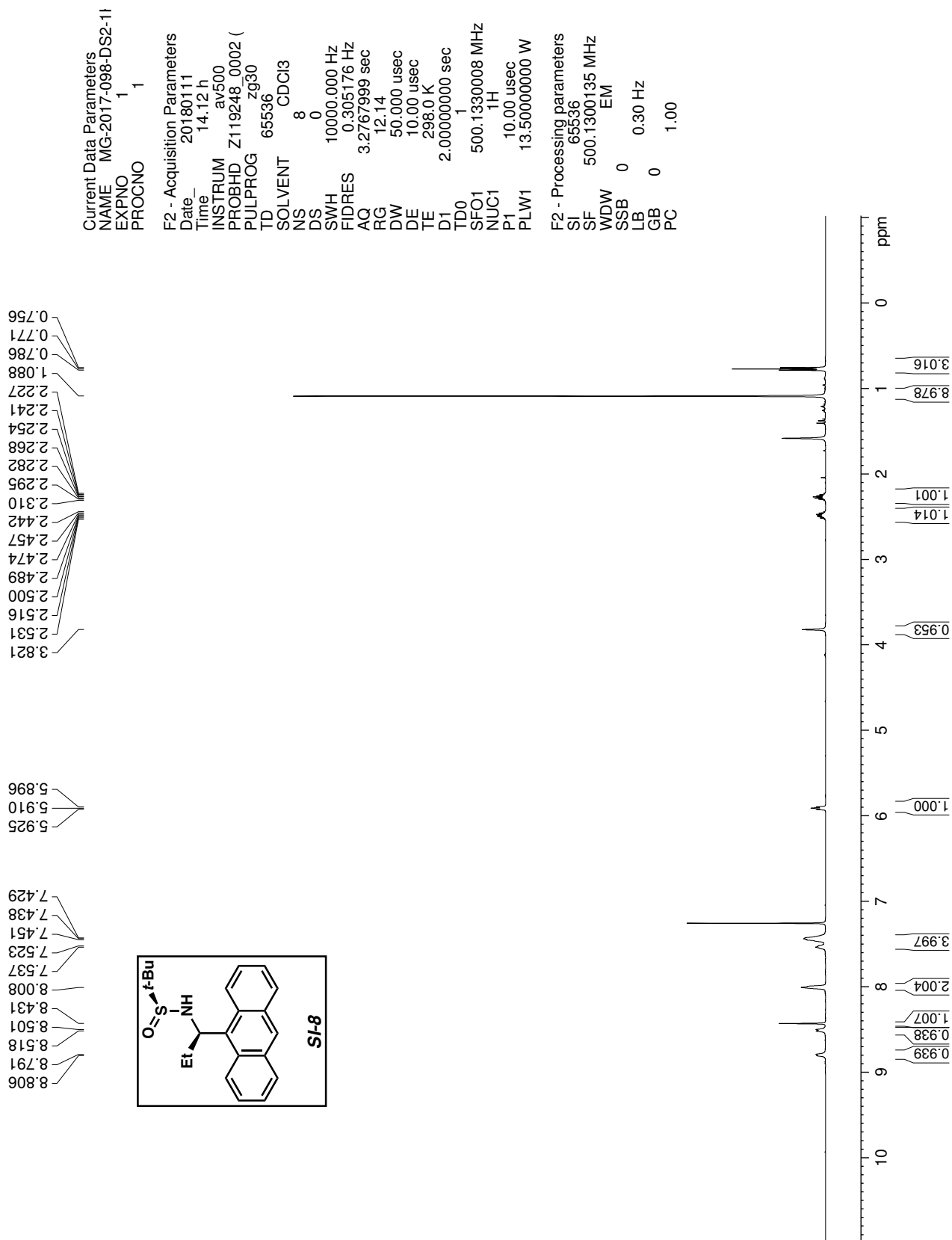


Figure S7 ^1H NMR (500 MHz, CDCl_3) of compound SI-8.

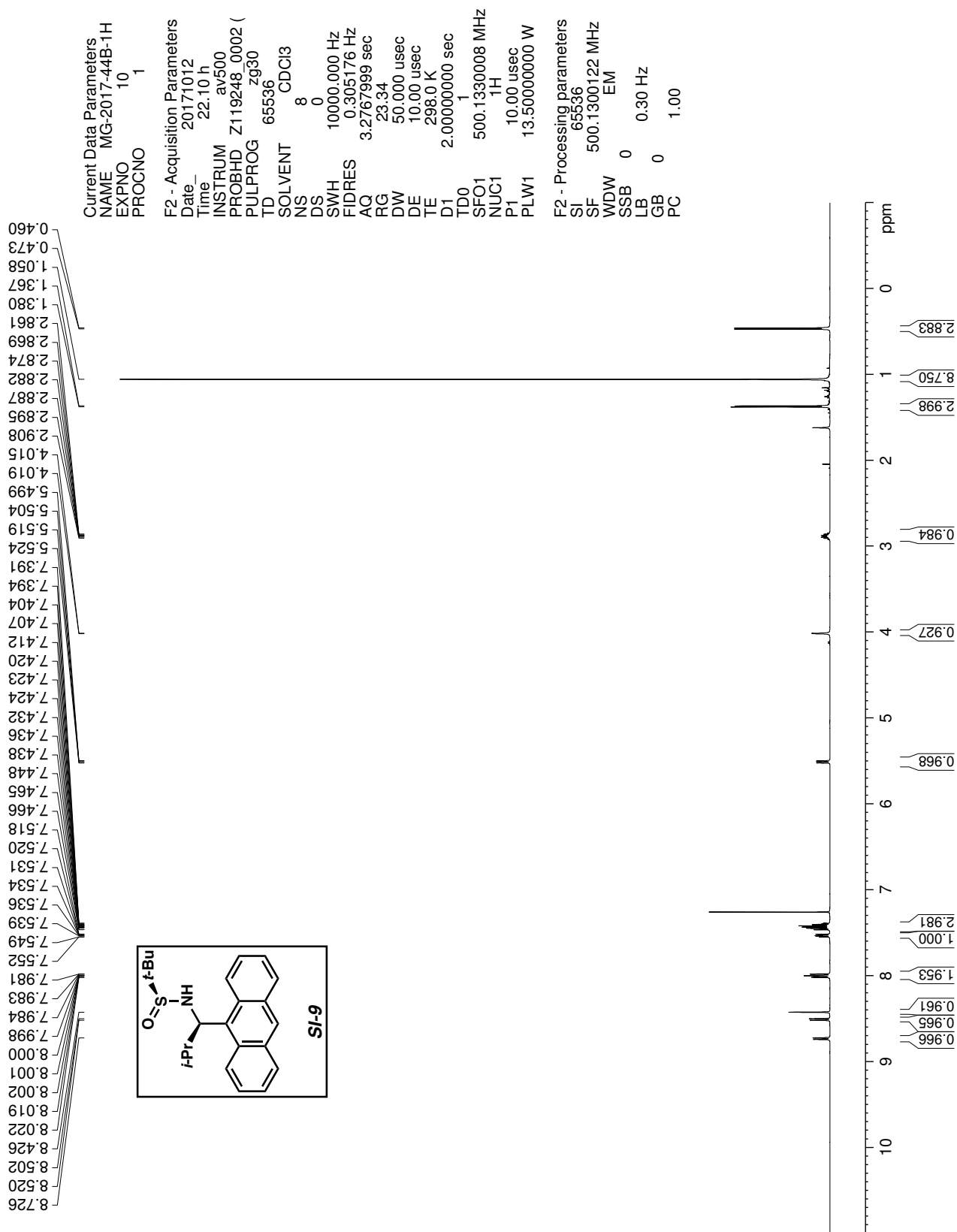


Figure S8 ^1H NMR (500 MHz, CDCl_3) of compound SI-9.

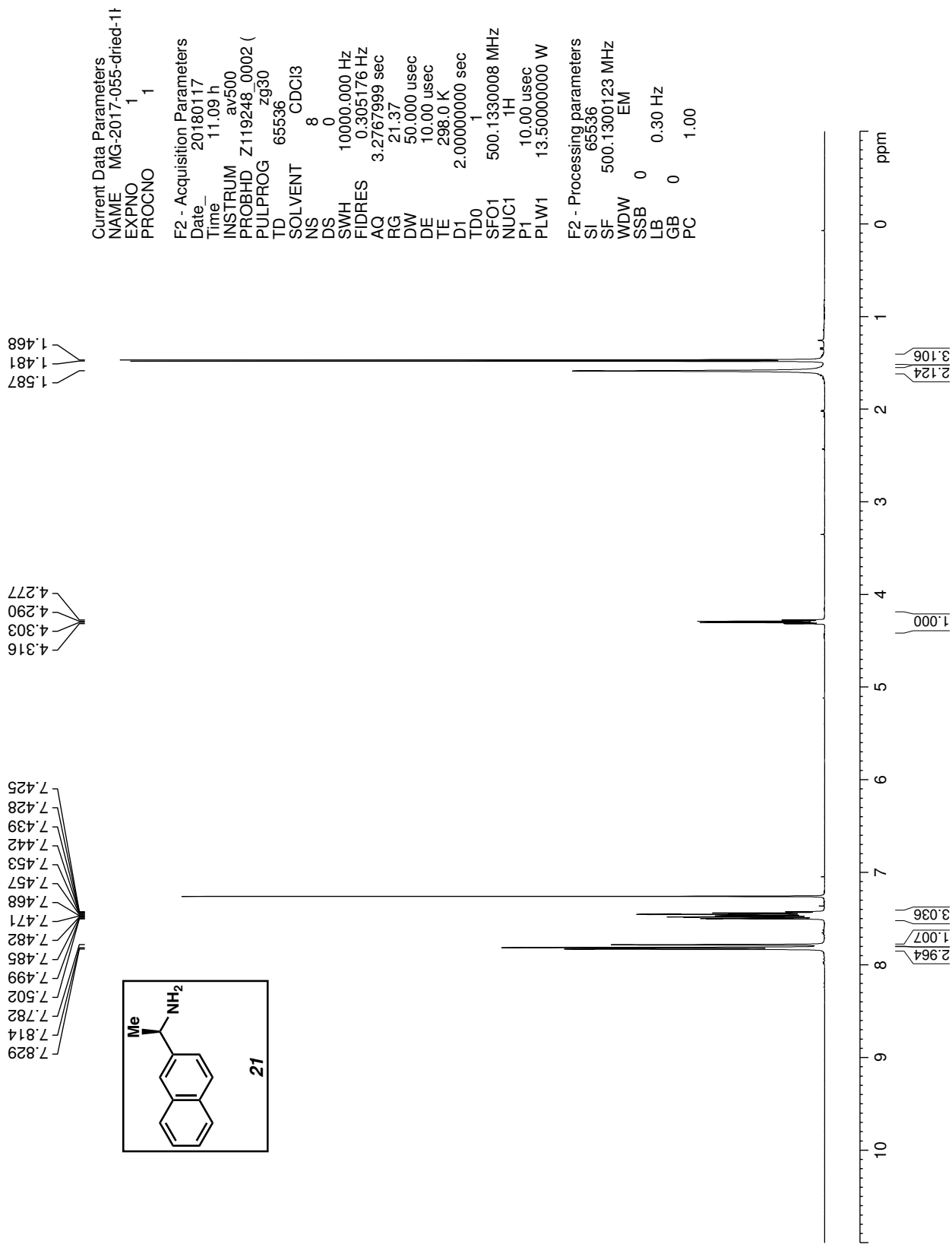


Figure S9 ^1H NMR (500 MHz, CDCl_3) of compound 21.

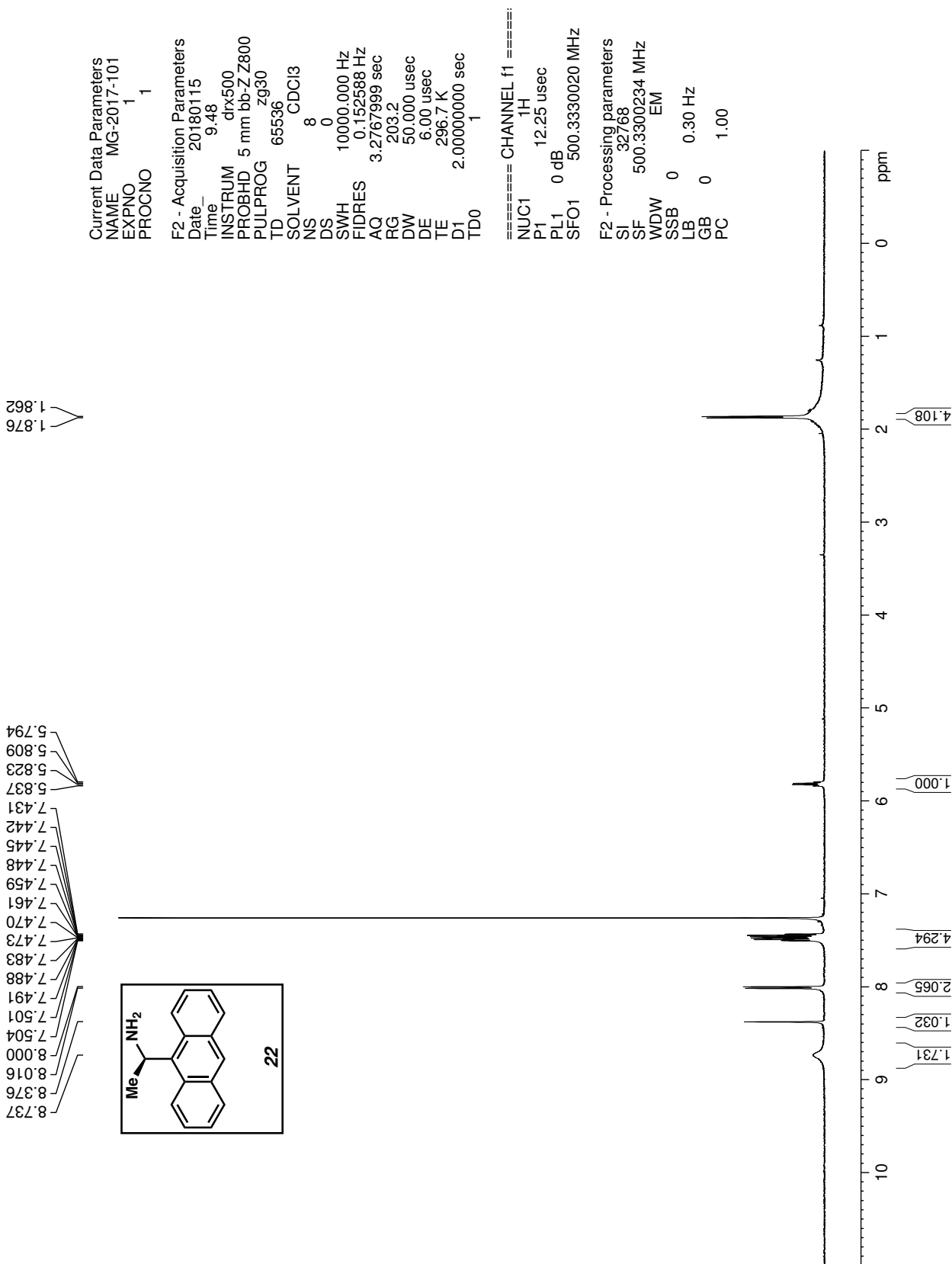


Figure S10 ^1H NMR (500 MHz, CDCl_3) of compound 22.

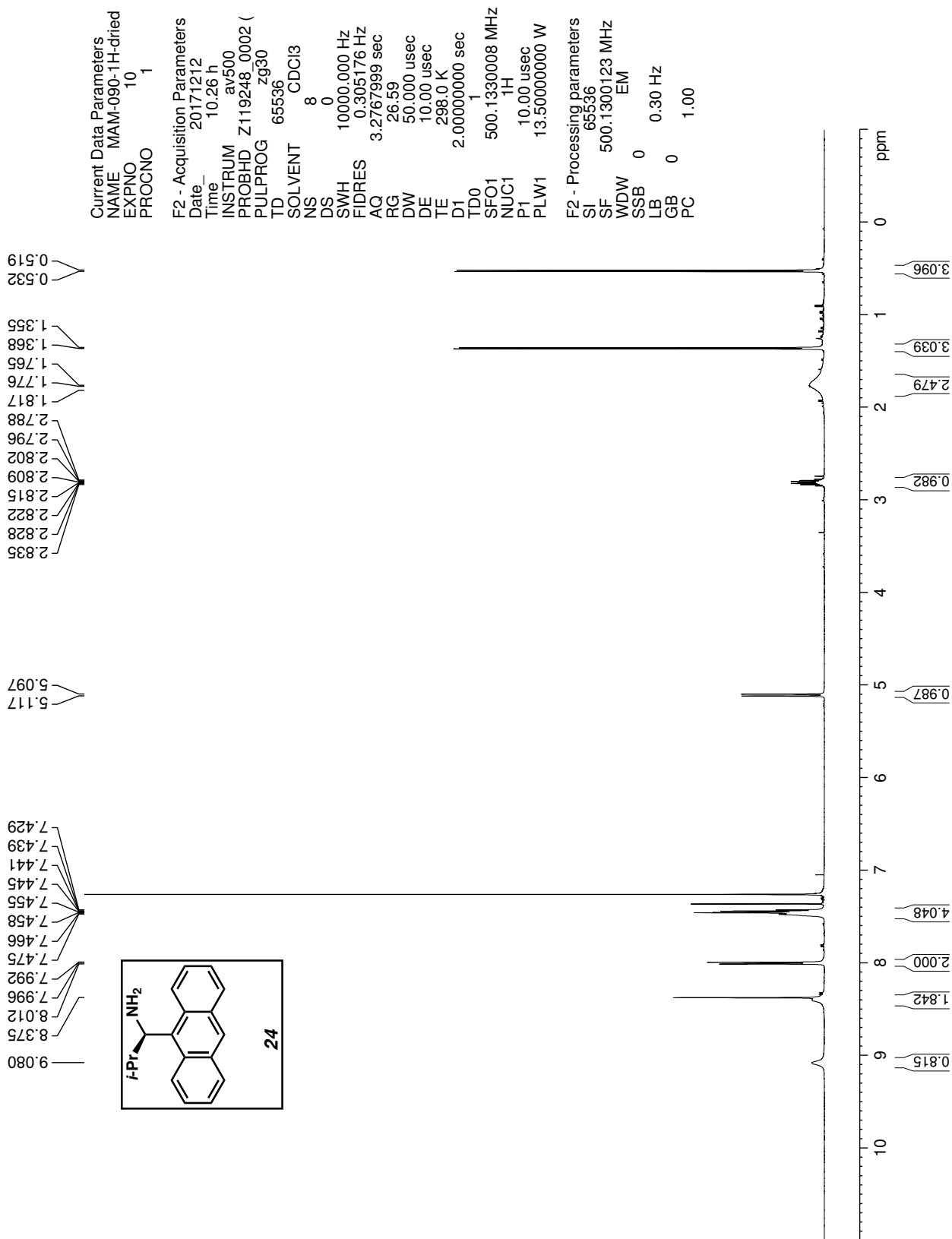


Figure S12 ^1H NMR (500 MHz, CDCl_3) of compound 24.

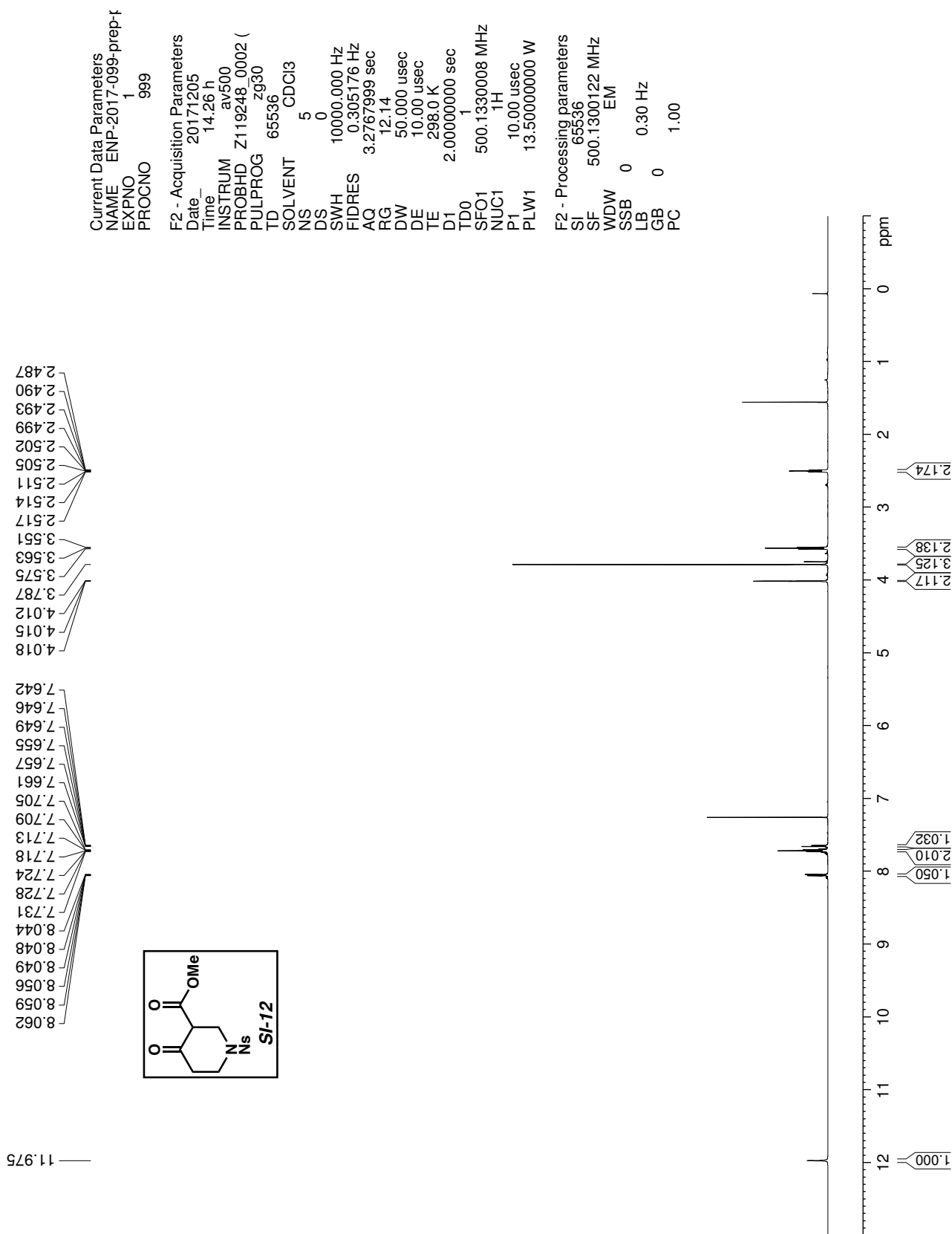


Figure S13 ¹H NMR (500 MHz, CDCl₃) of compound SI-12.

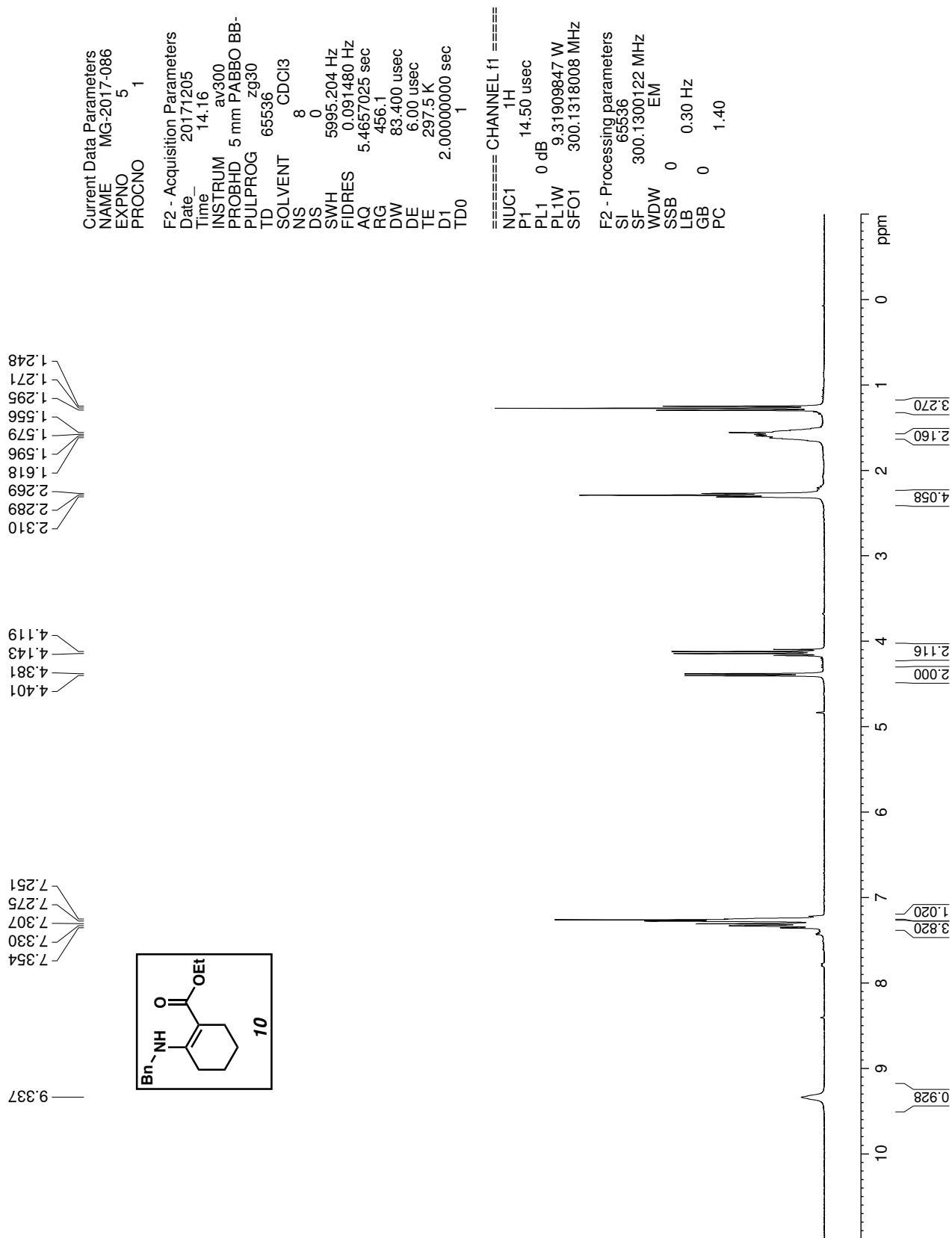


Figure S14 ^1H NMR (300 MHz, CDCl_3) of compound **10**.

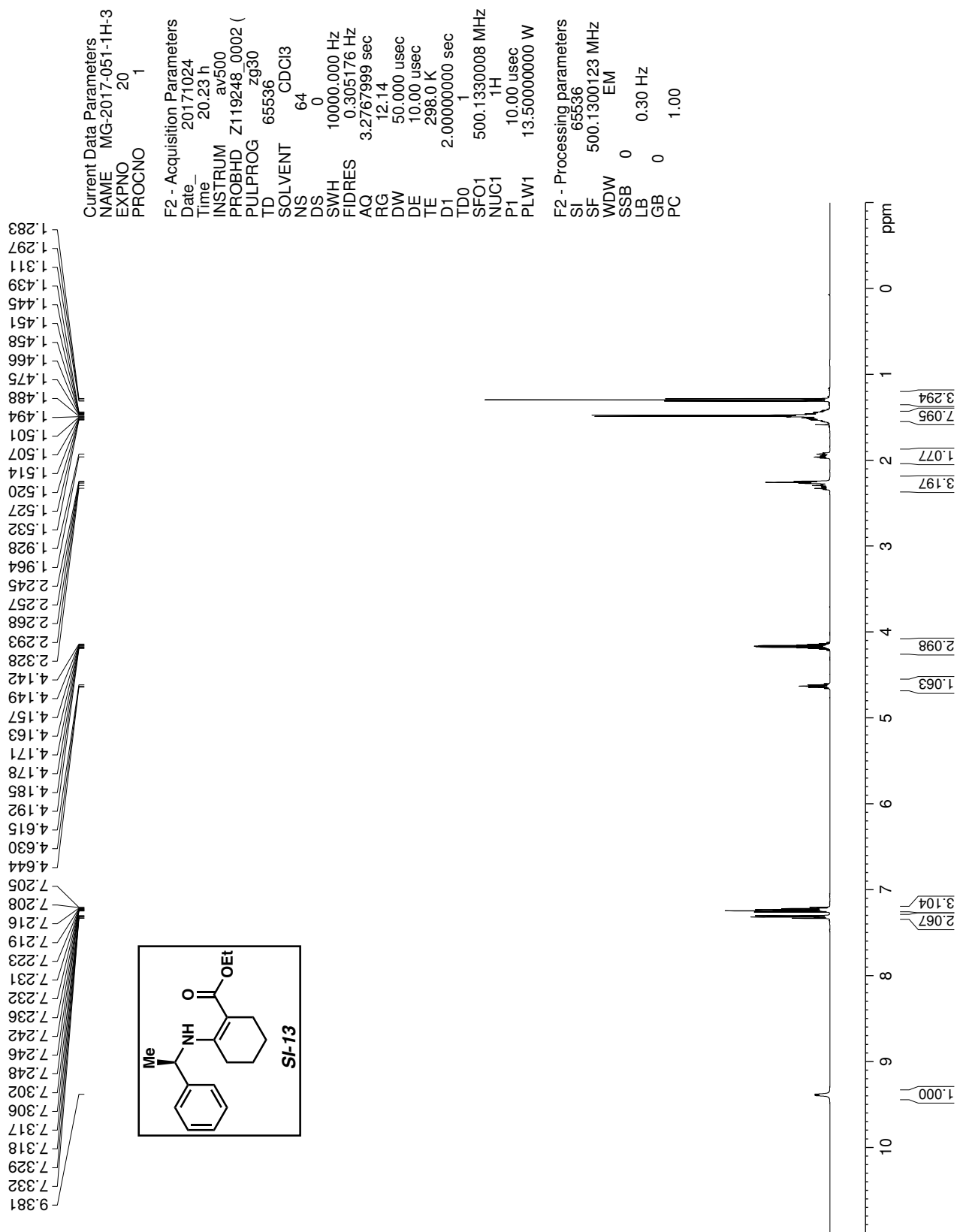


Figure S15 ¹H NMR (500 MHz, CDCl₃) of compound SI-13.

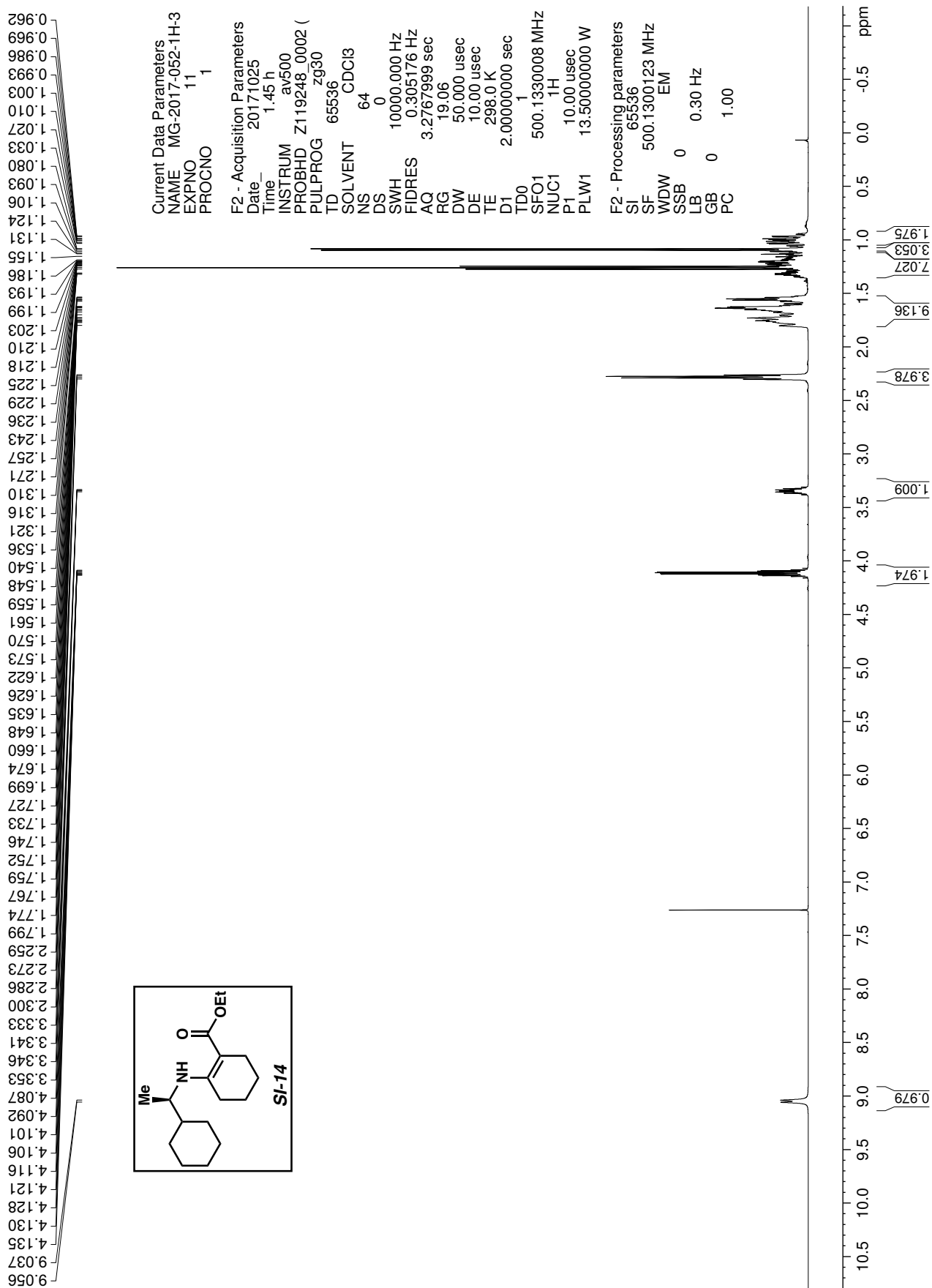


Figure S16 ^1H NMR (500 MHz, CDCl_3) of compound SI-14.

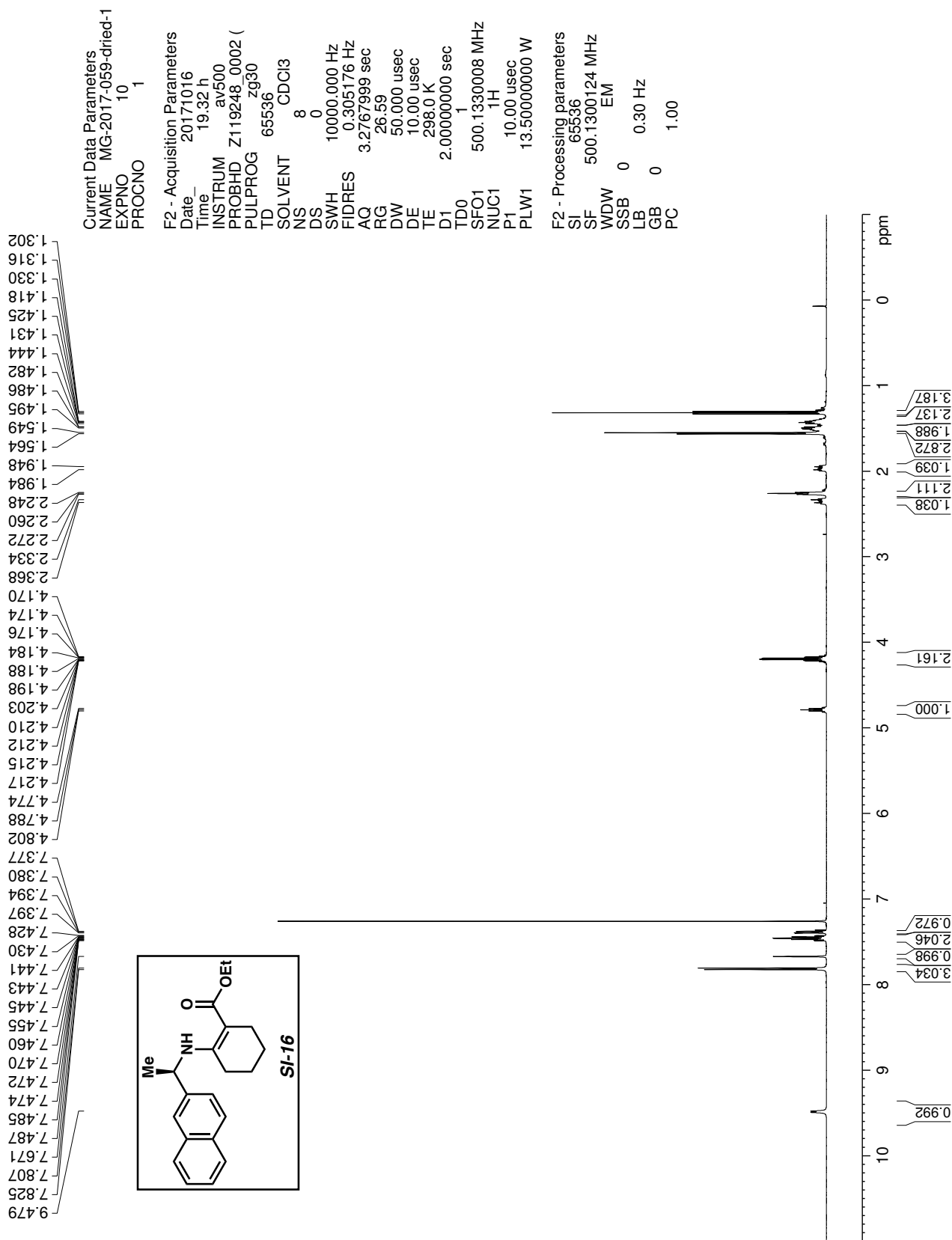


Figure S18 ^1H NMR (500 MHz, CDCl_3) of compound SI-16.

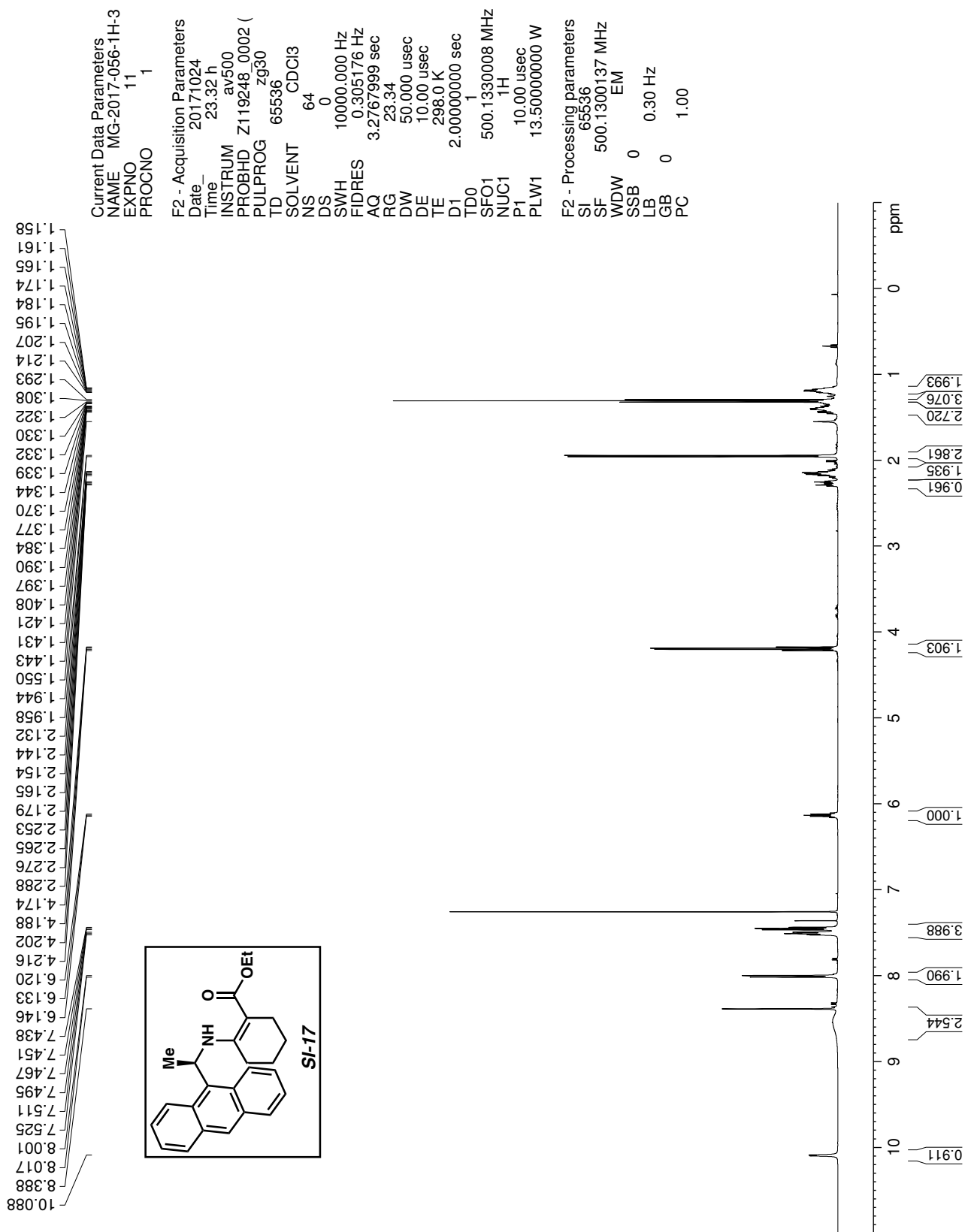


Figure S19 ^1H NMR (500 MHz, CDCl_3) of compound SI-17.

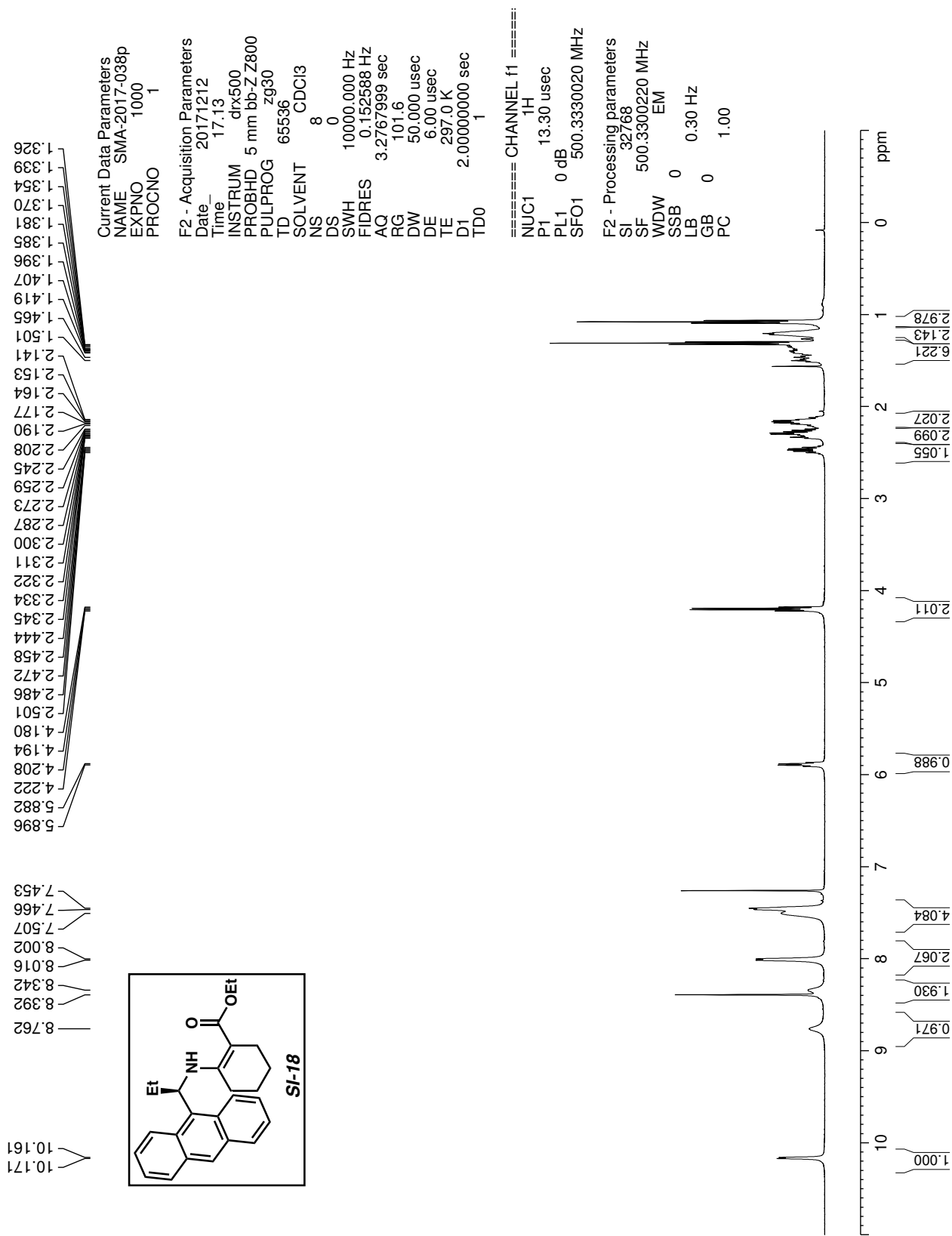


Figure S20 ¹H NMR (500 MHz, CDCl₃) of compound SI-18.

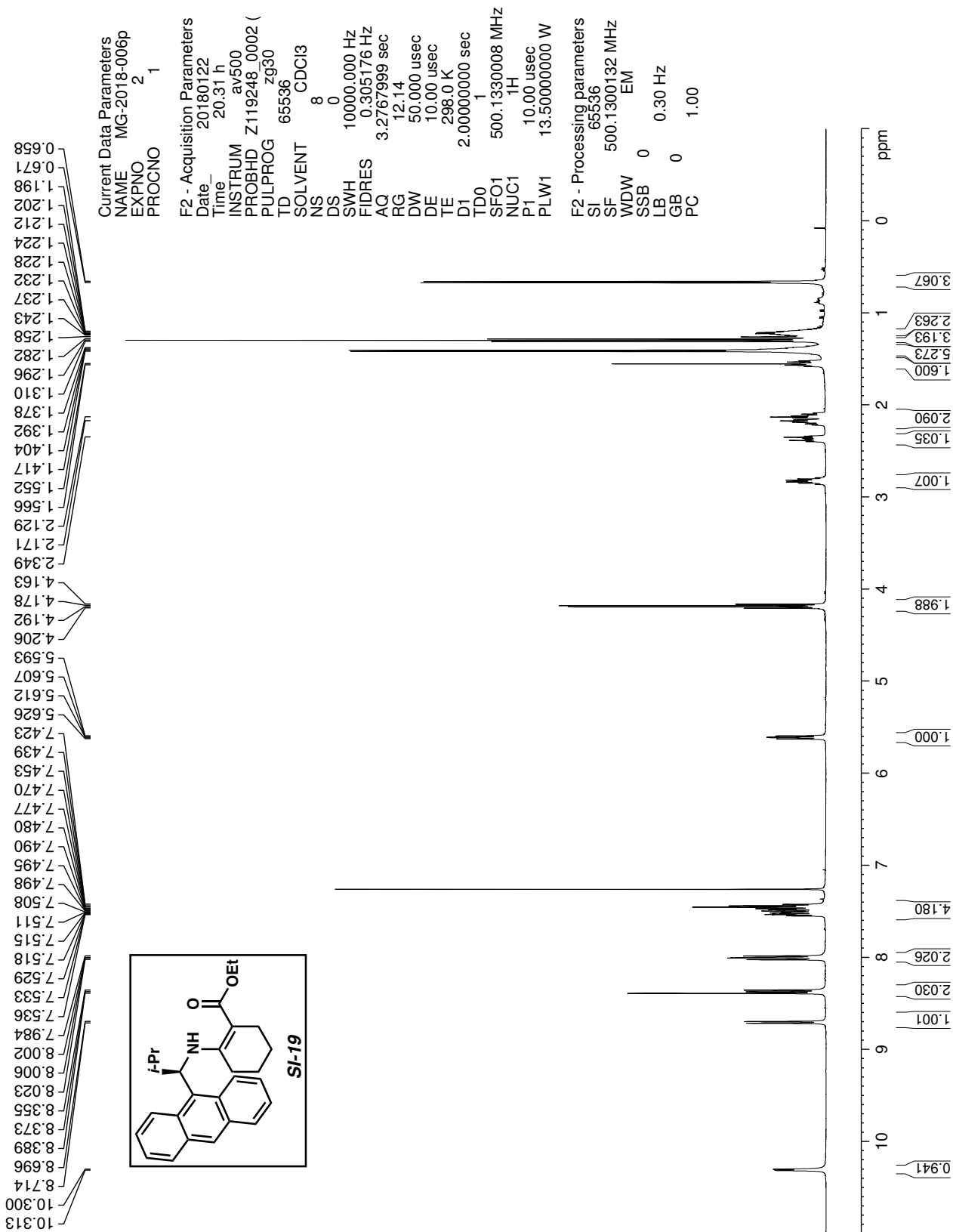


Figure S21 ^1H NMR (500 MHz, CDCl_3) of compound SI-19.

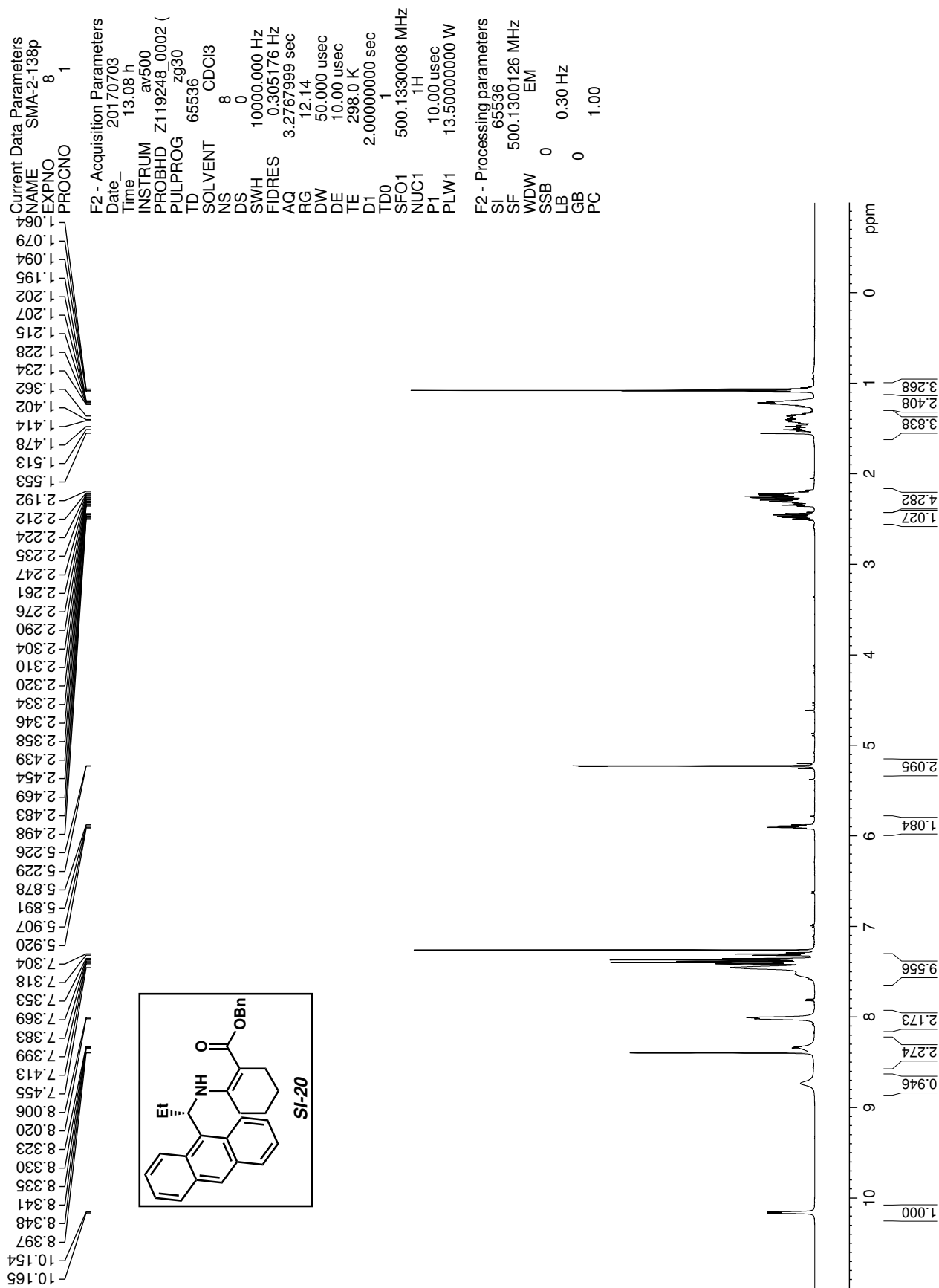


Figure S22 ^1H NMR (500 MHz, CDCl_3) of compound SI-20.

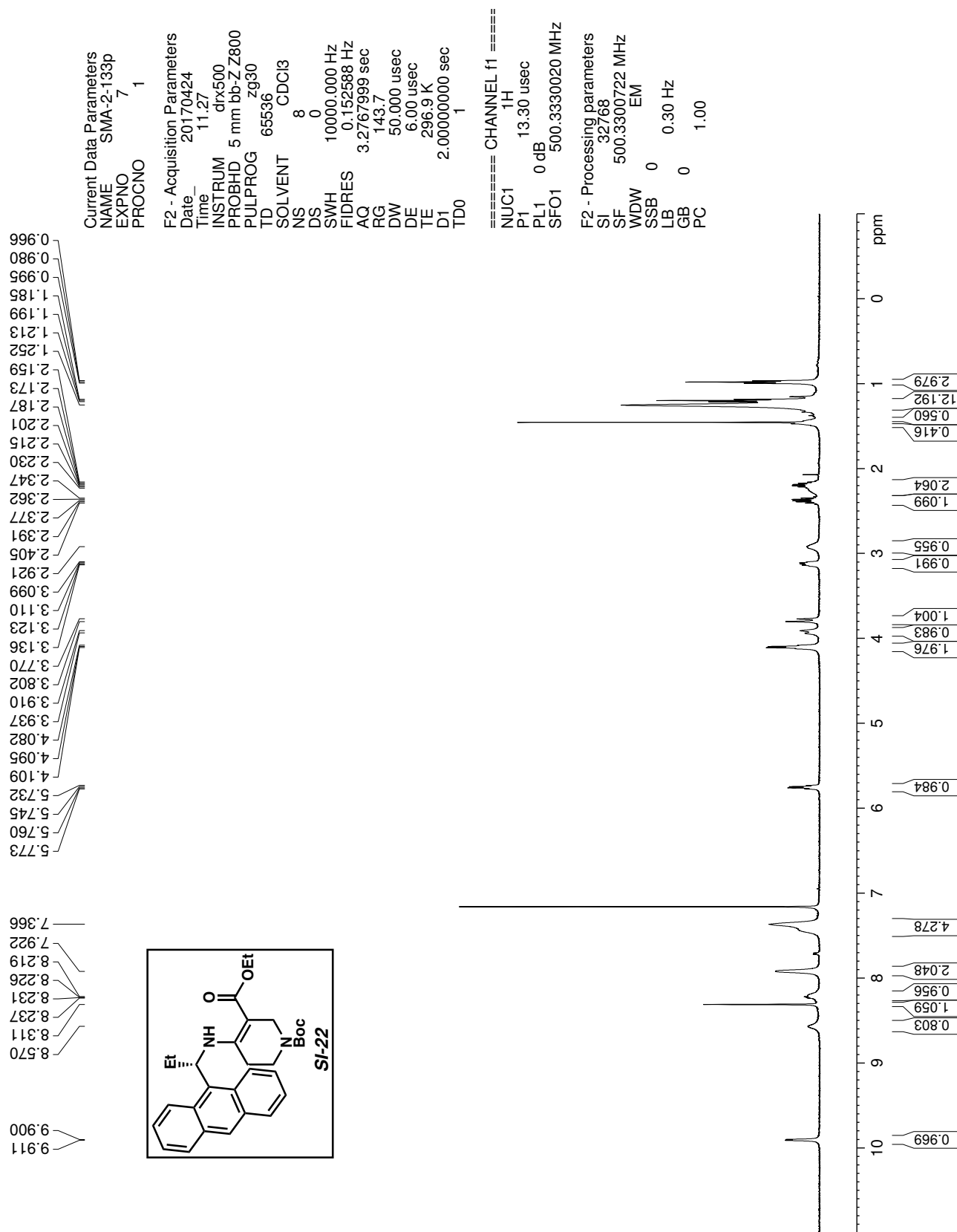


Figure S23 ^1H NMR (500 MHz, CDCl_3) of compound SI-22.

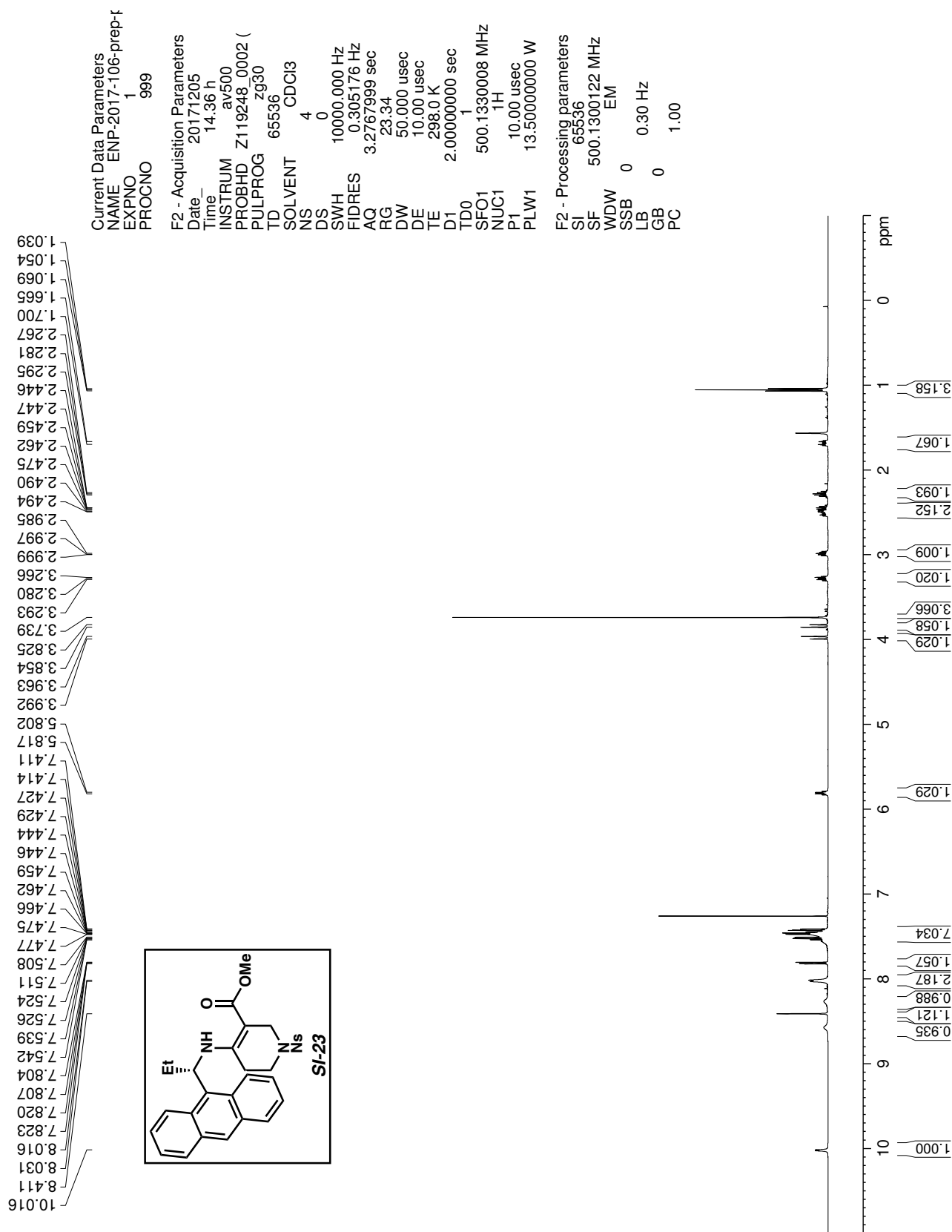


Figure S24 ^1H NMR (500 MHz, CDCl_3) of compound SI-23.

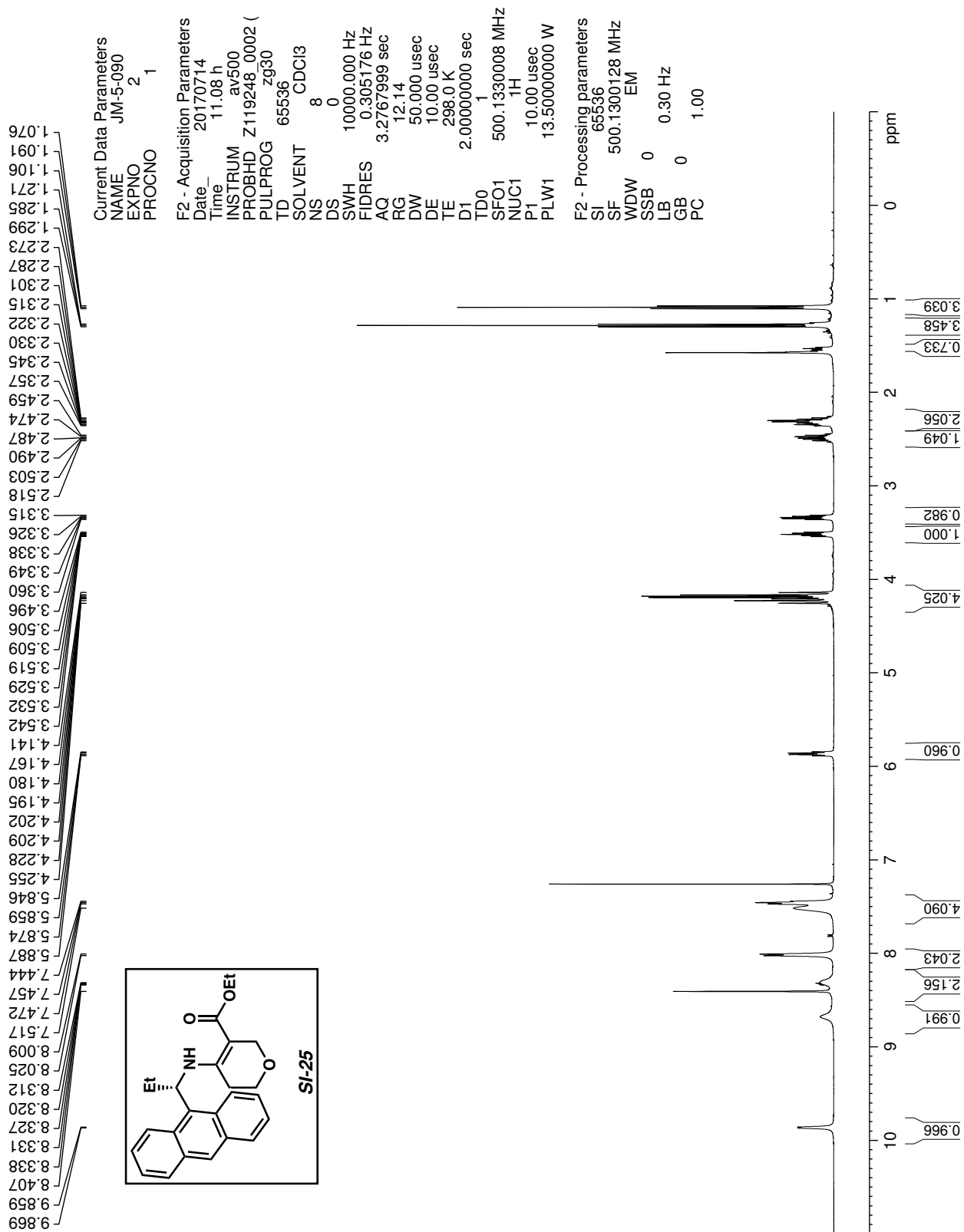


Figure S25 ^1H NMR (500 MHz, CDCl_3) of compound SI-25.

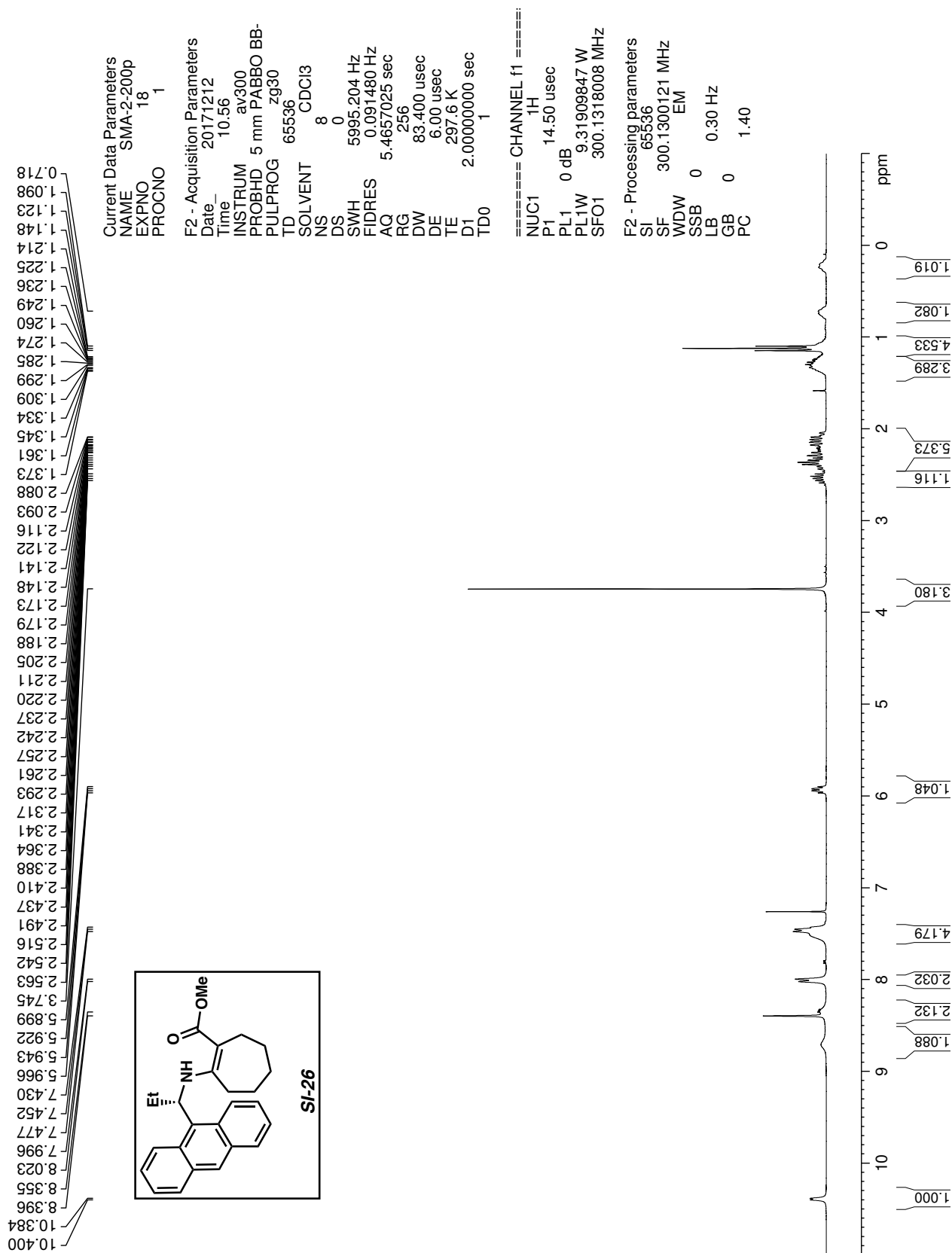


Figure S26 ^1H NMR (300 MHz, CDCl_3) of compound SI-26.

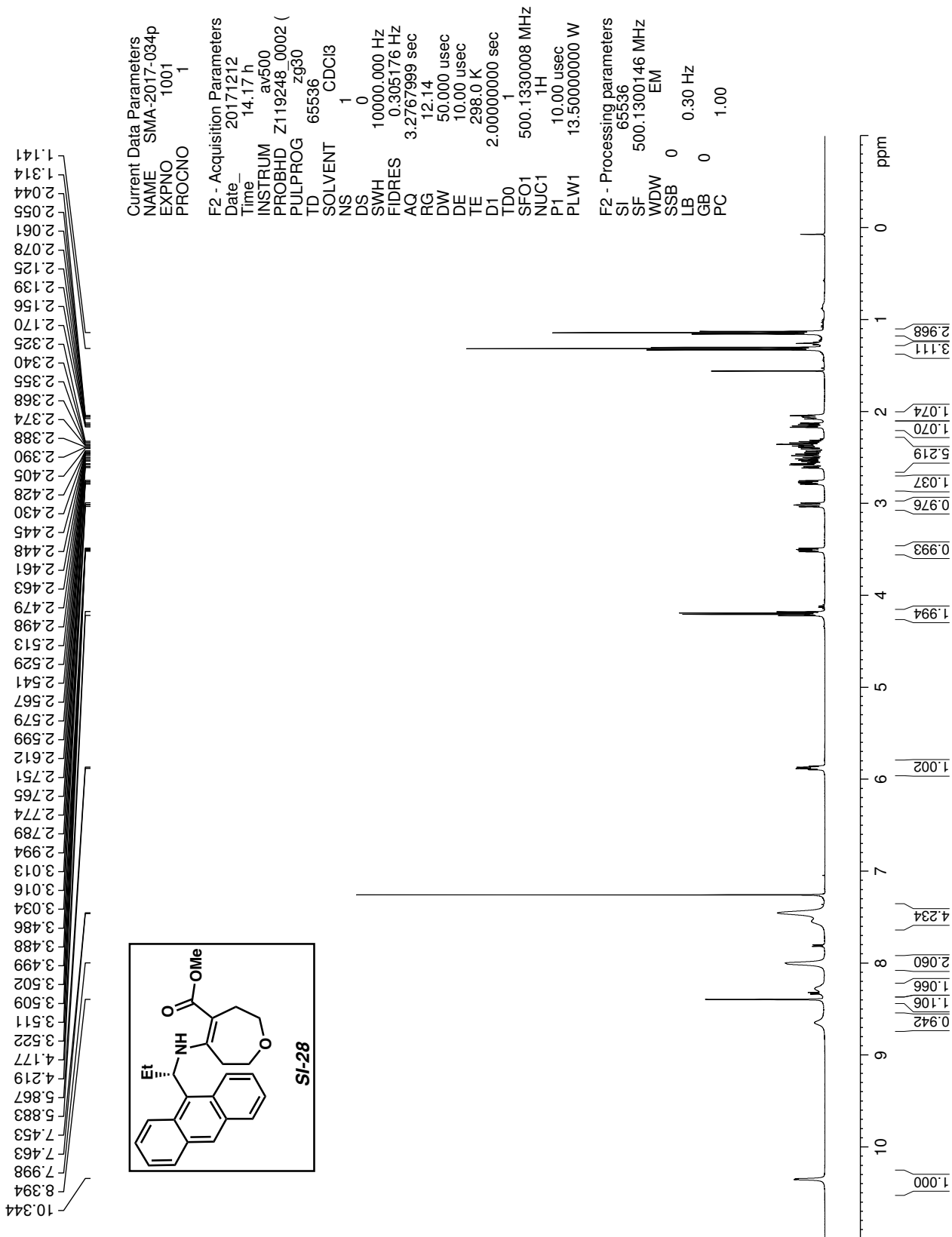


Figure S27 ^1H NMR (500 MHz, CDCl_3) of compound SI-28.

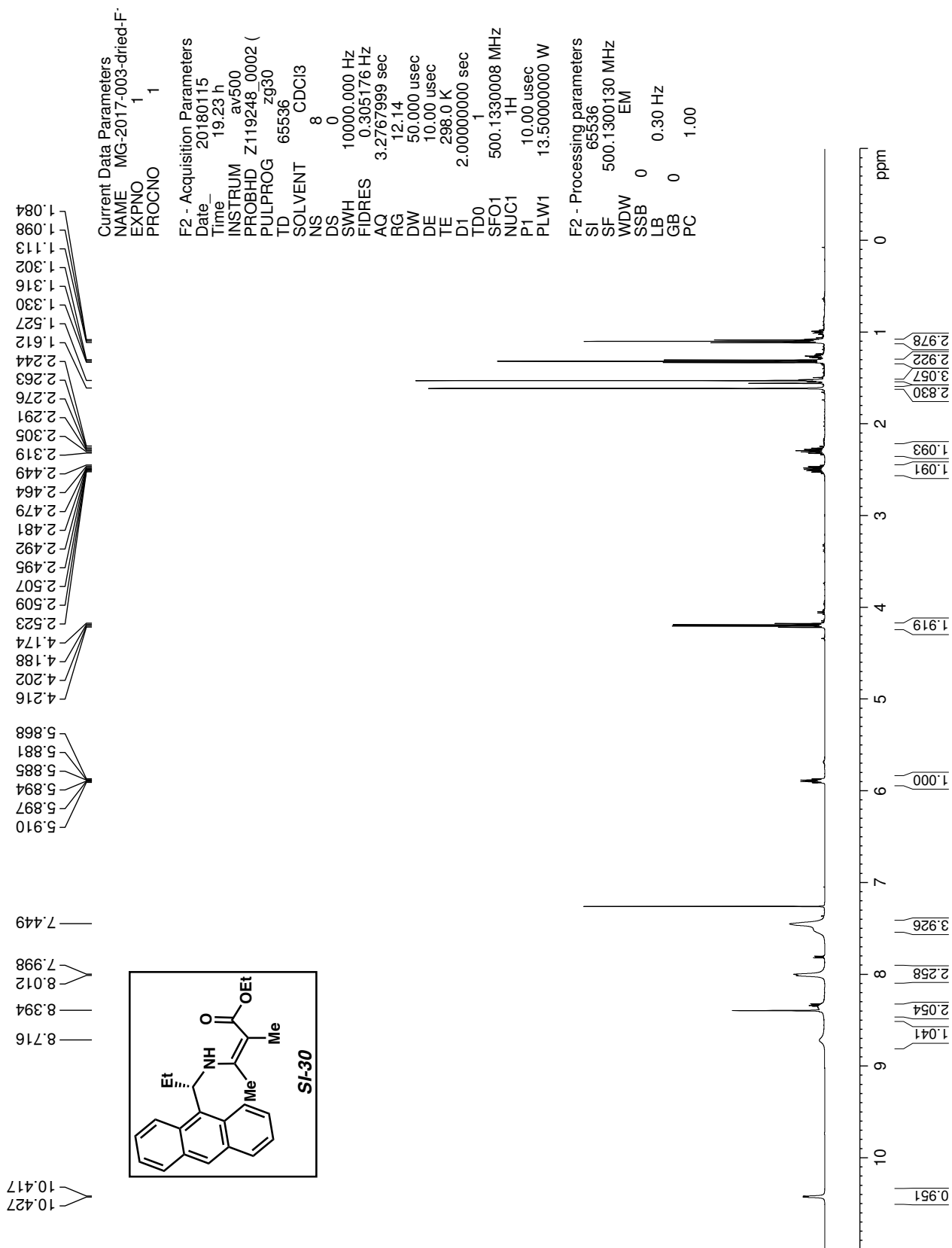


Figure S28 ^1H NMR (500 MHz, CDCl_3) of compound SI-30.

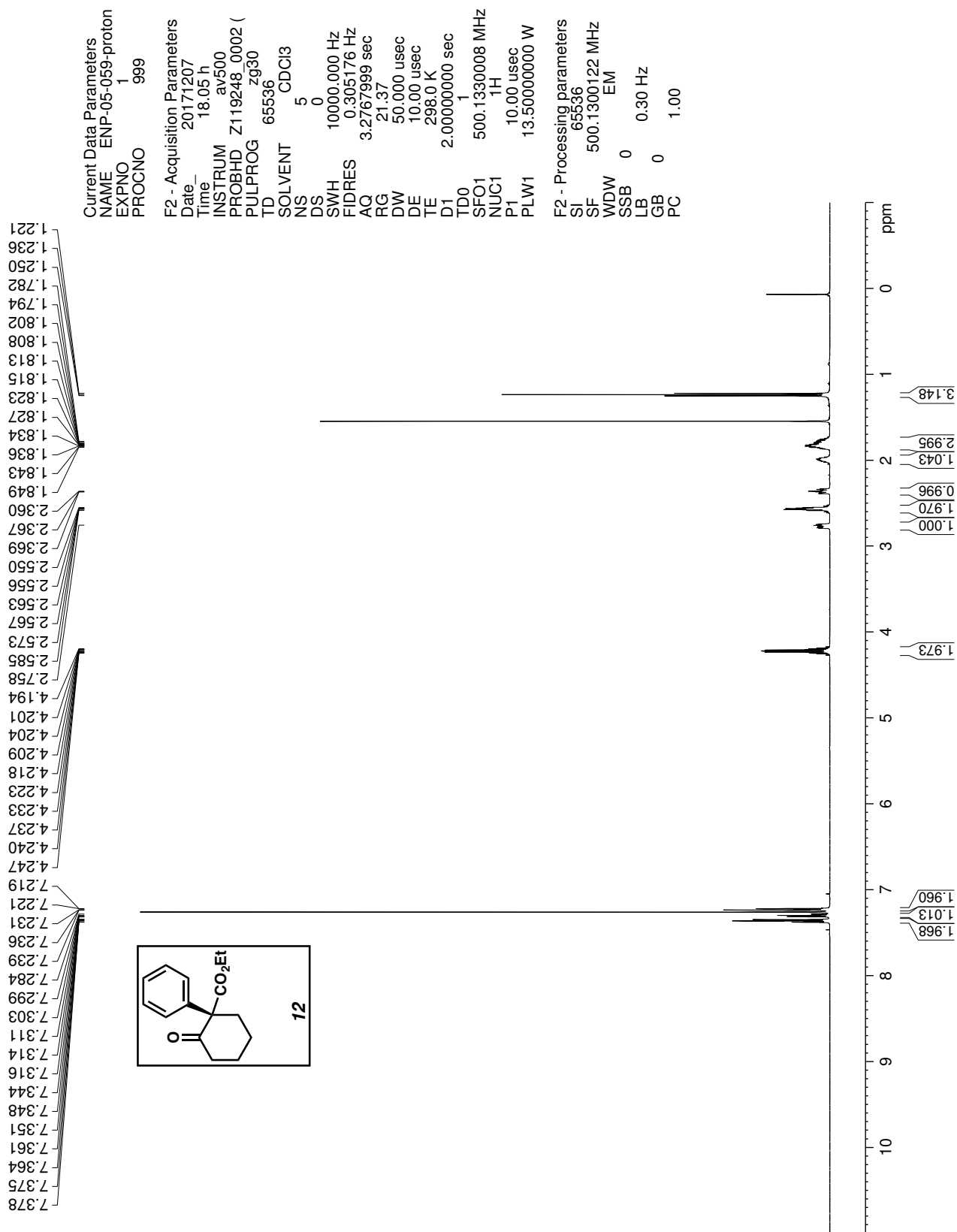


Figure S29 ^1H NMR (500 MHz, CDCl_3) of compound 12.

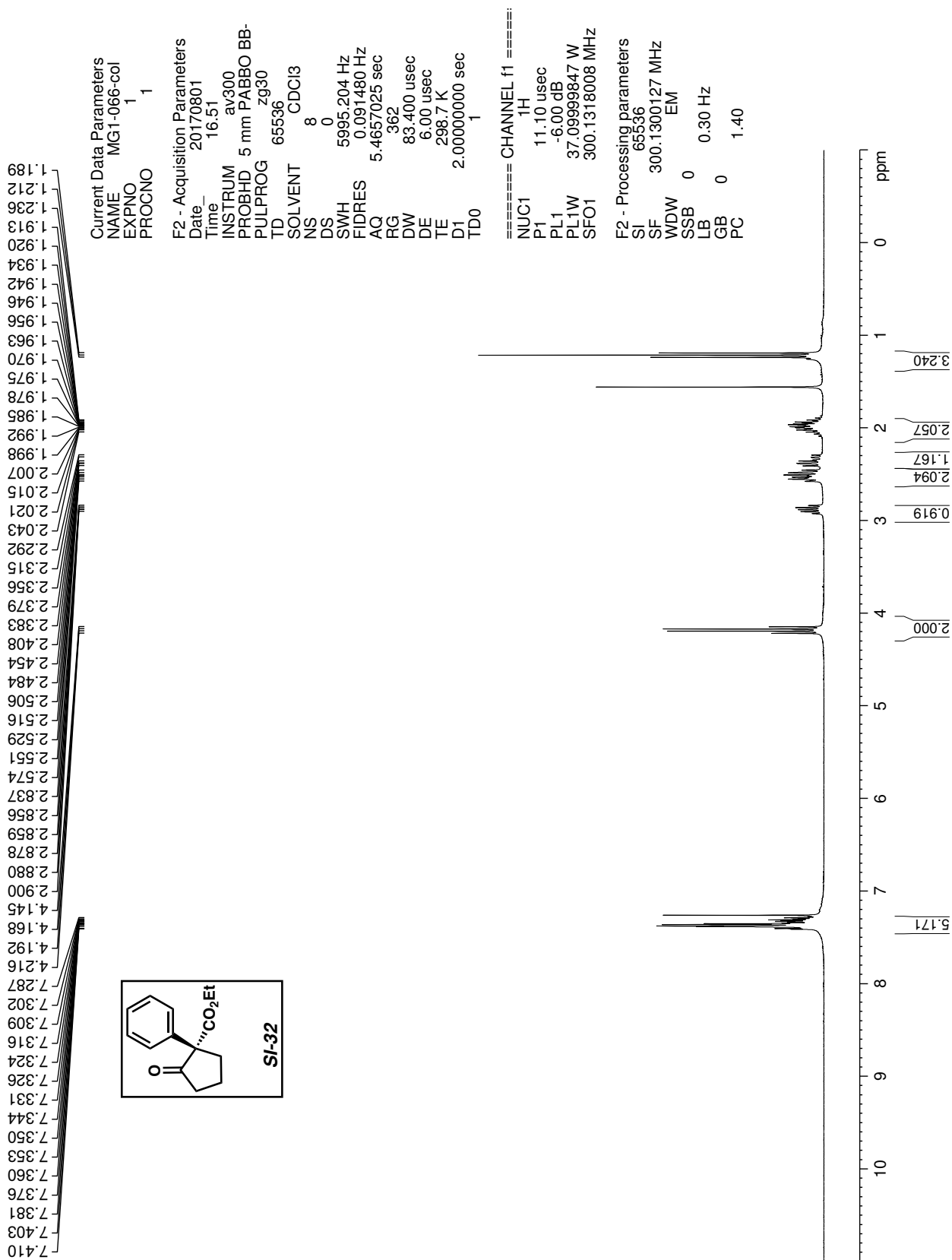


Figure S30 ^1H NMR (300 MHz, CDCl_3) of compound SI-32.

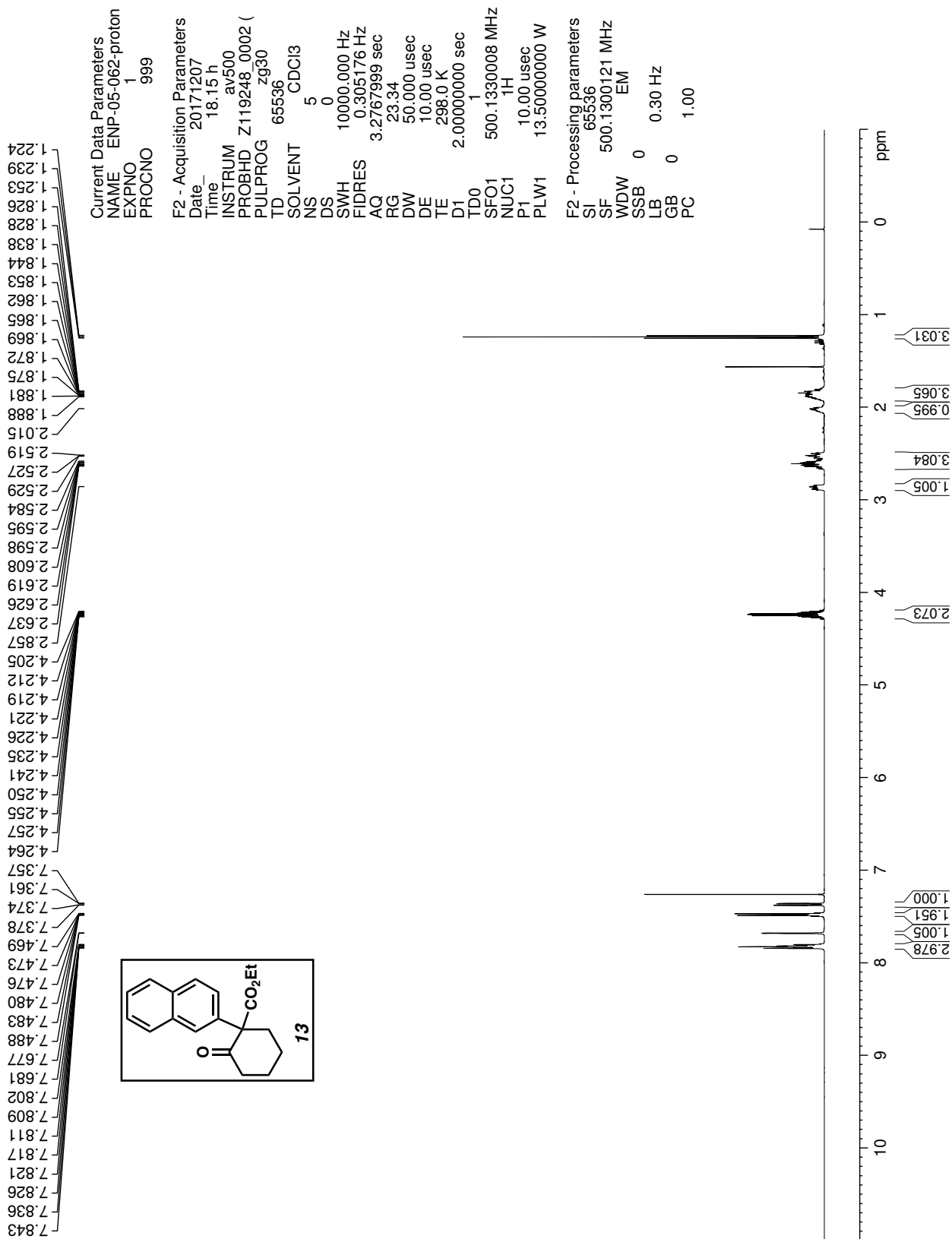


Figure S31 ^1H NMR (500 MHz, CDCl_3) of compound 13.

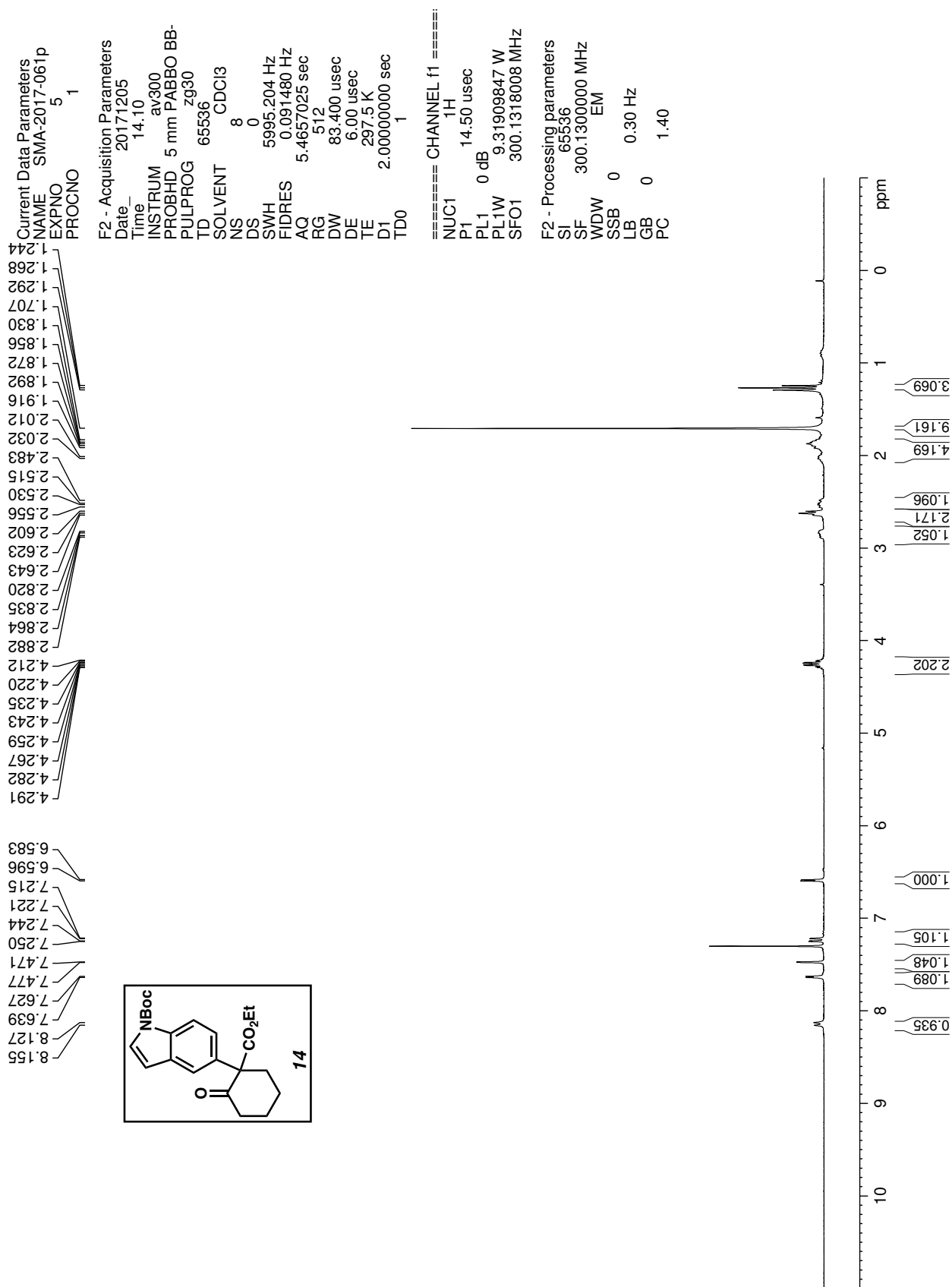


Figure S32 ^1H NMR (300 MHz, CDCl_3) of compound 14.

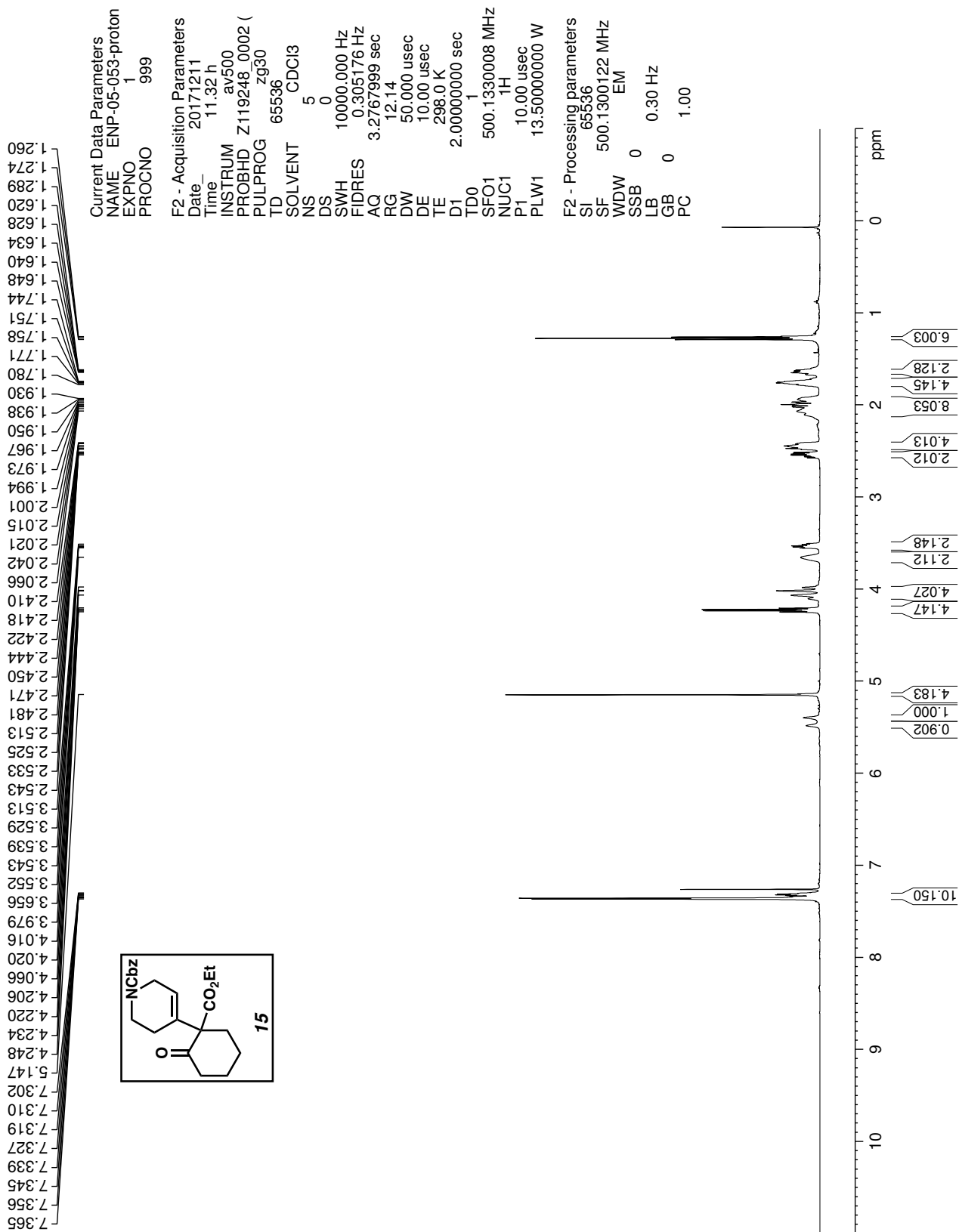


Figure S33 ^1H NMR (500 MHz, CDCl_3) of compound 15.

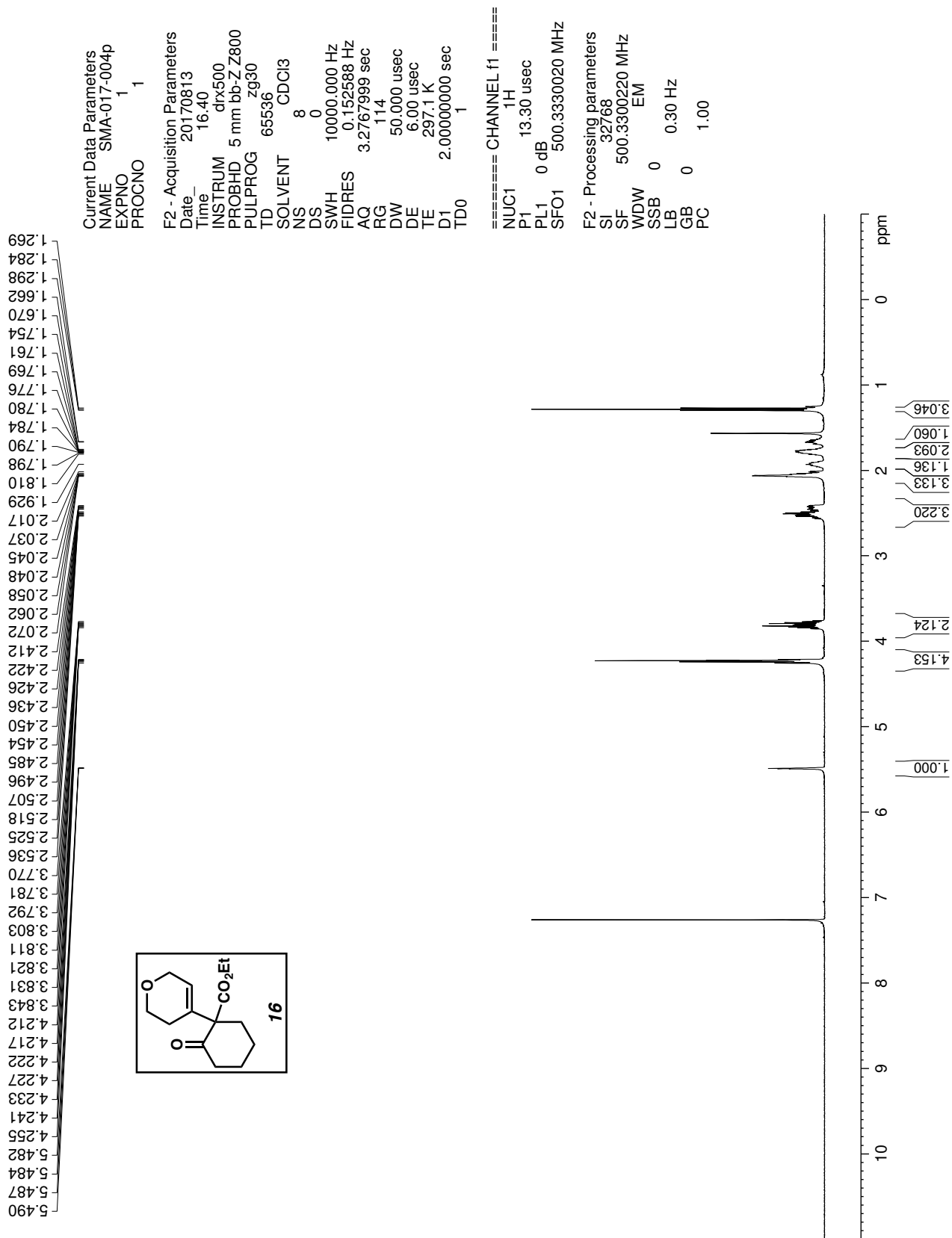


Figure S34 ^1H NMR (500 MHz, CDCl_3) of compound 16.

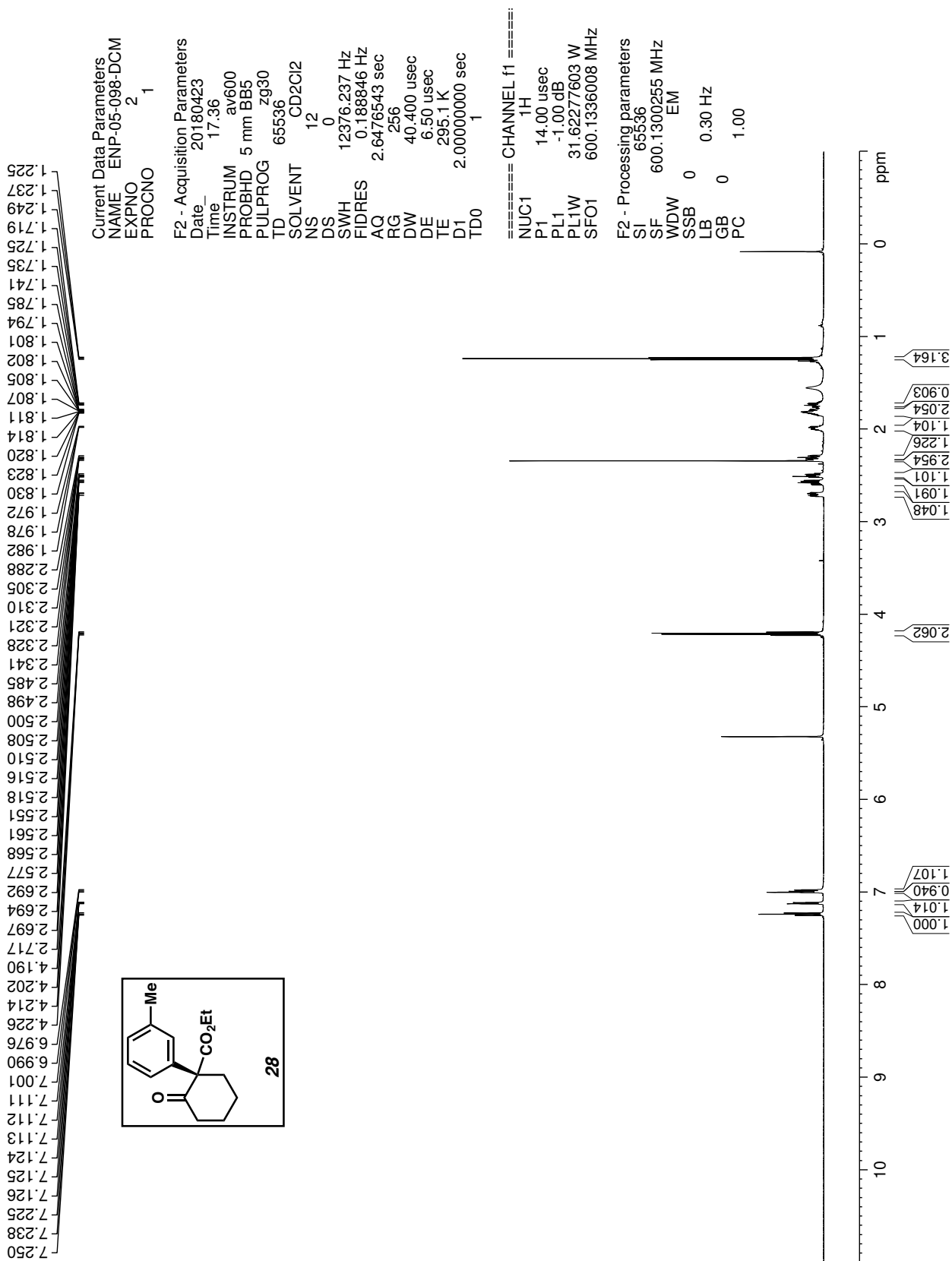


Figure S35 ^1H NMR (600 MHz, CD_2Cl_2) of compound 28.

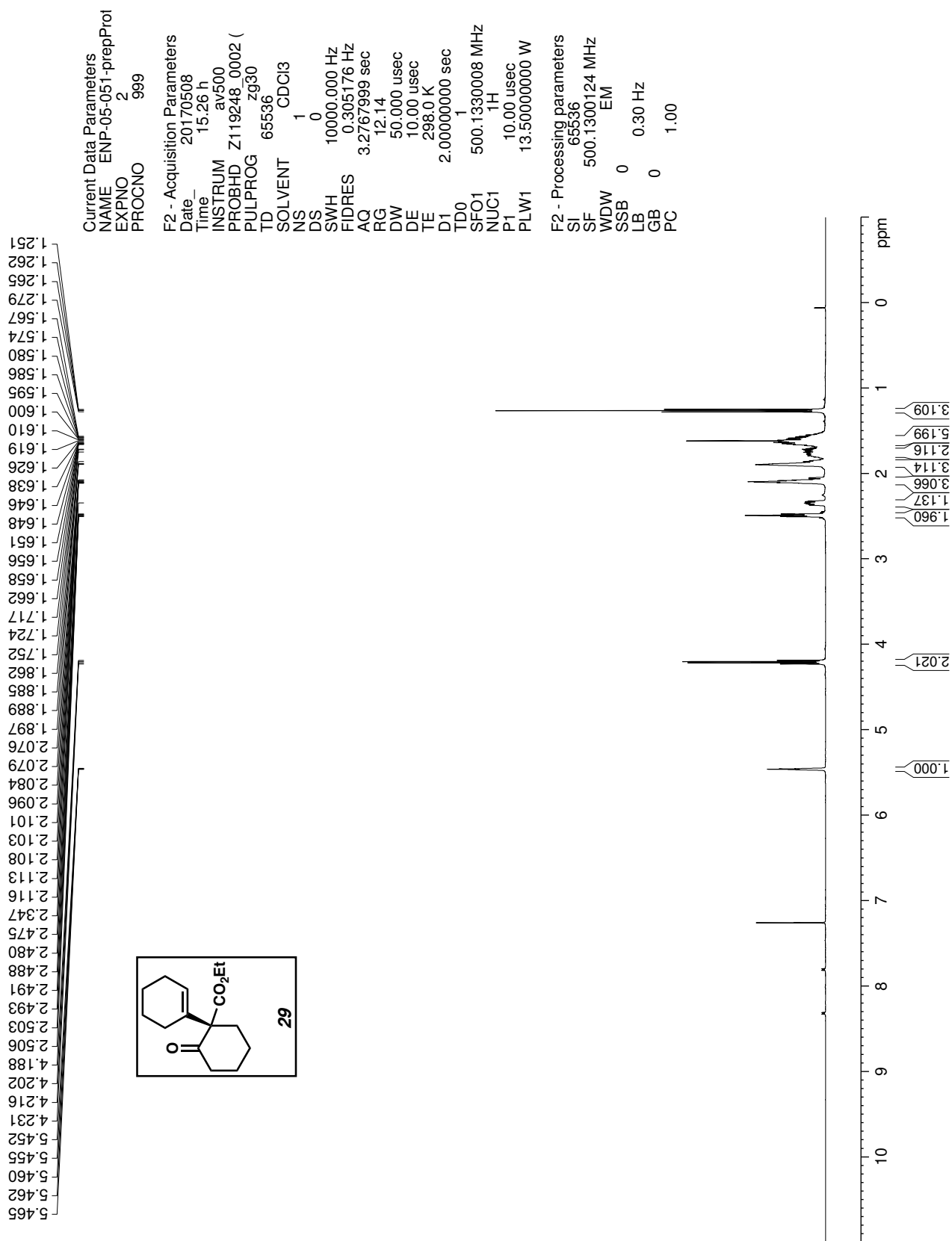


Figure S36 ^1H NMR (500 MHz, CDCl_3) of compound 29.

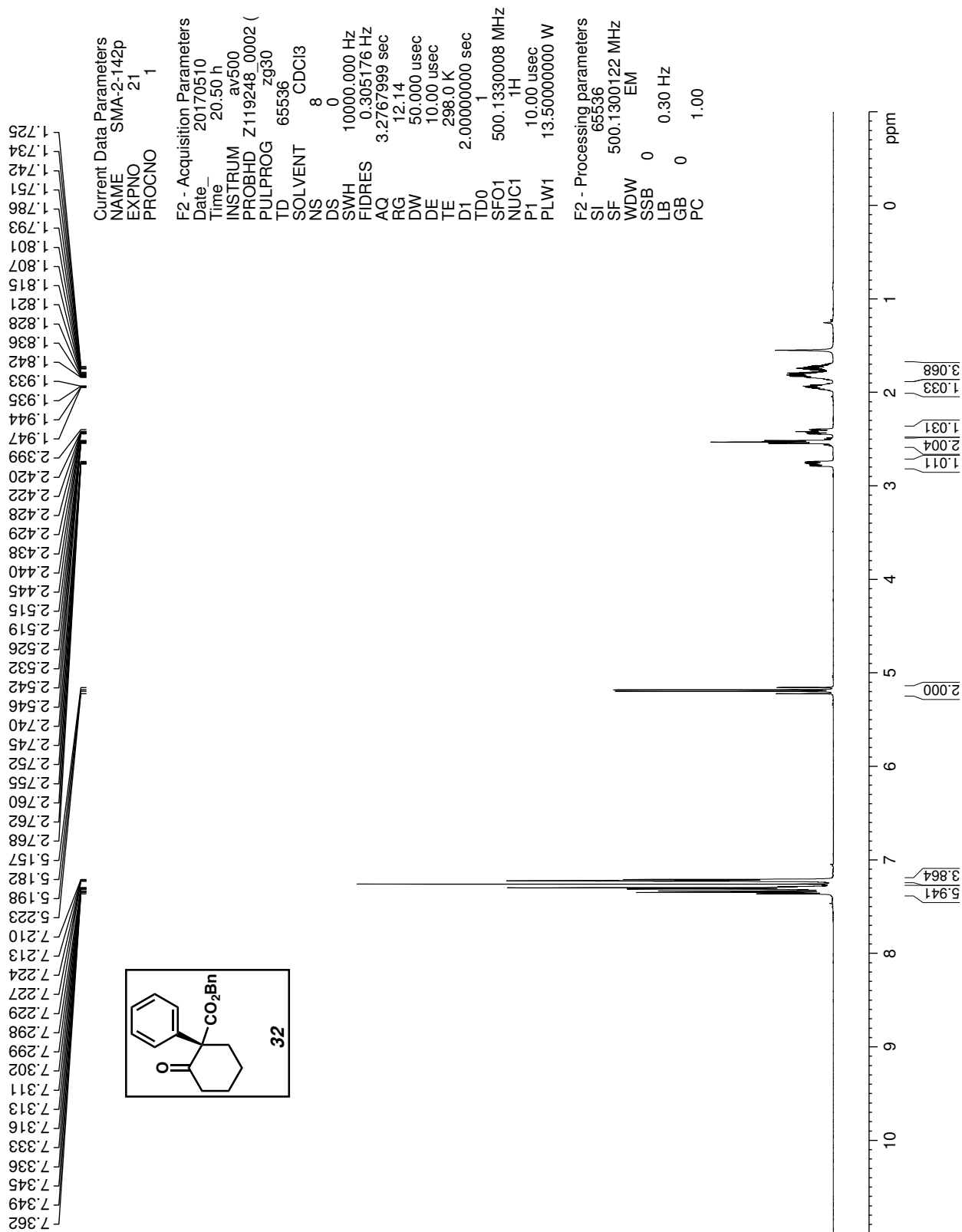


Figure S37 ^1H NMR (500 MHz, CDCl_3) of compound 32.

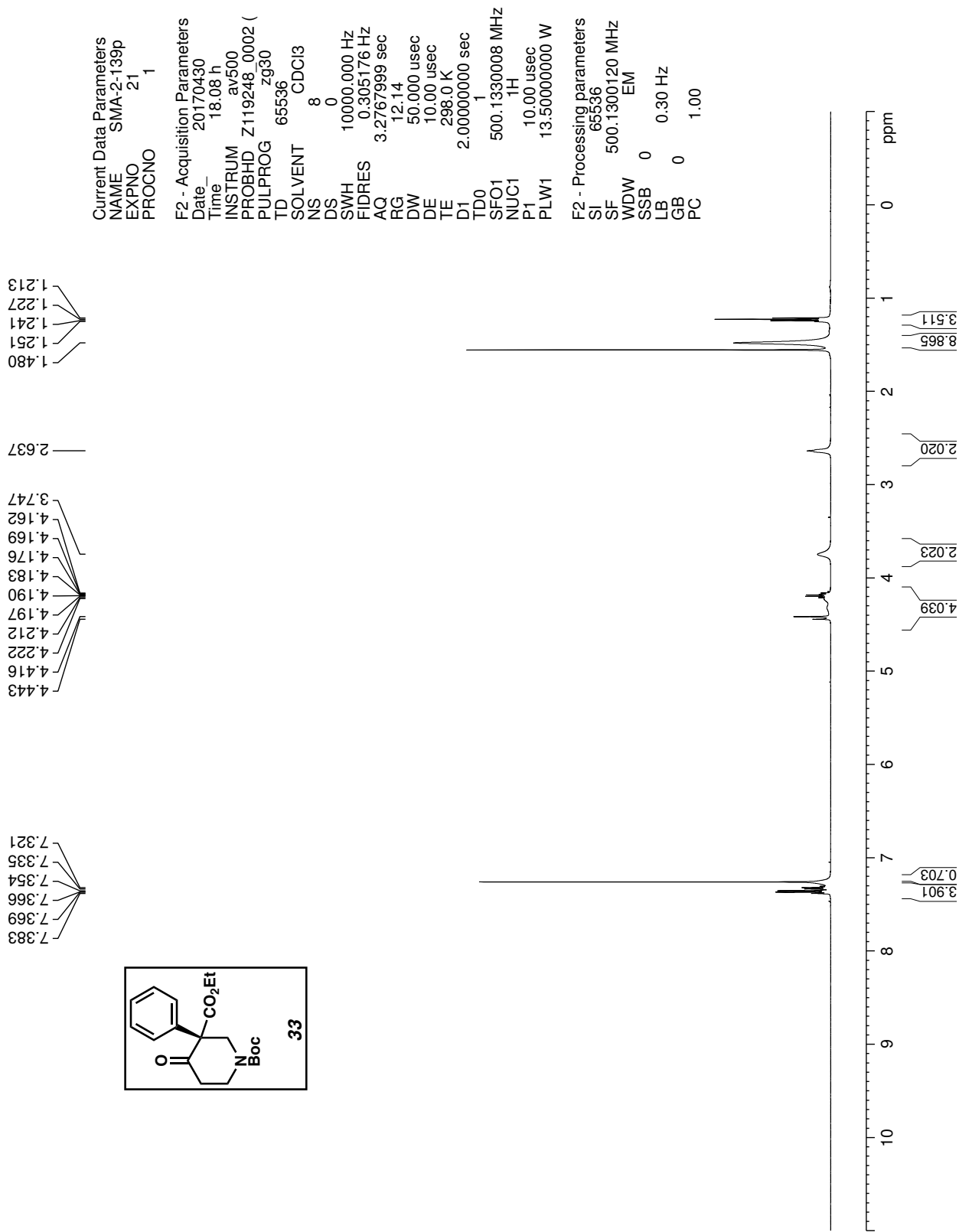


Figure S38 ^1H NMR (500 MHz, CDCl_3) of compound **33**.

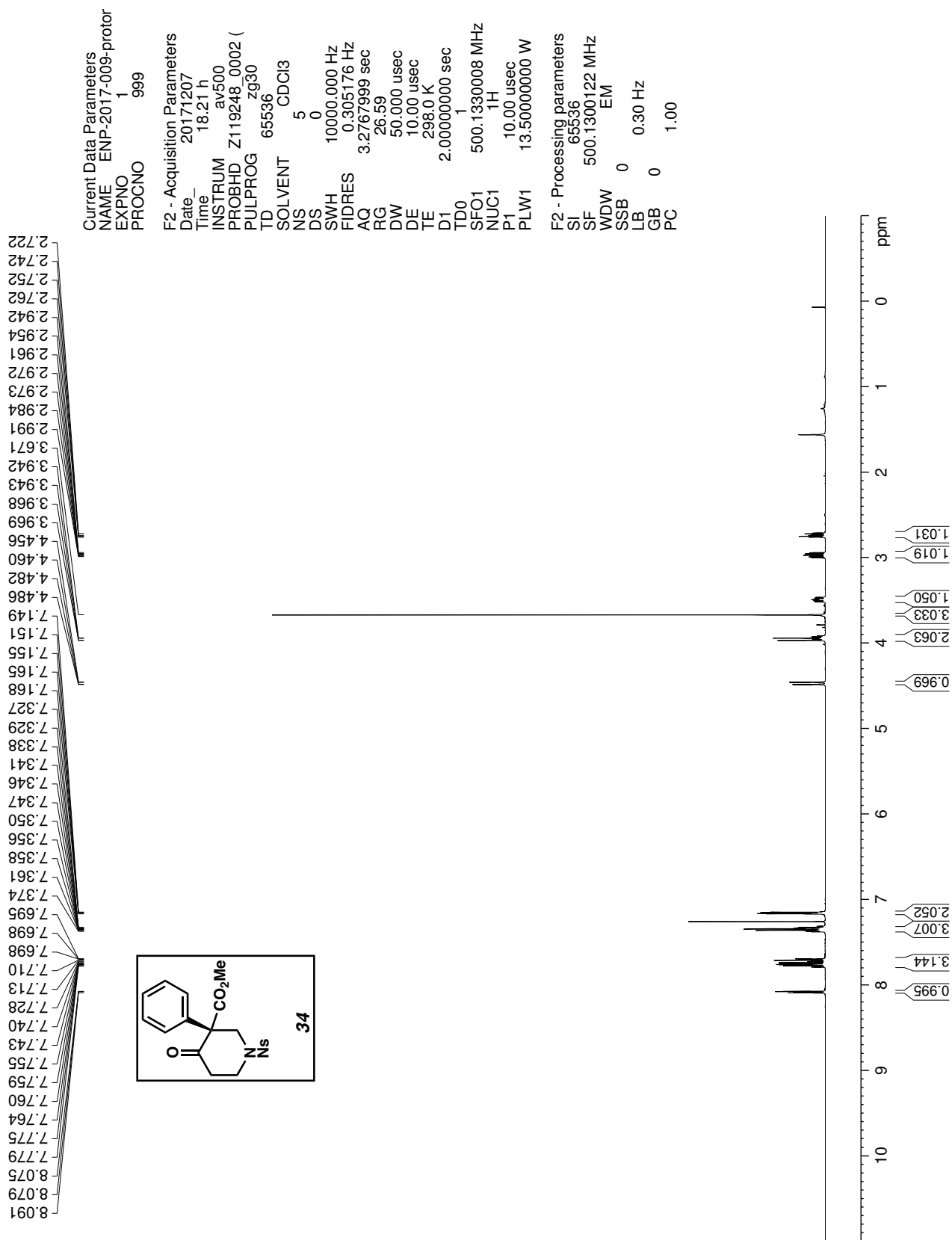


Figure S39 ¹H NMR (500 MHz, CDCl₃) of compound 34.

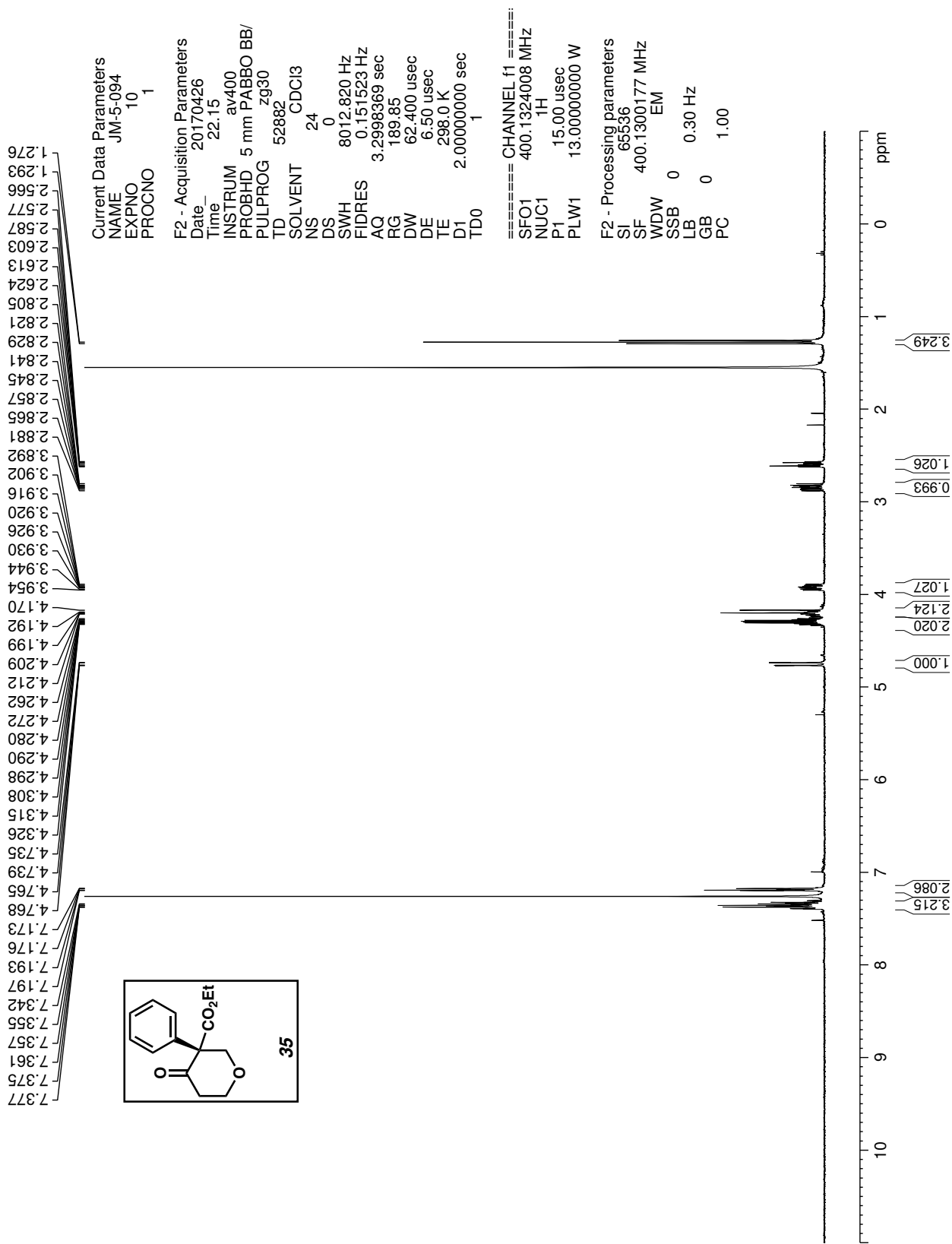


Figure S40 ^1H NMR (400 MHz, CDCl_3) of compound 35.

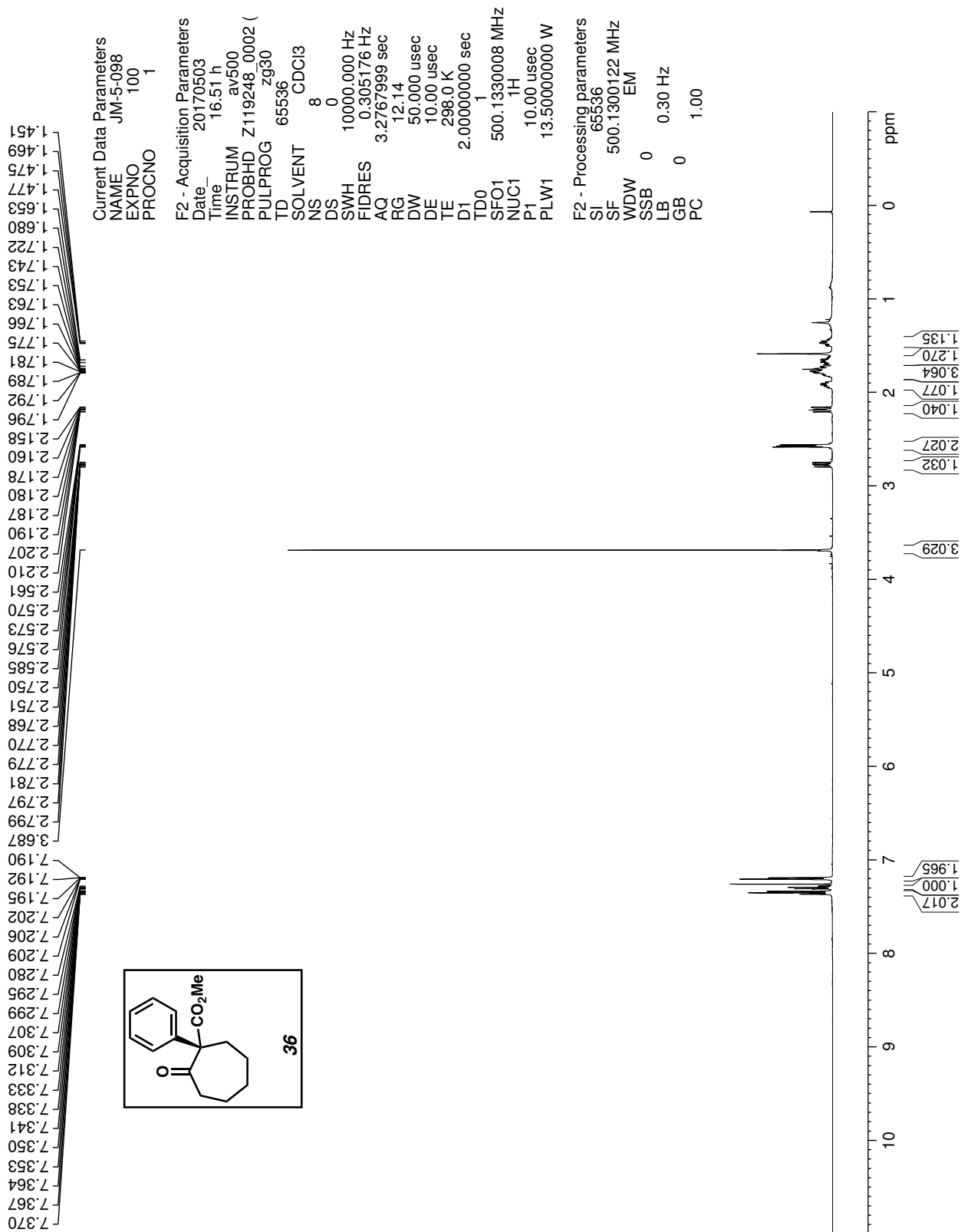


Figure S41 ^1H NMR (500 MHz, CDCl_3) of compound 36.

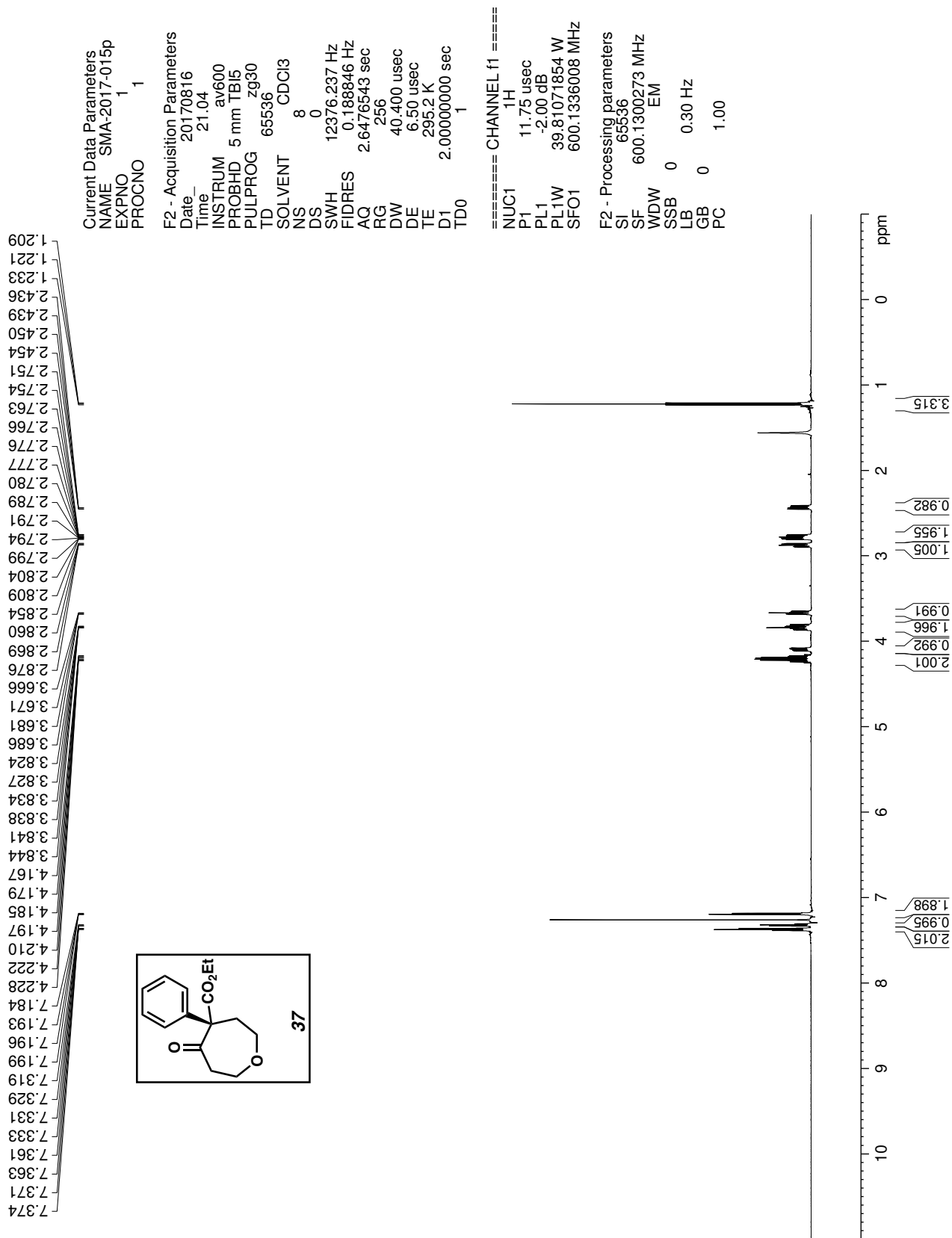


Figure S42 ^1H NMR (600 MHz, CDCl_3) of compound 37.

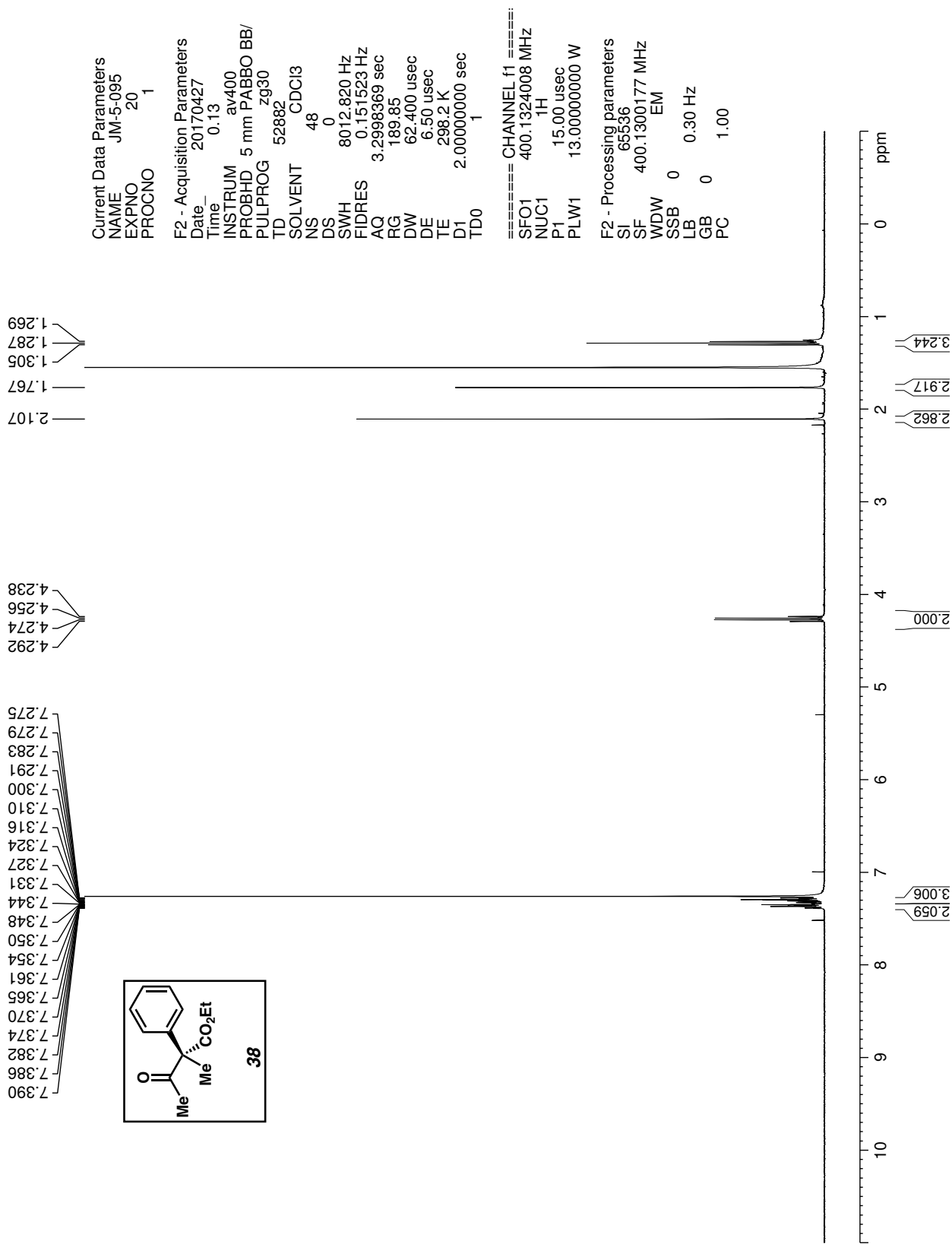


Figure S43 ^1H NMR (400 MHz, CDCl_3) of compound 38.

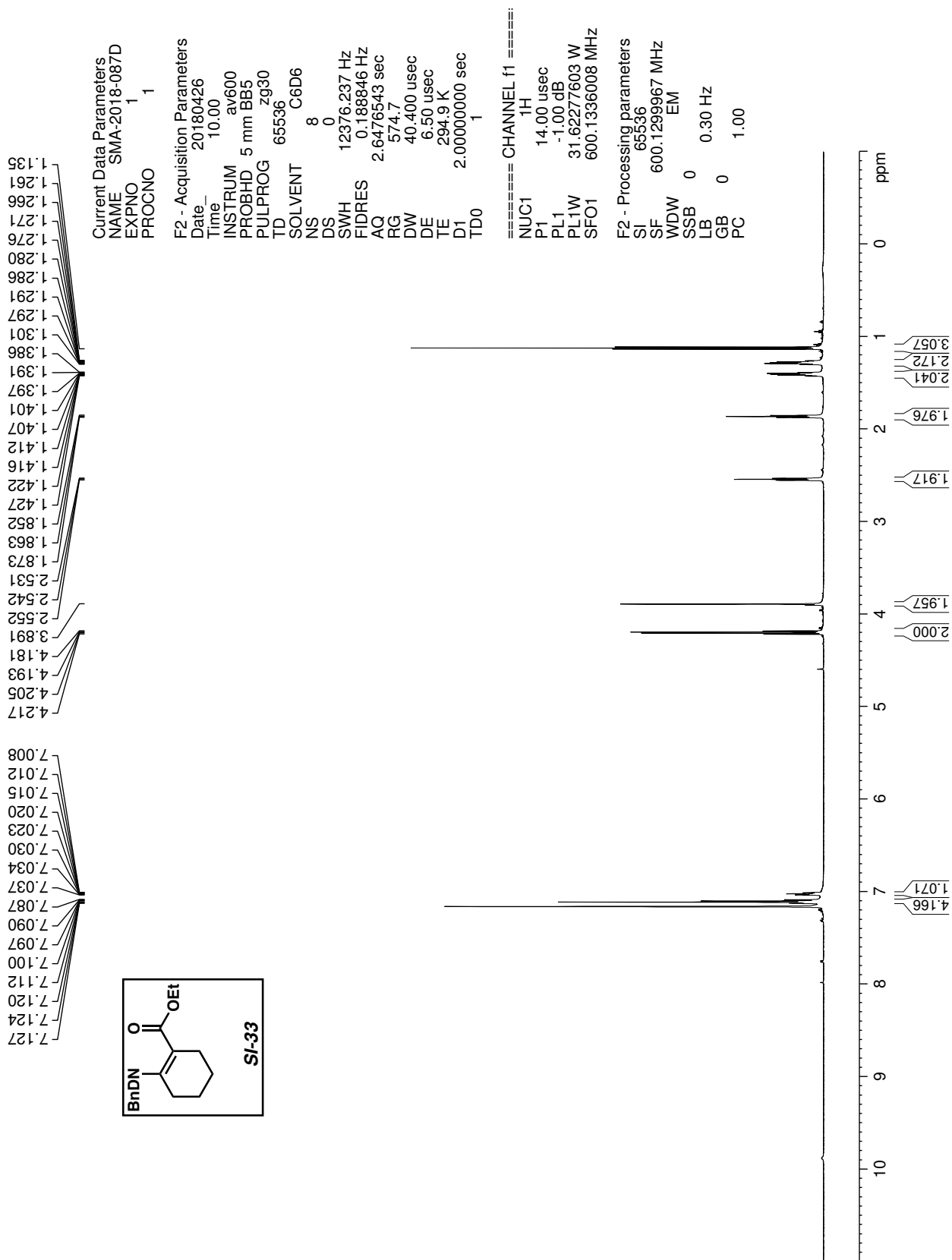


Figure S44 ^1H NMR (600 MHz, C_6D_6) of compound SI-33.

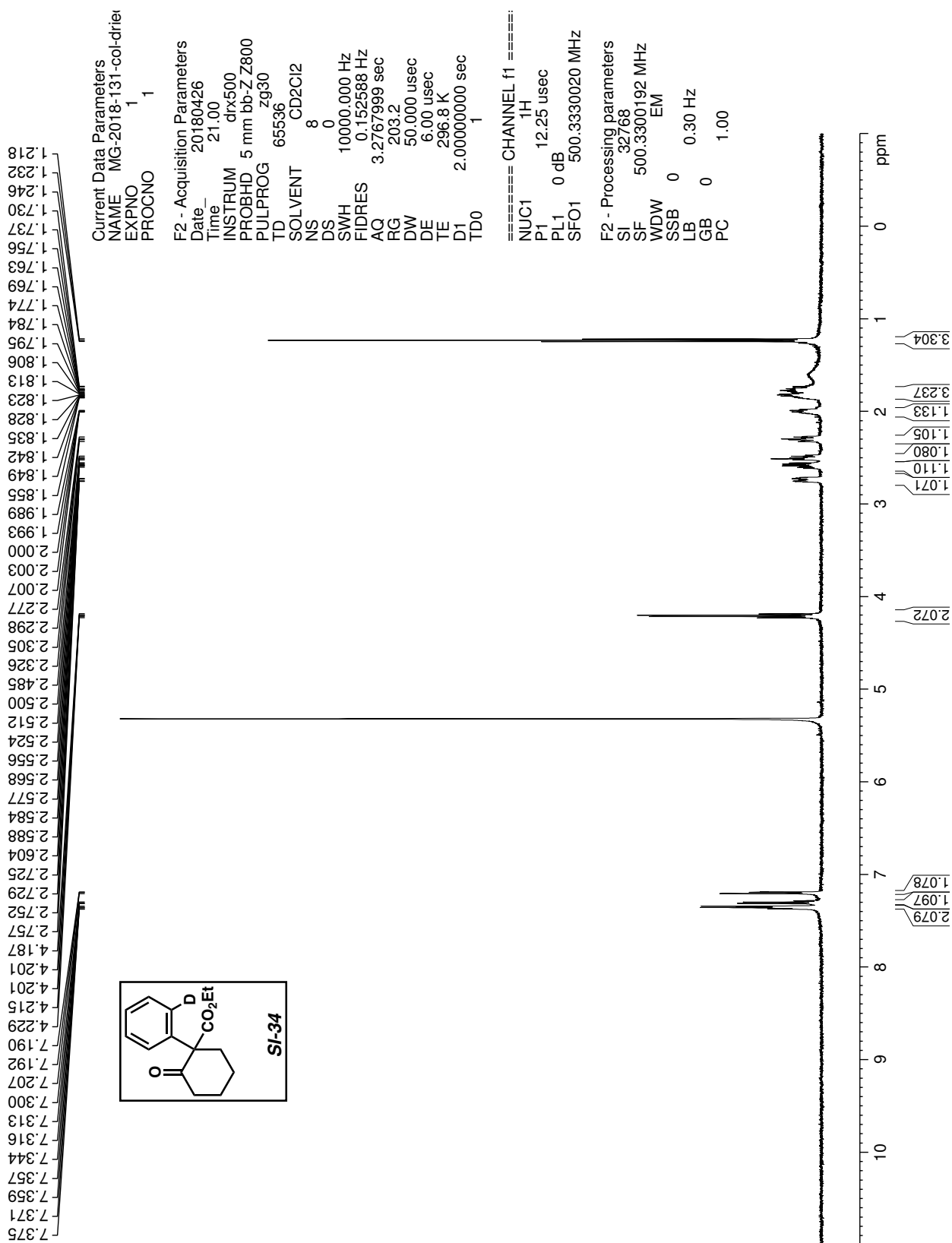


Figure S45 ^1H NMR (500 MHz, CD_2Cl_2) of compound SI-34.

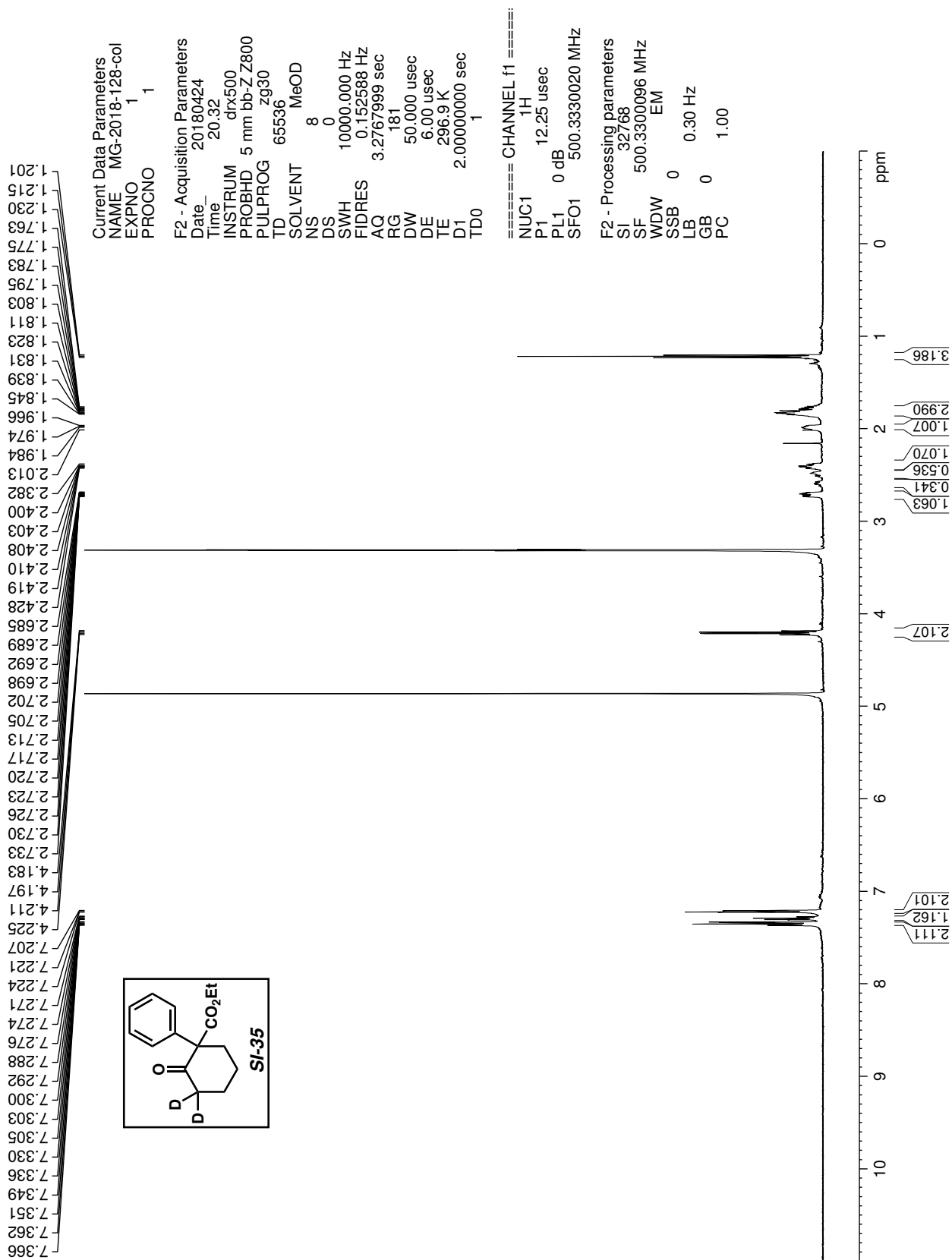


Figure S46 ^1H NMR (500 MHz, CD_3OD) of compound **SI-35**.

^{13}C NMR Spectra

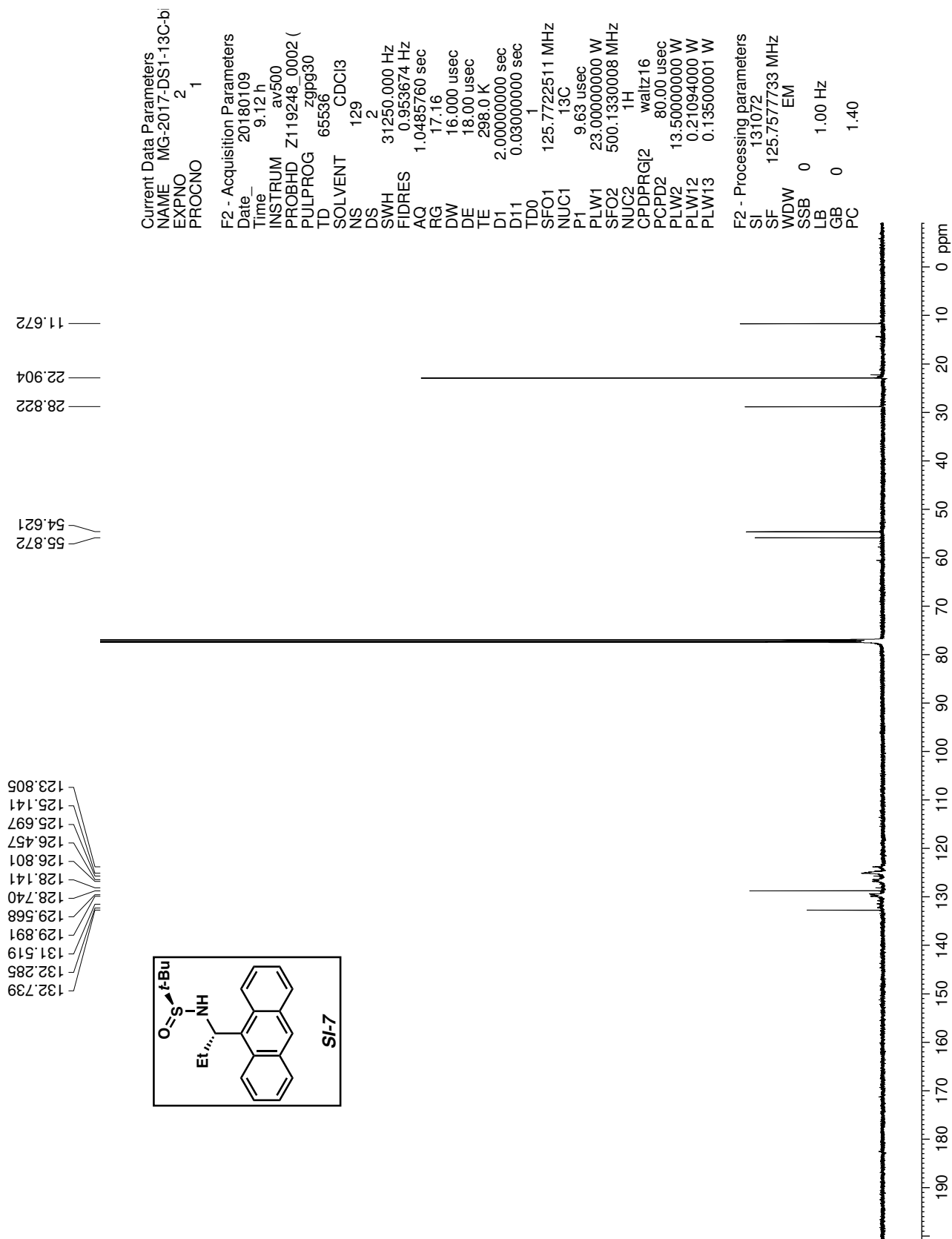
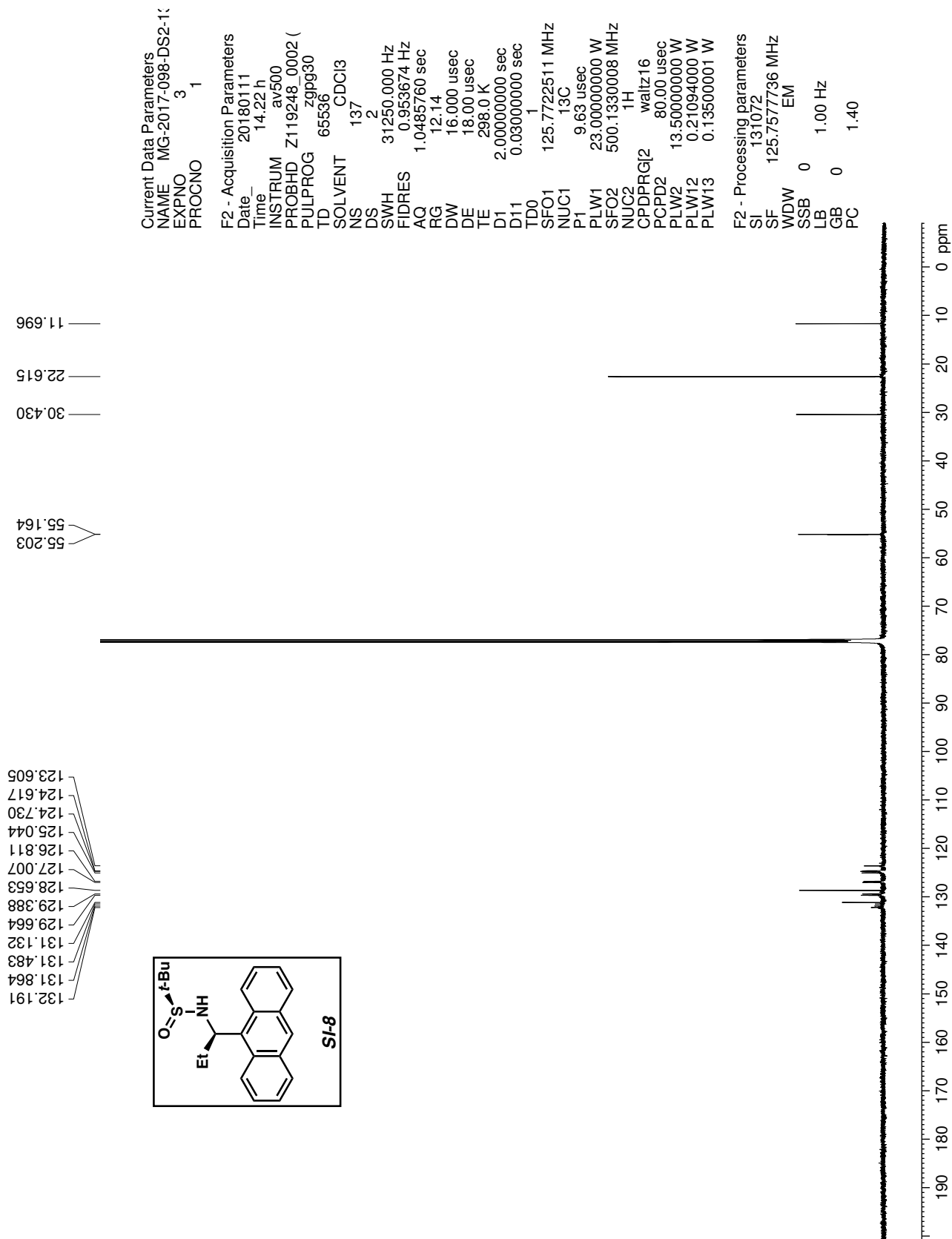


Figure S47 ^{13}C NMR (125 MHz, CDCl_3) of compound SI-7.



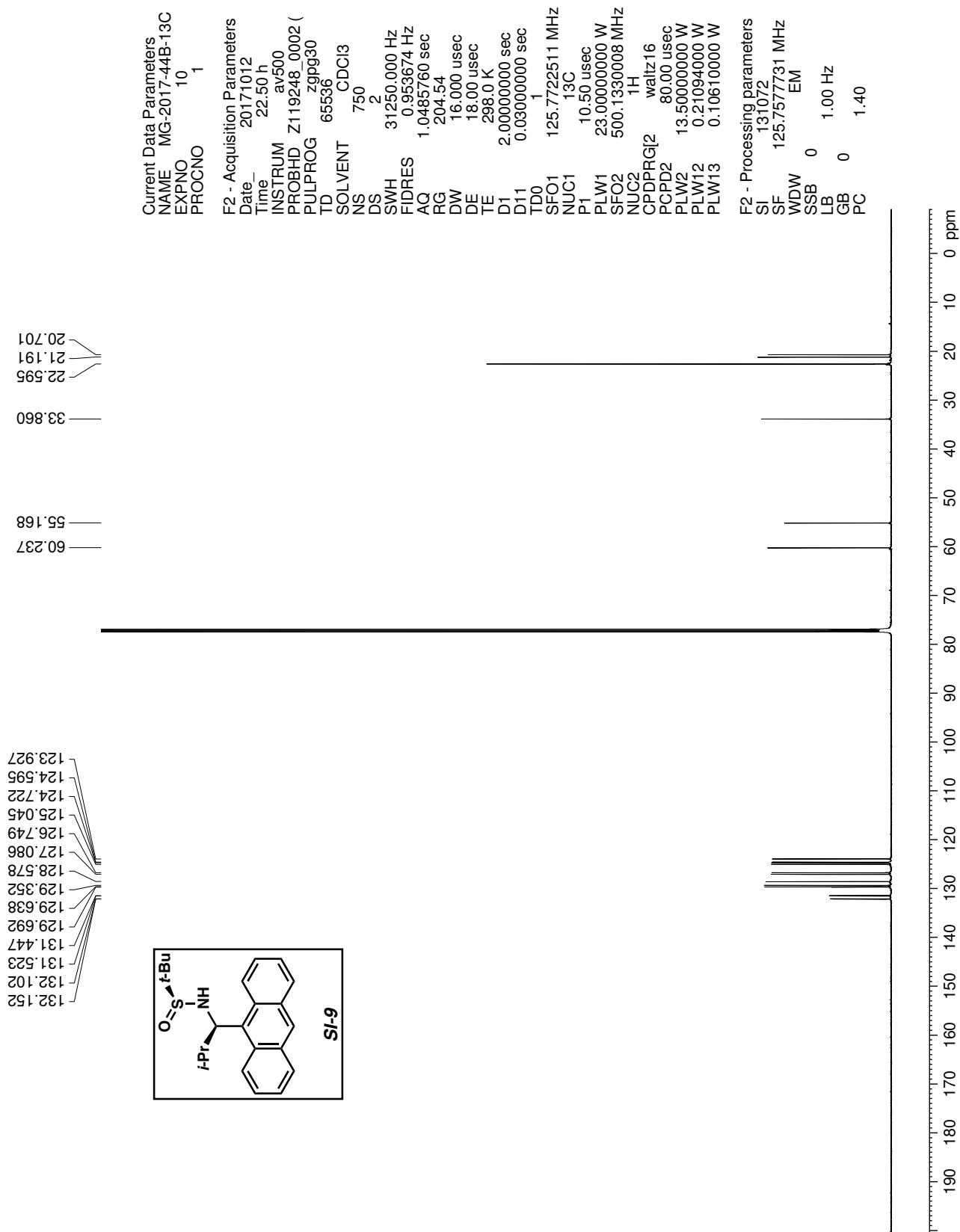


Figure S49 ^{13}C NMR (125 MHz, CDCl_3) of compound SI-9.

Current Data Parameters
 NAME MG-2017-108-13C
 EXPNO 2
 PROCNO 1

F2 - Acquisition Parameters

Date 20180109
 Time 8.58 h
 INSTRUM av500
 PROBHD Z119248_0002 (
 PULPROG zgpg30
 TD 65536
 SOLVENT CDCl3
 NS 99
 DS 2
 SWH 31250.000 Hz
 FIDRES 0.953674 Hz
 AQ 1.0485760 sec
 RG 17.16
 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 9.63 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 0.13500001 W

F2 - Processing parameters

SI 131072
 SF 125.7577768 MHz
 WDW EM
 SSB 0
 LB 1.00 Hz
 GB 0
 PC 1.40

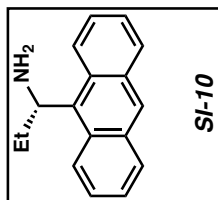
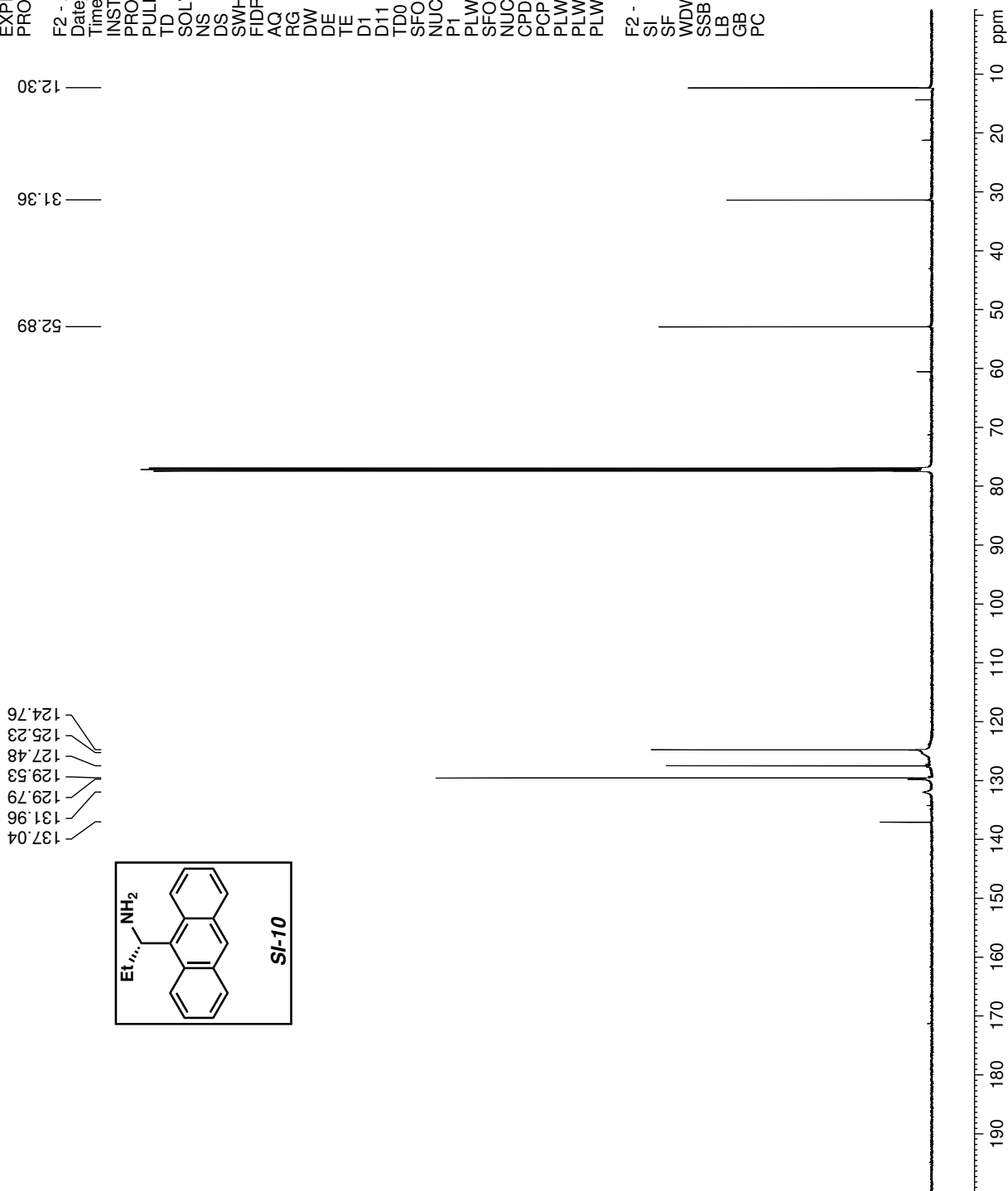
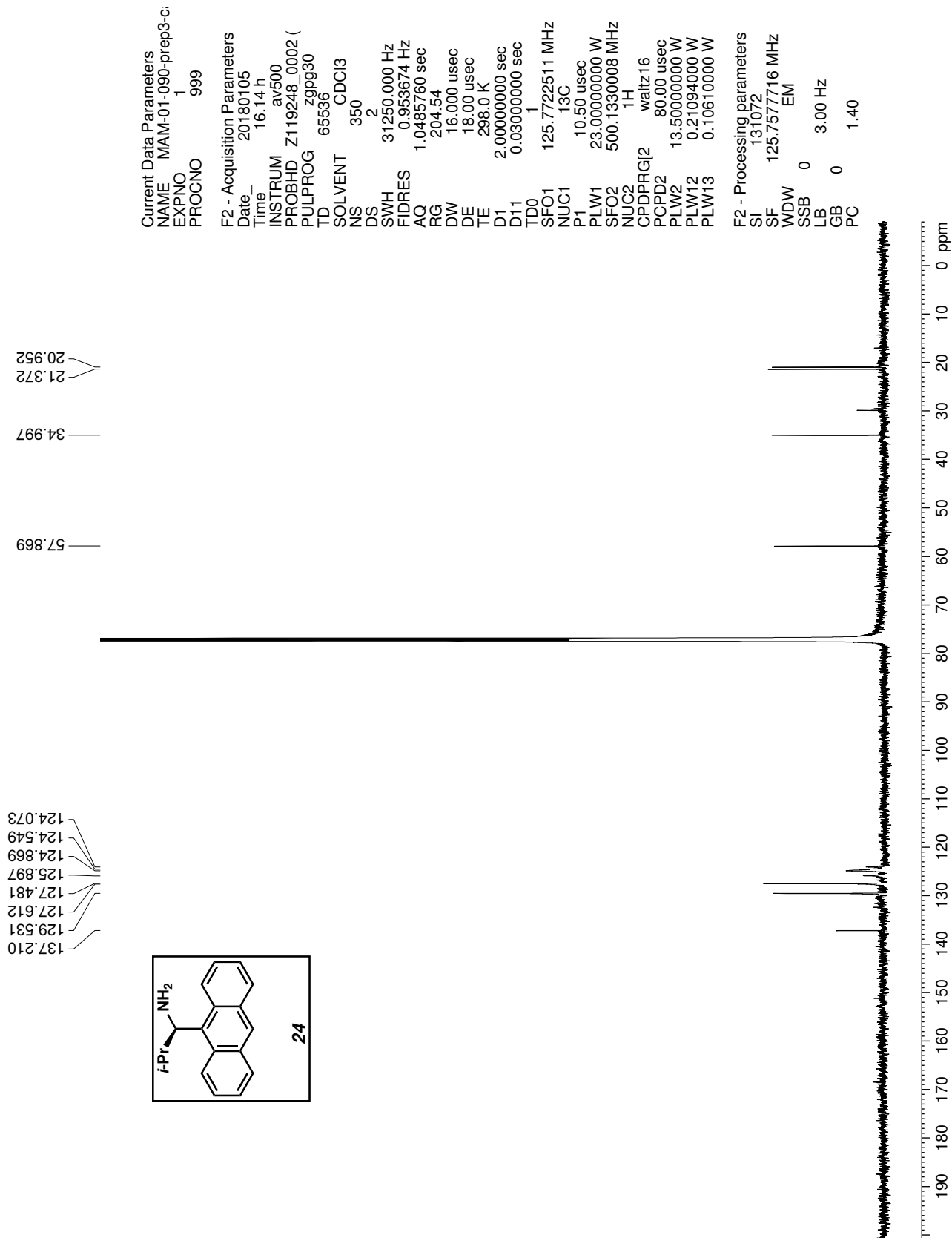


Figure S50 ¹³C NMR (125 MHz, CDCl₃) of compound SI-10.

Figure S51 ^{13}C NMR (125 MHz, CDCl_3) of compound **24**.

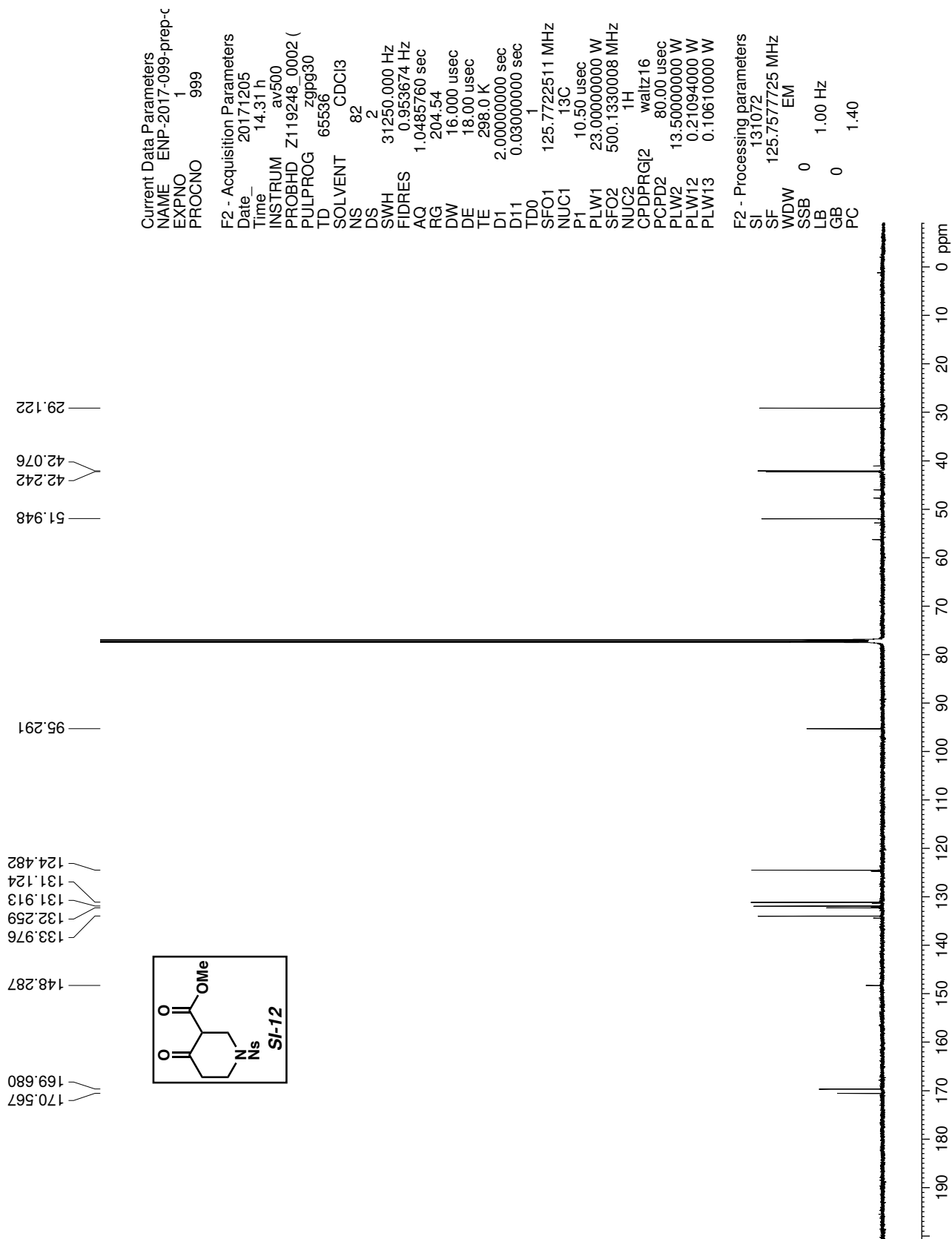


Figure S52 ^{13}C NMR (125 MHz, CDCl_3) of compound SI-12.

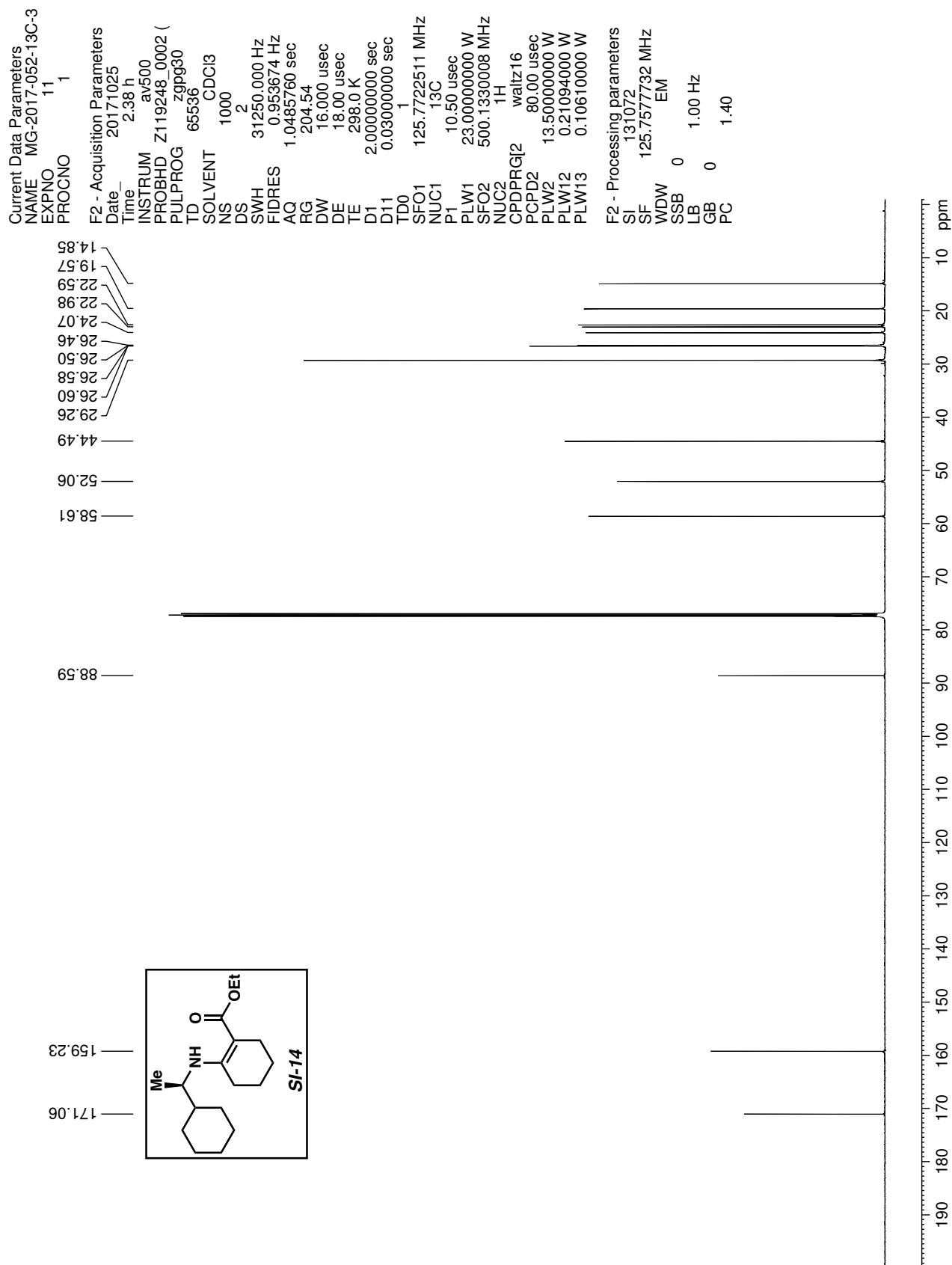


Figure S53 ^{13}C NMR (125 MHz, CDCl_3) of compound SI-14.

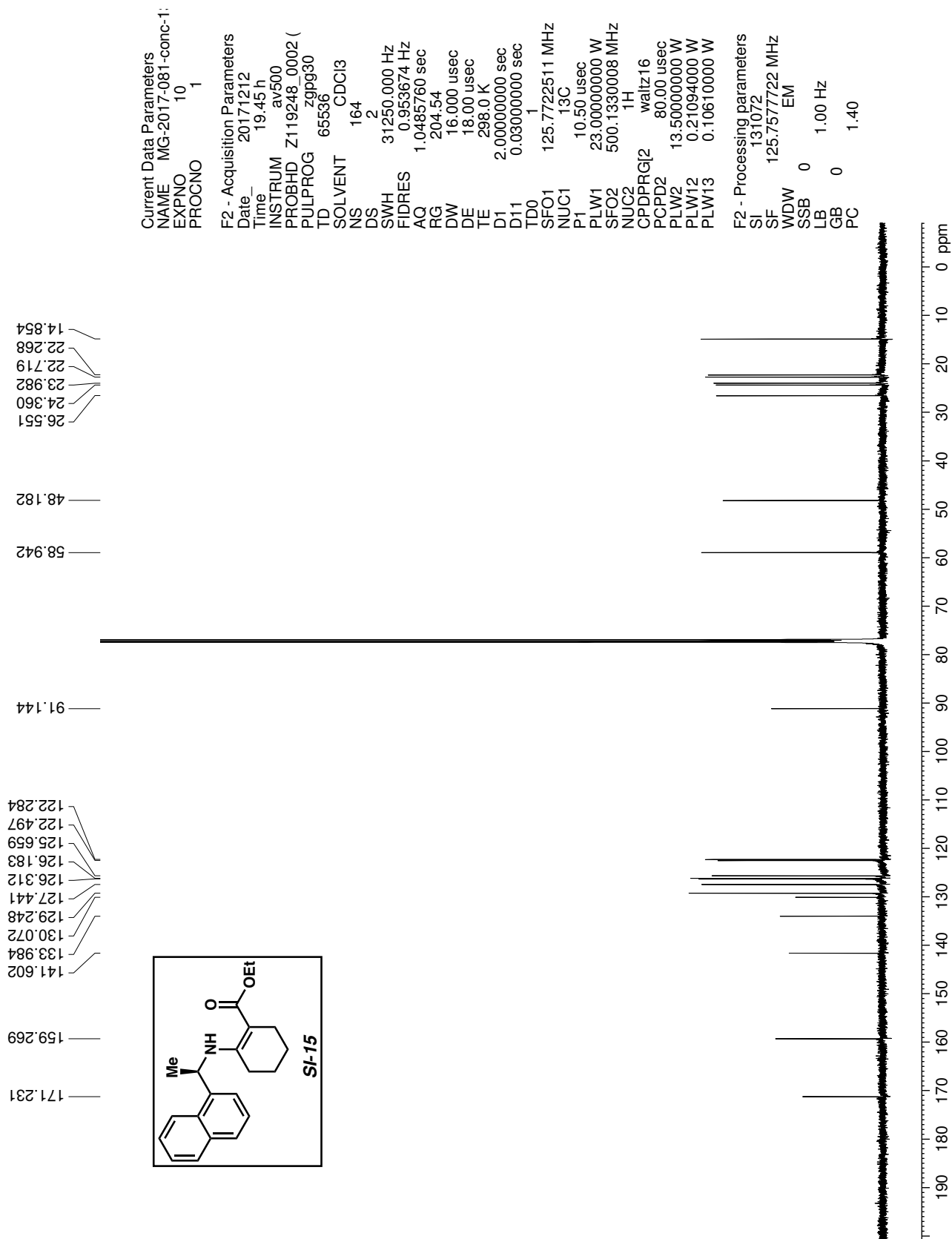


Figure S54 ^{13}C NMR (125 MHz, CDCl_3) of compound SI-15.

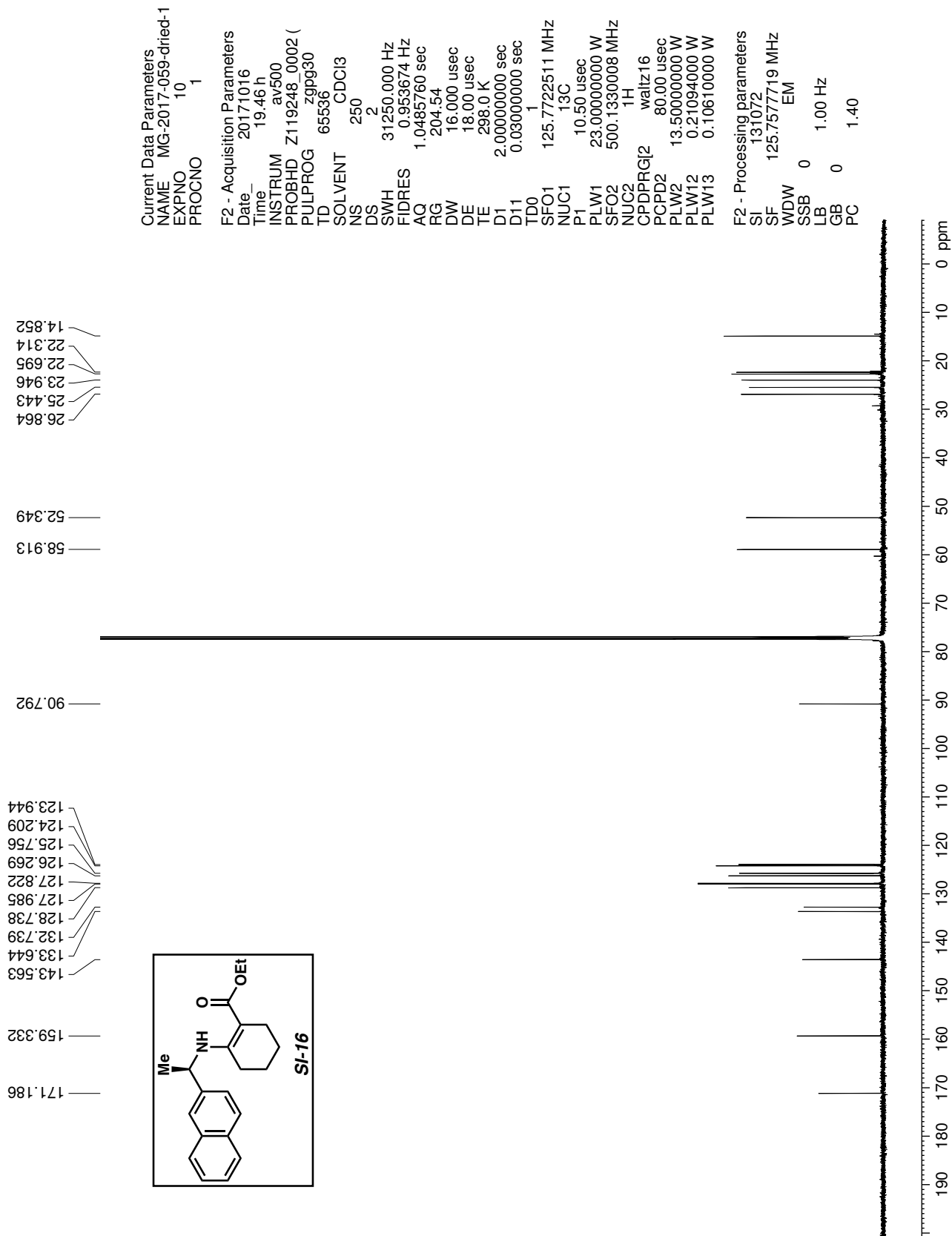


Figure S55 ¹³C NMR (125 MHz, CDCl₃) of compound SI-16.

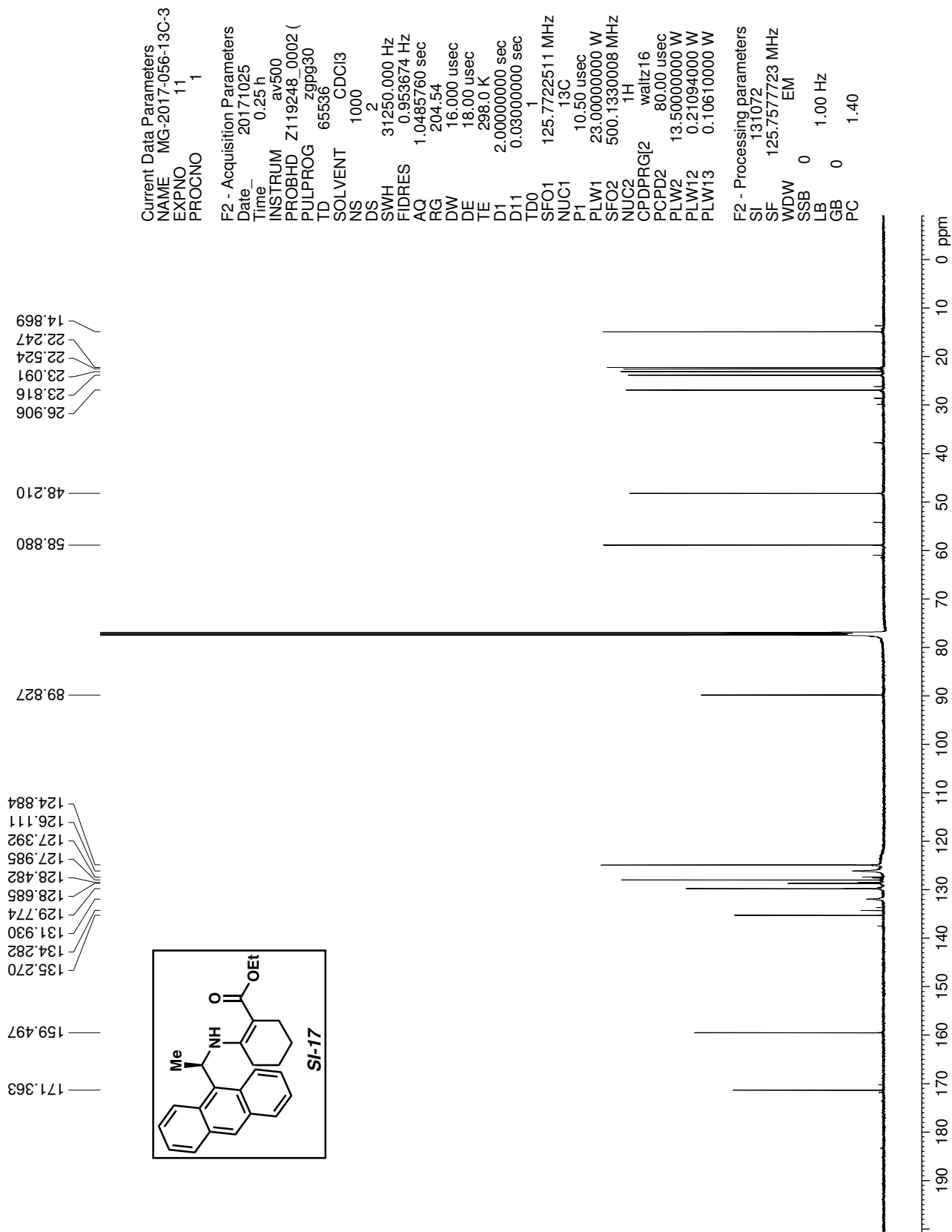


Figure S56 ^{13}C NMR (125 MHz, CDCl_3) of compound SI-17.

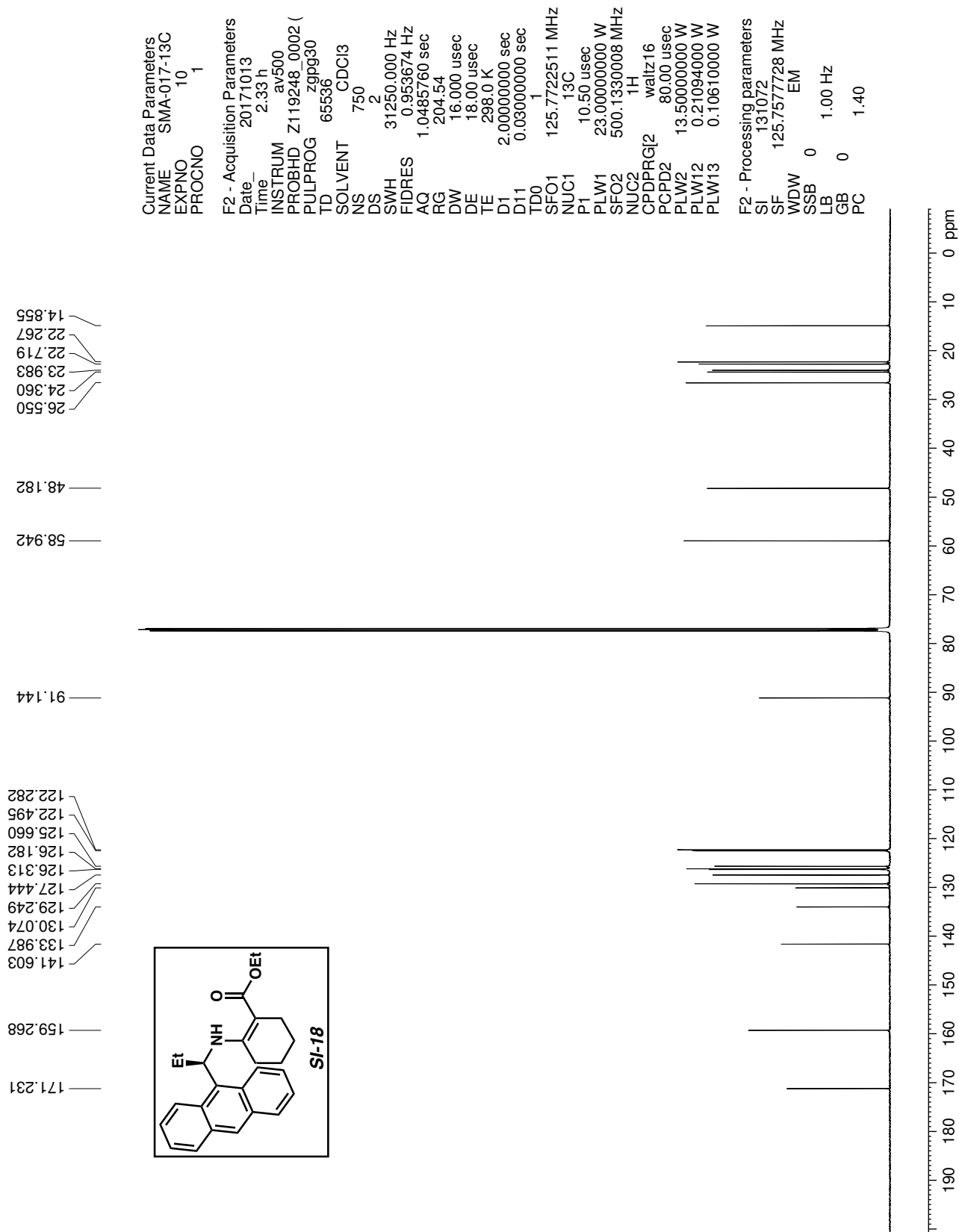


Figure S57 ^{13}C NMR (125 MHz, CDCl_3) of compound SI-18.

Current Data Parameters
 NAME MG-2018-006p
 EXPNO 17
 PROCNO 1

F2 - Acquisition Parameters
 Date_ 20180122
 Time_ 22.05 h
 INSTRUM av500
 PROBHD Z119248_0002 (
 PULPROG zgpg30
 TD 65536
 SOLVENT CDCl3
 NS 39
 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 9.63 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 0.135000001 W

F2 - Processing parameters
 SI 131072
 SF 125.7577728 MHz
 WDW EM
 SSB 0
 LB 1.00 Hz
 GB 0
 PC 1.40

14.86
 20.76
 21.62
 22.34
 22.55
 23.89
 27.15
 35.20

58.90
 58.82

89.40

123.28
 124.60
 124.98
 125.58
 126.04
 126.37
 126.37
 128.12
 129.36
 129.63
 129.93
 129.93
 130.25
 131.31
 132.37
 134.37

159.94
 171.38

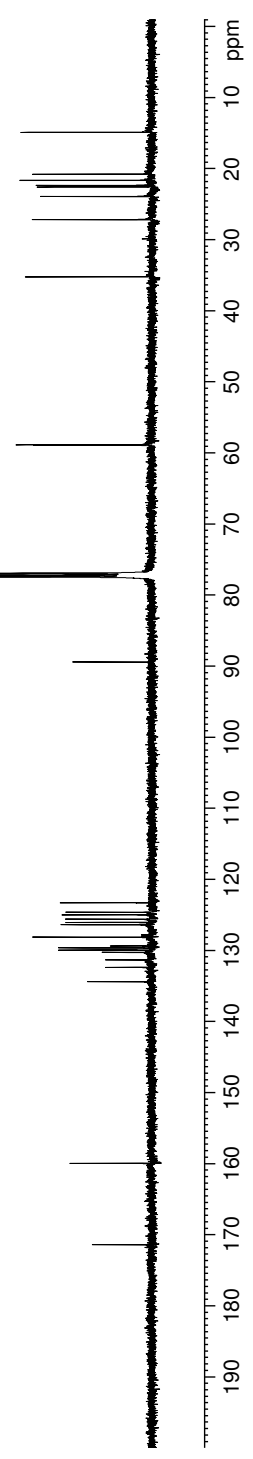
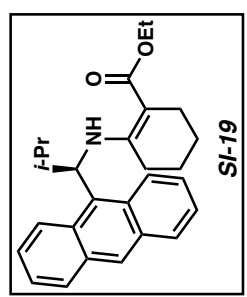


Figure S58 ^{13}C NMR (125 MHz, CDCl_3) of compound SI-19.

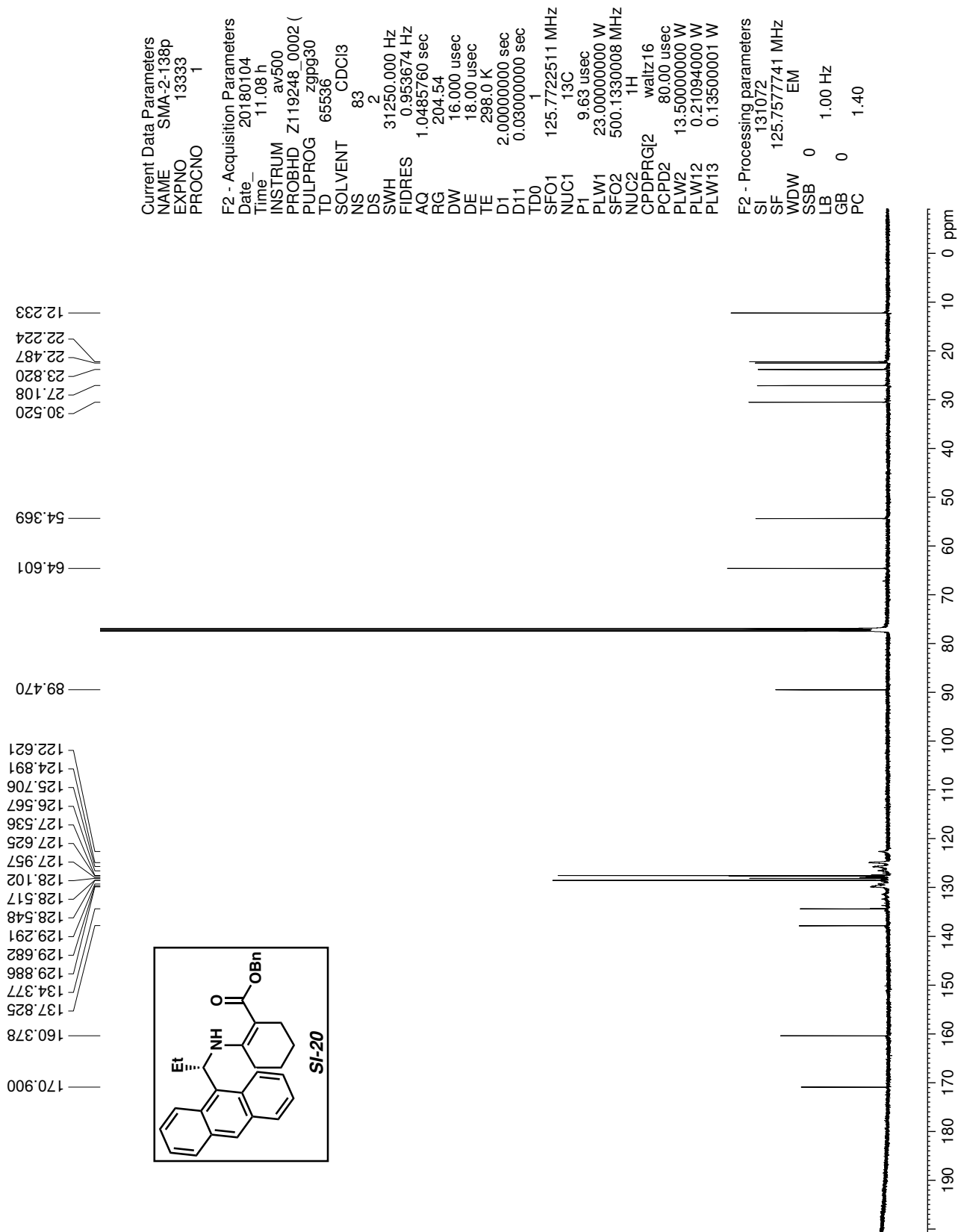


Figure S59 ^{13}C NMR (125 MHz, CDCl_3) of compound SI-20.

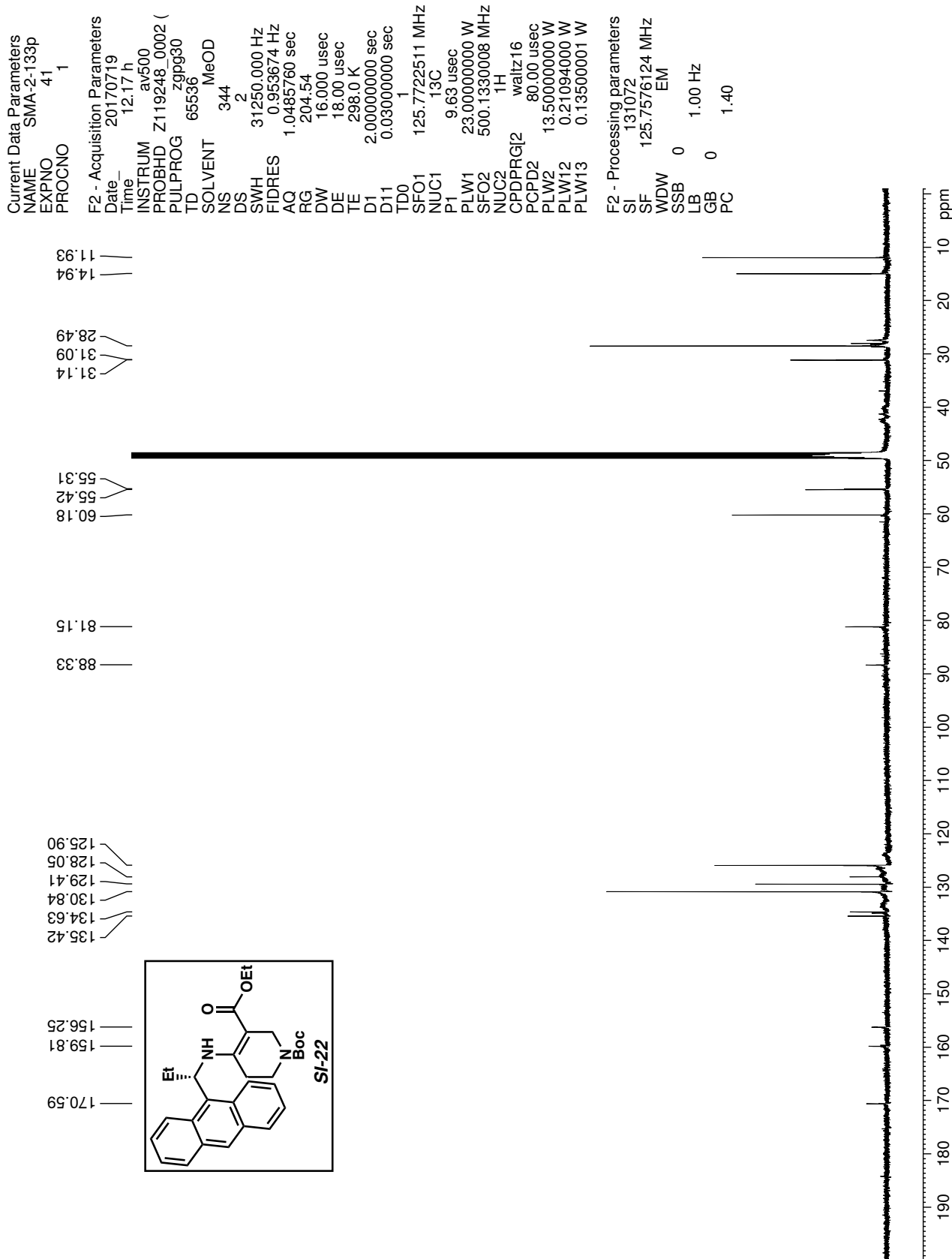


Figure S60 ^{13}C NMR (125 MHz, CD_3OD) of compound SI-22.

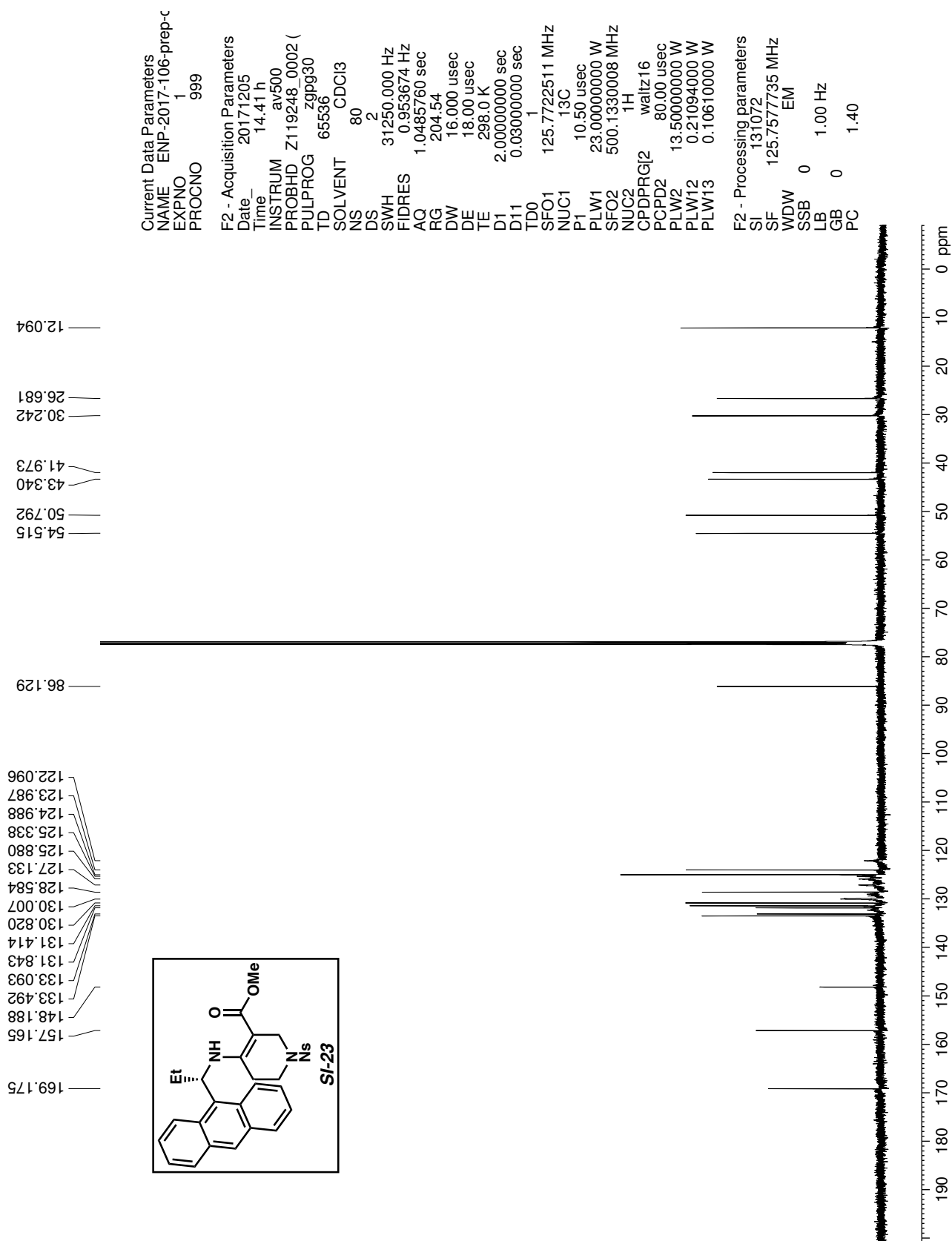


Figure S61 ^{13}C NMR (125 MHz, CDCl_3) of compound SI-23.

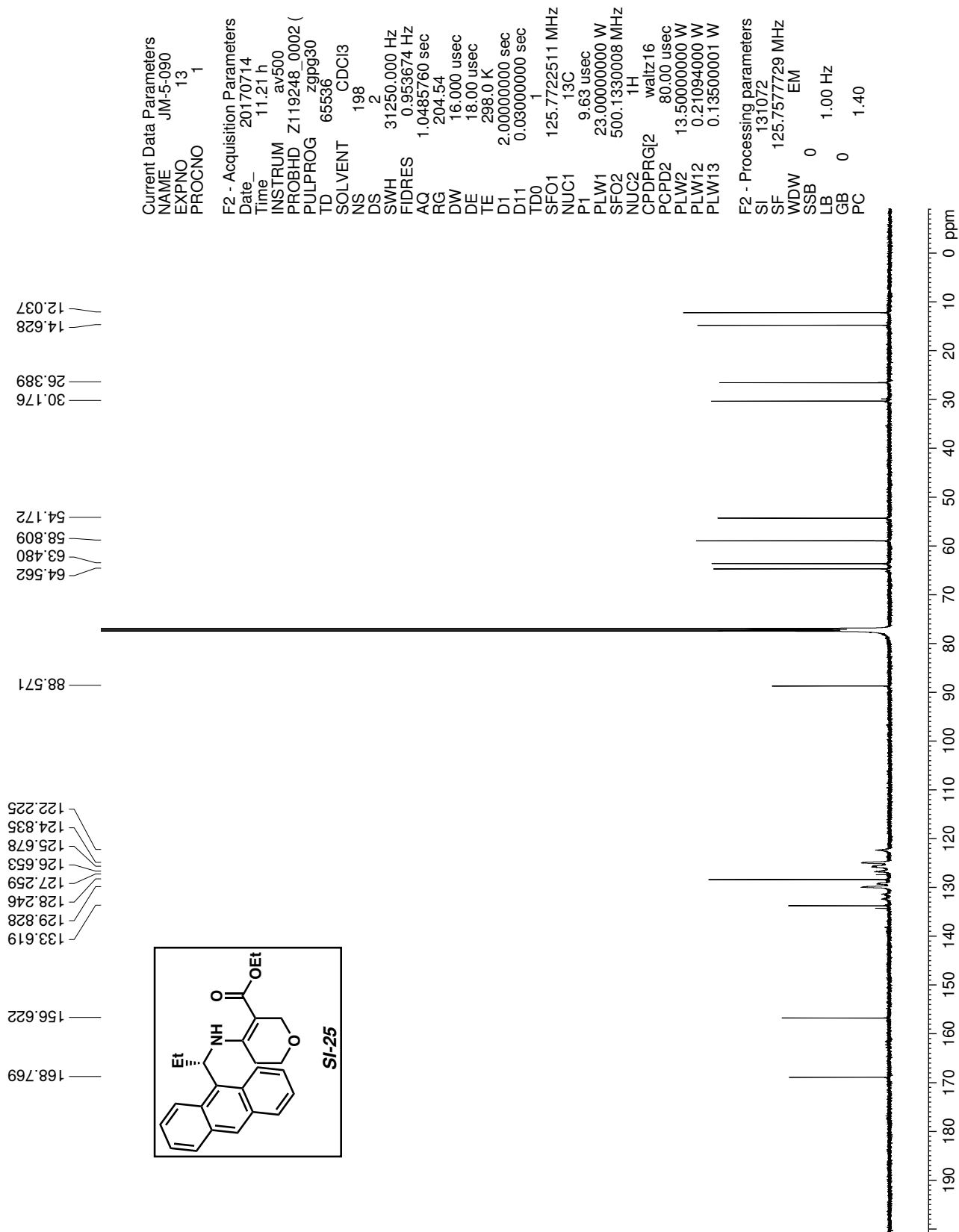


Figure S62 ¹³C NMR (125 MHz, CDCl₃) of compound SI-25.

Current Data Parameters
 NAME SMA-2-200p
 EXPNO 10
 PROCNO 1

F2 - Acquisition Parameters
 Date_ 20171212
 Time_ 12.31
 INSTRUM av400
 PROBHD 5 mm PABBO BB/
 PULPROG zgpg30
 TD 65536
 SOLVENT CDCl3
 NS 520
 DS 0
 SMH 25252.525 Hz
 FIDRES 0.385323 Hz
 AQ 1.2976128 sec
 RG 189.85
 DW 19.800 usec
 DE 6.50 usec
 TE 299.2 K
 D1 2.00000000 sec
 D11 0.03000000 sec
 TD0 1

==== CHANNEL f1 =====
 SFO1 100.6243395 MHz
 NUC1 13C
 P1 10.00 usec
 PLW1 52.00000000 W

==== CHANNEL f2 =====
 SFO2 400.1324008 MHz
 NUC2 1H
 CPDPRG2 waltz16
 PCPD2 90.00 usec
 PLW2 13.00000000 W
 PLW12 0.3611000 W
 PLW13 0.29249999 W

F2 - Processing parameters
 SI 65536
 SF 100.6127596 MHz
 WDW EM
 SSB 0
 LB 0
 GB 0
 PC 1.40

12.20
 24.03
 25.76
 28.39
 29.96
 30.23
 31.41

50.57
 55.28

94.30

122.35
 124.81
 125.72
 127.69
 127.94
 128.16
 129.26
 134.89

167.61
 171.47

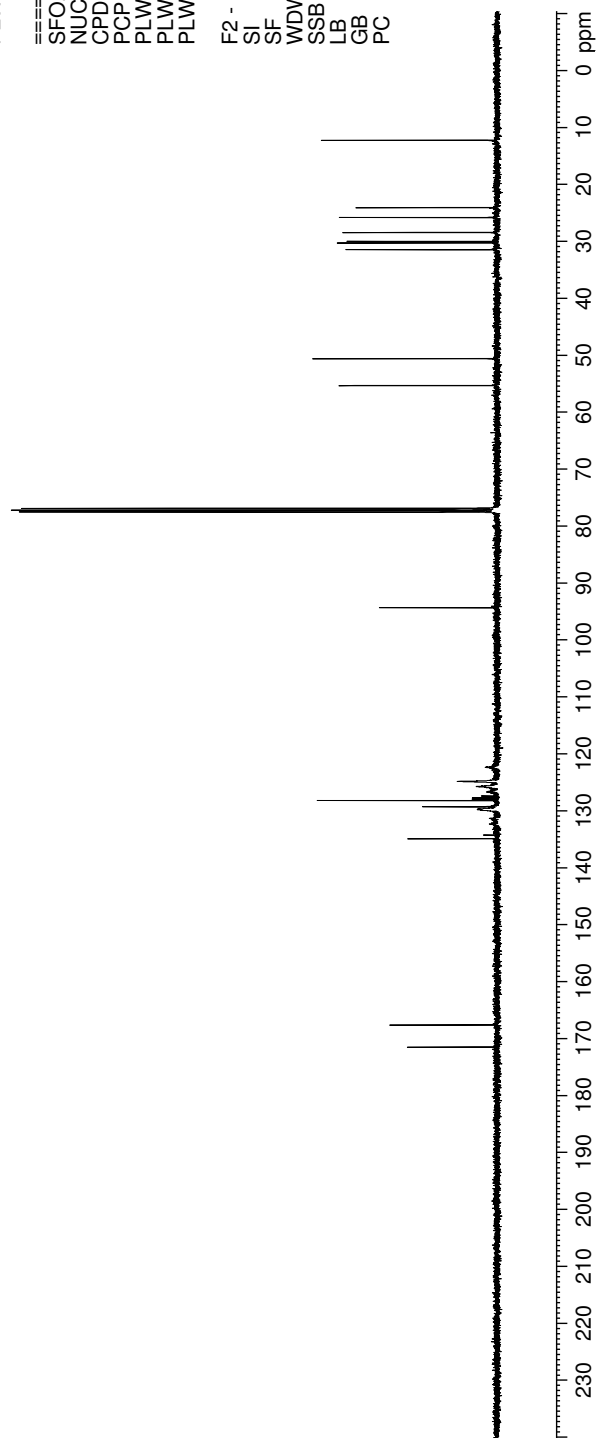
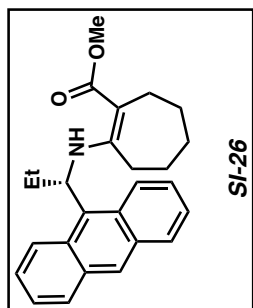


Figure S63 ^{13}C NMR (100 MHz, CDCl_3) of compound **SI-26**.

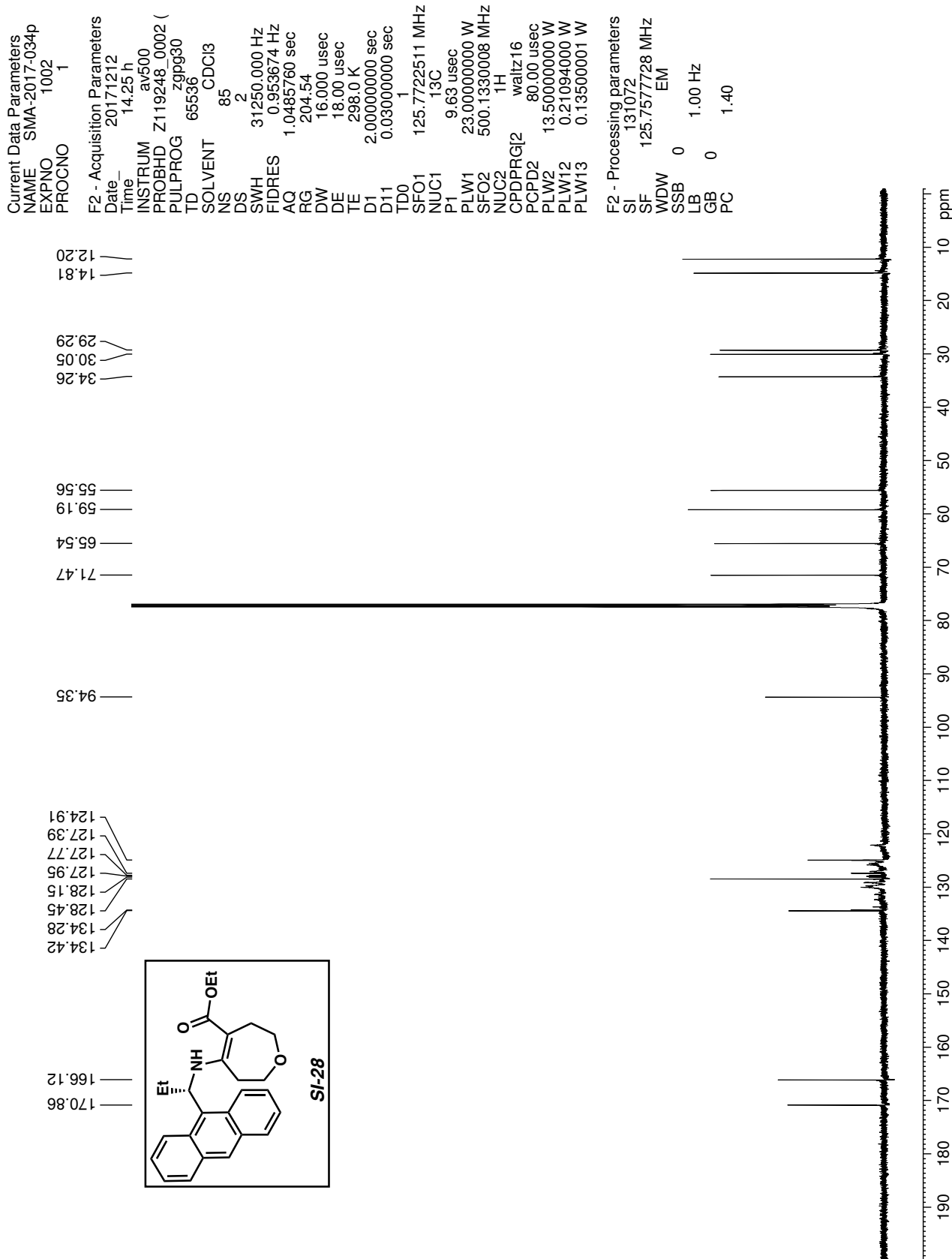


Figure S64 ^{13}C NMR (125 MHz, CDCl_3) of compound SI-28.

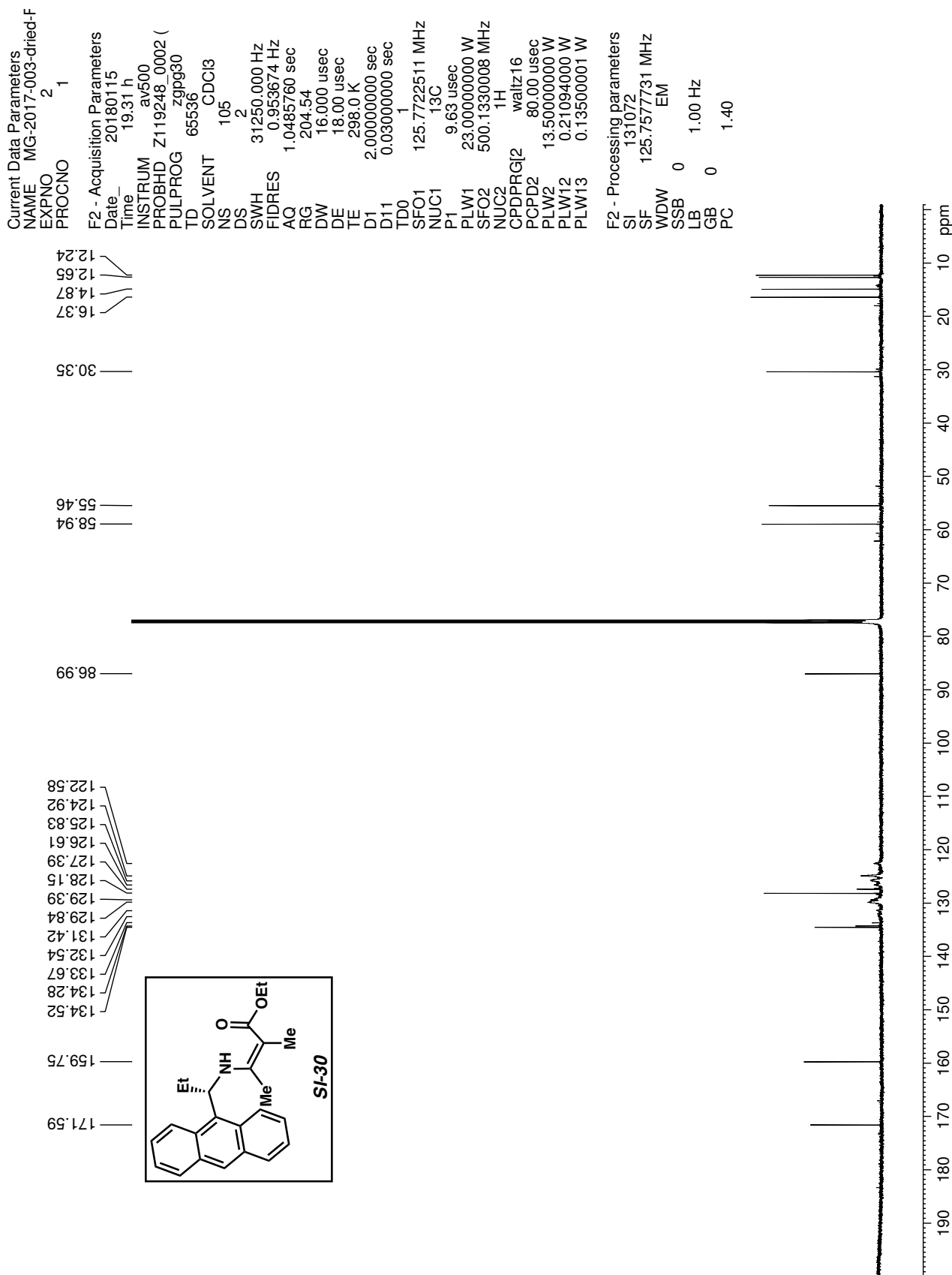


Figure S65 ^{13}C NMR (125 MHz, CDCl_3) of compound SI-30.

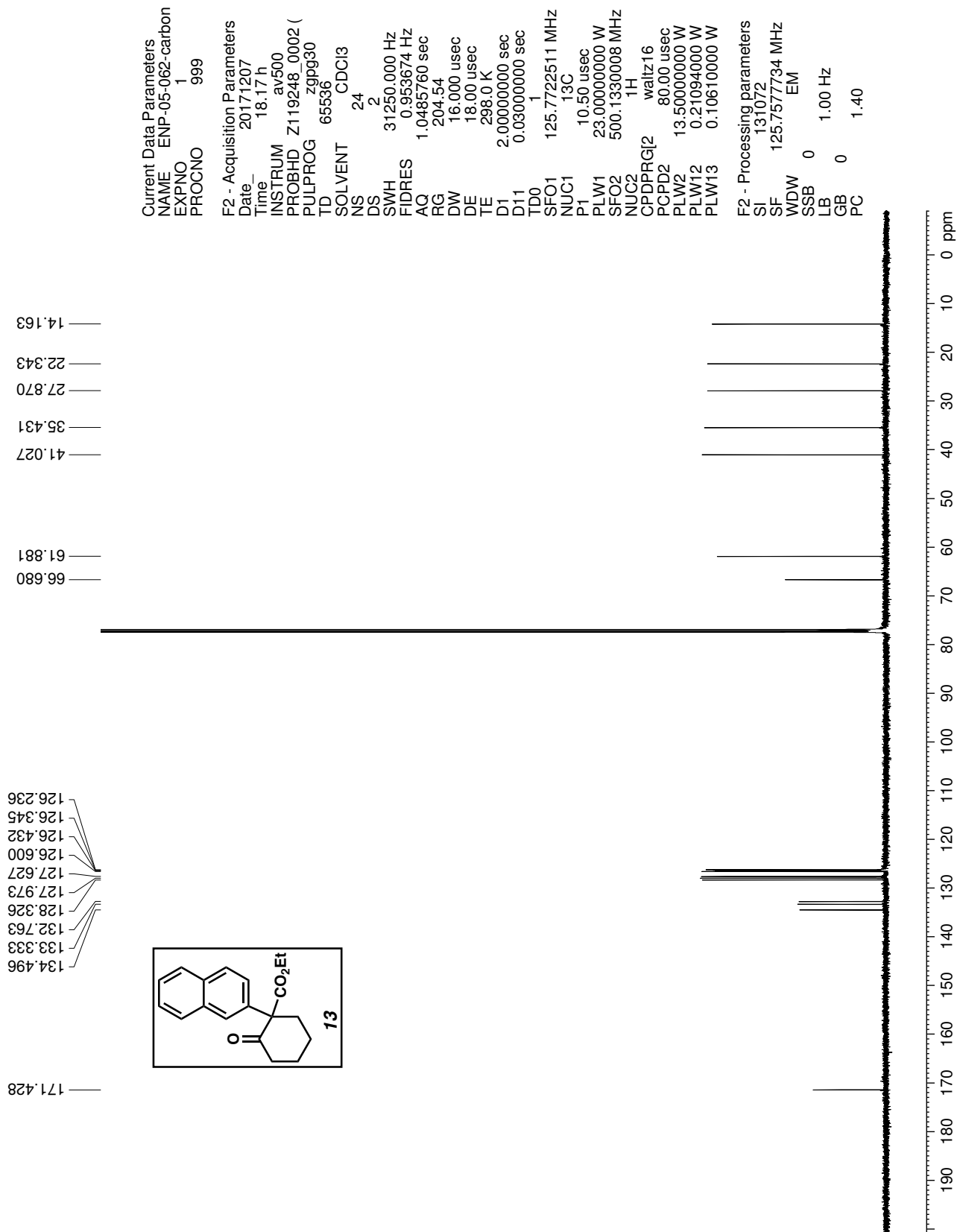


Figure S66 ^{13}C NMR (125 MHz, CDCl_3) of compound 13.

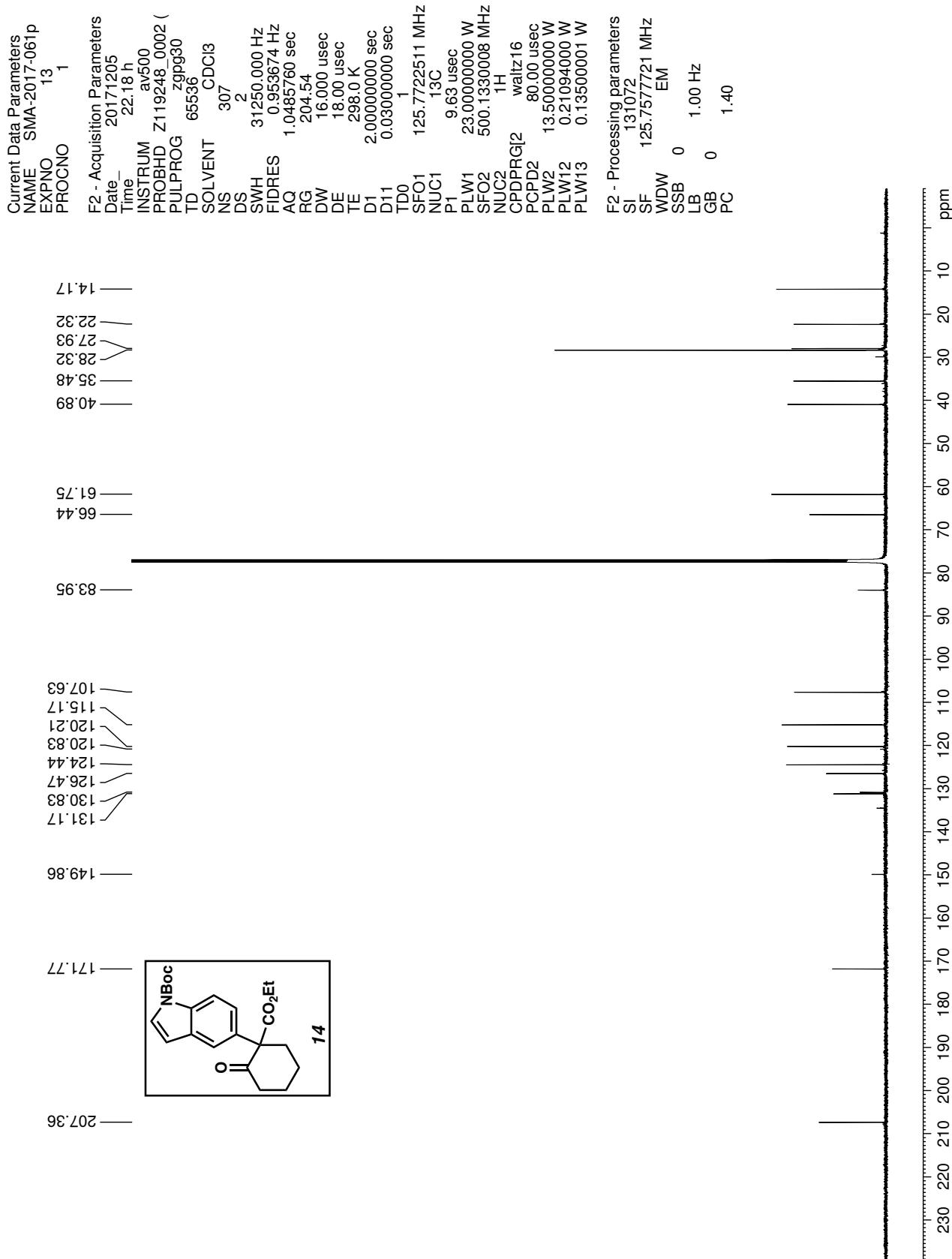


Figure S67 ^{13}C NMR (125 MHz, CDCl_3) of compound 14.

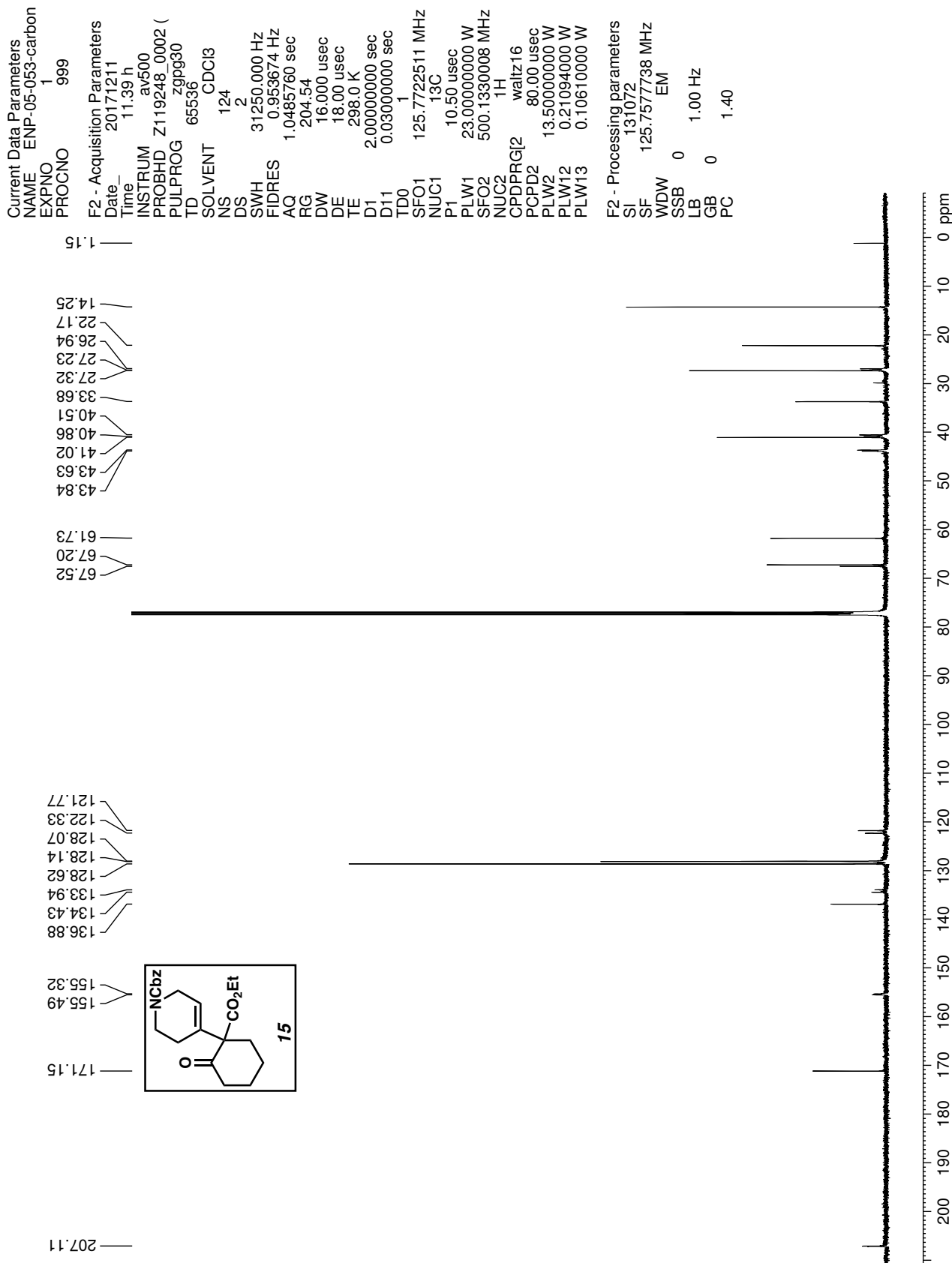


Figure S68 ^{13}C NMR (125 MHz, CDCl_3) of compound 15.

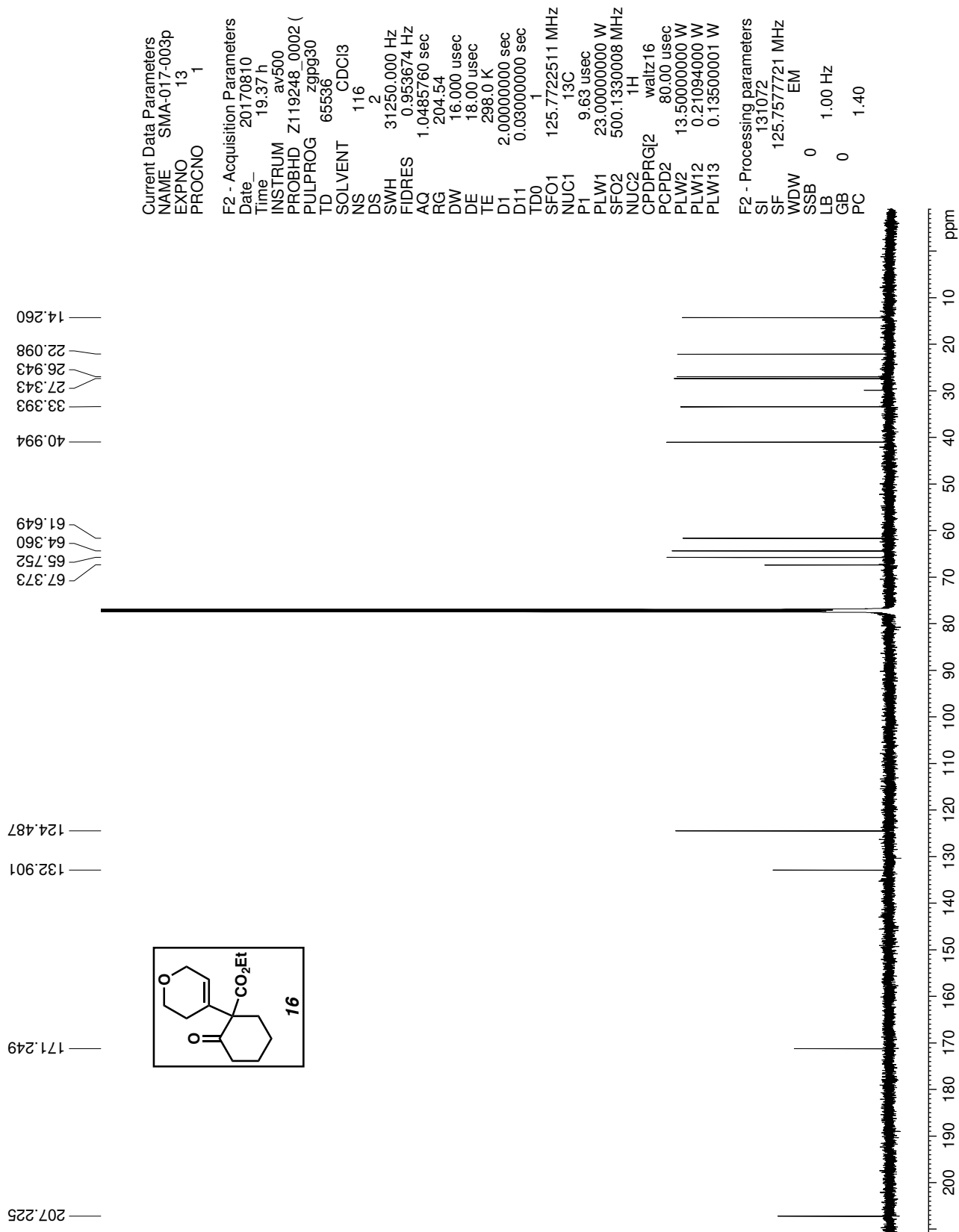


Figure S69 ^{13}C NMR (125 MHz, CDCl_3) of compound 16.

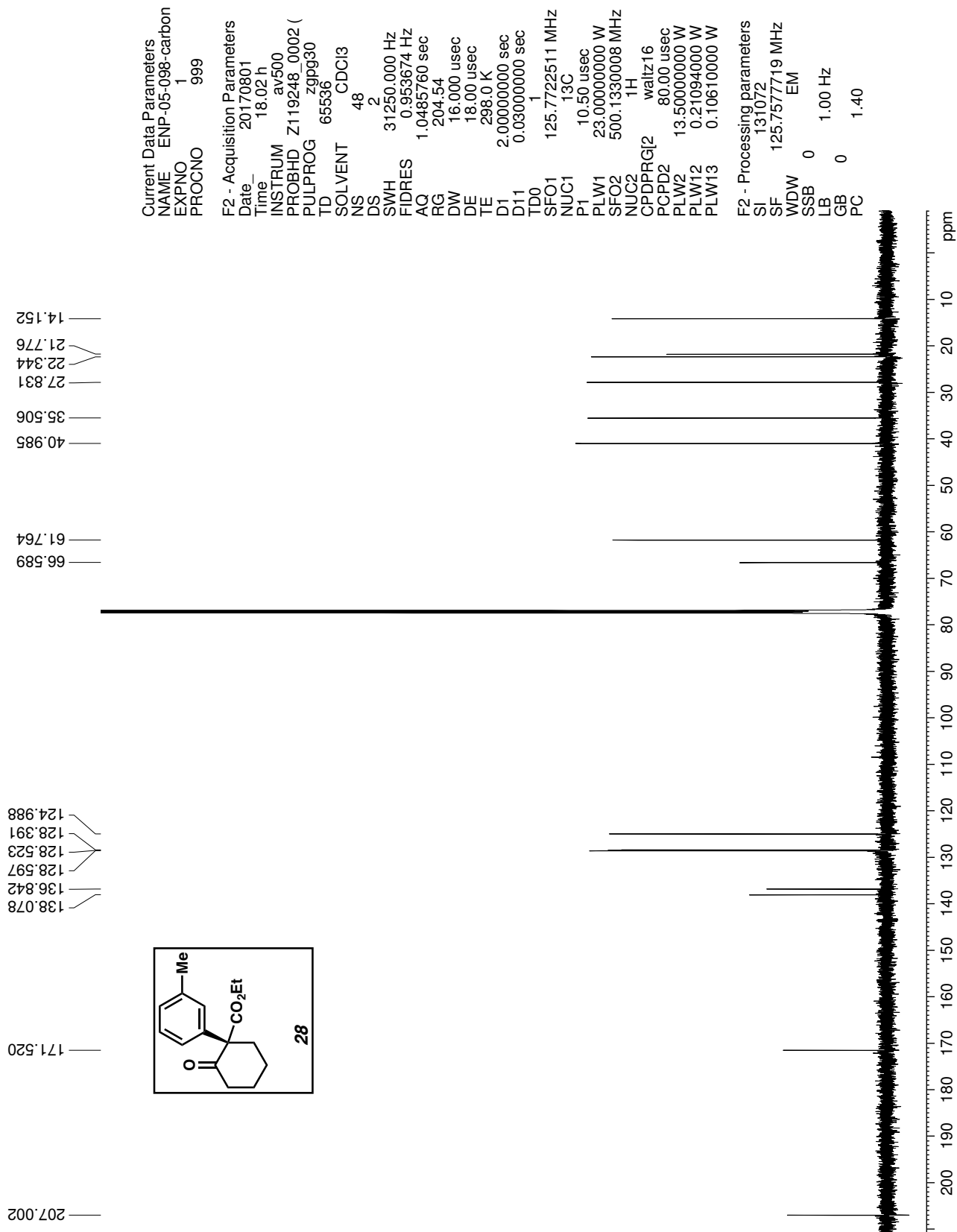


Figure S70 ^{13}C NMR (125 MHz, CDCl_3) of compound **28**.

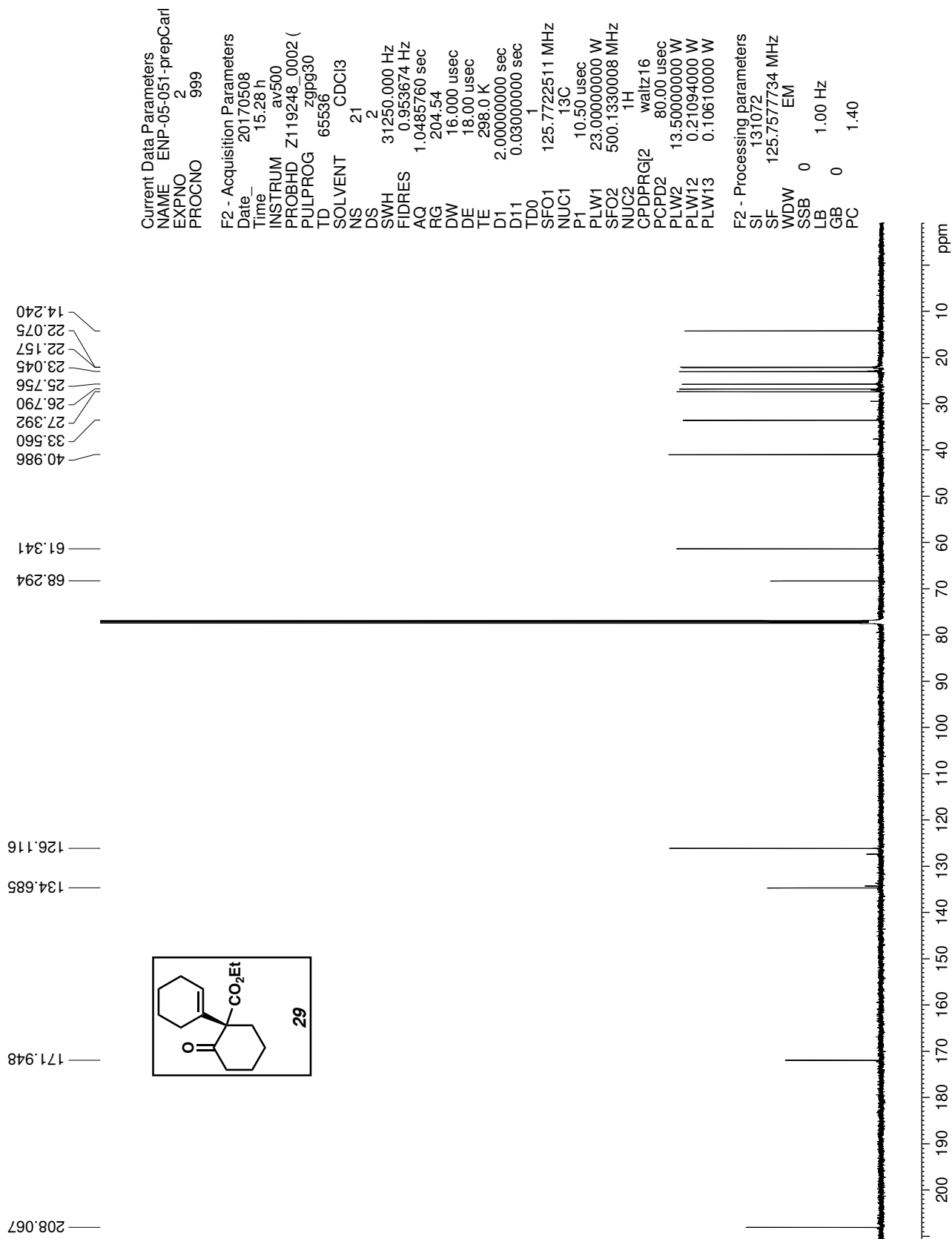


Figure S71 ^{13}C NMR (125 MHz, CDCl_3) of compound 29.

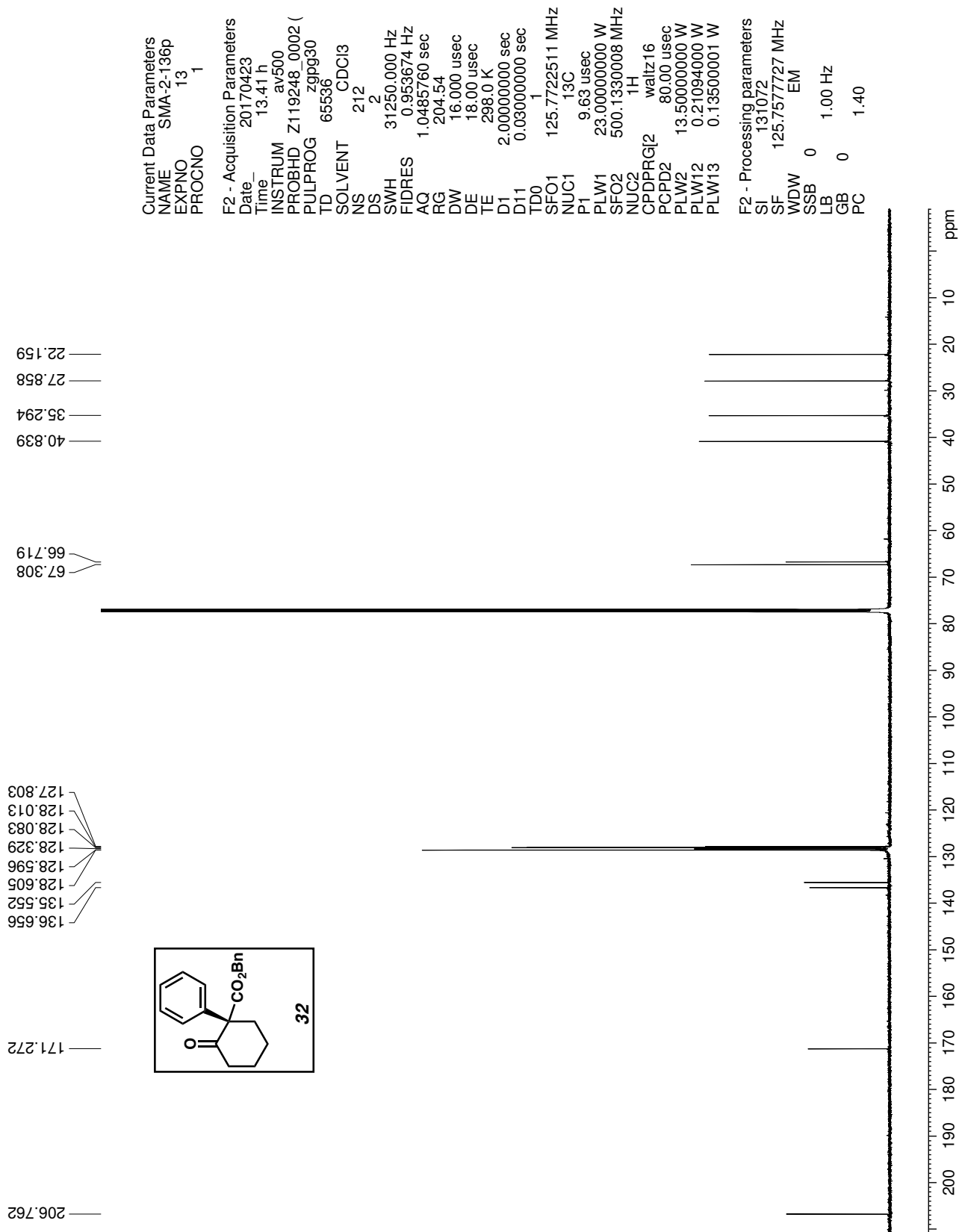


Figure S72 ^{13}C NMR (125 MHz, CDCl_3) of compound 32.

Current Data Parameters
 NAME SMA-2-139p
 EXPNO 23
 PROCNO 1

F2 - Acquisition Parameters
 Date_ 20170430
 Time_ 18.46 h
 INSTRUM av500
 PROBHD Z119248_0002 (
 PULPROG zgpg30
 TD 65536
 SOLVENT CDCl3
 NS 701
 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 9.63 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 0.13500001 W

F2 - Processing parameters
 SI 131072
 SF 125.7577892 MHz
 WDW EM
 SSB 0
 LB 1.00 Hz
 GB 0
 PC 1.40

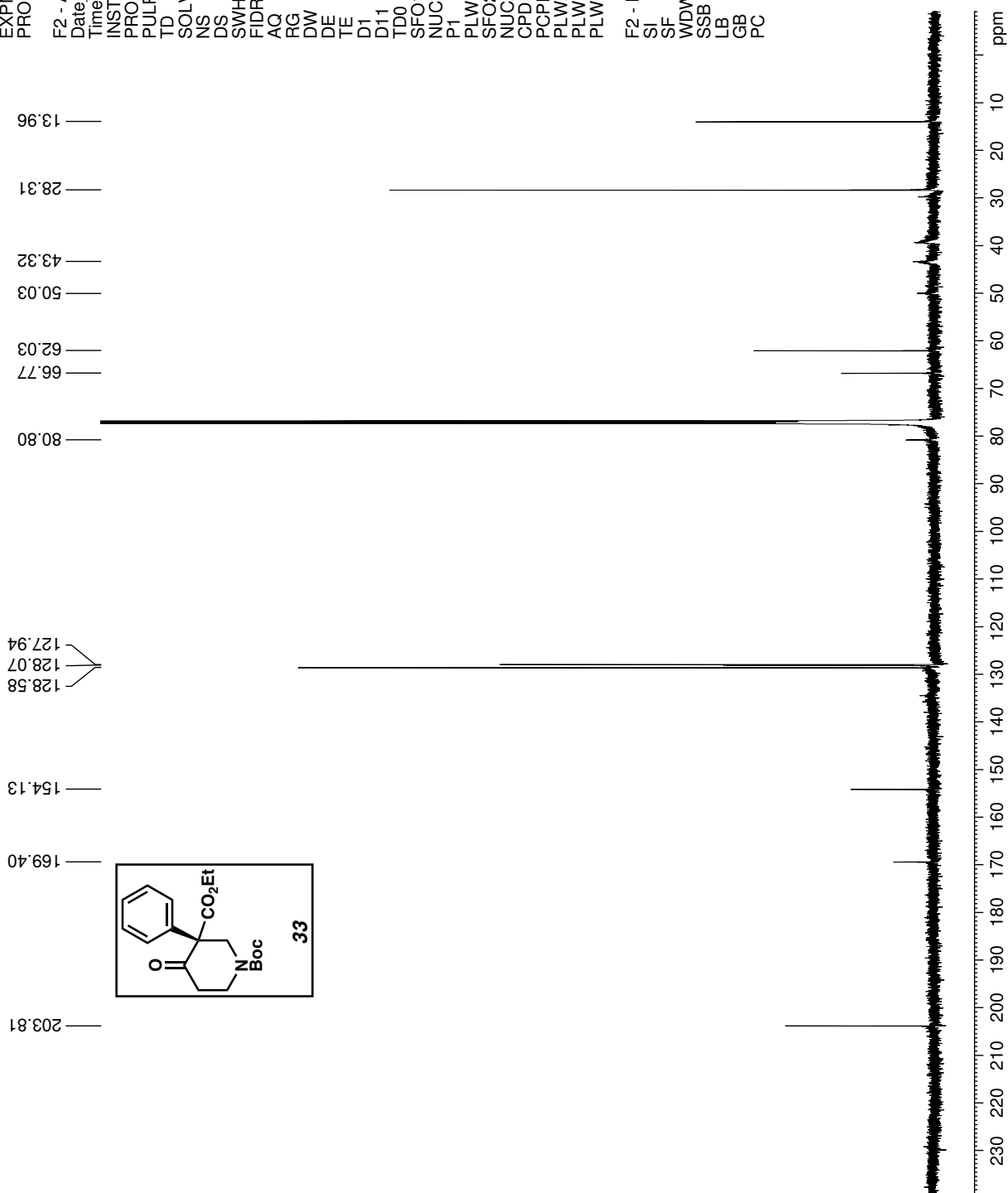


Figure S73 ^{13}C NMR (125 MHz, CDCl_3) of compound 33.

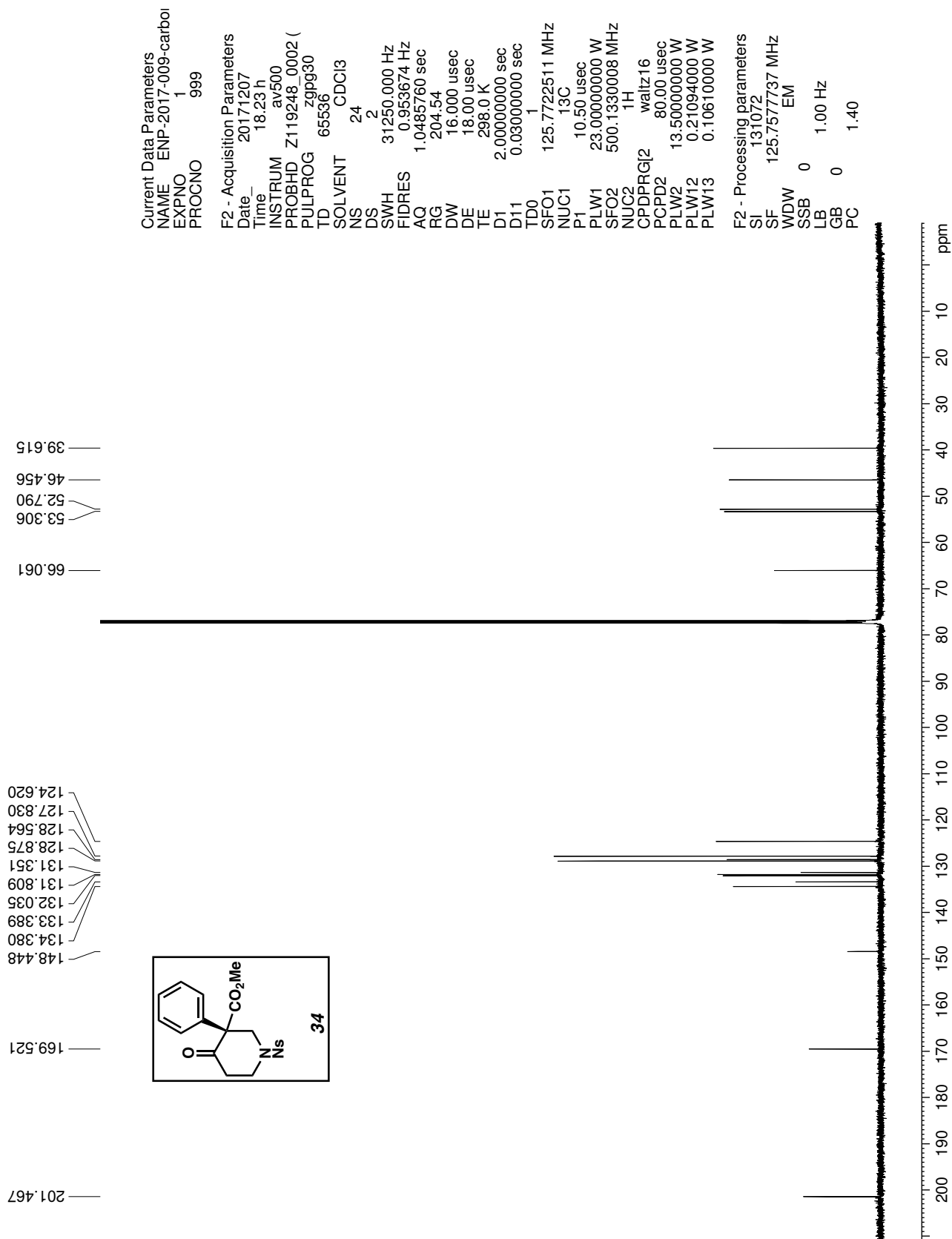


Figure S74 ^{13}C NMR (125 MHz, CDCl_3) of compound 34.

Current Data Parameters
 NAME JM-5-092
 EXPNO 101
 PROCNO 1

F2 - Acquisition Parameters
 Date_ 20170428
 Time_ 15.49 h
 INSTRUM av500
 PROBHD Z119248_0002 (
 PULPROG zgpg30
 TD 65536
 SOLVENT CDCl3
 NS 60
 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 125.7577733 MHz
 WDW EM
 SSB 0
 LB 1.00 Hz
 GB 0
 PC 1.40

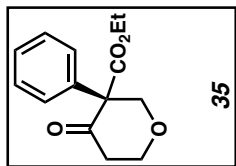
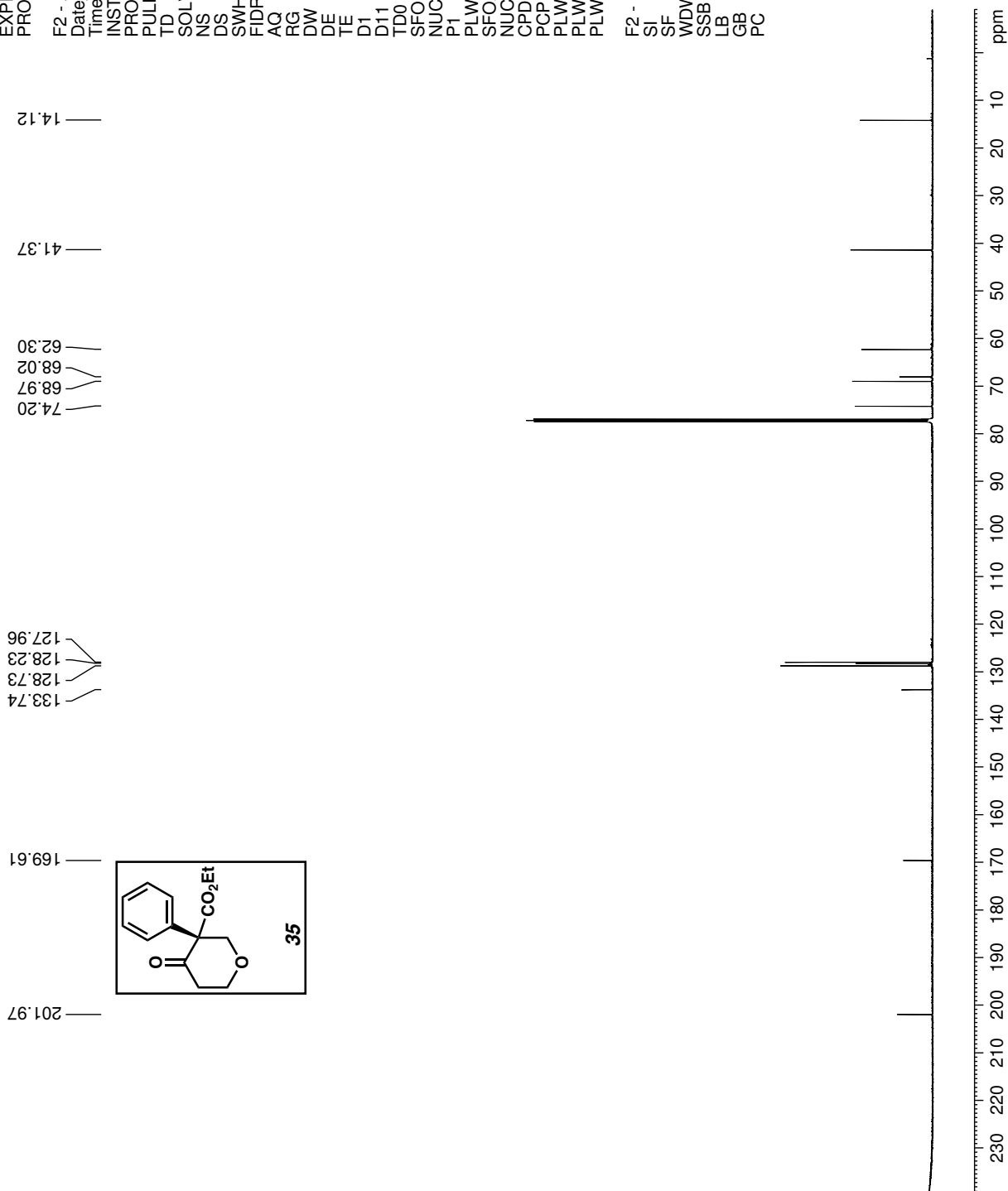


Figure S75 ^{13}C NMR (125 MHz, CDCl_3) of compound **35**.

Current Data Parameters
 NAME SMA-2017-015p
 EXPNO 13
 PROCNO 1

F2 - Acquisition Parameters
 Date_ 20170818
 Time_ 10.33 h
 INSTRUM av500
 PROBHD Z119248_0002 (
 PULPROG zgpg30
 TD 65536
 SOLVENT CDCI3
 NS 115
 DS 2
 SMH 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 9.63 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 0.13500001 W

F2 - Processing parameters
 SI 131072
 SF 125.7577892 MHz
 WDW EM
 SSB 0
 LB 1.00 Hz
 GB 0
 PC 1.40

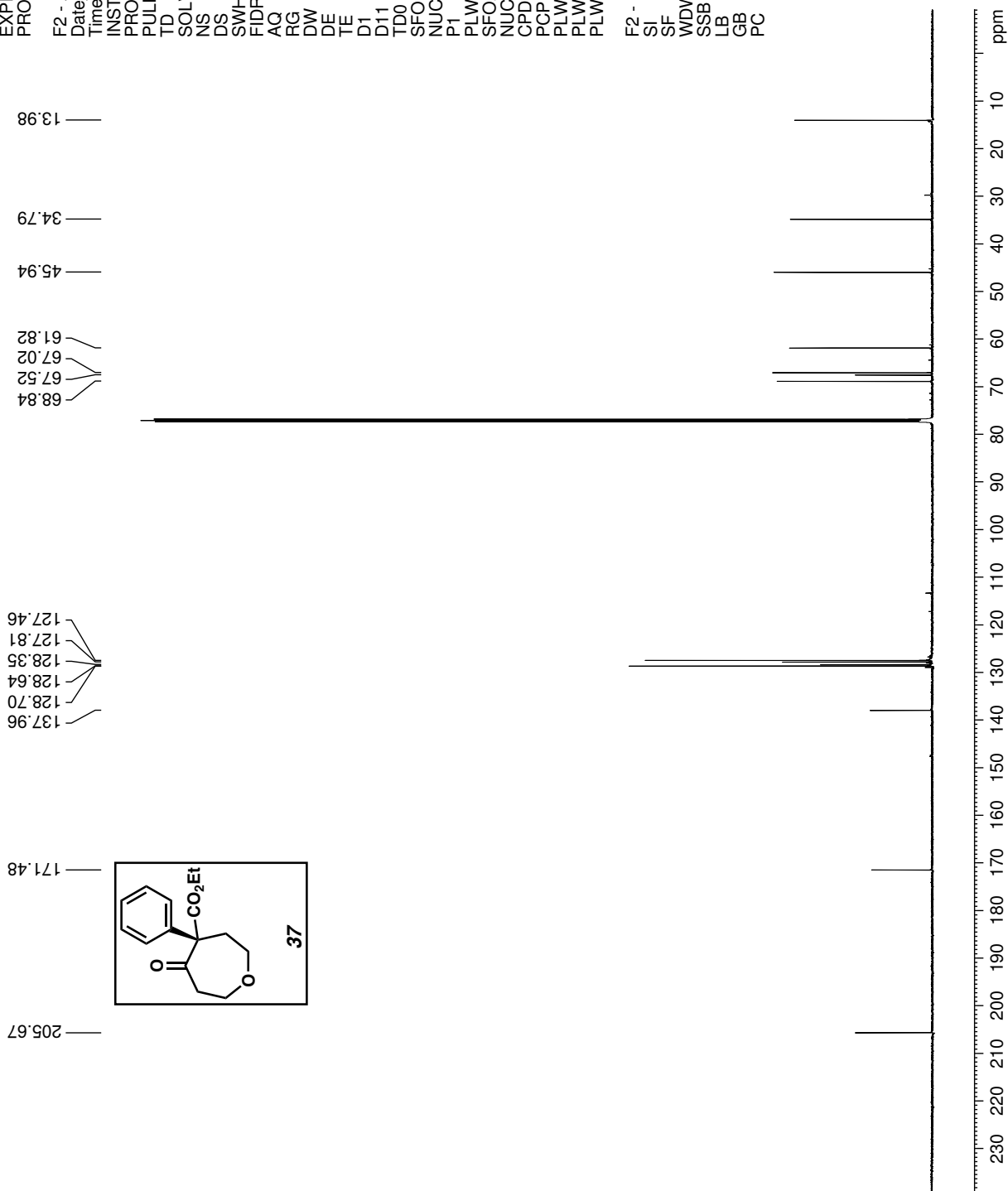


Figure S76 ^{13}C NMR (125 MHz, CDCl_3) of compound 37.

^2H NMR Spectra

9.264

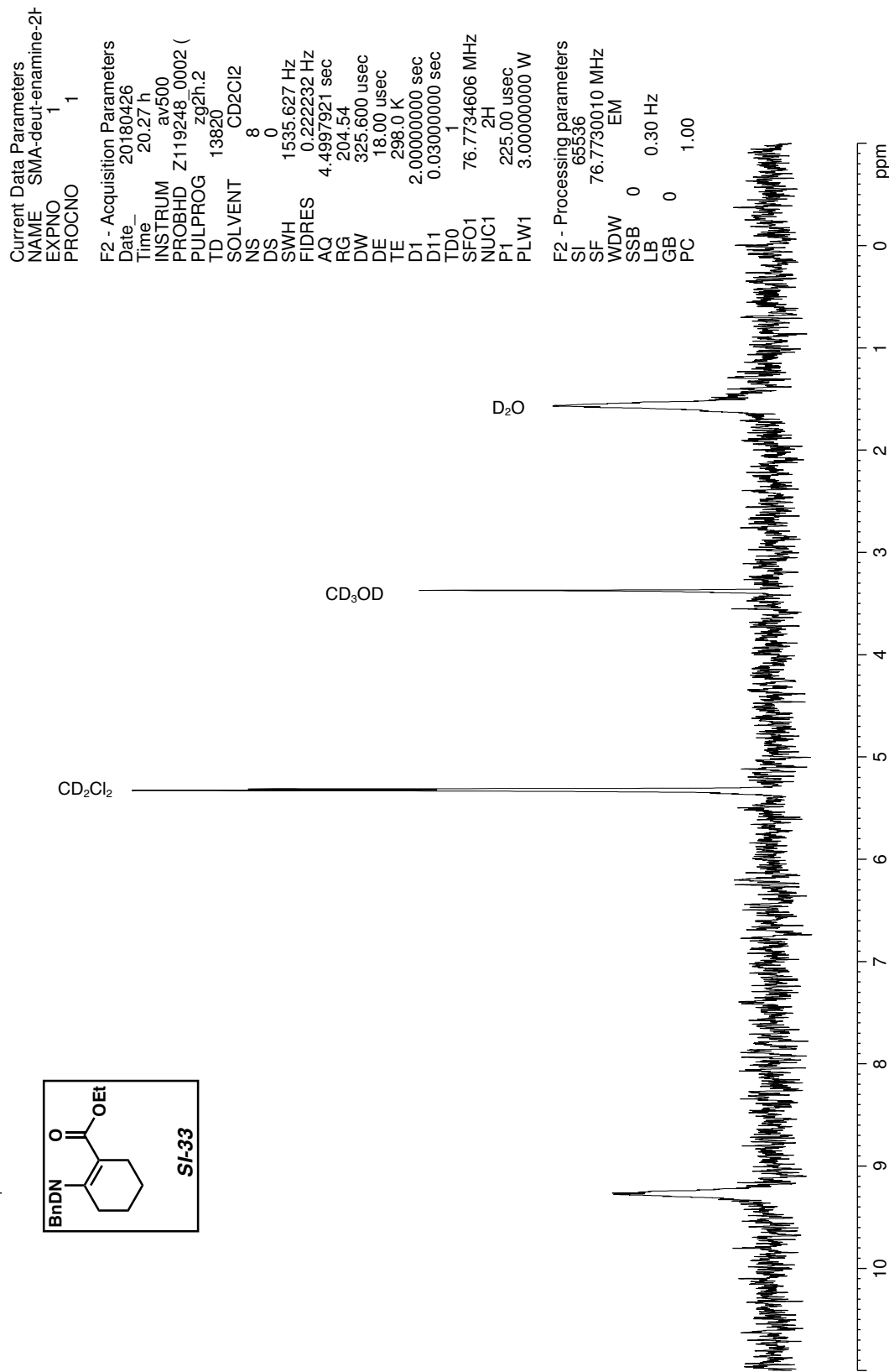
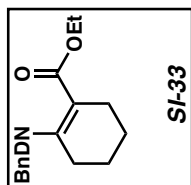
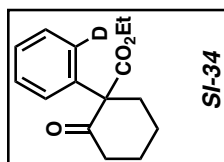


Figure S77 ^2H NMR (76 MHz, CH_2Cl_2) of compound **SI-33** with added CD_2Cl_2 and trace CD_3OD .

— 7.226



Current Data Parameters
 NAME MG-2018-131-coi-2H
 EXPNO 1
 PROCNO 1

F2 - Acquisition Parameters
 Date_ 20180426
 Time_ 20.24 h
 INSTRUM av500
 PROBHD Z119248_0002 (
 PULPROG zg2h.2
 TD 13820
 SOLVENT CD2Cl2
 NS 8
 DS 0
 SWH 1535.627 Hz
 FIDRES 0.222232 Hz
 AQ 4.4997921 sec
 RG 204.54
 DW 325.600 usec
 DE 18.00 usec
 TE 298.0 K
 D1 2.00000000 sec
 D11 0.03000000 sec
 TD0 1
 SFO1 76.7734606 MHz
 NUC1 ²H
 P1 225.00 usec
 PLW1 3.00000000 W

F2 - Processing parameters
 SI 65536
 SF 76.7730018 MHz
 WDW EM
 SSB 0
 LB 0.30 Hz
 GB 0
 PC 1.00

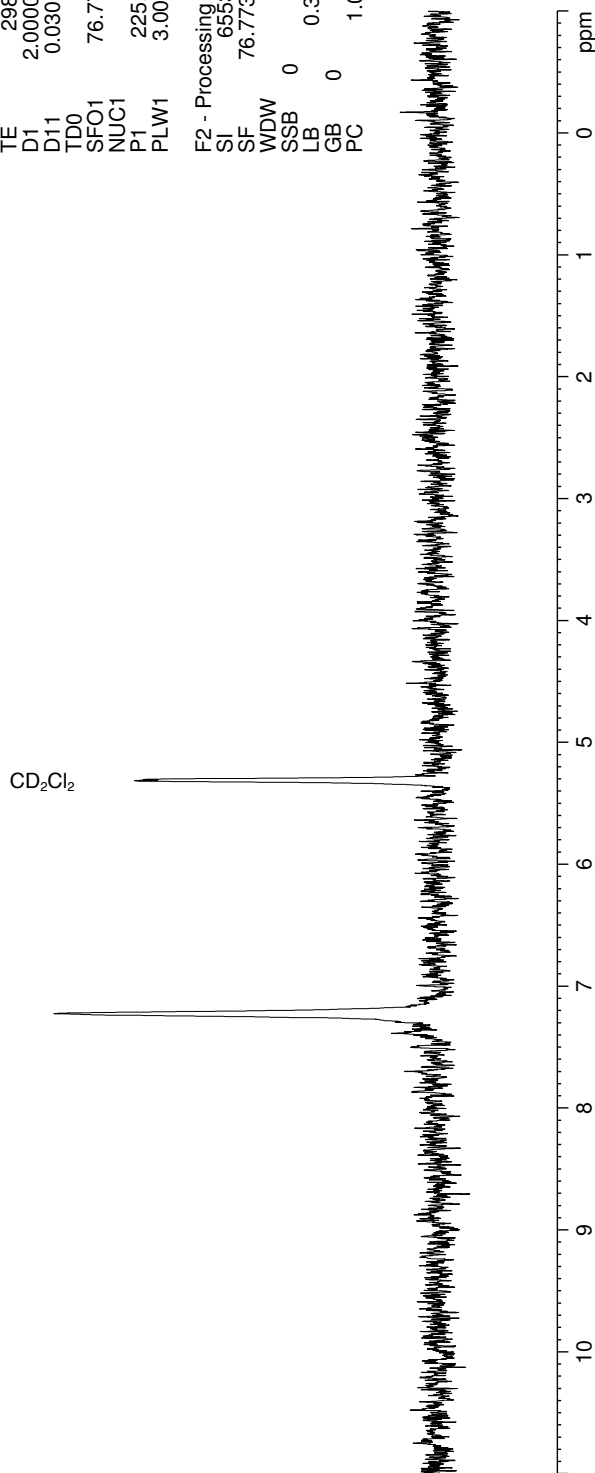


Figure S78 ¹H NMR (76 MHz, CH₂Cl₂) of compound SI-34 with added CD₂Cl₂.

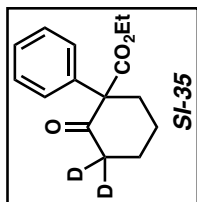
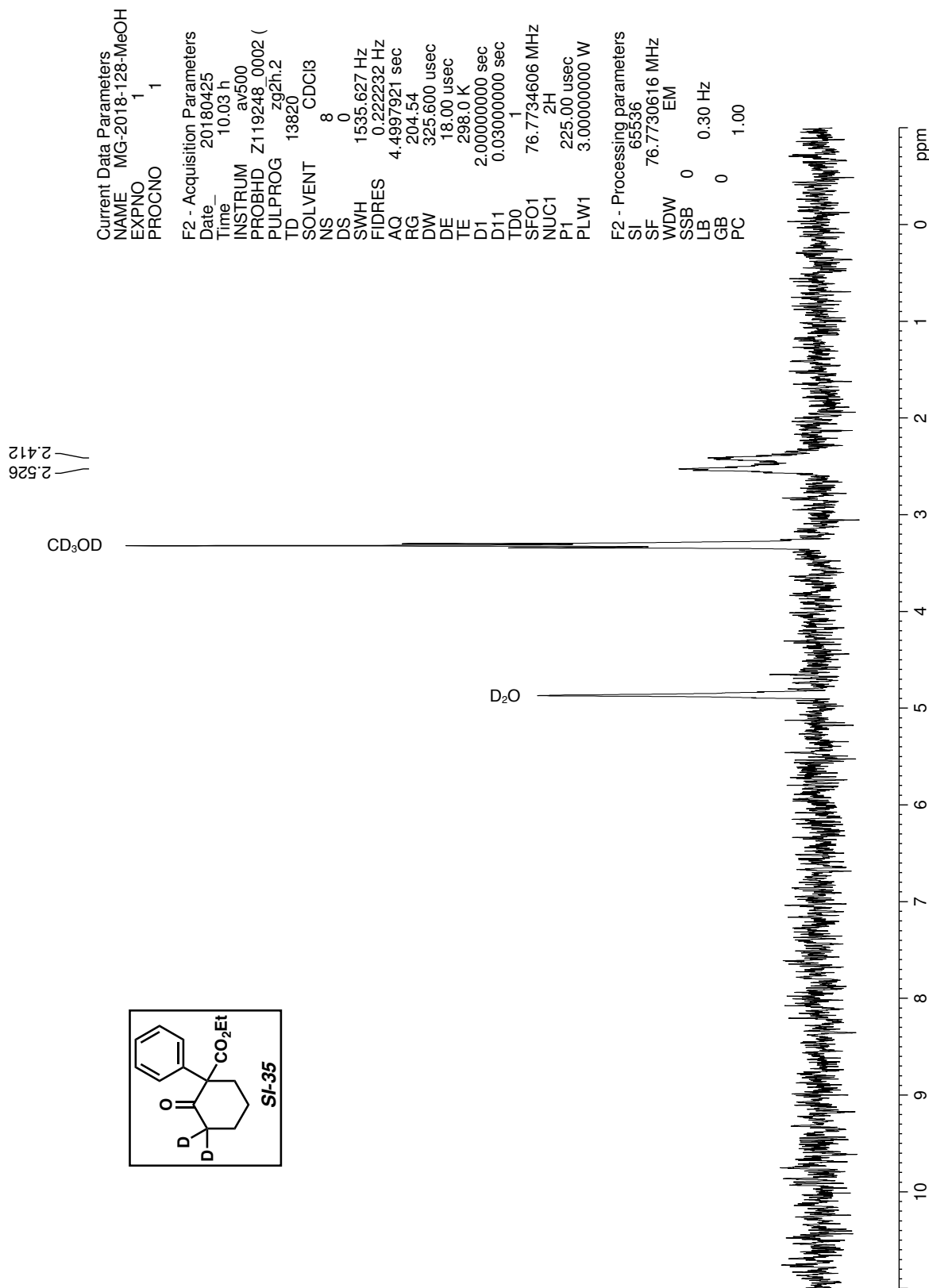


Figure S79 ¹H NMR (76 MHz, CH₃OH) of compound SI-35 with added CD₃OD.

SFC Traces

SFC traces from Table S1: Benzyne Arylation Reaction Optimization

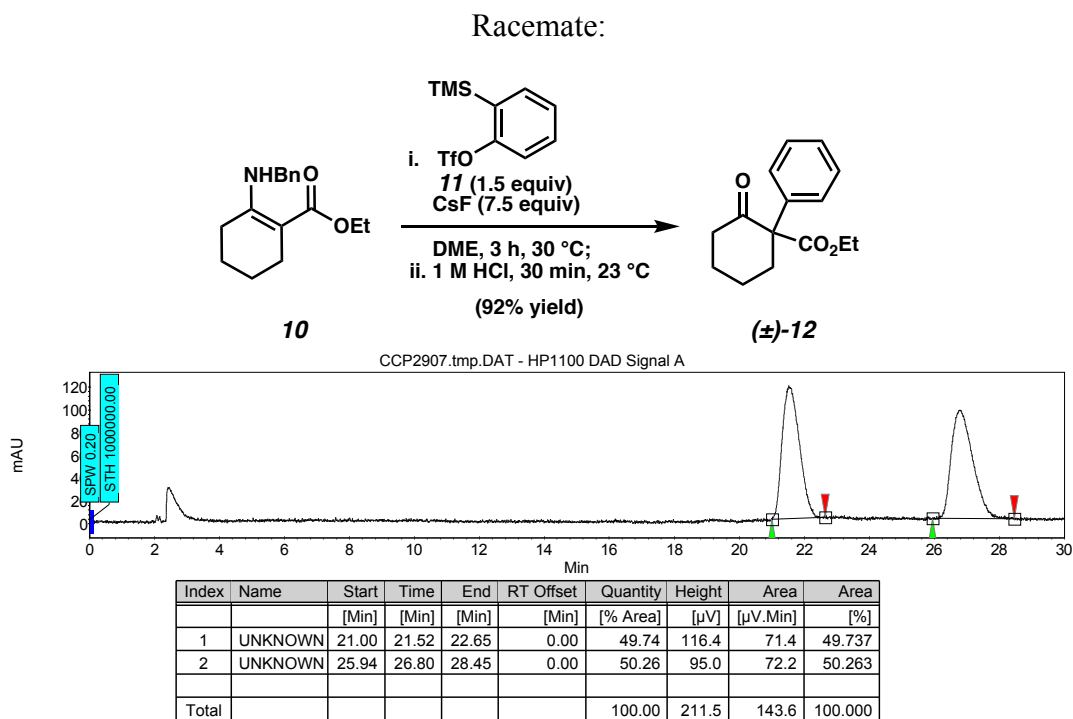
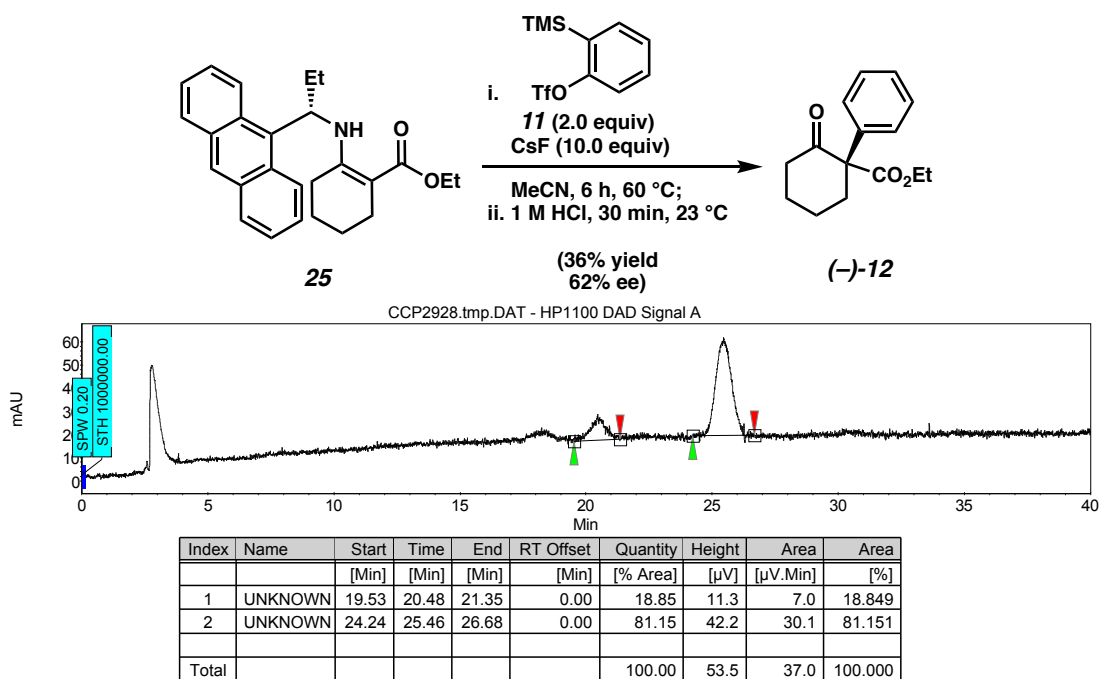
Figure S80 SFC trace of (\pm)-12Figure S81 SFC trace of ($-$)-12; (Table S1, Entry 1)

Figure S82 SFC trace of (–)-12; (Table S1, Entry 2)

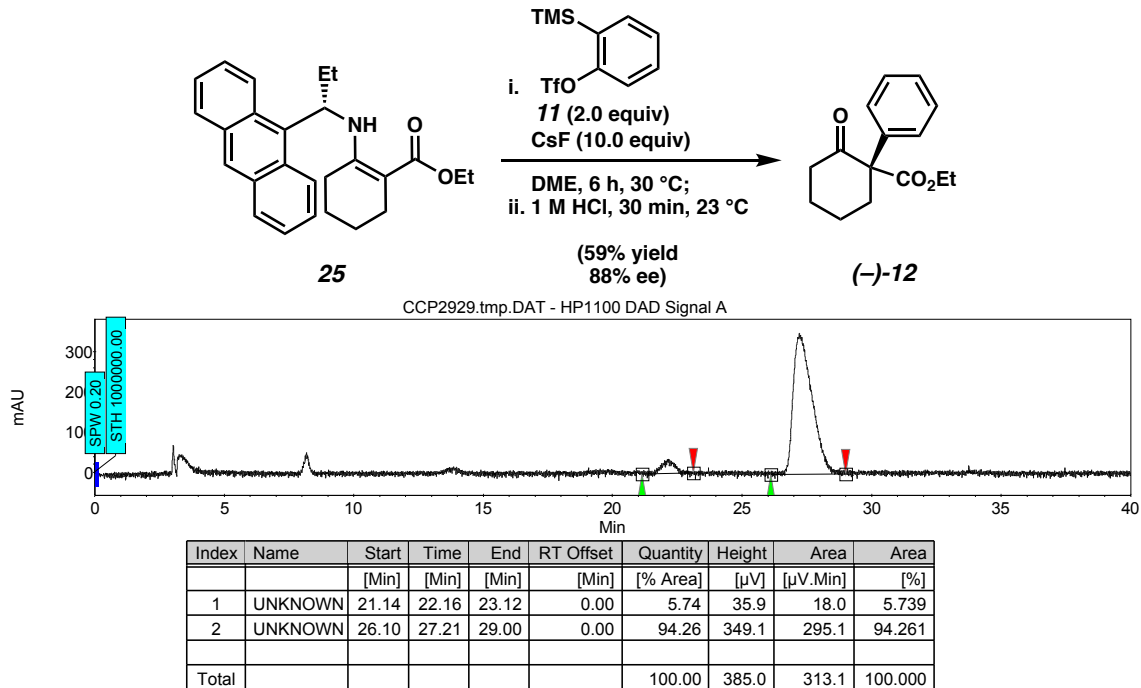


Figure S83 SFC trace of (–)-12; (Table S1, Entry 4)

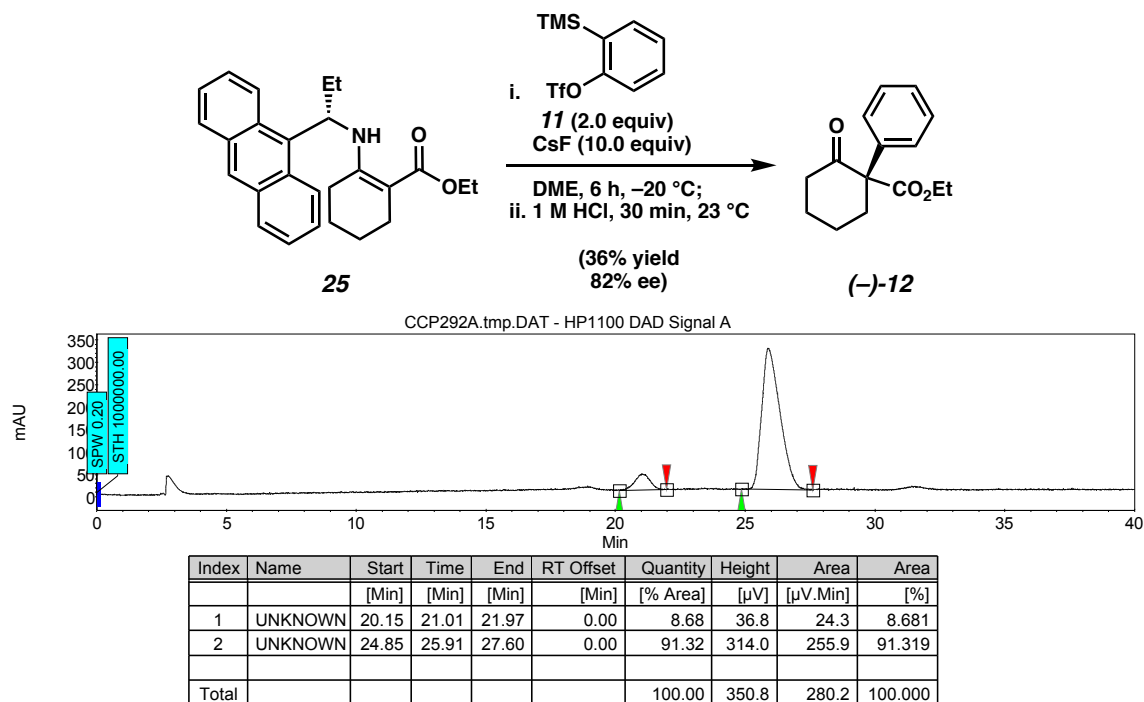


Figure S84 SFC trace of (–)-12; (Table S1, Entry 5)

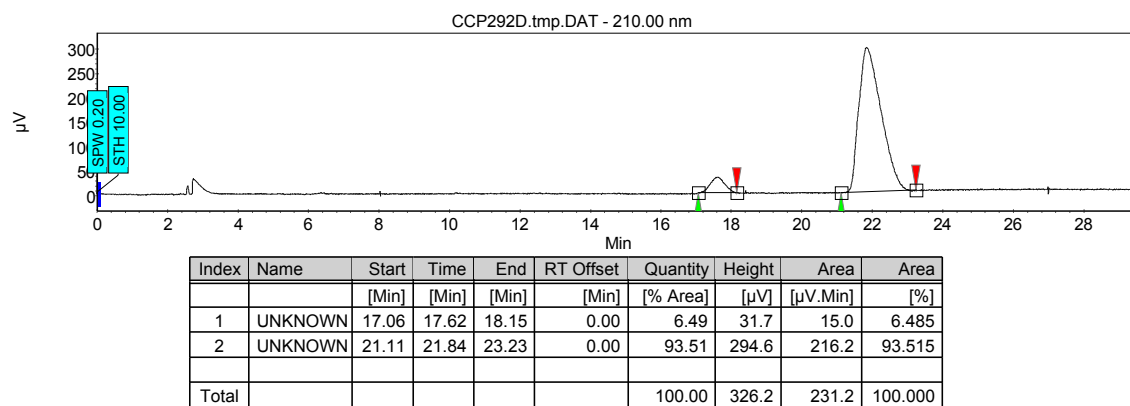
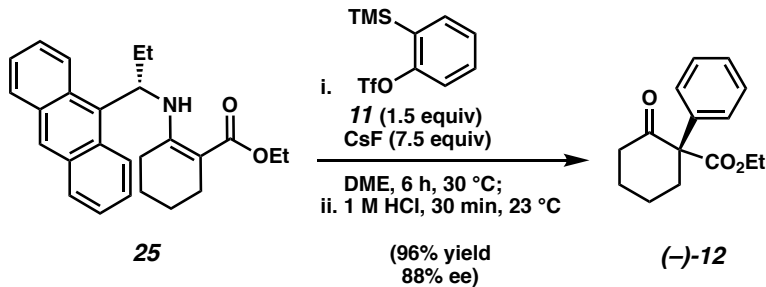


Figure S85 SFC trace of (–)-12; (Table S1, Entry 6)

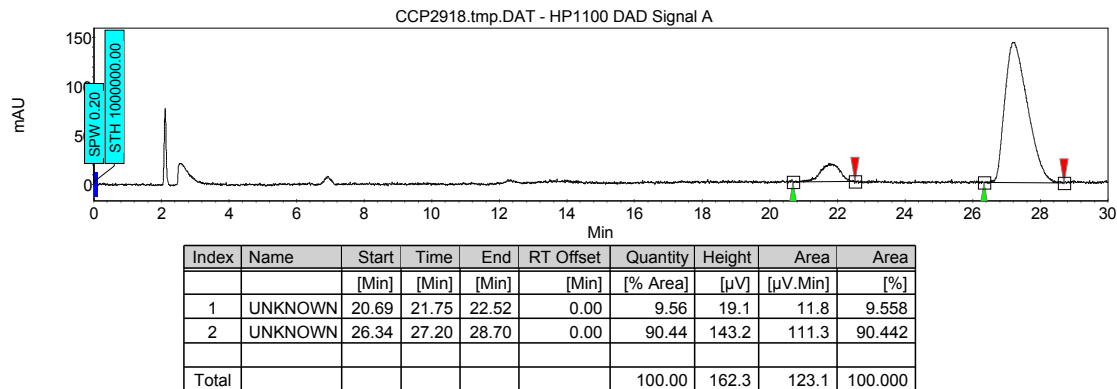
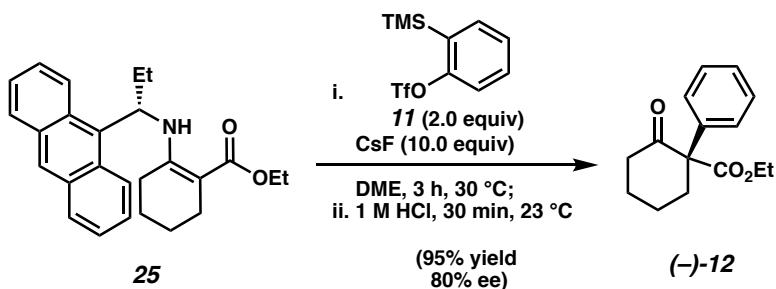
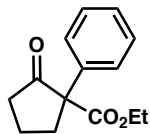
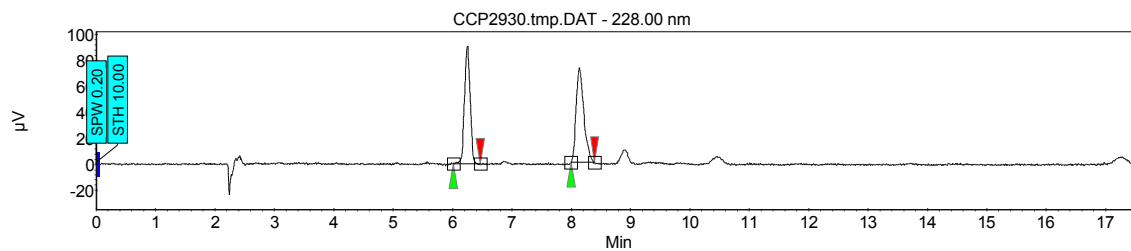
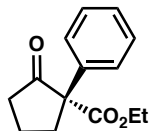


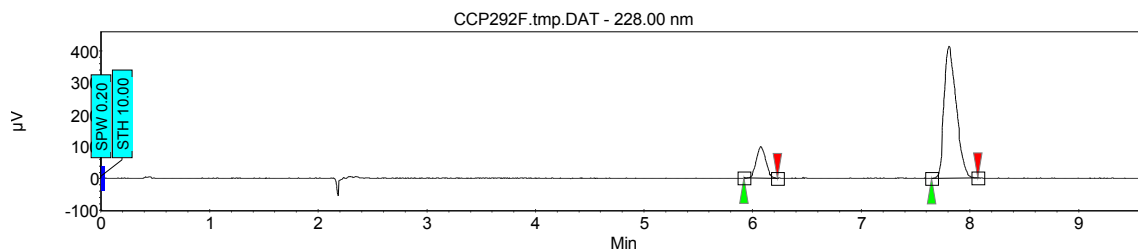
Figure S86 SFC trace of (\pm)-SI-32(\pm)-SI-32

Index	Name	Start [Min]	Time [Min]	End [Min]	RT Offset [Min]	Quantity [% Area]	Height [μV]	Area [μV.Min]	Area [%]
1	UNKNOWN	6.01	6.25	6.46	0.00	47.59	90.3	9.9	47.593
2	UNKNOWN	8.00	8.13	8.39	0.00	52.41	72.7	10.9	52.407
Total						100.00	163.0	20.8	100.000

Figure S87 SFC trace of (–)-SI-32



(–)-SI-32



Index	Name	Start [Min]	Time [Min]	End [Min]	RT Offset [Min]	Quantity [% Area]	Height [μV]	Area [μV.Min]	Area [%]
1	UNKNOWN	5.92	6.08	6.23	0.00	15.83	99.9	10.1	15.834
2	UNKNOWN	7.64	7.81	8.07	0.00	84.17	413.7	53.9	84.166
Total						100.00	513.6	64.0	100.000

SFC traces from Table 1: Amine Optimization

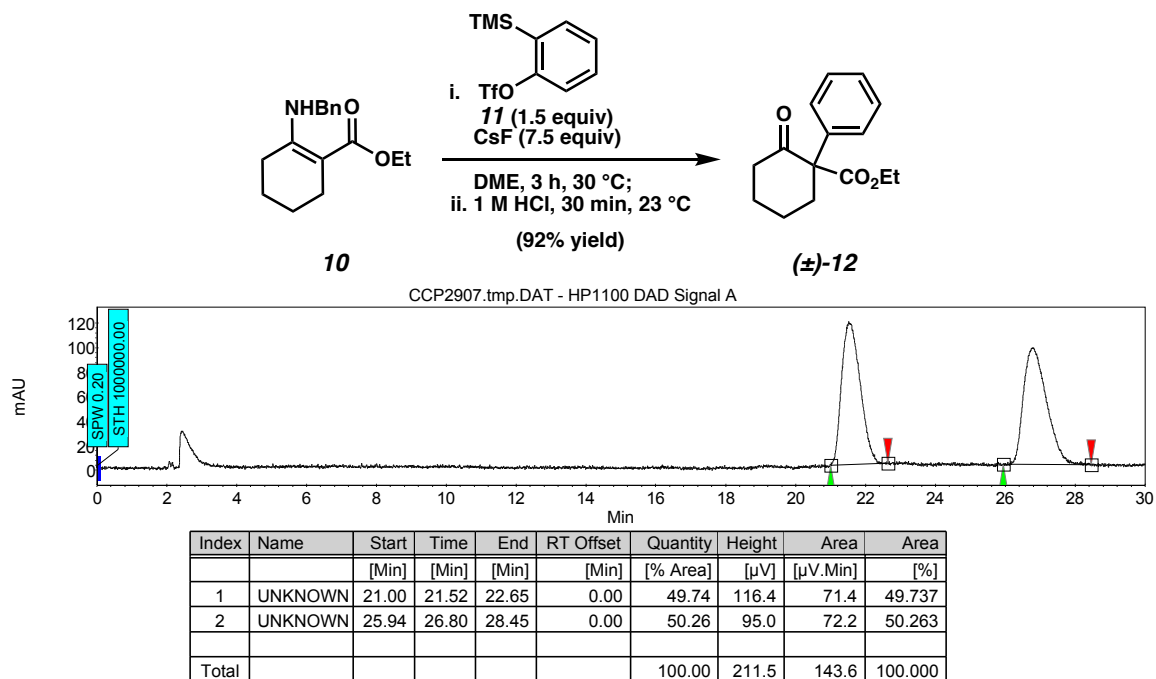
Figure S88 SFC trace of (\pm)-12

Figure S89 SFC trace of (+)-12; (Table 1, Entry 1)

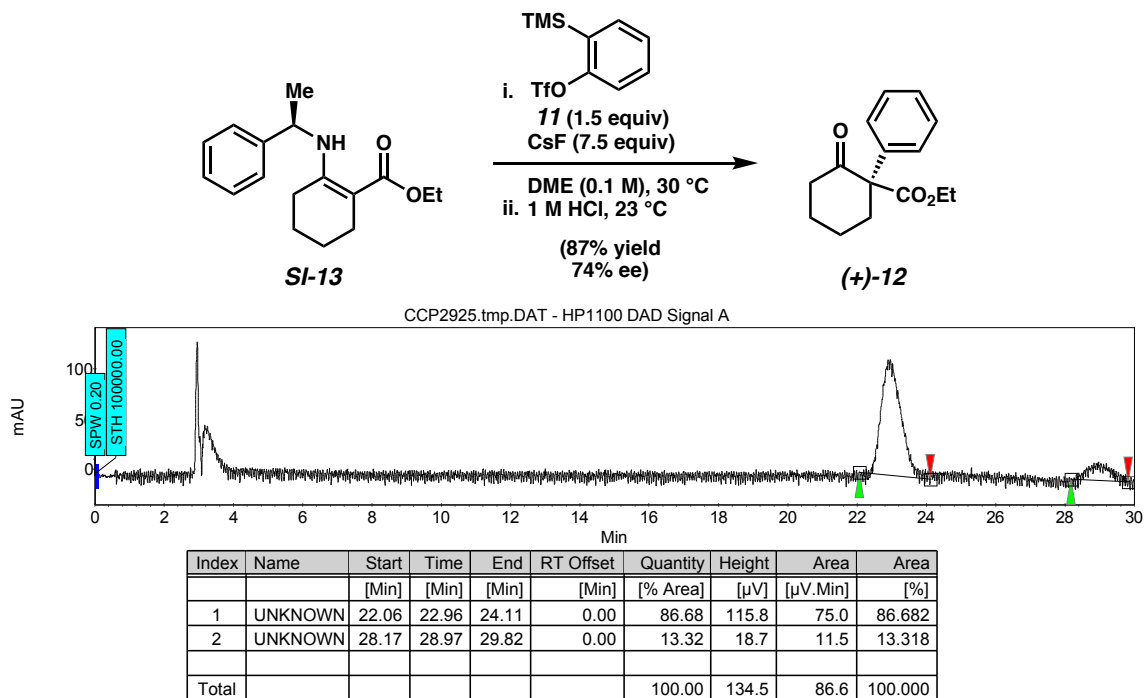


Figure S90 SFC trace of (+)-12; (Table 1, Entry 2)

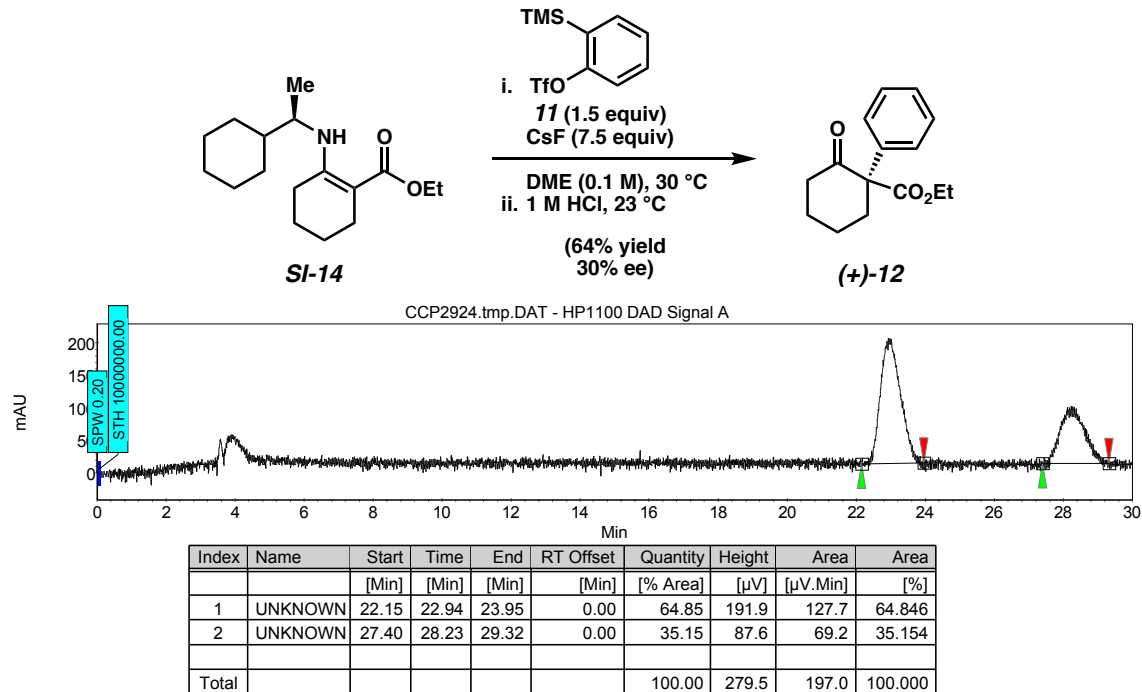


Figure S91 SFC trace of (+)-12; (Table 1, Entry 3)

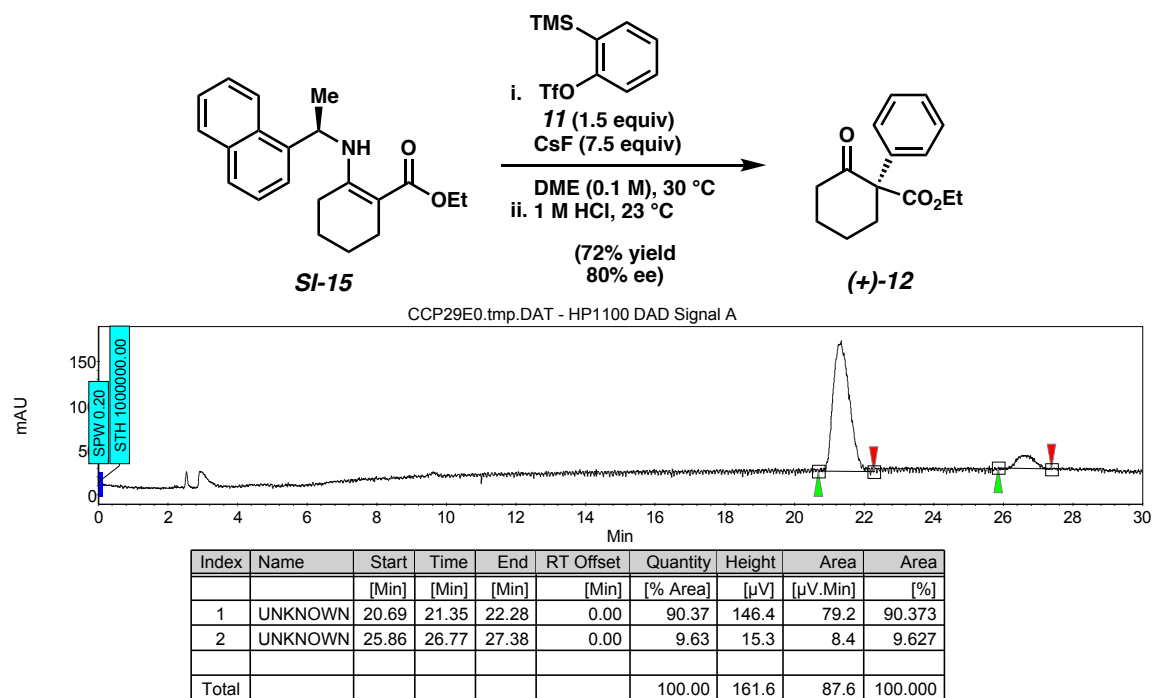


Figure S92 SFC trace of (+)-12; (Table 1, Entry 4)

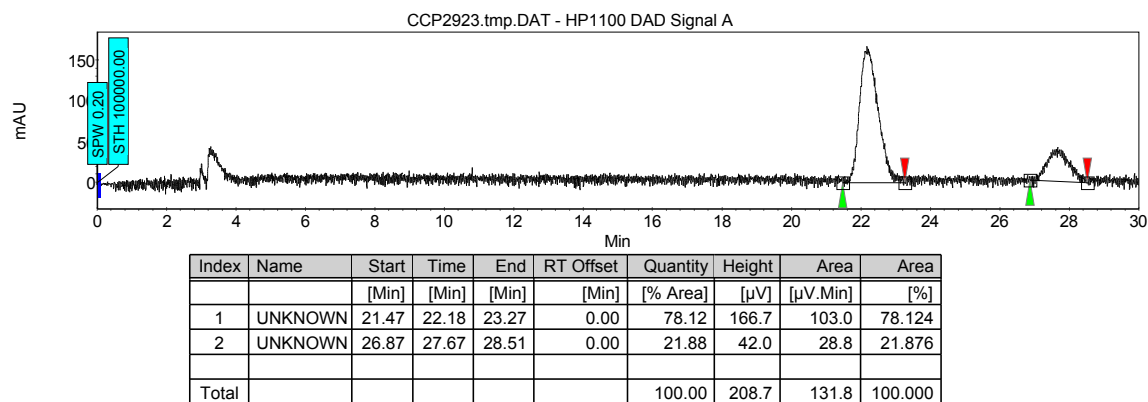
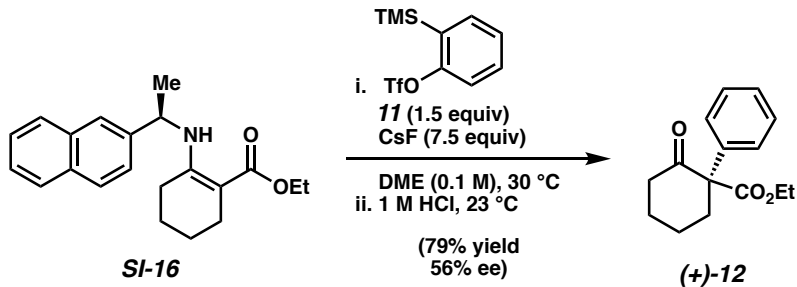


Figure S93 SFC trace of (+)-12; (Table 1, Entry 5)

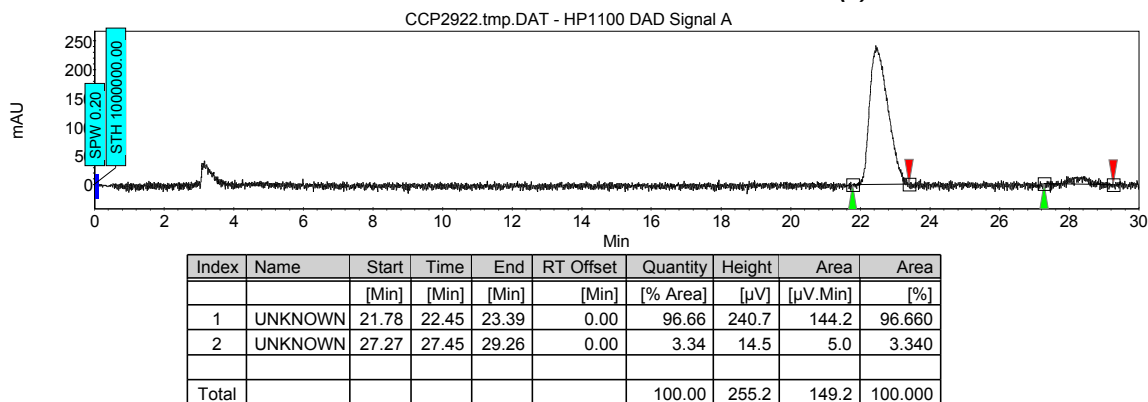
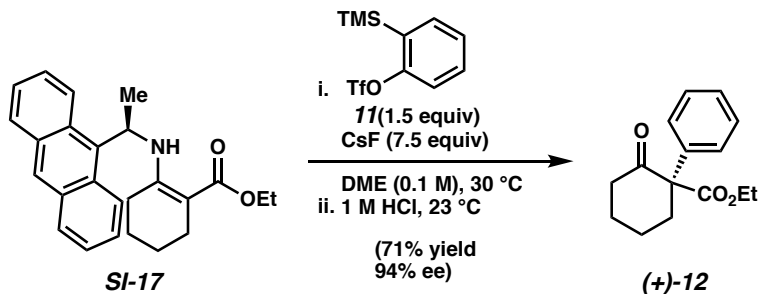


Figure S94 SFC trace of (+)-12; (Table 1, Entry 6)

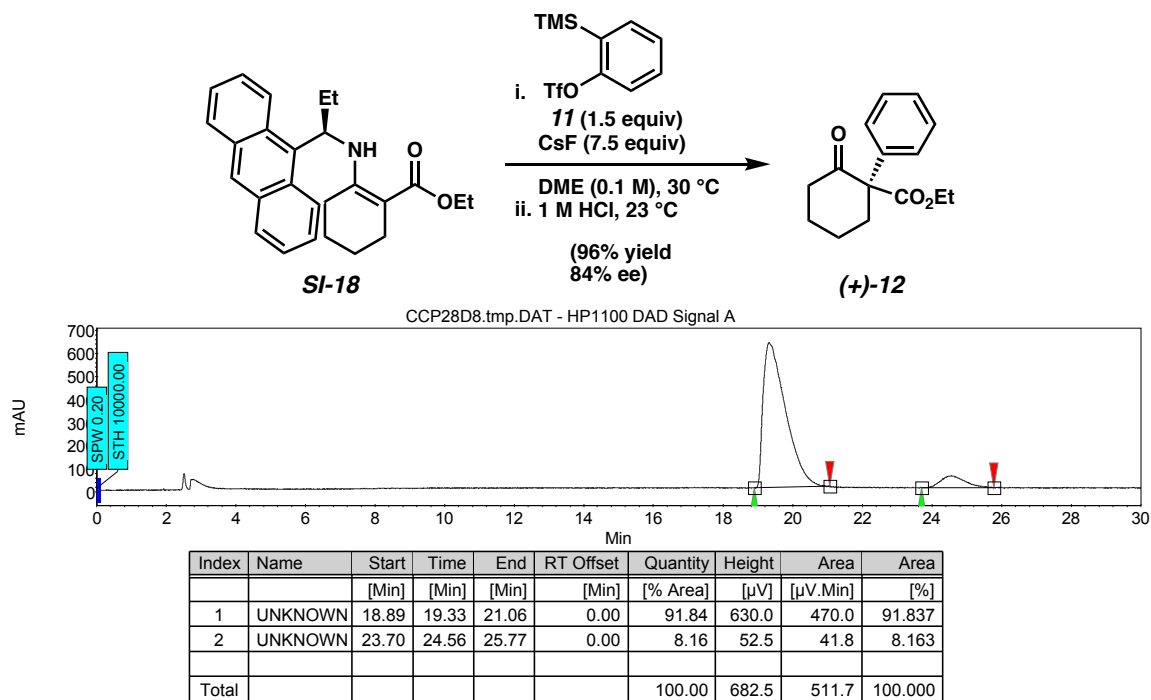
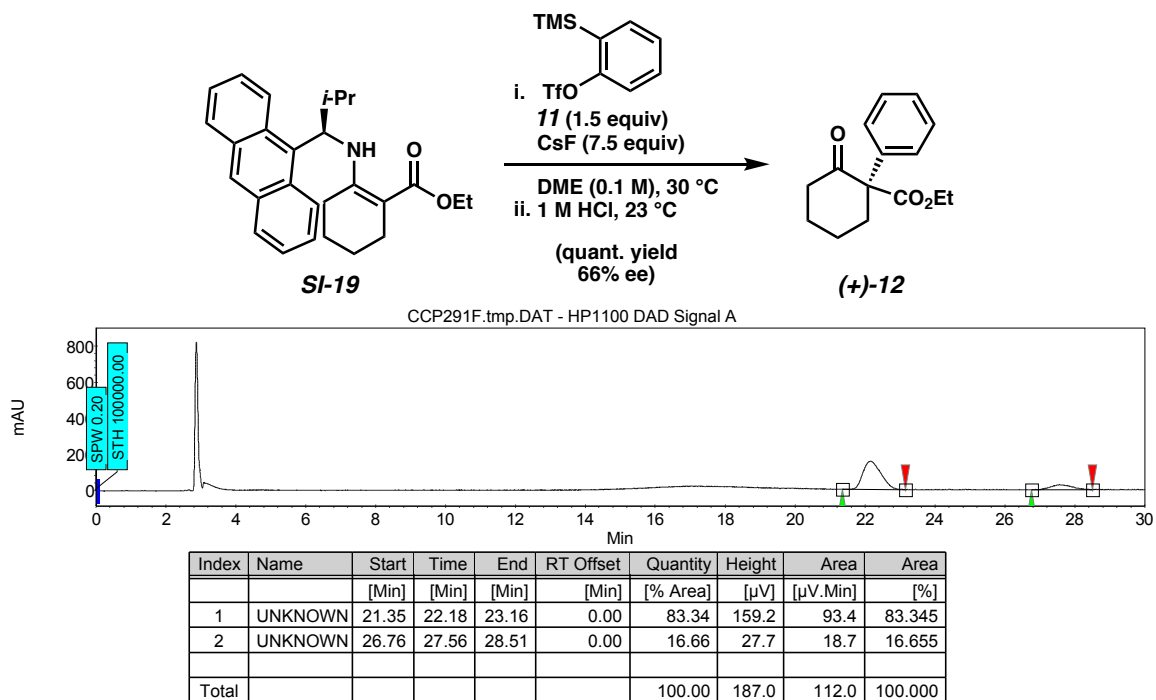
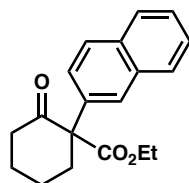
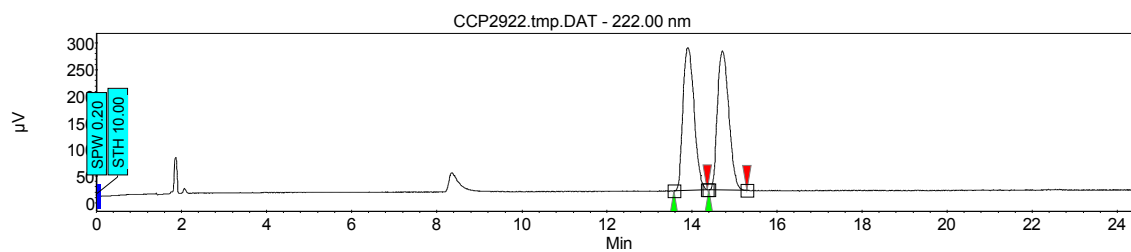


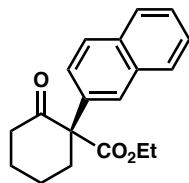
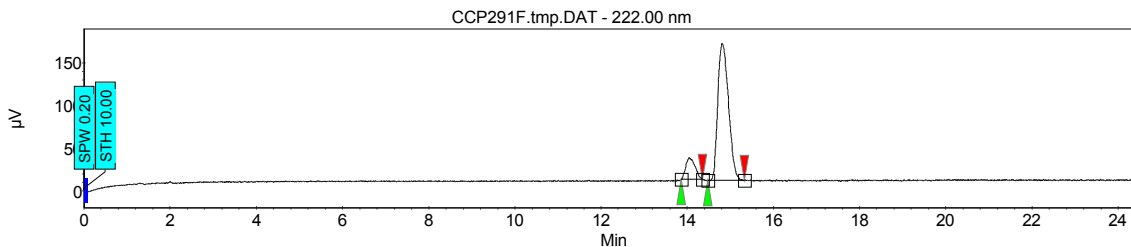
Figure S95 SFC trace of (+)-12; (Table 1, Entry 7)



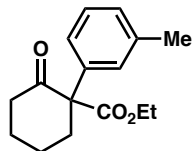
SFC traces from Figures 2 and 3: Electrophile Arylation Reactions

Figure S96 SFC trace of (\pm)-13**(\pm)-13**

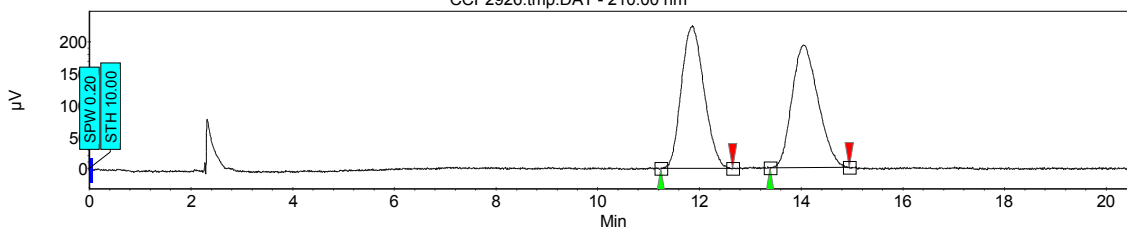
Index	Name	Start [Min]	Time [Min]	End [Min]	RT Offset [Min]	Quantity [% Area]	Height [μ V]	Area [μ V.Min]	Area [%]
1	UNKNOWN	13.58	13.91	14.37	0.00	50.06	267.8	81.7	50.064
2	UNKNOWN	14.40	14.72	15.29	0.00	49.94	261.3	81.5	49.936
Total						100.00	529.2	163.1	100.000

Figure S97 SFC trace of ($-$)-13**($-$)-13**

Index	Name	Start [Min]	Time [Min]	End [Min]	RT Offset [Min]	Quantity [% Area]	Height [μ V]	Area [μ V.Min]	Area [%]
1	UNKNOWN	13.87	14.05	14.36	0.00	12.03	25.7	6.3	12.033
2	UNKNOWN	14.48	14.81	15.32	0.00	87.97	160.7	46.2	87.967
Total						100.00	186.4	52.6	100.000

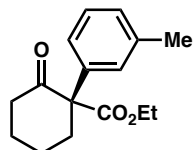
Figure S98 SFC trace of (\pm)-28**(\pm)-28**

CCP2926.tmp.DAT - 210.00 nm

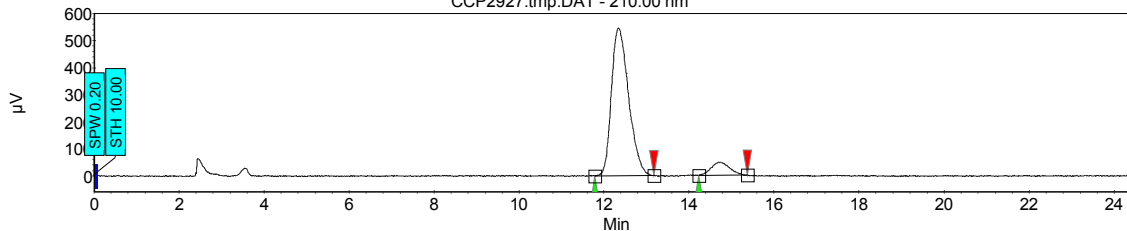


Index	Name	Start [Min]	Time [Min]	End [Min]	RT Offset [Min]	Quantity [% Area]	Height [μV]	Area [μV.Min]	Area [%]
1	UNKNOWN	11.24	11.86	12.65	0.00	50.25	225.9	116.5	50.255
2	UNKNOWN	13.39	14.04	14.94	0.00	49.75	194.2	115.3	49.745
Total						100.00	420.0	231.8	100.000

Figure S99 SFC trace of (–)-28

**(–)-28**

CCP2927.tmp.DAT - 210.00 nm



Index	Name	Start [Min]	Time [Min]	End [Min]	RT Offset [Min]	Quantity [% Area]	Height [μV]	Area [μV.Min]	Area [%]
1	UNKNOWN	11.79	12.35	13.18	0.00	91.57	545.5	255.7	91.568
2	UNKNOWN	14.23	14.74	15.37	0.00	8.43	47.5	23.5	8.432
Total						100.00	593.0	279.3	100.000

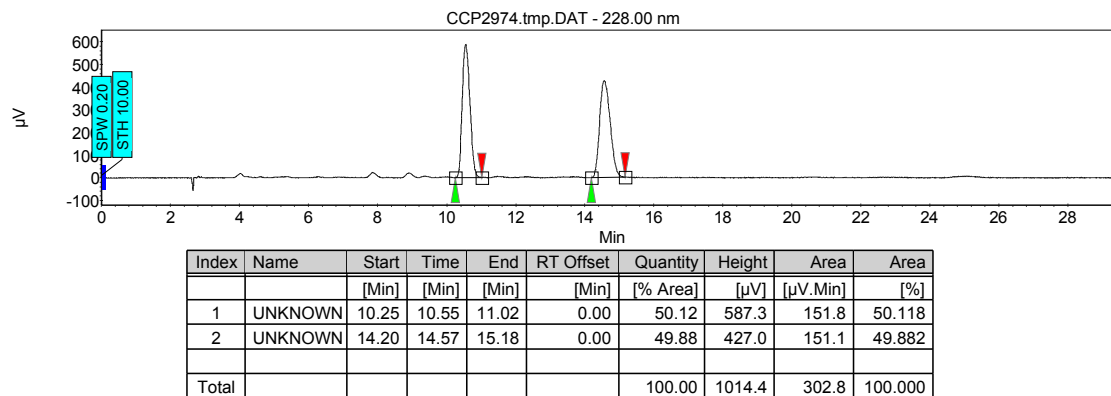
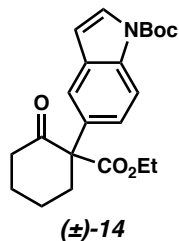
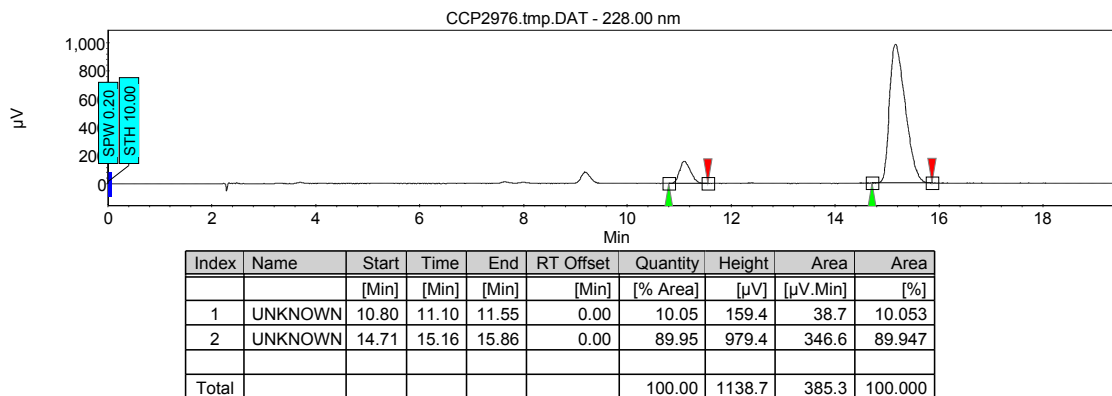
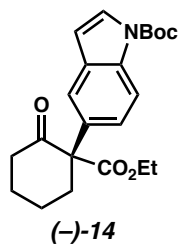
Figure S100 SFC trace of (\pm)-14**Figure S101** SFC trace of (–)-14

Figure S102 HPLC trace of (\pm)-29

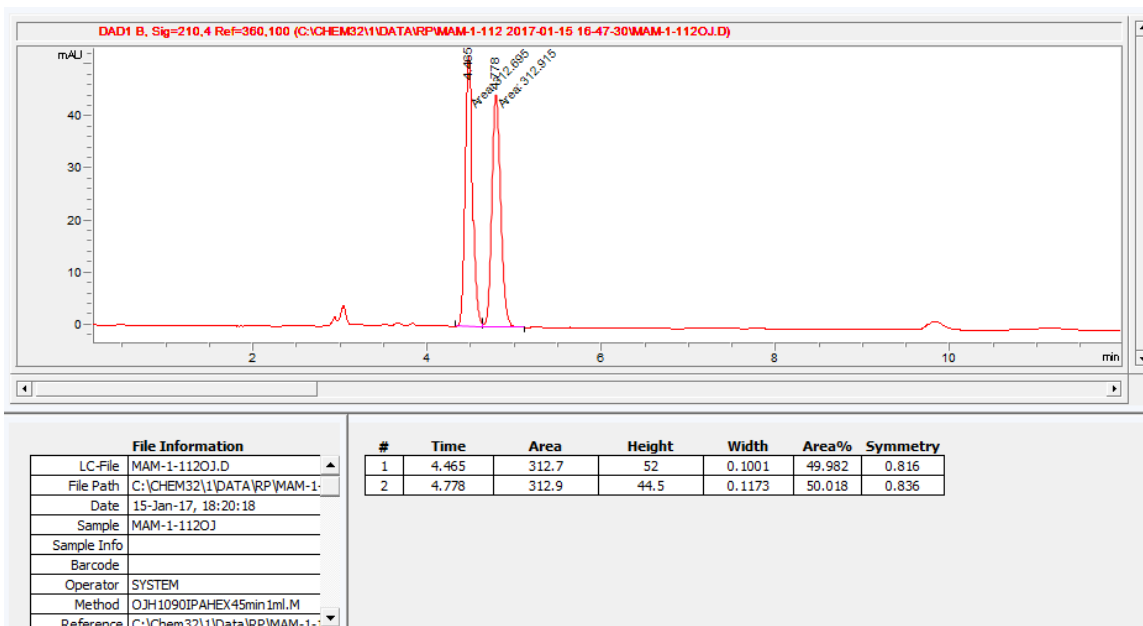
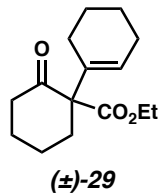


Figure S103 HPLC trace of (-)-29

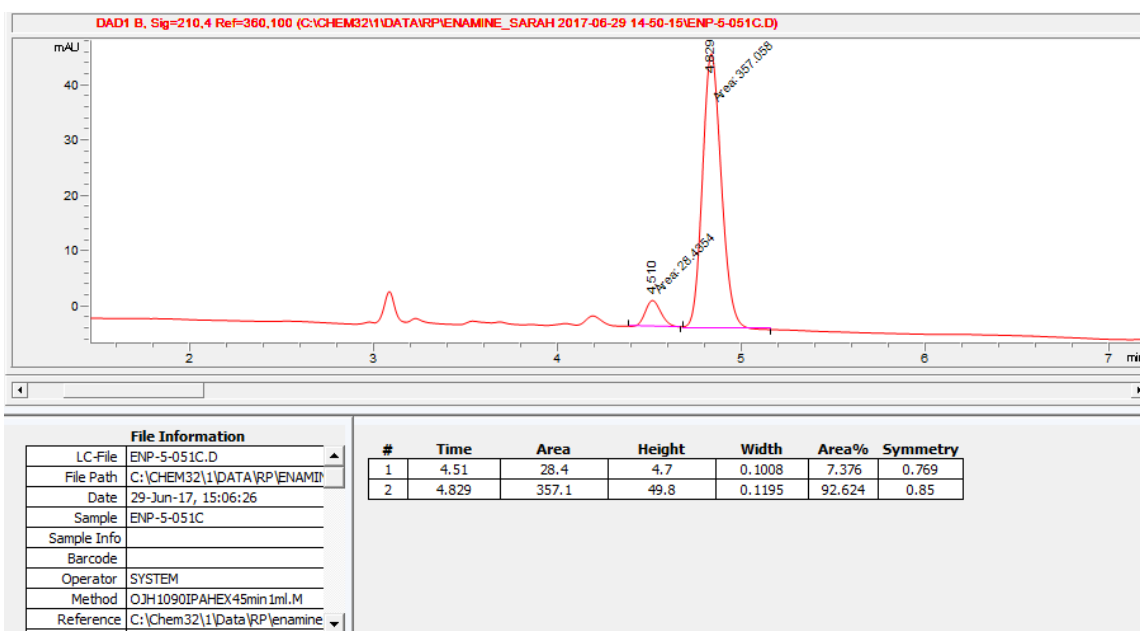
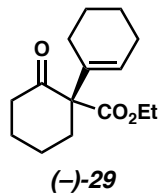
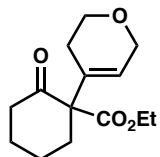
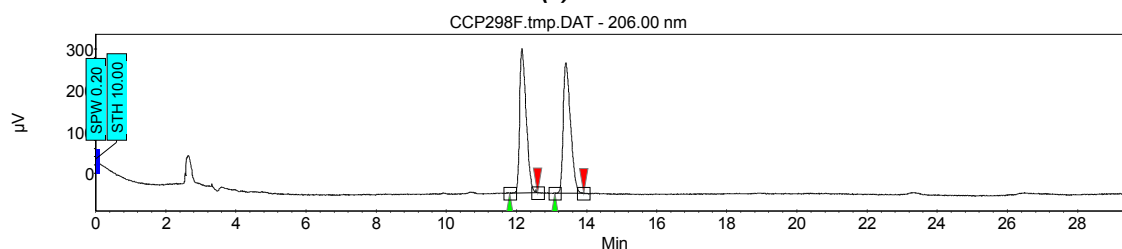
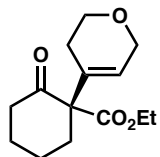
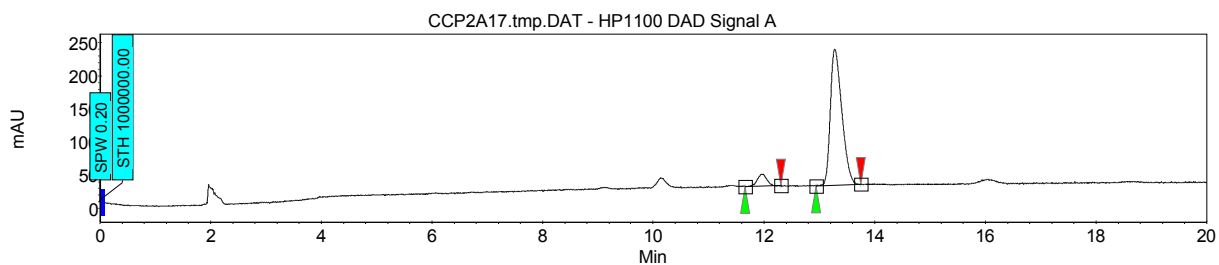


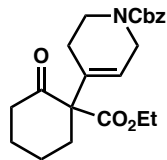
Figure S104 SFC trace of (\pm)-16**(\pm)-16**

Index	Name	Start [Min]	Time [Min]	End [Min]	RT Offset [Min]	Quantity [% Area]	Height [μ V]	Area [μ V.Min]	Area [%]
1	UNKNOWN	11.80	12.15	12.60	0.00	49.53	349.0	75.0	49.530
2	UNKNOWN	13.09	13.41	13.91	0.00	50.47	317.1	76.4	50.470
Total						100.00	666.1	151.4	100.000

Figure S105 SFC trace of ($-$)-16**($-$)-16**

Index	Name	Start [Min]	Time [Min]	End [Min]	RT Offset [Min]	Quantity [% Area]	Height [μ V]	Area [μ V.Min]	Area [%]
1	UNKNOWN	11.67	11.97	12.31	0.00	7.00	18.5	3.7	7.000
2	UNKNOWN	12.95	13.28	13.76	0.00	93.00	204.7	49.3	93.000
Total						100.00	223.2	53.1	100.000

Figure S106 HPLC trace of (\pm)-15



(\pm)-15

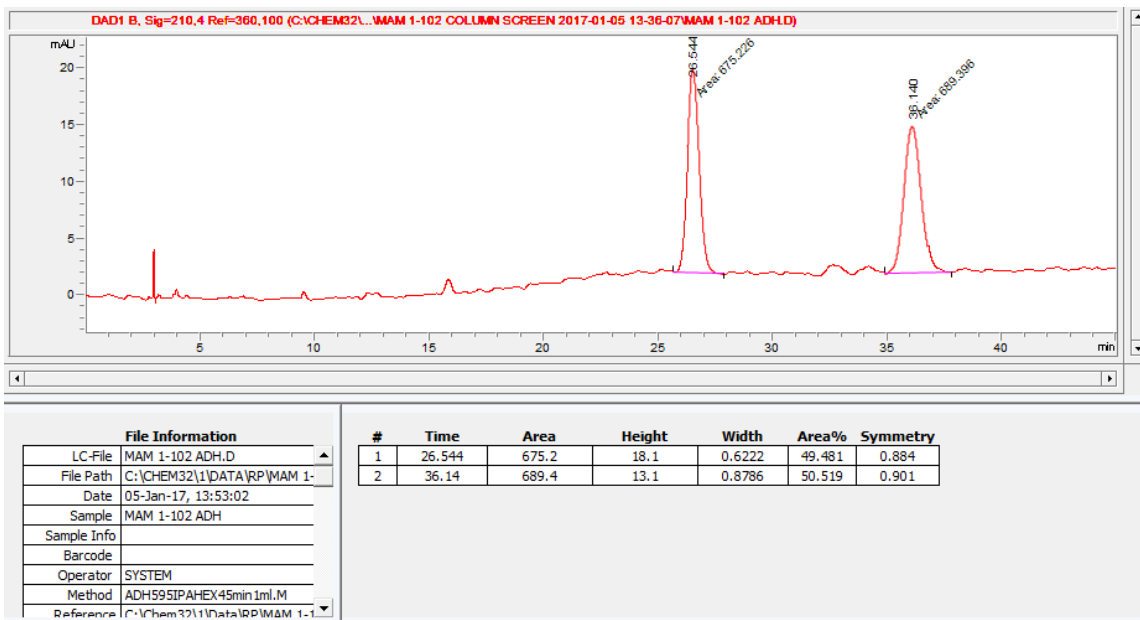
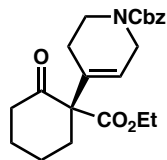
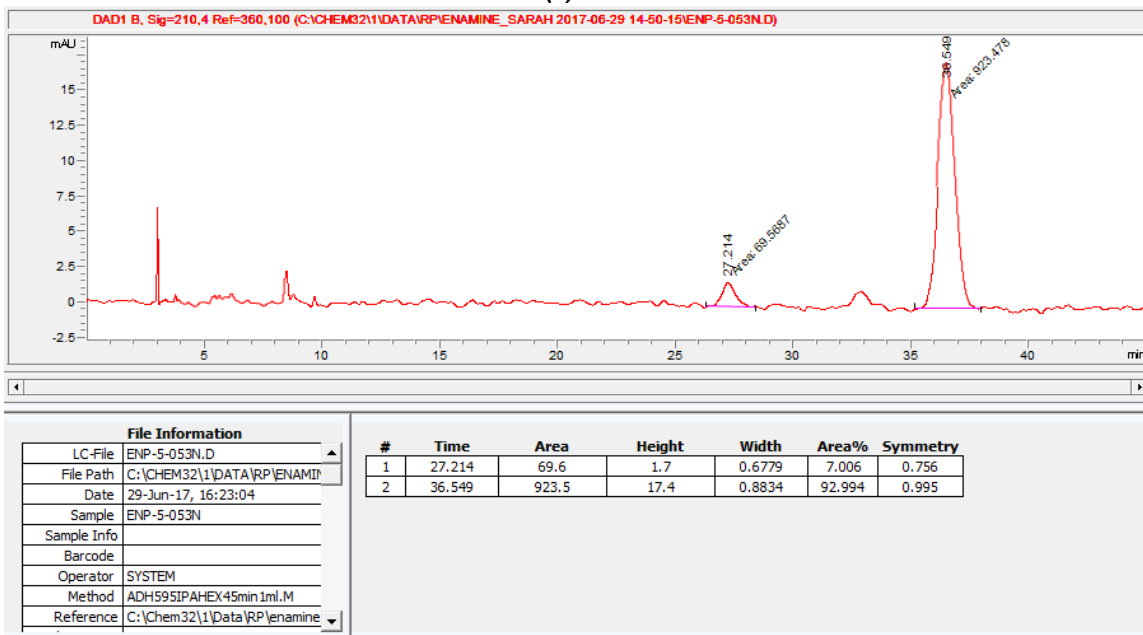


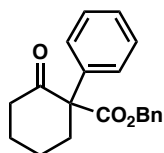
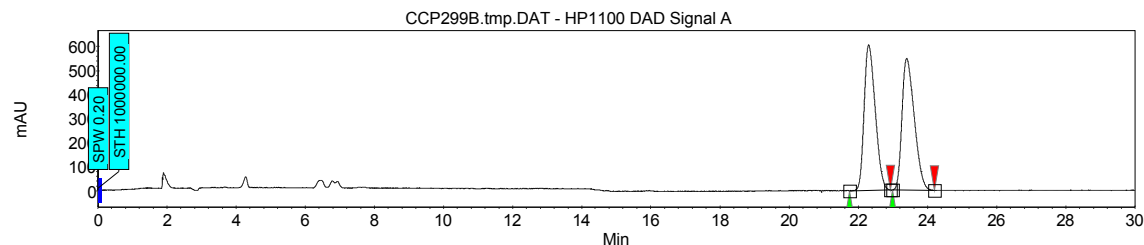
Figure S107 HPLC trace of (-)-15



(-)-15

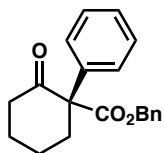


SFC traces from Figure 4: Nucleophile Arylation Reactions

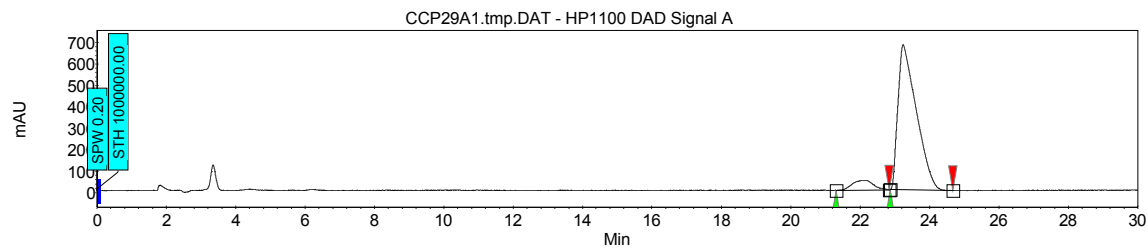
Figure S108 SFC trace of (\pm)-32(\pm)-32

Index	Name	Start [Min]	Time [Min]	End [Min]	RT Offset [Min]	Quantity [% Area]	Height [μ V]	Area [μ V.Min]	Area [%]
1	UNKNOWN	21.75	22.30	22.93	0.00	49.88	604.8	224.8	49.877
2	UNKNOWN	22.99	23.40	24.21	0.00	50.12	547.5	225.9	50.123
Total						100.00	1152.3	450.6	100.000

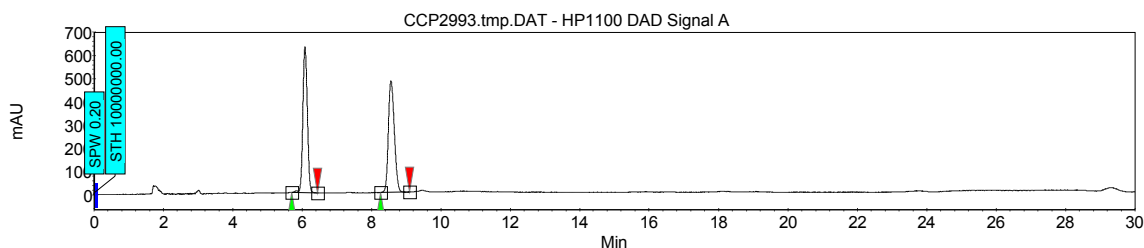
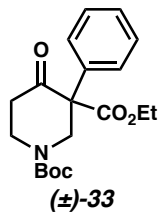
Figure S109 SFC trace of (–)-32



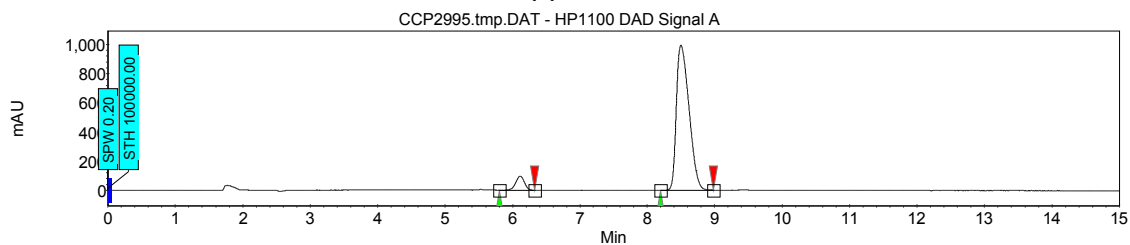
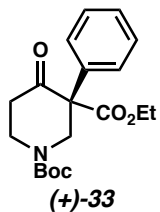
(–)-32



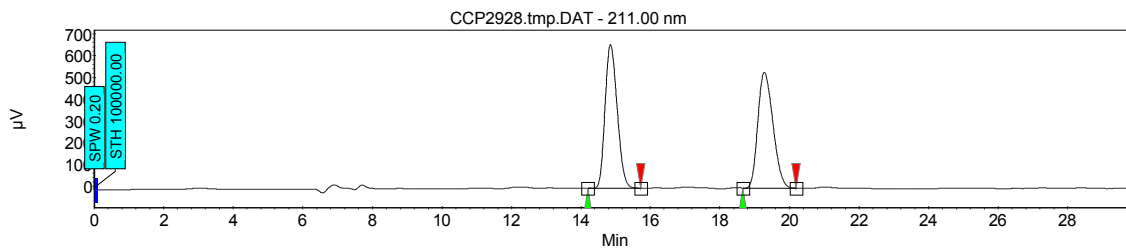
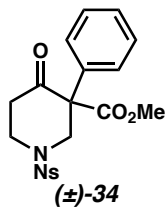
Index	Name	Start [Min]	Time [Min]	End [Min]	RT Offset [Min]	Quantity [% Area]	Height [μ V]	Area [μ V.Min]	Area [%]
1	UNKNOWN	21.31	22.10	22.84	0.00	7.04	45.1	31.4	7.044
2	UNKNOWN	22.87	23.24	24.67	0.00	92.96	674.9	414.1	92.956
Total						100.00	720.1	445.5	100.000

Figure S110 SFC trace of (\pm)-**33**

Index	Name	Start [Min]	Time [Min]	End [Min]	RT Offset [Min]	Quantity [% Area]	Height [μ V]	Area [μ V.Min]	Area [%]
1	UNKNOWN	5.70	6.08	6.44	0.00	49.58	627.2	94.4	49.576
2	UNKNOWN	8.25	8.55	9.09	0.00	50.42	481.6	96.0	50.424
Total						100.00	1108.8	190.4	100.000

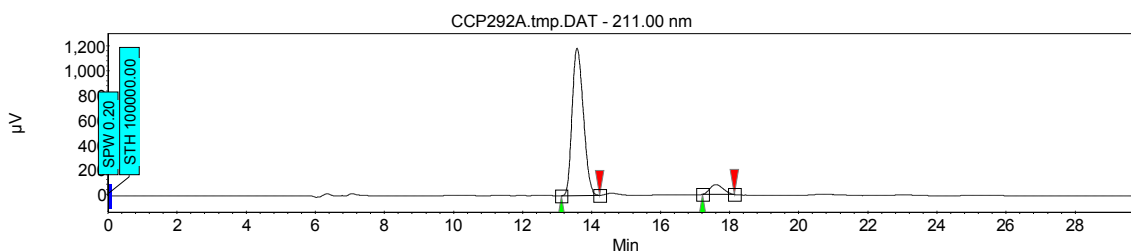
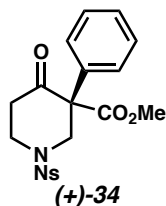
Figure S111 SFC trace of (+)-**33**

Index	Name	Start [Min]	Time [Min]	End [Min]	RT Offset [Min]	Quantity [% Area]	Height [μ V]	Area [μ V.Min]	Area [%]
2	UNKNOWN	5.81	6.11	6.32	0.00	6.17	95.7	14.2	6.172
1	UNKNOWN	8.20	8.50	8.98	0.00	93.83	993.7	215.6	93.828
Total						100.00	1089.4	229.8	100.000

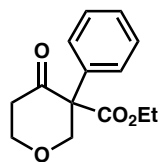
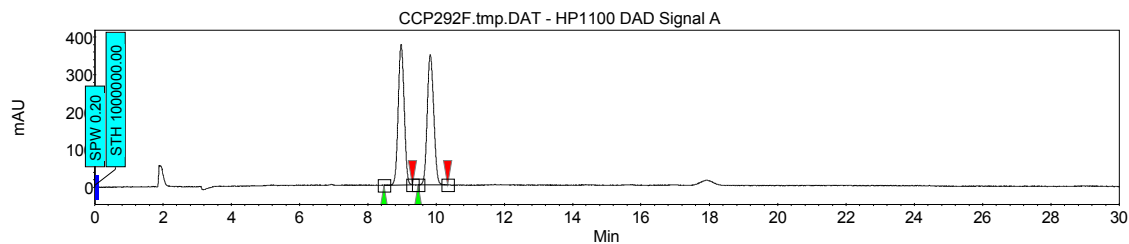
Figure S112 SFC trace of (\pm)-34

Index	Name	Start [Min]	Time [Min]	End [Min]	RT Offset [Min]	Quantity [% Area]	Height [μV]	Area [μV.Min]	Area [%]
1	UNKNOWN	14.20	14.85	15.72	0.00	49.87	661.5	267.2	49.874
2	UNKNOWN	18.66	19.28	20.18	0.00	50.13	534.1	268.5	50.126
Total						100.00	1195.6	535.7	100.000

Figure S113 SFC trace of (+)-34

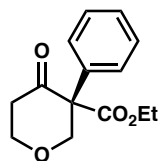
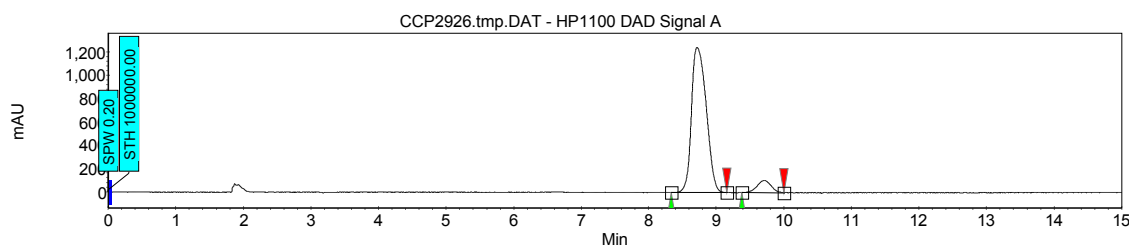


Index	Name	Start [Min]	Time [Min]	End [Min]	RT Offset [Min]	Quantity [% Area]	Height [μV]	Area [μV.Min]	Area [%]
1	UNKNOWN	13.13	13.57	14.24	0.00	92.78	1192.2	450.0	92.781
2	UNKNOWN	17.22	17.61	18.14	0.00	7.22	79.4	35.0	7.219
Total						100.00	1271.6	485.0	100.000

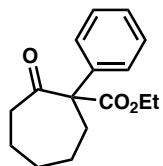
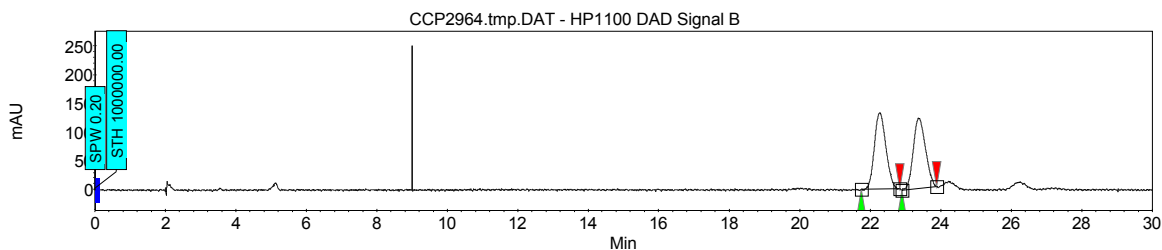
Figure S114 SFC trace of (\pm)-35**(\pm)-35**

Index	Name	Start [Min]	Time [Min]	End [Min]	RT Offset [Min]	Quantity [% Area]	Height [μ V]	Area [μ V.Min]	Area [%]
1	UNKNOWN	8.47	8.97	9.31	0.00	49.72	374.0	75.9	49.720
2	UNKNOWN	9.46	9.82	10.33	0.00	50.28	347.0	76.7	50.280
Total						100.00	721.0	152.6	100.000

Figure S115 SFC trace of (–)-35

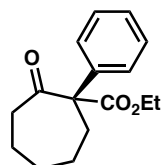
**(–)-35**

Index	Name	Start [Min]	Time [Min]	End [Min]	RT Offset [Min]	Quantity [% Area]	Height [μ V]	Area [μ V.Min]	Area [%]
1	UNKNOWN	8.33	8.72	9.16	0.00	92.71	1242.3	314.2	92.711
2	UNKNOWN	9.38	9.71	10.00	0.00	7.29	103.3	24.7	7.289
Total						100.00	1345.6	338.9	100.000

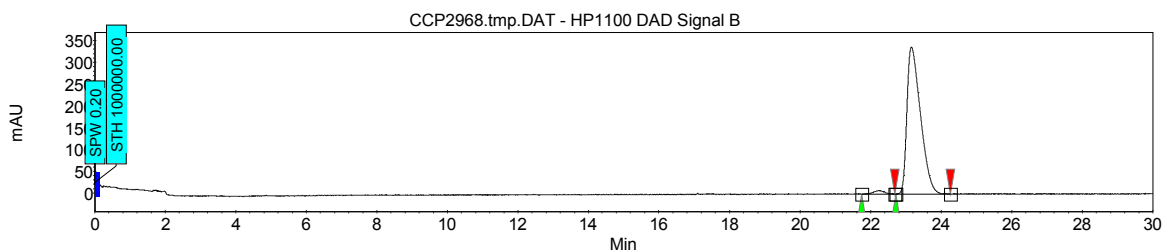
Figure S116 SFC trace of (\pm)-36(\pm)-36

Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[μ V]	[μ V.Min]	[%]
1	UNKNOWN	21.75	22.28	22.83	0.00	50.57	132.4	50.1	50.566
2	UNKNOWN	22.90	23.36	23.89	0.00	49.43	122.5	48.9	49.434
Total						100.00	254.9	99.0	100.000

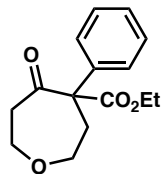
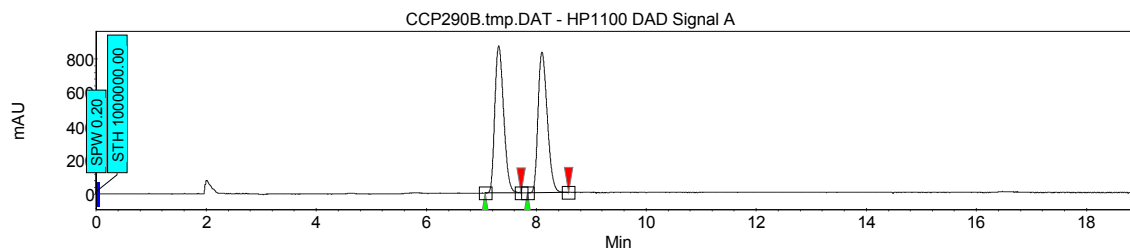
Figure S117 SFC trace of (+)-36



(+)-36

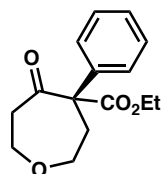
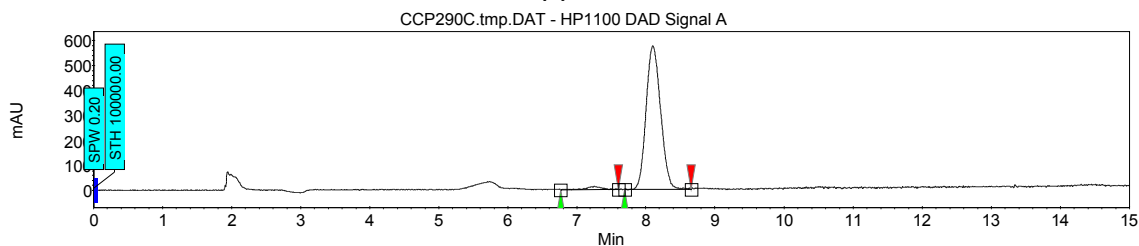


Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[μ V]	[μ V.Min]	[%]
1	UNKNOWN	21.75	22.22	22.68	0.00	1.81	8.3	2.8	1.814
2	UNKNOWN	22.71	23.16	24.26	0.00	98.19	337.9	150.5	98.186
Total						100.00	346.1	153.2	100.000

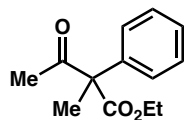
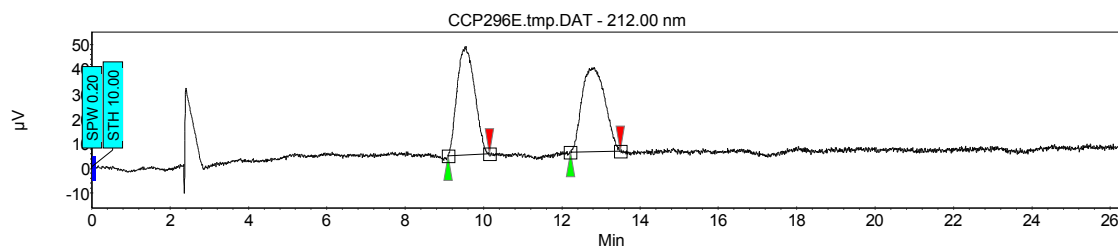
Figure S118 SFC trace of (\pm)-37**(\pm)-37**

Index	Name	Start Time [Min]	Time [Min]	End [Min]	RT Offset [Min]	Quantity [% Area]	Height [μ V]	Area [μ V.Min]	Area [%]
1	UNKNOWN	7.07	7.32	7.72	0.00	49.97	865.9	161.1	49.969
2	UNKNOWN	7.84	8.10	8.59	0.00	50.03	827.8	161.3	50.031
Total						100.00	1693.7	322.4	100.000

Figure S119 SFC trace of (+)-37

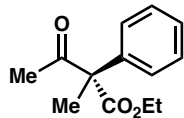
**(+)-37**

Index	Name	Start Time [Min]	Time [Min]	End [Min]	RT Offset [Min]	Quantity [% Area]	Height [μ V]	Area [μ V.Min]	Area [%]
1	UNKNOWN	6.76	7.26	7.60	0.00	1.81	13.3	2.6	1.811
2	UNKNOWN	7.69	8.10	8.66	0.00	98.19	574.6	139.8	98.189
Total						100.00	587.9	142.4	100.000

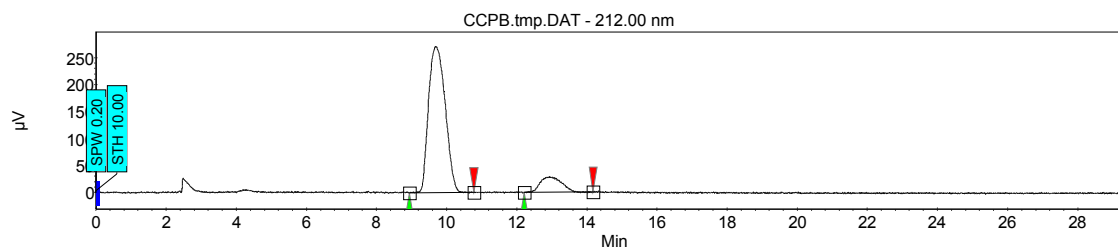
Figure S120 SFC trace of (\pm)-38(\pm)-38

Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[μ V]	[μ V.Min]	[%]
1	UNKNOWN	9.09	9.55	10.15	0.00	48.90	43.7	22.4	48.905
2	UNKNOWN	12.21	12.83	13.50	0.00	51.10	34.2	23.4	51.095
Total						100.00	77.8	45.9	100.000

Figure S121 SFC trace of (+)-38

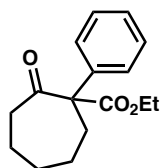
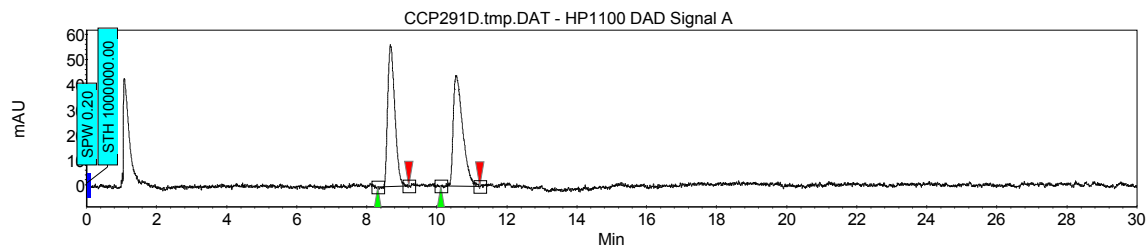


(+)-38

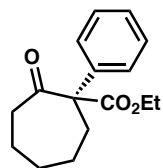
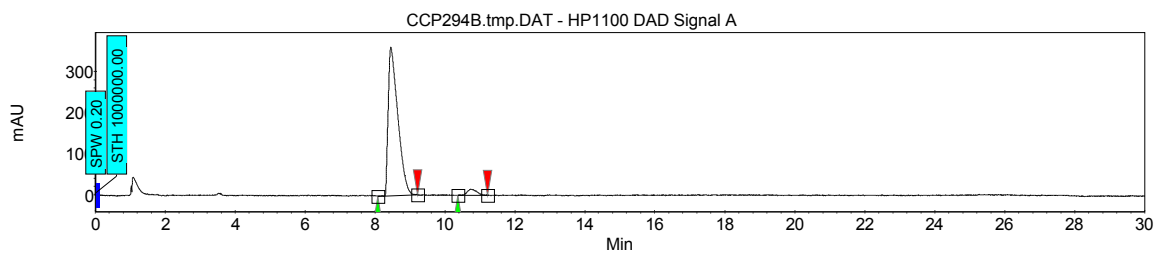


Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[μ V]	[μ V.Min]	[%]
1	UNKNOWN	8.94	9.68	10.77	0.00	88.70	270.9	149.5	88.696
2	UNKNOWN	12.21	12.93	14.17	0.00	11.30	28.2	19.0	11.304
Total						100.00	299.1	168.5	100.000

SFC traces from Figure 5: One-pot arylation reaction

Figure S122 SFC trace of (\pm)-36**(\pm)-36**

Index	Name	Start [Min]	Time [Min]	End [Min]	RT Offset [Min]	Quantity [% Area]	Height [μ V]	Area [μ V.Min]	Area [%]
1	UNKNOWN	8.31	8.67	9.20	0.00	49.01	56.5	13.2	49.014
2	UNKNOWN	10.11	10.57	11.23	0.00	50.99	44.2	13.7	50.986
Total						100.00	100.7	26.9	100.000

Figure S123 SFC trace of ($-$)-36**($-$)-36**

Index	Name	Start [Min]	Time [Min]	End [Min]	RT Offset [Min]	Quantity [% Area]	Height [μ V]	Area [μ V.Min]	Area [%]
1	UNKNOWN	8.07	8.44	9.21	0.00	96.12	360.9	114.8	96.125
2	UNKNOWN	10.36	10.73	11.20	0.00	3.88	15.3	4.6	3.875
Total						100.00	376.2	119.5	100.000

Part II: Computational Section

Computational Methods. All quantum chemical calculations were performed with Gaussian 09.¹⁹ Geometry optimizations and frequencies were calculated with the B3LYP²⁰ (in vacuo) density functional with the 6-31+G(d,p) basis set. Optimized geometries were verified by frequency calculations as minima (zero imaginary frequencies) or transition structures (a single imaginary frequency). Free energy corrections were determined using unscaled B3LYP/6-31+G(d,p) vibrational frequencies assuming a standard state of 1 atm and 298.15 K. Errors in the treatment of low modes as harmonic oscillations were mitigated by use of the quasiharmonic approximation proposed by Truhlar and coworkers.²¹ Single point energy calculations were performed on optimized geometries with the M06-2X²² functional and def2-TZVPP²³ basis set in conjunction with the SMD implicit solvation model.²⁴ The free energies reported herein were determined by adding zero-point energy and thermal correction determined using B3LYP/6-31+G(d,p) to electronic energies computed at the M06-2X/def2-TZVPP–SMD level of theory. Transition structures were also optimized at the B3LYP level of theory with the implicit SMD solvation method, which provided similar energies but yielded poor TS geometries. Transition structures optimized with M06-2X had convergence issues and often failed to locate a TS. This has been found in similar computational studies involving aryne intermediates.²⁵ The B3LYP functional has been shown to have better convergence on transition structures for these reactions. We selected the M06-2X/def2-TZVPP–SMD//B3LYP/6-31+G(d,p) level of theory due to providing a combination of accurate geometries and energies for these reactions, in addition to the examples provided by Goodman²⁶ and our group.²⁷

Monte Carlo conformational searches were performed on the reactive complexes using the OPLS3 force field²⁸ in Maestro/Macromodel.²⁹ Reactive conformations with the distance between the bond-forming atoms shorter than 4.0 Å were used as input geometries for transition structure optimizations. Molecular graphics were generated using CYLView.³⁰

Cartesian Coordinates, Energies, and Vibrational Frequencies.**TS1**

C	2.57994	-1.45346	1.86194
C	1.96211	-0.98045	0.55097
C	0.67960	-0.38393	0.54732
C	0.01712	0.05887	1.83192
C	0.53877	-0.65483	3.08400
C	2.06735	-0.68930	3.08560
H	3.66827	-1.38140	1.79581
H	2.37124	-2.52573	1.99364
H	0.19149	1.14256	1.92488
H	-1.06553	-0.07419	1.74645
H	0.15176	-0.14597	3.97387
H	0.14846	-1.68119	3.11160
H	2.44231	-1.16569	3.99885
H	2.45652	0.33706	3.07459
N	0.10453	-0.02771	-0.60354
H	0.61059	-0.32321	-1.44114
C	-1.16282	0.68707	-0.77825
H	-1.19283	1.48012	-0.02728
C	2.46071	-1.59977	-0.68720
O	1.95961	-1.49952	-1.80917
O	3.58190	-2.33435	-0.48475
C	4.16678	-2.92364	-1.65884
H	5.05054	-3.45420	-1.30420
H	3.46645	-3.61627	-2.13214
H	4.44454	-2.14814	-2.37673
C	-4.63960	-1.92095	-0.36600
C	-2.38788	-0.21734	-0.60163
C	-2.29943	-1.57035	-0.87017
C	-3.42149	-2.42563	-0.75660
H	-5.50568	-2.57084	-0.27241
H	-1.34519	-1.99268	-1.16927
H	-3.31008	-3.48295	-0.97835
C	-3.65083	0.33762	-0.19935
C	-4.78589	-0.53688	-0.07763
C	-6.03943	-0.00151	0.32861
C	-6.18657	1.33962	0.60453
C	-5.07441	2.20667	0.48454
C	-3.84456	1.71970	0.09324
H	-6.88680	-0.67675	0.41635
H	-7.15048	1.73392	0.91234
H	-5.19017	3.26470	0.70109

H	-3.01620	2.41397	0.00625
C	-1.14741	1.34640	-2.16850
H	-0.29250	2.02297	-2.25053
H	-2.07216	1.90427	-2.33507
H	-1.07124	0.58400	-2.95119
C	3.02262	1.02582	0.03724
C	4.23636	1.18802	0.68050
C	4.86818	2.39734	0.32877
C	4.27437	3.28644	-0.58315
C	3.03191	3.00010	-1.17819
C	2.42111	1.79421	-0.80406
H	4.69594	0.49119	1.37365
H	5.83257	2.63870	0.76913
H	4.78971	4.21152	-0.83326
H	2.59511	3.70012	-1.88834

Electronic energy = -1212.206643

Zero-point electronic energy = -1211.738914

Enthalpy = -1211.711953

Free energy = -1211.796629

Free energy with quasiharmonic approximation = -1211.790229

Frequencies = -100.87 17.16 25.57 31.94 37.92 40.54

SCF (M06-2X/def2-TZVPP) = -1212.099989

TS2

C	-2.85303	-1.47087	1.74696
C	-2.17152	-1.12088	0.42886
C	-0.75994	-1.10210	0.34149
C	0.10544	-1.20770	1.57870
C	-0.60242	-1.82419	2.78985
C	-1.98264	-1.19398	2.97512
H	-3.12917	-2.53564	1.73742
H	-3.80178	-0.93327	1.81927
H	1.01319	-1.77258	1.34258
H	0.44740	-0.19269	1.82424
H	-0.71187	-2.90788	2.64623
H	0.02247	-1.68433	3.67892
H	-1.87180	-0.11154	3.12274
H	-2.47404	-1.59149	3.87063
N	-0.15166	-0.87536	-0.83121
H	-0.79566	-0.79801	-1.62204
C	1.27973	-1.01458	-1.13812
H	1.61061	-1.95929	-0.69415
C	-2.95265	-1.32432	-0.79989
O	-2.52715	-1.26810	-1.95509

O	-4.25692	-1.59720	-0.54585
C	-5.09993	-1.75672	-1.69932
H	-6.09696	-1.94871	-1.30245
H	-5.09444	-0.84725	-2.30494
H	-4.76165	-2.59672	-2.31123
C	3.78315	2.24736	0.31613
C	2.16344	0.11219	-0.59611
C	1.65979	1.39161	-0.46997
C	2.46586	2.46242	-0.01496
H	4.40828	3.06342	0.66944
H	0.61562	1.57379	-0.70917
H	2.02997	3.45322	0.07391
C	3.53918	-0.14253	-0.26625
C	4.35089	0.94929	0.20140
C	5.71207	0.71375	0.53979
C	6.27045	-0.53994	0.42541
C	5.48018	-1.61823	-0.03840
C	4.15650	-1.42372	-0.37531
H	6.30926	1.55094	0.89237
H	7.31164	-0.70351	0.68722
H	5.91955	-2.60721	-0.13237
H	3.58630	-2.27315	-0.73497
C	1.41681	-1.13802	-2.66623
H	0.85300	-1.99933	-3.03939
H	1.04090	-0.23339	-3.15473
H	2.46692	-1.25915	-2.94267
C	-2.90874	3.80649	-0.16120
C	-2.02522	3.13736	-1.02866
C	-1.82826	1.77215	-0.77709
C	-2.45416	1.21632	0.19714
C	-3.33672	1.75639	1.11436
C	-3.55129	3.13164	0.89073
H	-3.10113	4.86768	-0.30491
H	-1.53753	3.67780	-1.83770
H	-3.83659	1.22989	1.92005
H	-4.23012	3.67320	1.54499

Electronic energy = -1212.203996

Zero-point electronic energy = -1211.736279

Enthalpy = -1211.709335

Free energy = -1211.793447

Free energy with quasiharmonic approximation = -1211.787691

Frequencies = -95.44 20.31 26.96 30.29 42.06 57.46

SCF (M06-2X/def2-TZVPP) = -1212.096632

TS3

C	-2.67502	0.67522	2.34948
C	-2.12920	0.67502	0.92711
C	-0.91291	0.01918	0.62949
C	-0.26095	-0.91035	1.62669
C	-0.68063	-0.66303	3.07972
C	-2.19907	-0.51818	3.18231
H	-3.76715	0.70443	2.31665
H	-2.37728	1.60751	2.85234
H	-0.53501	-1.93603	1.33261
H	0.82597	-0.84400	1.52930
H	-0.31690	-1.48745	3.70315
H	-0.19859	0.25141	3.45106
H	-2.50528	-0.38245	4.22611
H	-2.67872	-1.43820	2.82344
N	-0.40106	0.07288	-0.60202
H	-0.93157	0.66191	-1.24674
C	0.75882	-0.66159	-1.13061
H	0.61413	-1.69468	-0.82018
C	-2.62228	1.71386	0.01499
O	-2.17839	1.97724	-1.10655
O	-3.66829	2.40664	0.53059
C	-4.24149	3.40811	-0.32658
H	-5.06145	3.84183	0.24612
H	-3.50069	4.17203	-0.57563
H	-4.61280	2.95482	-1.24891
C	4.69121	0.54419	0.38159
C	2.13182	-0.20351	-0.60771
H	5.66452	0.83176	0.77260
C	2.49168	1.16902	-0.52982
C	3.79444	1.53907	-0.01393
C	4.16112	2.92008	0.07674
C	3.30876	3.90923	-0.33412
C	2.03385	3.55911	-0.86151
C	1.64045	2.24741	-0.95202
H	5.14280	3.16355	0.47492
H	3.59936	4.95330	-0.26494
H	1.35844	4.34055	-1.19726
H	0.65853	2.04212	-1.34984
C	0.68940	-0.63871	-2.66749
H	1.49644	-1.24928	-3.08124
H	0.80417	0.37610	-3.05957
H	-0.27188	-1.04047	-3.00084

C	-3.39501	-0.98462	-0.22536
C	-2.88615	-1.43008	-1.31811
C	-3.60137	-2.37794	-2.06454
C	-4.84332	-2.77784	-1.53671
C	-5.33221	-2.24340	-0.33217
C	-4.59326	-1.28712	0.39361
H	-3.24605	-2.80050	-3.00253
H	-5.44139	-3.51352	-2.07043
H	-6.29827	-2.56566	0.04886
C	4.37556	-0.81116	0.26865
C	3.07871	-1.20248	-0.24490
C	2.83983	-2.61615	-0.36287
C	3.77916	-3.54632	0.00751
C	5.04151	-3.14584	0.52890
C	5.32478	-1.81202	0.65144
H	1.90490	-2.98142	-0.76868
H	3.55640	-4.60359	-0.10379
H	5.77120	-3.89564	0.81935
H	6.28565	-1.48336	1.03905
H	-4.96807	-0.86117	1.31825

Electronic energy = -1365.841995

Zero-point electronic energy = -1365.327482

Enthalpy = -1365.297748

Free energy = -1365.388062

Free energy with quasiharmonic approximation = -1365.381332

Frequencies = -70.25 18.04 23.56 34.76 39.11 41.22

SCF (M06-2X/def2-TZVPP) = -1365.72377

TS4

C	4.22909	-0.27480	0.89949
C	2.83267	0.24704	0.57498
C	1.72066	-0.16912	1.34918
C	1.83227	-1.35616	2.28235
C	3.26007	-1.65435	2.75323
C	4.22562	-1.65101	1.56877
H	4.73968	0.44398	1.55760
H	4.82577	-0.29790	-0.01531
H	1.18074	-1.21618	3.14901
H	1.43871	-2.22735	1.73425
H	3.57338	-0.89644	3.48417
H	3.27102	-2.61900	3.27316
H	3.92044	-2.41824	0.84545
H	5.24097	-1.90281	1.89623
N	0.50579	0.32776	1.09952

H	0.49209	1.07381	0.40297
C	-0.75866	-0.06444	1.75183
H	-0.66184	-1.12311	1.96557
C	2.75939	1.53840	-0.13094
O	1.75024	2.22435	-0.29598
O	3.96304	1.93520	-0.61231
C	3.96170	3.15599	-1.37231
H	4.99482	3.29827	-1.68974
H	3.30066	3.06541	-2.23751
H	3.63058	3.99424	-0.75420
C	-4.29611	0.39241	-0.77569
C	-1.96077	0.10421	0.81737
H	-5.19379	0.50395	-1.37959
C	-2.34014	1.38593	0.33432
C	-3.53181	1.52199	-0.47686
C	-3.92302	2.80979	-0.96358
C	-3.18435	3.92841	-0.68586
C	-2.00339	3.80842	0.09851
C	-1.60054	2.59182	0.58884
H	-4.82407	2.87586	-1.56793
H	-3.48779	4.89981	-1.06466
H	-1.40354	4.68986	0.30449
H	-0.68490	2.56239	1.16238
C	-0.96898	0.62761	3.12004
H	-1.86014	0.20961	3.59927
H	-0.11206	0.45037	3.77742
H	-1.11037	1.70501	3.03129
C	1.33354	-2.18691	-3.46147
C	0.38283	-1.56500	-2.63137
C	0.88190	-0.90447	-1.50164
C	2.15284	-0.88759	-1.28384
C	3.17770	-1.44948	-2.02693
C	2.70676	-2.12952	-3.16721
H	1.00407	-2.72175	-4.35004
H	-0.67565	-1.61335	-2.87910
H	4.23873	-1.39192	-1.80488
H	3.42174	-2.61213	-3.82925
C	-3.93387	-0.87719	-0.32294
C	-2.74109	-1.03738	0.48462
C	-2.42997	-2.37986	0.89463
C	-3.22003	-3.44911	0.55482
C	-4.39563	-3.27278	-0.22765
C	-4.73450	-2.01711	-0.65362
H	-1.53998	-2.58298	1.47624

H -2.93835 -4.44599 0.88140
H -5.00943 -4.13030 -0.48645
H -5.62330 -1.85827 -1.25887
Electronic energy = -1365.836501
Zero-point electronic energy = -1365.322021
Enthalpy = -1365.292288
Free energy = -1365.382729
Free energy with quasiharmonic approximation = -1365.375623
Frequencies = -124.20 14.45 23.84 27.56 39.06 45.10
SCF (M06-2X/def2-TZVPP) = -1365.720222

Benzyne

C -0.62658 -1.23819 -0.00006
C 0.62601 -1.23811 0.00002
C 1.46344 -0.13426 0.00001
C 0.70423 1.05943 -0.00000
C -0.70383 1.05966 -0.00001
C -1.46338 -0.13377 0.00007
H 2.54757 -0.13604 -0.00001
H 1.23035 2.01101 -0.00002
H -1.22967 2.01139 -0.00009
H -2.54752 -0.13497 -0.00006
Electronic energy = -230.928372
Zero-point electronic energy = -230.853306
Enthalpy = -230.847853
Free energy = -230.88069
Free energy with quasiharmonic approximation = -230.88069
Frequencies = 393.59 405.49 433.72 587.14 619.73 750.65
SCF (M06-2X/def2-TZVPP) = -230.9027525

Enamine_Anthracene

C 3.58237 -1.64183 -1.39482
C 2.92497 -0.83845 -0.28046
C 1.59234 -1.02134 0.07169
C 0.71668 -2.02521 -0.65340
C 1.31002 -2.53398 -1.97086
C 2.78500 -2.88903 -1.78801
H 4.59181 -1.93056 -1.08482
H 3.72038 -1.00821 -2.28423
H 0.54560 -2.87495 0.02495
H -0.26676 -1.58047 -0.83246
H 0.72919 -3.39563 -2.31958

H	1.21619	-1.75522	-2.73961
H	3.19945	-3.32133	-2.70635
H	2.87981	-3.65454	-1.00449
N	1.01495	-0.33448	1.09272
H	1.65951	0.29094	1.57719
C	-0.36367	-0.43848	1.57388
H	-0.57668	-1.50366	1.66405
C	3.72064	0.15489	0.41142
O	3.35959	0.87111	1.36025
O	4.98678	0.26592	-0.08409
C	5.82928	1.23495	0.55483
H	6.78714	1.17087	0.03732
H	5.40865	2.23943	0.45709
H	5.95105	1.00463	1.61658
C	-3.50352	1.18295	-1.02768
C	-1.45221	0.16459	0.66196
H	-4.28019	1.56675	-1.68525
C	-1.30452	1.43871	0.04919
C	-2.35158	1.94358	-0.81651
C	-2.20662	3.22353	-1.44179
C	-1.09963	3.99858	-1.22383
C	-0.07235	3.52367	-0.36050
C	-0.16793	2.29621	0.24574
H	-3.00678	3.56906	-2.09140
H	-1.00258	4.96973	-1.70015
H	0.80387	4.13925	-0.17926
H	0.64477	1.97778	0.87954
C	-0.42911	0.15064	2.99521
H	-1.43348	0.02200	3.40756
H	-0.20318	1.22104	2.99453
H	0.28723	-0.35591	3.65039
C	-3.69010	-0.04943	-0.39847
C	-2.65724	-0.56981	0.47423
C	-2.94017	-1.82649	1.11525
C	-4.11222	-2.50786	0.89858
C	-5.10710	-1.99366	0.02025
C	-4.89448	-0.79481	-0.60588
H	-2.22893	-2.25996	1.80697
H	-4.28415	-3.45116	1.40911
H	-6.02649	-2.54803	-0.14242
H	-5.64425	-0.37838	-1.27369

Electronic energy = -1134.912092

Zero-point electronic energy = -1134.474467

Enthalpy = -1134.449861

Free energy = -1134.528545

Free energy with quasiharmonic approximation = -1134.523663

Frequencies = 16.76 18.80 36.57 63.42 81.67 91.84

SCF (M06-2X/def2-TZVPP) = -1134.811617

Enamine_Naphthalene

C	-3.62670	-1.66015	0.60682
C	-2.83551	-0.50270	0.01289
C	-1.51128	-0.64071	-0.38155
C	-0.76708	-1.95086	-0.19911
C	-1.48102	-2.95317	0.71400
C	-2.96825	-3.02231	0.36975
H	-4.63782	-1.65944	0.18705
H	-3.76033	-1.50820	1.68870
H	-0.62052	-2.39831	-1.19382
H	0.23461	-1.74207	0.19105
H	-1.00039	-3.93376	0.61933
H	-1.36442	-2.64270	1.76108
H	-3.47260	-3.78895	0.96957
H	-3.08420	-3.31475	-0.68370
N	-0.82090	0.37092	-0.97688
H	-1.35414	1.23603	-1.07290
C	0.59551	0.38267	-1.32332
H	0.84096	-0.58803	-1.76493
C	-3.49485	0.78279	-0.11926
O	-3.01579	1.81861	-0.60619
O	-4.76755	0.78162	0.37175
C	-5.47889	2.02376	0.27587
H	-5.57121	2.33862	-0.76696
H	-6.46219	1.82729	0.70466
H	-4.96633	2.80895	0.83803
C	3.20192	1.15319	2.09838
C	1.52179	0.61898	-0.12122
C	1.05359	1.28914	0.99291
C	1.88873	1.56141	2.10312
H	3.84963	1.35540	2.94744
H	0.01653	1.60841	1.02140
H	1.48172	2.09276	2.95850
C	2.89072	0.18262	-0.15242
C	3.73394	0.45566	0.98001
C	5.08878	0.02307	0.96237
C	5.60843	-0.65183	-0.11983
C	4.78460	-0.92441	-1.23792
C	3.46644	-0.51800	-1.25282

H	5.71208	0.23762	1.82683
H	6.64522	-0.97503	-0.11871
H	5.19368	-1.45725	-2.09152
H	2.86517	-0.73940	-2.12757
C	0.80942	1.45936	-2.40400
H	0.51809	2.44380	-2.02224
H	0.20660	1.23674	-3.29009
H	1.86124	1.51287	-2.69550

Electronic energy = -981.277826

Zero-point electronic energy = -980.886678

Enthalpy = -980.864906

Free energy = -980.937341

Free energy with quasiharmonic approximation = -980.933222

Frequencies = 18.19 27.70 32.79 82.52 91.45 99.05

SCF (M06-2X/def2-TZVPP) = -981.1883372

References:

- Medina, J. M.; Mackey, J. L.; Garg, N. K.; Houk, K. N. *J. Am. Chem. Soc.* **2014**, *136*, 15798–15805.
- Devlin, A. S.; Du Bois, J. *Chem. Sci.* **2013**, *4*, 1059–1063.
- McMahon, T. C.; Medina, J. M.; Yang, Y.-F.; Simmons, B. J.; Houk, K. N.; Garg, N. K. *J. Am. Chem. Soc.* **2015**, *137*, 4082–4085.
- Shah, T. K.; Medina, J. M.; Garg, N. K. *J. Am. Chem. Soc.* **2016**, *138*, 4948–4954.
- Matsuo, J.-i.; Okano, M.; Takeuchi, K.; Tanaka, H.; Ishibashi, H. *Tetrahedron: Asymmetry* **2007**, *18*, 1906–1910.
- Masami, O.; Noriyasu, H.; Masanori, I.; Hironori, M.; Hironao, S.; Yoshihiro, S.; Yomoyuki, T. Imidazopyridin-2-one Derivatives. U. S. Patent 2011082138, September 18, 2014.
- Laetitia, B. G.; Manning, M. A.; Arkless, H. L.; Stephens, T. C.; Unsworth, W. P. *Chem. Eur. J.* **2017**, *23*, 2225–2230.
- Bolshan, Y.; Batey, R. A. *Org. Lett.* **2005**, *7*, 1481–1484.
- Oldenhuis, N. J.; Dong, V. M.; Guan, Z. *J. Am. Chem. Soc.* **2014**, *136*, 12548–12551.
- Hernández-Rodríguez, M.; Castillo-Hernández, T.; Trejo-Huizar, K. E. *Synthesis* **2011**, *17*, 2817–2821.
- Pallavivini, M.; Bolchi, C.; Fumagalli, L.; Valoti, E.; Villa, L. *Tetrahedron: Asymmetry* **2002**, *13*, 2277–2282.
- Roje, M.; Hameršak, Z.; Šunjić, V. *Synth. Commun.* **2002**, *32*, 3413–3417.
- Harrad, M. A.; Outtouch, R.; Ali, M. A.; Firdoussia, L. E.; Karim, A.; Alain, R. *Cat. Commun.* **2010**, *11*, 442–446.

- ¹⁴ Hayashi, Y.; Rohde, J. J.; Corey, E. J. *J. Am. Chem. Soc.* **1996**, *118*, 5502–5503.
- ¹⁵ Huang, X.; Maulide, N. *J. Am. Chem. Soc.* **2011**, *133*, 8510–8513.
- ¹⁶ Li, W.; Tan, F.; Hao, X.; Wang, G.; Tang, Y.; Liu, X.; Lin, L.; Feng, X. *Angew. Chem., Int. Ed.* **2015**, *54*, 1608–1611.
- ¹⁷ Tambar, U. K.; Stoltz, B. M. *J. Am. Chem. Soc.* **2005**, *127*, 5340–5341.
- ¹⁸ Mermerian, A. H.; Fu, G. C. *J. Am. Chem. Soc.* **2005**, *127*, 5604–5607.
- ¹⁹ Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Scalmani, G.; Barone, V.; Mennucci, B.; Petersson, G. A.; Nakatsuji, H.; Caricato, M.; Li, X.; Hratchian, H. P.; Izmaylov, A. F.; Bloino, J.; Zheng, G.; Sonnenberg, J. L.; Hada, M.; Ehara, M.; Toyota, K.; Fukuda, R.; Hasegawa, J.; Ishida, M.; Nakajima, T.; Honda, Y.; Kitao, O.; Nakai, H.; Vreven, T.; Montgomery, J. A., Jr.; Peralta, J. E.; Ogliaro, F.; Bearpark, M.; Heyd, J. J.; Brothers, E.; Kudin, K. N.; Staroverov, V. N.; Keith, T.; Kobayashi, R.; Normand, J.; Raghavachari, K.; Rendell, A.; Burant, J. C.; Iyengar, S. S.; Tomasi, J.; Cossi, M.; Rega, N.; Millam, J. M.; Klene, M.; Knox, J. E.; Cross, J. B.; Bakken, V.; Adamo, C.; Jaramillo, J.; Gomperts, R.; Stratmann, R. E.; Yazyev, O.; Austin, A. J.; Cammi, R.; Pomelli, C.; Ochterski, J. W.; Martin, R. L.; Morokuma, K.; Zakrzewski, V. G.; Voth, G. A.; Salvador, P.; Dannenberg, J. J.; Dapprich, S.; Daniels, A. D.; Farkas, O.; Foresman, J. B.; Ortiz, J. V.; Cioslowski, J.; Fox, D. J. *Gaussian 09*, Rev. D.01; Gaussian, Inc.: Wallingford, CT, 2013.
- ²⁰ a) Vosko, S. H.; Wilk, L.; Nusair, M. *Can. J. Phys.* **1980**, *58*, 1200–1211. b) Lee, C.; Yang, W.; Parr, R. G. *Phys. Rev. B: Condens. Matter Mater. Phys.* **1988**, *37*, 785–789. c) Becke, A. D. *J. Chem. Phys.* **1993**, *98*, 5648–5652. d) Stephens, P. J.; Devlin, F. J.; Chabalowski, C. F.; Frisch, M. J. *J. Phys. Chem.* **1994**, *98*, 11623–11627.
- ²¹ a) Ribeiro, R. F.; Marenich, A. V.; Cramer, C. J.; Truhlar, D. G. *J. Phys. Chem. B* **2011**, *115*, 14556–14562. b) Zhao, Y.; Truhlar, D. G. *Phys. Chem. Chem. Phys.* **2008**, *10*, 2813–2818.
- ²² Zhao, Y.; Truhlar, D. G. *Theor. Chem. Acc.* **2008**, *120*, 215–241.
- ²³ Weigend, F.; Ahlrichs, R. *Phys. Chem. Chem. Phys.* **2005**, *7*, 3297–3305.
- ²⁴ Marenich, A. V.; Cramer, C. J.; Truhlar, D. G. *J. Phys. Chem. B* **2009**, *113*, 6378–6396.
- ²⁵ a) Bronner, S. M.; Mackey, J. L.; Houk, K. N.; Garg, N. K. *J. Am. Chem. Soc.* **2012**, *134*, 13966–13969. b) Medina, J. M.; Mackey, J. L.; Garg, N. K.; Houk, K. N. *J. Am. Chem. Soc.* **2014**, *136*, 15798–15805.
- ²⁶ Simoń, L.; Goodman, J. M. *Org. Biomol. Chem.* **2011**, *9*, 689–700.
- ²⁷ a) Simon, A.; Lam, Y.-H.; Houk, K. N. *J. Am. Chem. Soc.* **2016**, *138*, 503–506. b) Simon, A.; Yeh, A. J.; Lam, Y.-H.; Houk, K. N. *J. Org. Chem.* **2016**, *81*, 12408–12415.
- ²⁸ Harder, E.; Damm, W.; Maple, J.; Wu, C.; Reboul, M.; Xiang, J.Y.; Wang, L.; Lupyan, D.; Dahlgren, M. K.; Knight, J. L.; Kaus, J. W.; Cerutti, D.; Krilov, G.; Jorgensen, W. L.; Abel, R.; and Friesner, R. A. *J. Chem. Theory Comput.* **2016**, *12*, 281–296.
- ²⁹ *Schrödinger Release 2017–3: MacroModel*; Schrödinger, LLC: New York, NY, 2017.

³⁰ Legault, C. Y. *CYLview*, 1.0b; Université de Sherbrooke, 2009; <http://www.cylview.org>.