

SUPPORTING INFORMATION

Enantioselective Synthesis of α -Acetal- β' -Amino Ketone Derivatives by Rhodium-Catalyzed Asymmetric Hydrogenation

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1. General

All reactions were run under argon atmosphere unless specified. Reaction vessels were oven-dried, cooled under vacuum and flushed with argon before use. Methanol was distilled over sodium. THF, CH₂Cl₂, DMF were dried over alumina columns in an Innovative Technologies apparatus. Reagent grade ethanol was purchased and used without further purification. Every reagent was either purified following the methods described in the literature or used without further purification.

Acros Silica Gel 60 (0.0040-0.0063 mm) was employed for flash column chromatography. Analytical thin layer chromatography (TLC) was carried out using commercial silica-gel plates (Merck 60 F254), spots were detected with UV light (254 nm) and revealed with a KMnO₄ or para-anisaldehyde stain.

Proton nuclear magnetic resonance (¹H NMR) spectra were recorded using a Bruker AVANCE 300 (300 MHz) or a Bruker AVANCE 400 (400 MHz). Chemical shifts are reported in delta (δ) units part per million (ppm) relative to the signal of the solvent. Coupling constants are reported in Hertz (Hz). The following abbreviations are used: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, brd = broad singlet. Carbon-13 nuclear magnetic resonance (¹³C NMR) spectra were recorded using a Bruker AVANCE 300 (75 MHz) or a Bruker AVANCE 400 (100 MHz). Fluor-19 nuclear magnetic resonance (¹⁹F NMR) spectra were recorded using a Bruker AVANCE 300 (282 MHz). Chemical shifts are reported in delta (δ) units part per million (ppm) relative to the center line of the triplet at 77.16 ppm for deuteriochloroform. ¹³C NMR experiments were routinely run with broadband decoupling.

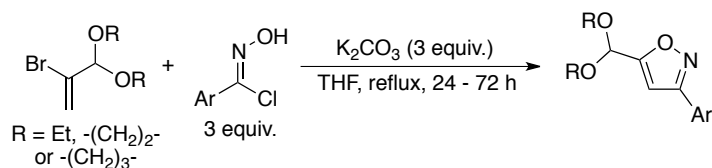
Mass spectra (Chemical ionization, NH₃ or Electrospray) were recorded at ENSCP Chimie ParisTech. HRMS (ion trap) analyses were performed at the Université Pierre et Marie Curie. Chloroximes were prepared according to the procedures described in the literature. Spectral data were in accordance with the literature values.¹ [Rh(cod)₂]BF₄ was prepared from [Rh(cod)Cl]₂.²

¹ a) Sanders, B. C.; Friscourt, F.; Ledin, P. A.; Mbua, N. E.; Arumugam, S.; Guo, J.; Boltje, T. J.; Popik, V. V.; Boons, G.-J. *J. Am. Chem. Soc.* **2011**, *133*, 949. b) Di Nunno, L.; Vitalea, P.; Scilimati, A.; Simonea, L.; Capitelli, F. *Tetrahedron* **2008**, *64*, 11198. c) da Silva-Alves, D. C. B.; dos Anjos, J. V.; Cavalcante, N. N. M.; Santos, G. K. N.; Navarro, D.; Srivastava, R. M. *Bioorg. Med. Chem.* **2013**, *21*, 940. d) Di Nunno, L.; Vitalea, P.; Scilimati, A.; Simonea, L.; Capitelli, F. *Tetrahedron* **2007**, *63*, 12388. e) Tóth, M.; Kun, S.; Bokor, E.; Bentlifa, M.; Tallec, G.; Vidal, S.; Docsa, T.; Gergely, P.; Somsák, L.; Praly, J.-P. *Bioorg. Med. Chem.* **2009**, *17*, 4773. f) Dubrovskiy, A. V.; Larock, R. C. *Org. Lett.* **2010**, *12*, 1180. g) Krompiec, S.; Bujak, P.; Malarz, J.; Krompiec, M.; Skórka, Ł.; Pluta, T.; Danikiewicz, W.; Kania, M.; Kusz, J. *Tetrahedron* **2012**, *68*, 6018. h) Di Nunno, L.; Vitale, P.; Scilimati, A.; Tacconelli, S.; Patrignani, P. *J. Med. Chem.* **2004**, *47*, 4881. i) Schwarz, L.; Girreser, U.; Clement, B. *Eur. J. Org. Chem.* **2014**, *2014*, 1961. j) Vo, Q. V.; Trenerry, C.; Rochfort, S.; Wadeson, J.; Leyton, C.; Hughes, A. B. *Bioorg. Med. Chem.* **2013**, *21*, 5945.

² Ensing, S. C.; Venable, E. P.; Kortman, G. D.; Weir, L. J.; Hull, K. L. *J. Am. Chem. Soc.* **2015**, *137*, 13748.

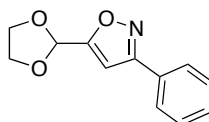
2. Synthesis of the Isoxazoles 4a – 4u

General procedure



In a flask filled with argon was added 2-(1-bromovinyl)-1,3-dioxane (2.5 mmol, 1.0 equiv.), chloro-oxime (7.5 mmol, 3 equiv.), K_2CO_3 (7.5 mmol, 3 equiv.) and dry THF (150 mL). The mixture was stirred at 70 °C until complete conversion (24 h for the diethoxy acetal compound, 48 h for the dioxolane compound and 72 h for the dioxane compound), then filtered and concentrated. The crude product was then purified by column chromatography (PET/EtOAc 8/2).

5-(1,3-dioxolan-2-yl)-3-phenylisoxazole **4a**



Slightly yellow oil, 90% yield (491 mg)

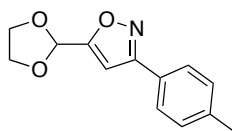
Chemical formula: $C_{12}H_{11}NO_3$

1H NMR (300 MHz, $CDCl_3$) δ 7.82 – 7.78 (m, 2H), 7.48 – 7.44 (m, 3H), 6.64 (d, J = 0.5 Hz, 1H), 6.13 (d, J = 0.5 Hz, 1H), 4.19 – 3.07 (m, 4H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 169.7, 162.3, 130.3, 129.1, 128.9, 127.0, 100.7, 96.6, 65.6.

Mass (CI/ NH_3) MH^+ 218

5-(1,3-dioxolan-2-yl)-3-(*p*-tolyl)isoxazole **4b**



Slightly yellow oil, 68% yield (393 mg)

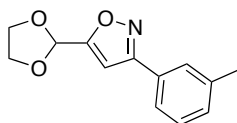
Chemical formula: $C_{13}H_{13}NO_3$

1H NMR (400 MHz, $CDCl_3$) δ 7.69 (d, J = 8.0 Hz, 2H), 7.26 (d, J = 8.0 Hz, 2H), 6.61 (s, 1H), 6.11 (s, 1H), 4.36 – 3.83 (m, 4H), 2.39 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 169.4, 162.2, 140.4, 129.7, 126.8, 125.9, 100.6, 96.6, 65.5, 21.5.

Mass (CI/NH₃) MH⁺ 232

5-(1,3-dioxolan-2-yl)-3-(*m*-tolyl)isoxazole **4c**



Slightly yellow oil, 63% yield (365 mg)

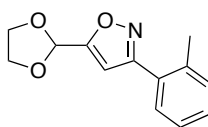
Chemical formula: C₁₃H₁₃NO₃

¹H NMR (300 MHz, CDCl₃) δ 7.51 (dd, *J* = 7.5, 1.1 Hz, 1H), 7.42 – 7.19 (m, 3H), 6.53 (s, 1H), 6.16 (s, 1H), 4.33 – 3.97 (m, 4H), 2.49 (s, 3H).

¹³C NMR (75 MHz, CDCl₃) δ 168.7, 162.8, 137.1, 131.2, 129.7, 129.6, 128.6, 126.1, 103.3, 96.6, 65.6, 21.2.

Mass (CI/NH₃) MH⁺ 232

5-(1,3-dioxolan-2-yl)-3-(*o*-tolyl)isoxazole **4d**



Slightly yellow oil, 57% yield (331 mg)

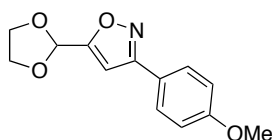
Chemical formula: C₁₃H₁₃NO₃

¹H NMR (300 MHz, CDCl₃) δ 7.65 – 7.63 (m, 1H), 7.58 (d, *J* = 7.6 Hz, 1H), 7.34 (t, *J* = 7.6 Hz, 1H), 7.27 – 7.25 (m, 1H), 6.63 (s, 1H), 6.12 (s, 1H), 4.28 – 3.96 (m, 4H), 2.41 (s, 3H).

¹³C NMR (75 MHz, CDCl₃) δ 169.4, 162.2, 138.7, 130.9, 128.8, 128.6, 127.5, 123.9, 100.6, 96.5, 65.4, 21.4.

Mass (CI/NH₃) MH⁺ 232

5-(1,3-dioxolan-2-yl)-3-(4-methoxyphenyl)isoxazole **4e**



Slightly yellow oil, 65% yield (403 mg)

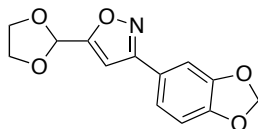
Chemical formula: C₁₃H₁₃NO₄

¹H NMR (300 MHz, CDCl₃) δ 7.76 – 7.70 (m, 2H), 7.99 – 6.94 (m, 2H), 6.58 (d, *J* = 0.5 Hz, 1H), 6.10 (s, 1H), 4.17 – 4.05 (m, 4H), 3.84 (s, 3H).

^{13}C NMR (75 MHz, CDCl_3) δ 169.4, 161.9, 161.2, 128.4, 121.4, 114.5, 100.5, 96.6, 65.5, 55.5.

Mass (CI/NH_3) MH^+ 248

3-(benzo[*d*][1,3]dioxol-5-yl)-5-(1,3-dioxolan-2-yl)isoxazole **4f**



Yellow oil, 60% yield (393 mg)

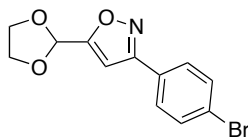
Chemical formula: $\text{C}_{13}\text{H}_{11}\text{NO}_5$

^1H NMR (300 MHz, CDCl_3) δ 7.26 (d, J = 1.5 Hz, 1H), 7.21 (dd, J = 8.0, 1.5 Hz, 1H), 6.82 (d, J = 8.0 Hz, 1H), 6.50 (d, J = 0.5 Hz, 1H), 6.05 (s, 1H), 5.97 (s, 2H), 4.24 – 3.89 (m, 4H).

^{13}C NMR (75 MHz, CDCl_3) δ 169.5, 161.8, 149.4, 148.4, 122.8, 121.4, 108.7, 107.1, 101.6, 100.5, 96.6, 65.5.

Mass (CI/NH_3) MH^+ 262

3-(4-bromophenyl)-5-(1,3-dioxolan-2-yl)isoxazole **4g**



Slightly yellow oil, 76% yield (562 mg)

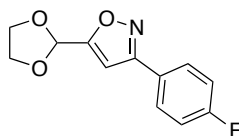
Chemical formula: $\text{C}_{12}\text{H}_{10}\text{BrNO}_3$

^1H NMR (400 MHz, CDCl_3) δ 7.65 (d, J = 8.5 Hz, 2H), 7.57 (d, J = 8.5 Hz, 2H), 6.61 (s, 1H), 6.10 (s, 1H), 4.27 – 3.86 (m, 4H).

^{13}C NMR (101 MHz, CDCl_3) δ 169.9, 161.3, 132.3, 128.4, 127.7, 124.6, 100.5, 96.5, 65.5.

Mass (CI/NH_3) MH^+ 296

5-(1,3-dioxolan-2-yl)-3-(4-fluorophenyl)isoxazole **4h**



Slightly yellow oil, 33% yield (195 mg)

Chemical formula: $\text{C}_{12}\text{H}_{10}\text{FNO}_3$

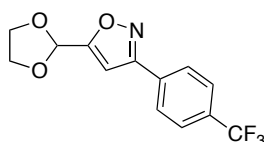
^1H NMR (300 MHz, CDCl_3) δ 7.89 – 7.63 (m, 2H), 7.20 – 6.98 (m, 2H), 6.60 (s, 1H), 6.10 (s, 1H), 4.22 – 3.99 (m, 4H).

^{13}C NMR (75 MHz, CDCl_3) δ 169.9, 163.9 (d, $^1J_{\text{CF}} = 250.2$ Hz), 161.3, 128.9 (d, $^3J_{\text{CF}} = 8.5$ Hz), 125.1 (d, $^4J_{\text{CF}} = 3.4$ Hz), 116.2 (d, $^2J_{\text{CF}} = 22.0$ Hz), 100.5, 96.5, 65.5.

^{19}F NMR (282 MHz, CDCl_3) δ -108.59 – -110.17 (m).

Mass (CI/ NH_3) MH^+ 236

5-(1,3-dioxolan-2-yl)-3-(4-(trifluoromethyl)phenyl)isoxazole **4i**



White solid (mp = 84 – 87 °C), 81% yield (581 mg)

Chemical formula: $\text{C}_{13}\text{H}_{10}\text{F}_3\text{NO}_3$

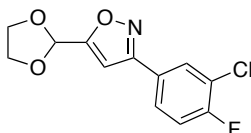
^1H NMR (300 MHz, CDCl_3) δ 7.92 (d, $J = 8.0$ Hz, 2H), 7.71 (d, $J = 8.0$ Hz, 2H), 6.68 (s, 1H), 6.13 (s, 1H), 4.32 – 3.93 (m, 4H).

^{13}C NMR (75 MHz, CDCl_3) δ 170.4, 161.2, 132.3, 132.1 (q, $^2J_{\text{CF}} = 31.5$ Hz), 127.3, 126.1 (q, $^3J_{\text{CF}} = 4.5$ Hz), 123.9 (q, $^1J_{\text{CF}} = 272.5$ Hz), 100.7, 96.5, 65.6.

^{19}F NMR (282 MHz, CDCl_3) δ – 63.83 (s).

Mass (CI/ NH_3) MH^+ 287

3-(3-chloro-4-fluorophenyl)-5-(1,3-dioxolan-2-yl)isoxazole **4j**



Slightly yellow oil, 58% yield (392 mg)

Chemical formula: $\text{C}_{12}\text{H}_9\text{ClFNO}_3$

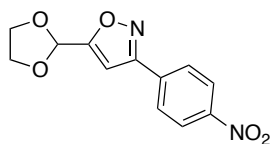
^1H NMR (300 MHz, CDCl_3) δ 7.86 (dd, $J = 7.0, 2.0$ Hz, 1H), 7.67 (ddd, $J = 8.5, 4.5, 2.0$ Hz, 1H), 7.22 (t, $J = 8.5$ Hz, 1H), 6.60 (s, 1H), 6.11 (s, 1H), 4.23 – 3.93 (m, 4H).

^{13}C NMR (75 MHz, CDCl_3) δ 170.3, 160.4, 159.3 (d, $^1J_{\text{CF}} = 252.7$ Hz), 129.4, 126.9 (d, $^3J_{\text{CF}} = 7.6$ Hz), 126.2 (d, $^3J_{\text{CF}} = 3.7$ Hz), 122.1 (d, $^2J_{\text{CF}} = 18.1$ Hz), 117.4 (d, $^2J_{\text{CF}} = 21.7$ Hz), 100.5, 96.5, 65.6.

^{19}F NMR (282 MHz, CDCl_3) δ – 112.51 (q, $J = 6.8$ Hz).

Mass (CI/ NH_3) MH^+ 270

5-(1,3-dioxolan-2-yl)-3-(4-nitrophenyl)isoxazole **4k**



Yellow solid (mp = 135-138 °C), 94% yield (618 mg)

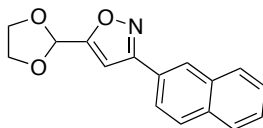
Chemical formula: C₁₂H₁₀N₂O₅

¹H NMR (400 MHz, CDCl₃) δ 8.32 (d, *J* = 9.0 Hz, 2H), 7.99 (d, *J* = 9.0 Hz, 2H), 6.72 (s, 1H), 6.14 (s, 1H), 4.37 – 3.87 (m, 4H).

¹³C NMR (100 MHz, CDCl₃) δ 170.8, 160.5, 148.9, 134.9, 127.8, 124.4, 100.8, 96.4, 65.7.

Mass (CI/NH₃) MH⁺ 263

5-(1,3-dioxolan-2-yl)-3-(naphthalen-2-yl)isoxazole **4l**



Yellow oil, 73% yield (489 mg)

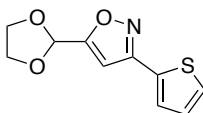
Chemical formula: C₁₆H₁₃NO₃

¹H NMR (300 MHz, CDCl₃) δ 8.24 (d, *J* = 1.5 Hz, 1H), 8.08 – 7.74 (m, 4H), 7.58 – 7.45 (m, 2H), 6.78 (s, 1H), 6.16 (s, 1H), 4.29 – 3.99 (m, 4H).

¹³C NMR (75 MHz, CDCl₃) δ 169.6, 162.3, 134.2, 133.3, 128.9, 128.6, 127.9, 127.2, 126.8, 126.3, 124.0, 100.8, 96.6, 65.6.

Mass (CI/NH₃) MH⁺ 268

5-(1,3-dioxolan-2-yl)-3-(thiophen-2-yl)isoxazole **4m**



Dark yellow oil, 60% yield (336 mg)

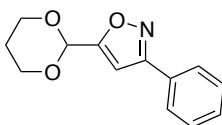
Chemical formula: C₁₀H₉NO₃S

¹H NMR ¹H NMR (300 MHz, Chloroform-*d*) δ 7.45 (dd, *J* = 3.5, 1.2 Hz, 1H), 7.42 (dd, *J* = 5.0, 1.2 Hz, 1H), 7.11 (dd, *J* = 5.0, 3.5 Hz, 1H), 6.56 (s, 1H), 6.10 (s, 1H), 4.22 – 3.96 (m, 4H).

¹³C NMR (75 MHz, CDCl₃) δ 169.7, 157.5, 130.5, 127.9, 127.8, 127.7, 100.7, 96.5, 65.5.

Mass (CI/NH₃) MH⁺ 224

5-(1,3-dioxan-2-yl)-3-phenylisoxazole **4n**



Slightly yellow oil, 87% yield (505 mg)

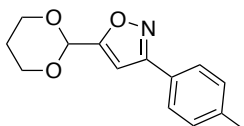
Chemical formula: C₁₃H₁₃NO₃

¹H NMR (300 MHz, CDCl₃) δ 7.87 – 7.72 (m, 2H), 7.54 – 7.37 (m, 3H), 6.69 (d, *J* = 1.0 Hz, 1H), 5.74 (s, 1H), 4.31 – 4.25 (m, 2H), 4.04 – 3.95 (m, 2H), 2.38 – 2.13 (m, 1H), 1.53 – 1.46 (m, 1H).

¹³C NMR (100 MHz, CDCl₃) δ 168.8, 162.3, 130.1, 129.0 (2C), 126.9, 100.3, 95.0, 67.4, 25.6.

Mass (CI/NH₃) MH⁺ 232

5-(1,3-dioxan-2-yl)-3-phenylisoxazole **4o**



Slightly yellow solid (mp = 78 – 80 °C), 95% yield (584 mg)

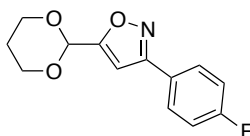
Chemical formula: C₁₄H₁₃NO₃

¹H NMR (300 MHz, CDCl₃) δ 7.65 (d, *J* = 8.0 Hz, 1H), 7.21 (d, *J* = 8.0 Hz, 1H), 6.62 (s, 1H), 5.69 (s, 1H), 4.27 – 4.21 (m, 2H), 4.01 – 3.92 (m, 2H), 2.35 (s, 3H), 2.28 – 2.15 (m, 1H), 1.54 – 1.43 (m, 1H).

¹³C NMR (75 MHz, CDCl₃) δ 168.7, 162.3, 140.3, 129.7, 126.9, 126.2, 100.2, 95.1, 67.4, 25.7, 21.5.

Mass (CI/NH₃) MH⁺ 246

5-(1,3-dioxan-2-yl)-3-(4-fluorophenyl)isoxazole **4p**



Slightly yellow solid (mp = 80 – 82 °C), 51% yield (315 mg)

Chemical formula: C₁₃H₁₂FNO₃

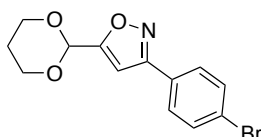
¹H NMR (300 MHz, CDCl₃) δ 7.80 – 7.76 (m, 2H), 7.26 – 7.10 (m, 2H), 6.64 (s, 1H), 5.73 (s, 1H), 4.31 – 4.25 (m, 2H), 4.04 – 3.95 (m, 2H), 2.31 – 2.19 (m, 1H), 1.53 – 1.46 (m, 1H).

^{13}C NMR (75 MHz, CDCl_3) δ 169.1, 163.9 (d, $J = 250.0$ Hz), 161.4, 128.9 (d, $J = 8.5$ Hz), 125.2 (d, $J = 3.3$ Hz), 116.2 (d, $J = 21.9$ Hz), 100.2, 94.9, 67.4, 25.6.

^{19}F NMR (282 MHz, CDCl_3) δ -111.40 – -111.60 (m).

Mass (CI/ NH_3) MH^+ 249

3-(4-bromophenyl)-5-(1,3-dioxan-2-yl)isoxazole **4q**



Slightly yellow solid (mp = 111 – 114 °C), 86% yield (667 mg)

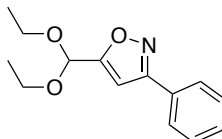
Chemical formula: $\text{C}_{13}\text{H}_{12}\text{BrNO}_3$

^1H NMR (300 MHz, CDCl_3) δ 7.70 – 7.62 (m, 2H), 7.60 – 7.52 (m, 2H), 6.65 (s, 1H), 5.72 (s, 1H), 4.30 – 4.24 (m, 2H), 4.03 – 3.94 (m, 2H), 2.33 – 2.16 (m, 1H), 1.53 – 1.45 (m, 1H).

^{13}C NMR (75 MHz, CDCl_3) δ 169.2, 161.4, 132.3, 128.5, 127.9, 124.5, 100.1, 94.9, 67.4, 25.6.

Mass (CI/ NH_3) MH^+ 310

5-(diethoxymethyl)-3-phenylisoxazole **4r**



Slightly yellow oil, 56% yield (347 mg)

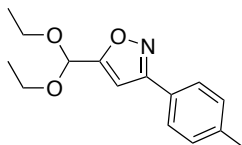
Chemical formula: $\text{C}_{14}\text{H}_{17}\text{NO}_3$

^1H NMR (300 MHz, CDCl_3) δ 7.93 – 7.71 (m, 2H), 7.47 – 7.39 (m, 3H), 6.67 (d, $J = 1.0$ Hz, 1H), 5.68 (d, $J = 1.0$ Hz, 1H), 3.76 – 3.61 (m, 4H), 1.27 (t, $J = 7.0$ Hz, 6H).

^{13}C NMR (100 MHz, CDCl_3) δ 170.0, 162.3, 130.1, 129.0 (2C), 126.9, 101.1, 95.4, 61.9, 15.2.

Mass (ESI) MH^+ 248

5-(diethoxymethyl)-3-(*p*-tolyl)isoxazole **4s**



Slightly yellow oil, 45% yield (295 mg)

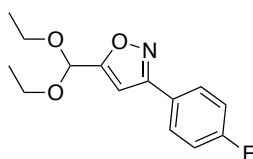
Chemical formula: $\text{C}_{15}\text{H}_{19}\text{NO}_3$

^1H NMR (300 MHz, CDCl_3) δ 7.70 (d, $J = 8.0$ Hz, 1H), 7.25 (d, $J = 8.0$ Hz, 1H), 6.64 (d, $J = 1.0$ Hz, 1H), 5.67 (d, $J = 1.0$ Hz, 1H), 3.91 – 3.45 (qd, $J = 7.0, 3.5$ Hz, 4H), 2.39 (s, 3H), 1.27 (t, $J = 7.0$ Hz, 6H).

^{13}C NMR (100 MHz, CDCl_3) δ 169.8, 162.2, 140.3, 129.7, 126.8, 126.2, 101.0, 95.4, 61.9, 21.5, 15.2.

Mass (ESI) MH^+ 262

5-(diethoxymethyl)-3-(4-fluorophenyl)isoxazole **4t**



Slightly yellow oil, 64% yield (424 mg)

Chemical formula: $\text{C}_{14}\text{H}_{16}\text{FNO}_3$

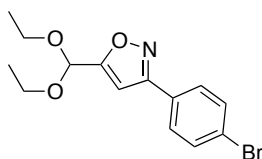
^1H NMR (300 MHz, CDCl_3) δ 7.82 – 7.64 (m, 2H), 7.16 – 7.09 (m, 2H), 6.62 (s, 1H), 5.66 (s, 1H), 3.72 – 3.62 (m, 4H), 1.26 (t, $J = 7.1$ Hz, 6H).

^{13}C NMR (75 MHz, CDCl_3) δ 170.2, 163.9 (d, $^1J_{\text{CF}} = 250.0$ Hz), 161.3, 128.9 (d, $^3J_{\text{CF}} = 8.4$ Hz), 125.3 (d, $^4J_{\text{CF}} = 3.3$ Hz), 116.1 (d, $^2J_{\text{CF}} = 22.0$ Hz), 100.9, 95.3, 62.0, 15.2.

^{19}F NMR (282 MHz, CDCl_3) δ -106.84 – -116.95 (m)

Mass (ESI) MH^+ 265

3-(4-bromophenyl)-5-(diethoxymethyl)isoxazole **4u**



Slightly yellow oil, 91% yield (742 mg)

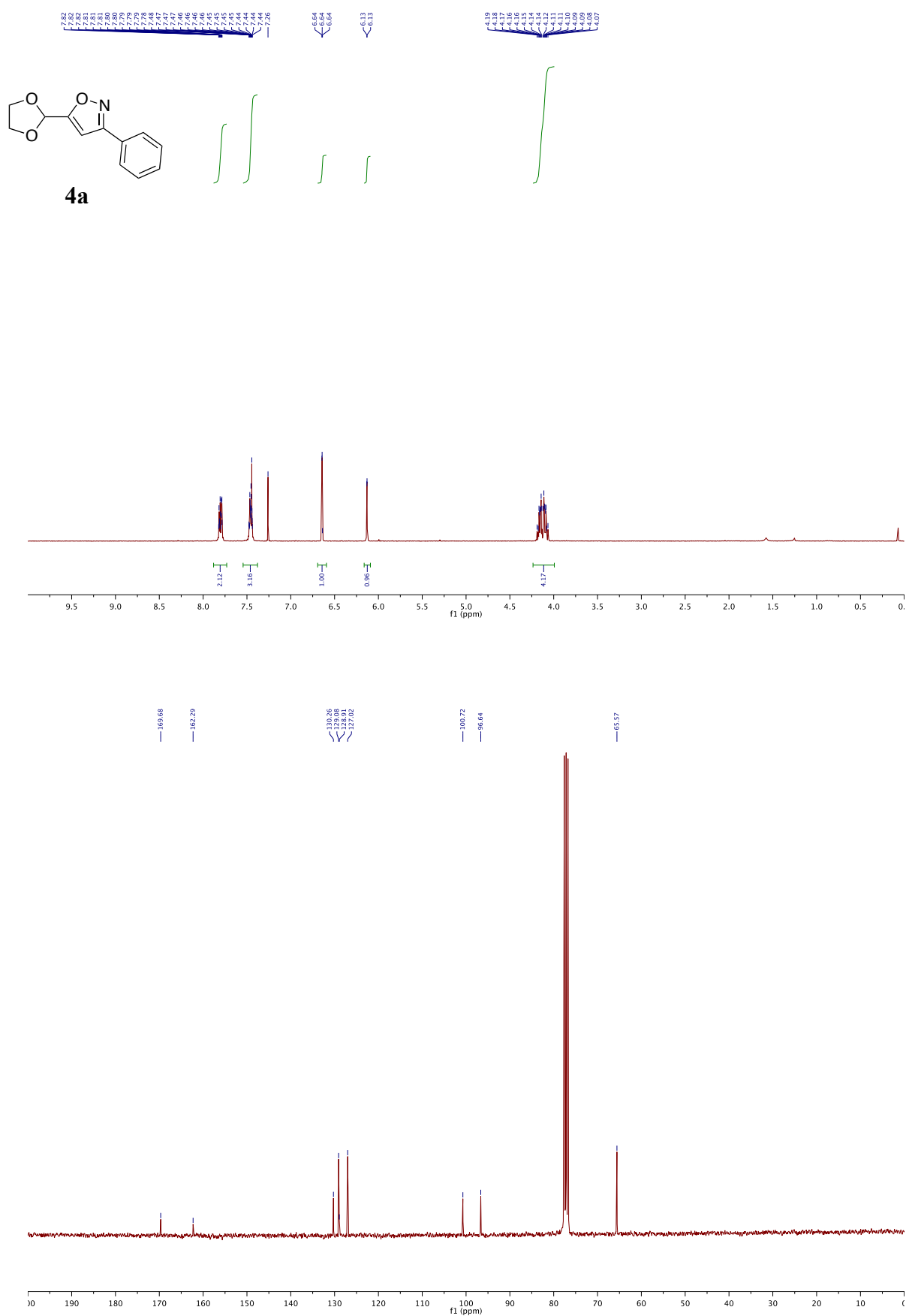
Chemical formula: $\text{C}_{14}\text{H}_{16}\text{BrNO}_3$

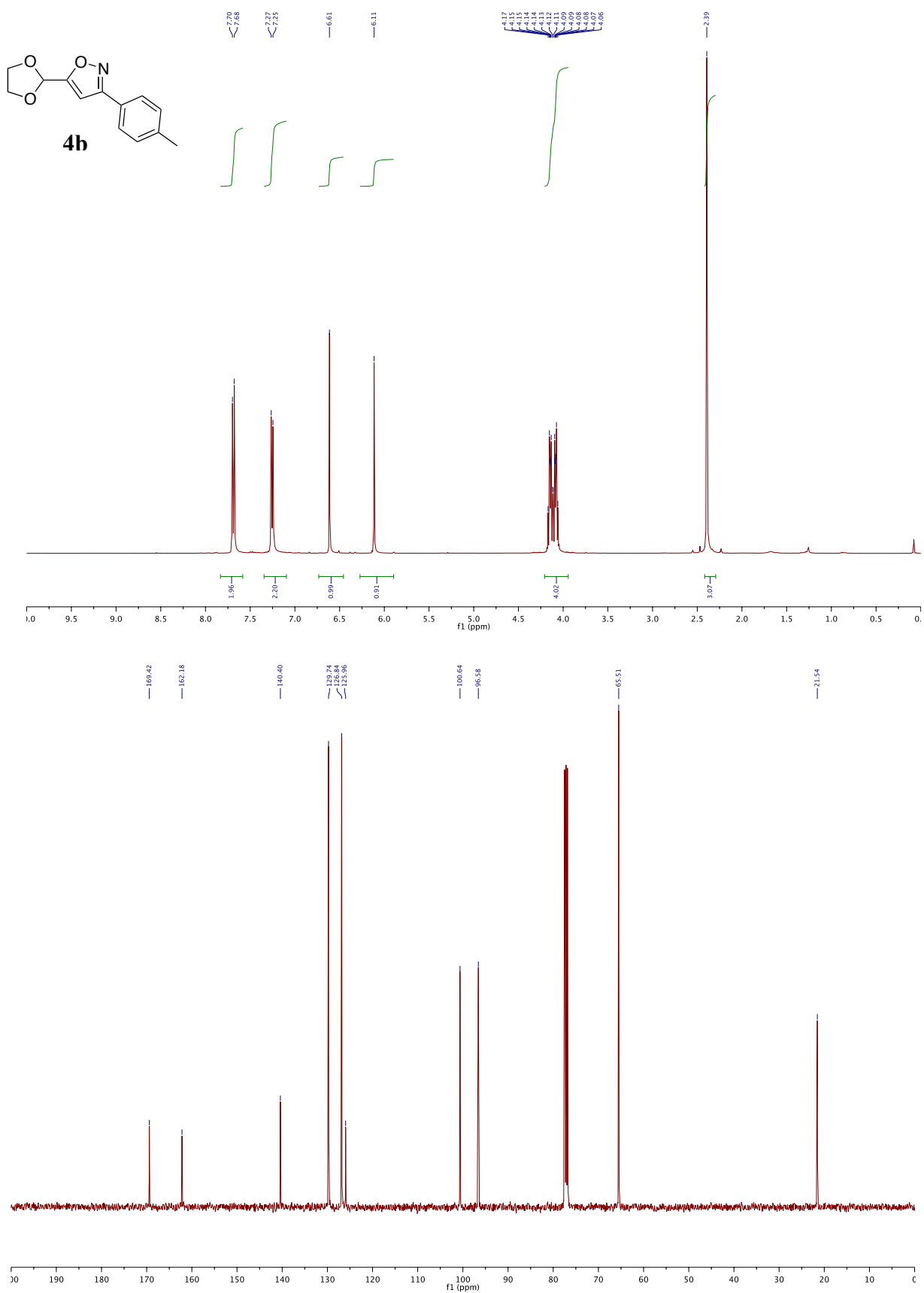
^1H NMR (300 MHz, CDCl_3) δ 7.68 (d, $J = 8.5$ Hz, 2H), 7.58 (d, $J = 8.5$ Hz, 2H), 6.64 (s, 1H), 5.67 (s, 1H), 3.91 – 3.42 (m, 4H), 1.27 (t, $J = 7.0$ Hz, 6H).

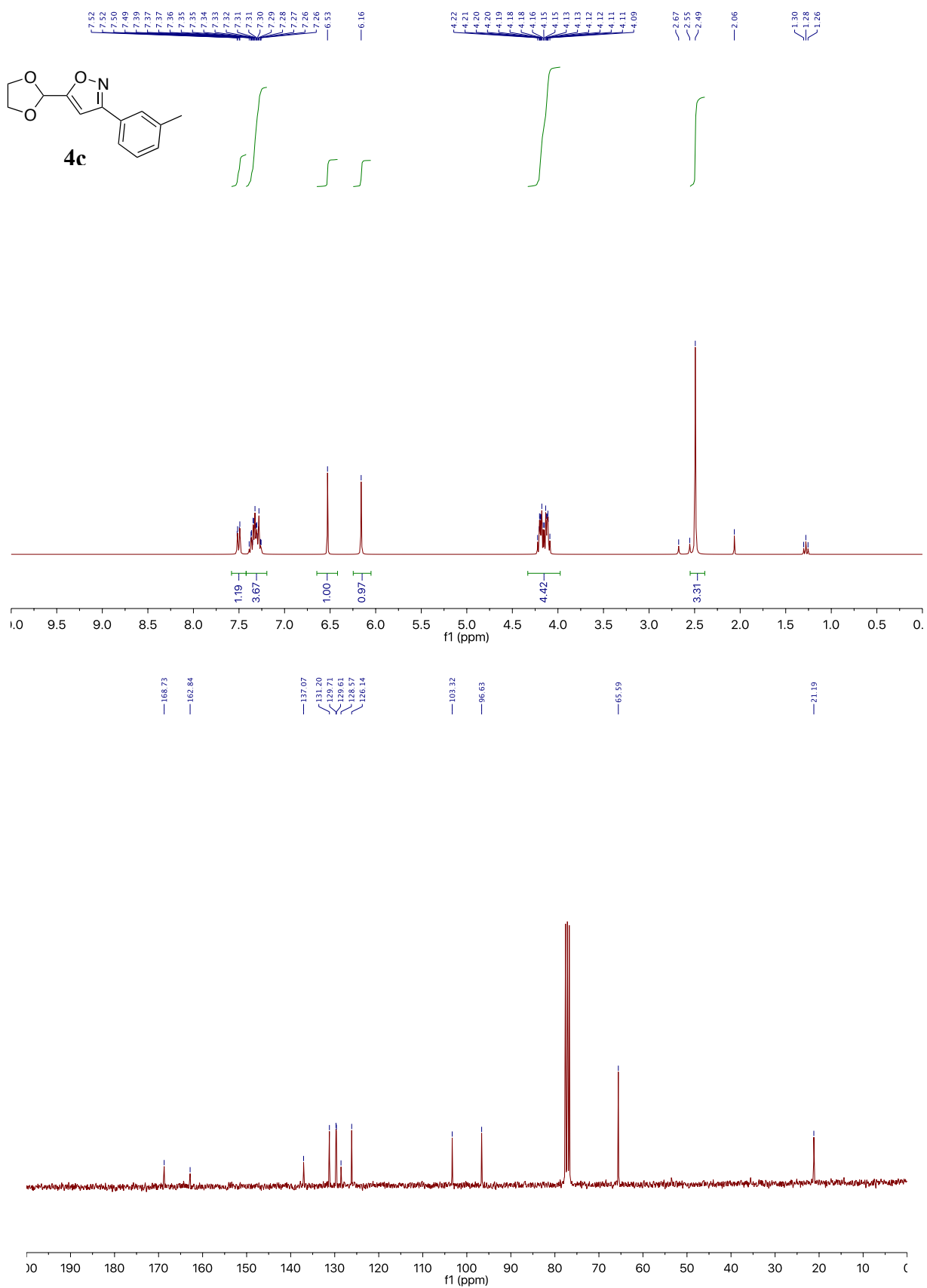
^{13}C NMR (75 MHz, CDCl_3) δ 170.4, 161.4, 132.3, 128.5, 127.9, 124.5, 100.9, 95.3, 62.0, 15.2.

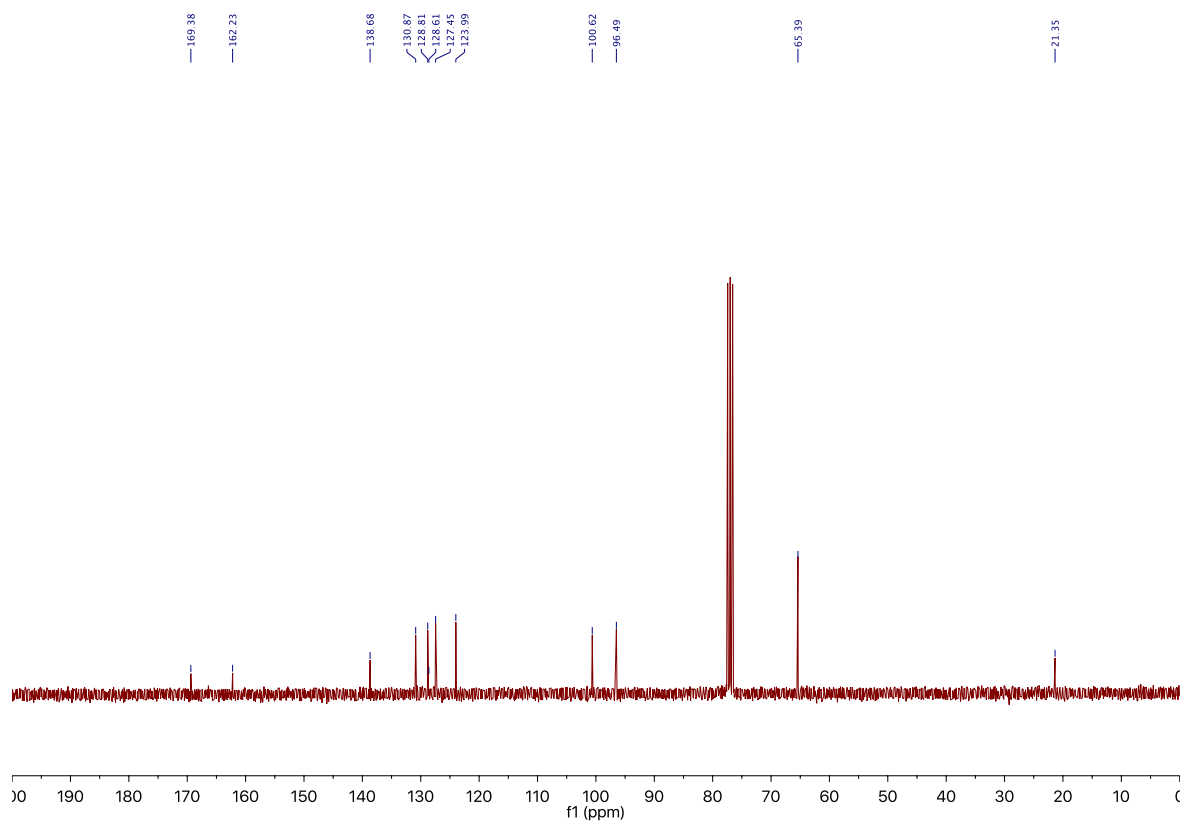
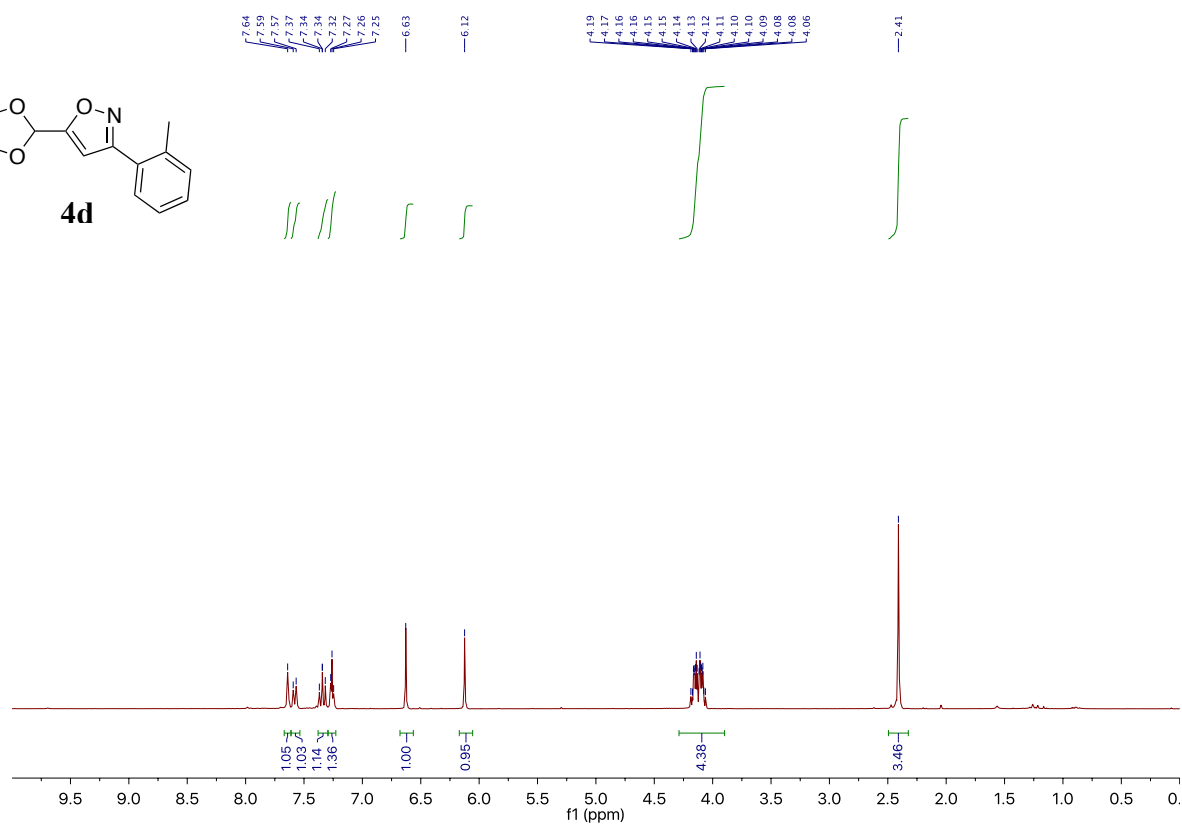
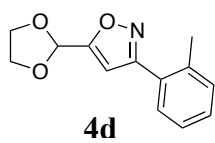
Mass (ESI) MH^+ 326

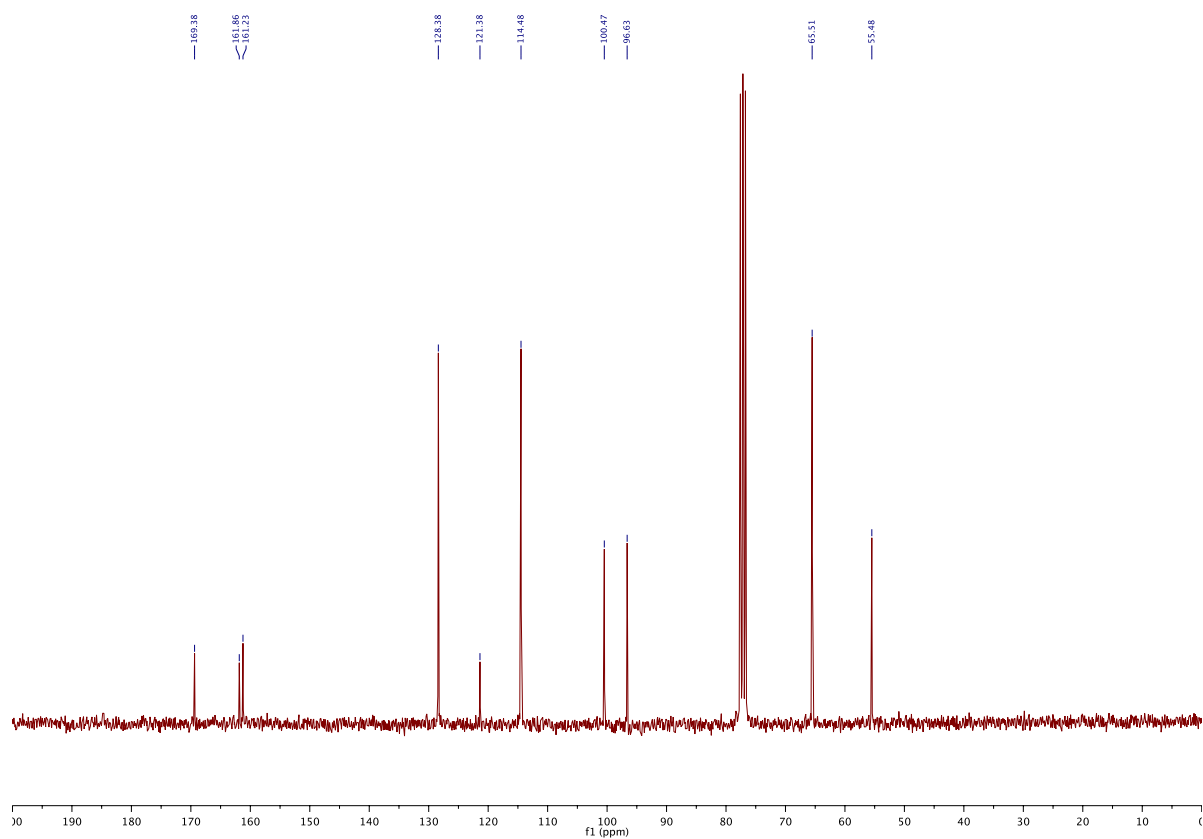
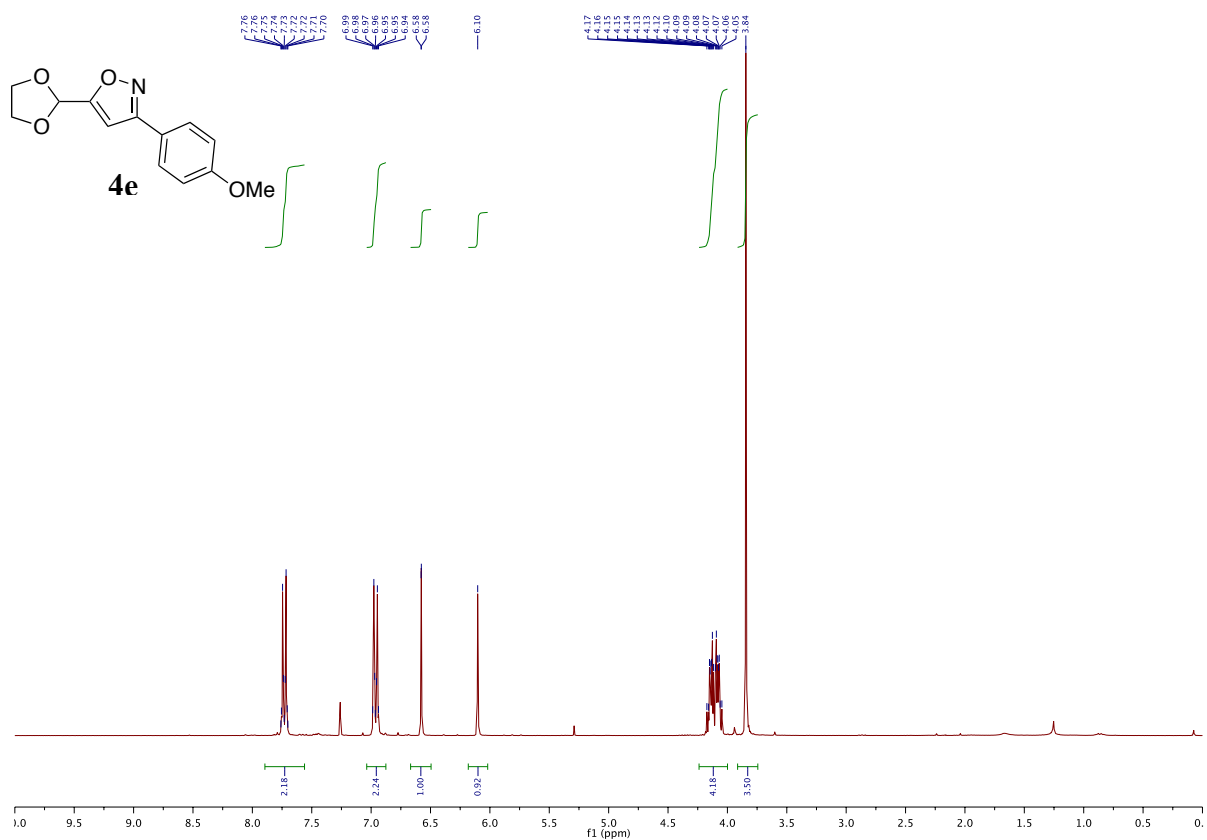
3. NMR spectra of compounds 4a – 4u

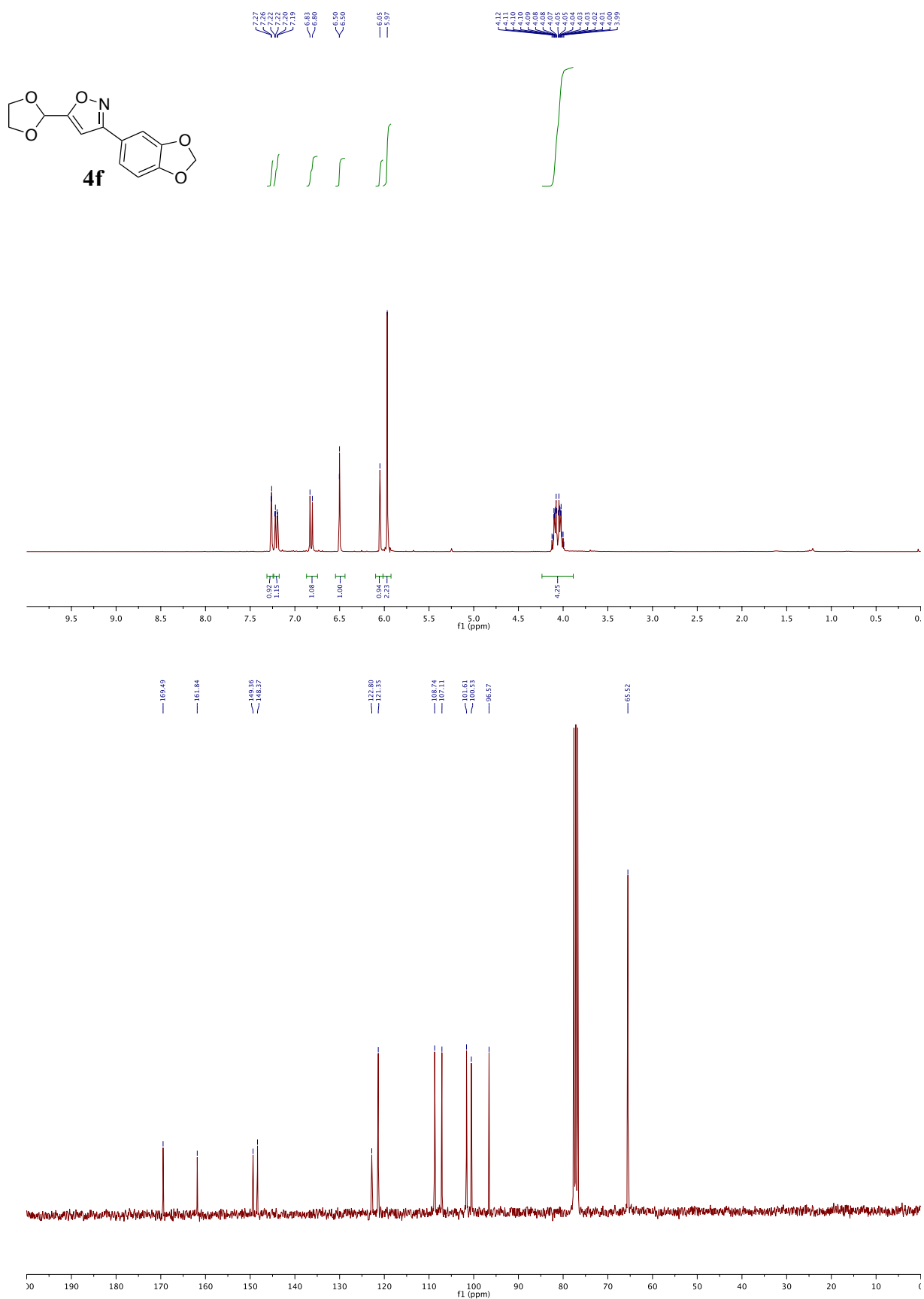


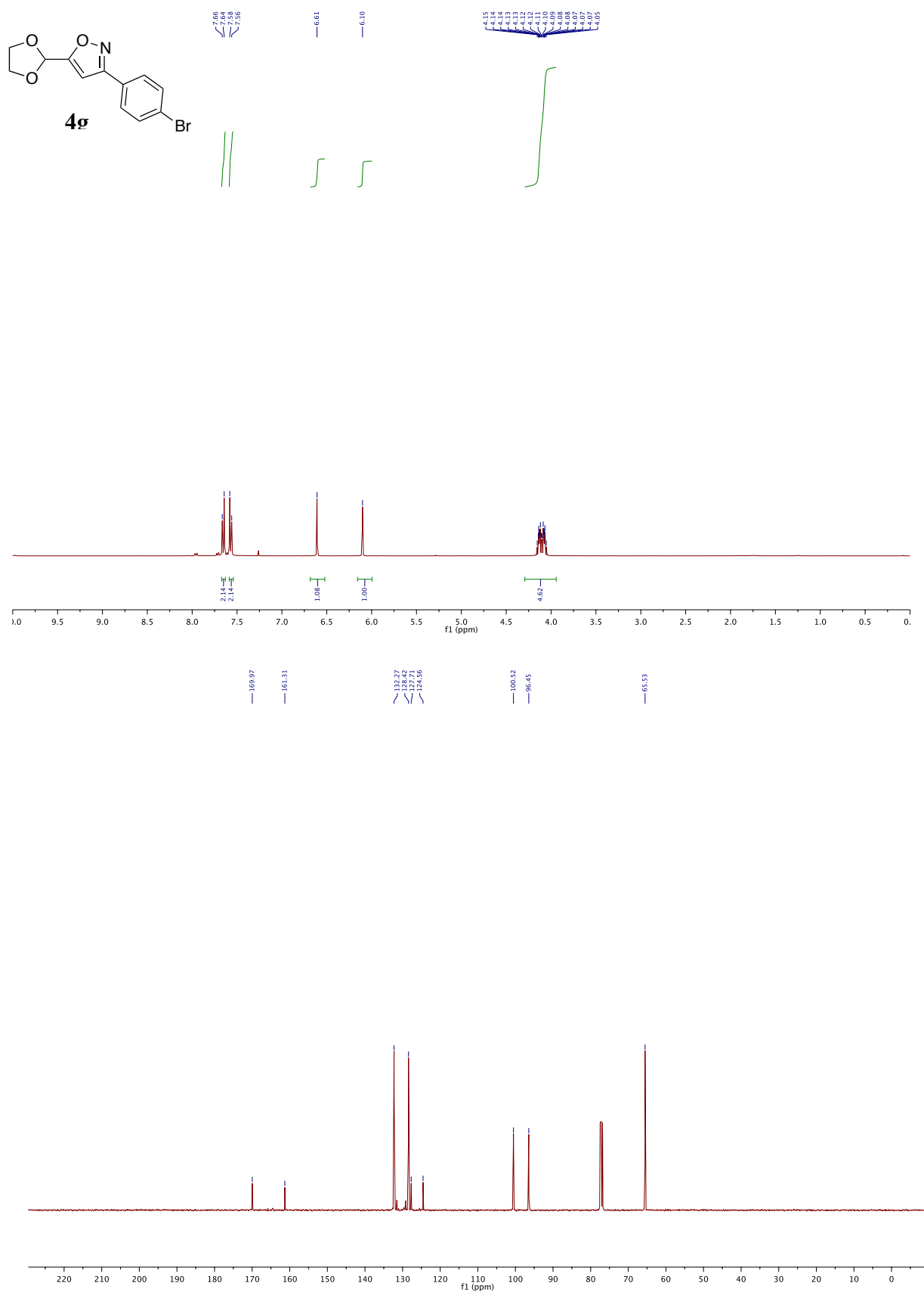


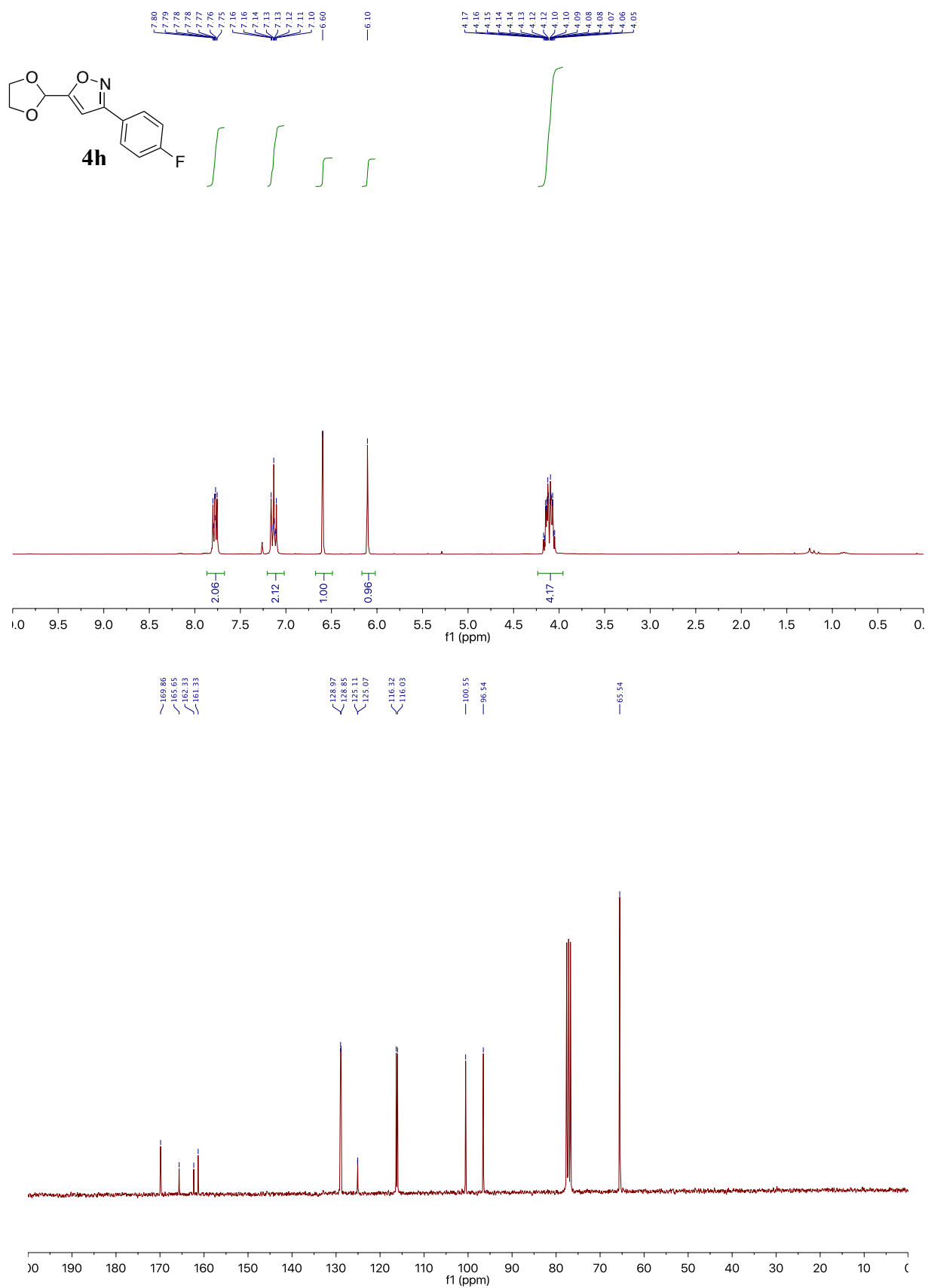


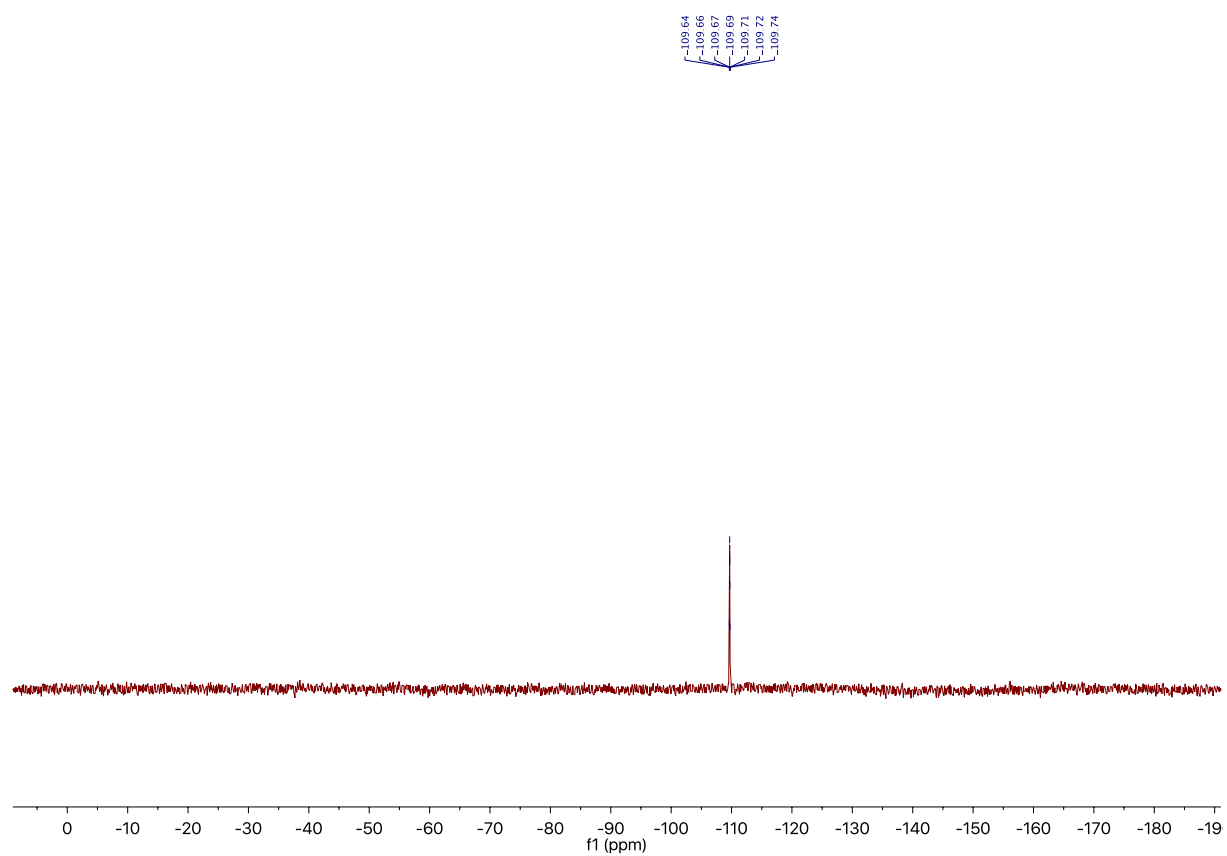


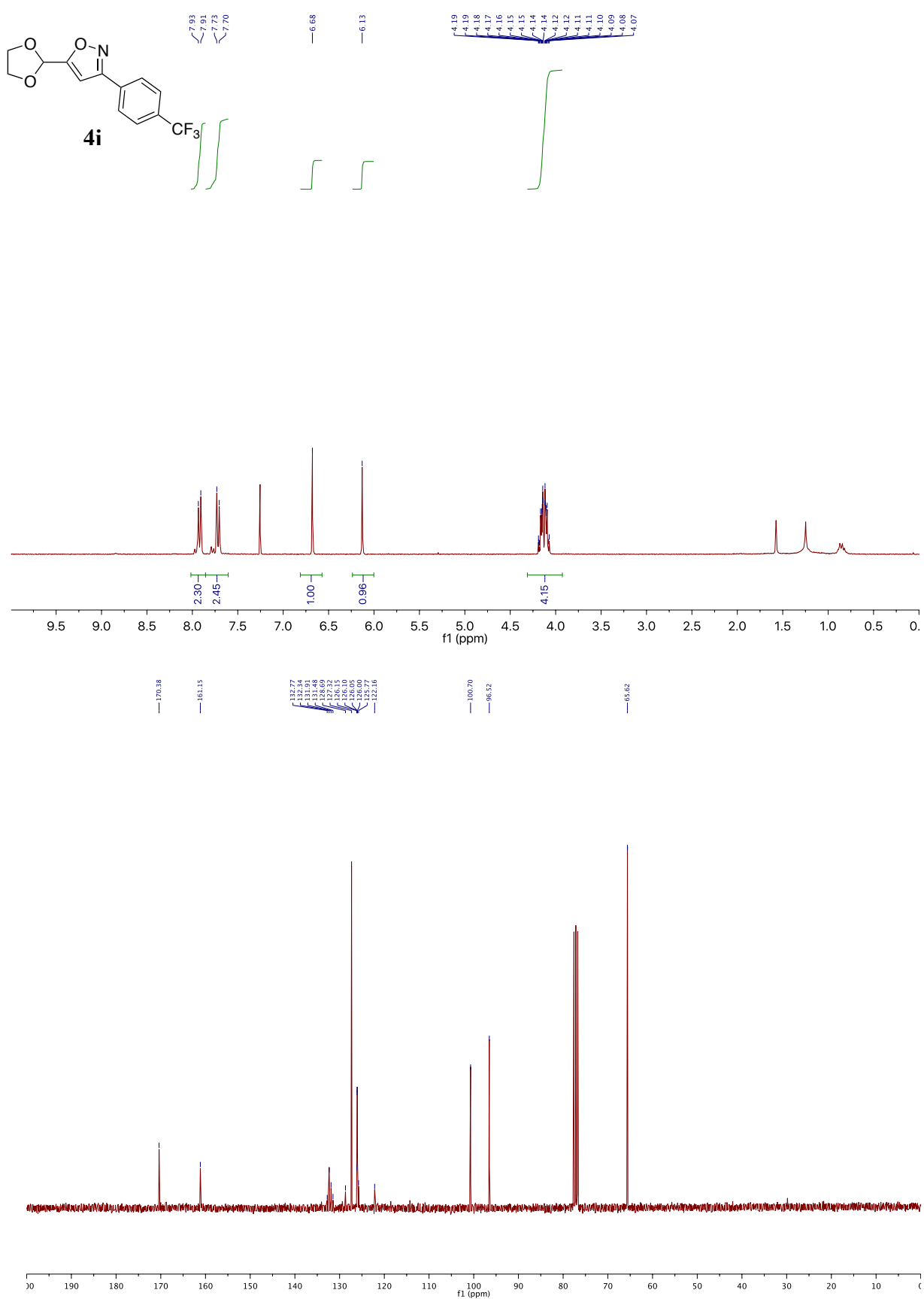


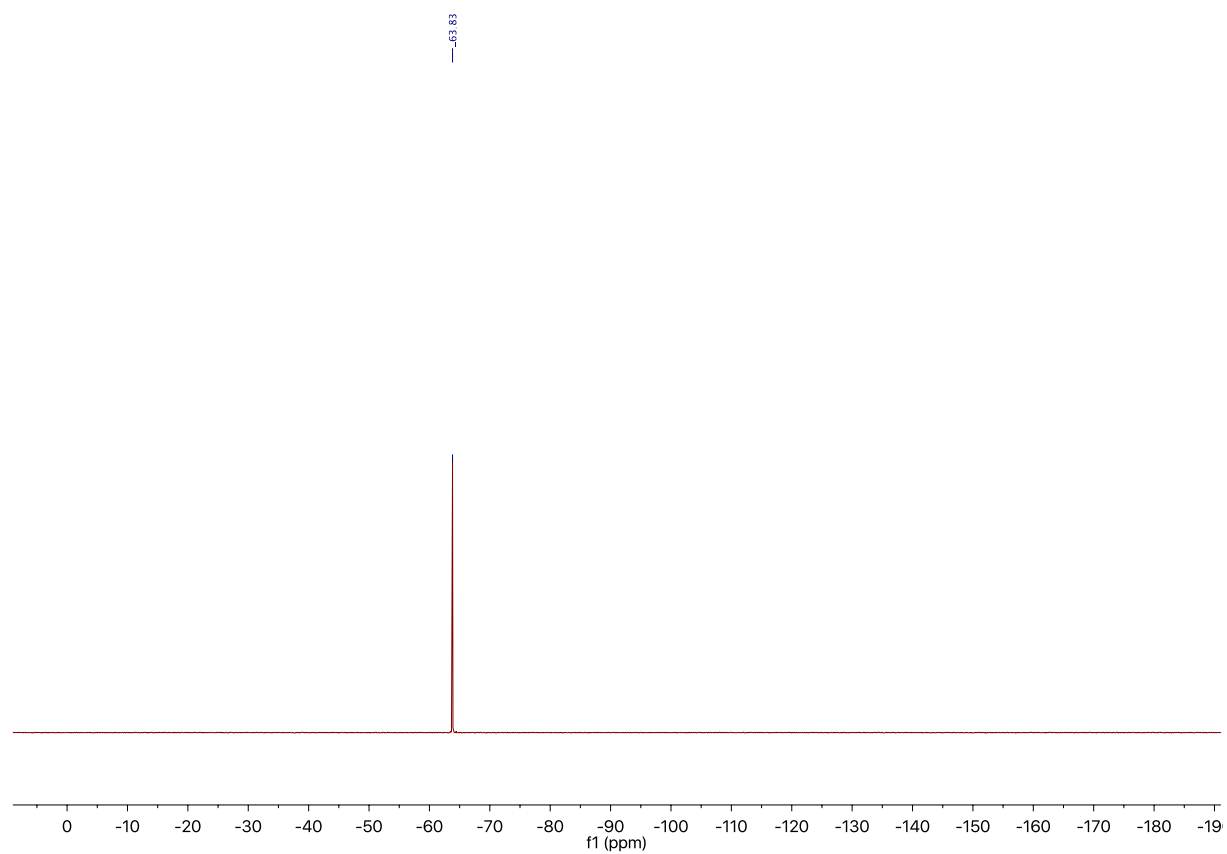


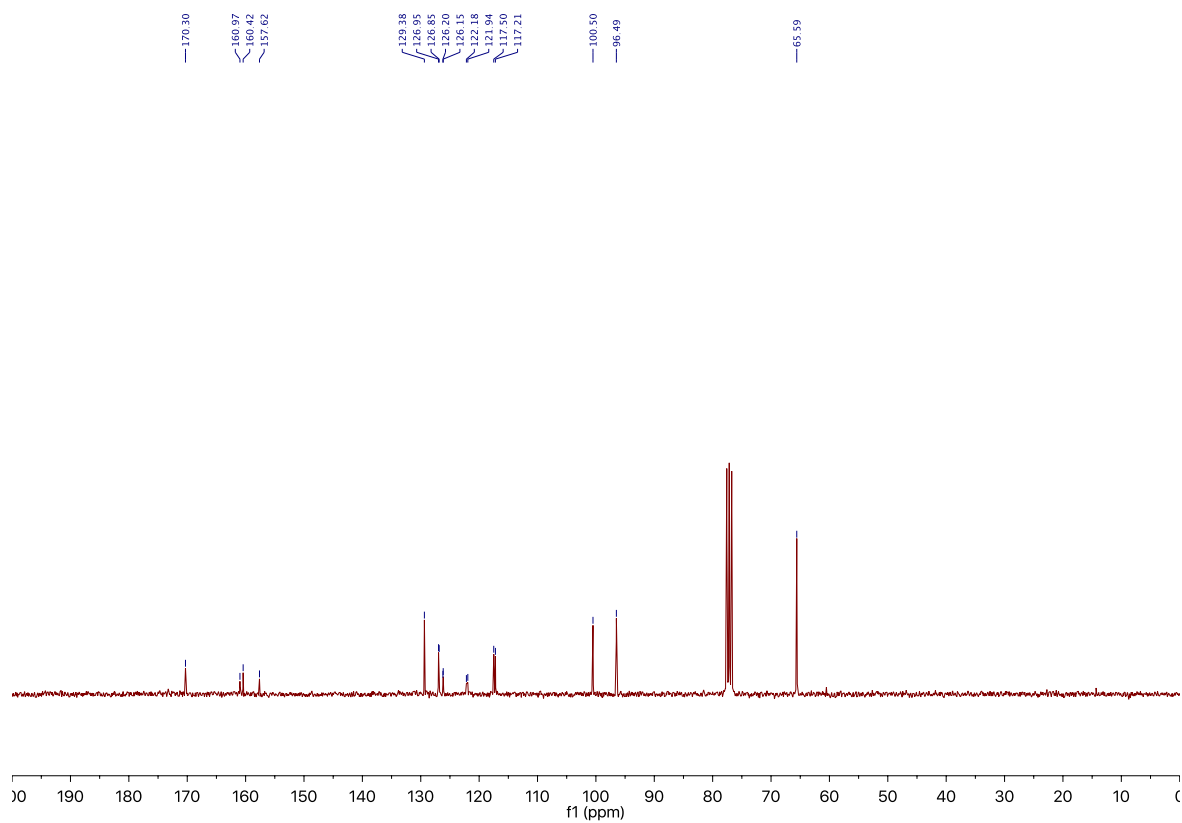
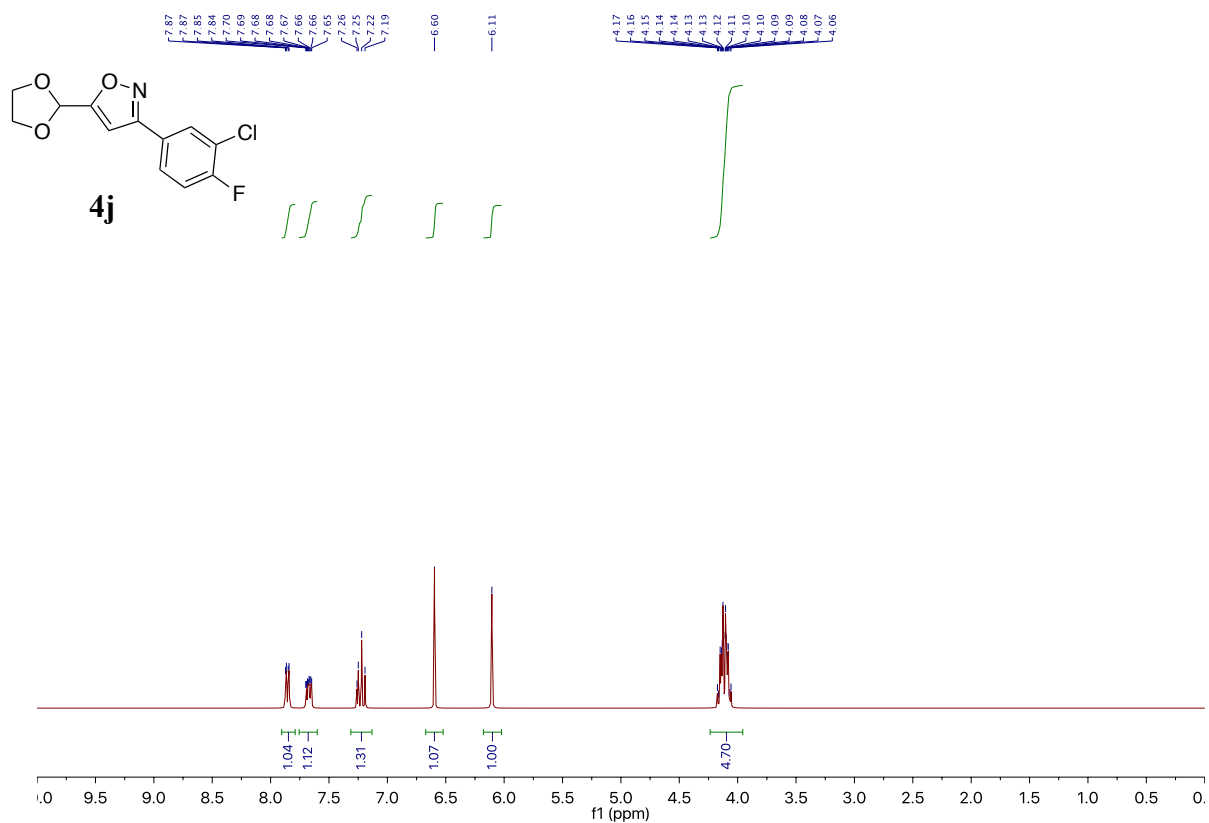


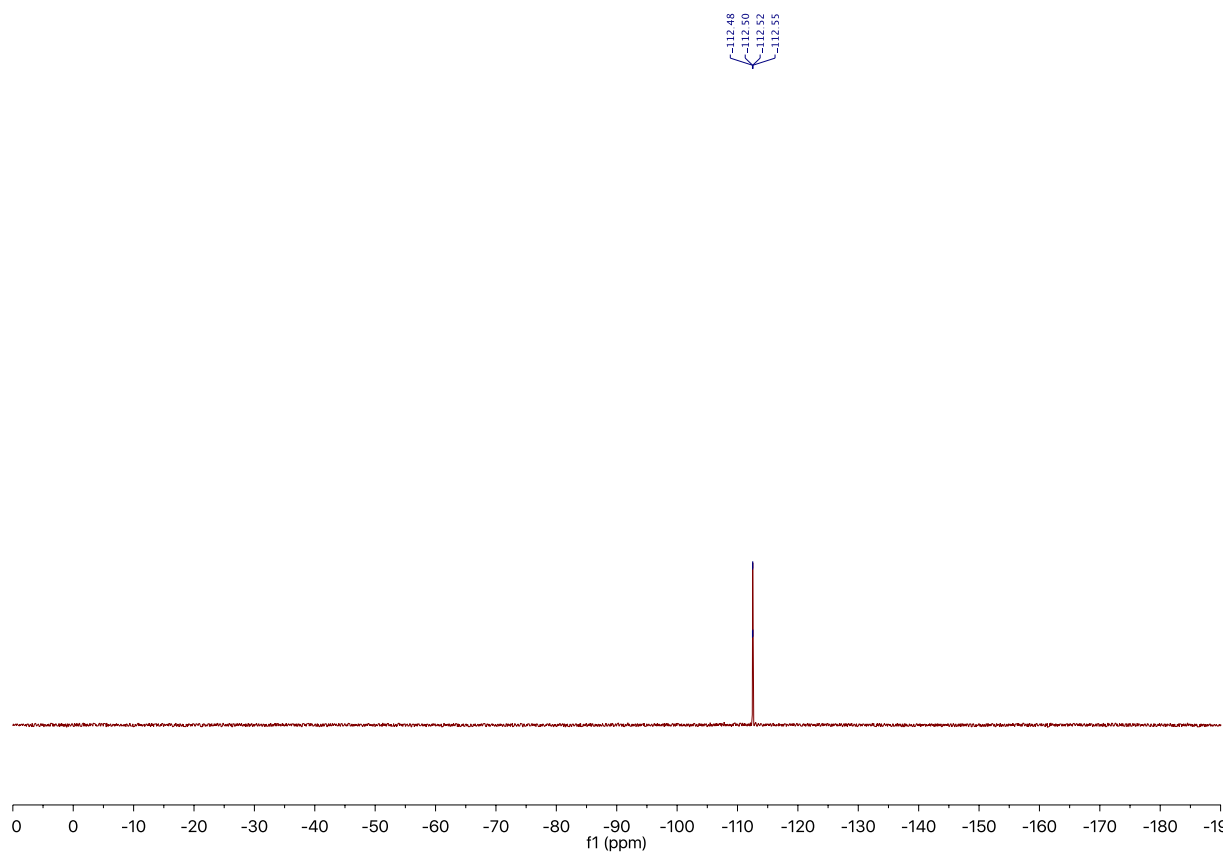


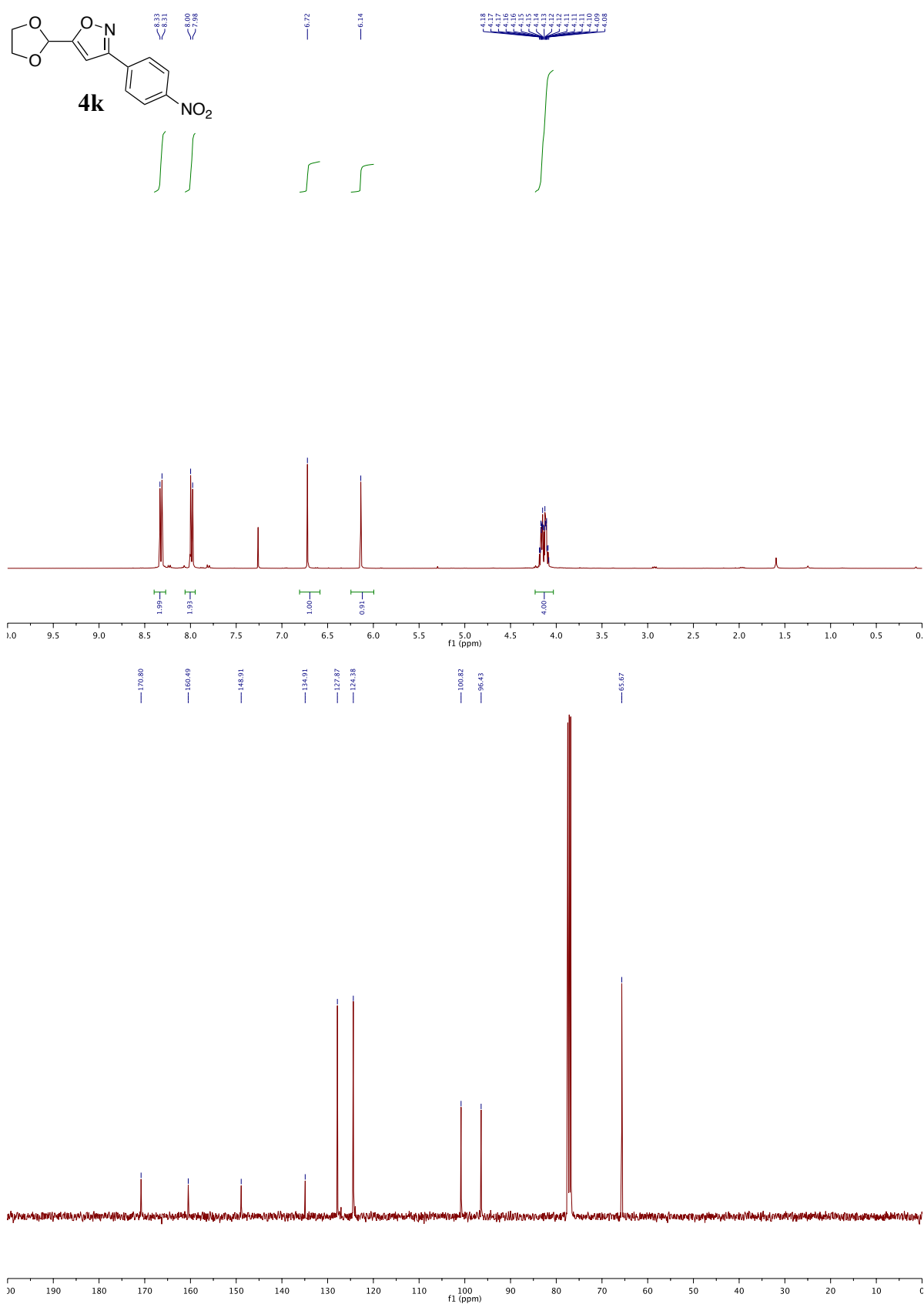


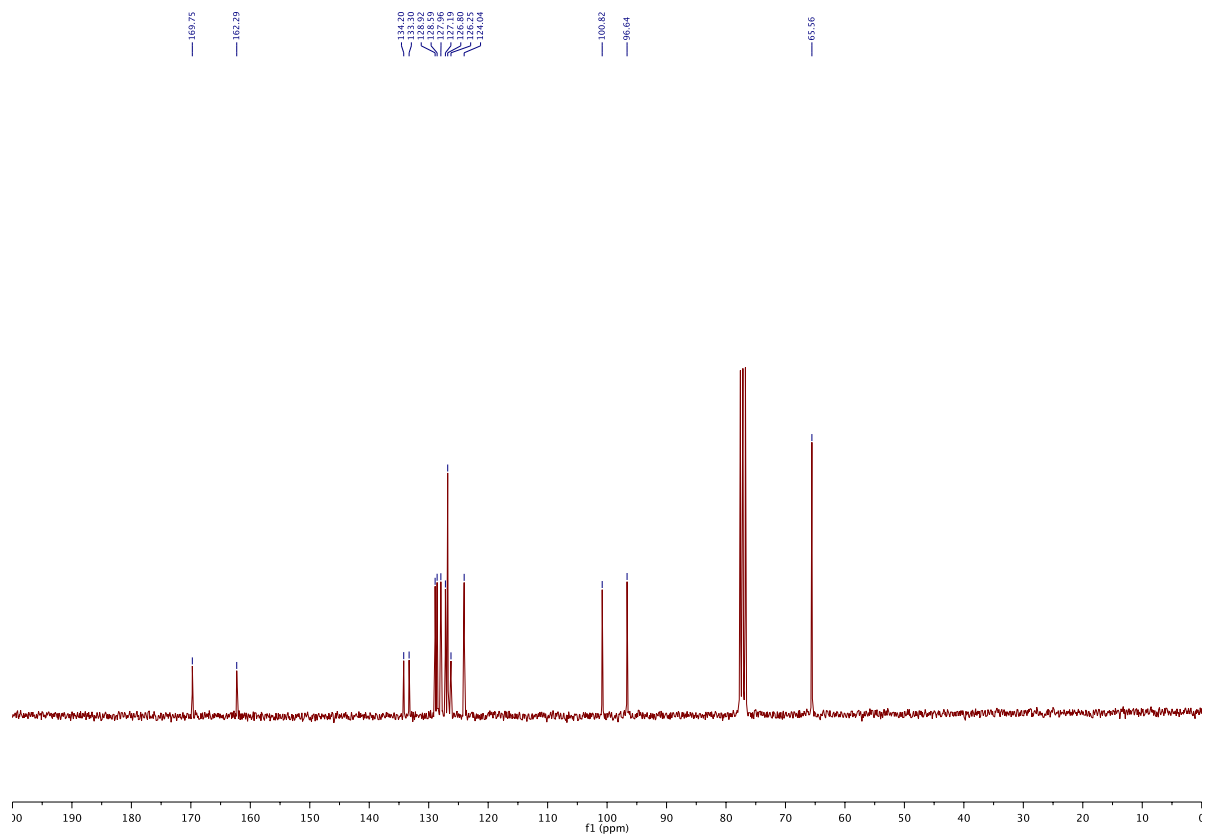
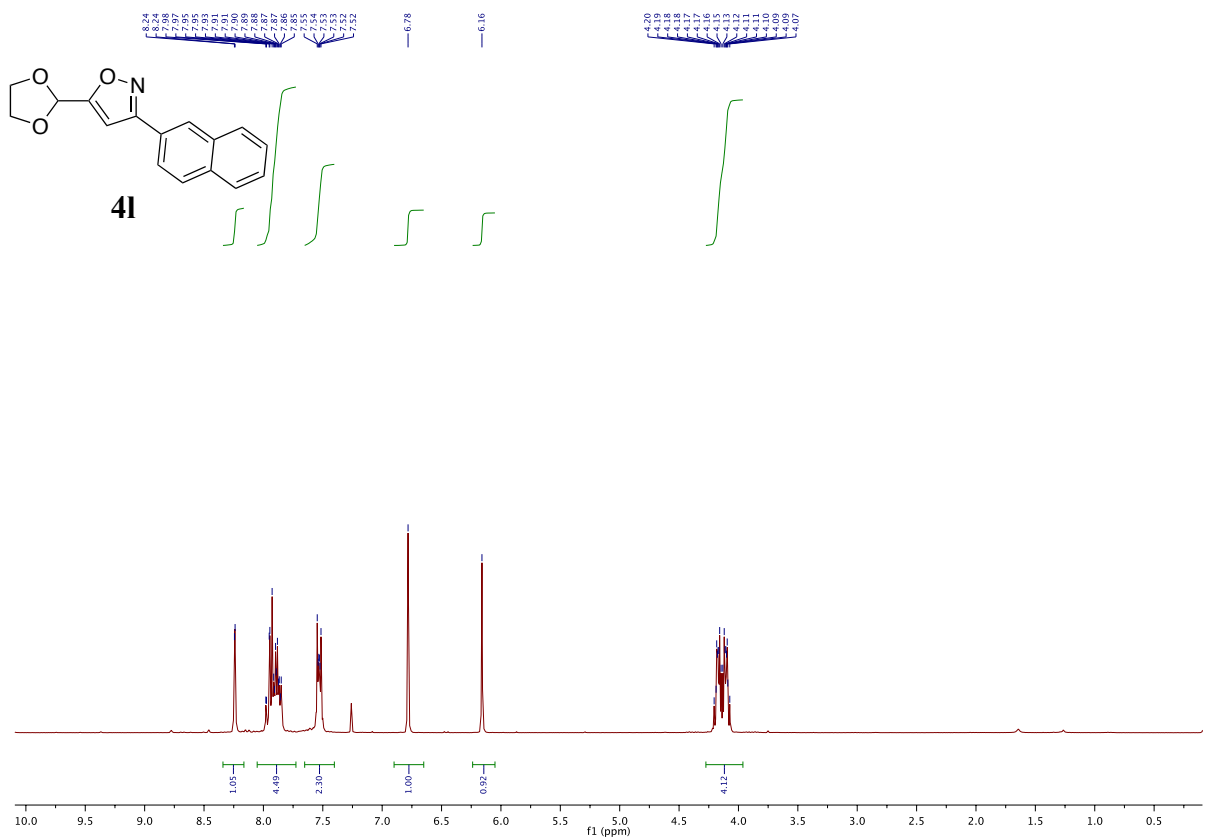


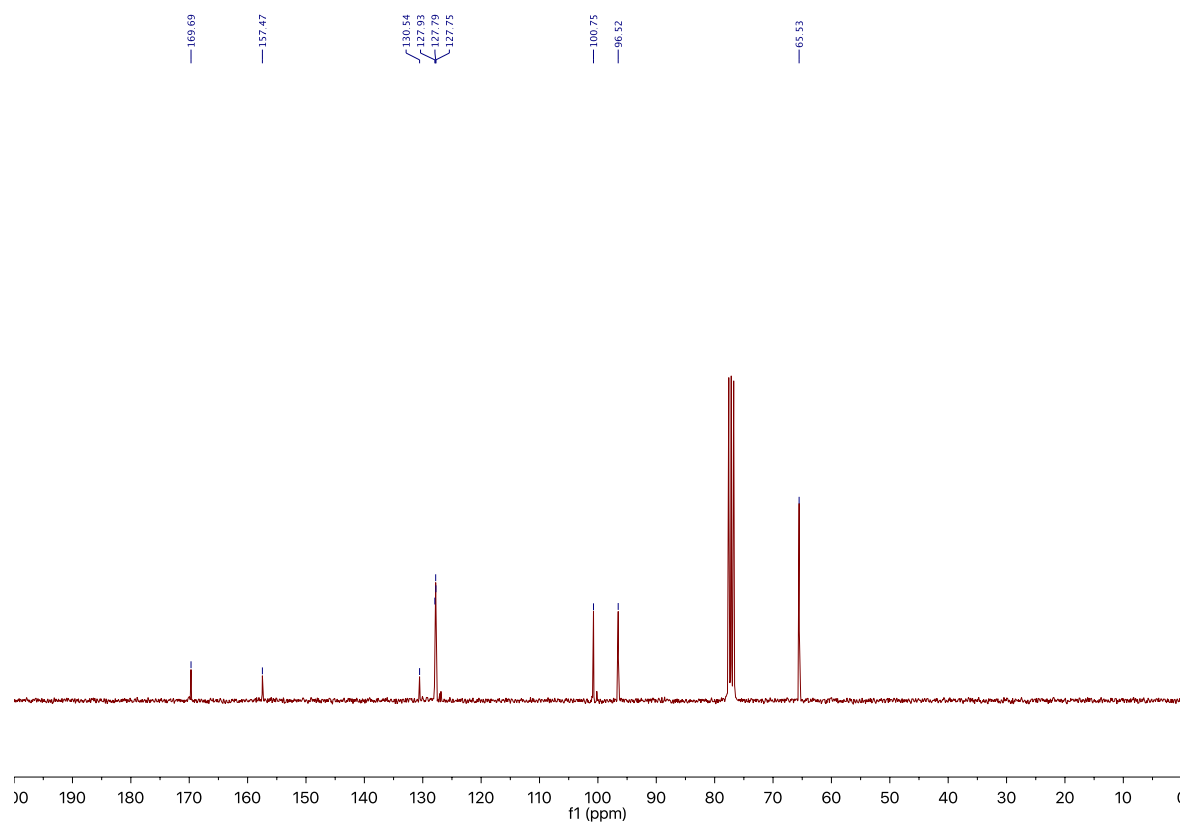
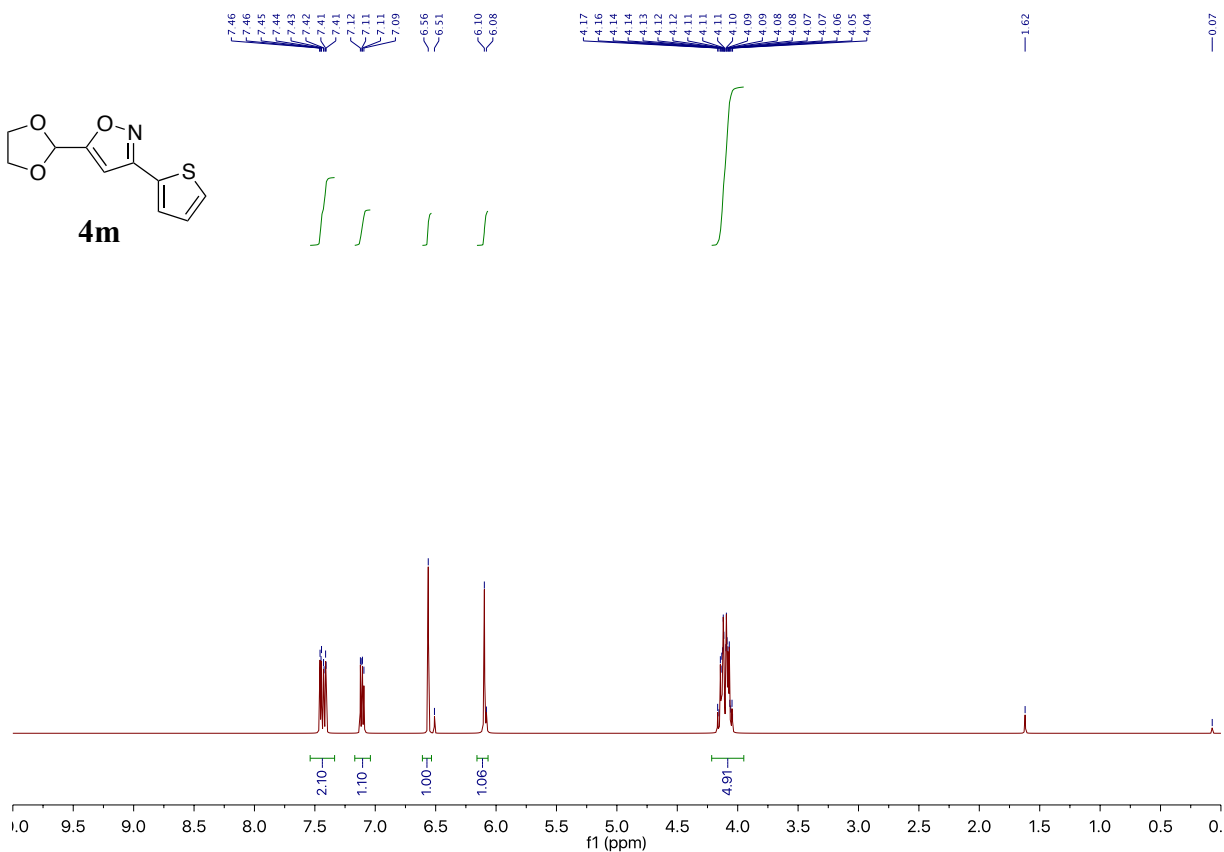
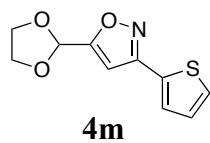


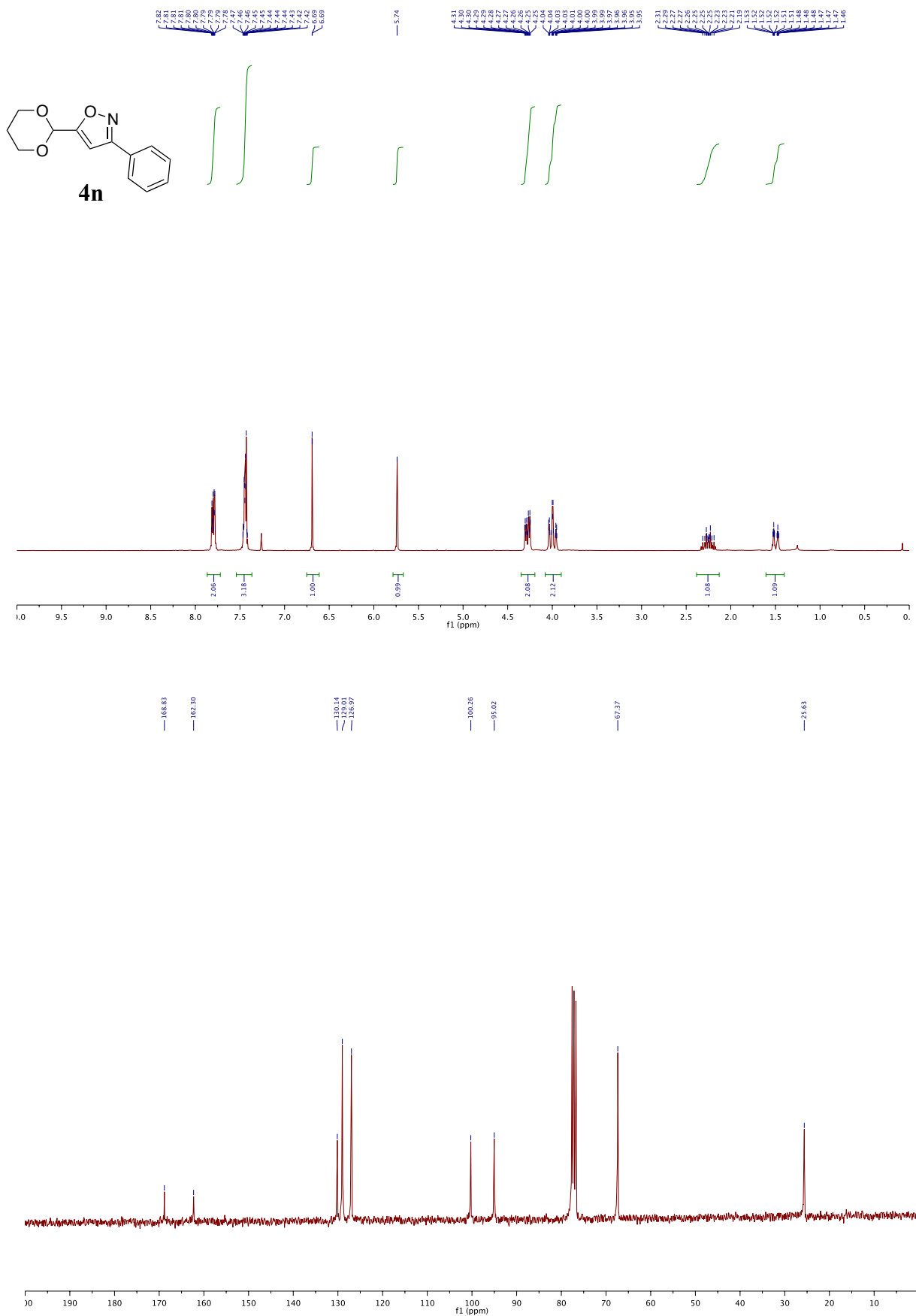


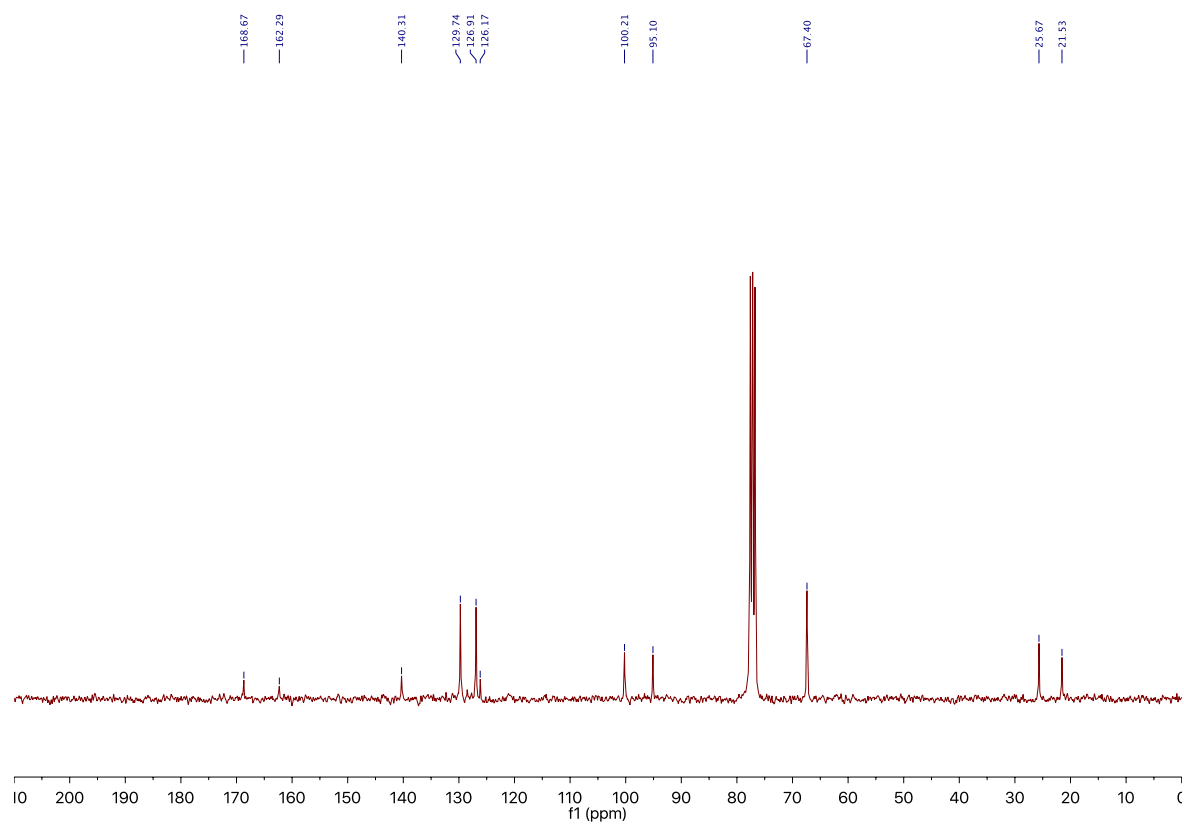
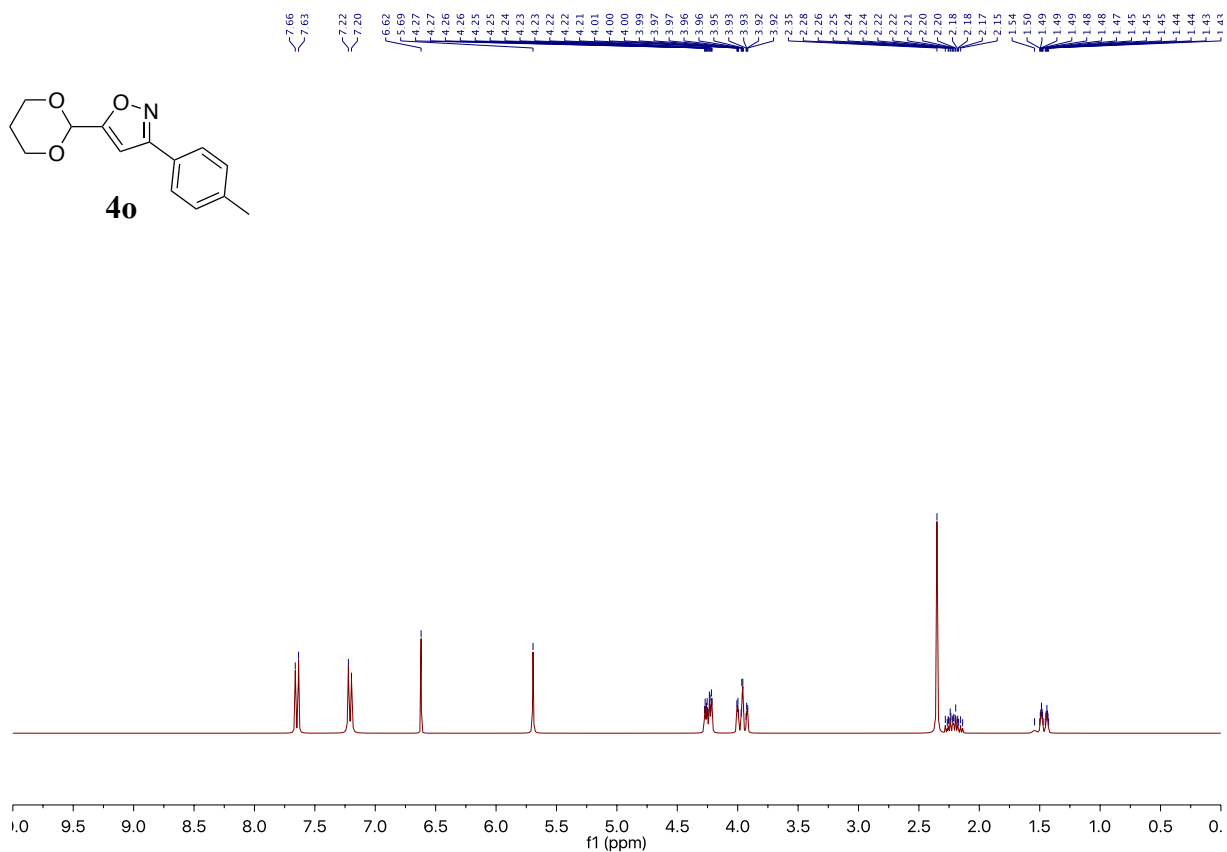
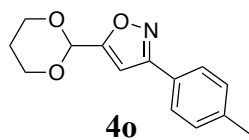


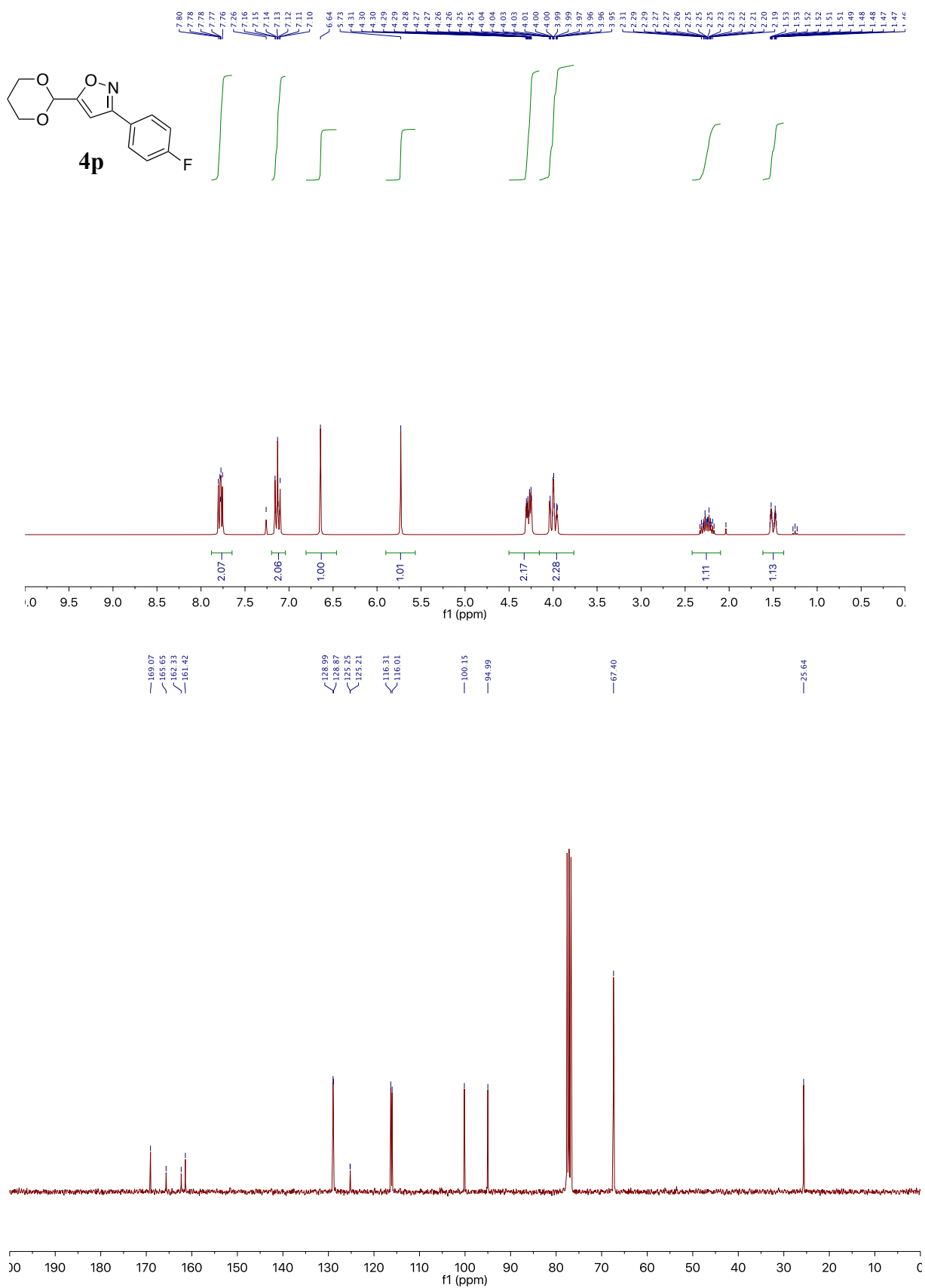


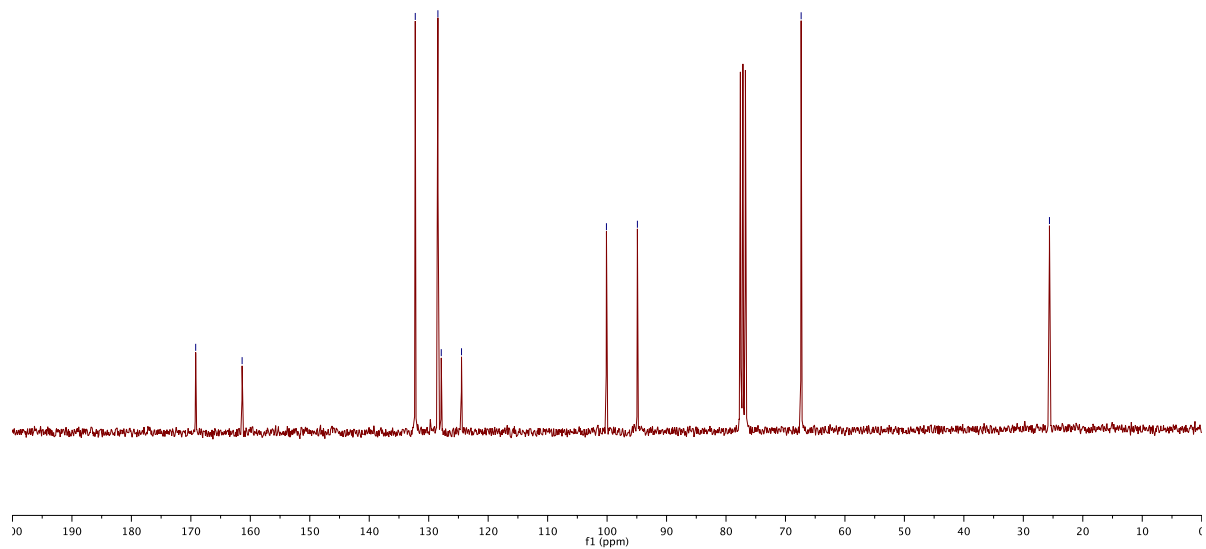
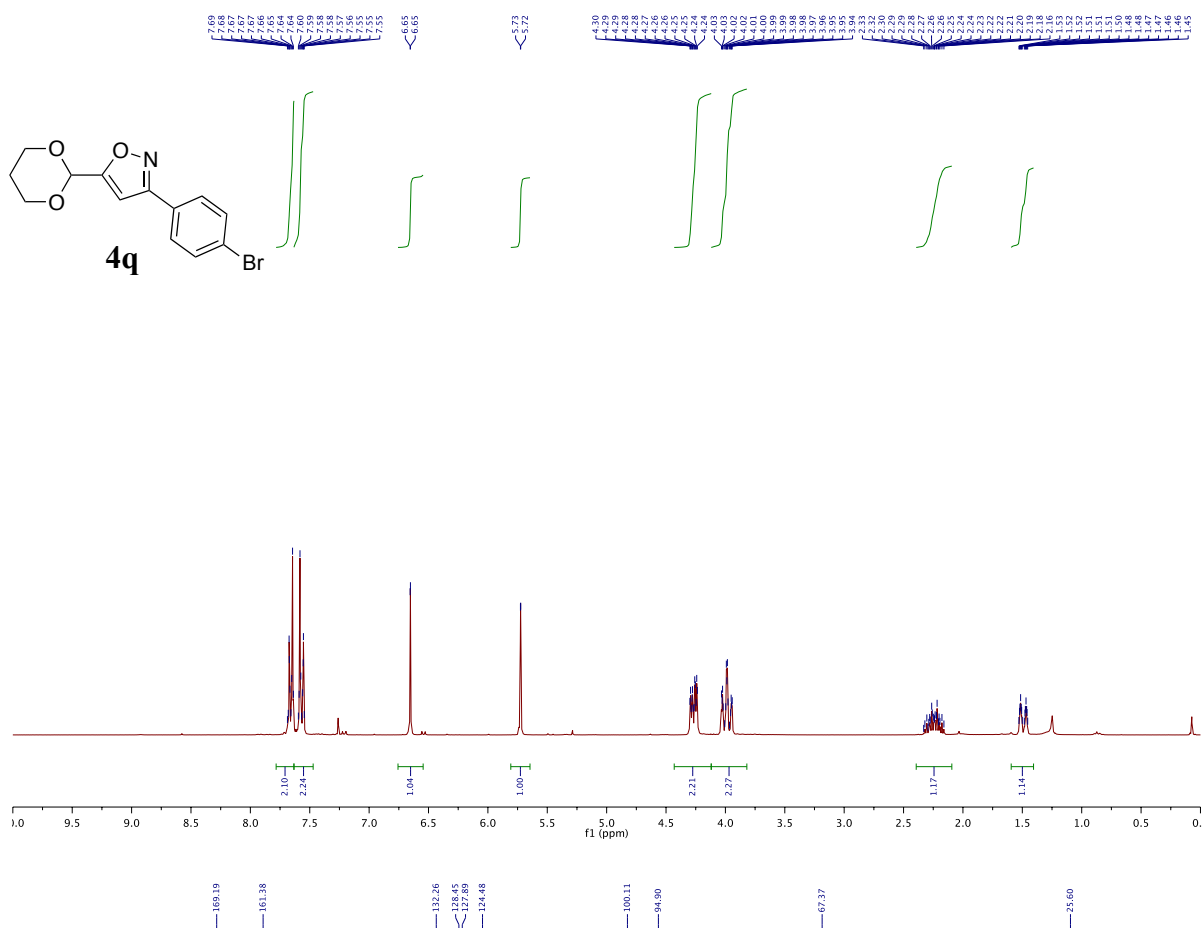


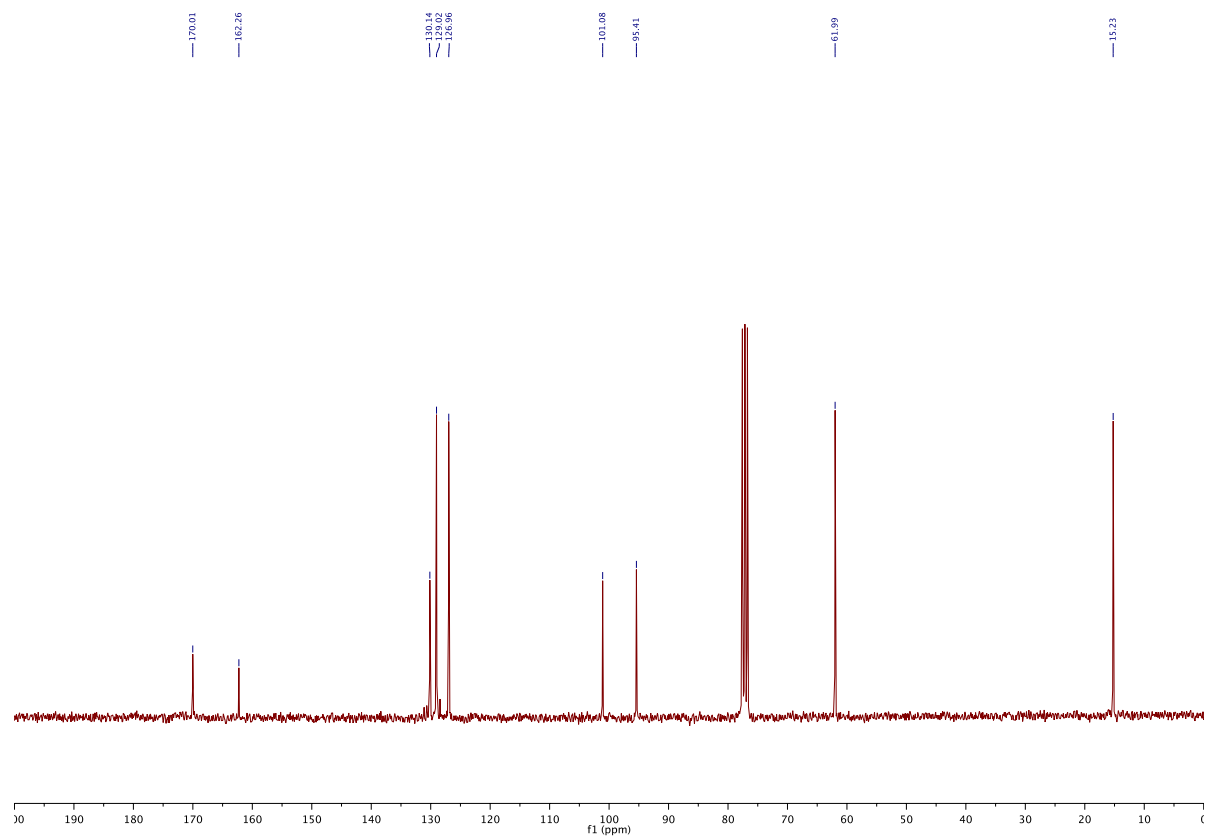
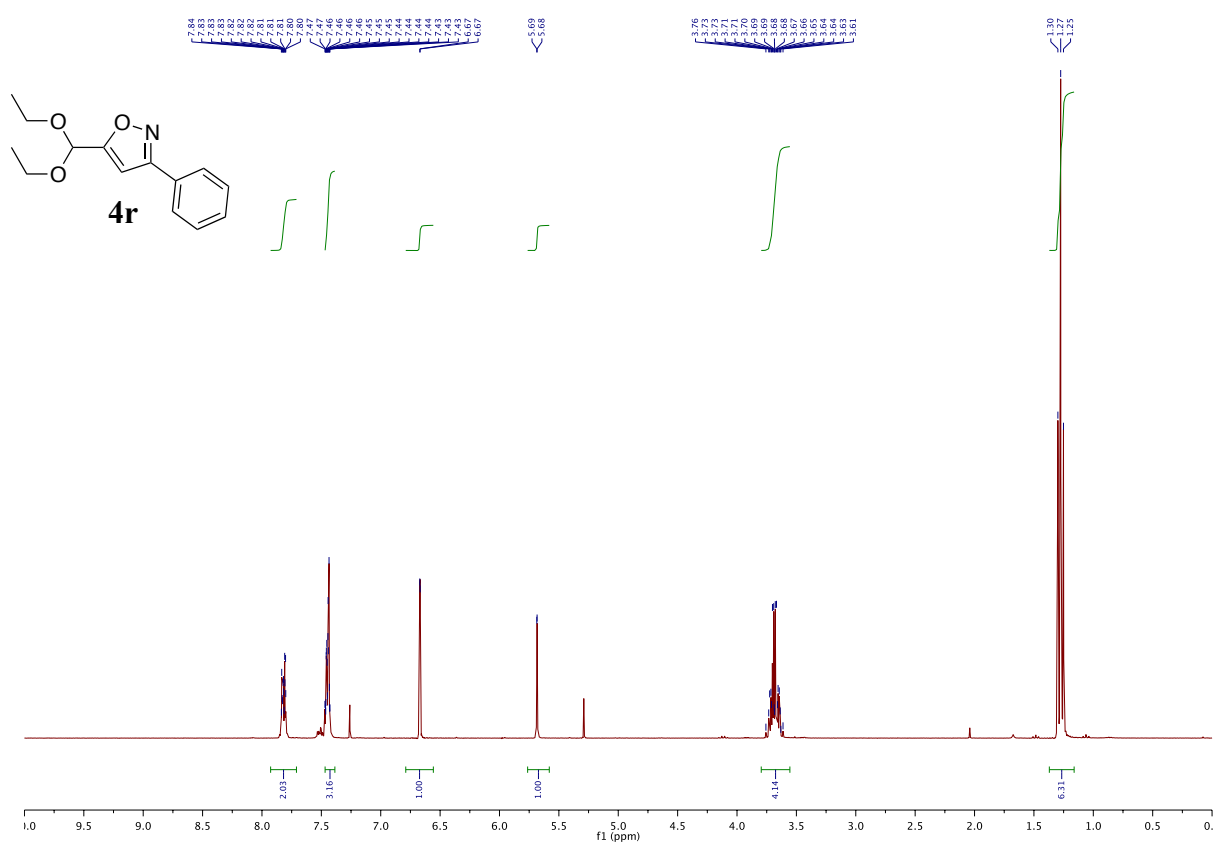


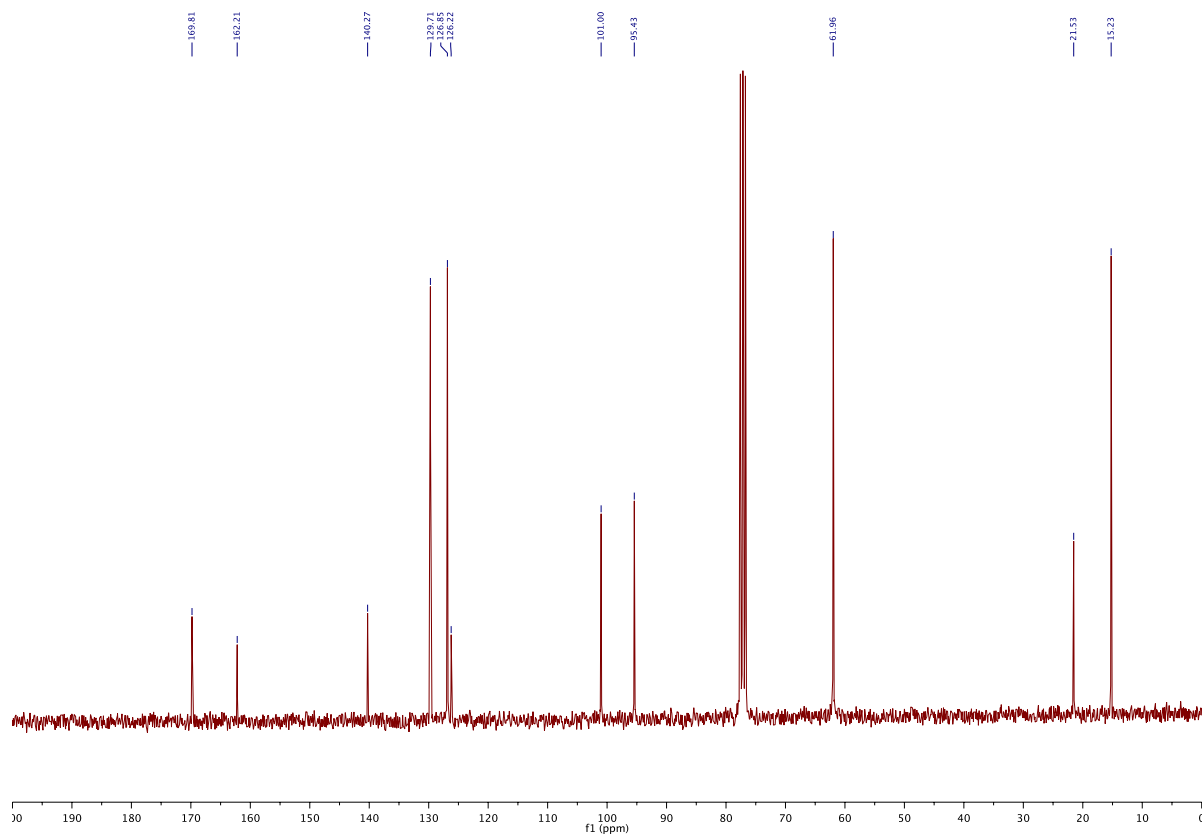
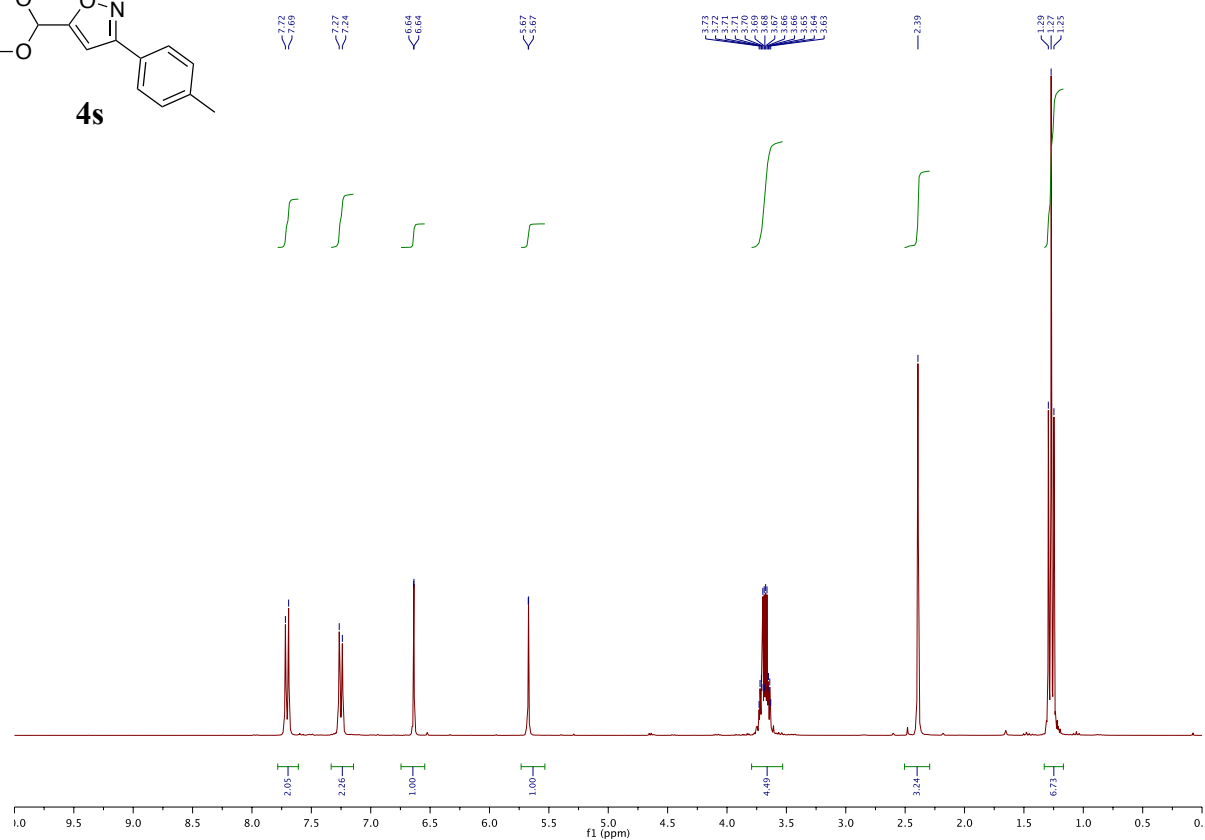
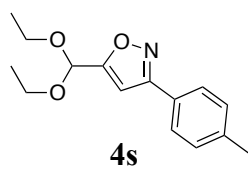


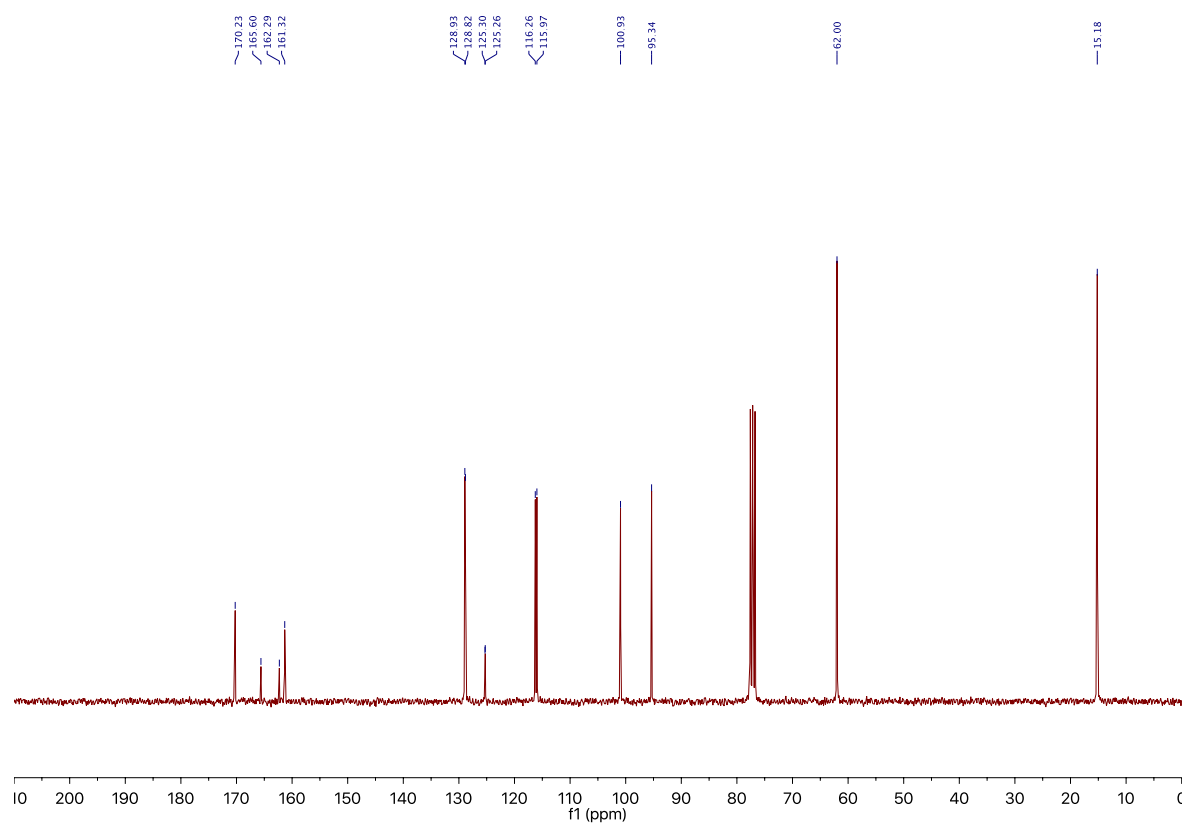
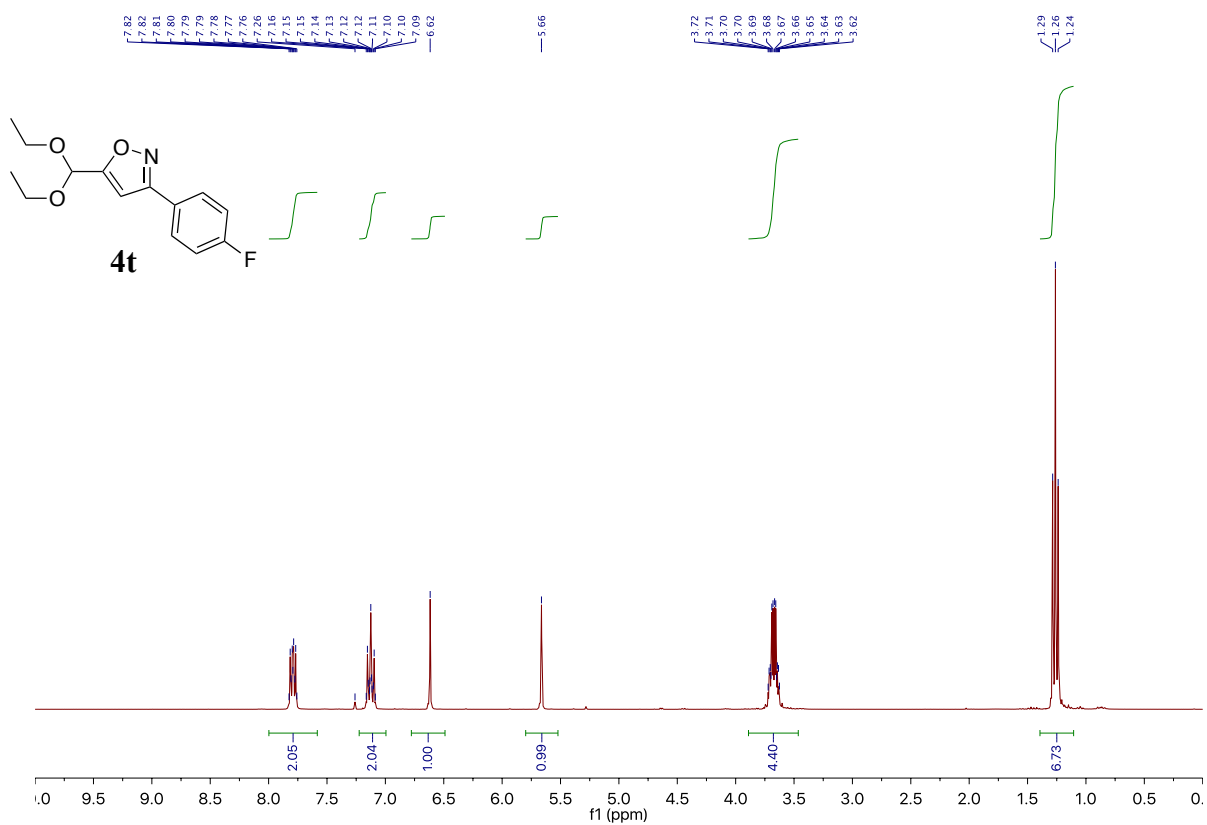


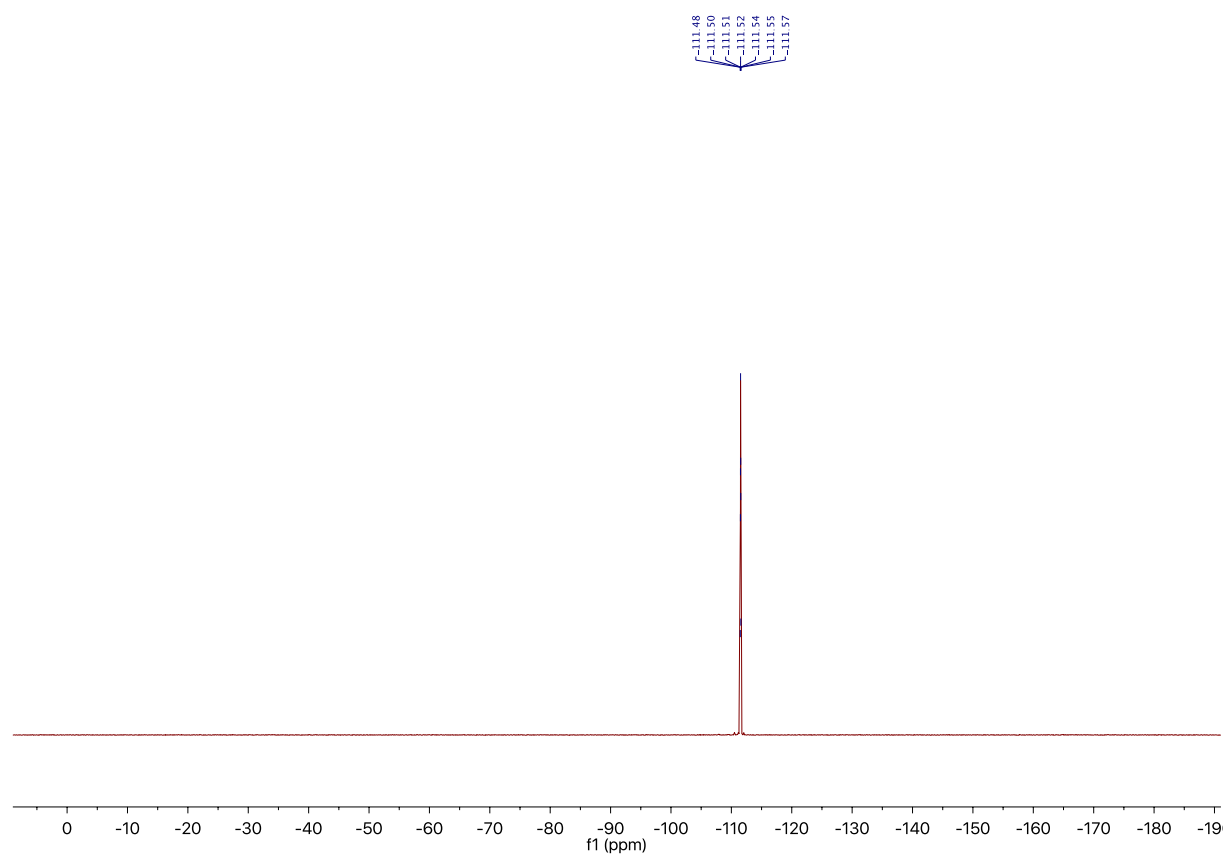


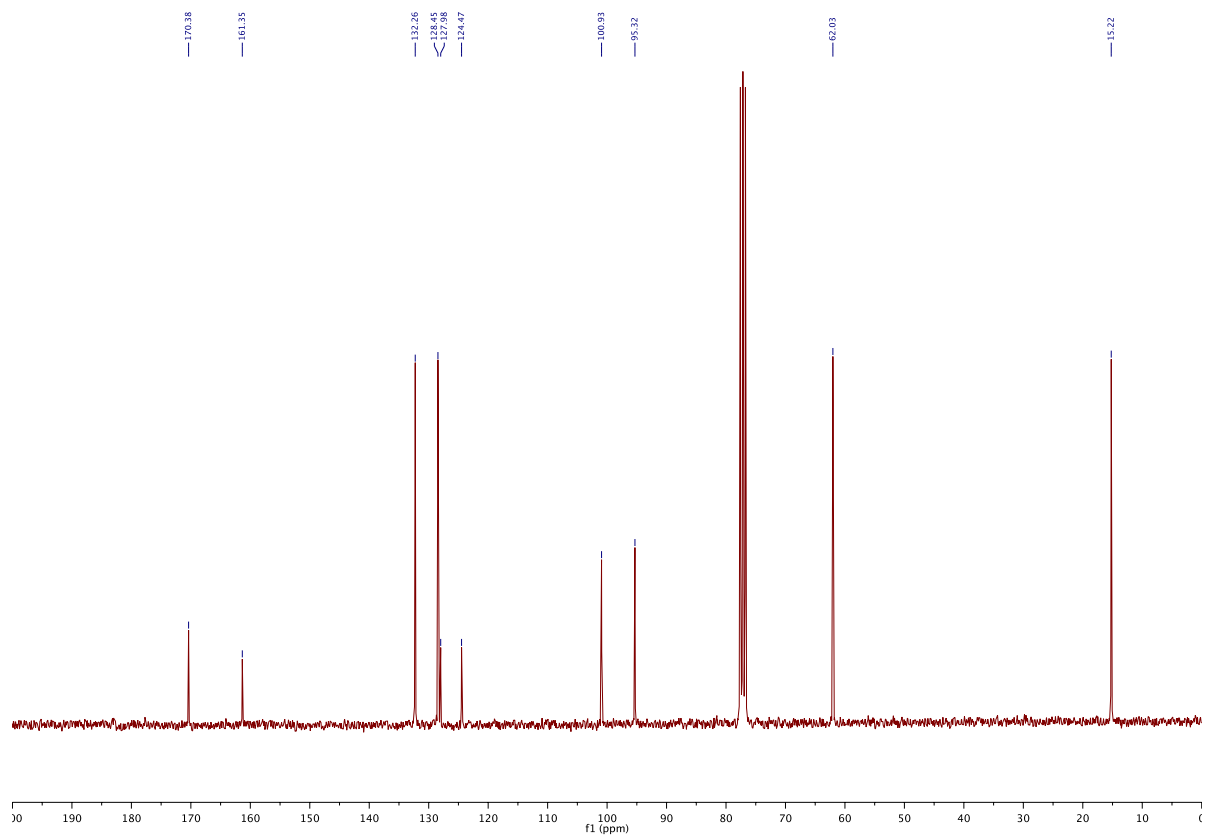
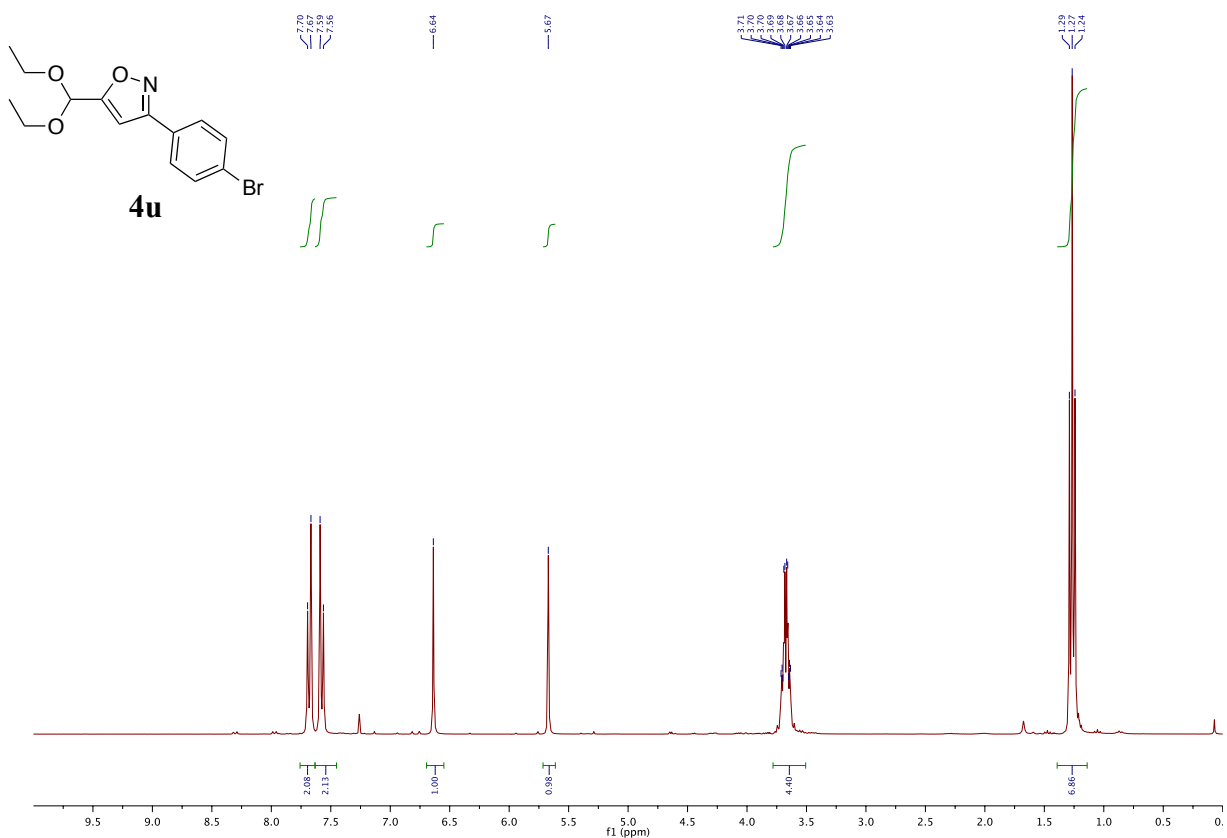






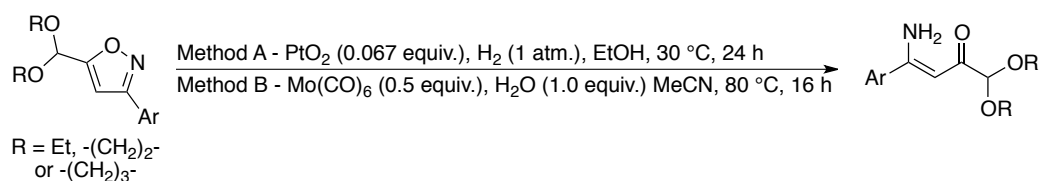






4. Synthesis of the Enamines 5a – 5u

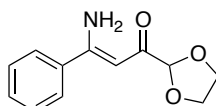
General procedure



Method A: In a Schlenk flask under argon were introduced the isoxazole (1.0 equiv.), PtO_2 (0.067 equiv.) and ethanol ($c = 0.20$ mol/L). After 3 cycles of vacuum/argon, 3 cycles of vacuum/hydrogen were performed. The resulting mixture was stirred at room temperature for 16 h under 1 atm of hydrogen. The solution was then filtered over a pad of celite and concentrated *in vacuo*. The crude product was purified by silica gel column chromatography (petroleum ether/ethyl acetate: 1/1) to afford the pure compound.

Method B: In a sealed tube under argon were introduced the isoxazole (1 equiv.), Mo(CO)_6 (0.5 equiv.), MeCN ($c = 1$ mol/L) and water (1 equiv.). The resulting mixture was stirred at 80 °C for 16 h. The solution was then filtered over a pad of celite and concentrated *in vacuo*. Crude product was purified by silica gel column chromatography (petroleum ether/ethyl acetate : 1/1) to afford the pure compound.

(Z)-3-amino-1-(1,3-dioxolan-2-yl)-3-phenylprop-2-en-1-one **5a**



Method A, yellow oil, 90% yield (446 mg)

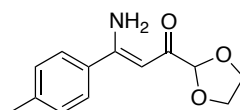
Chemical formula: $\text{C}_{12}\text{H}_{13}\text{NO}_3$

^1H NMR (300 MHz, CDCl_3) δ 10.15 (brd, 1H), 7.67 – 7.53 (m, 2H), 7.53 – 7.32 (m, 3H), 5.83 (brd, 1H), 5.72 (s, 1H), 5.15 (s, 1H), 4.22 – 3.76 (m, 4H).

^{13}C NMR (75 MHz, CDCl_3) δ 192.7, 164.3, 136.7, 131.0, 129.0, 126.4, 102.4, 90.0, 65.5.

Mass (CI/NH_3) MH^+ 220

(Z)-3-amino-1-(1,3-dioxolan-2-yl)-3-(p-tolyl)prop-2-en-1-one **5b**



Method A, yellow oil, 64% yield (255 mg)

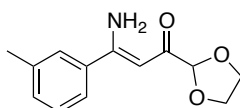
Chemical formula: $\text{C}_{13}\text{H}_{15}\text{NO}_3$

^1H NMR (300 MHz, CDCl_3) δ 10.19 (brd, 1H), 7.47 (d, $J = 8.0$ Hz, 2H), 7.23 (d, $J = 8.0$ Hz, 2H), 5.73 (s, 2H), 5.17 (s, 1H), 4.24 – 3.83 (m, 4H), 2.38 (s, 3H).

^{13}C NMR (75 MHz, CDCl_3) δ 192.6, 164.3, 141.6, 133.8, 129.7, 126.3, 102.5, 89.7, 65.5, 21.4.

Mass (CI/ NH_3) MH^+ 234

(*Z*)-3-amino-1-(1,3-dioxolan-2-yl)-3-(*m*-tolyl)prop-2-en-1-one **5c**



Method A, yellow oil, 75% yield (274 mg)

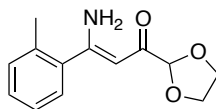
Chemical formula: $\text{C}_{13}\text{H}_{15}\text{NO}_3$

^1H NMR (300 MHz, CDCl_3) δ 10.05 (brd, 1H), 7.32 – 7.03 (m, 4H), 5.38 (brd, 1H), 5.35 (s, 1H), 5.05 (s, 1H), 4.09 – 3.76 (m, 4H), 2.32 (s, 3H).

^{13}C NMR (75 MHz, CDCl_3) δ 192.9, 165.5, 137.3, 135.1, 130.9, 129.6, 127.8, 126.1, 102.4, 92.4, 65.5, 19.7.

Mass (CI/ NH_3) MH^+ 234

(*Z*)-3-amino-1-(1,3-dioxolan-2-yl)-3-(*o*-tolyl)prop-2-en-1-one **5d**



Method A, yellow oil, 82% yield (274 mg)

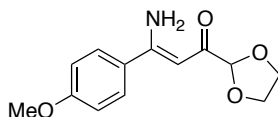
Chemical formula: $\text{C}_{13}\text{H}_{15}\text{NO}_3$

^1H NMR (300 MHz, CDCl_3) δ 10.17 (brd, 1H), 7.46 – 7.17 (m, 4H), 5.73 (s, 1H), 5.64 (brd, 1H), 5.18 (s, 1H), 4.23 – 3.82 (m, 4H), 2.39 (s, 3H).

^{13}C NMR (75 MHz, CDCl_3) δ 192.8, 164.5, 138.9, 136.8, 131.9, 129.1, 127.1, 123.5, 102.5, 90.1, 65.5, 21.5.

Mass (CI/ NH_3) MH^+ 234

(*Z*)-3-amino-1-(1,3-dioxolan-2-yl)-3-(4-methoxyphenyl)prop-2-en-1-one **5e**



Method A, yellow oil, 59% yield (241 mg)

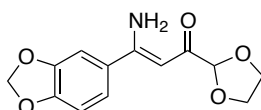
Chemical formula: $\text{C}_{13}\text{H}_{15}\text{NO}_4$

¹H NMR (300 MHz, CDCl₃) δ 10.16 (brd, 1H), 7.47 (d, *J* = 8.5 Hz, 2H), 6.85 (d, *J* = 8.5 Hz, 2H), 5.84 (brd, 1H), 5.63 (s, 1H), 5.08 (s, 1H), 4.13 – 3.79 (m, 4H), 3.75 (s, 3H).

¹³C NMR (75 MHz, CDCl₃) δ 192.1, 164.0, 161.9, 128.5, 127.9, 114.3, 102.5, 89.2, 65.4, 55.5.

Mass (CI/NH₃) MH⁺ 250

(*Z*)-3-amino-3-(benzo[*d*][1,3]dioxol-5-yl)-1-(1,3-dioxolan-2-yl)prop-2-en-1-one **5f**



Method B, yellow solid (mp = 74-78 °C), 50% yield (198 mg)

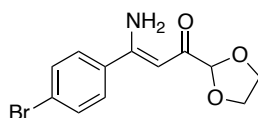
Chemical formula: C₁₃H₁₃NO₅

¹H NMR (300 MHz, CDCl₃) δ 10.11 (brd, 1H), 7.06 (dd, *J* = 8.0, 2.0 Hz, 1H), 6.98 (d, *J* = 2.0 Hz, 1H), 6.76 (d, *J* = 8.0 Hz, 1H), 5.94 (s, 2H), 5.72 (brd, 1H), 5.59 (s, 1H), 5.08 (s, 1H), 4.05 – 3.80 (m, 4H).

¹³C NMR (75 MHz, CDCl₃) δ 192.4, 163.9, 150.1, 148.3, 130.6, 120.9, 108.6, 106.8, 102.5, 101.8, 89.6, 65.5.

Mass (CI/NH₃) MH⁺ 264

(*Z*)-3-amino-3-(4-bromophenyl)-1-(1,3-dioxolan-2-yl)prop-2-en-1-one **5g**



Method B, yellow oil, 47% yield (493 mg)

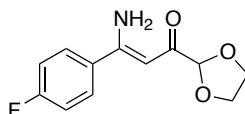
Chemical formula: C₁₂H₁₂BrNO₃

¹H NMR (300 MHz, CDCl₃) δ 10.09 (brd, 1H), 7.57 (d, *J* = 8.5 Hz, 2H), 7.45 (d, *J* = 8.5 Hz, 2H), 5.69 (s, 1H), 5.69 (brd, 1H), 5.15 (s, 1H), 4.23 – 3.84 (m, 4H).

¹³C NMR (75 MHz, CDCl₃) δ 193.1, 162.9, 135.7, 132.3, 128.0, 125.5, 102.4, 90.2, 65.6.

Mass (CI/NH₃) MH⁺ 298

(*Z*)-3-amino-1-(1,3-dioxolan-2-yl)-3-(4-fluorophenyl)prop-2-en-1-one **5h**



Method B, yellow oil, 64% yield (126 mg)

Chemical formula: C₁₂H₁₂FNO₃

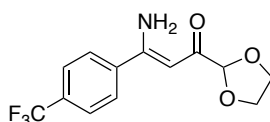
¹H NMR (300 MHz, CDCl₃) δ 10.14 (brd, 1H), 7.75 – 7.43 (m, 2H), 7.18 – 6.92 (m, 2H), 5.72 (brd, 1H), 5.69 (s, 1H), 5.15 (s, 1H), 4.22 – 3.76 (m, 4H).

¹³C NMR (75 MHz, CDCl₃) δ 192.9, 164.5 (d, ¹J_{CF} = 252.0 Hz), 163.2, 132.9 (d, ⁴J_{CF} = 2.5 Hz), 128.6 (d, ³J_{CF} = 8.5 Hz), 116.2 (d, ²J_{CF} = 22.0 Hz), 102.5, 90.2, 65.5.

¹⁹F NMR (282 MHz, CDCl₃) δ -107.19 – -111.19 (m).

Mass (CI/NH₃) MH⁺ 238

(Z)-3-amino-1-(1,3-dioxolan-2-yl)-3-(4-(trifluoromethyl)phenyl)prop-2-en-1-one **5i**



Method A, colorless oil, 63% yield (372 mg)

Chemical formula: C₁₃H₁₂F₃NO₃

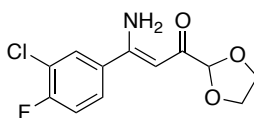
¹H NMR (300 MHz, CDCl₃) δ 10.03 (brd, 1H), 7.86 – 7.49 (m, 4H), 6.18 (brd, 1H), 5.68 (s, 1H), 5.08 (s, 1H), 4.15 – 3.75 (m, 4H).

¹³C NMR (75 MHz, CDCl₃) δ 193.1, 162.8, 140.2, 132.6 (q, ²J_{CF} = 32.5 Hz), 127.1, 125.9 (q, ³J_{CF} = 4.0 Hz), 123.7 (q, ¹J_{CF} = 272.5 Hz), 102.2, 90.5, 65.4.

¹⁹F NMR (282 MHz, CDCl₃) δ -63.93 (s).

Mass (CI/NH₃) MH⁺ 288

(Z)-3-amino-3-(3-chloro-4-fluorophenyl)-1-(1,3-dioxolan-2-yl)prop-2-en-1-one **5j**



Method B, yellow oil, 46% yield (181 mg)

Chemical formula: C₁₂H₁₁ClFNO₃

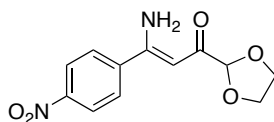
¹H NMR (300 MHz, CDCl₃) δ 10.07 (brd, 1H), 7.65 (dd, *J* = 7.0, 2.3 Hz, 1H), 7.47 (ddd, *J* = 8.5, 4.4, 2.3 Hz, 1H), 7.21 (t, *J* = 8.5 Hz, 1H), 5.67 (s, 1H), 5.56 (brd, 1H), 5.16 (brd, 1H), 4.19 – 3.86 (m, 4H).

¹³C NMR (75 MHz, CDCl₃) 193.3, 161.6, 159.7 (d, ¹J_{CF} = 254.5 Hz), 134.1 (d, ³J_{CF} = 3.7 Hz), 129.1, 126.6 (d, ³J_{CF} = 7.8 Hz), 122.2 (d, ²J_{CF} = 18.3 Hz), 117.4 (d, ²J_{CF} = 21.6 Hz), 102.4, 90.6, 65.6.

¹⁹F NMR (282 MHz, CDCl₃) δ -112.64 (q, *J* = 6.8 Hz).

Mass (CI/NH₃) MH⁺ 272

(Z)-3-amino-3-(3-chloro-4-fluorophenyl)-1-(1,3-dioxolan-2-yl)prop-2-en-1-one **5k**



Method B, yellow solid (mp = 117-119 °C), 50% yield (311 mg)

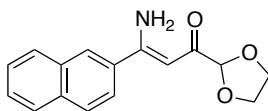
Chemical formula: C₁₂H₁₂N₂O₅

¹H NMR (300 MHz, CDCl₃) δ 10.01 (brd, 1H), 8.28 (d, *J* = 9.0 Hz, 2H), 7.76 (d, *J* = 9.0 Hz, 2H), 5.74 (s, 1H), 5.69 (brd, 1H), 5.14 (s, 1H), 4.19 – 3.86 (m, 4H).

¹³C NMR (75 MHz, CDCl₃) δ 193.7, 161.2, 149.3, 142.9, 127.7, 124.3, 102.3, 91.4, 65.6.

Mass (CI/NH₃) MH⁺ 265

(*Z*)-3-amino-1-(1,3-dioxolan-2-yl)-3-(naphthalen-2-yl)prop-2-en-1-one **5l**



Method A, yellow solid (mp = 85-89 °C), 61% yield (301 mg)

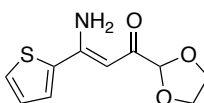
Chemical formula: C₁₆H₁₅NO₃

¹H NMR (300 MHz, CDCl₃) δ 10.26 (brd, 1H), 8.07 (d, *J* = 2.0 Hz, 1H), 8.00 – 7.75 (m, 3H), 7.65 (dd, *J* = 8.5, 2.0 Hz, 1H), 7.58 – 7.42 (m, 2H), 5.91 (brd, 1H), 5.87 (s, 1H), 5.22 (s, 1H), 4.27 – 3.87 (m, 4H).

¹³C NMR (75 MHz, CDCl₃) δ 192.8, 164.3, 134.5, 133.9, 132.9, 128.9, 128.7, 127.8, 127.6, 127.0, 126.5, 123.4, 102.5, 90.5, 65.5.

Mass (CI/NH₃) MH⁺ 270

(*Z*)-3-amino-1-(1,3-dioxolan-2-yl)-3-(thiophen-2-yl)prop-2-en-1-one **5m**



Method A, yellow oil, 75% yield (254 mg)

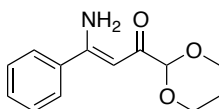
Chemical formula: C₁₀H₁₁NO₃S

¹H NMR (300 MHz, Chloroform-*d*) δ 10.07 (brd, 1H), 7.48 (dd, *J* = 3.8, 1.2 Hz, 1H), 7.45 (dd, *J* = 5.0, 1.2 Hz, 1H), 7.10 (dd, *J* = 5.1, 3.8 Hz, 1H), 5.84 (s, 1H), 5.64 (brd, 1H), 5.17 (s, 1H), 4.24 – 3.86 (m, 4H).

¹³C NMR (75 MHz, CDCl₃) δ 192.9, 156.6, 139.1, 128.8, 128.3, 127.2, 102.4, 89.6, 65.5.

Mass (CI/NH₃) MH⁺ 226

(Z)-3-amino-1-(1,3-dioxan-2-yl)-3-phenylprop-2-en-1-one **5n**



Method A, slightly yellow oil, 78% yield (506 mg)

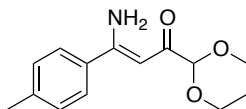
Chemical formula: C₁₃H₁₅NO₃

¹H NMR (300 MHz, CDCl₃) δ 10.14 (brd, 1H), 7.76 – 7.51 (m, 2H), 7.51 – 7.34 (m, 3H), 5.82 (s, 1H), 5.69 (brd, 1H), 4.87 (s, 1H), 4.24 – 4.18 (m, 2H), 3.91 – 3.82 (m, 2H), 2.37 – 2.01 (m, 1H), 1.43 – 1.35 (m, 1H).

¹³C NMR (75 MHz, CDCl₃) δ 190.8, 164.4, 136.9, 130.9, 129.0, 126.5, 101.0, 90.1, 67.2, 25.9.

Mass (CI/NH₃) MH⁺ 233

(Z)-3-amino-1-(1,3-dioxan-2-yl)-3-(*p*-tolyl)prop-2-en-1-one **5o**



Method A, white solid (mp = 129 – 131 °C), 77% yield (453 mg)

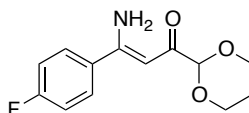
Chemical formula: C₁₄H₁₇NO₃

¹H NMR (300 MHz, CDCl₃) δ 10.18 (brd, 1H), 7.47 (d, *J* = 8.2 Hz, 2H), 7.21 (d, *J* = 8.2 Hz, 2H), 5.81 (s, 1H), 5.67 (brd, 1H), 4.86 (s, 1H), 4.24 – 4.18 (m, 2H), 3.99 – 3.73 (m, 2H), 2.37 (s, 3H), 2.24 – 2.08 (m, 1H), 1.42 – 1.35 (m, 1H).

¹³C NMR (75 MHz, CDCl₃) δ 190.6, 164.4, 141.4, 133.9, 129.7, 126.3, 101.1, 89.7, 67.2, 25.9, 21.4.

Mass (CI/NH₃) MH⁺ 248

(Z)-3-amino-1-(1,3-dioxan-2-yl)-3-(4-fluorophenyl)prop-2-en-1-one **5p**



Method B, slightly yellow oil, 55% yield (with 15% of an inseparable impurity)(170 mg)

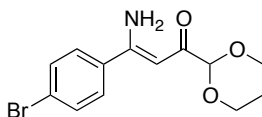
Chemical formula: C₁₃H₁₄FNO₃

¹H NMR (300 MHz, CDCl₃) δ 10.14 (brd, 1H), 7.72 – 7.46 (m, 2H), 7.20 – 7.00 (m, 2H), 5.79 (s, 1H), 5.50 (brd, 1H), 4.88 (s, 1H), 4.26 – 4.20 (m, 2H), 4.93 – 3.83 (m, 2H), 2.24 – 2.11 (m, 1H), 1.63 – 1.37 (m, 1H).

¹³C NMR (75 MHz, CDCl₃) δ 190.9, 164.4 (d, *J* = 251.5 Hz), 163.2, 133.1 (d, *J* = 2.8 Hz), 128.6 (d, *J* = 8.6 Hz), 116.2 (d, *J* = 21.9 Hz), 101.1, 90.3, 67.3, 25.9.

Mass (CI/NH₃) MH⁺ 252

(*Z*)-3-amino-3-(4-bromophenyl)-1-(1,3-dioxan-2-yl)prop-2-en-1-one **5q**



Method B, white solid (mp = 175 – 177 °C), 57% yield (386 mg)

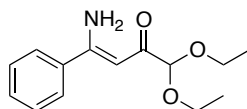
Chemical formula: C₁₃H₁₄BrNO₃

¹H NMR (300 MHz, CDCl₃) δ 10.08 (brd, 1H), 7.57 (d, *J* = 8.6 Hz, 2H), 7.46 (d, *J* = 8.6 Hz, 2H), 5.80 (s, 1H), 5.47 (brd, 1H), 4.87 (s, 1H), 4.26 – 4.20 (m, 2H), 3.93 – 3.84 (m, 2H), 2.26 – 2.10 (m, 1H), 1.45 – 1.37 (m, 1H).

¹³C NMR (75 MHz, CDCl₃) δ 191.2, 162.9, 135.9, 132.3, 128.1, 125.4, 101.0, 90.4, 67.3, 25.9.

Mass (CI/NH₃) MH⁺ 312

(*Z*)-4-amino-1,1-diethoxy-4-phenylbut-3-en-2-one **5r**



Method A, slightly yellow oil, 91% yield (318 mg)

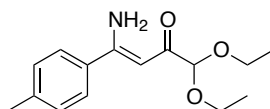
Chemical formula: C₁₄H₁₉NO₃

¹H NMR (300 MHz, CDCl₃) δ 10.11 (brd, 1H), 7.70 – 7.55 (m, 2H), 7.55 – 7.35 (m, 3H), 5.86 (s, 1H), 5.46 (brd, 1H), 4.74 (s, 1H), 3.94 – 3.42 (m, 4H), 1.26 (t, *J* = 7.0 Hz, 6H).

¹³C NMR (75 MHz, CDCl₃) δ 193.9, 163.6, 137.2, 130.9, 129.1, 126.5, 102.6, 90.9, 62.6, 15.4.

Mass (ESI) MH⁺ 250

(*Z*)-4-amino-1,1-diethoxy-4-(*p*-tolyl)but-3-en-2-one **5s**



Method A, slightly yellow oil, 69% yield (205 mg)

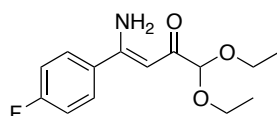
Chemical formula: C₁₅H₂₁NO₃

¹H NMR (300 MHz, CDCl₃) δ 10.13 (brd, 1H), 7.48 (d, *J* = 8.0 Hz, 2H), 7.24 (d, *J* = 8.0 Hz, 2H), 5.85 (s, 1H), 5.46 (brd, 1H), 4.74 (s, 1H), 3.88 – 3.45 (m, 4H), 2.39 (s, 3H), 1.26 (t, *J* = 7.0 Hz, 6H).

¹³C NMR (75 MHz, CDCl₃) δ 193.6, 163.6, 141.4, 134.2, 129.8, 126.4, 102.6, 90.5, 62.6, 21.5, 15.4.

Mass (ESI) MH⁺ 264

(*Z*)-4-amino-1,1-diethoxy-4-(4-fluorophenyl)but-3-en-2-one **5t**



Method B, slightly yellow oil, 66% yield (282 mg)

Chemical formula: C₁₄H₁₈FNO₃

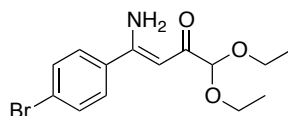
¹H NMR (300 MHz, CDCl₃) δ 10.08 (brd, 1H), 7.73 – 7.41 (m, 2H), 7.21 – 7.00 (m, 2H), 5.81 (s, 1H), 5.38 (brd, 1H), 4.73 (s, 1H), 3.87 – 3.44 (m, 4H), 1.26 (t, *J* = 7.0 Hz, 6H).

¹³C NMR (75 MHz, CDCl₃) δ 193.9, 164.4 (d, *J* = 251.3 Hz), 162.4, 133.3 (d, *J* = 2.9 Hz), 128.6 (d, *J* = 8.6 Hz), 116.2 (d, *J* = 21.9 Hz), 102.6, 90.9, 62.7, 15.4.

¹⁹F NMR (282 MHz, CDCl₃) δ -110.06 – -110.16 (m).

Mass (ESI) MH⁺ 267

(*Z*)-4-amino-4-(4-bromophenyl)-1,1-diethoxybut-3-en-2-one **5u**



Method B, slightly yellow oil, 57% yield (424 mg)

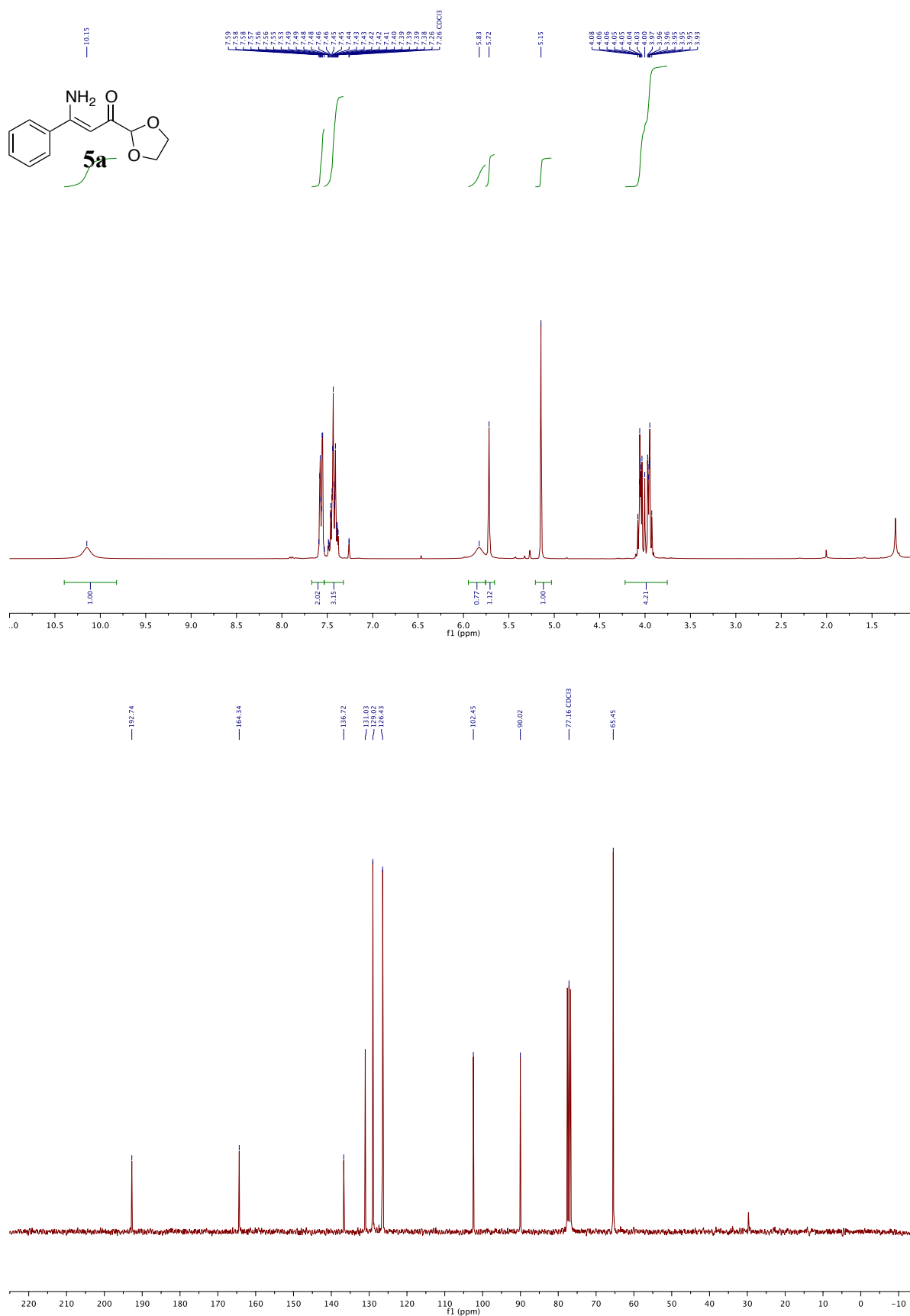
Chemical formula: C₁₄H₁₈BrNO₃

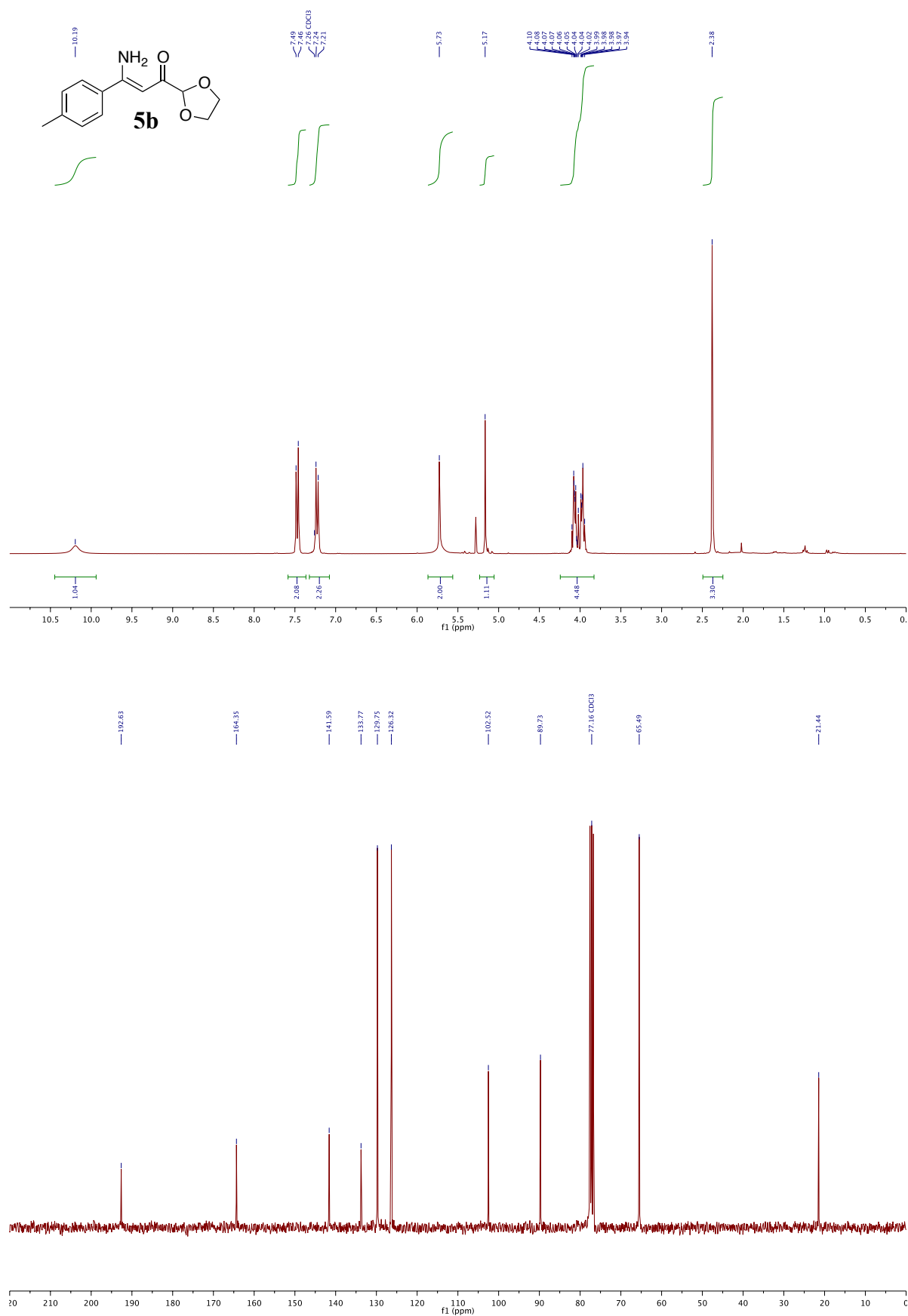
¹H NMR (300 MHz, CDCl₃) δ 9.99 (brd, 1H), 7.54 (d, *J* = 8.6 Hz, 2H), 7.44 (d, *J* = 8.6 Hz, 2H), 5.78 (s, 1H), 5.62 (brd, 1H), 4.69 (s, 1H), 3.92 – 3.38 (m, 4H), 1.23 (t, *J* = 7.0 Hz, 6H).

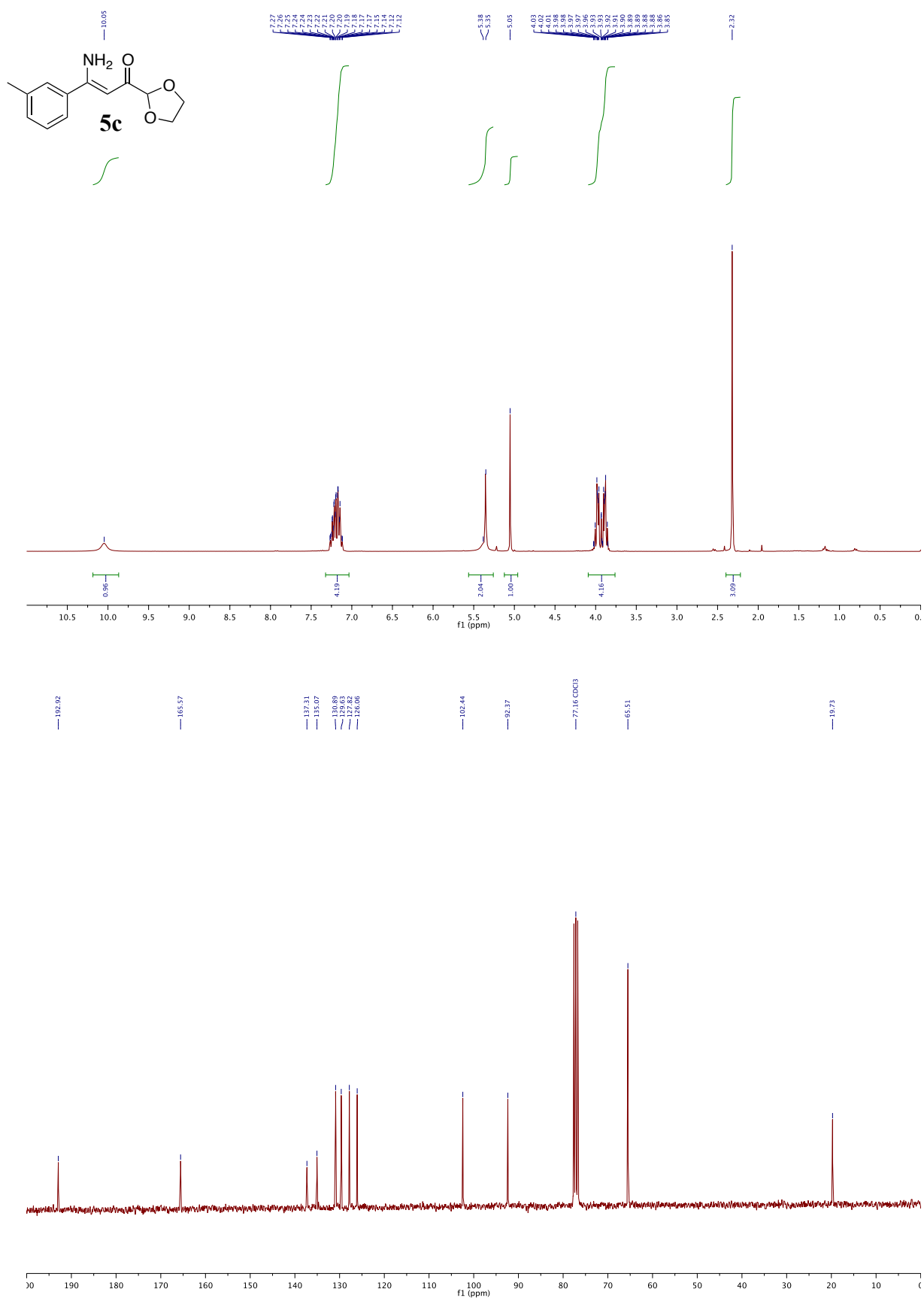
¹³C NMR (75 MHz, CDCl₃) δ 193.9, 162.3, 135.9, 132.2, 128.1, 125.2, 102.5, 90.8, 62.7, 15.3.

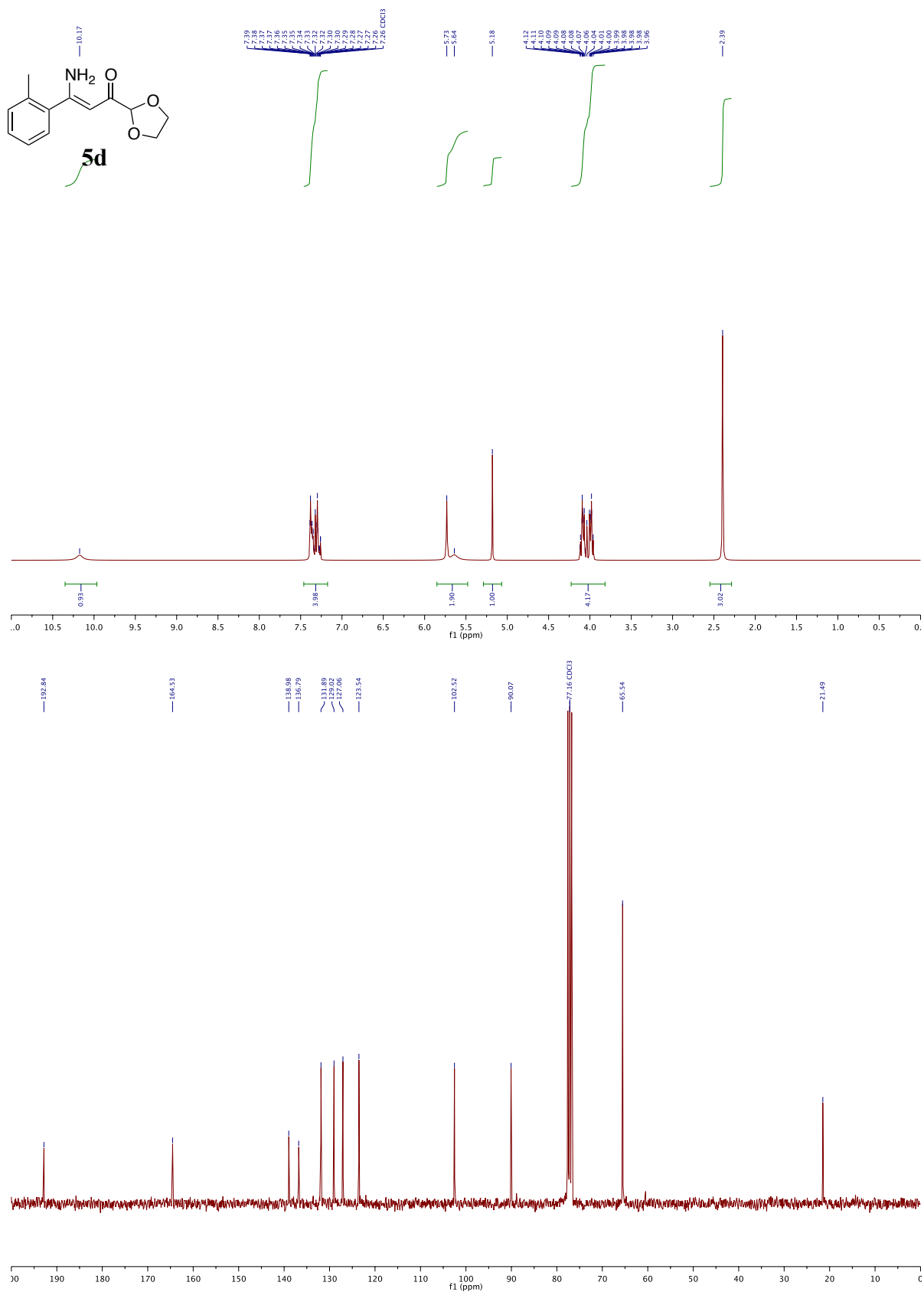
Mass (ESI) MH⁺ 328

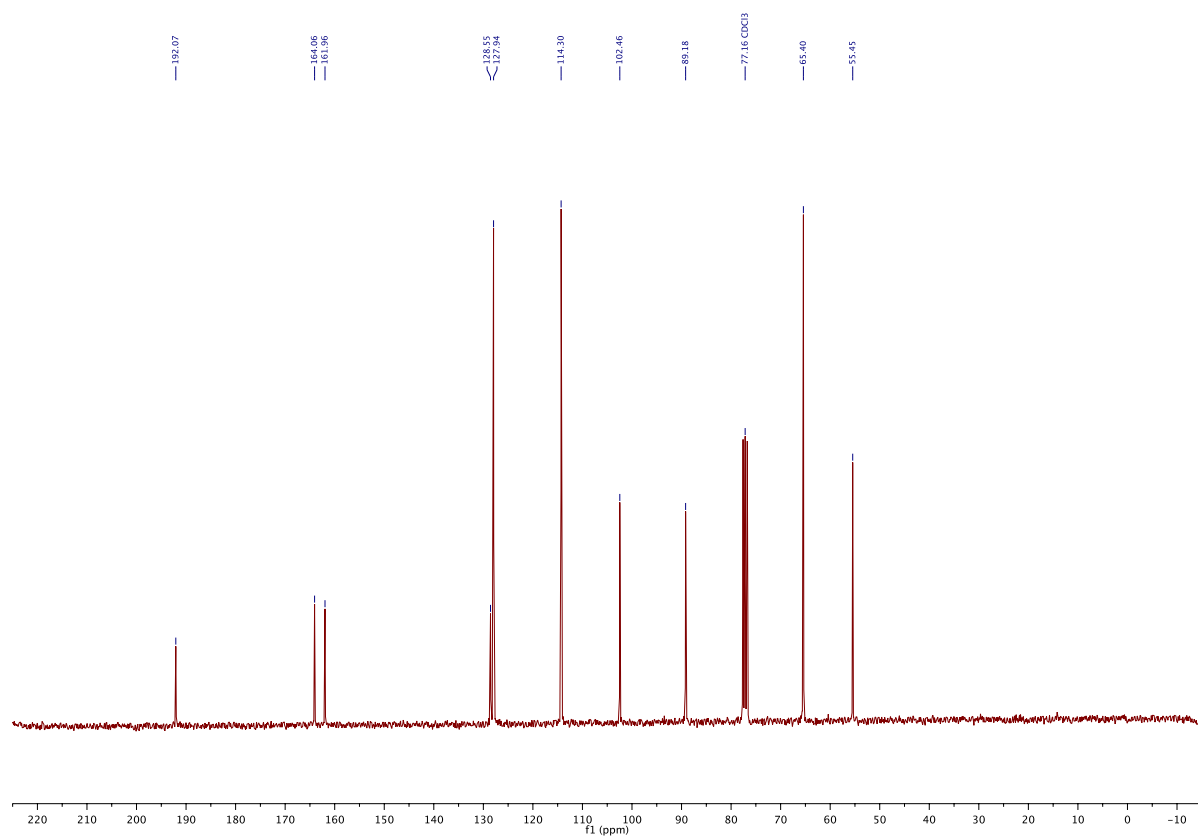
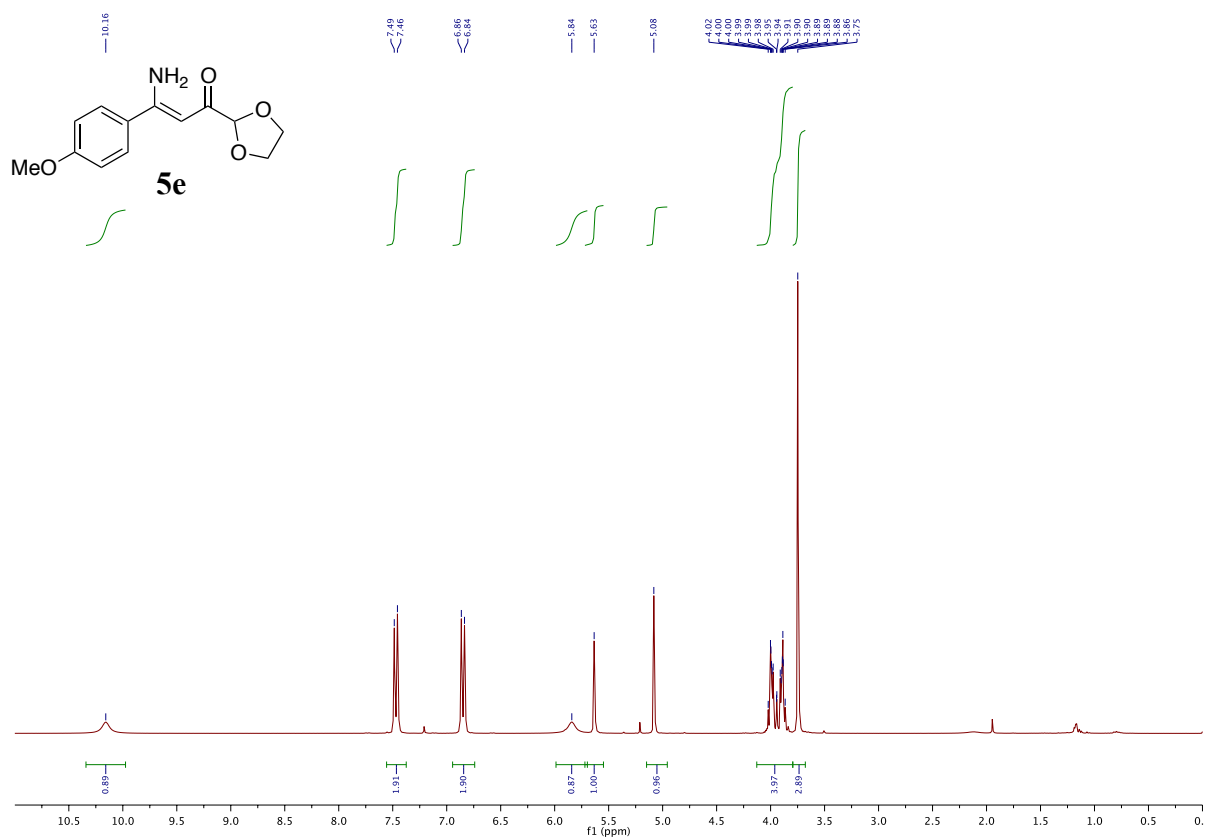
5. NMR spectra of compounds 5a – 5u

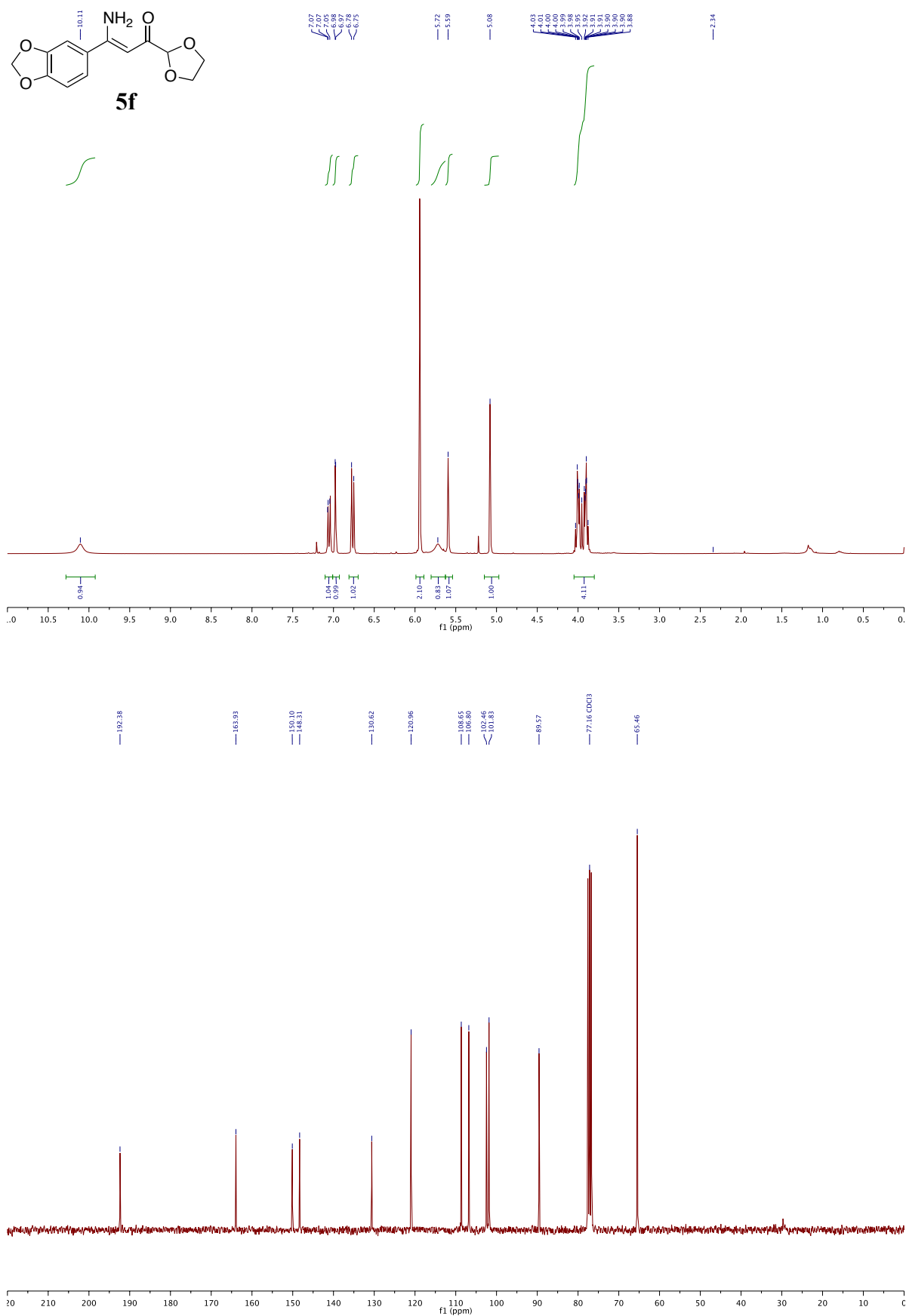


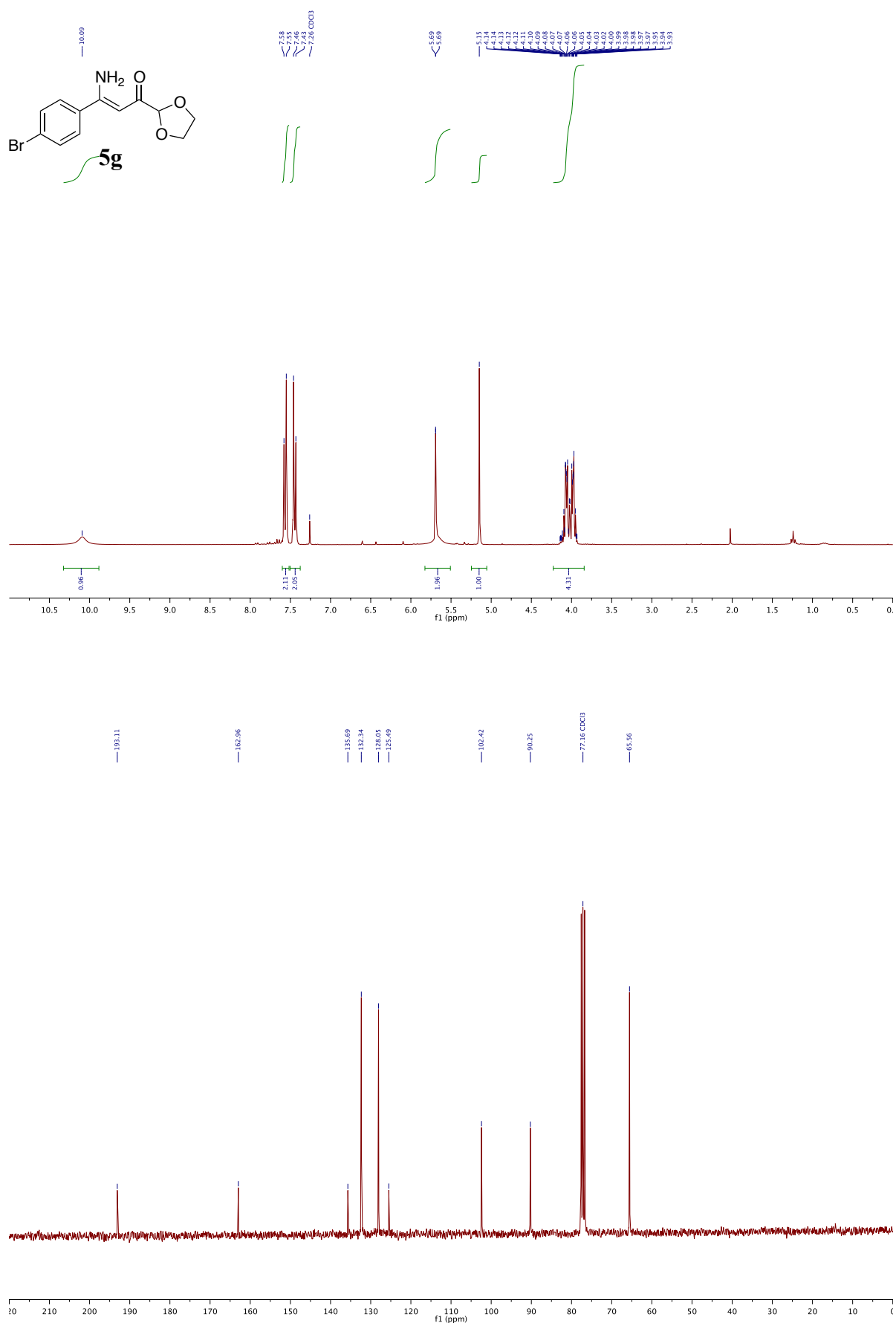


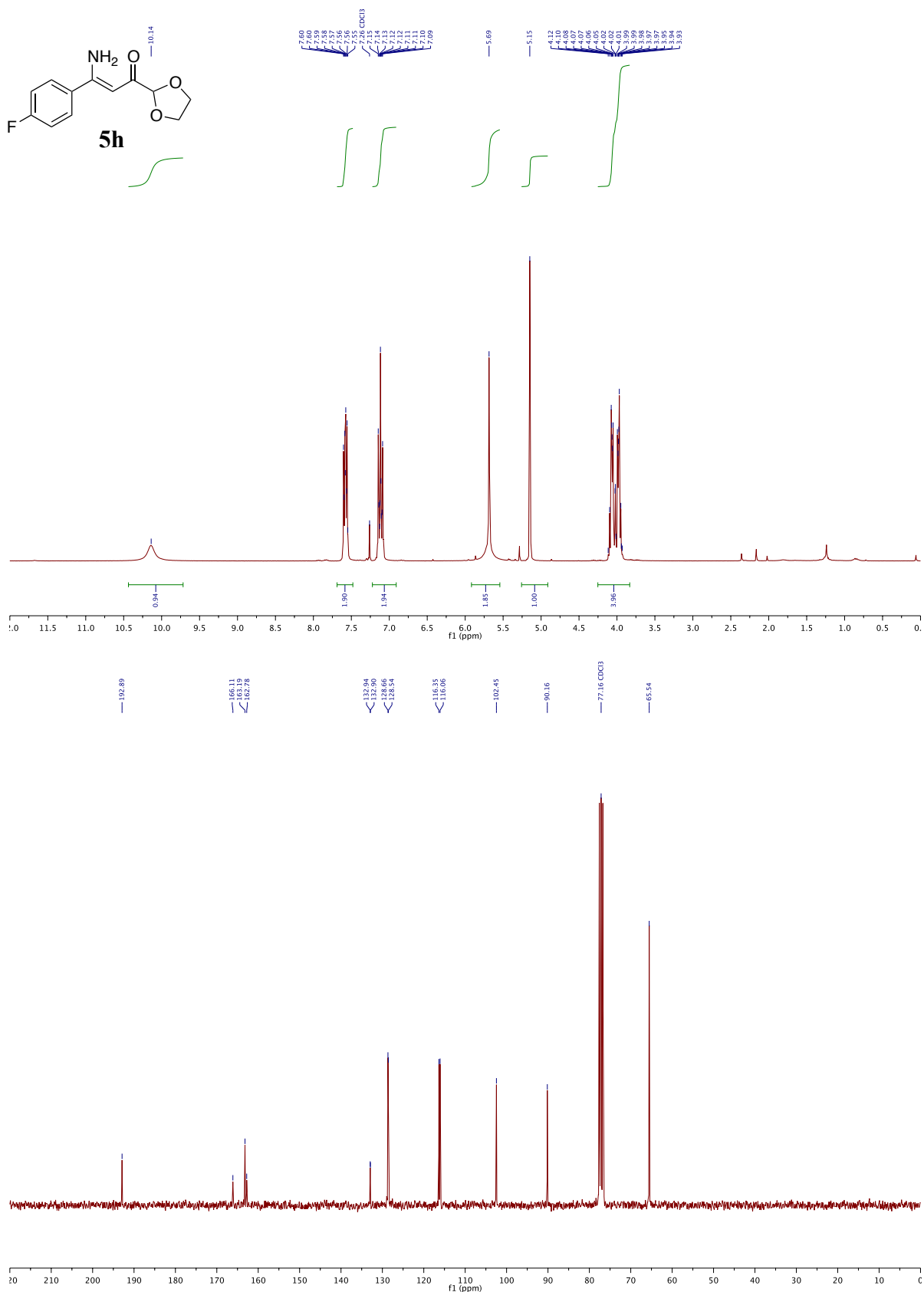


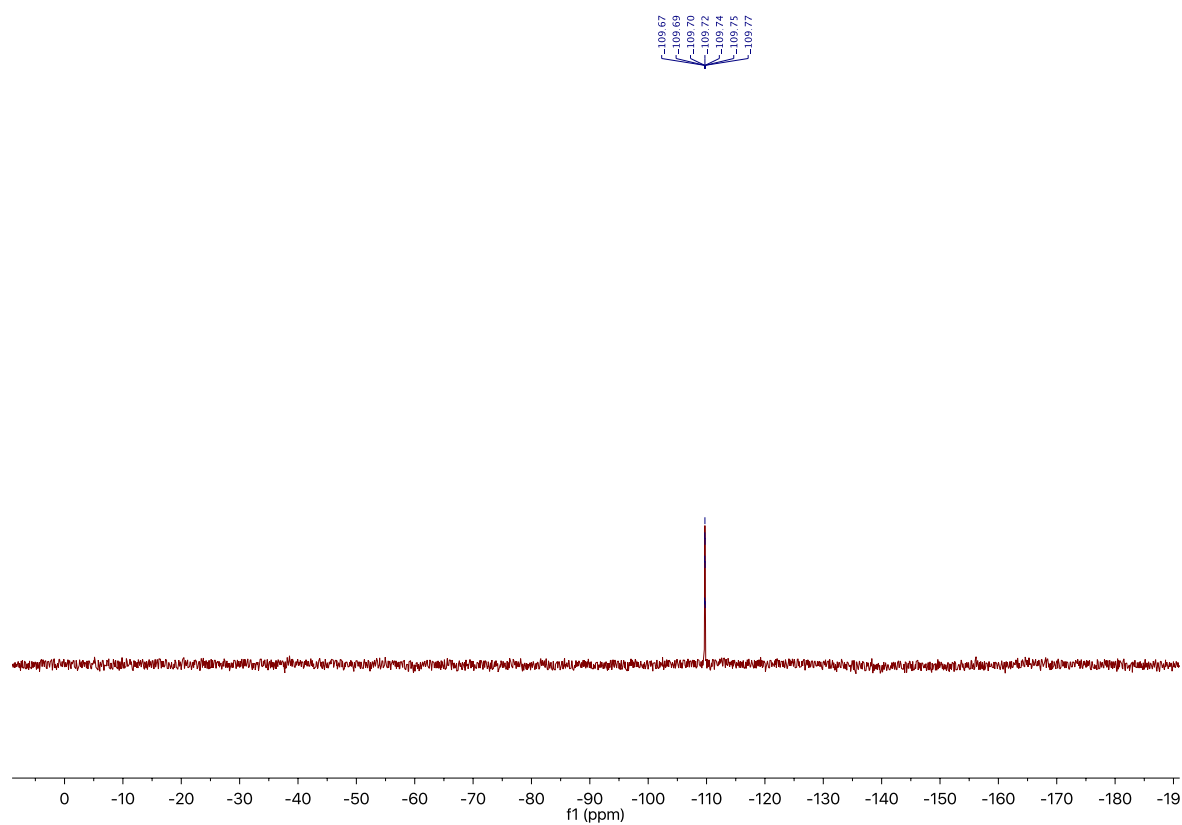


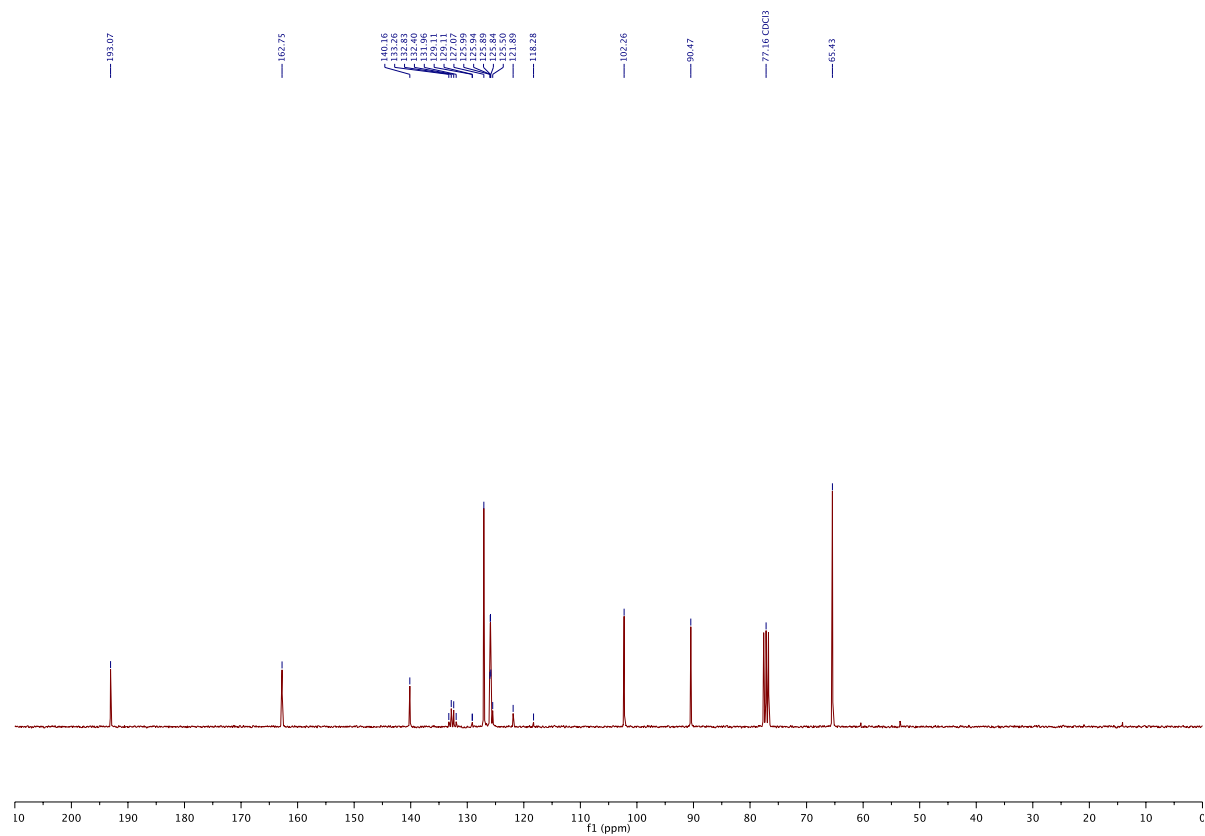
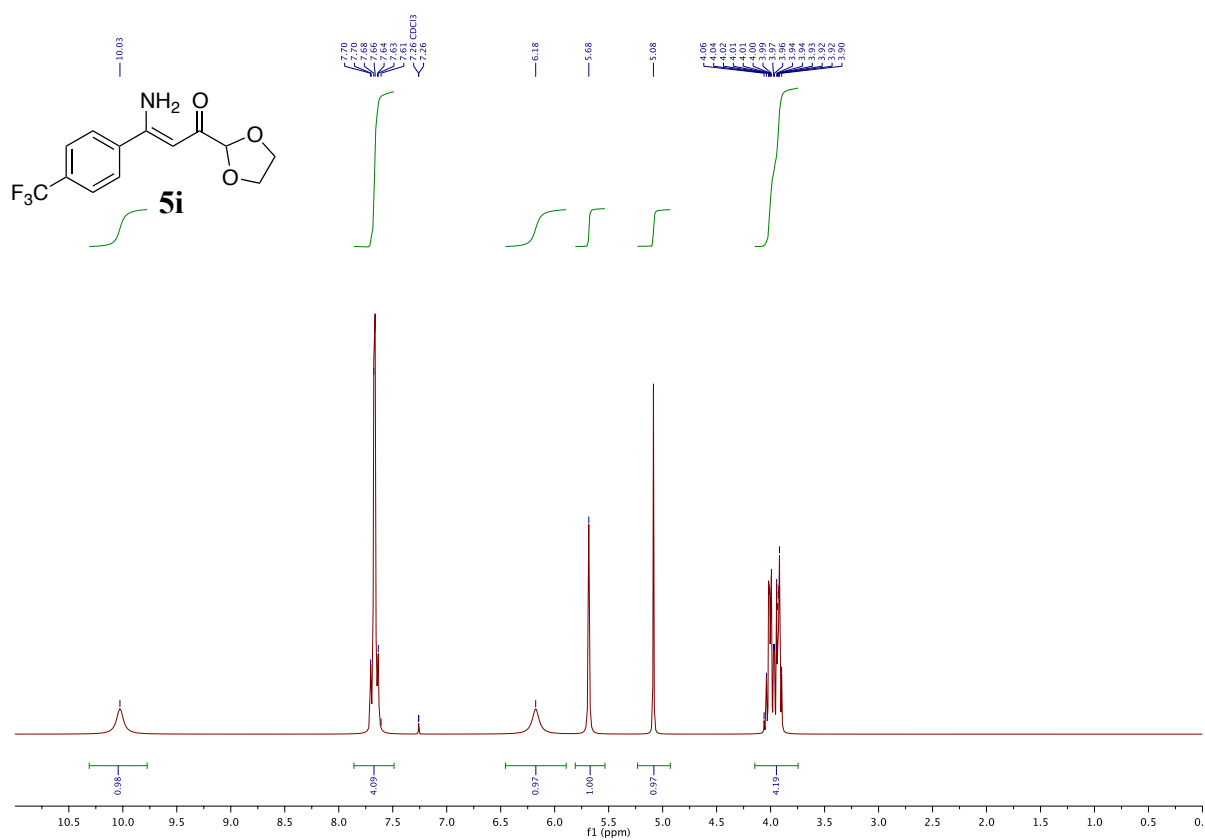


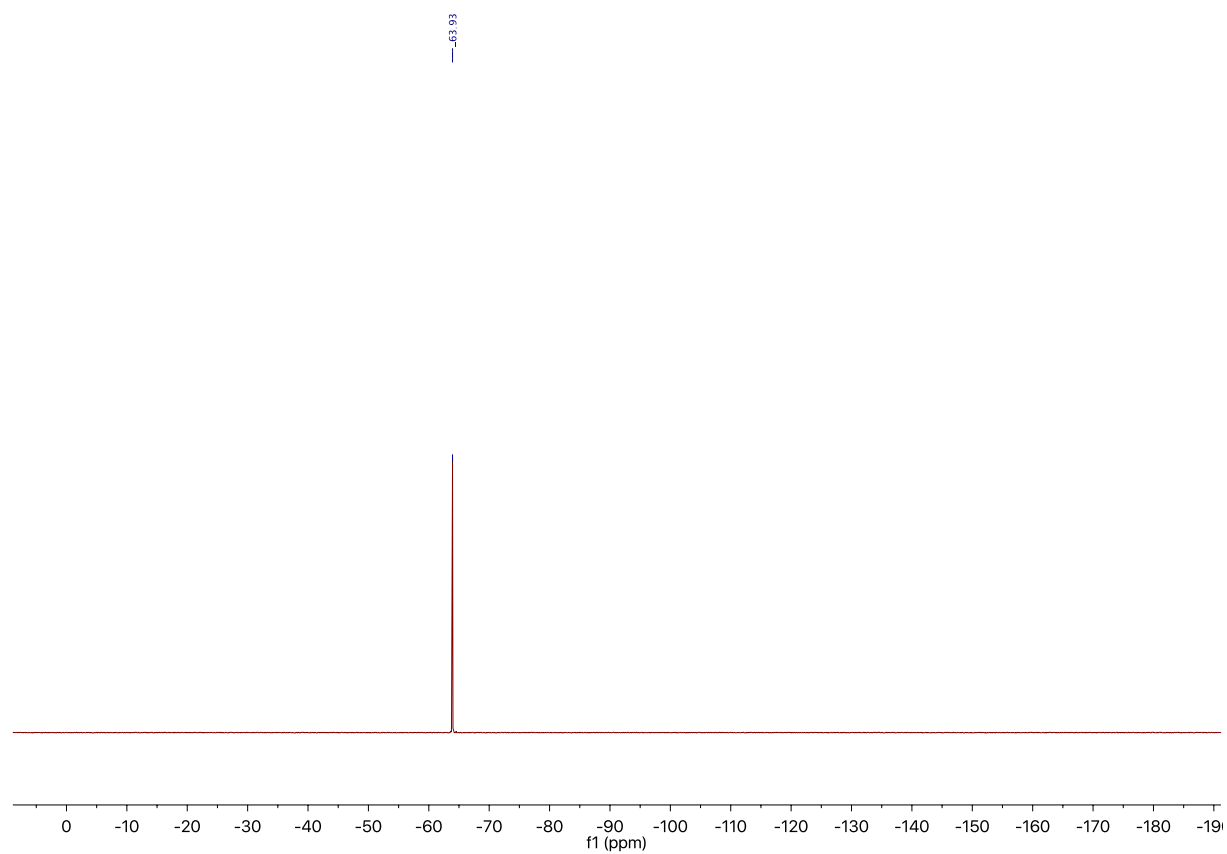


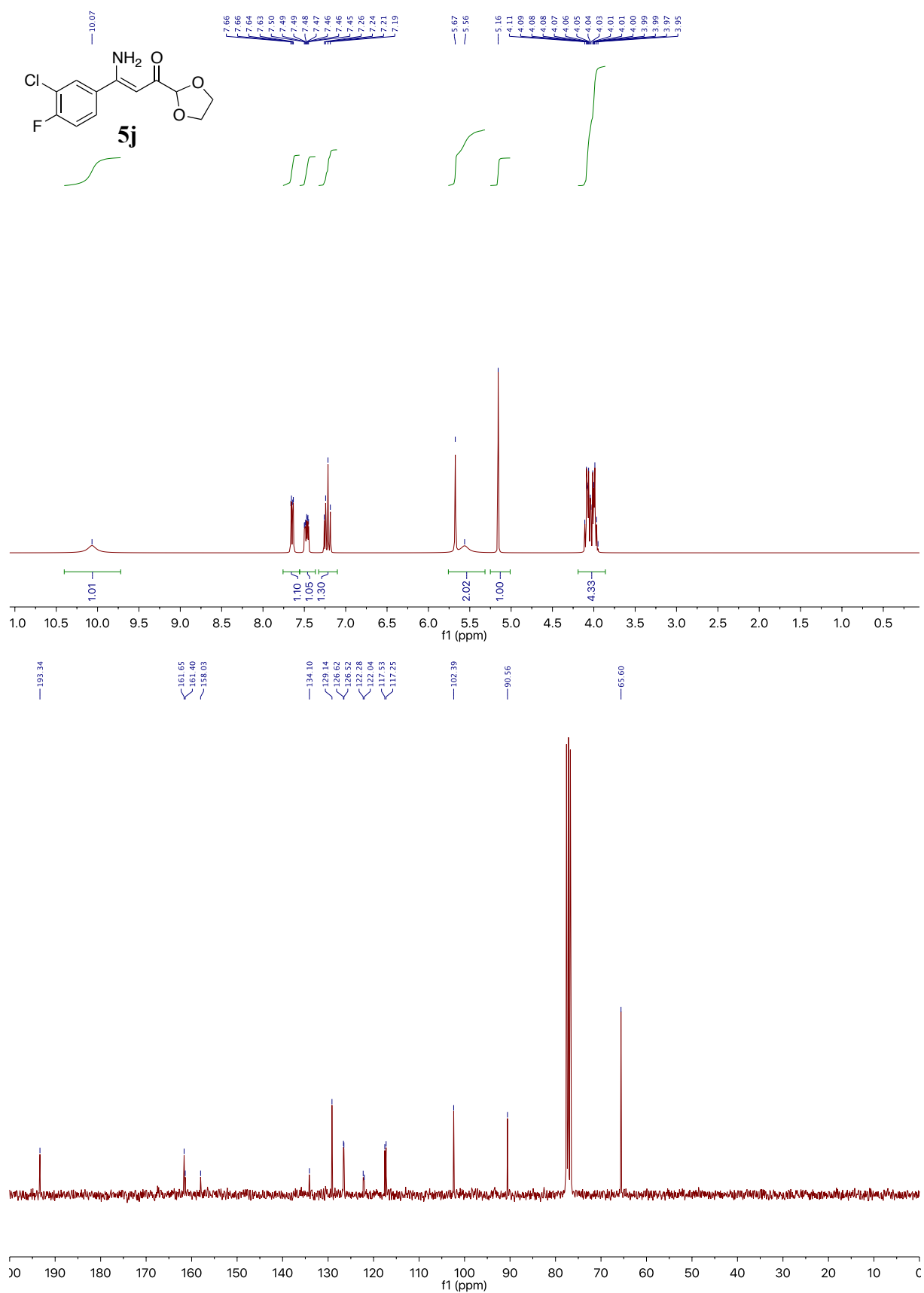


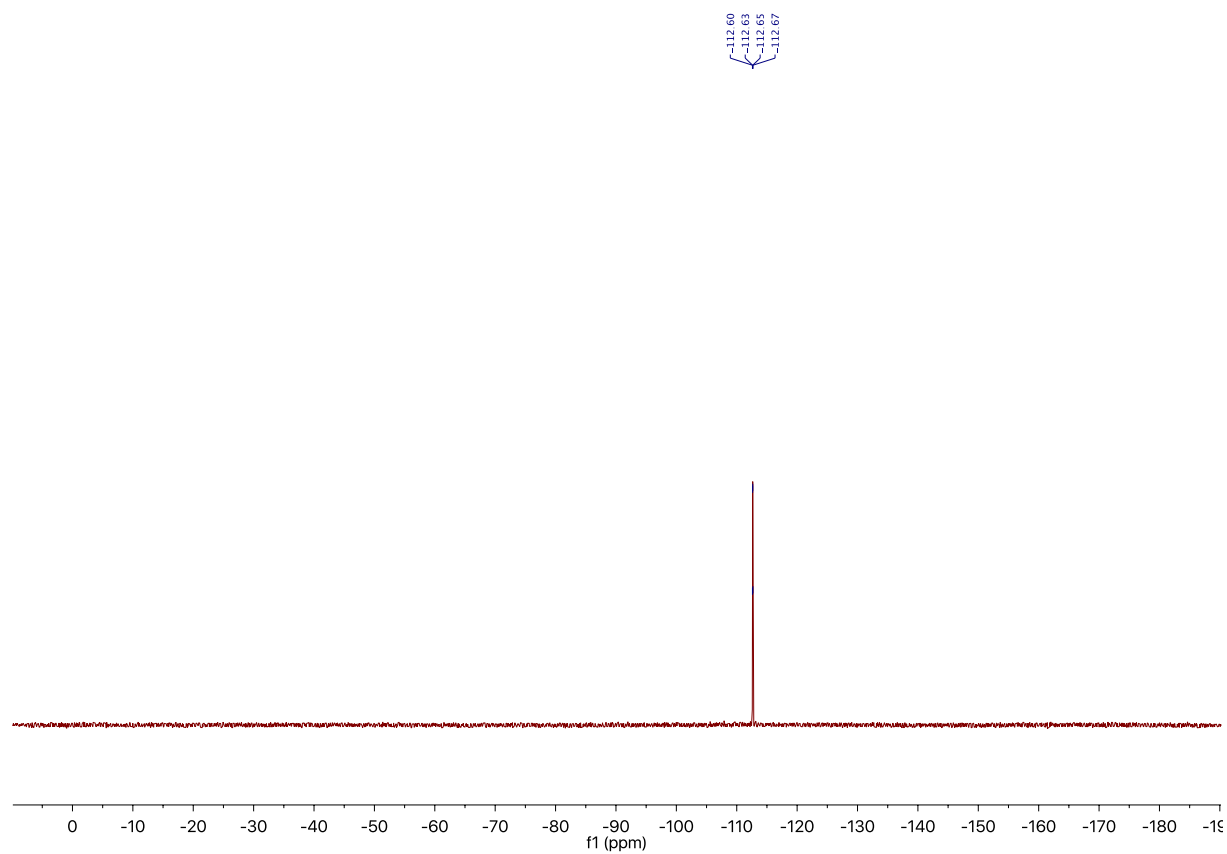


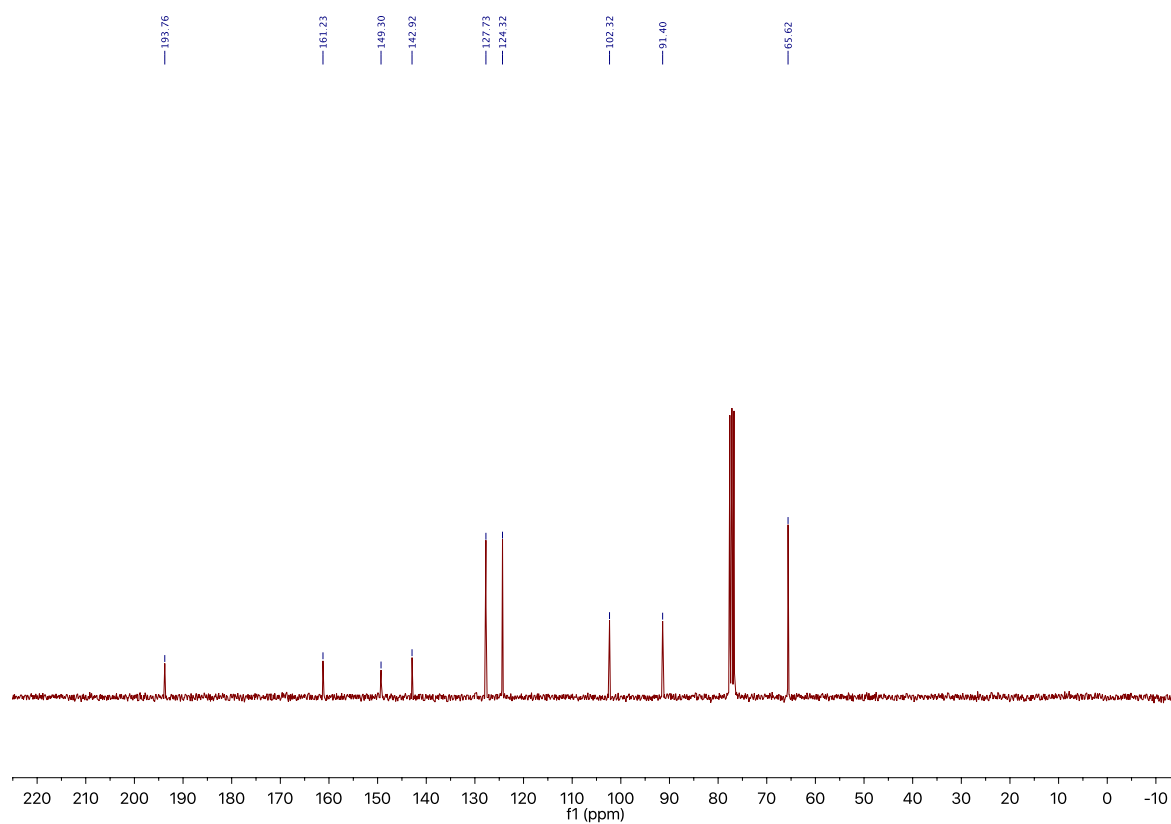
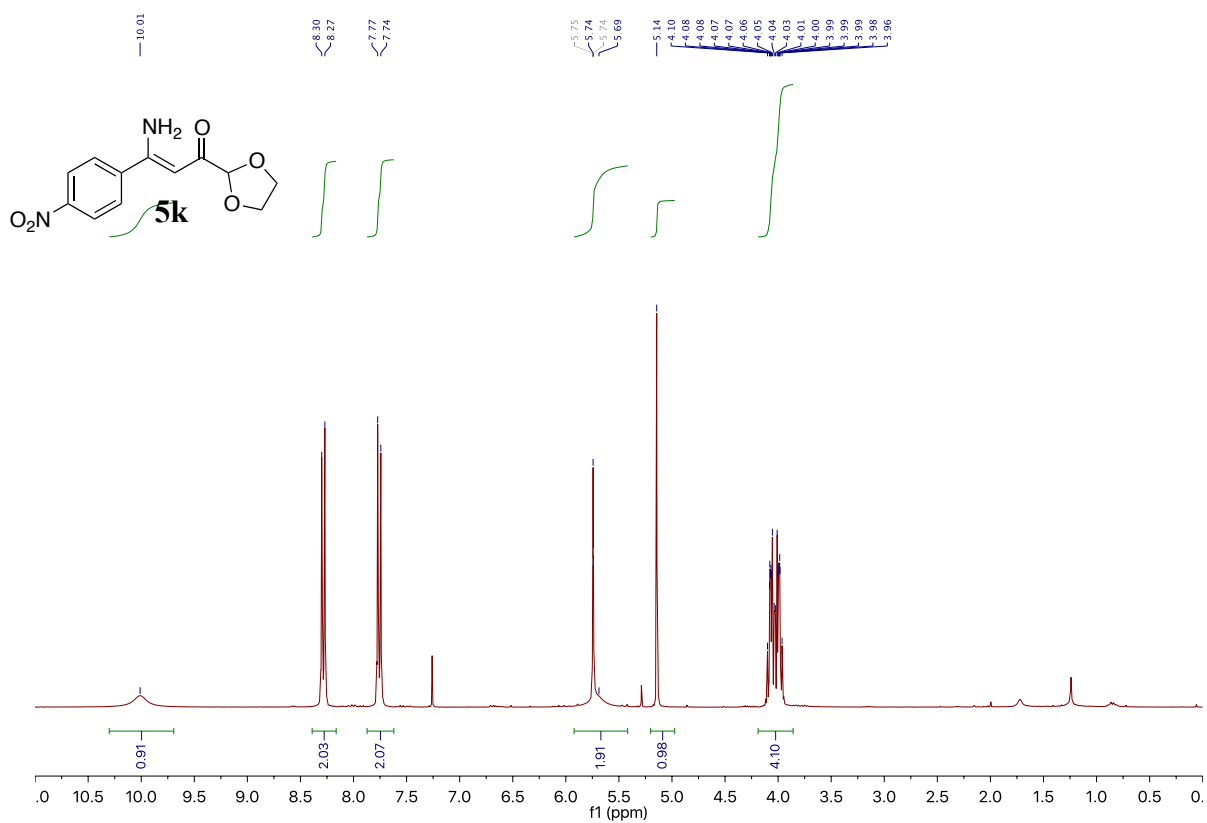


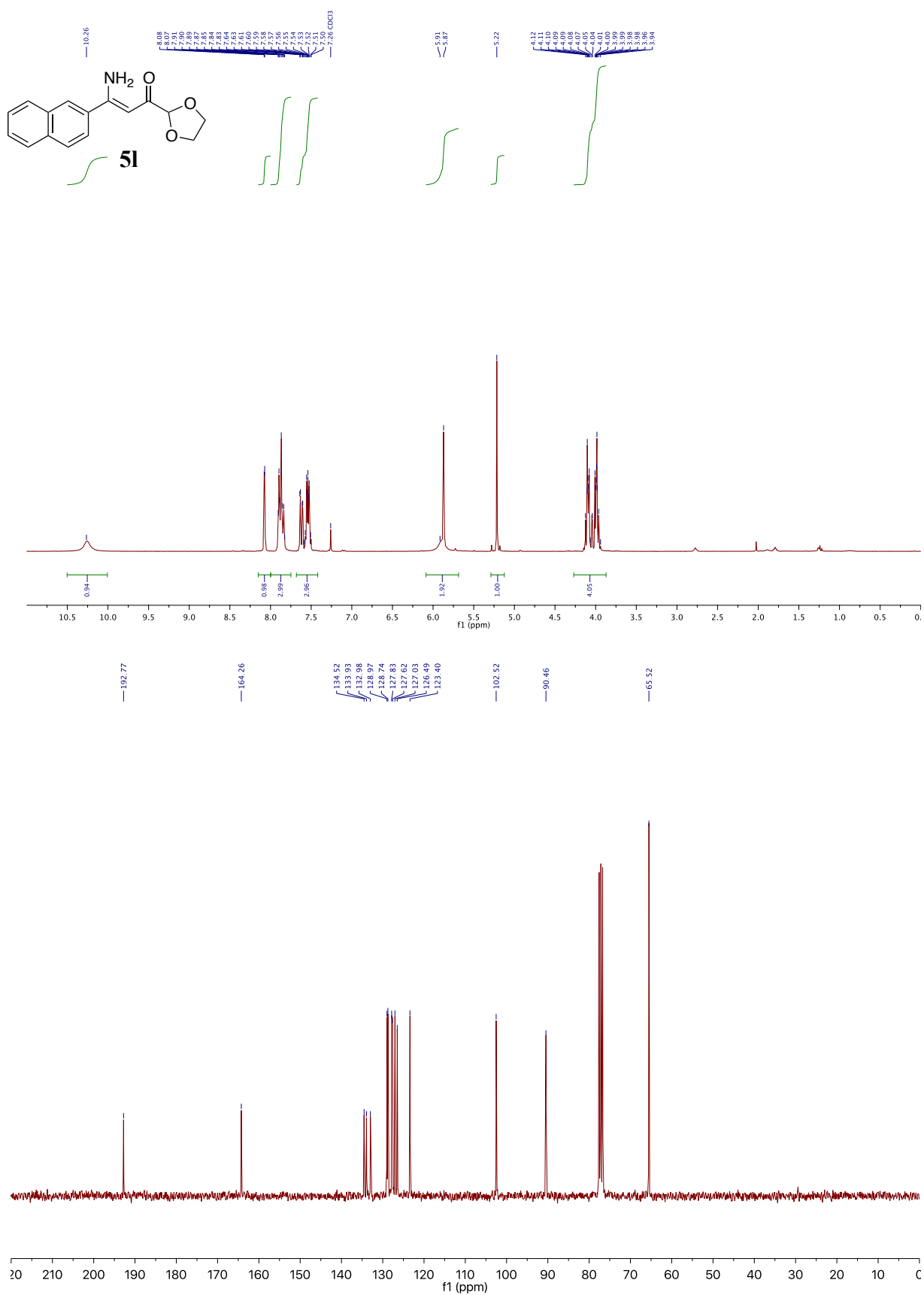


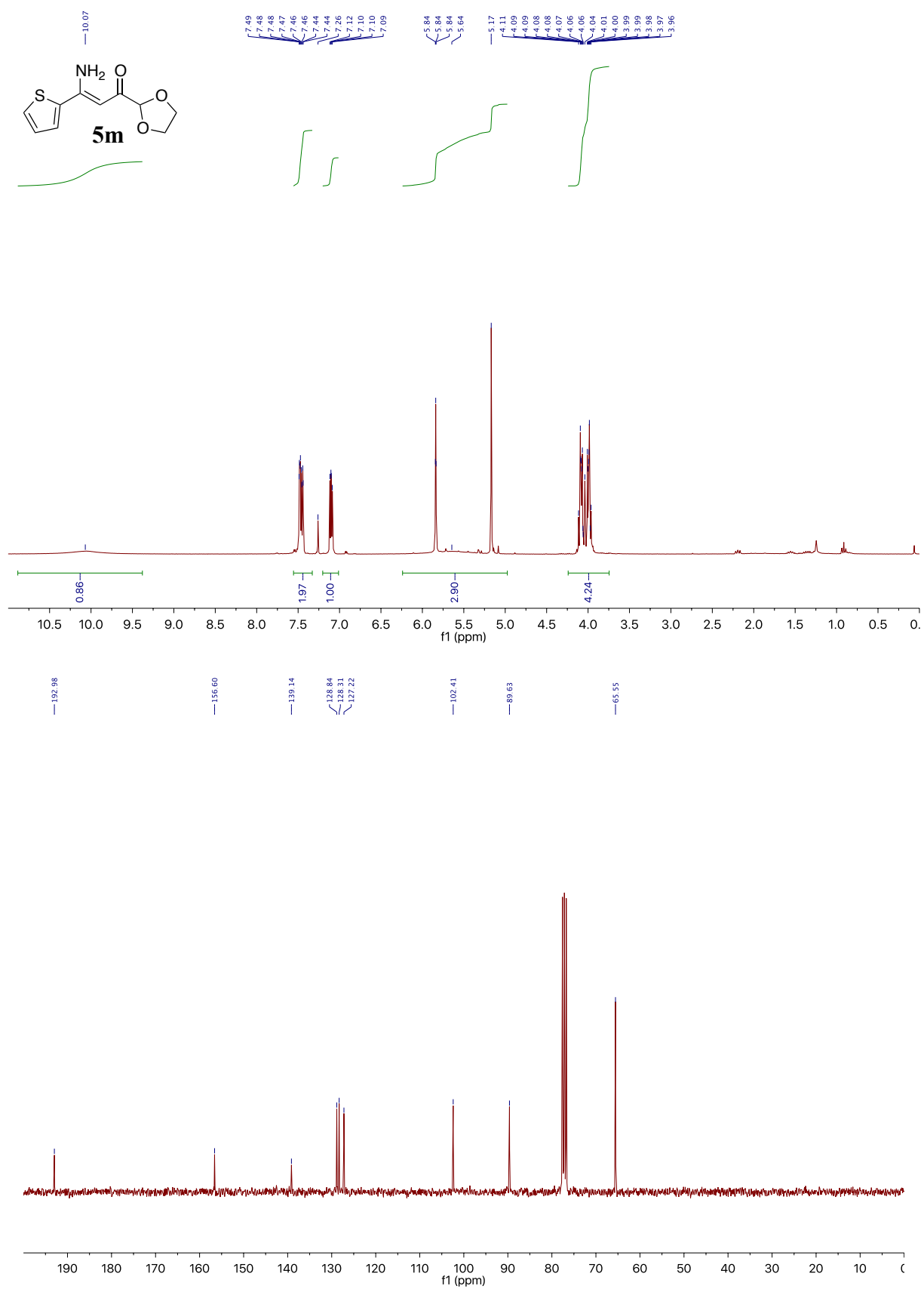


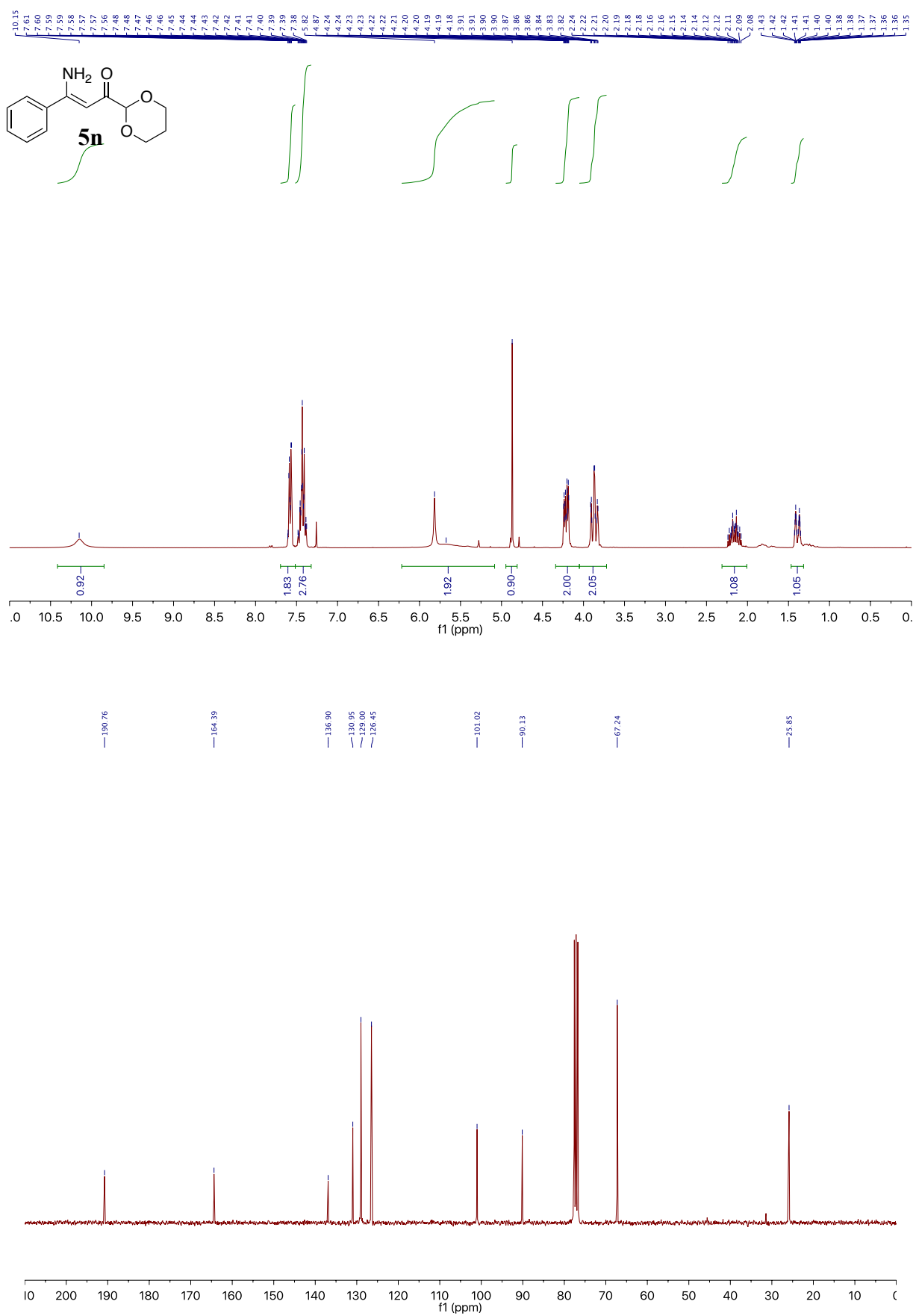


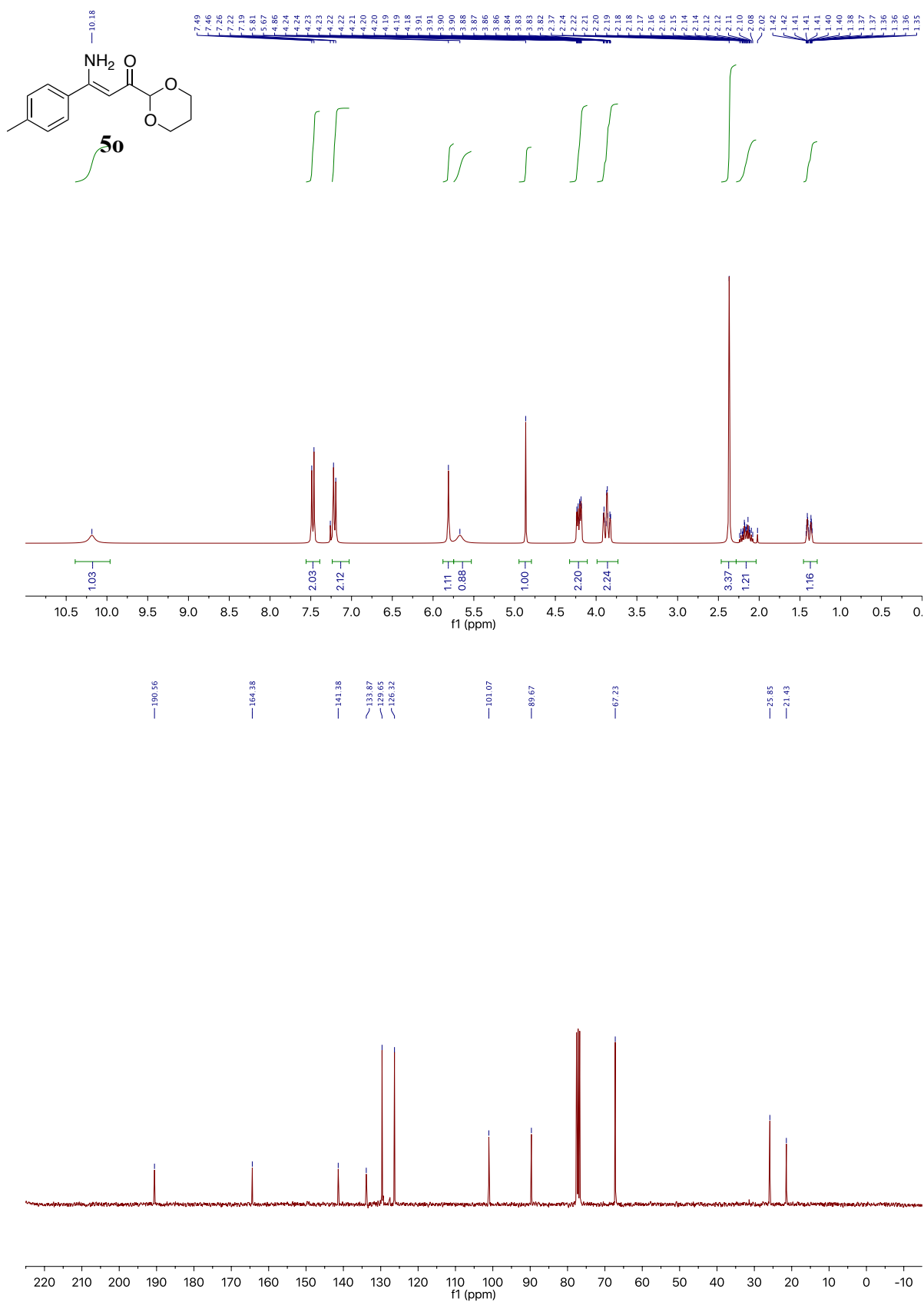


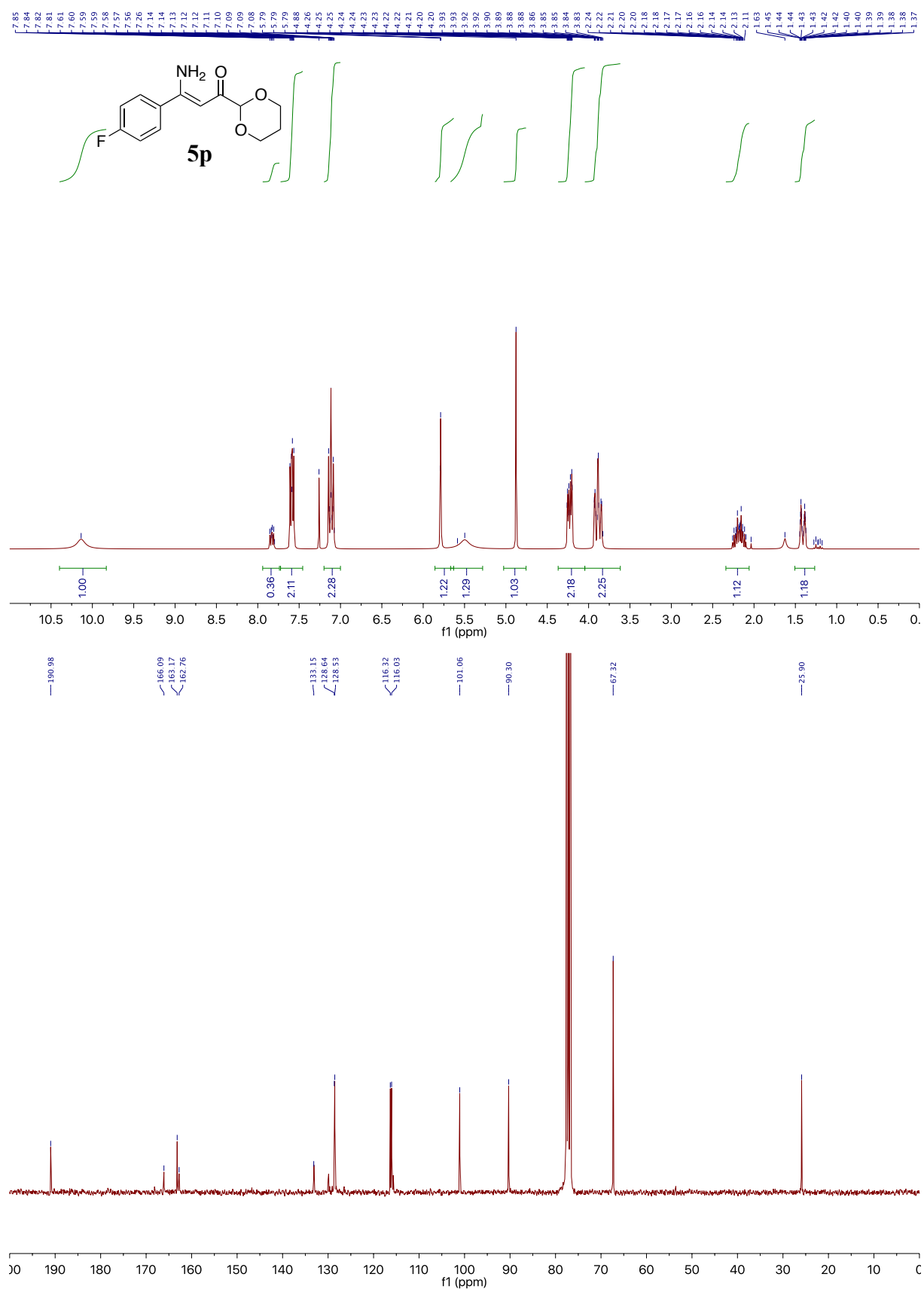


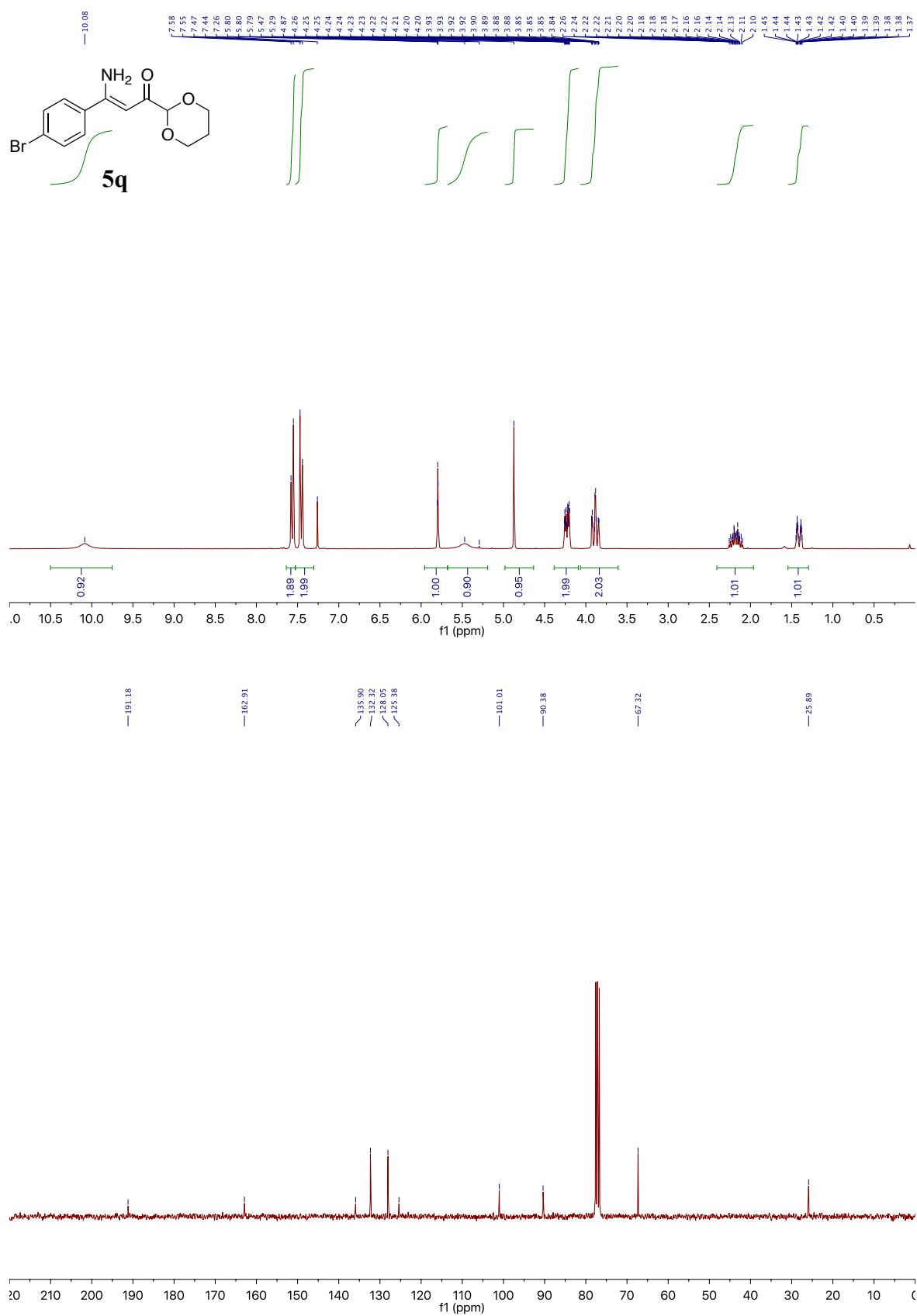


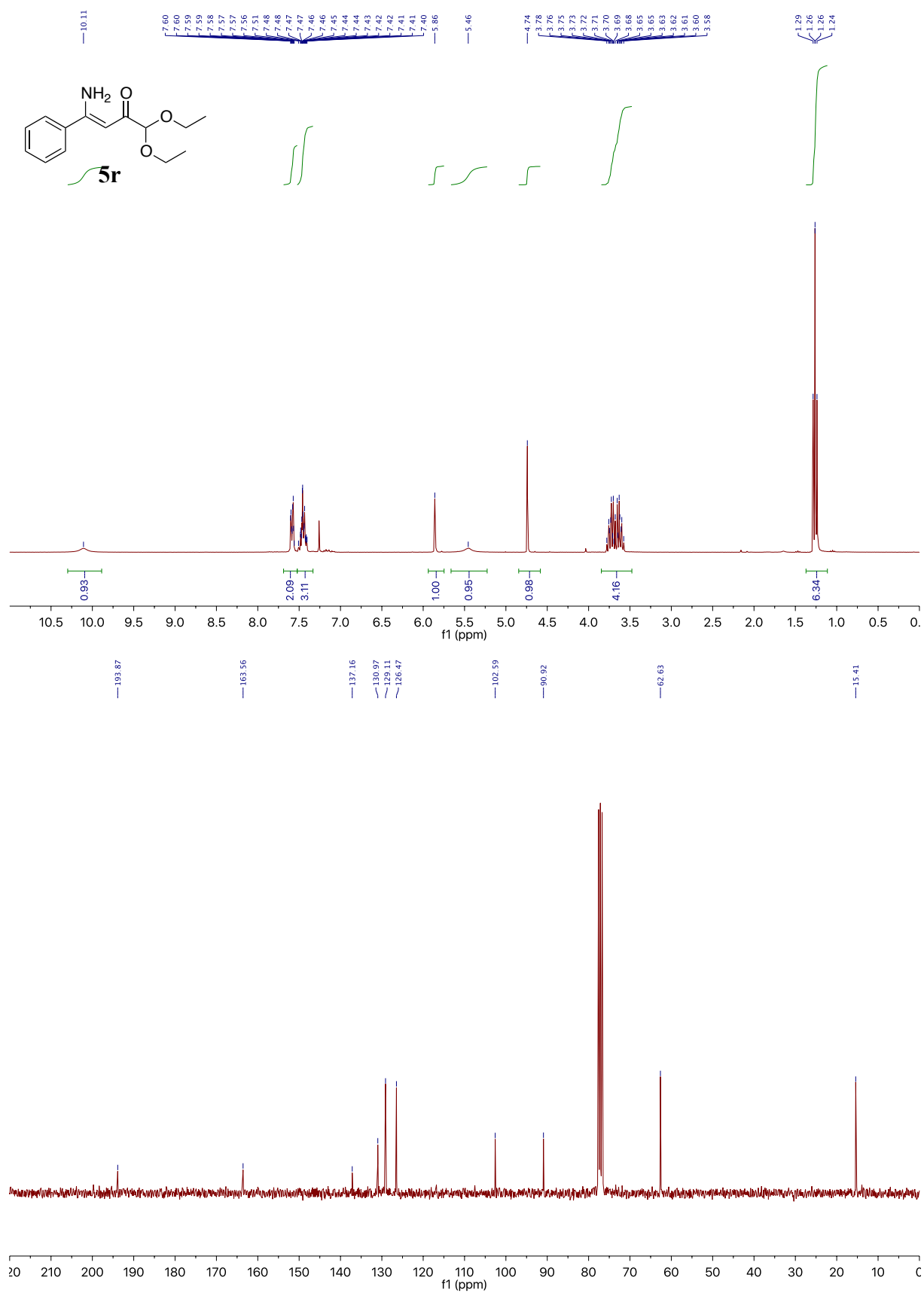


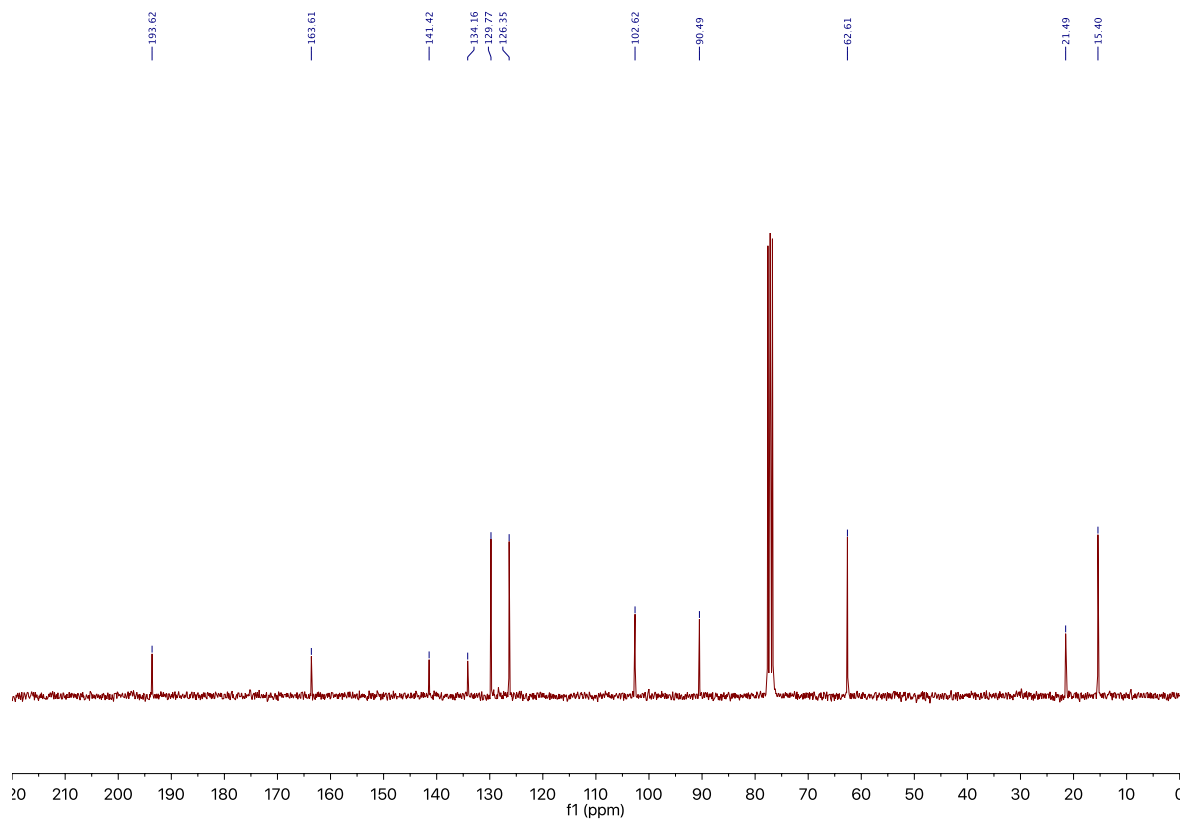
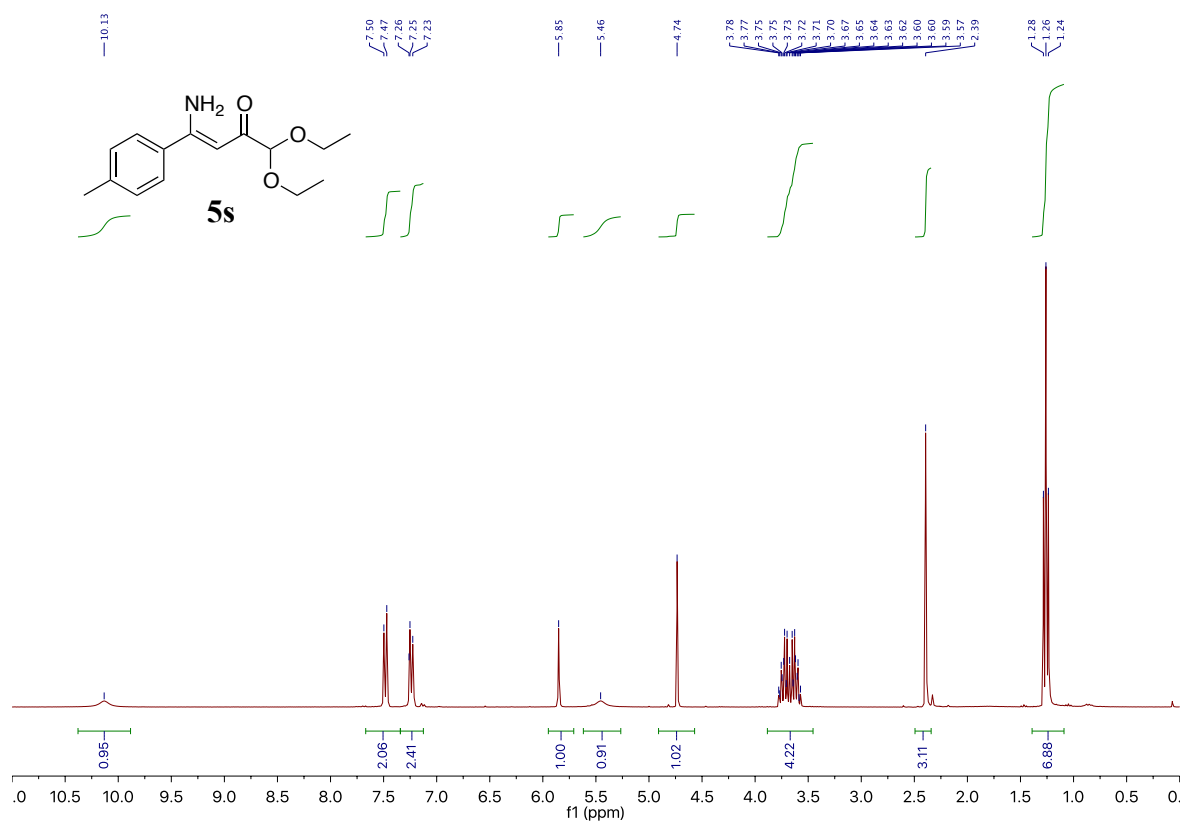


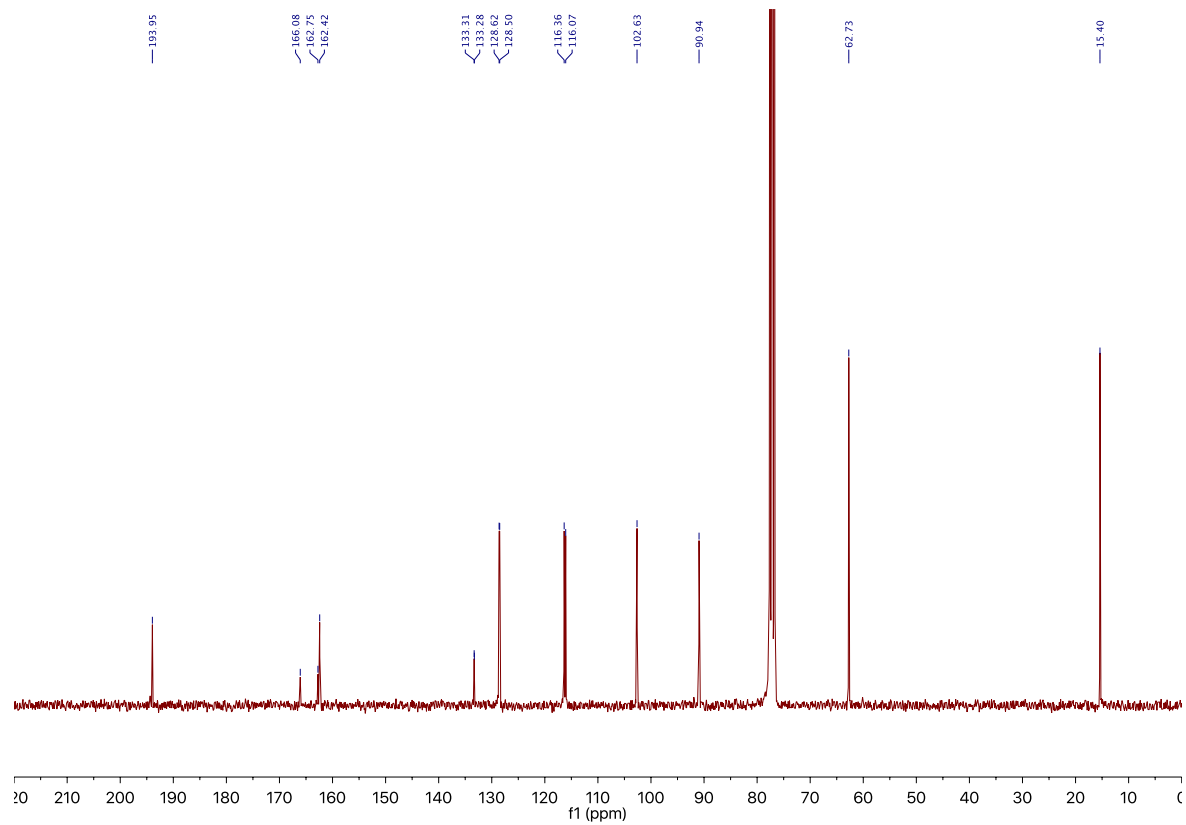
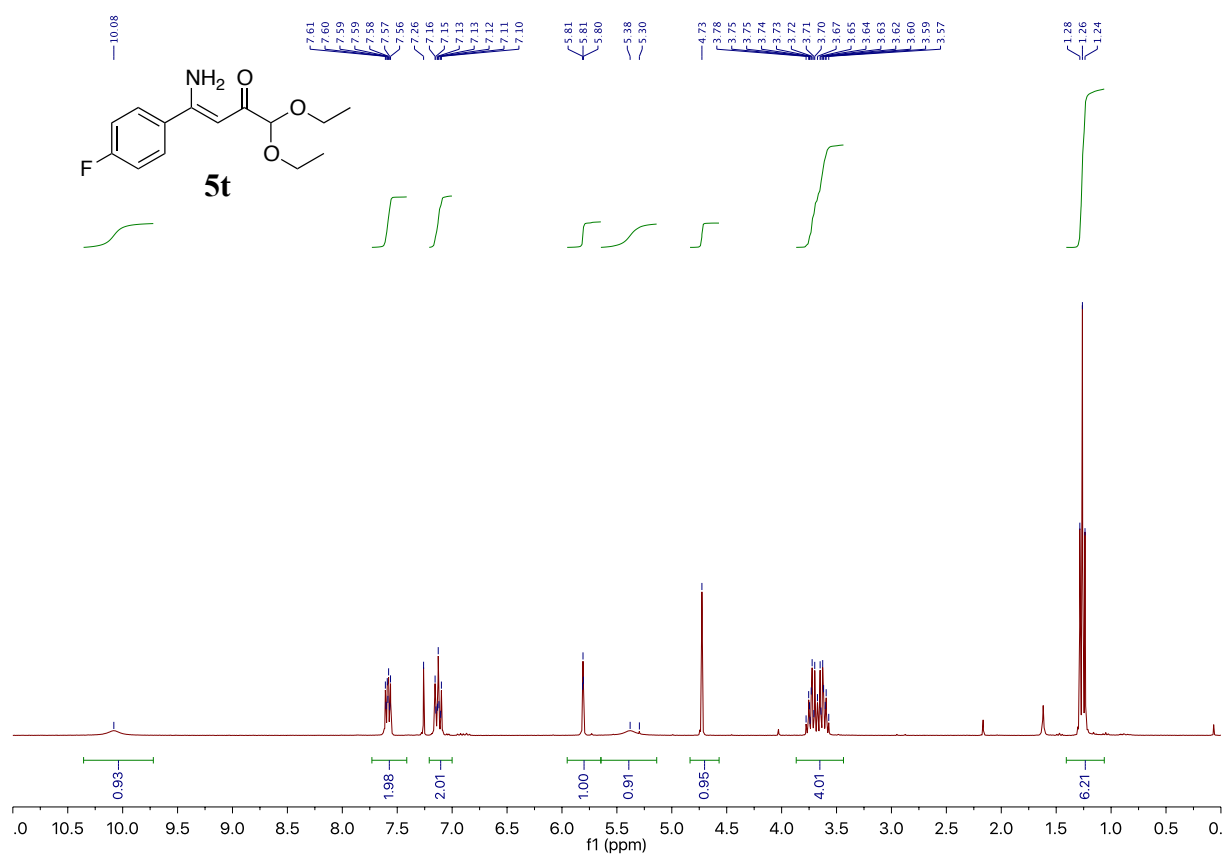


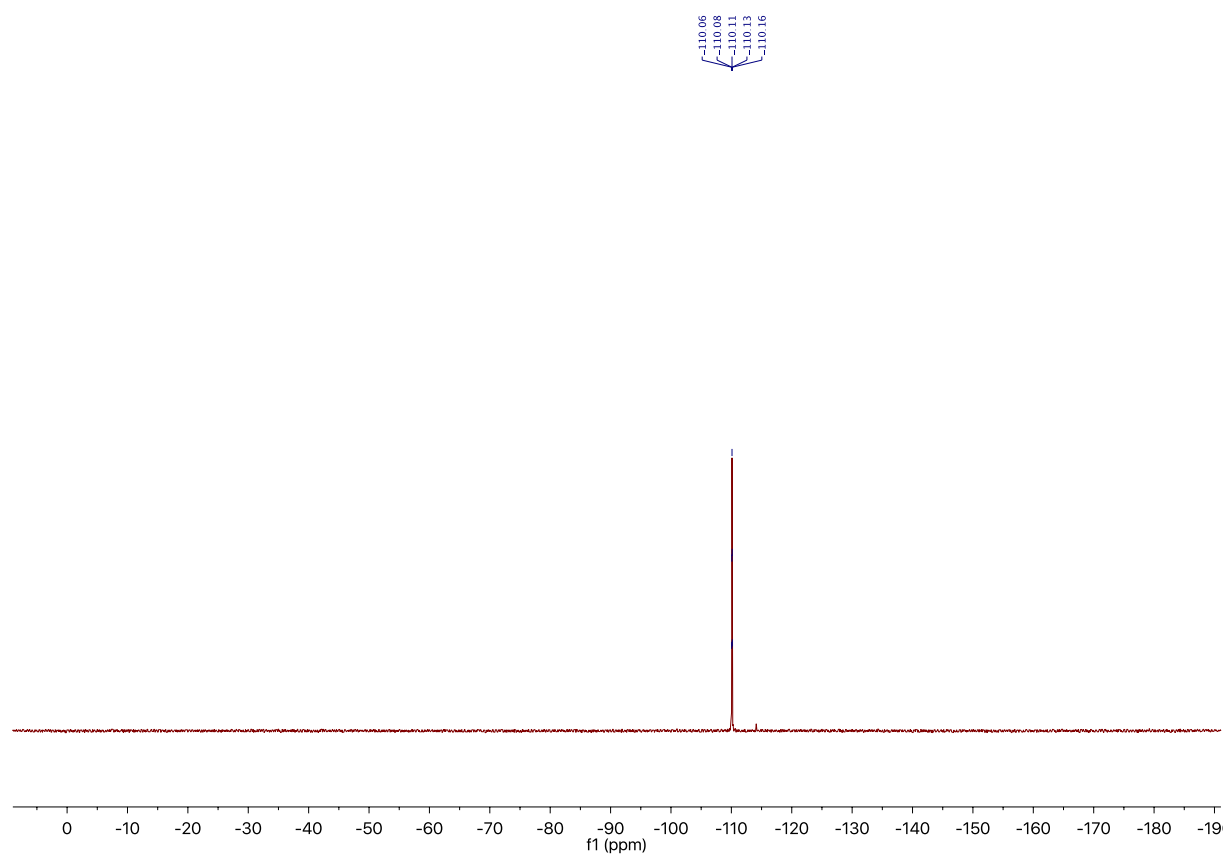


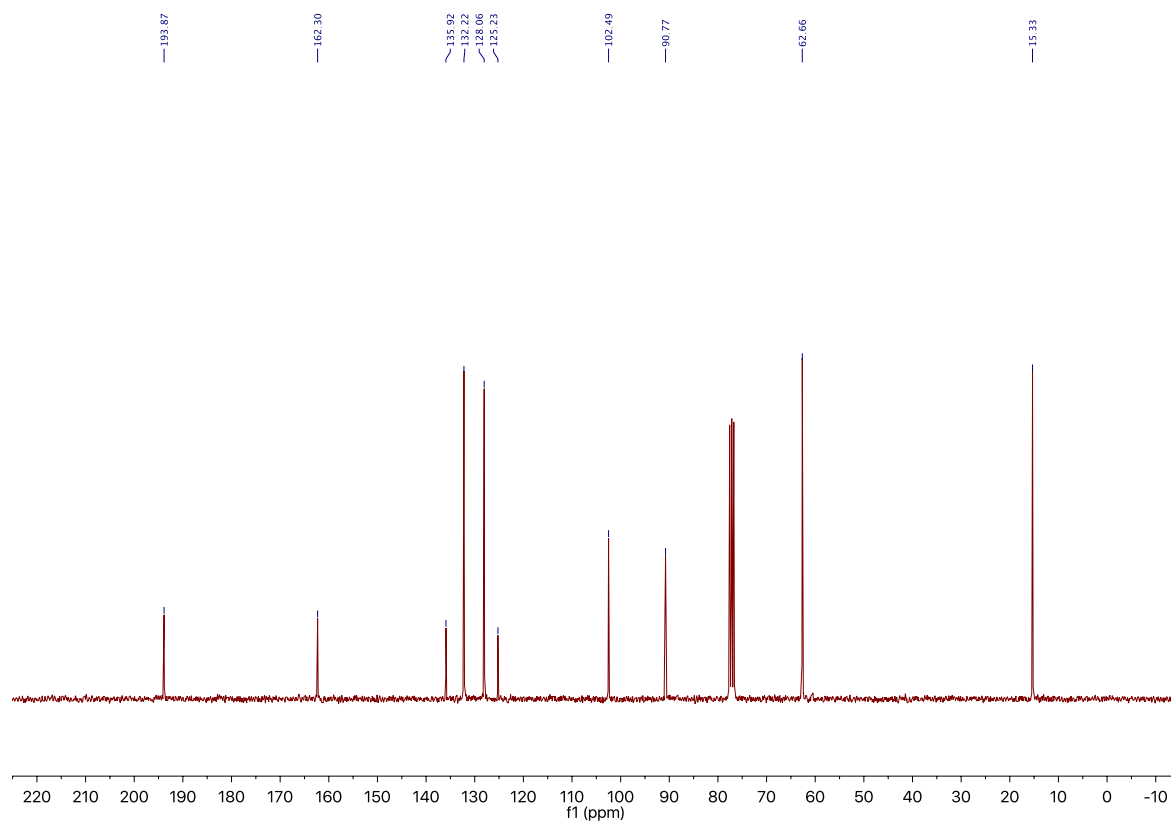
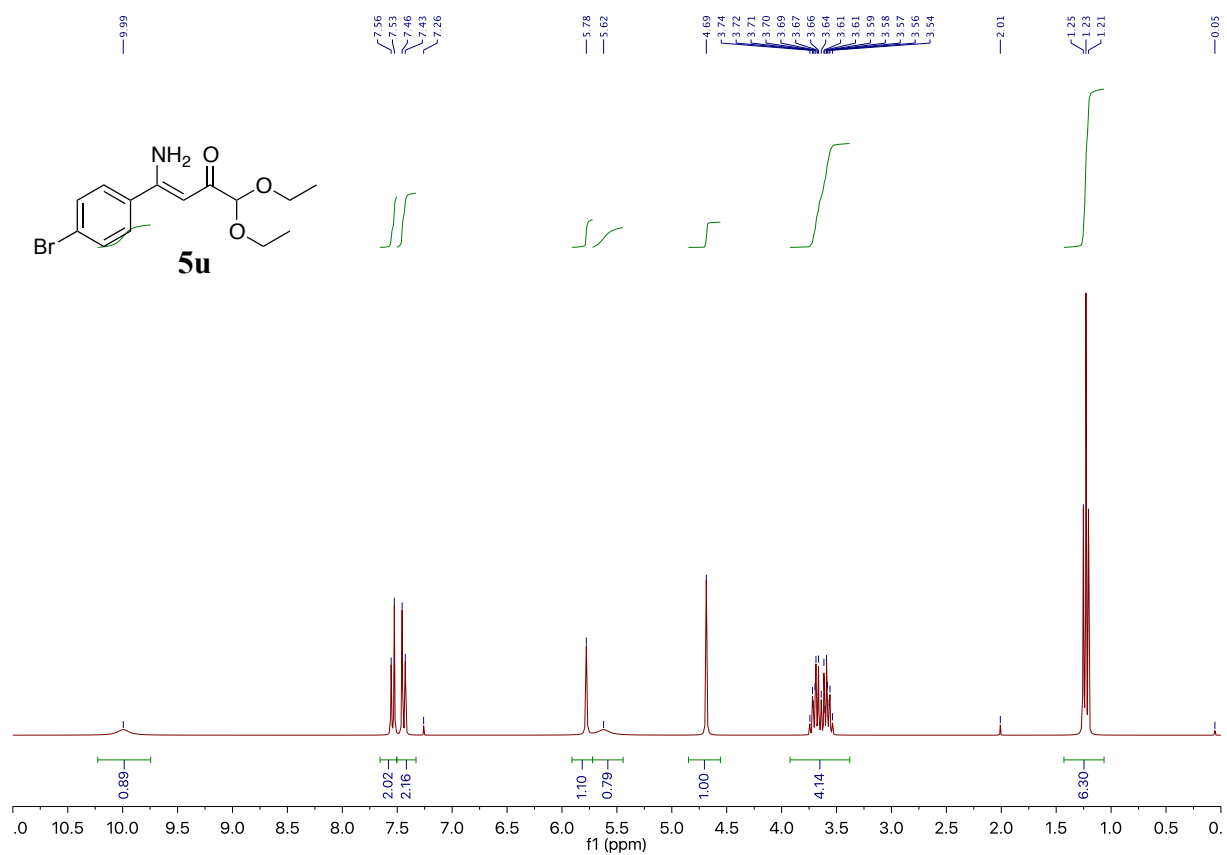






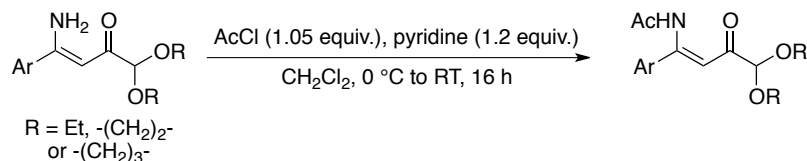






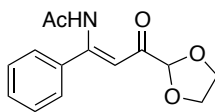
6. Synthesis of the Enamides 1a – 1u

General procedure



In a round bottom flask charged with argon were introduced the enamine (1.0 equiv.) and dichloromethane (c = 1.0 M). At 0 °C, acetyl chloride (1.05 equiv) and pyridine (1.2 equiv) were sequentially added dropwise. The mixture was allowed to reach room temperature, stirred for 16 h and hydrolyzed with aqueous NaHCO_3 . The product was then extracted with dichloromethane. Combined organic layers were dried over MgSO_4 and concentrated *in vacuo* to afford the crude compound which was purified by silica gel column chromatography (PET/EtOAc: 7/3).

(Z)-N-(3-(1,3-dioxolan-2-yl)-3-oxo-1-phenylprop-1-en-1-yl)acetamide **1a**



White solid (mp = 63 – 65 °C), 71% yield (325 mg).

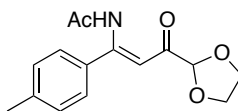
Chemical Formula: $\text{C}_{14}\text{H}_{15}\text{NO}_4$

^1H NMR (300 MHz, CDCl_3) δ 11.69 (brd, 1H), 7.53 – 7.30 (m, 5H), 5.87 (s, 1H), 5.15 (s, 1H), 4.18 – 3.84 (m, 4H), 2.17 (s, 3H).

^{13}C NMR (75 MHz, CDCl_3) δ 196.0, 168.6, 157.7, 135.5, 130.1, 128.0, 127.5, 103.0, 102.0, 65.6, 24.9.

Mass (CI/ NH_3) MH^+ 262

(Z)-N-(3-(1,3-dioxolan-2-yl)-3-oxo-1-(p-tolyl)prop-1-en-1-yl)acetamide **1b**



Slightly yellow oil, 86% yield (258 mg).

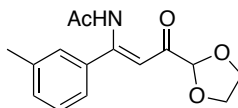
Chemical formula: $\text{C}_{15}\text{H}_{17}\text{NO}_4$

^1H NMR (300 MHz, CDCl_3) δ 11.70 (brd, 1H), 7.31 (d, J = 8.0 Hz, 2H), 7.18 (d, J = 8.0 Hz, 2H), 5.88 (s, 1H), 5.16 (s, 1H), 4.21 – 3.84 (m, 4H), 2.38 (s, 3H), 2.18 (s, 3H).

^{13}C NMR (75 MHz, CDCl_3) δ 196.0, 168.8, 158.1, 140.7, 132.6, 128.9, 127.6, 102.7, 102.1, 65.7, 25.2, 21.5.

Mass (CI/NH_3) MH^+ 276

(*Z*)-*N*-(3-(1,3-dioxolan-2-yl)-3-oxo-1-(*m*-tolyl)prop-1-en-1-yl)acetamide **1c**



Slightly yellow oil, 79% yield (255 mg).

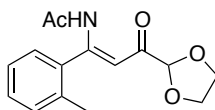
Chemical Formula: $\text{C}_{15}\text{H}_{17}\text{NO}_4$

^1H NMR (300 MHz, CDCl_3) δ 11.72 (brd, 1H), 7.43 – 7.08 (m, 4H), 5.89 (s, 1H), 5.18 (s, 1H), 4.24 – 3.85 (m, 4H), 2.39 (s, 3H), 2.20 (s, 3H).

^{13}C NMR (75 MHz, CDCl_3) δ 196.1, 168.7, 158.1, 137.8, 135.5, 131.0, 127.9 (2C), 124.7, 102.9, 102.1, 65.7, 25.1, 21.4.

Mass (CI/NH_3) MH^+ 276

(*Z*)-*N*-(3-(1,3-dioxolan-2-yl)-3-oxo-1-(*o*-tolyl)prop-1-en-1-yl)acetamide **1d**



White solid (mp = 87 – 90 °C), 75% yield (242 mg).

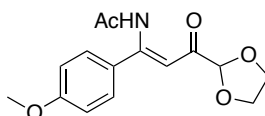
Chemical Formula: $\text{C}_{15}\text{H}_{17}\text{NO}_4$

^1H NMR (300 MHz, CDCl_3) δ 12.03 (brd, 1H), 7.20 (dd, J = 7.5, 1.5 Hz, 1H), 7.19 – 7.02 (m, 3H), 5.59 (s, 1H), 5.07 (s, 1H), 4.12 – 3.72 (m, 4H), 2.27 (s, 3H), 2.06 (s, 3H).

^{13}C NMR (75 MHz, CDCl_3) δ 196.5, 168.1, 158.1, 135.9, 135.1, 129.8, 129.1, 127.2, 125.6, 102.1, 101.8, 65.7, 24.9, 19.5.

Mass (CI/NH_3) MH^+ 276

(*Z*)-*N*-(3-(1,3-dioxolan-2-yl)-1-(4-methoxyphenyl)-3-oxoprop-1-en-1-yl)acetamide **1e**



Slightly yellow solid (mp = 67 – 70 °C), quantitative yield (280 mg).

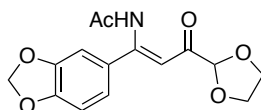
Chemical Formula: $\text{C}_{15}\text{H}_{17}\text{NO}_5$

¹H NMR (300 MHz, CDCl₃) δ 11.70 (brd, 1H), 7.37 (d, *J* = 8.9 Hz, 2H), 6.88 (d, *J* = 8.9 Hz, 2H), 5.87 (s, 1H), 5.15 (s, 1H), 4.13 – 3.92 (m, 4H), 3.82 (s, 3H), 2.19 (s, 3H).

¹³C NMR (75 MHz, CDCl₃) δ 195.8, 169.0, 161.6, 157.7, 129.4, 127.5, 113.6, 102.3, 102.1, 65.7, 55.4, 25.2.

Mass (CI/NH₃) MH⁺ 292

(*Z*)-*N*-(1-(benzo[*d*][1,3]dioxol-5-yl)-3-(1,3-dioxolan-2-yl)-3-oxoprop-1-en-1-yl)acetamide **1f**



Slightly yellow solid (mp = 104 – 107 °C), 72% yield (165 mg).

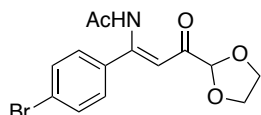
Chemical Formula: C₁₅H₁₅NO₆

¹H NMR (300 MHz, CDCl₃) δ 11.61 (s, 1H), 6.95 (dd, *J* = 8.0, 2.0 Hz, 1H), 6.85 (d, *J* = 2.0 Hz, 1H), 6.79 (d, *J* = 8.0 Hz, 1H), 5.99 (s, 2H), 5.87 (s, 1H), 5.14 (s, 1H), 4.17 – 3.85 (m, 4H), 2.18 (s, 3H).

¹³C NMR (75 MHz, CDCl₃) δ 195.8, 168.8, 157.3, 149.6, 147.5, 129.2, 122.2, 108.10, 108.07, 102.5, 102.0, 101.6, 65.6, 25.1.

Mass (CI/NH₃) MH⁺ 306

(*Z*)-*N*-(1-(4-bromophenyl)-3-(1,3-dioxolan-2-yl)-3-oxoprop-1-en-1-yl)acetamide **1g**



Slightly yellow solid (mp = 91 – 95 °C), 68% yield (382 mg).

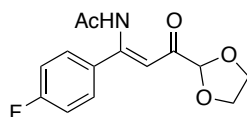
Chemical Formula: C₁₄H₁₄BrNO₄

¹H NMR (300 MHz, CDCl₃) δ 11.67 (brd, 1H), 7.51 (d, *J* = 8.5 Hz, 2H), 7.27 (d, *J* = 8.5 Hz, 2H), 5.86 (s, 1H), 5.16 (s, 1H), 4.21 – 3.83 (m, 4H), 2.20 (s, 3H).

¹³C NMR (75 MHz, CDCl₃) δ 196.2, 168.7, 156.5, 134.5, 131.4, 129.1, 124.6, 103.2, 102.0, 65.7, 25.0.

Mass (CI/NH₃) MH⁺ 340

(*Z*)-*N*-(3-(1,3-dioxolan-2-yl)-1-(4-fluorophenyl)-3-oxoprop-1-en-1-yl)acetamide **1h**



Slightly yellow solid (mp = 80 – 84 °C), 72% yield (319 mg).

Chemical Formula: C₁₄H₁₄FNO₄

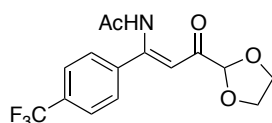
¹H NMR (300 MHz, CDCl₃) δ 11.70 (brd, 1H), 7.51 – 7.30 (m, 2H), 7.14 – 6.86 (m, 2H), 5.84 (s, 1H), 5.15 (s, 1H), 4.19 – 3.81 (m, 4H), 2.19 (s, 3H).

¹³C NMR (75 MHz, CDCl₃) δ 196.1, 168.8, 163.9 (d, ¹J_{CF} = 250.7 Hz), 156.7, 131.5 (d, ⁴J_{CF} = 3.1 Hz), 129.7 (d, ³J_{CF} = 8.5 Hz), 115.3 (d, ²J_{CF} = 22.1 Hz), 103.1, 102.1, 65.7, 25.1.

¹⁹F NMR (282 MHz, CDCl₃) δ -107.72 – -115.89 (m).

Mass (CI/NH₃) MH⁺ 280

(*Z*)-*N*-(3-(1,3-dioxolan-2-yl)-3-oxo-1-(4-(trifluoromethyl)phenyl)prop-1-en-1-yl)acetamide **1i**



White solid (mp = 103 – 106 °C), 75% yield (319 mg).

Chemical Formula: C₁₅H₁₄F₃NO₄

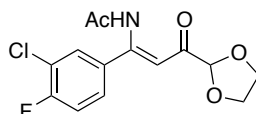
¹H NMR (300 MHz, CDCl₃) δ 11.67 (s, 1H), 7.61 (d, *J* = 8.1 Hz, 2H), 7.48 (d, *J* = 8.1 Hz, 2H), 5.85 (s, 1H), 5.13 (s, 1H), 4.14 – 3.88 (m, 4H), 2.18 (s, 3H).

¹³C NMR (75 MHz, CDCl₃) δ 196.3, 168.7, 155.8, 139.3, 131.8 (q, ²J_{CF} = 32.3 Hz), 127.8, 125.1 (q, ³J_{CF} = 3.9 Hz), 123.8 (q, ¹J_{CF} = 272.3 Hz), 103.7, 101.9, 65.7, 24.8.

¹⁹F NMR (282 MHz, CDCl₃) δ -63.83 (s).

Mass (CI/NH₃) MH⁺ 330

(*Z*)-*N*-(1-(3-chloro-4-fluorophenyl)-3-(1,3-dioxolan-2-yl)-3-oxoprop-1-en-1-yl)acetamide **1j**



Slightly yellow solid (mp = 85 – 88 °C), 72% yield (152 mg).

Chemical Formula: C₁₄H₁₃ClFNO₄

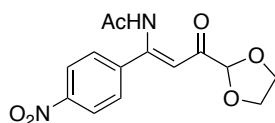
¹H NMR (300 MHz, CDCl₃) δ 11.57 (brd, 1H), 7.37 (dd, *J* = 6.6, 2.2 Hz, 1H), 7.20 (ddd, *J* = 8.6, 6.5, 2.2 Hz, 1H), 7.06 (t, *J* = 8.6 Hz, 1H), 5.76 (s, 1H), 5.08 (s, 1H), 4.22 – 3.63 (m, 4H), 2.13 (s, 3H).

¹³C NMR (75 MHz, CDCl₃) δ 196.2, 168.8, 159.1 (d, ¹J_{CF} = 253.0 Hz), 155.1, 132.7 (d, ³J_{CF} = 3.9 Hz), 129.8, 127.7 (d, ³J_{CF} = 7.6 Hz), 121.2 (d, ²J_{CF} = 18.3 Hz), 116.4 (d, ²J_{CF} = 21.8 Hz), 103.4, 102.0, 65.8, 25.1.

¹⁹F NMR (282 MHz, CDCl₃) δ -113.49 – -113.56 (m).

Mass (Cl/NH₃) MH⁺ 314

(Z)-N-(3-(1,3-dioxolan-2-yl)-1-(4-nitrophenyl)-3-oxoprop-1-en-1-yl)acetamide **1k**



Yellow solid (mp = 145 – 147 °C), 85% yield (307 mg).

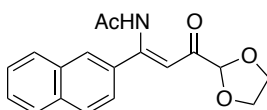
Chemical Formula: C₁₄H₁₄N₂O₆

¹H NMR (300 MHz, CDCl₃) δ 11.67 (s, 1H), 8.22 (d, *J* = 8.8 Hz, 2H), 7.53 (d, *J* = 8.8 Hz, 2H), 5.87 (s, 1H), 5.15 (s, 1H), 4.27 – 3.86 (m, 4H), 2.21 (s, 3H).

¹³C NMR (75 MHz, CDCl₃) δ 196.4, 168.8, 154.8, 148.5, 142.2, 128.4, 123.5, 104.1, 101.9, 65.9, 24.9.

Mass (Cl/NH₃) MH⁺ 307

(Z)-N-(3-(1,3-dioxolan-2-yl)-1-(naphthalen-2-yl)-3-oxoprop-1-en-1-yl)acetamide **1l**



Slightly yellow solid (mp = 104 – 106 °C), 83% yield (288 mg).

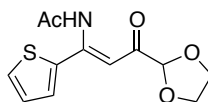
Chemical Formula: C₁₈H₁₇NO₄

¹H NMR (300 MHz, CDCl₃) δ 11.82 (brd, 1H), 8.09 – 7.69 (m, 4H), 7.69 – 7.34 (m, 3H), 6.00 (s, 1H), 5.21 (s, 1H), 4.24 – 3.84 (m, 4H), 2.22 (s, 3H).

¹³C NMR (75 MHz, CDCl₃) δ 196.1, 168.8, 157.9, 134.2, 133.3, 132.9, 128.7, 127.8, 127.5, 127.3, 127.0, 126.6, 125.1, 103.4, 102.2, 65.8, 25.1.

Mass (Cl/NH₃) MH⁺ 312

(Z)-N-(3-(1,3-dioxolan-2-yl)-3-oxo-1-(thiophen-2-yl)prop-1-en-1-yl)acetamide **1m**



Dark yellow oil, 57% yield (172 mg).

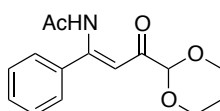
Chemical Formula: C₁₂H₁₃NSO₄

¹H NMR (300 MHz, CDCl₃) δ 11.49 (s, 1H), 7.45 (dd, *J* = 5.0, 1.3 Hz, 1H), 7.37 (dd, *J* = 3.7, 1.3 Hz, 1H), 7.04 (dd, *J* = 5.0, 3.7 Hz, 1H), 6.08 (s, 1H), 5.15 (s, 1H), 4.28 – 3.78 (m, 4H), 2.20 (s, 3H).

¹³C NMR (75 MHz, CDCl₃) δ 195.9, 169.1, 150.3, 136.9, 130.4, 129.4, 127.5, 102.8, 102.0, 65.7, 25.2.

Mass (CI/NH₃) MH⁺ 268

(*Z*)-*N*-(3-(1,3-dioxan-2-yl)-3-oxo-1-phenylprop-1-en-1-yl)acetamide **1n**



Slightly yellow solid (mp = 112 – 114 °C), 76% yield (355 mg).

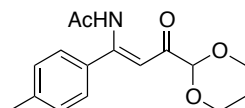
Chemical Formula: C₁₅H₁₇NO₄

¹H NMR (300 MHz, CDCl₃) δ 11.73 (brd, 1H), 7.59 – 7.30 (m, 5H), 5.99 (s, 1H), 4.89 (s, 1H), 4.22 (ddt, *J* = 10.5, 5.0, 1.5 Hz, 2H), 3.87 (tdd, *J* = 10.5, 2.5, 1.5 Hz, 2H), 2.17 (s, 3H), 2.26 – 2.02 (m, 1H), 1.42 (dtt, *J* = 13.65, 2.5, 1.5 Hz, 1H).

¹³C NMR (75 MHz, CDCl₃) δ 193.6, 168.7, 157.9, 135.7, 130.1, 128.1, 127.6, 103.4, 100.3, 67.2, 25.7, 25.1.

Mass (CI/NH₃) MH⁺ 276

(*Z*)-*N*-(3-(1,3-dioxan-2-yl)-3-oxo-1-(*p*-tolyl)prop-1-en-1-yl)acetamide **1o**



Slightly yellow oil, 80% yield (422 mg).

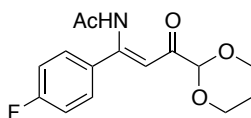
Chemical Formula: C₁₆H₁₉NO₄

¹H NMR (300 MHz, CDCl₃) δ 11.70 (brd, 1H), 7.30 (d, *J* = 8.0 Hz, 2H), 7.16 (d, *J* = 8.0 Hz, 2H), 5.99 (s, 1H), 4.87 (s, 1H), 4.20 (ddt, *J* = 10.6, 5.0, 1.5 Hz, 2H), 3.92 – 3.74 (m, 2H), 2.36 (s, 3H), 2.16 (s, 3H), 2.25 – 2.03 (m, 1H), 1.40 (dtt, *J* = 13.6, 2.5, 1.0 Hz, 1H).

¹³C NMR (75 MHz, CDCl₃) δ 193.4, 168.7, 157.9, 140.4, 132.6, 128.7, 127.5, 102.9, 100.2, 67.1, 25.6, 25.0, 21.4.

Mass (CI/NH₃) MH⁺ 290

(Z)-N-(3-(1,3-dioxan-2-yl)-1-(4-fluorophenyl)-3-oxoprop-1-en-1-yl)acetamide **1p**



Slightly yellow solid (mp = 120-123 °C), 82% yield (169 mg).

Chemical Formula: C₁₅H₁₆FNO₄

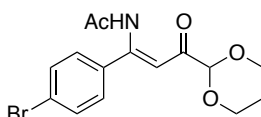
¹H NMR (300 MHz, CDCl₃) δ 11.71 (brd, 1H), 7.53 – 7.31 (m, 2H), 7.15 – 6.82 (m, 2H), 5.96 (s, 1H), 4.88 (s, 1H), 4.22 (ddt, *J* = 10.5, 5.1, 1.6 Hz, 2H), 4.02 – 3.62 (m, 2H), 2.17 (s, 3H), 2.36 – 2.01 (m, 1H), 1.42 (dtt, *J* = 13.6, 2.7, 1.6 Hz, 1H).

¹³C NMR (75 MHz, CDCl₃) δ 193.6, 168.8, 163.9 (d, ¹*J*_{CF} = 250.3 Hz), 156.7, 131.6 (d, ⁴*J*_{CF} = 2.7 Hz), 129.7 (d, ³*J*_{CF} = 8.5 Hz), 115.2 (d, ²*J*_{CF} = 21.9 Hz), 103.3, 100.3, 67.2, 25.7, 25.1.

¹⁹F NMR (282 MHz, CDCl₃) δ -111.11 – -111.20 (m).

Mass (CI/NH₃) MH⁺ 294

(Z)-N-(3-(1,3-dioxan-2-yl)-1-(4-bromophenyl)-3-oxoprop-1-en-1-yl)acetamide **1q**



Slightly yellow solid (mp = 125 – 127 °C), 57% yield (252 mg).

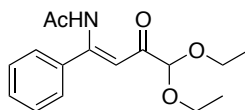
Chemical Formula: C₁₅H₁₆BrNO₄

¹H NMR (300 MHz, CDCl₃) δ 11.68 (brd, 1H), 7.49 (d, *J* = 8.6 Hz, 2H), 7.27 (d, *J* = 8.6 Hz, 2H), 5.97 (s, 1H), 4.88 (s, 1H), 4.23 (ddt, *J* = 10.7, 5.2, 1.5 Hz, 2H), 4.05 – 3.73 (m, 2H), 2.18 (s, 3H), 2.46 – 1.98 (m, 1H), 1.43 (dtd, *J* = 13.6, 2.6, 1.5 Hz, 1H).

¹³C NMR (75 MHz, CDCl₃) δ 193.8, 168.8, 156.6, 134.7, 131.4, 129.2, 124.6, 103.5, 100.3, 67.3, 25.7, 25.1.

Mass (CI/NH₃) MH⁺ 356

(Z)-N-(4,4-diethoxy-3-oxo-1-phenylbut-1-en-1-yl)acetamide **1r**



Yellow oil, 72% yield (263 mg).

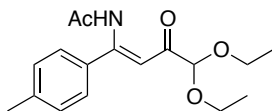
Chemical Formula: C₁₆H₂₁NO₄

¹H NMR (300 MHz, CDCl₃) δ 11.70 (brd, 1H), 7.55 – 7.30 (m, 5H), 6.01 (s, 1H), 4.72 (s, 1H), 3.85 – 3.47 (m, 4H), 2.18 (s, 3H), 1.26 (t, *J* = 7.0 Hz, 6H).

^{13}C NMR (75 MHz, CDCl_3) δ 196.6, 168.8, 157.1, 135.7, 130.1, 128.1, 127.6, 103.9, 102.2, 63.0, 25.1, 15.3.

Mass (ESI) MH^+ 292

(*Z*)-*N*-(4,4-diethoxy-3-oxo-1-(*p*-tolyl)but-1-en-1-yl)acetamide **1s**



Yellow oil, 69% yield (165 mg).

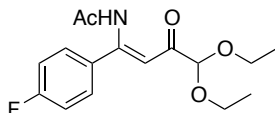
Chemical Formula: $\text{C}_{17}\text{H}_{23}\text{NO}_4$

^1H NMR (300 MHz, CDCl_3) δ 11.70 (brd, 1H), 7.31 (d, $J = 8.0$ Hz, 2H), 7.18 (d, $J = 8.0$ Hz, 2H), 6.01 (s, 1H), 4.72 (s, 1H), 3.81 – 3.41 (m, 4H), 2.38 (s, 3H), 2.18 (s, 3H), 1.26 (t, $J = 7.0$ Hz, 6H).

^{13}C NMR (75 MHz, CDCl_3) δ 196.6, 168.9, 157.3, 140.6, 132.8, 128.9, 127.6, 103.6, 102.2, 62.9, 25.2, 21.6, 15.3.

Mass (ESI) MH^+ 306

(*Z*)-*N*-(4,4-diethoxy-1-(4-fluorophenyl)-3-oxobut-1-en-1-yl)acetamide **1t**



Slightly yellow solid (mp = 124 – 126 °C), 68% yield (224 mg).

Chemical Formula: $\text{C}_{16}\text{H}_{20}\text{FNO}_4$

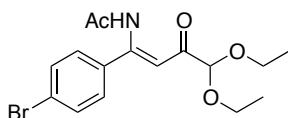
^1H NMR (300 MHz, CDCl_3) δ 11.69 (brd, 1H), 7.55 – 7.31 (m, 2H), 7.20 – 6.89 (m, 2H), 5.97 (s, 1H), 4.70 (brd, 1H), 3.84 – 3.44 (m, 4H), 2.18 (s, 3H), 1.26 (t, $J = 7.0$ Hz, 6H).

^{13}C NMR (75 MHz, CDCl_3) δ 196.6, 168.9, 163.9 (d, $^1J_{\text{CF}} = 250.4$ Hz), 155.9, 131.7 (d, $^4J_{\text{CF}} = 3.4$ Hz), 129.6 (d, $^3J_{\text{CF}} = 8.6$ Hz), 115.3 (d, $^2J_{\text{CF}} = 22.1$ Hz), 103.9, 102.3, 63.1, 25.1, 15.3.

^{19}F NMR (282 MHz, CDCl_3) δ -111.15 – -111.24 (m).

Mass (ESI) MH^+ 310

(*Z*)-*N*-(1-(4-bromophenyl)-4,4-diethoxy-3-oxobut-1-en-1-yl)acetamide **1u**



Pink oil, 67% yield (237 mg).

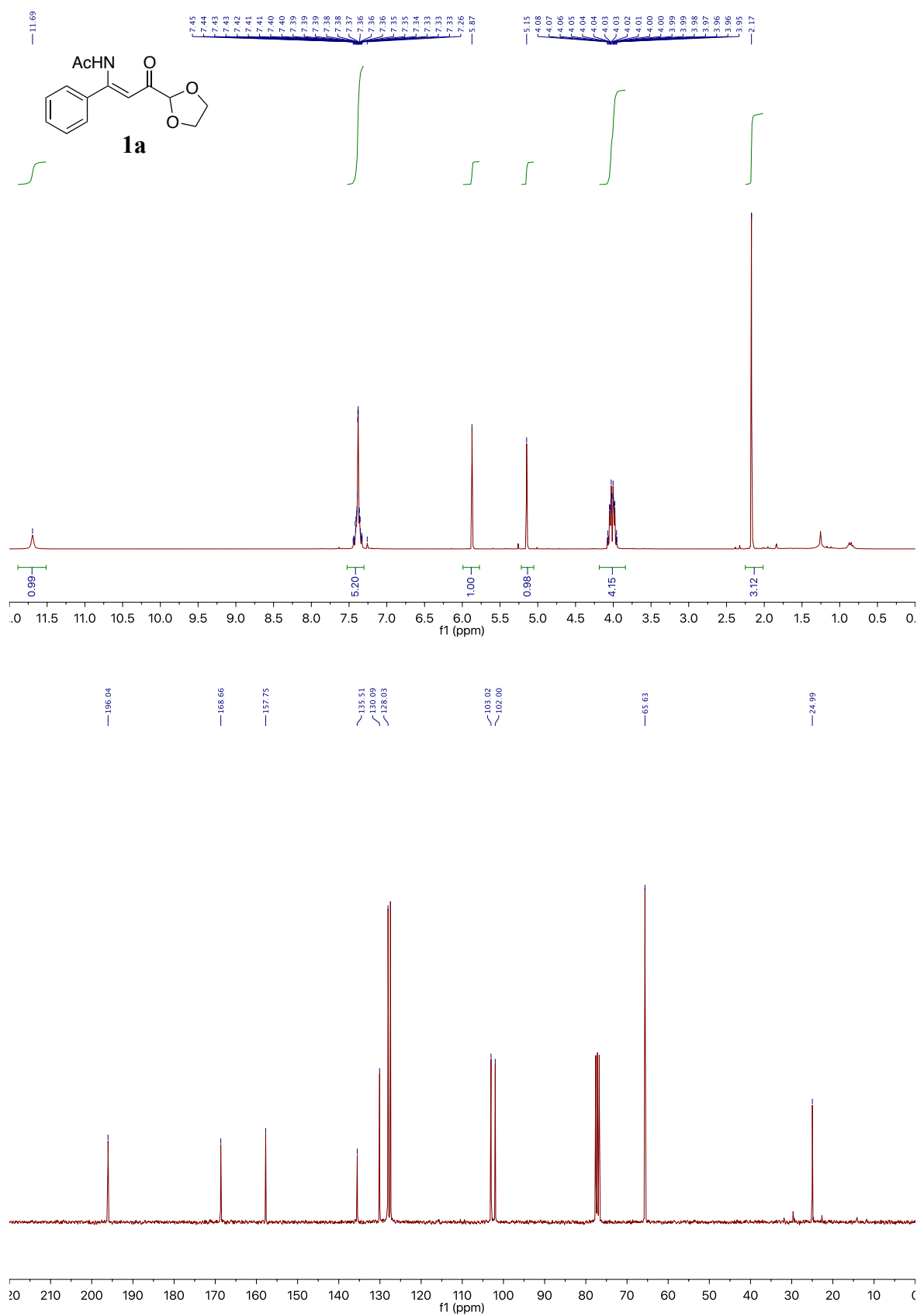
Chemical Formula: C₁₆H₂₀BrNO₄

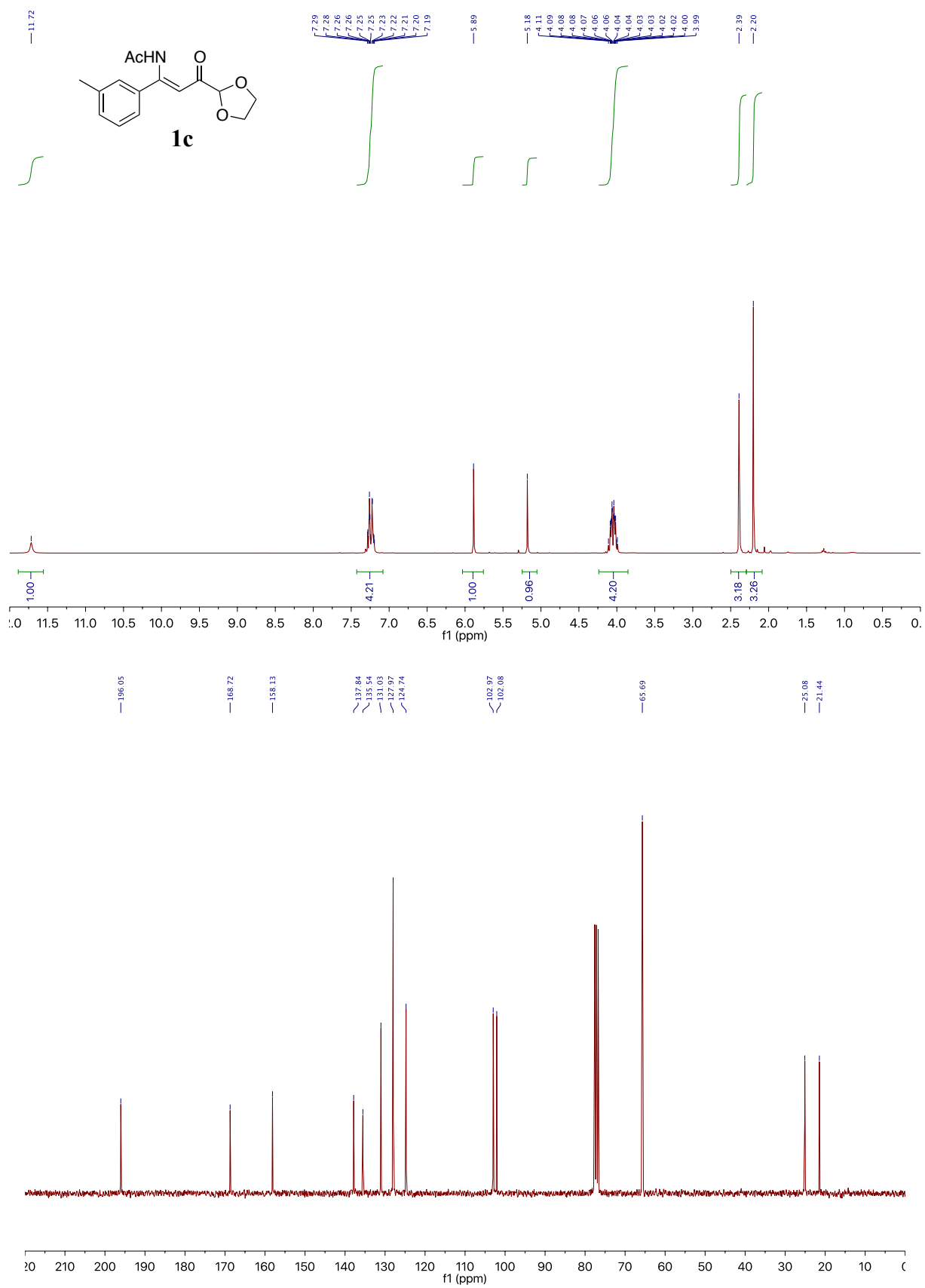
¹H NMR (300 MHz, CDCl₃) δ 11.66 (s, 1H), 7.50 (d, *J* = 8.5 Hz, 2H), 7.27 (d, *J* = 8.5 Hz, 2H), 5.98 (s, 1H), 4.70 (s, 1H), 3.85 – 3.42 (m, 4H), 2.19 (s, 3H), 1.26 (t, *J* = 7.0 Hz, 6H).

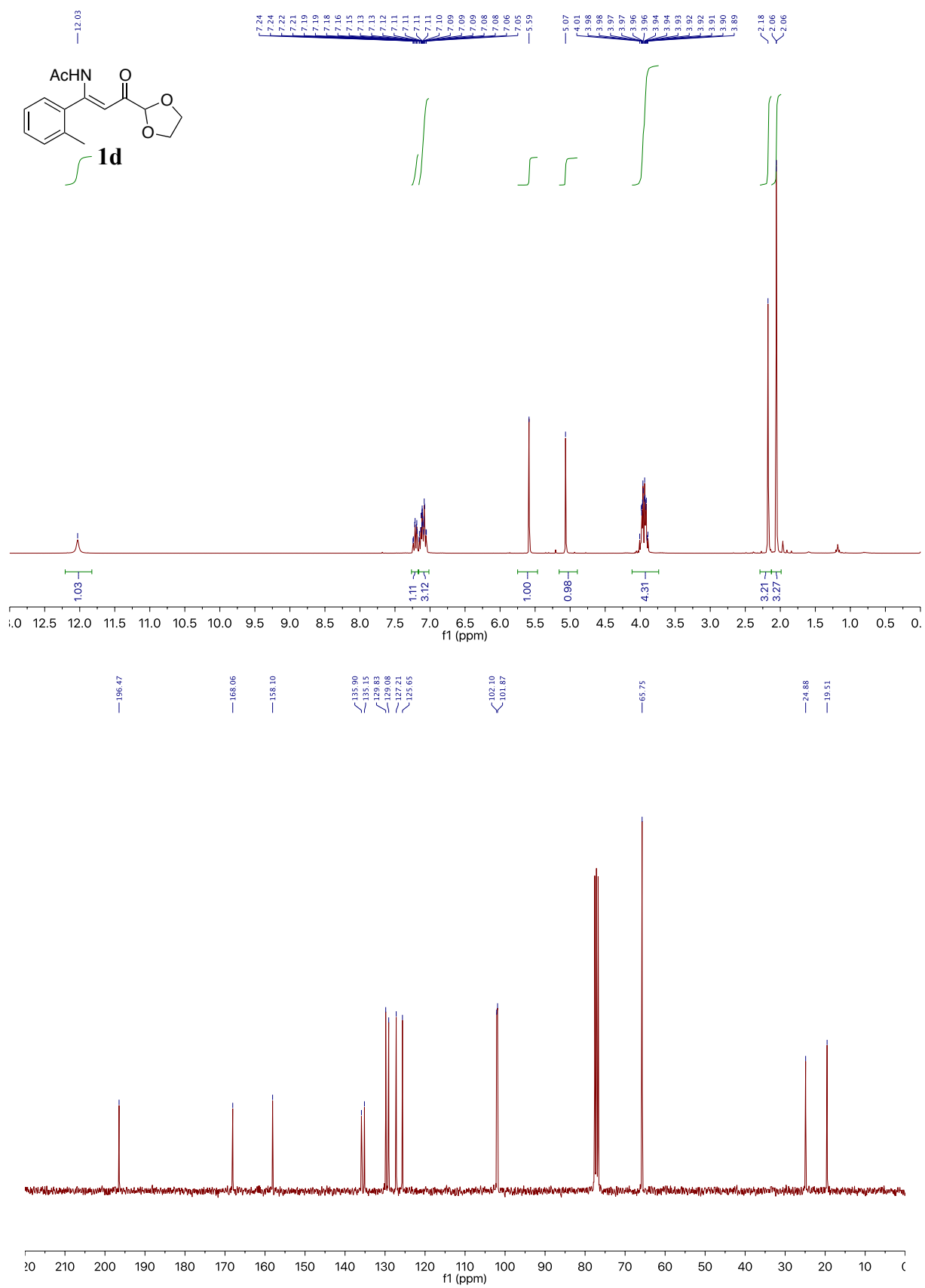
¹³C NMR (75 MHz, CDCl₃) δ 196.7, 168.9, 155.8, 134.7, 131.4, 129.2, 124.5, 104.1, 102.3, 63.2, 25.1, 15.3.

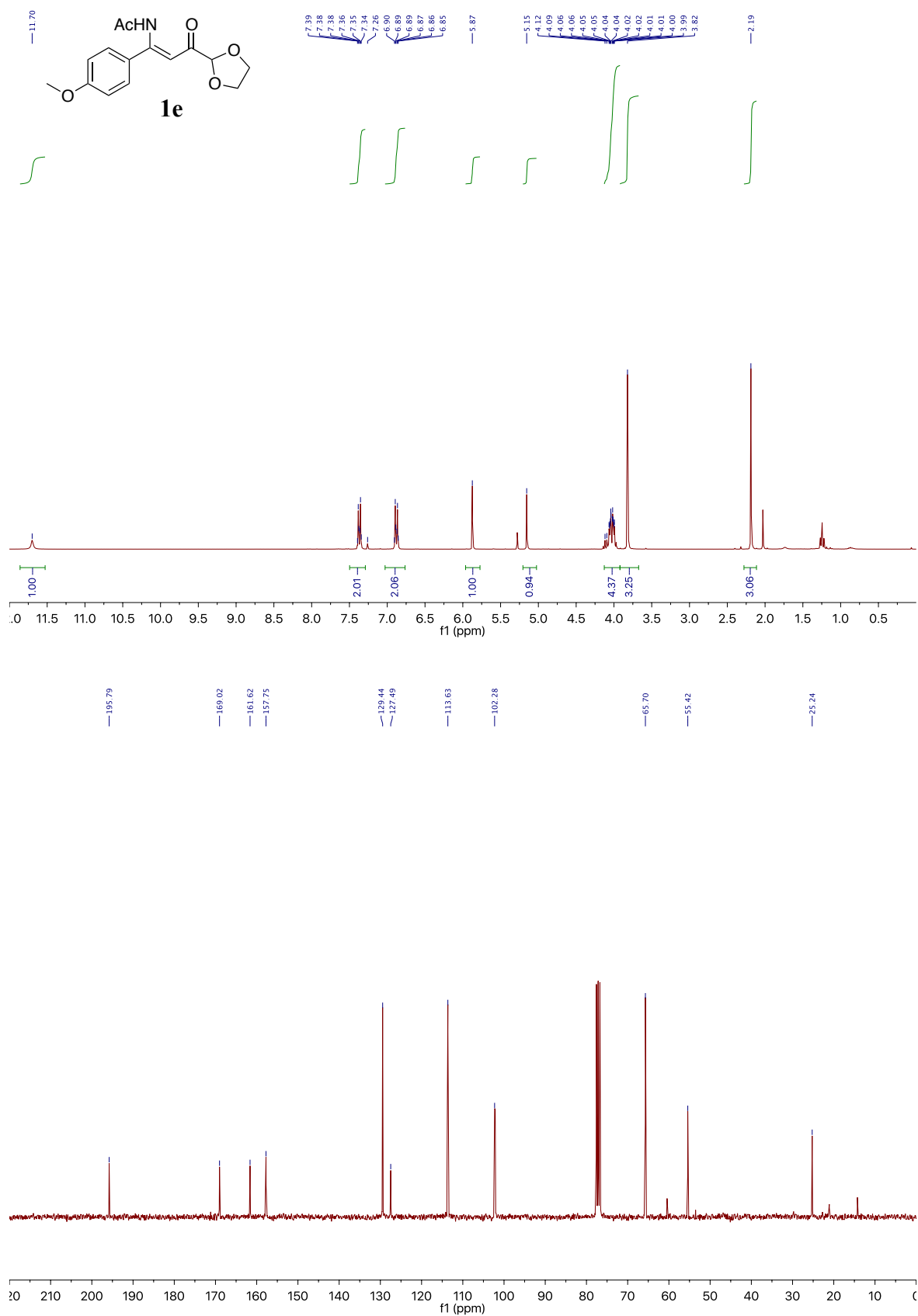
Mass (ESI) MH⁺ 272

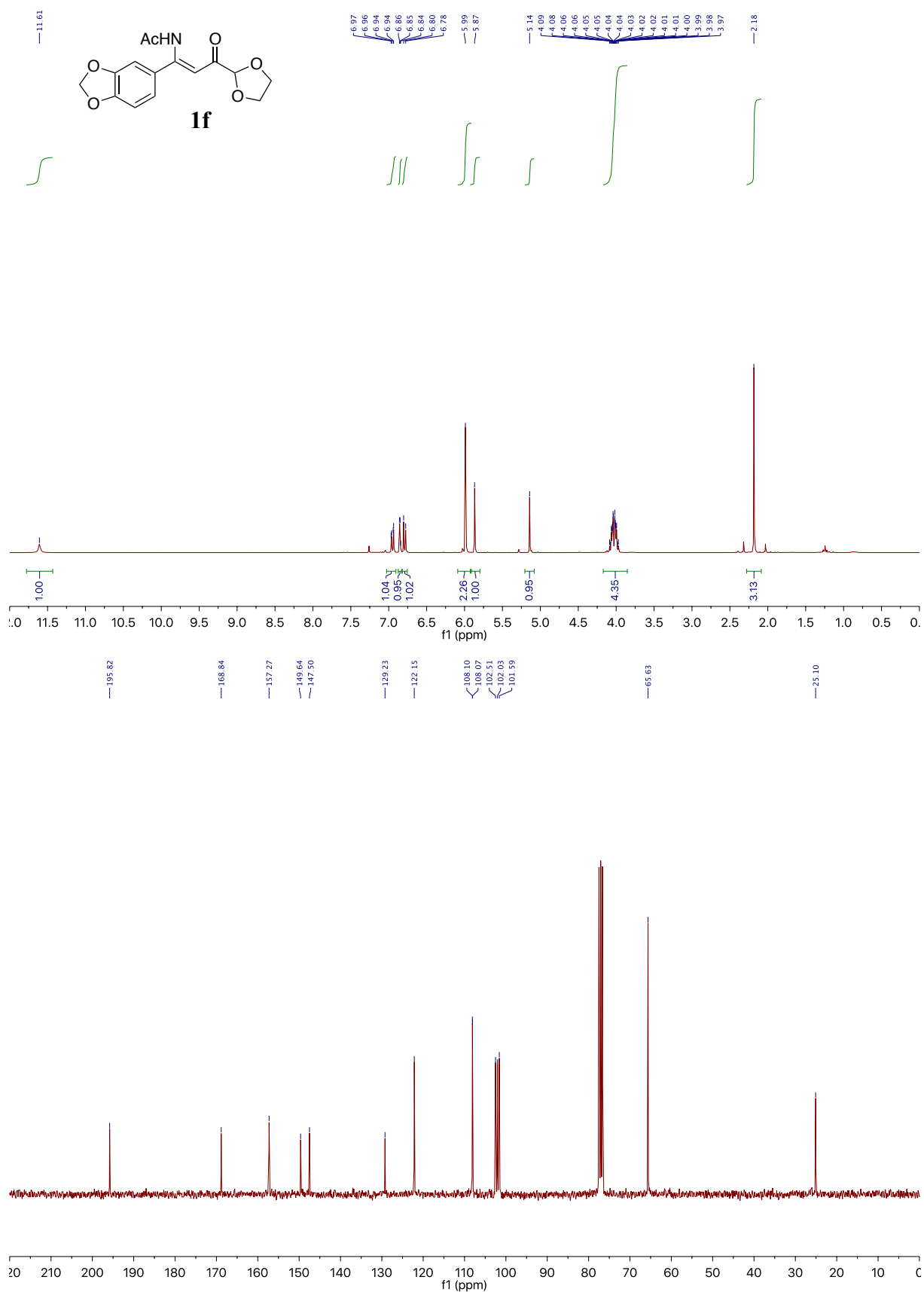
7. NMR spectra of compounds 1a – 1u

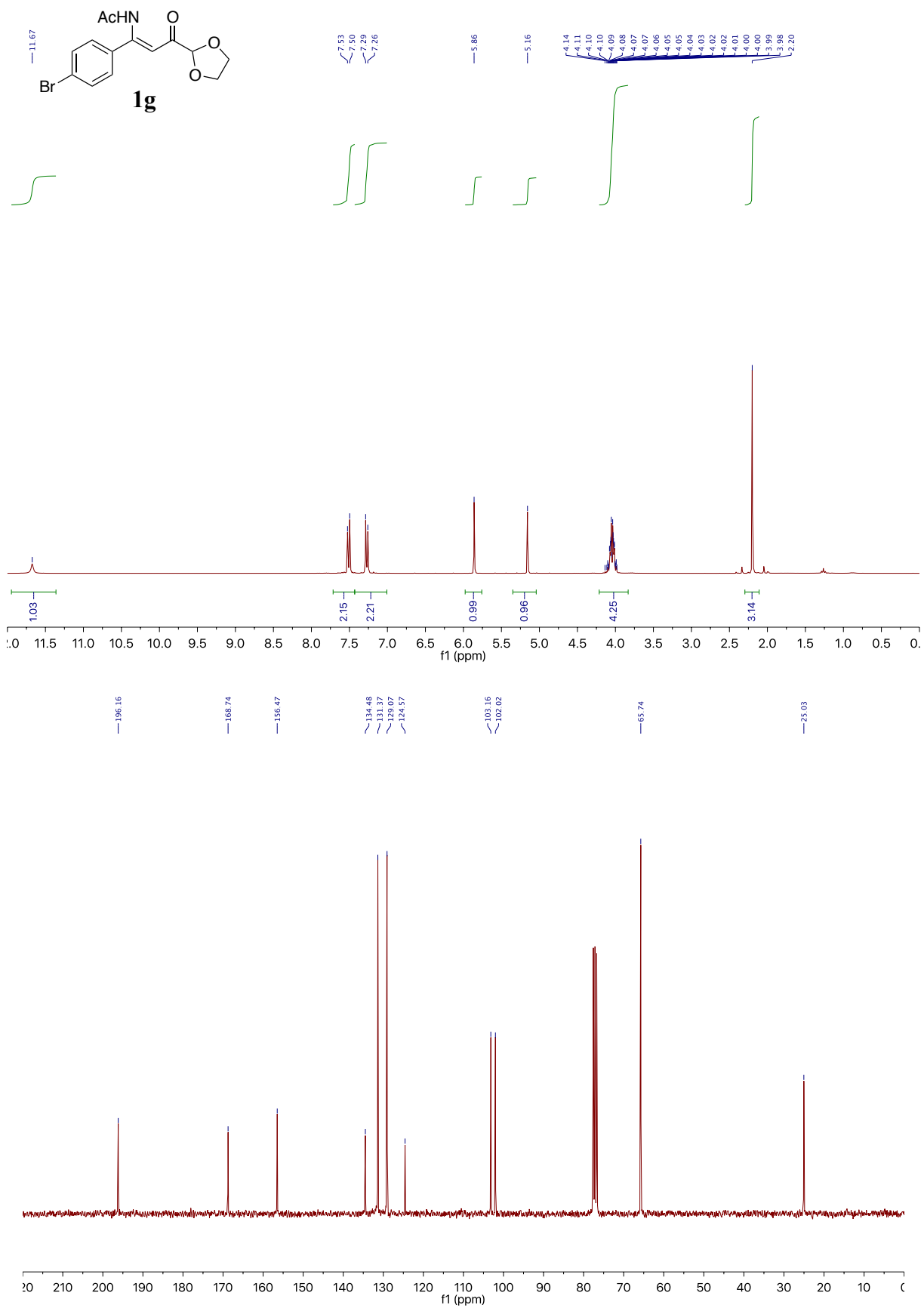


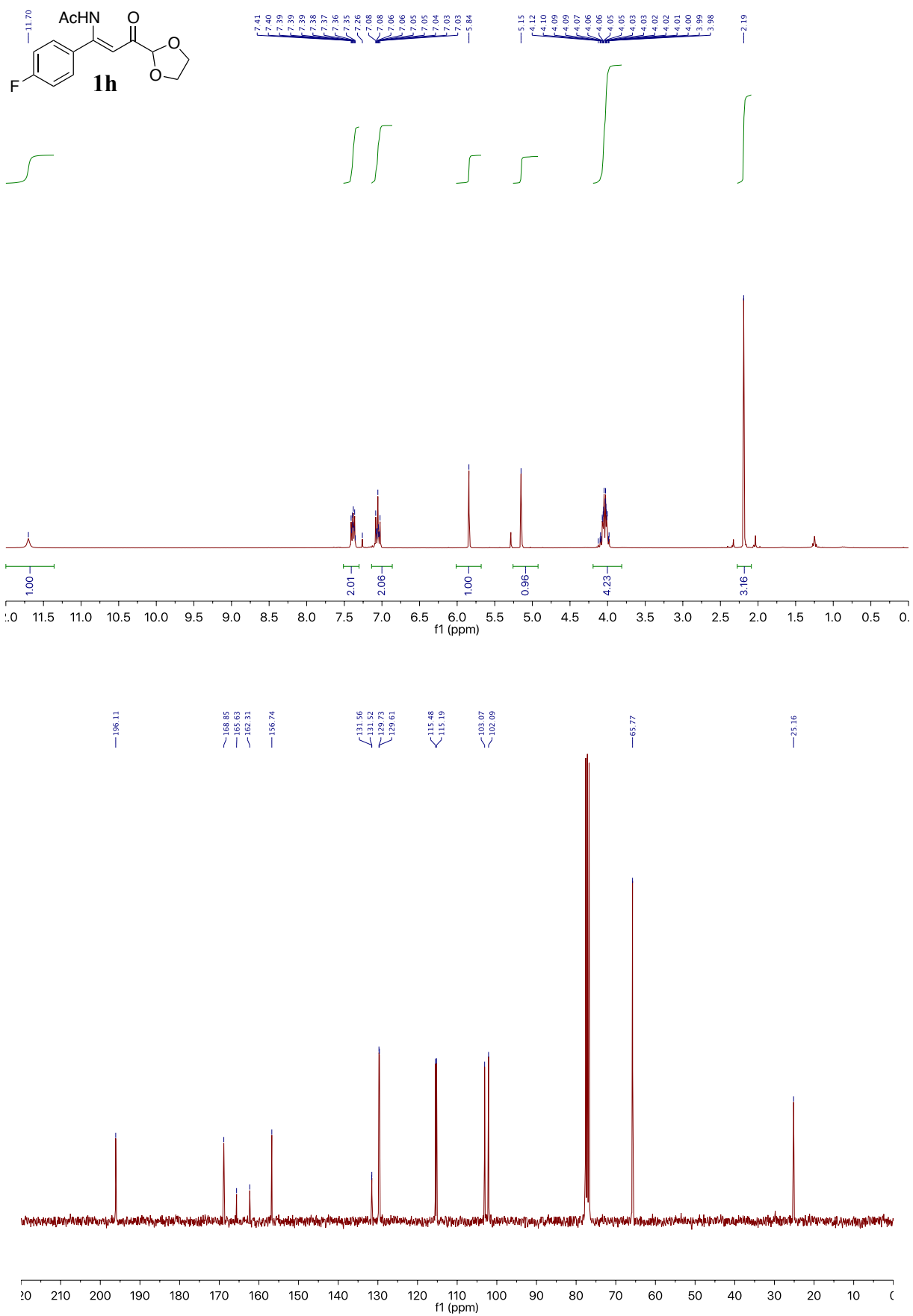


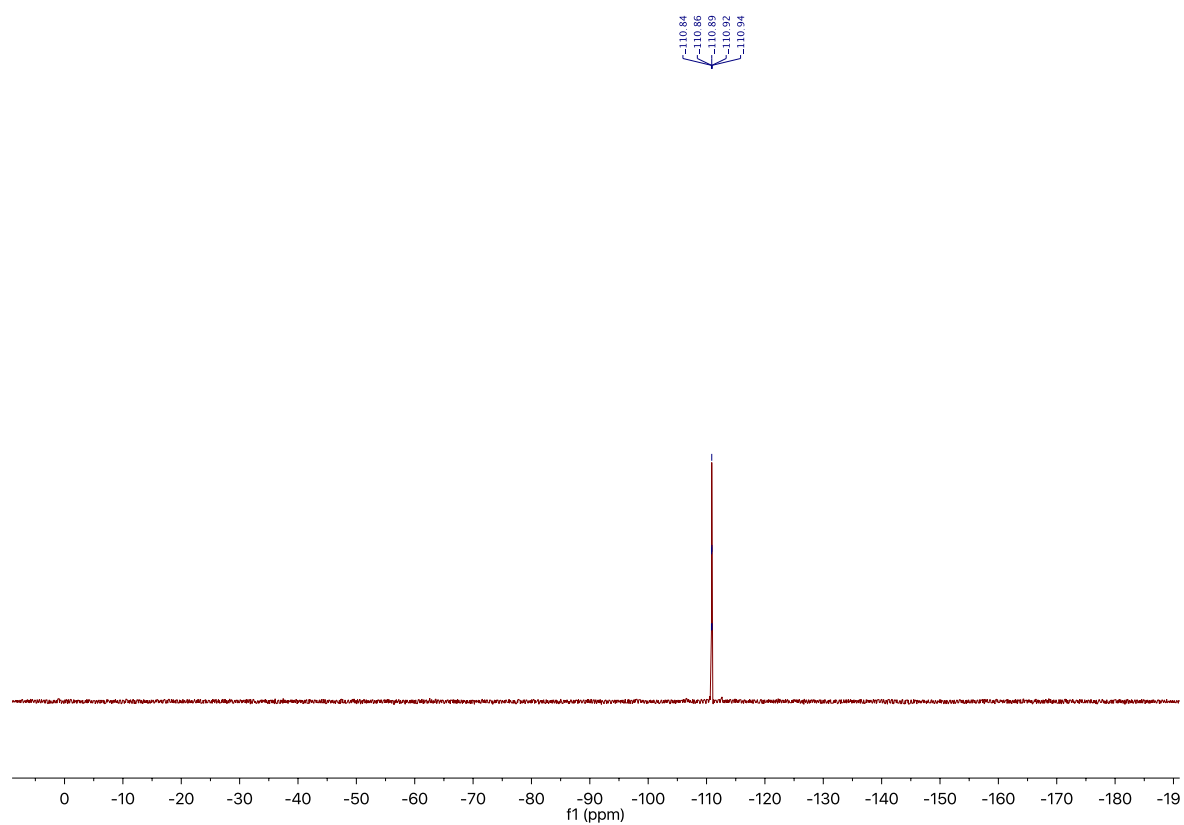


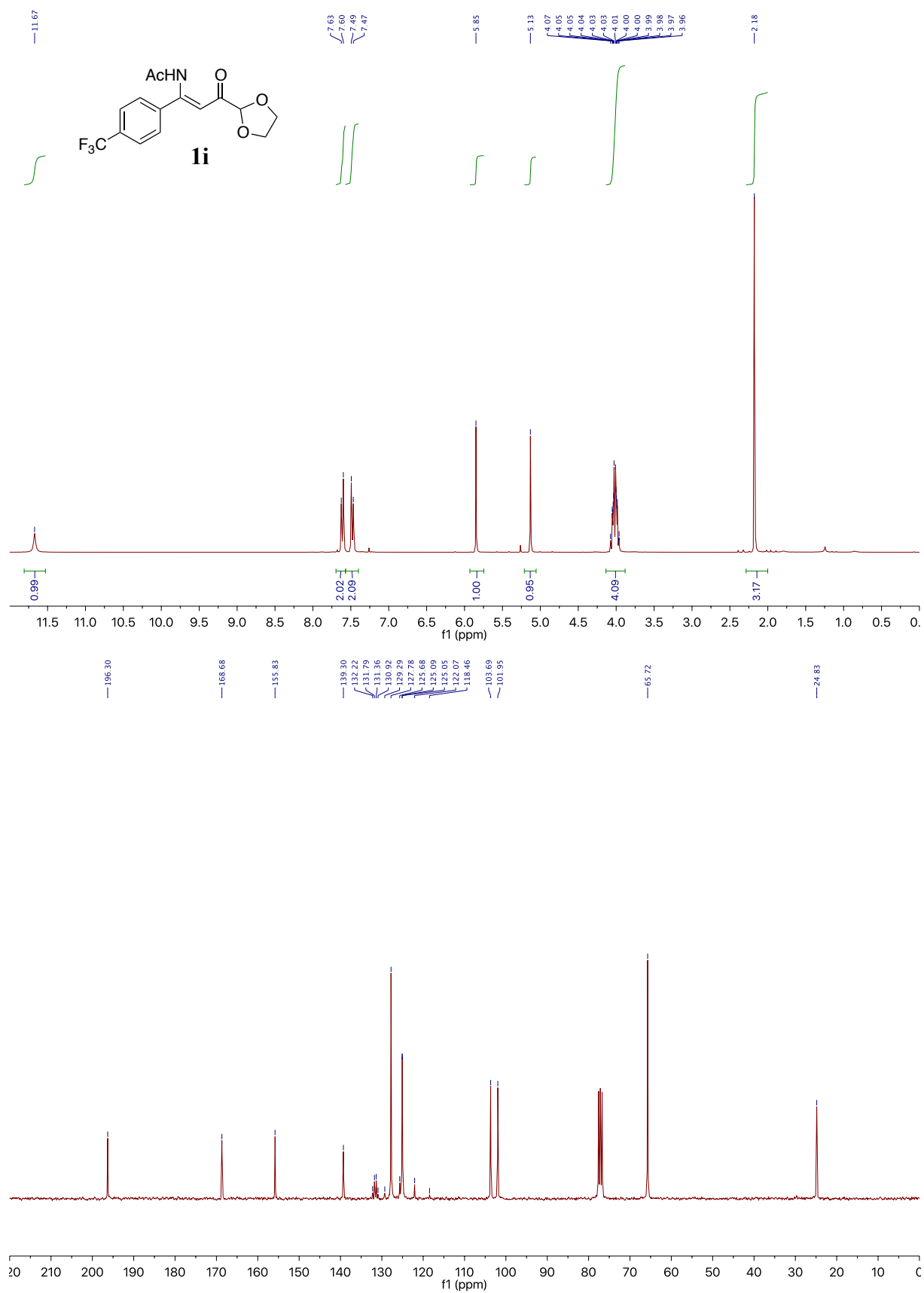


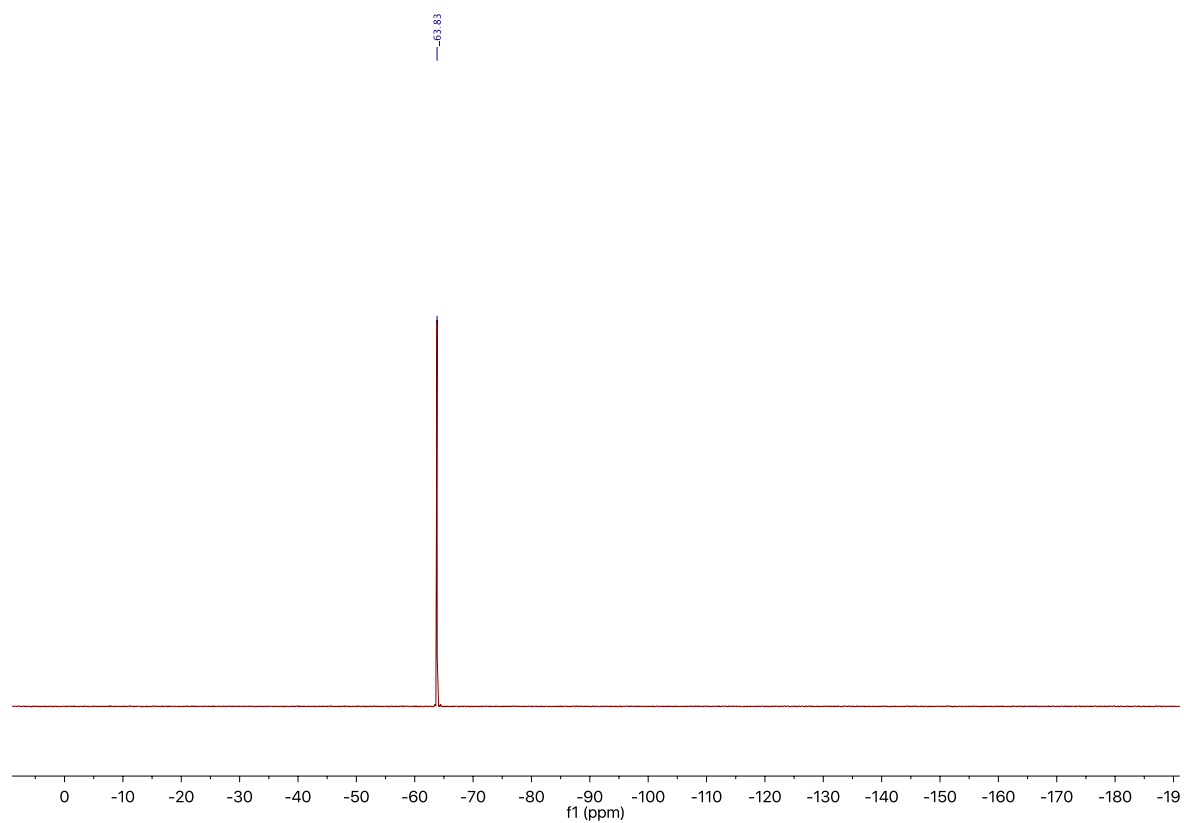


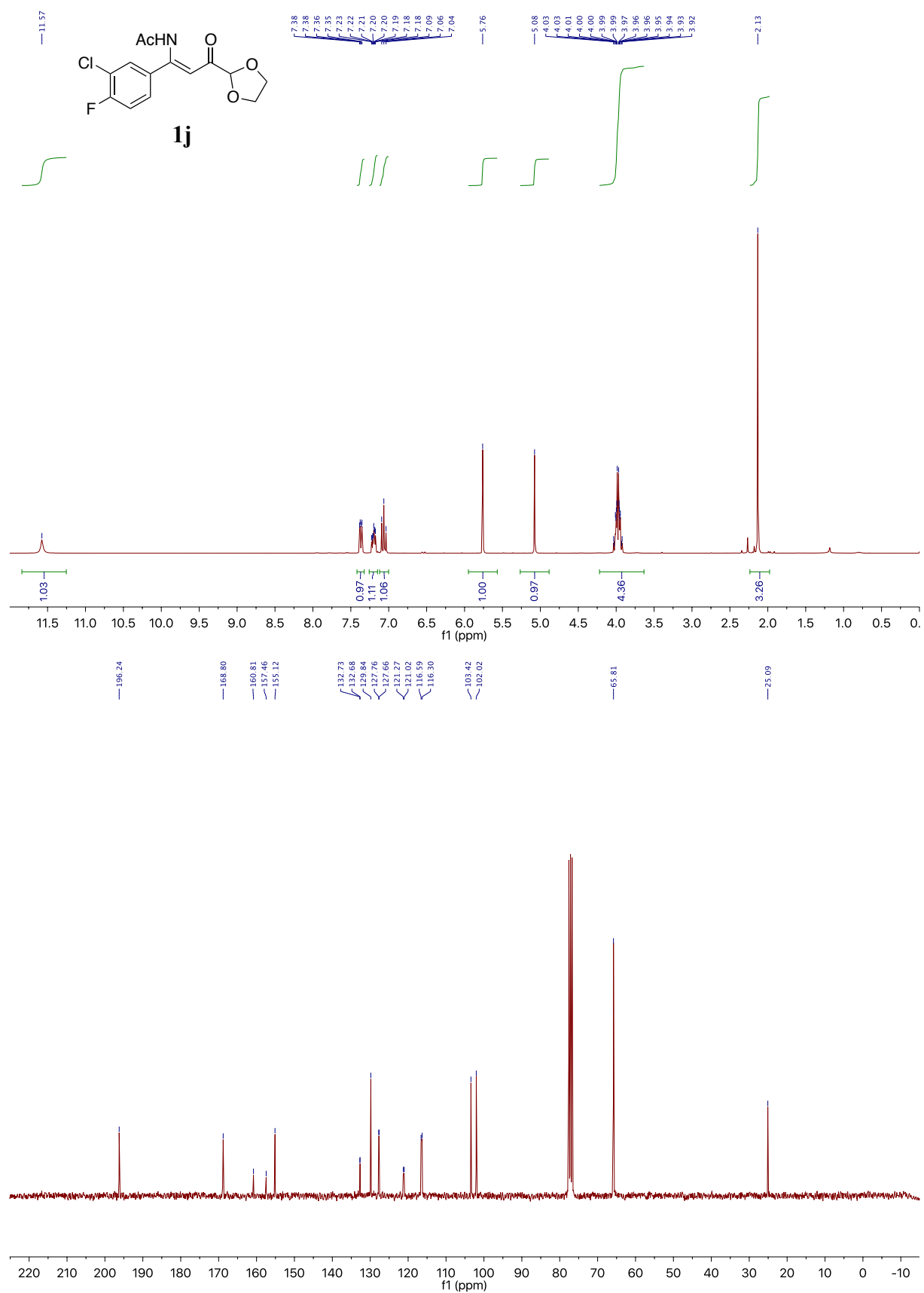


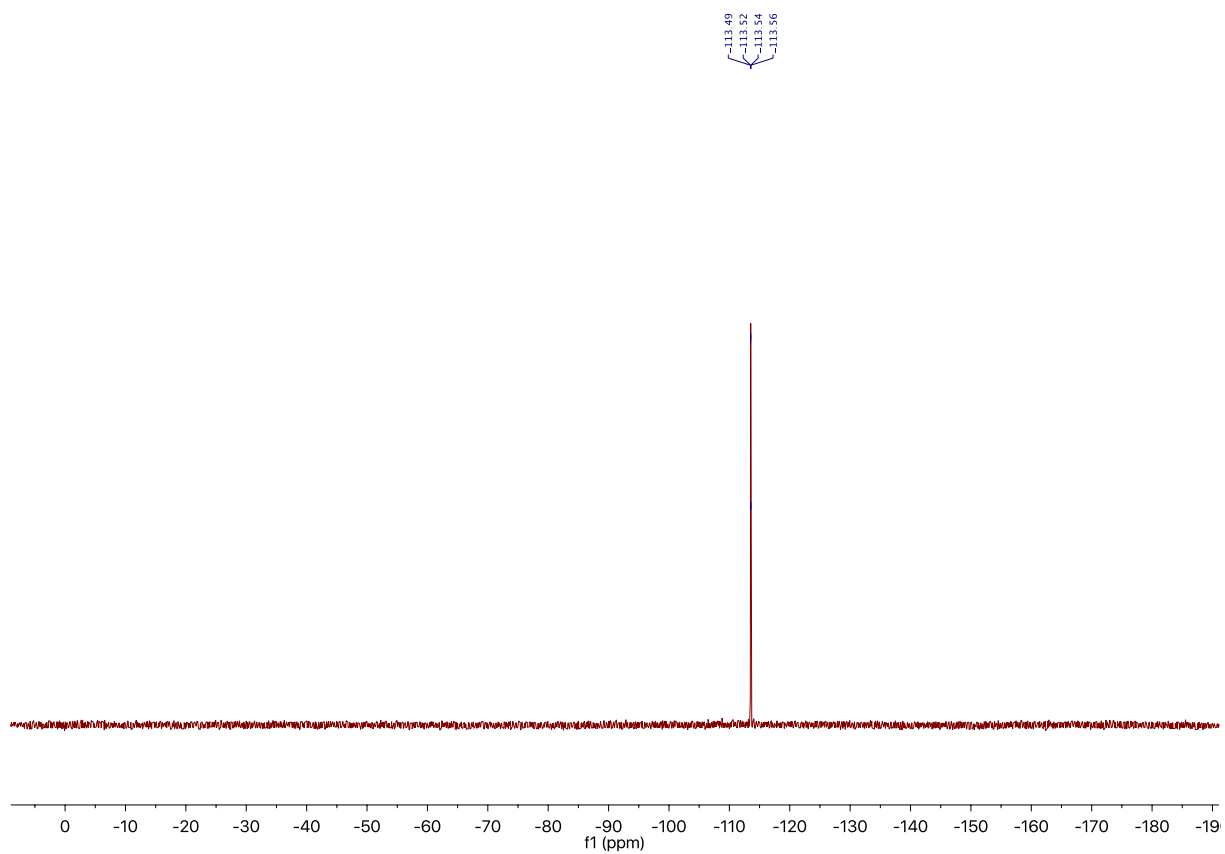


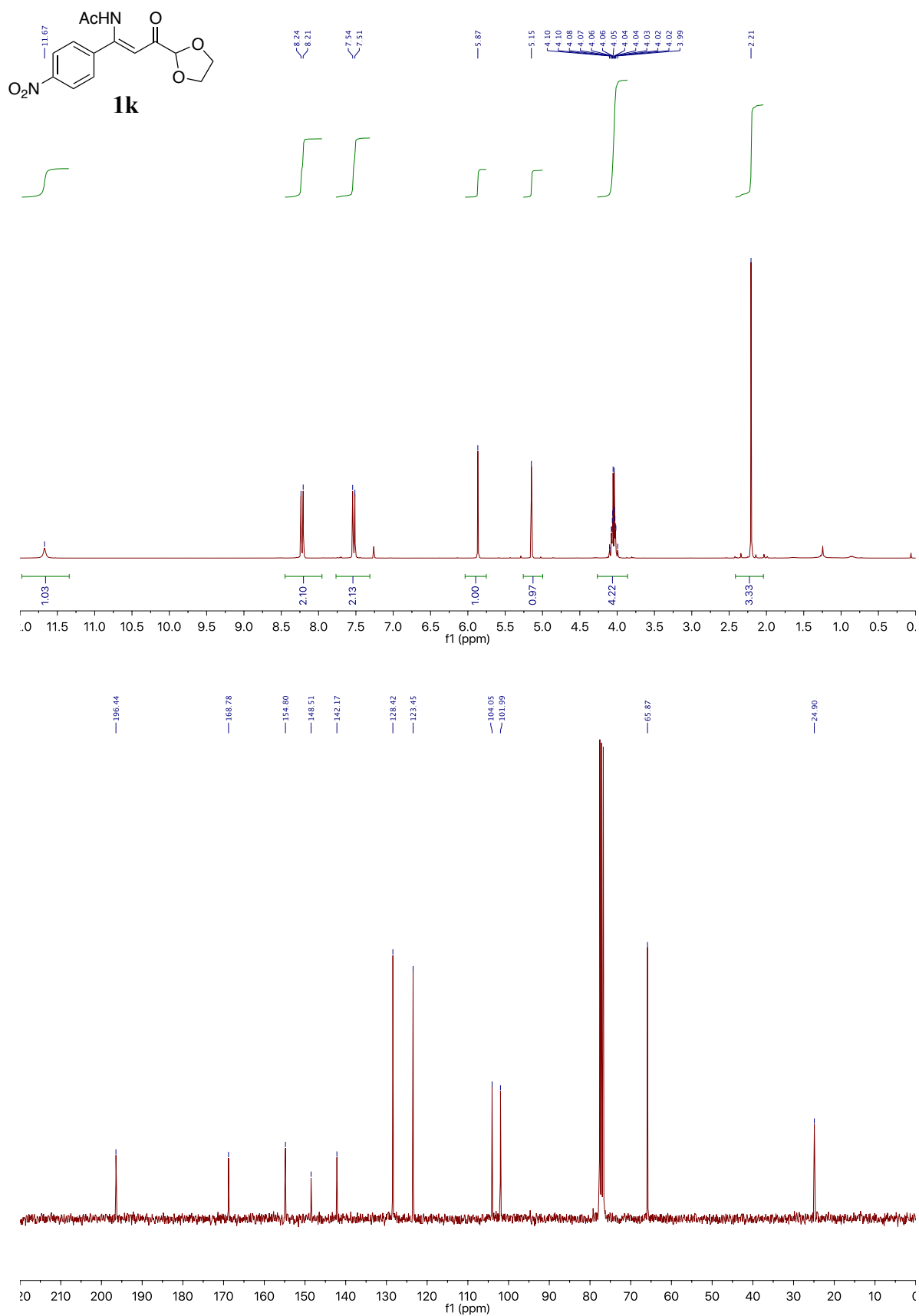




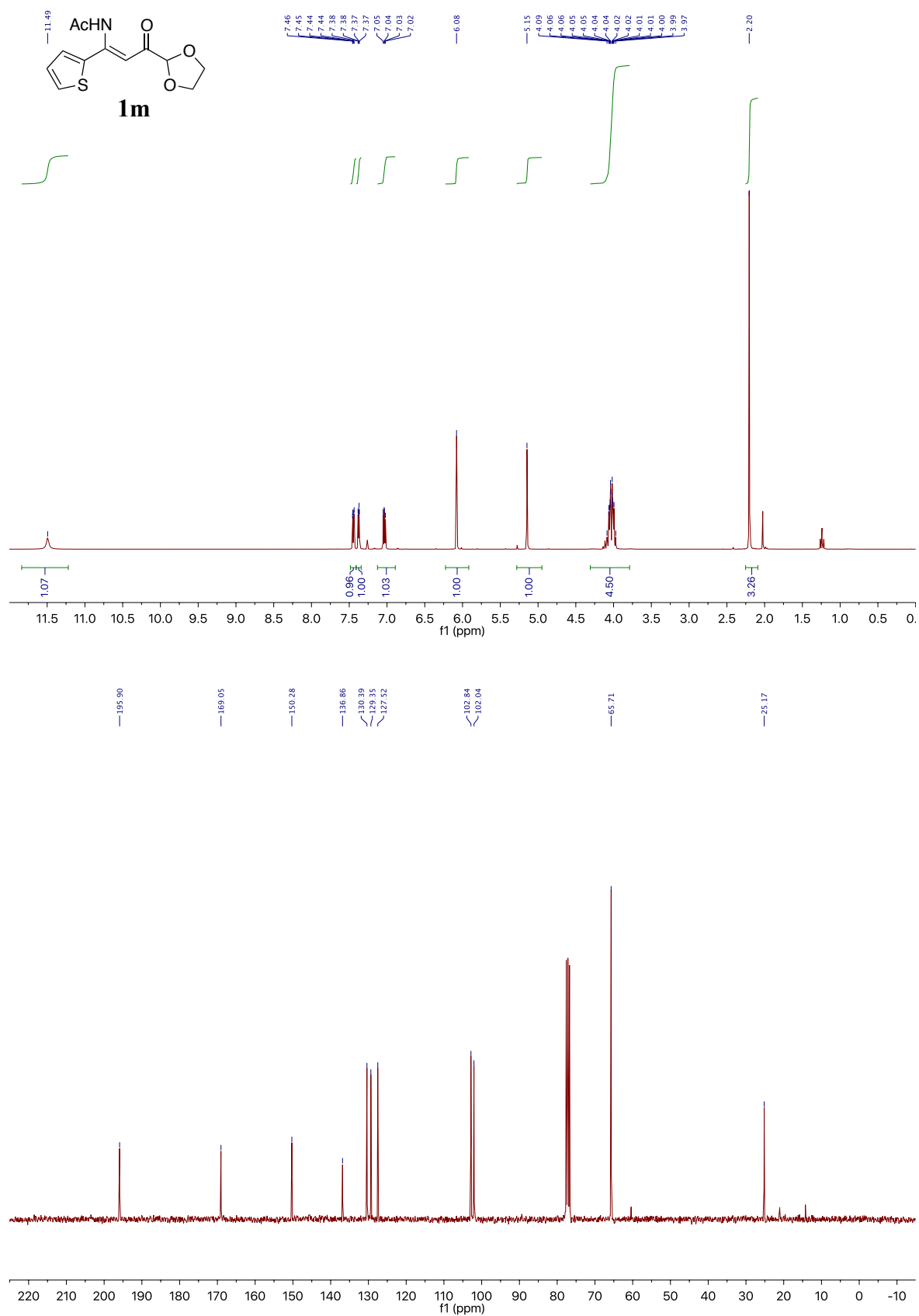


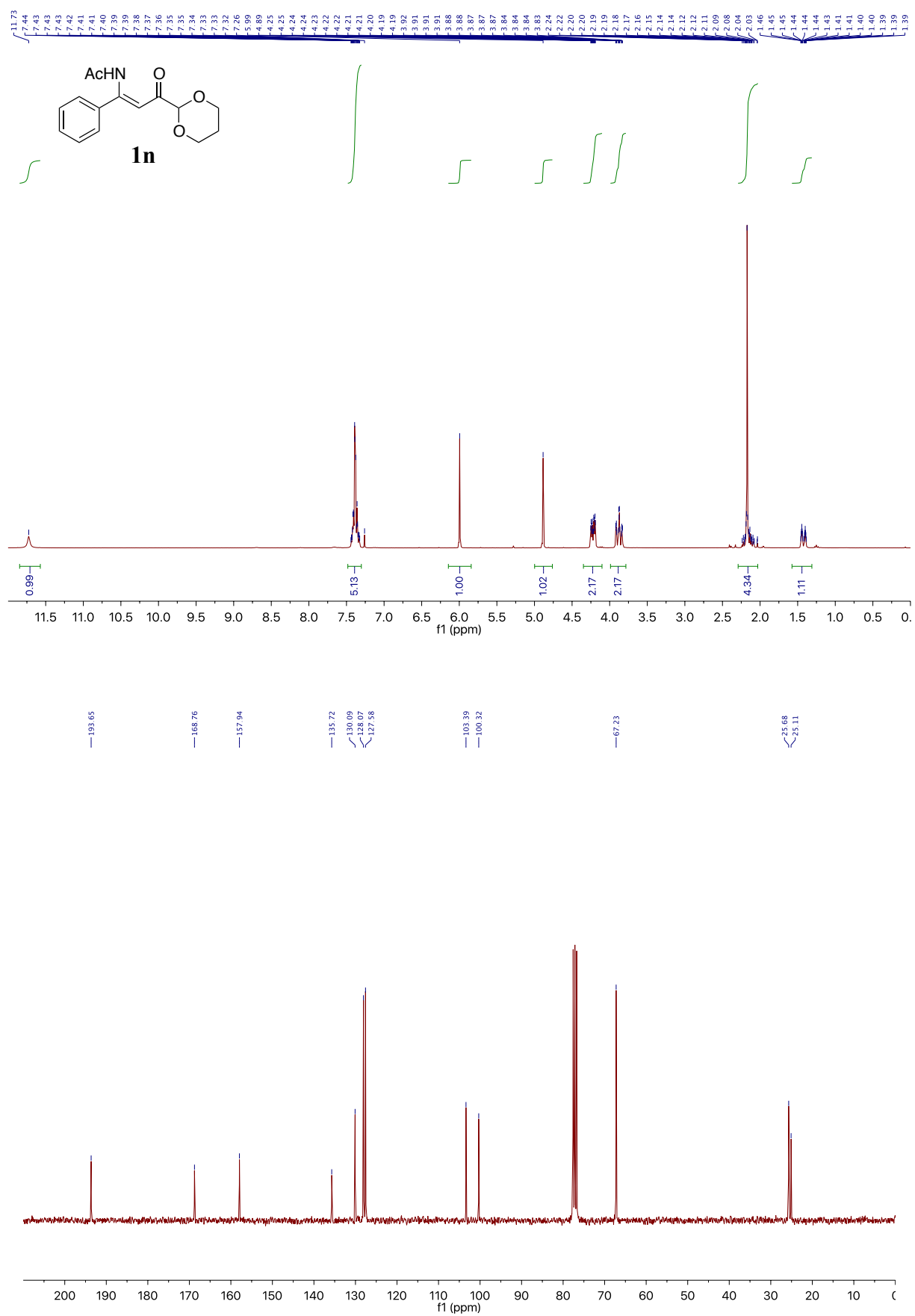


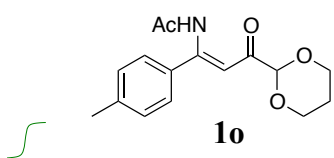


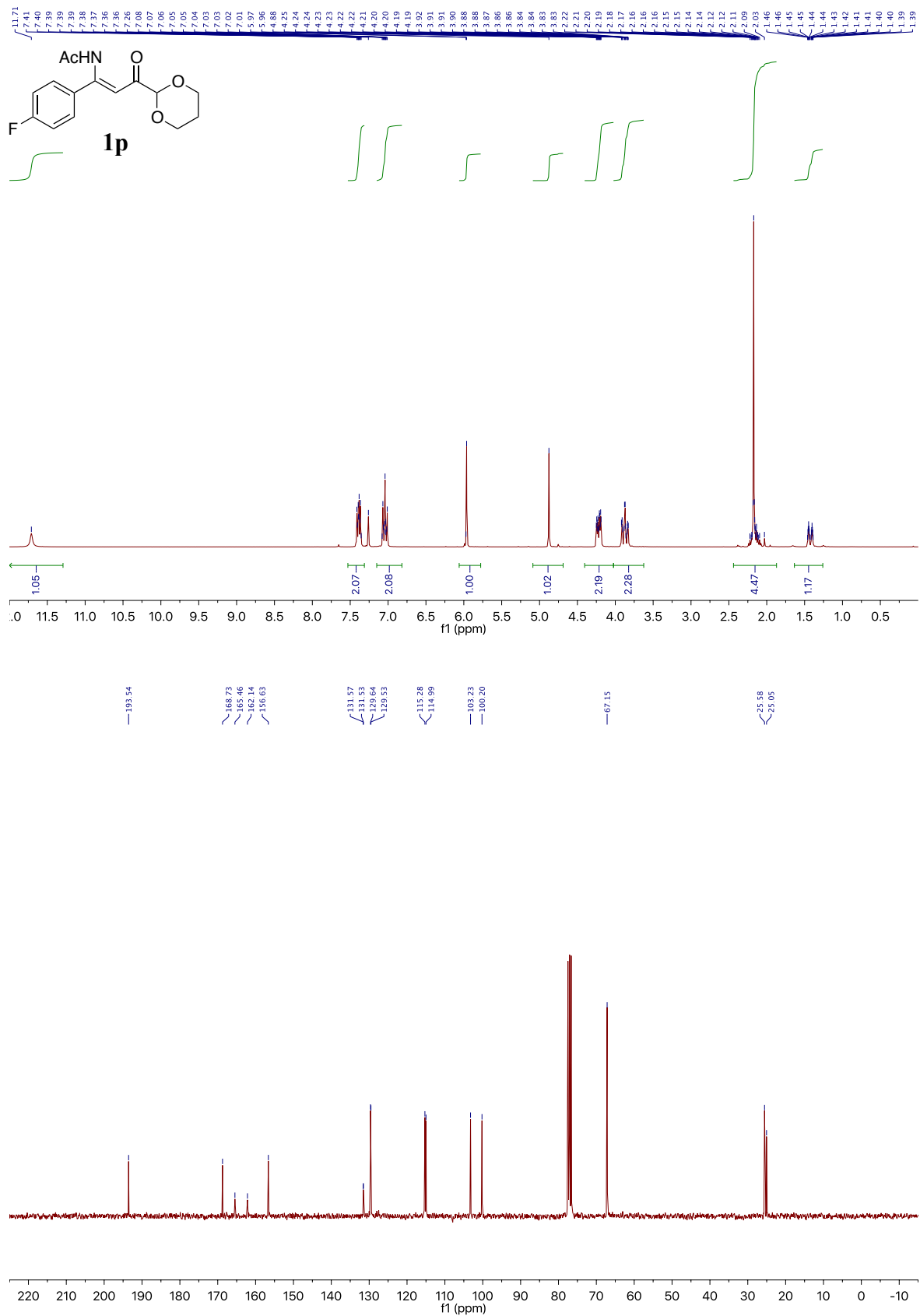


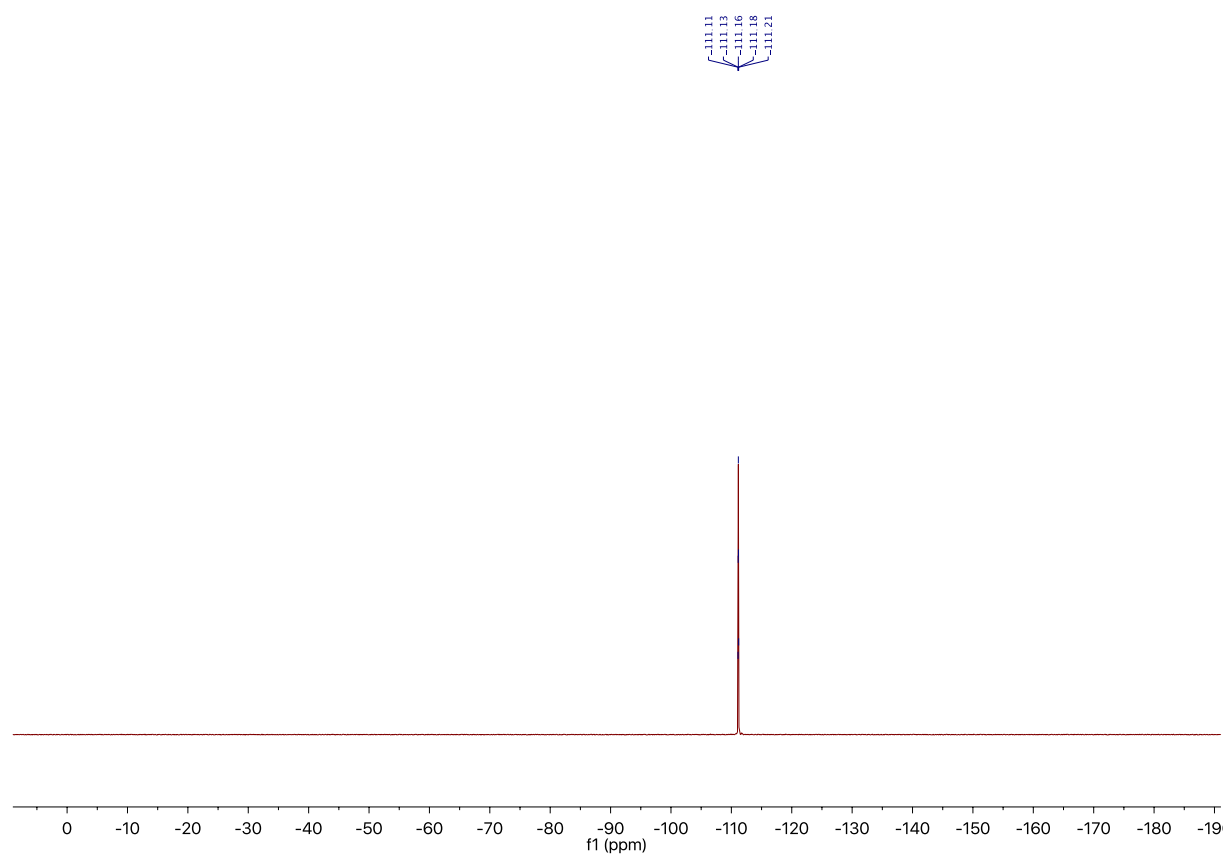


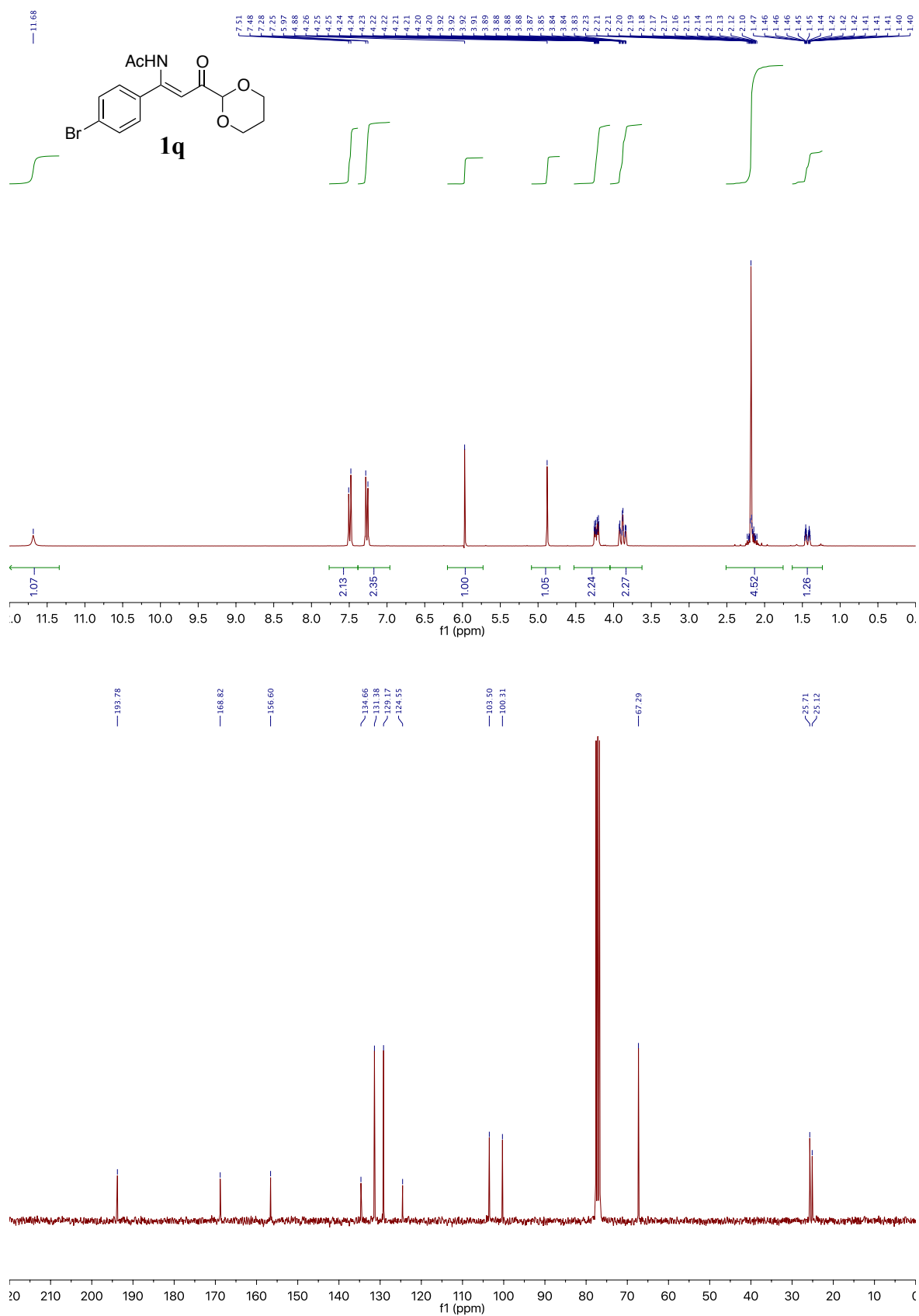


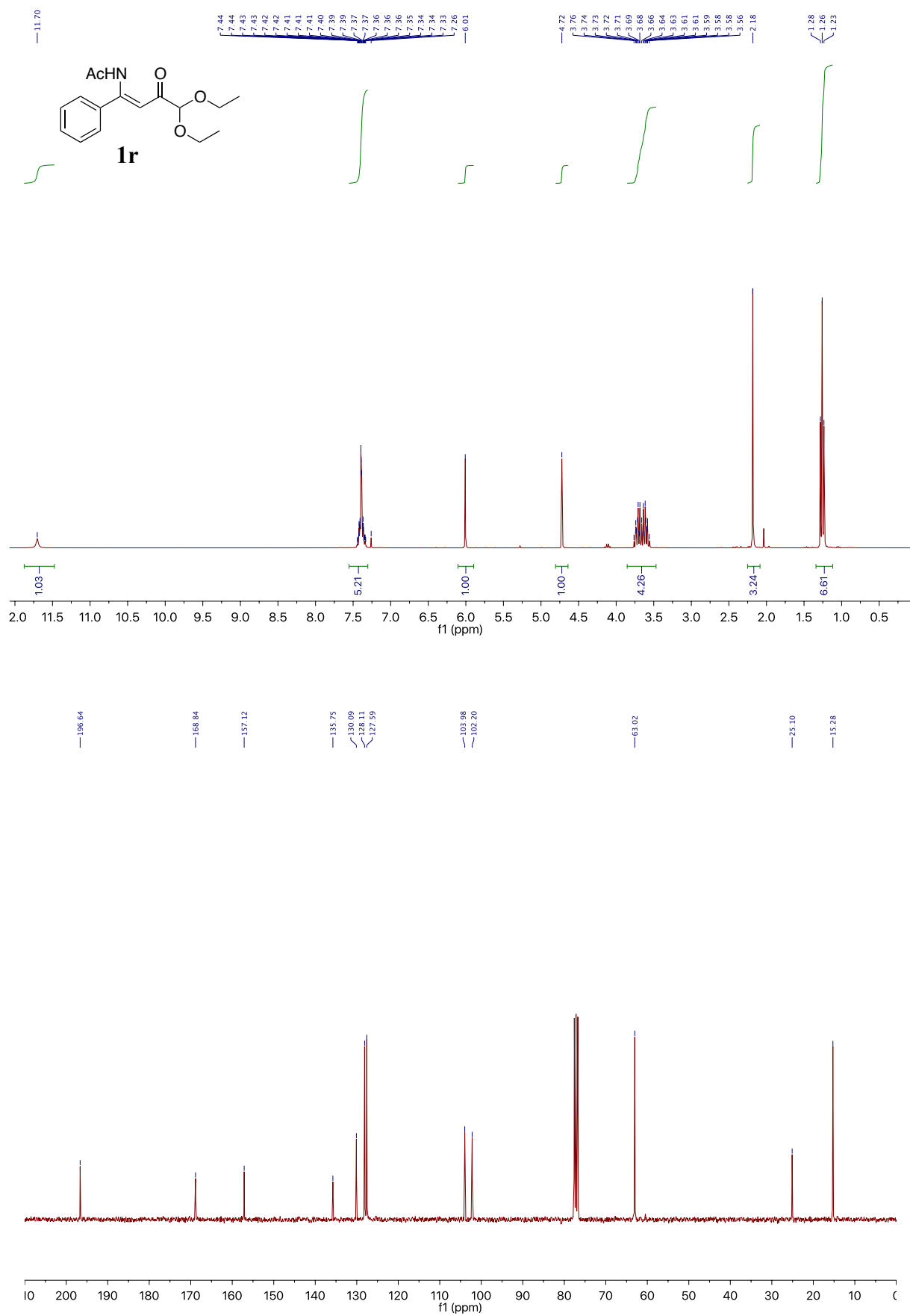


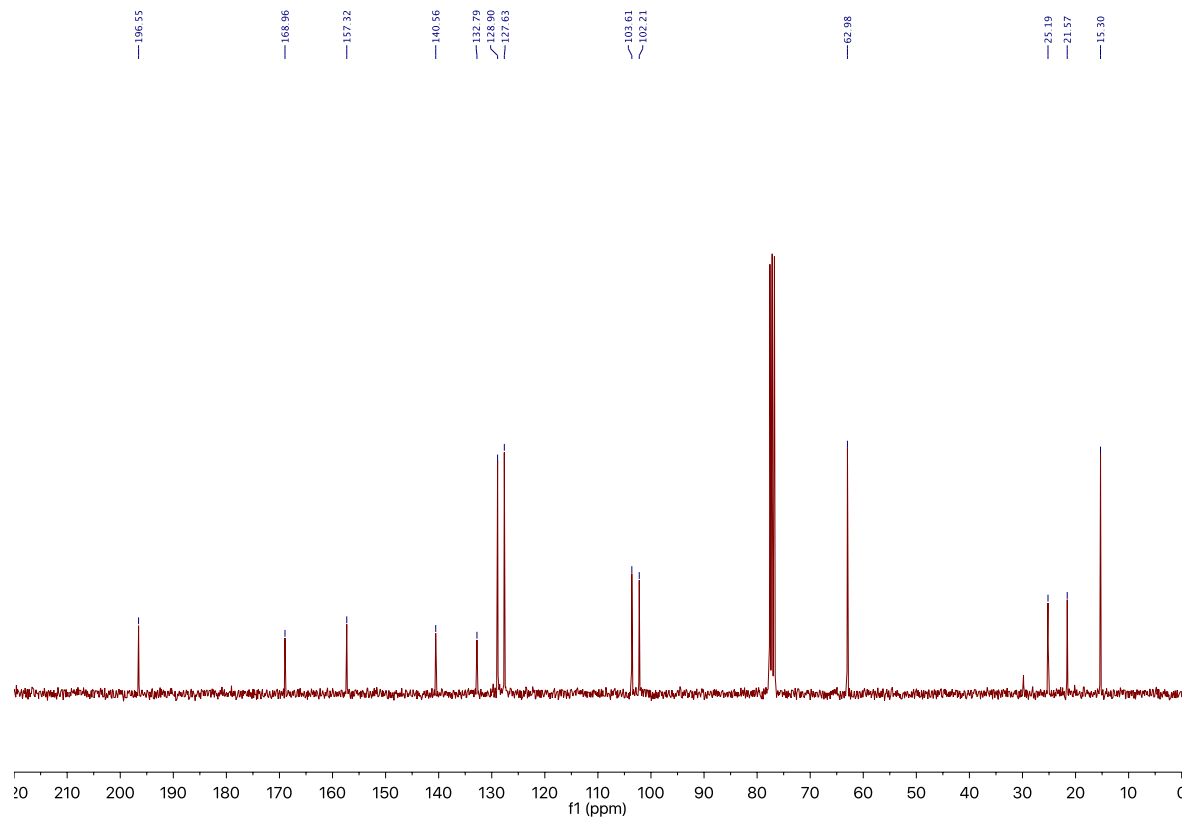
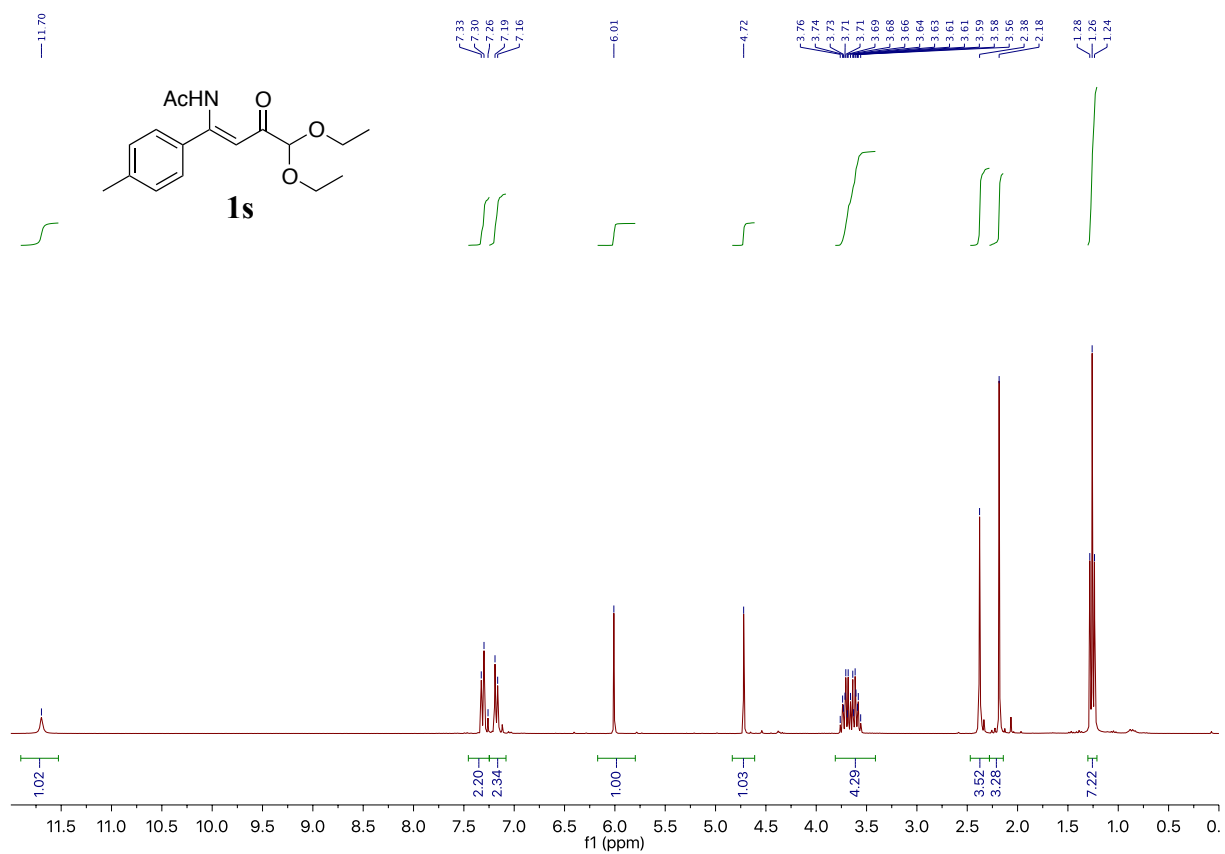


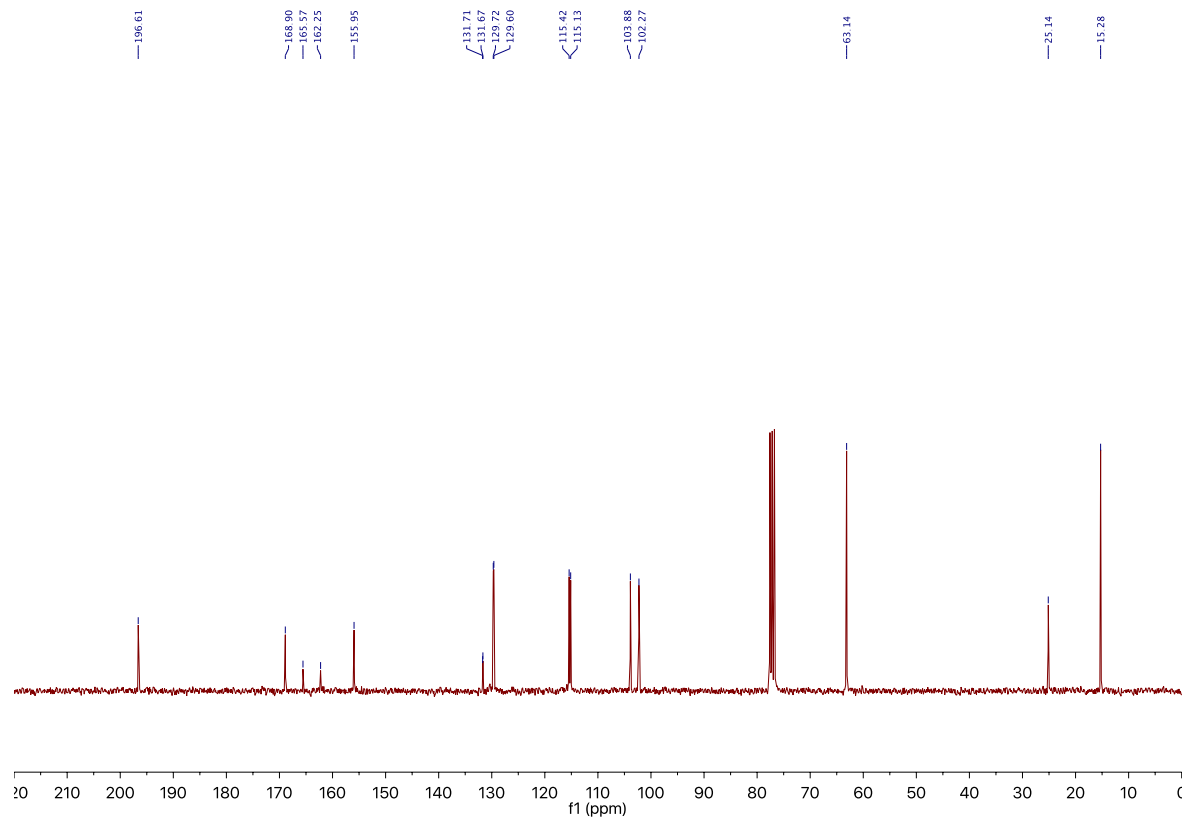
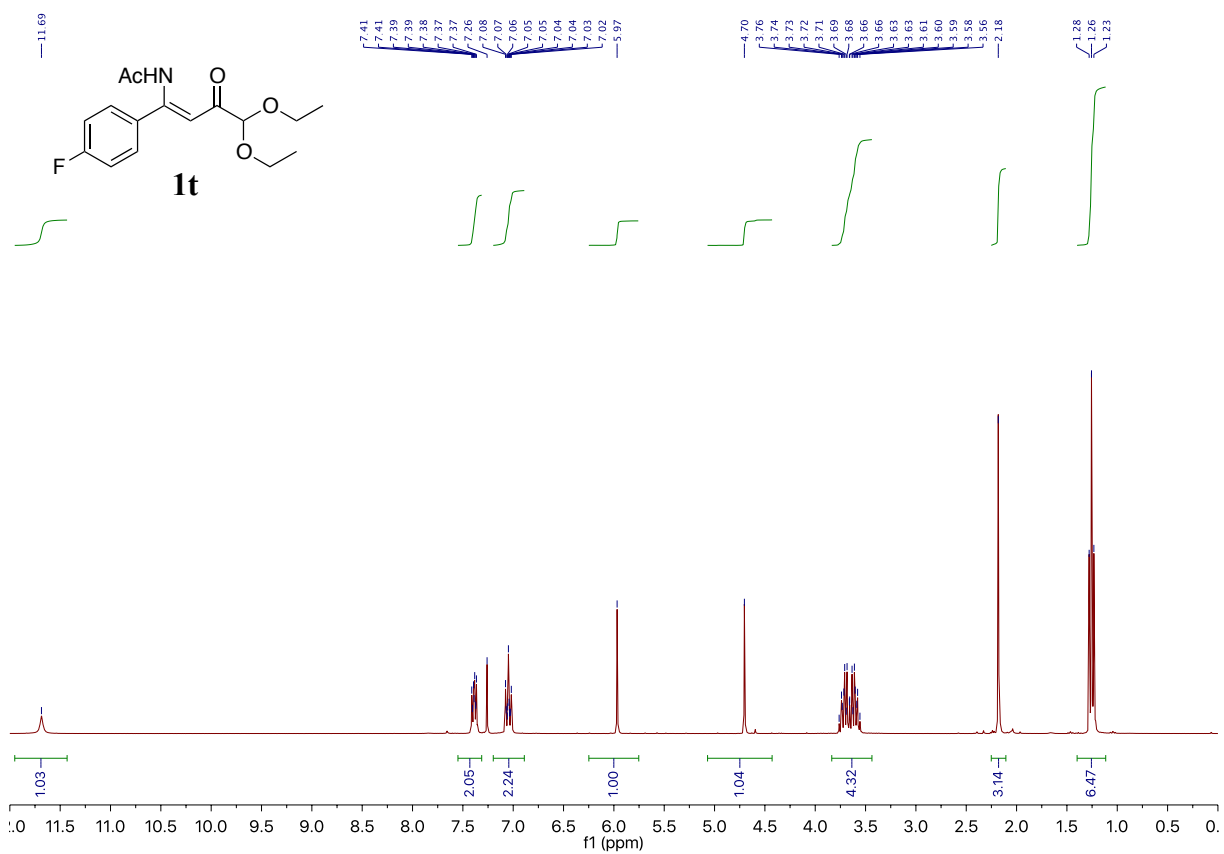


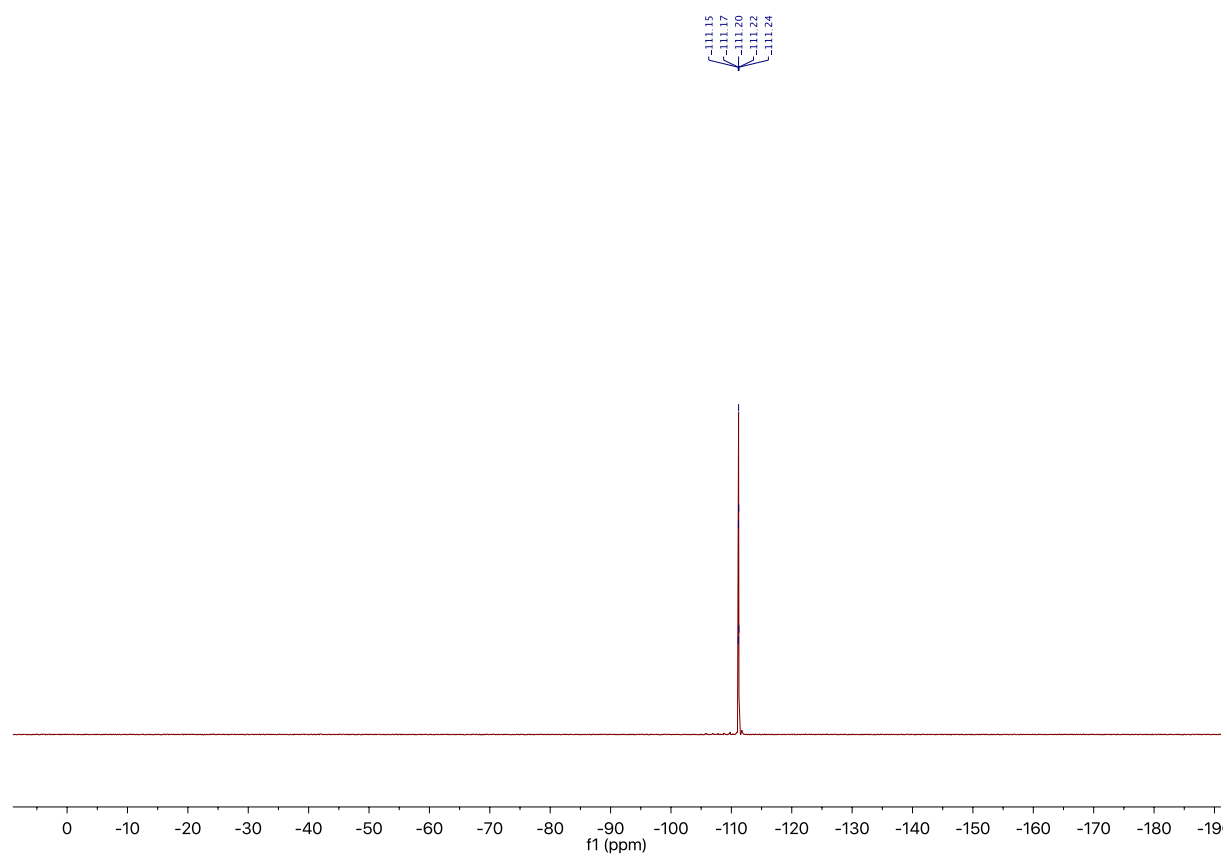


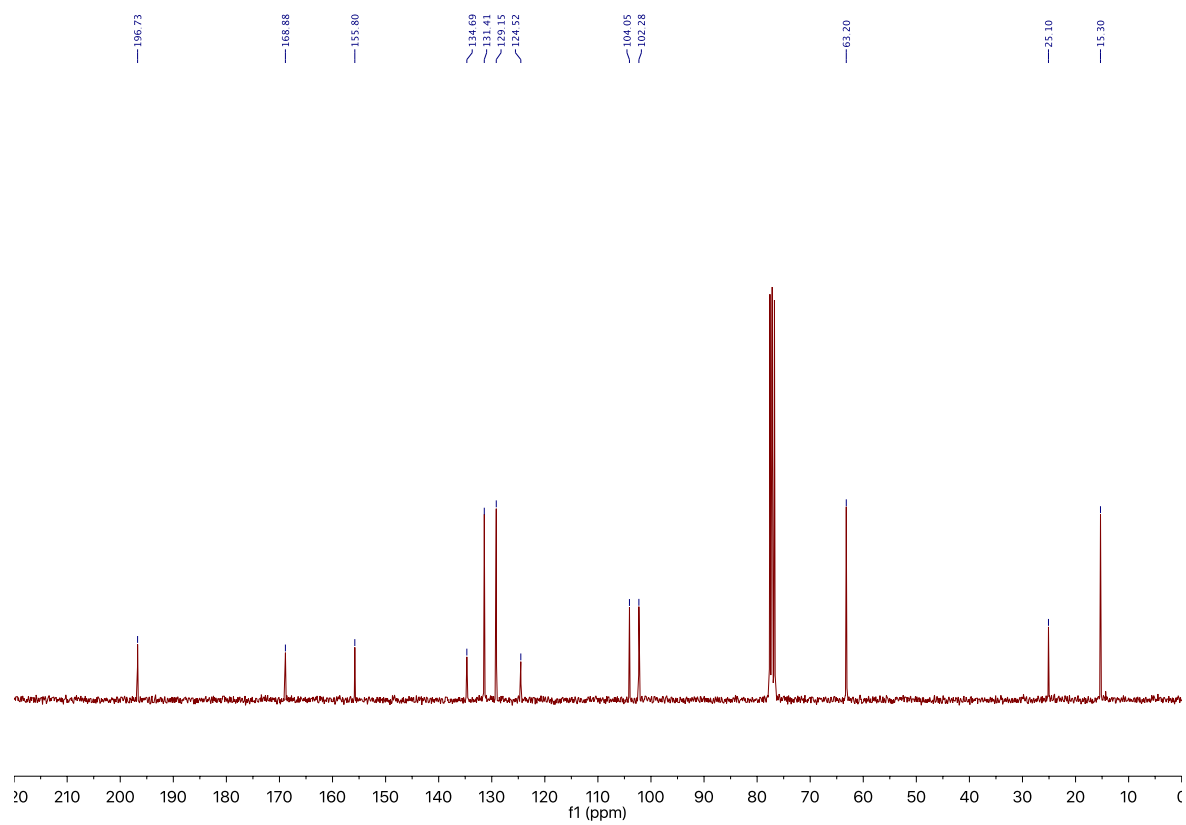
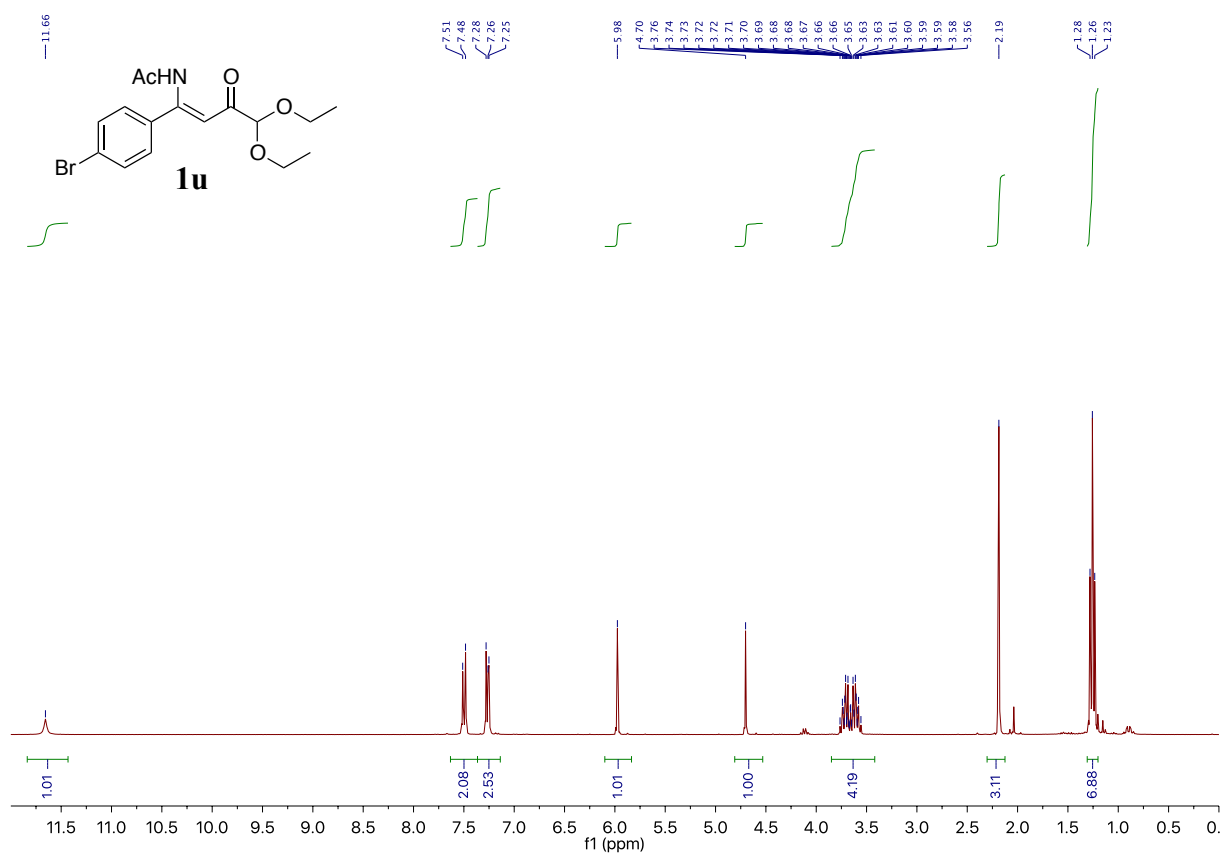






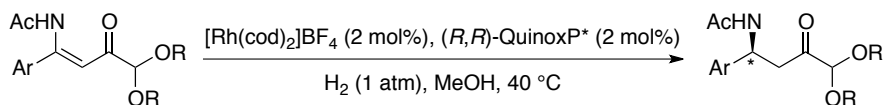






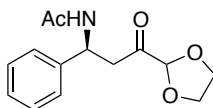
8. Asymmetric hydrogenation of enamides

General procedure



In a Schlenk flask under argon were introduced $[\text{Rh}(\text{cod})_2]\text{BF}_4$ (0.02 equiv.), (*R,R*)-QuinoxP* (0.02 equiv.) and MeOH ($c = 10 \text{ M}$). The mixture was degassed, filled with argon 3 times and stirred for 30 min. Enamide (0.35 mmol, 1 equiv.) in MeOH ($c = 1 \text{ M}$) was then added, and 3 cycles of vacuum/hydrogen were performed. The resulting mixture was stirred at 40°C under 1 atm of hydrogen until total conversion, monitored by TLC. The solution was then filtered over a pad of celite, washed with EtAOc and concentrated *in vacuo* to afford the pure compound.

(*S*)-*N*-(3-(1,3-dioxolan-2-yl)-3-oxo-1-phenylpropyl)acetamide **6a**



Yellow oil, quantitative yield, 95% ee (88 mg).

Chemical Formula: $\text{C}_{14}\text{H}_{17}\text{NO}_4$

^1H NMR (300 MHz, CDCl_3) δ 7.28 – 7.14 (m, 5H), 6.41 (brd, $J = 8.3 \text{ Hz}$, 1H), 5.38 (dt, $J = 8.3, 6.0 \text{ Hz}$, 1H), 4.88 (s, 1H), 4.08 – 3.67 (m, 4H), 3.17 (dd, $J = 17.1, 6.0 \text{ Hz}$, 1H), 2.97 (dd, $J = 17.1, 6.0 \text{ Hz}$, 1H), 1.90 (s, 3H).

^{13}C NMR (75 MHz, CDCl_3) δ 204.2, 169.5, 140.8, 128.8, 127.6, 126.5, 101.8, 65.8, 49.3, 42.0, 23.4.

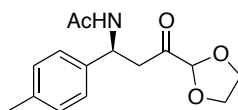
Mass (CI/ NH_3) MH^+ 264

HRMS (ESI): m/z $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{14}\text{H}_{17}\text{NO}_4\text{Na}$: 286.1050, found: 286.1049.

$[\alpha]_{\text{D}}^{20} - 27.3$ (c 1.07, CHCl_3)

SFC: CHIRALPAK IA, $\text{scCO}_2/\text{iPrOH}$ (90:10), 4 mL/min, $P = 150 \text{ bar}$, $\lambda = 215 \text{ nm}$; t_{R} [minor] = 7.52 min, t_{R} [major] = 8.77 min.

(*S*)-*N*-(3-(1,3-dioxolan-2-yl)-3-oxo-1-(*p*-tolyl)propyl)acetamide **6b**



Yellow oil, 97% yield, 97% ee (94 mg).

Chemical Formula: C₁₅H₁₉NO₄

¹H NMR (300 MHz, CDCl₃) δ 7.18 (d, *J* = 8.4 Hz, 2H), 7.12 (d, *J* = 8.4 Hz, 2H), 6.33 (brd, *J* = 8.2 Hz, 1H), 5.42 (dt, *J* = 8.3, 6.0 Hz, 1H), 4.96 (s, 1H), 4.12 – 3.82 (m, 4H), 3.24 (dd, *J* = 17.1, 6.0 Hz, 1H), 3.03 (dd, *J* = 17.1, 6.0 Hz, 1H), 2.31 (s, 3H), 1.98 (s, 3H).

¹³C NMR (75 MHz, CDCl₃) δ 204.4, 169.5, 137.7, 137.4, 129.5, 126.4, 101.9, 65.8, 49.1, 42.0, 23.5, 21.1.

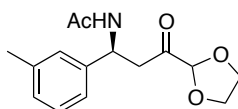
HRMS (ESI): *m/z* [M+Na]⁺ calcd for C₁₅H₁₉NO₄Na: 300.1206, found: 300.1207.

Mass (CI/NH₃) MH⁺ 278

[α]_D²⁰ – 45.5 (*c* 0.25, CHCl₃)

SFC: CHIRALPAK IA, scCO₂/iPrOH (90:10), 4 mL/min, P = 150 bar, λ = 215 nm; *t*_R [minor] = 8.94 min, *t*_R [major] = 10.04 min.

(*S*)-*N*-(3-(1,3-dioxolan-2-yl)-3-oxo-1-(*m*-tolyl)propyl)acetamide **6c**



Slightly yellow solid (mp = 125 – 127 °C), 99% yield, 97% ee (96 mg).

Chemical Formula: C₁₅H₁₉NO₄

¹H NMR (300 MHz, CDCl₃) δ 7.20 (t, *J* = 7.5 Hz, 1H), 7.13 – 6.97 (m, 3H), 6.34 (brd, *J* = 8.5 Hz, 1H), 5.42 (dt, *J* = 8.5, 6.0 Hz, 1H), 4.97 (s, 1H), 4.07 – 3.85 (m, 4H), 3.23 (dd, *J* = 17.0, 6.0 Hz, 1H), 3.03 (dd, *J* = 17.0, 6.0 Hz, 1H), 2.33 (s, 3H), 1.99 (s, 3H).

¹³C NMR (75 MHz, CDCl₃) δ 204.3, 169.4, 140.7, 138.5, 128.7, 128.4, 127.4, 123.4, 101.9, 65.8, 49.3, 42.1, 23.5, 21.6.

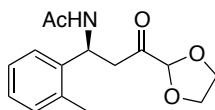
Mass (CI/NH₃) MH⁺ 278

HRMS (ESI): *m/z* [M+Na]⁺ calcd for C₁₅H₁₉NO₄Na: 300.1206, found: 300.1207.

[α]_D²⁰ – 43.6 (*c* 0.36, CHCl₃)

SFC: CHIRALPAK IA, scCO₂/iPrOH (90:10), 4 mL/min, P = 150 bar, λ = 215 nm; *t*_R [minor] = 6.89 min, *t*_R [major] = 8.05 min.

(*S*)-*N*-(3-(1,3-dioxolan-2-yl)-3-oxo-1-(*o*-tolyl)propyl)acetamide **6d**



Slightly yellow solid (mp = 60 – 64 °C), 98% yield, 89% ee (95 mg).

Chemical Formula: C₁₅H₁₉NO₄

¹H NMR (300 MHz, CDCl₃) δ 7.40 – 7.05 (m, 4H), 6.21 (brd, 1H), 5.62 (dt, *J* = 7.5, 6.5 Hz, 1H), 4.97 (s, 1H), 3.95 (s, 4H), 3.12 (dd, *J* = 16.7, 3.4 Hz, 1H), 3.04 (dd, *J* = 16.5, 3.5 Hz, 1H), 2.42 (s, 3H), 1.93 (s, 3H).

¹³C NMR (75 MHz, CDCl₃) δ 203.8, 169.4, 139.0, 136.1, 130.9, 127.7, 126.4, 125.2, 101.8, 65.7, 46.2, 41.9, 23.3, 19.4.

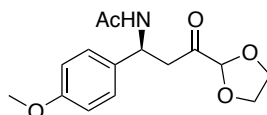
Mass (CI/NH₃) MH⁺ 278

HRMS (ESI): *m/z* [M+Na]⁺ calcd for C₁₅H₁₉NO₄Na: 300.1206, found: 300.1207.

[α]_D²⁰ – 42.8 (*c* 1.12, CHCl₃)

SFC: CHIRALPAK ID, scCO₂/iPrOH (90:10), 4 mL/min, P = 150 bar, λ = 215 nm; *t*_R [major] = 12.18 min, *t*_R [minor] = 16.43 min.

(*S*)-*N*-(3-(1,3-dioxolan-2-yl)-1-(4-methoxyphenyl)-3-oxopropyl)acetamide **6e**



Yellow oil, 95% yield, 99% ee (102 mg).

Chemical Formula: C₁₅H₁₉NO₅

¹H NMR (300 MHz, CDCl₃) δ 7.26 – 7.12 (m, 2H), 6.93 – 6.72 (m, 2H), 6.31 (brd, *J* = 8.0 Hz, 1H), 5.40 (dt, *J* = 8.0, 6.0 Hz, 1H), 4.96 (s, 1H), 4.09 – 3.86 (m, 4H), 3.77 (s, 3H), 3.23 (dd, *J* = 17.1, 6.0 Hz, 1H), 3.02 (dd, *J* = 17.1, 6.0 Hz, 1H), 1.97 (s, 3H).

¹³C NMR (75 MHz, CDCl₃) δ 204.4, 169.4, 159.1, 132.9, 127.7, 114.2, 101.9, 65.8, 55.4, 48.8, 42.1, 23.5.

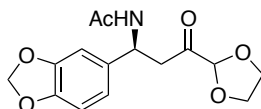
Mass (CI/NH₃) MH⁺ 294

HRMS (ESI): *m/z* [M+Na]⁺ calcd for C₁₅H₁₉NO₅Na: 316.1155, found: 316.1157.

[α]_D²⁰ – 41.1 (*c* 0.41, CHCl₃)

SFC: CHIRALPAK IA, scCO₂/iPrOH (90:10), 4 mL/min, P = 150 bar, λ = 215 nm; *t*_R [minor] = 12.18 min, *t*_R [major] = 16.43 min.

(*S*)-*N*-(1-(benzo[*d*][1,3]dioxol-5-yl)-3-(1,3-dioxolan-2-yl)-3-oxopropyl)acetamide **6f**



White solid (mp = 115 – 118 °C), 93% yield, 97% ee (100 mg).

Chemical Formula: C₁₅H₁₇NO₆

¹H NMR (300 MHz, CDCl₃) δ 6.89 – 6.62 (m, 3H), 6.37 (brd, *J* = 8.0 Hz, 1H), 5.92 (s, 2H), 5.34 (dt, *J* = 8.0, 6.0 Hz, 1H), 4.95 (s, 1H), 4.08 – 3.89 (m, 4H), 3.19 (dd, *J* = 17.0, 6.0 Hz, 1H), 2.98 (dd, *J* = 17.0, 6.0 Hz, 1H), 1.96 (s, 3H).

¹³C NMR (75 MHz, CDCl₃) δ 204.2, 169.4, 148.0, 147.0, 134.8, 119.8, 108.4, 107.2, 101.9, 101.2, 65.8, 49.2, 42.2, 23.5.

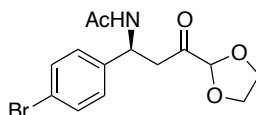
Mass (CI/NH₃) MH⁺ 308

HRMS (ESI): *m/z* [M+Na]⁺ calcd for C₁₅H₁₇NO₆Na: 330.0948, found: 330.0950.

[α]_D²⁰ – 46.5 (*c* 1.03, CHCl₃)

SFC: CHIRALPAK OD-H, scCO₂/iPrOH (80:20) + 0.1% Et₃N, 4 mL/min, P = 150 bar, λ = 215 nm; *t*_R [minor] = 3.98 min, *t*_R [major] = 7.53 min.

(*S*)-*N*-(1-(4-bromophenyl)-3-(1,3-dioxolan-2-yl)-3-oxopropyl)acetamide **6g**



White solid (mp = 125-127 °C), 94% yield, 95% ee (113 mg).

Chemical Formula: C₁₄H₁₆BrNO₄

¹H NMR (300 MHz, CDCl₃) δ 7.43 (d, *J* = 8.5 Hz, 2H), 7.16 (d, *J* = 8.5 Hz, 2H), 6.45 (brd, *J* = 8.0 Hz, 1H), 5.39 (dt, *J* = 8.0, 6.0 Hz, 1H), 4.93 (s, 1H), 4.08 – 3.89 (m, 4H), 3.23 (dd, *J* = 17.5, 6.0 Hz, 1H), 3.00 (dd, *J* = 17.5, 6.0 Hz, 1H), 1.99 (s, 3H).

¹³C NMR (75 MHz, CDCl₃) δ 204.2, 169.5, 139.9, 131.8, 128.3, 121.4, 101.8, 65.9, 48.7, 41.6, 23.5.

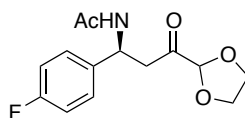
Mass (CI/NH₃) MH⁺ 342

HRMS (ESI): *m/z* [M+Na]⁺ calcd for C₁₄H₁₆BrNO₄Na: 364.0155, found: 364.0157.

[α]_D²⁰ – 36.9 (*c* 0.53, CHCl₃)

SFC: CHIRALPAK OD-H, scCO₂/MeOH (90:10), 4 mL/min, P = 150 bar, λ = 215 nm; *t*_R [minor] = 11.92 min, *t*_R [major] = 14.92 min.

(*S*)-*N*-(3-(1,3-dioxolan-2-yl)-1-(4-fluorophenyl)-3-oxopropyl)acetamide **6h**



Chemical Formula: C₁₄H₁₆FNO₄

White solid (mp = 80 – 83 °C), 95% yield, 97% ee (94 mg).

¹H NMR (300 MHz, CDCl₃) δ 7.41 – 7.11 (m, 2H), 7.11 – 6.89 (m, 2H), 6.41 (brd, *J* = 8.5 Hz, 1H), 5.42 (dt, *J* = 8.5, 5.9 Hz, 1H), 4.94 (s, 1H), 4.10 – 3.83 (m, 4H), 3.24 (dd, *J* = 17.4, 5.9 Hz, 1H), 3.01 (dd, *J* = 17.4, 5.9 Hz, 1H), 1.99 (s, 3H).

¹³C NMR (75 MHz, CDCl₃) δ 204.31, 169.5, 162.2 (d, ¹*J*_{CF} = 245.5 Hz), 136.6 (d, ⁴*J*_{CF} = 3.1 Hz), 128.2 (d, ³*J*_{CF} = 8.2 Hz), 115.6 (d, ²*J*_{CF} = 21.4 Hz), 101.9, 65.9, 48.7, 41.8, 23.5.

¹⁹F NMR (282 MHz, CDCl₃) δ -112.89 – -116.66 (m).

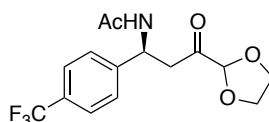
Mass (CI/NH₃) MH⁺ 282

HRMS (ESI): *m/z* [M+Na]⁺ calcd for C₁₄H₁₆FNO₄Na: 304.0956, found: 304.0956.

[α]_D²⁰ – 24.6 (*c* 0.31, CHCl₃)

SFC: CHIRALPAK IA, scCO₂/iPrOH (90:10), 4 mL/min, P = 150 bar, λ = 215 nm; *t*_R [major] = 5.65 min, *t*_R [minor] = 6.83 min.

(*S*)-*N*-(3-(1,3-dioxolan-2-yl)-3-oxo-1-(4-(trifluoromethyl)phenyl)propyl)acetamide **6i**



White solid (mp = 106 – 109 °C), 95% yield, 94% ee (110 mg).

Chemical Formula: C₁₅H₁₆F₃NO₄

¹H NMR (300 MHz, CDCl₃) δ 7.55 (d, *J* = 8.2 Hz, 2H), 7.39 (d, *J* = 8.2 Hz, 2H), 6.72 (brd, *J* = 8.2 Hz, 1H), 5.47 (dt, *J* = 8.2, 6.0 Hz, 1H), 4.92 (s, 1H), 4.11 – 3.82 (m, 4H), 3.24 (dd, *J* = 17.6, 6.0 Hz, 1H), 3.02 (dd, *J* = 17.6, 6.0 Hz, 1H), 1.97 (s, 3H).

¹³C NMR (75 MHz, CDCl₃) δ 203.9, 169.8, 145.0, 129.8 (q, ²*J*_{CF} = 32.7 Hz), 126.9, 125.7 (q, ³*J*_{CF} = 3.4 Hz), 124.1 (q, ¹*J*_{CF} = 272.1 Hz), 101.7, 65.8, 48.8, 41.6, 23.3.

¹⁹F NMR (282 MHz, CDCl₃) δ – 63.59 (s).

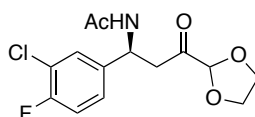
Mass (CI/NH₃) MH⁺ 332

HRMS (ESI): *m/z* [M+Na]⁺ calcd for C₁₅H₁₆F₃NO₄Na: 354.0924, found: 354.0924.

[α]_D²⁰ – 19.2 (*c* 1.06, CHCl₃)

SFC: CHIRALPAK IA, scCO₂/iPrOH (90:10), 4 mL/min, P = 150 bar, λ = 215 nm; *t*_R [minor] = 4.66 min, *t*_R [major] = 6.63 min.

(*S*)-*N*-(1-(3-chloro-4-fluorophenyl)-3-(1,3-dioxolan-2-yl)-3-oxopropyl)acetamide **6j**



White solid (mp = 110 – 113 °C), 95% yield, 95% ee (105 mg).

Chemical Formula: C₁₄H₁₅ClFNO₄

¹H NMR (300 MHz, CDCl₃) δ 7.32 (dd, *J* = 6.5, 2.3 Hz, 1H), 7.15 (ddd, *J* = 8.7, 6.5, 2.3 Hz, 1H), 7.05 (t, *J* = 8.7 Hz, 1H), 6.65 (brd, *J* = 8.2 Hz, 1H), 5.37 (dt, *J* = 8.2, 6.0 Hz, 1H), 4.93 (s, 1H), 4.11 – 3.84 (m, 4H), 3.19 (dd, *J* = 17.5, 6.0 Hz, 1H), 2.98 (dd, *J* = 17.5, 6.0 Hz, 1H), 1.97 (s, 3H).

¹³C NMR (75 MHz, CDCl₃) δ 203.9, 169.6, 157.4 (d, ¹*J*_{CF} = 249.0 Hz), 138.2 (d, ³*J*_{CF} = 3.9 Hz), 128.8, 126.4 (d, ³*J*_{CF} = 7.1 Hz), 121.1 (d, ²*J*_{CF} = 17.9 Hz), 116.7 (d, ²*J*_{CF} = 21.2 Hz), 101.7, 65.9, 48.3, 41.7, 23.4.

¹⁹F NMR (282 MHz, CDCl₃) δ -113.49 – -113.56 (m).

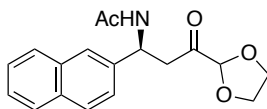
Mass (CI/NH₃) MH⁺ 316

HRMS (ESI): *m/z* [M+Na]⁺ calcd for C₁₄H₁₅ClFNO₄Na: 338.0566, found: 338.0566.

[α]_D²⁰ – 23.3 (*c* 1.24, CHCl₃)

SFC: CHIRALPAK ADH, scCO₂/iPrOH (90:10), 4 mL/min, P = 150 bar, λ = 215 nm; *t*_R [minor] = 5.38 min, *t*_R [major] = 6.89 min.

(*S*)-*N*-(3-(1,3-dioxolan-2-yl)-1-(naphthalen-2-yl)-3-oxopropyl)acetamide **6I**



White solid (mp = 116 – 118 °C), 90% yield, 96% ee (99 mg).

Chemical Formula: C₁₈H₁₉NO₄

¹H NMR (300 MHz, CDCl₃) δ 7.92 – 7.66 (m, 4H), 7.56 – 7.34 (m, 3H), 6.52 (brd, *J* = 8.5 Hz, 1H), 5.63 (dt, *J* = 8.5, 6.0 Hz, 1H), 4.97 (s, 1H), 4.09 – 3.86 (m, 4H), 3.34 (dd, *J* = 17.2, 6.0 Hz, 1H), 3.13 (dd, *J* = 17.2, 6.0 Hz, 1H), 2.02 (s, 3H).

¹³C NMR (75 MHz, CDCl₃) δ 206.6, 171.8, 140.4, 135.6, 135.1, 130.9, 130.4, 130.0, 128.7, 128.4, 127.4, 127.0, 104.2, 68.1, 51.7, 44.2, 25.8.

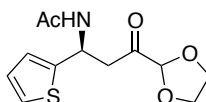
Mass (CI/NH₃) MH⁺ 314

HRMS (ESI): *m/z* [M+Na]⁺ calcd for C₁₈H₁₉NO₄Na: 336.1206, found: 336.1209.

[α]_D²⁰ – 18.5 (*c* 1.12, CHCl₃)

SFC: CHIRALPAK IA, scCO₂/MeOH (95:5), 4 mL/min, P = 150 bar, λ = 215 nm; *t*_R [minor] = 10.46 min, *t*_R [major] = 13.40 min.

(*S*)-*N*-(3-(1,3-dioxolan-2-yl)-3-oxo-1-(thiophen-2-yl)propyl)acetamide **6m**



Yellow oil, 72% yield, 96% ee (68 mg).

Chemical Formula: C₁₂H₁₅NO₄S

¹H NMR (400 MHz, CDCl₃) δ 7.22 – 7.10 (m, 1H), 7.01 – 6.85 (m, 2H), 6.46 (d, *J* = 8.5 Hz, 1H), 5.72 (dt, *J* = 8.5, 5.5 Hz, 1H), 5.00 (s, 1H), 4.06 – 3.99 (m, 4H), 3.32 (dd, *J* = 17.7, 5.5 Hz, 1H), 3.11 (dd, *J* = 17.7, 5.5 Hz, 1H), 1.99 (s, 3H).

¹³C NMR (101 MHz, CDCl₃) δ 204.3, 169.32 144.45 127.0, 124.74, 124.67, 101.9, 65.9, 45.2, 42.1, 23.5.

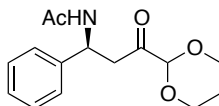
Mass (CI/NH₃) MH⁺ 269

HRMS (ESI): *m/z* [M+Na]⁺ calcd for C₁₂H₁₅NO₄SNa: 292.0619, found: 292.0617.

[α]_D²⁰ – 20.2 (*c* 1.20, CHCl₃)

SFC: CHIRALPAK IA, scCO₂/iPrOH (90:10), 4 mL/min, P = 150 bar, λ = 215 nm; *t*_R [minor] = 7.83 min, *t*_R [major] = 8.85 min.

(*S*)-*N*-(3-(1,3-dioxan-2-yl)-3-oxo-1-phenylpropyl)acetamide **6n**



White solid (mp = 120 – 124 °C), 93% yield, 99% ee (91 mg).

Chemical Formula: C₁₅H₁₉NO₄

¹H NMR (300 MHz, CDCl₃) δ 7.63 – 7.09 (m, 5H), 6.39 (brd, *J* = 8.3 Hz, 1H), 5.42 (dt, *J* = 8.3, 6.0 Hz, 1H), 4.70 (s, 1H), 4.16 (ddt, *J* = 12.1, 5.0, 1.5 Hz, 2H), 3.80 (tt, *J* = 12.1, 2.6 Hz, 2H), 3.24 (dd, *J* = 17.4, 6.0 Hz, 1H), 3.08 (dd, *J* = 17.4, 6.0 Hz, 1H), 2.11 (dtt, *J* = 13.6, 12.1, 5.0 Hz, 1H), 1.94 (s, 3H), 1.38 (ddq, *J* = 13.6, 2.6, 1.5 Hz, 1H).

¹³C NMR (75 MHz, CDCl₃) δ 202.1, 169.4, 141.1, 128.7, 127.5, 126.5, 100.3, 67.1, 49.1, 42.5, 25.7, 23.5.

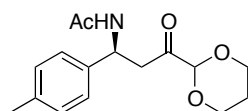
Mass (CI/NH₃) MH⁺ 278

HRMS (ESI): *m/z* [M+Na]⁺ calcd for C₁₅H₁₉NO₄Na: 300.1206, found: 300.1204.

[α]_D²⁰ – 19.3 (*c* 1.0, CHCl₃)

SFC: CHIRALPAK IA, scCO₂/MeOH (90:10), 4 mL/min, P = 150 bar, λ = 215 nm; *t*_R [minor] = 10.70 min, *t*_R [major] = 12.99 min.

(S)-N-(3-(1,3-dioxan-2-yl)-3-oxo-1-(p-tolyl)propyl)acetamide **6o**



Slightly yellow solid (mp = 143 – 146 °C), 95% yield, 97% ee (97 mg).

Chemical Formula: C₁₆H₂₁NO₄

¹H NMR (300 MHz, CDCl₃) δ 7.17 (d, *J* = 8.0 Hz, 2H), 7.10 (d, *J* = 8.0 Hz, 2H), 6.41 (brd, *J* = 8.0 Hz, 1H), 5.40 (dt, *J* = 8.0, 6.0 Hz, 1H), 4.72 (s, 1H), 4.25 – 4.07 (m, 2H), 3.81 (tt, *J* = 12.2, 2.8 Hz, 2H), 3.23 (dd, *J* = 17.3, 6.5 Hz, 1H), 3.09 (dd, *J* = 17.3, 5.8 Hz, 1H), 2.29 (s, 3H), 2.23 – 1.99 (m, 1H), 1.94 (s, 3H), 1.40 (dtt, *J* = 13.7, 2.8, 1.5 Hz, 1H).

¹³C NMR (75 MHz, CDCl₃) δ 202.1, 169.4, 138.1, 137.1, 129.4, 126.4, 100.2, 67.1, 48.8, 42.6, 25.6, 23.4, 21.1.

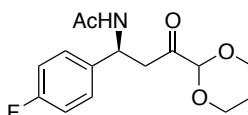
Mass (CI/NH₃) MH⁺ 292

HRMS (ESI): *m/z* [M+Na]⁺ calcd for C₁₆H₂₁NO₄Na: 314.1363, found: 314.1363.

[α]_D²⁰ – 37.9 (*c* 0.11, CHCl₃)

SFC: CHIRALPAK IA, scCO₂/iPrOH (90:10), 4 mL/min, P = 150 bar, λ = 215 nm; *t*_R [minor] = 5.99 min, *t*_R [major] = 6.67min.

(S)-N-(3-(1,3-dioxan-2-yl)-1-(4-fluorophenyl)-3-oxopropyl)acetamide **6p**



White solid (mp = 142 – 144 °C), 98% yield, 95% ee (102 mg).

Chemical Formula: C₁₅H₁₈FNO₄

¹H NMR (300 MHz, CDCl₃) δ 7.48 – 7.11 (m, 2H), 7.11 – 6.78 (m, 2H), 6.43 (brd, *J* = 7.5 Hz, 1H), 5.41 (dt, *J* = 7.5, 6.0 Hz, 1H), 4.71 (s, 1H), 4.35 – 4.05 (m, 2H), 3.82 (tt, *J* = 12.1, 2.5 Hz, 2H), 3.27 (dd, *J* = 17.6, 6.0 Hz, 1H), 3.07 (dd, *J* = 17.6, 6.0 Hz, 1H), 2.29 – 2.03 (m, 1H), 1.97 (s, 3H), 1.41 (dtt, *J* = 13.6, 2.7, 1.5 Hz, 1H).

¹³C NMR (75 MHz, CDCl₃) δ 202.1, 169.5, 162.1 (d, ¹*J*_{CF} = 245.8 Hz), 136.9 (d, ⁴*J*_{CF} = 2.9 Hz), 128.2 (d, ³*J*_{CF} = 8.1 Hz), 115.5 (d, ²*J*_{CF} = 21.5 Hz), 100.3, 67.2, 48.5, 42.3, 25.7, 23.5.

¹⁹F NMR (282 MHz, CDCl₃) δ -101.78 – -146.66 (m).

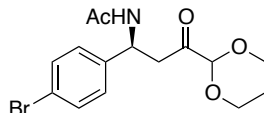
Mass (CI/NH₃) MH⁺ 296

HRMS (ESI): *m/z* [M+Na]⁺ calcd for C₁₅H₁₈FNO₄Na: 318.1112, found: 318.1112.

[α]_D²⁰ – 26.4 (*c* 0.97, CHCl₃)

SFC: CHIRALPAK IA, scCO₂/iPrOH (93:7), 4 mL/min, P = 150 bar, λ = 215 nm; t_R [minor] = 8.66 min, t_R [major] = 10.04 min.

(*S*)-*N*-(1-(4-bromophenyl)-3-(1,3-dioxan-2-yl)-3-oxopropyl)acetamide **6q**



White solid (mp = 140 – 142 °C), 98% yield, 96% ee (122 mg).

Chemical Formula: C₁₅H₁₈BrNO₄

¹H NMR (300 MHz, CDCl₃) δ 7.41 (d, J = 8.5 Hz, 2H), 7.16 (d, J = 8.5 Hz, 2H), 6.48 (brd, J = 8.5 Hz, 1H), 5.37 (dt, J = 8.5, 6.0 Hz, 1H), 4.71 (s, 1H), 4.28 – 4.05 (m, 2H), 3.82 (tt, J = 12.2, 2.5 Hz, 2H), 3.26 (dd, J = 17.7, 6.3 Hz, 1H), 3.06 (dd, J = 17.7, 5.5 Hz, 1H), 2.14 (dtt, J = 13.7, 12.4, 5.0 Hz, 1H), 1.96 (s, 3H), 1.41 (dtt, J = 13.7, 2.5, 1.5 Hz, 1H).

¹³C NMR (75 MHz, CDCl₃) δ 201.9, 169.5, 140.2, 131.7, 128.3, 121.4, 100.3, 67.1, 48.6, 42.1, 25.6, 23.4.

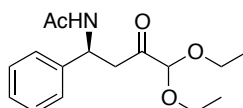
Mass (CI/NH₃) MH⁺ 356

HRMS (ESI): m/z [M+Na]⁺ calcd for C₁₅H₁₈BrNO₄Na: 378.0311, found: 378.0317.

$[\alpha]_D^{20}$ – 33.6 (c 1.1, CHCl₃)

SFC: CHIRALPAK IA, scCO₂/iPrOH (85:15), 4 mL/min, P = 150 bar, λ = 215 nm; t_R [minor] = 8.75 min, t_R [major] = 9.63 min.

(*S*)-*N*-(4,4-diethoxy-3-oxo-1-phenylbutyl)acetamide **6r**



Yellow oil, quantitative yield, 96% ee (103 mg).

Chemical Formula: C₁₆H₂₃NO₄

¹H NMR (300 MHz, CDCl₃) δ 7.31 – 7.14 (m, 5H), 6.60 (brd, J = 8.3 Hz, 1H), 5.41 (dt, J = 8.3, 6.0 Hz, 1H), 4.42 (s, 1H), 3.59 (dq, J = 9.5, 7.0 Hz, 2H), 3.43 (dq, J = 9.5, 7.0 Hz, 2H), 3.23 (dd, J = 17.0, 6.3 Hz, 1H), 3.01 (dd, J = 17.0, 6.0 Hz, 1H), 1.95 (s, 3H), 1.16 (t, J = 7.0 Hz, 3H), 1.16 (t, J = 7.0 Hz, 3H).

¹³C NMR (75 MHz, CDCl₃) δ 204.3, 169.4, 141.1, 128.6, 127.5, 126.5, 102.6, 63.6, 49.5, 42.0, 23.4, 15.2.

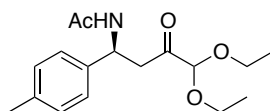
Mass (ESI) MH⁺ 294

HRMS (ESI): m/z [M+Na]⁺ calcd for C₁₆H₂₃NO₄Na: 316.1519, found: 316.1517.

$[\alpha]_D^{20} - 37.2$ (c 1.0, CHCl_3)

SFC: CHIRALPAK IA, $\text{scCO}_2/\text{iPrOH}$ (90:10), 4 mL/min, $P = 150$ bar, $\lambda = 215$ nm; t_R [minor] = 3.48 min, t_R [major] = 4.47 min.

(*S*)-*N*-(4,4-diethoxy-3-oxo-1-(*p*-tolyl)butyl)acetamide **6s**



Yellow oil, 99% yield, 98% ee (107 mg).

Chemical Formula: $\text{C}_{17}\text{H}_{25}\text{NO}_4$

^1H NMR (300 MHz, CDCl_3) δ 7.18 (d, $J = 8.0$ Hz, 2H), 7.10 (d, $J = 8.0$ Hz, 2H), 6.41 (brd, $J = 8.0$ Hz, 1H), 5.40 (dt, $J = 8.0, 6.0$ Hz, 1H), 4.44 (s, 1H), 3.62 (dq, $J = 9.5, 7.0, 1.5$ Hz, 2H), 3.55 – 3.35 (m, 2H), 3.24 (dd, $J = 17.0, 6.0$ Hz, 1H), 3.02 (dd, $J = 17.0, 6.0$ Hz, 1H), 2.30 (s, 3H), 1.96 (s, 3H), 1.19 (t, $J = 7.0$ Hz, 6H).

^{13}C NMR (75 MHz, CDCl_3) δ 204.5, 169.3, 138.2, 137.2, 129.3, 126.4, 102.7, 63.7, 49.2, 42.1, 23.5, 21.1, 15.2.

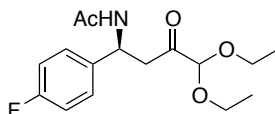
Mass (ESI) MH^+ 308

HRMS (ESI): m/z $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{17}\text{H}_{25}\text{NO}_4\text{Na}$: 330.1676, found: 330.1677.

$[\alpha]_D^{20} - 33.6$ (c 0.61, CHCl_3)

SFC: CHIRALPAK IA, $\text{scCO}_2/\text{iPrOH}$ (90:10), 4 mL/min, $P = 150$ bar, $\lambda = 215$ nm; t_R [minor] = 4.16 min, t_R [major] = 5.17 min.

(*S*)-*N*-(4,4-diethoxy-1-(4-fluorophenyl)-3-oxobutyl)acetamide **6t**



Yellow oil, 97% yield, 97% ee (72 mg).

Chemical Formula: $\text{C}_{16}\text{H}_{22}\text{FNO}_4$

^1H NMR (300 MHz, CDCl_3) δ 7.41 – 7.17 (m, 2H), 7.10 – 6.89 (m, 2H), 6.59 (brd, $J = 8.0$ Hz, 1H), 5.40 (dt, $J = 8.0, 6.0$ Hz, 1H), 4.44 (s, 1H), 3.64 (dq, $J = 9.5, 7.0, 1.1$ Hz, 2H), 3.46 (dq, $J = 9.5, 7.0, 6.0$ Hz, 2H), 3.24 (dd, $J = 17.2, 6.0$ Hz, 1H), 3.01 (dd, $J = 17.2, 6.0$ Hz, 1H), 1.97 (s, 3H), 1.20 (t, $J = 7.0$ Hz, 3H), 1.19 (t, $J = 7.0$ Hz, 3H).

^{13}C NMR (75 MHz, CDCl_3) δ 204.2, 169.4, 162.1 (d, $^1J_{\text{CF}} = 245.7$ Hz), 137.0 (d, $^4J_{\text{CF}} = 2.6$ Hz), 128.2 (d, $^3J_{\text{CF}} = 8.0$ Hz), 115.4 (d, $^2J_{\text{CF}} = 21.5$ Hz), 102.7, 63.8, 48.8, 41.8, 23.4, 15.2.

^{19}F NMR (282 MHz, CDCl_3) δ -116.30 – -116.40 (m).

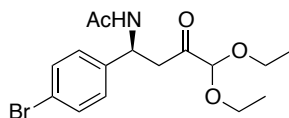
Mass (ESI) MH^+ 212

HRMS (ESI): m/z $[M+Na]^+$ calcd for $C_{16}H_{22}FNO_4Na$: 334.1425, found: 334.1426.

$[\alpha]_D^{20} - 17.8$ (c 0.12, $CHCl_3$)

SFC: CHIRALPAK IA, $scCO_2/iPrOH$ (90:10), 4 mL/min, $P = 150$ bar, $\lambda = 215$ nm; t_R [minor] = 2.84 min, t_R [major] = 3.70 min.

(*S*)-*N*-(1-(4-bromophenyl)-4,4-diethoxy-3-oxobutyl)acetamide **6u**



Yellow oil, 90% yield, 95% ee (117 mg).

Chemical Formula: $C_{16}H_{22}BrNO_4$

1H NMR (400 MHz, $CDCl_3$) δ 7.43 (d, $J = 8.5$ Hz, 2H), 7.18 (d, $J = 8.5$ Hz, 2H), 6.50 (brd, $J = 8.0$ Hz, 1H), 5.38 (dt, $J = 8.0, 6.0$ Hz, 1H), 4.43 (s, 1H), 3.64 (dq, $J = 9.5, 7.0, 1.2$ Hz, 2H), 3.56 – 3.35 (m, 2H), 3.26 (dd, $J = 17.3, 6.0$ Hz, 1H), 2.99 (dd, $J = 17.3, 6.0$ Hz, 1H), 2.00 (s, 3H), 1.21 (t, $J = 7.0$ Hz, 3H), 1.19 (t, $J = 7.0$ Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 204.4, 169.4, 140.2, 131.7, 128.3, 121.4, 102.8, 63.9, 48.9, 41.5, 23.5, 15.2.

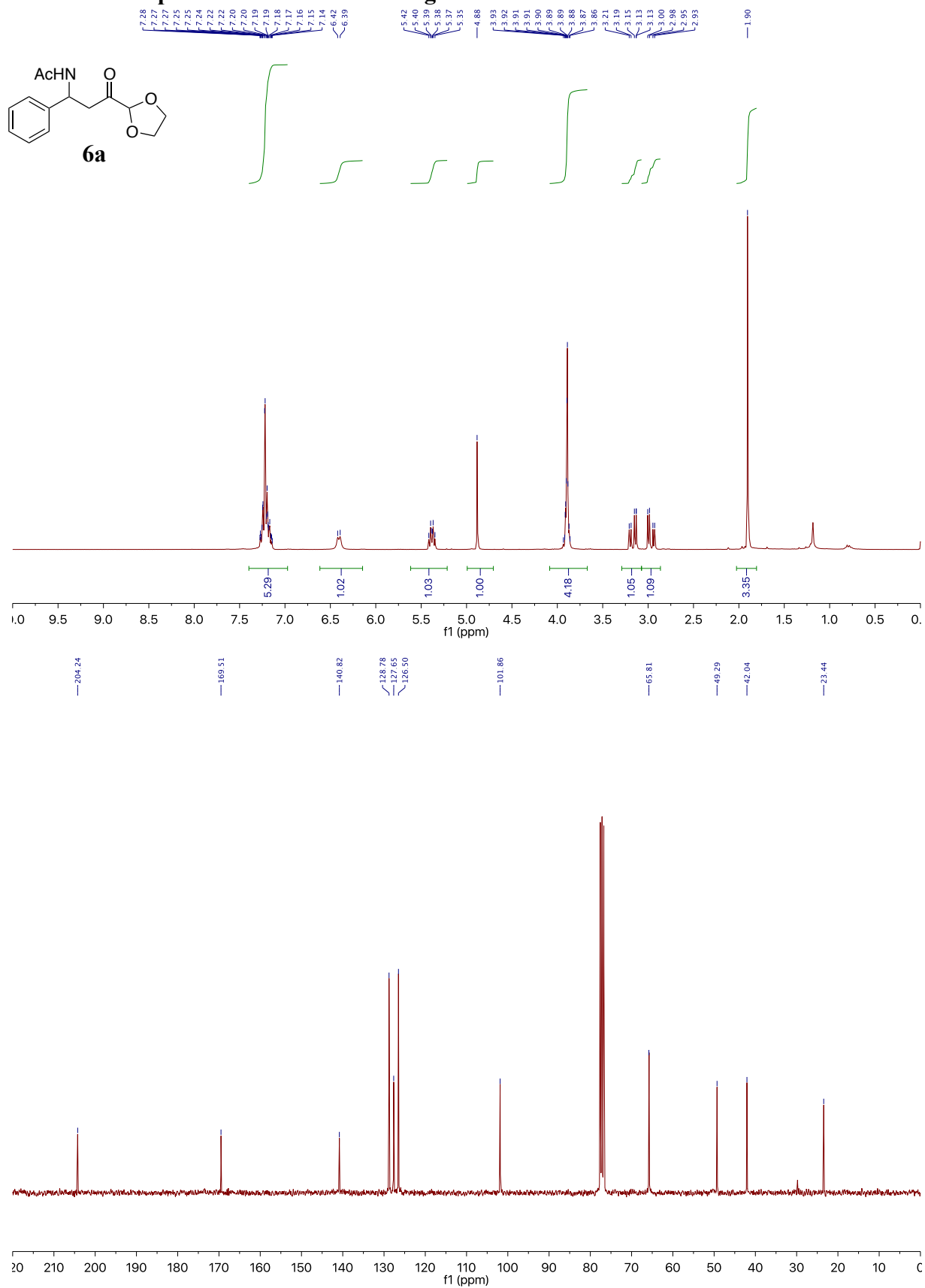
Mass (ESI) MH^+ 372

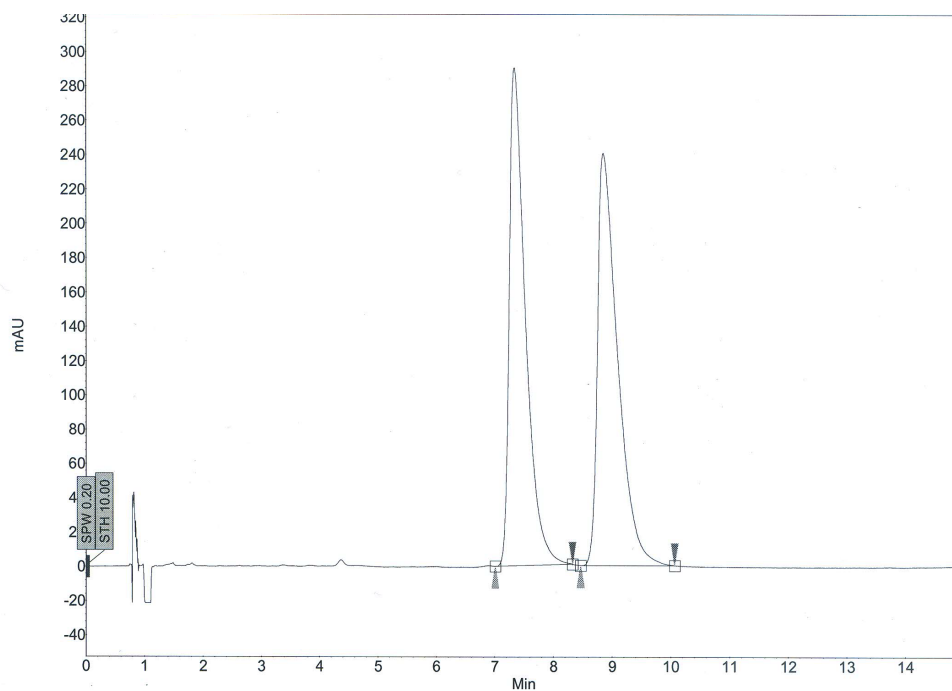
HRMS (ESI): m/z $[M+Na]^+$ calcd for $C_{16}H_{22}BrNO_4Na$: 394.0624, found: 394.0623.

$[\alpha]_D^{20} - 35.2$ (c 0.19, $CHCl_3$)

SFC: CHIRALPAK IA, $scCO_2/iPrOH$ (90:10), 4 mL/min, $P = 150$ bar, $\lambda = 215$ nm; t_R [minor] = 5.24 min, t_R [major] = 7.35 min.

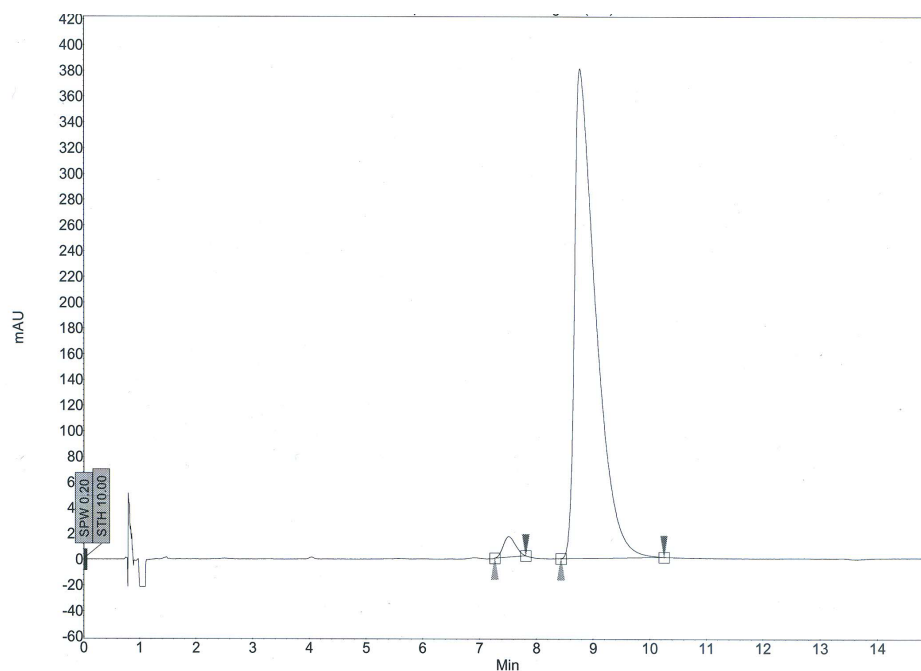
9. NMR spectra and SFC chromatograms for 6a – 6u





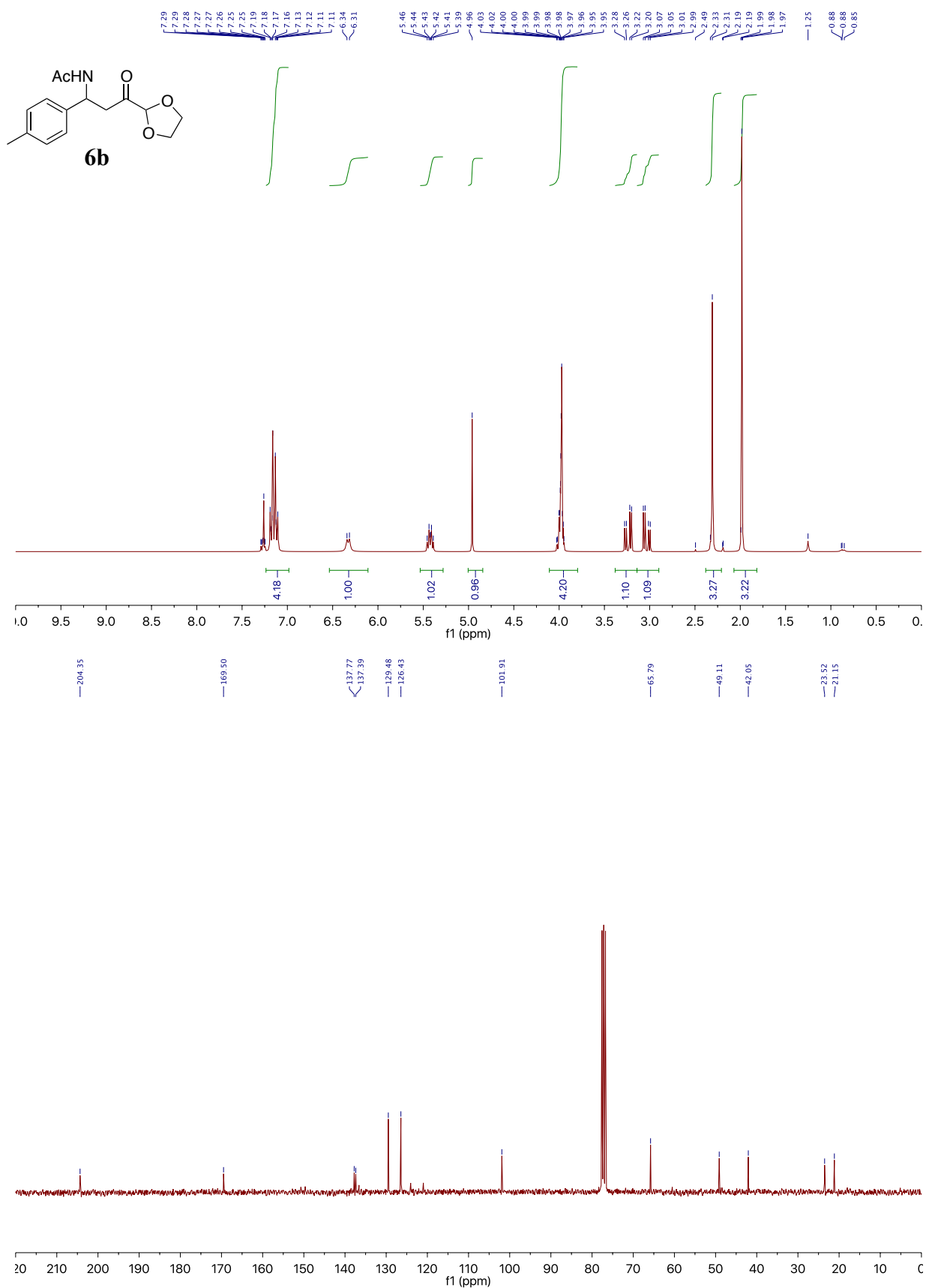
Results Table:

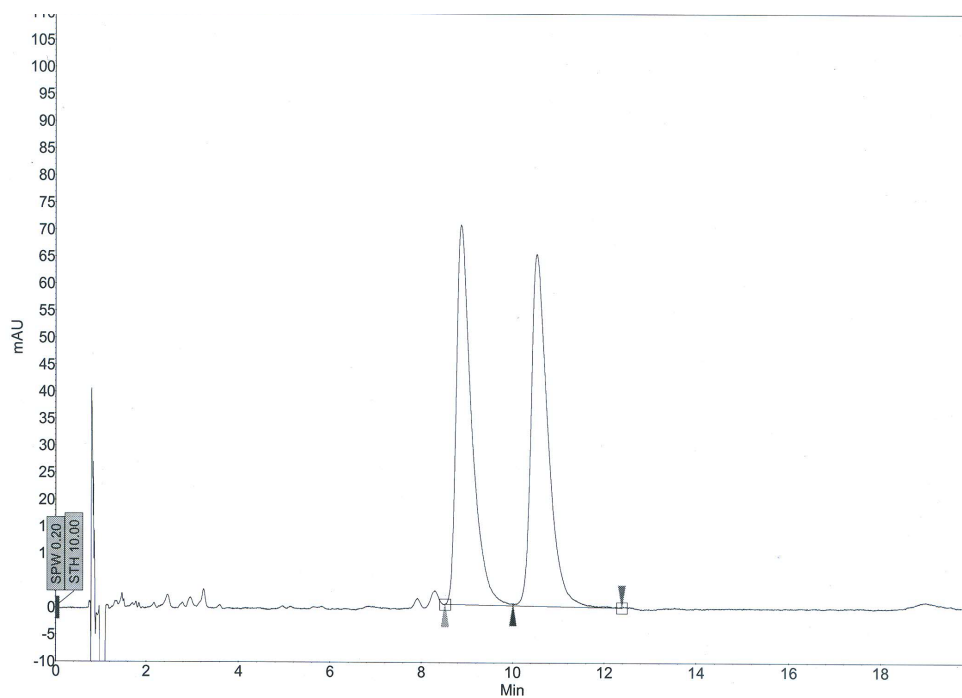
Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[μ V]	[μ V.Min]	[%]
1	UNKNOWN	7.01	7.34	8.33	0.00	49.47	290.2	93.0	49.466
2	UNKNOWN	8.47	8.85	10.06	0.00	50.53	240.3	95.0	50.534
Total						100.00	530.6	188.0	100.000



Results Table:

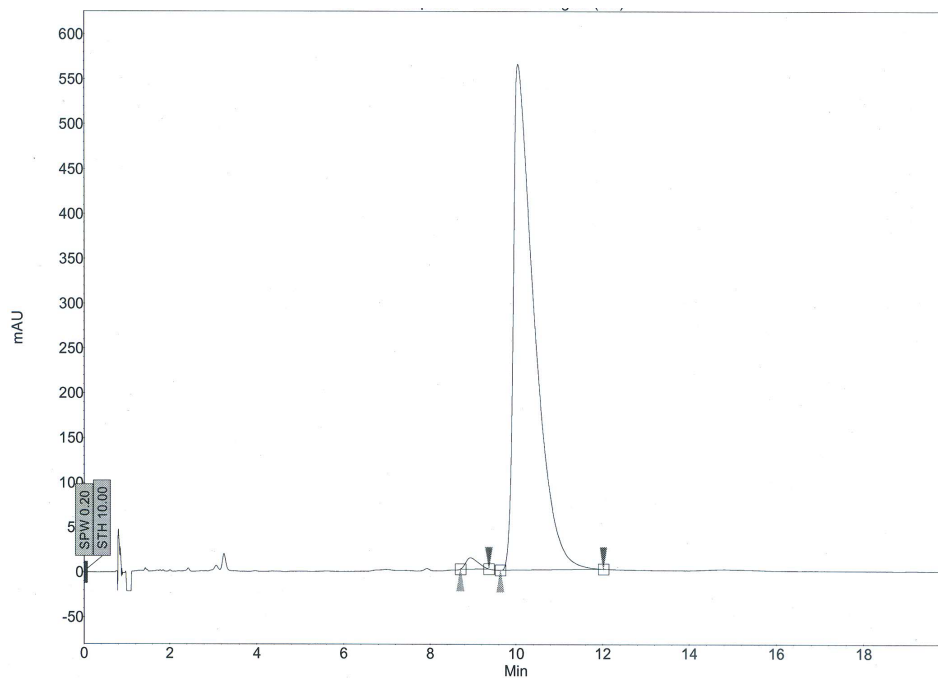
Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[μ V]	[μ V.Min]	[%]
2	UNKNOWN	7.27	7.52	7.82	0.00	2.39	16.0	4.0	2.387
1	UNKNOWN	8.44	8.77	10.25	0.00	97.61	380.6	164.4	97.613
Total						100.00	396.6	168.4	100.000





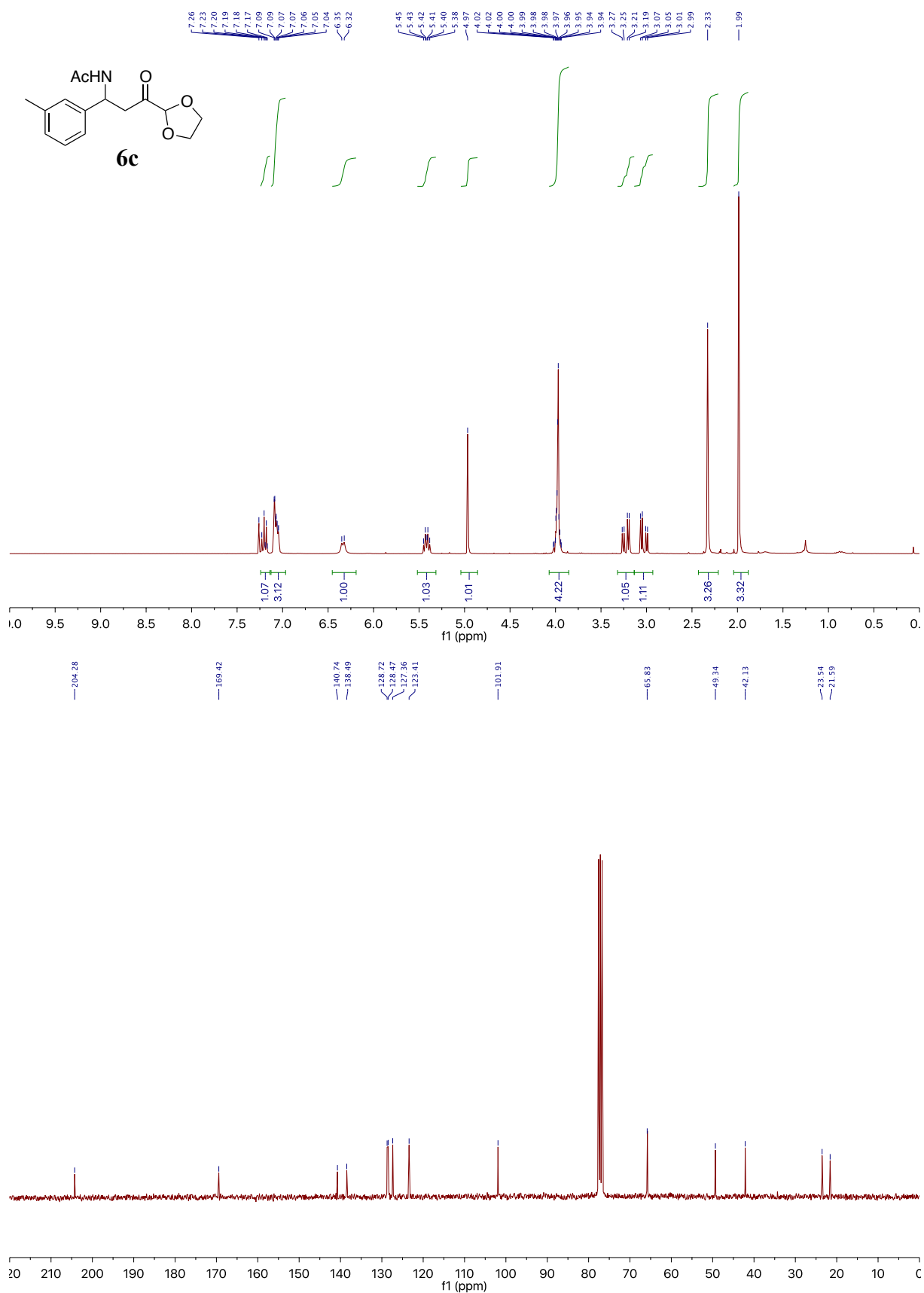
Results Table:

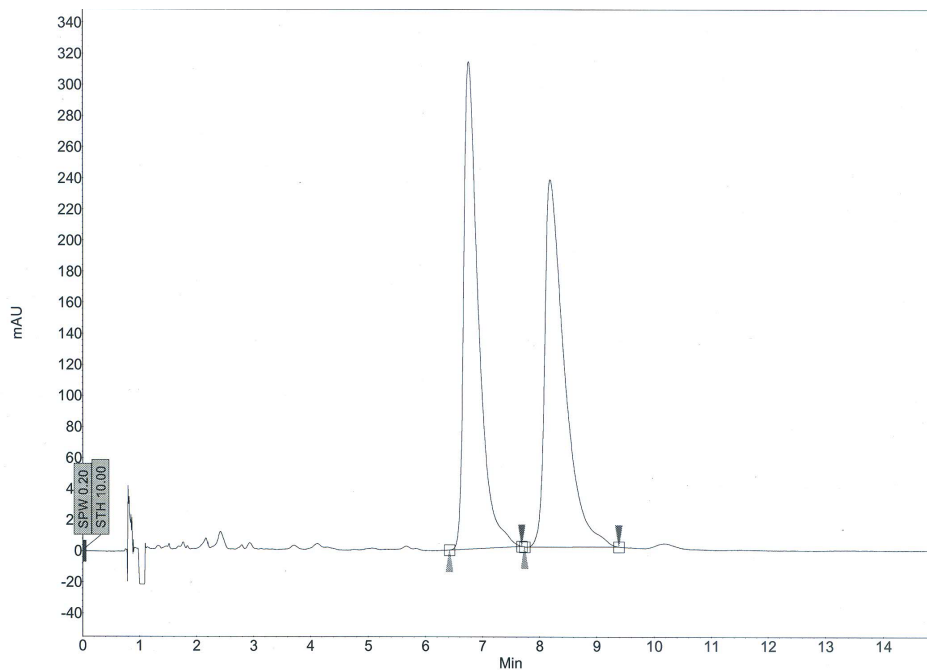
Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[μV]	[μV.Min]	[%]
1	UNKNOWN	8.52	8.88	10.01	0.00	49.76	70.2	27.4	49.756
2	UNKNOWN	10.01	10.52	12.39	0.00	50.24	65.2	27.7	50.244
Total						100.00	135.4	55.1	100.000



Results Table:

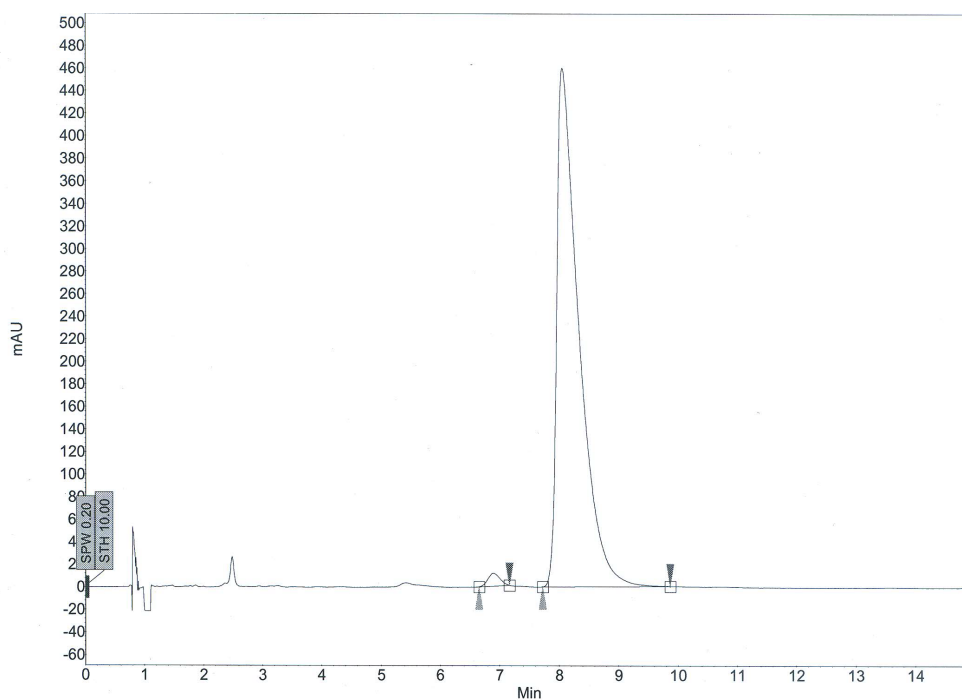
Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[μV]	[μV.Min]	[%]
1	UNKNOWN	8.71	8.94	9.37	0.00	1.32	12.8	4.2	1.318
2	UNKNOWN	9.64	10.04	12.01	0.00	98.68	564.0	315.3	98.682
Total						100.00	576.8	319.5	100.000





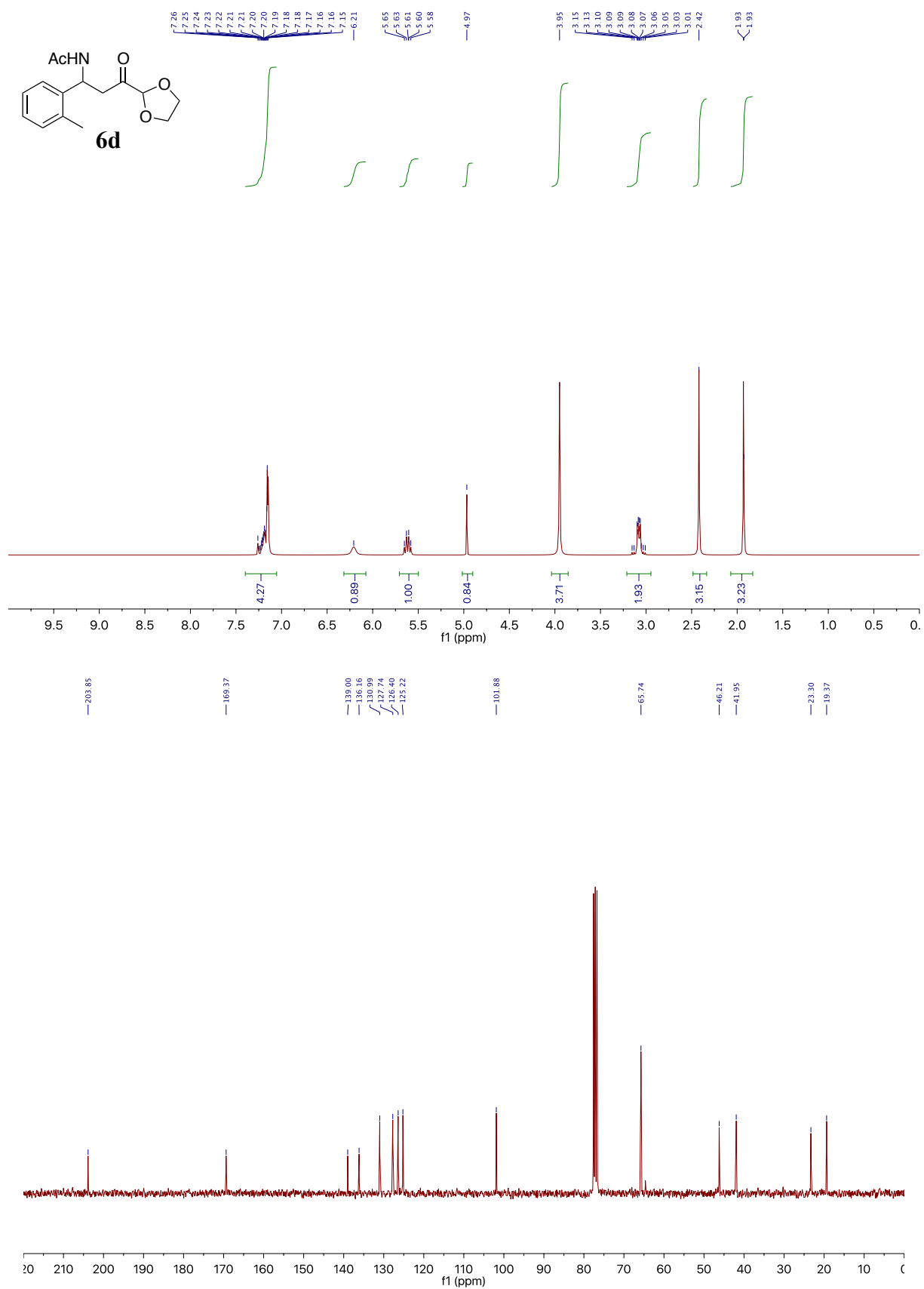
Results Table:

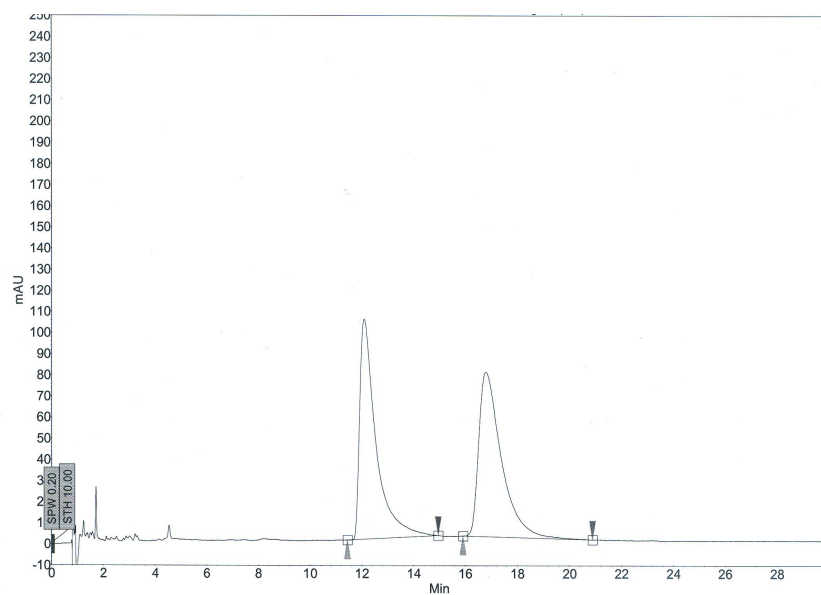
Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[μ V]	[μ V.Min]	[%]
1	UNKNOWN	6.42	6.76	7.69	0.00	49.86	313.5	94.1	49.863
2	UNKNOWN	7.74	8.19	9.38	0.00	50.14	236.3	94.7	50.137
Total						100.00	549.8	188.8	100.000



Results Table:

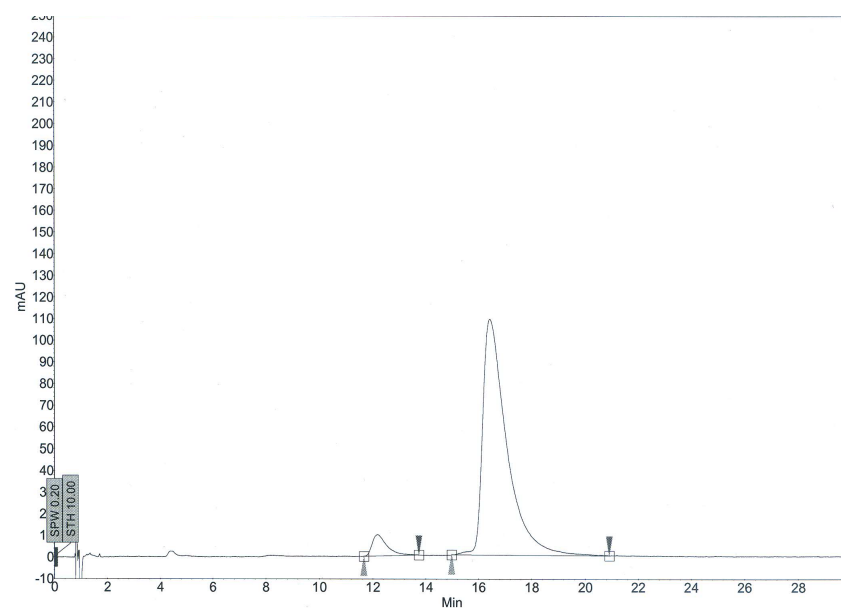
Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[μ V]	[μ V.Min]	[%]
1	UNKNOWN	6.65	6.89	7.16	0.00	1.36	11.5	2.7	1.356
2	UNKNOWN	7.72	8.05	9.86	0.00	98.64	459.8	196.7	98.644
Total						100.00	471.2	199.4	100.000





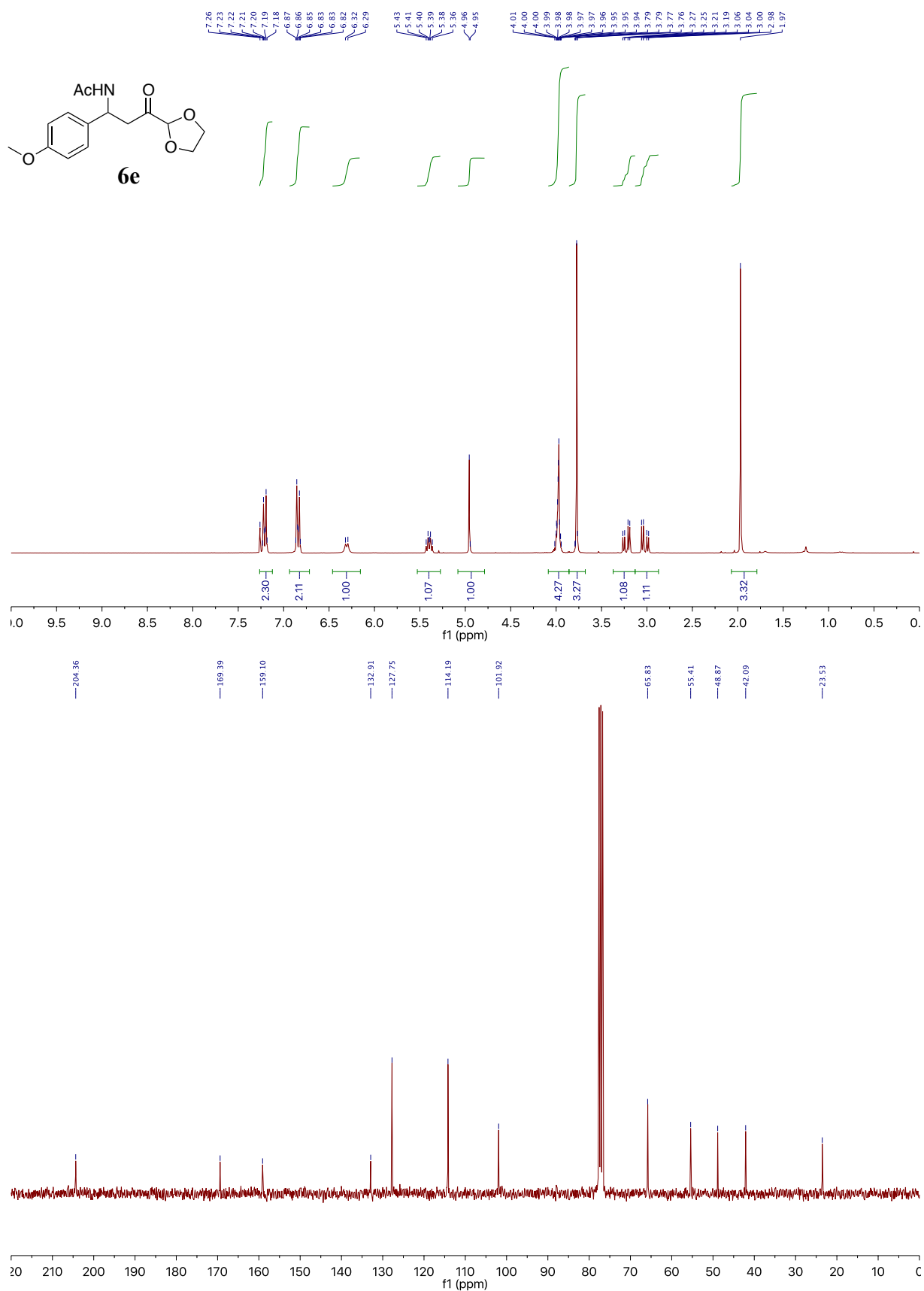
Results Table:

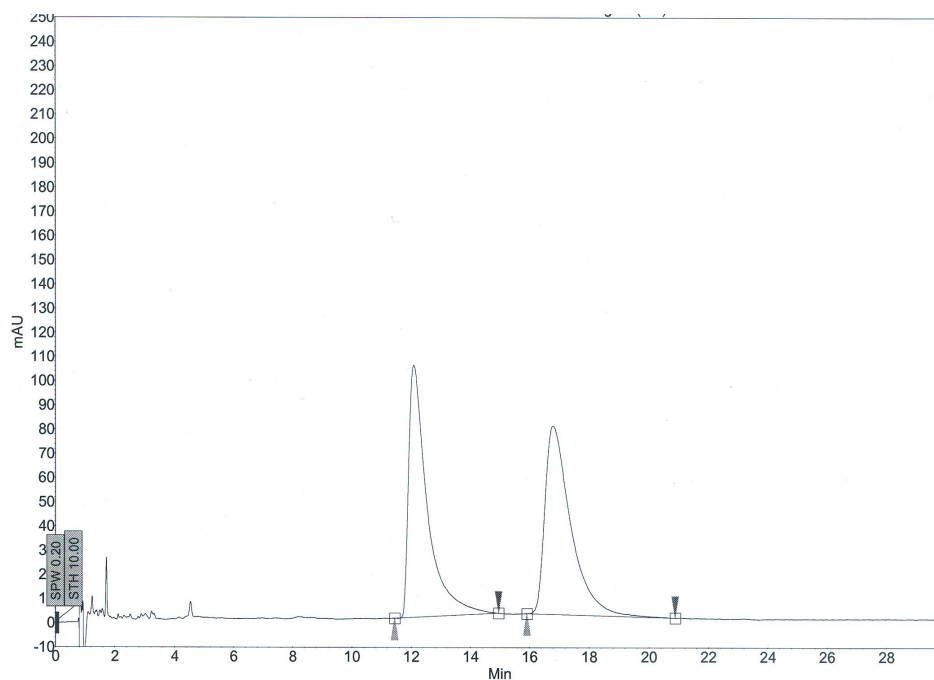
Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[μV]	[μV.Min]	[%]
1	UNKNOWN	11.45	12.09	14.95	0.00	49.21	104.1	75.9	49.212
2	UNKNOWN	15.91	16.80	20.88	0.00	50.79	77.8	78.3	50.788
Total						100.00	181.9	154.2	100.000



Results Table:

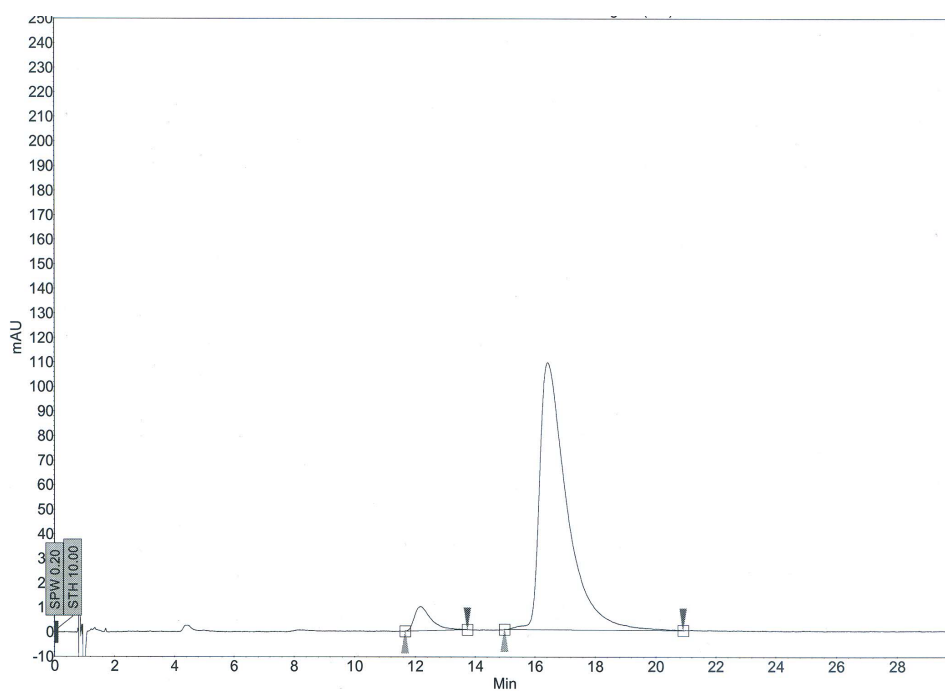
Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[μV]	[μV.Min]	[%]
1	UNKNOWN	11.66	12.18	13.74	0.00	5.22	9.9	6.3	5.220
2	UNKNOWN	14.98	16.43	20.91	0.00	94.78	108.8	114.3	94.780
Total						100.00	118.7	120.6	100.000





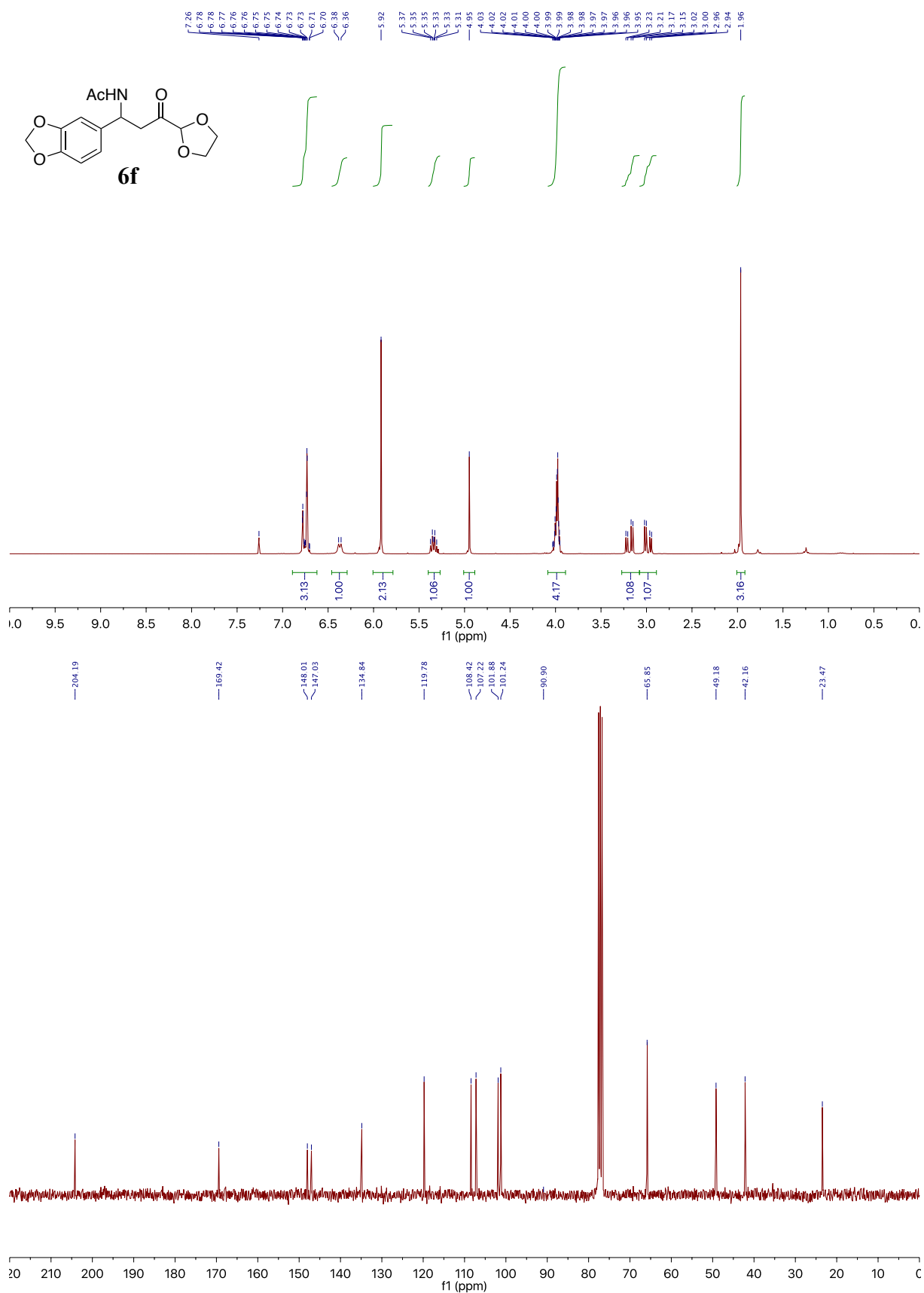
Results Table:

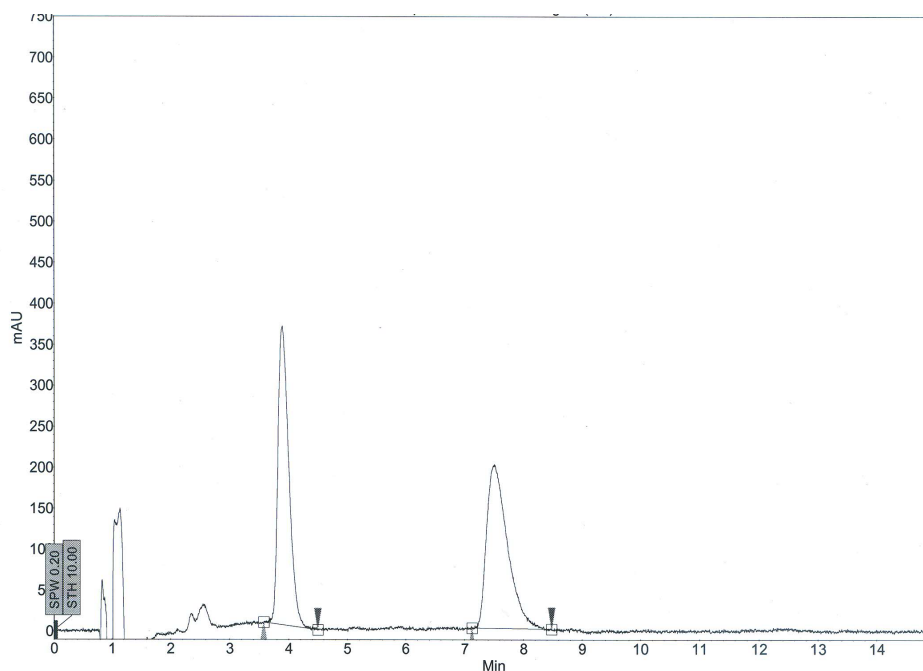
Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[μ V]	[μ V.Min]	[%]
1	UNKNOWN	11.45	12.09	14.95	0.00	49.21	104.1	75.9	49.212
2	UNKNOWN	15.91	16.80	20.88	0.00	50.79	77.8	78.3	50.788
Total						100.00	181.9	154.2	100.000



Results Table:

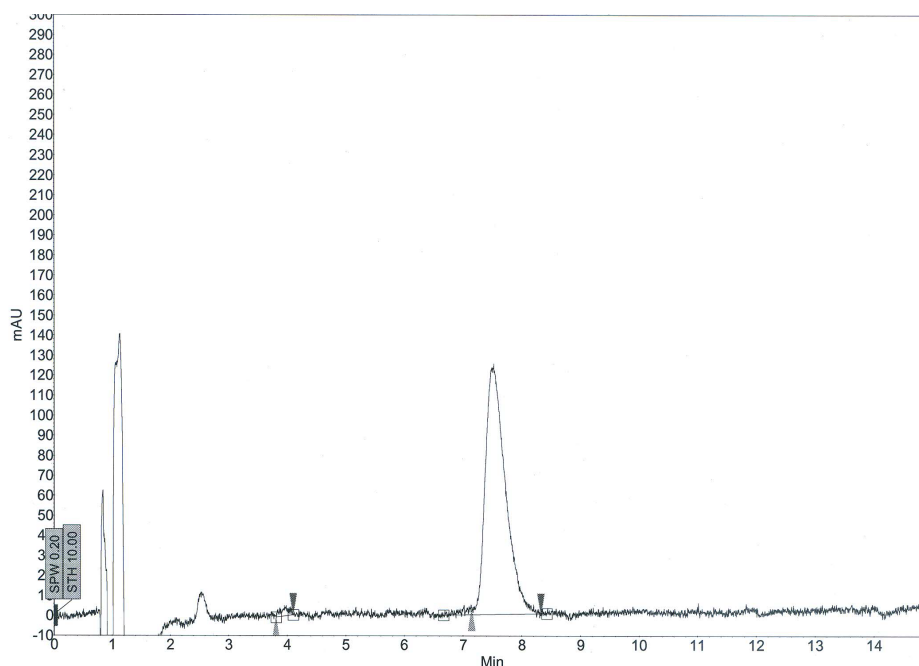
Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[μ V]	[μ V.Min]	[%]
1	UNKNOWN	11.66	12.18	13.74	0.00	5.22	9.9	6.3	5.220
2	UNKNOWN	14.98	16.43	20.91	0.00	94.78	108.8	114.3	94.780
Total						100.00	118.7	120.6	100.000





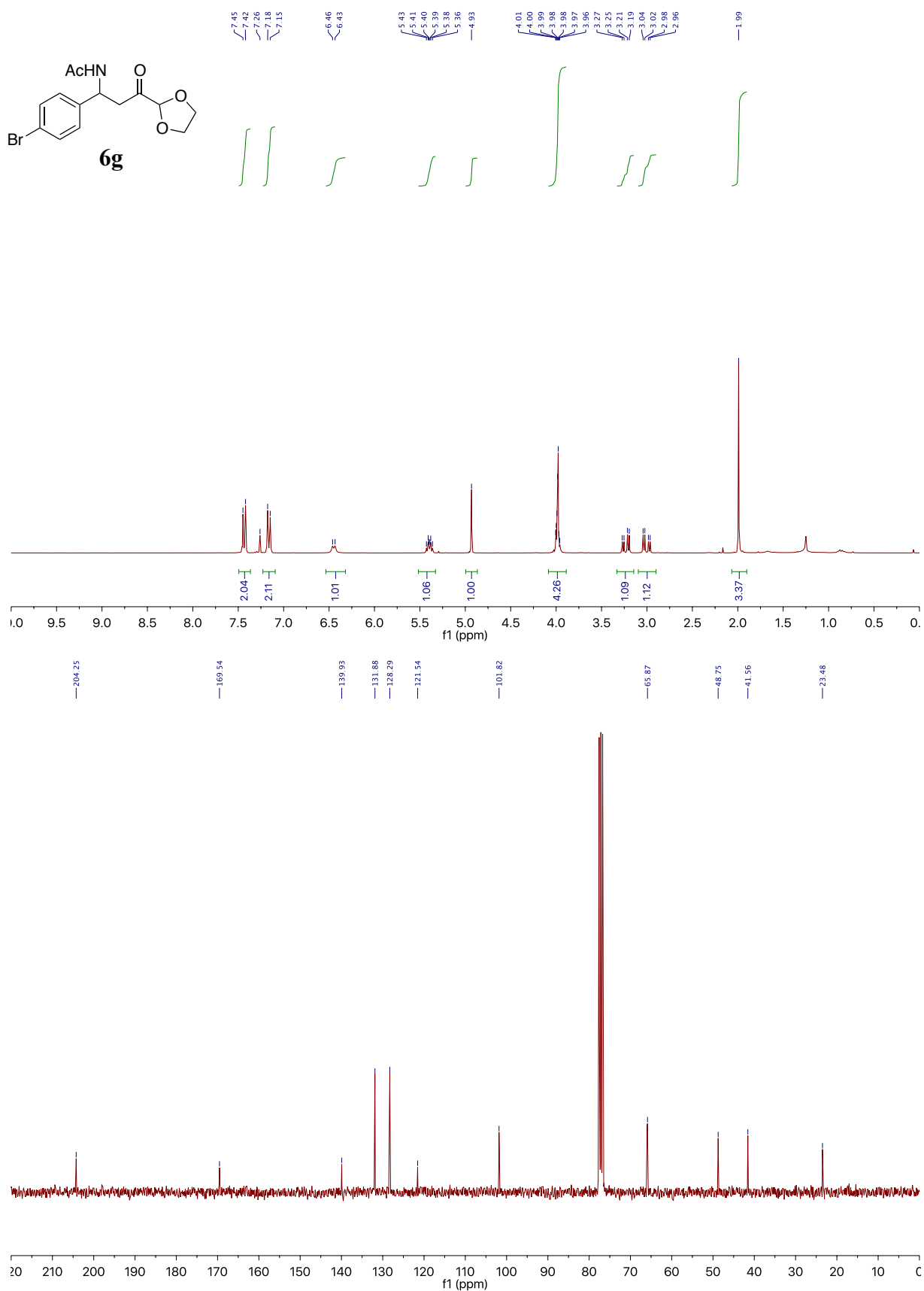
Results Table:

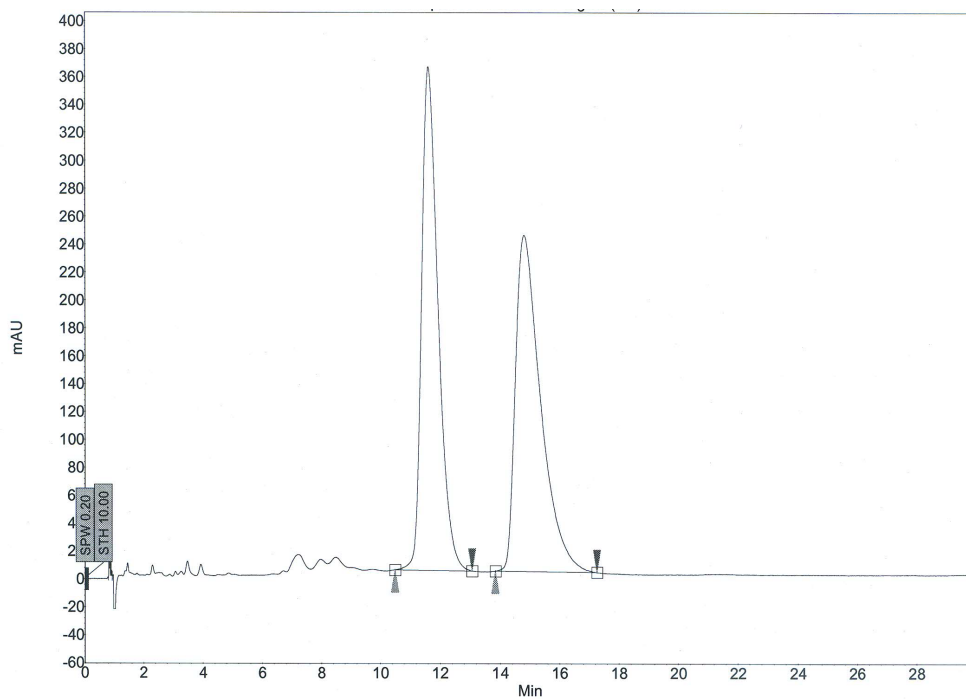
Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[μV]	[μV.Min]	[%]
2	UNKNOWN	3.58	3.89	4.50	0.00	48.83	362.6	78.0	48.829
1	UNKNOWN	7.12	7.50	8.48	0.00	51.17	196.9	81.8	51.171
Total						100.00	559.5	159.8	100.000



Results Table:

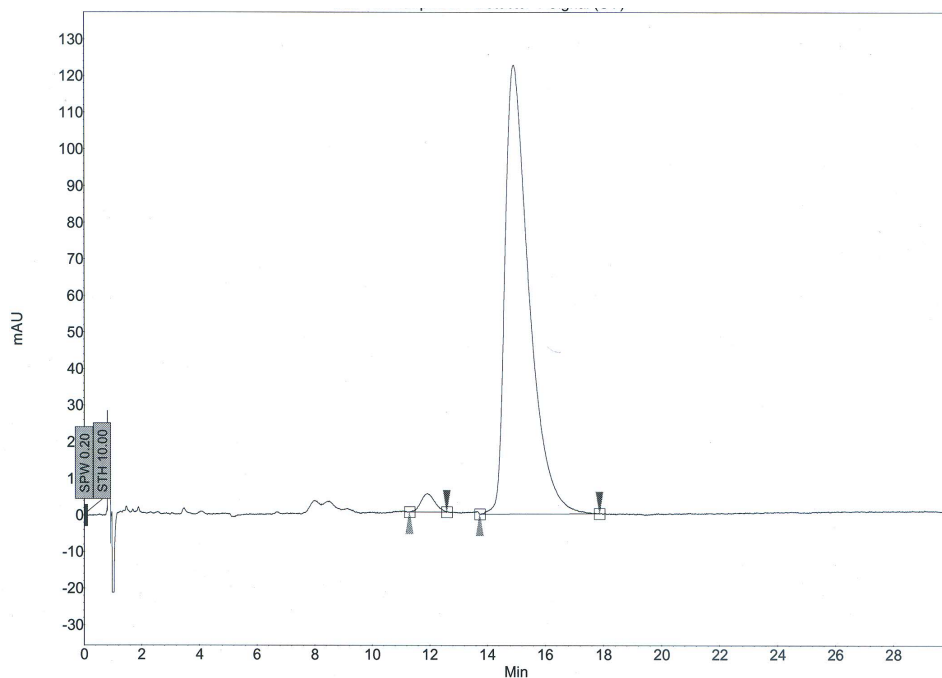
Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[μV]	[μV.Min]	[%]
2	UNKNOWN	3.81	3.98	4.11	0.00	1.48	3.9	0.7	1.483
1	UNKNOWN	7.15	7.53	8.33	0.00	98.52	125.2	48.9	98.517
Total						100.00	129.0	49.7	100.000





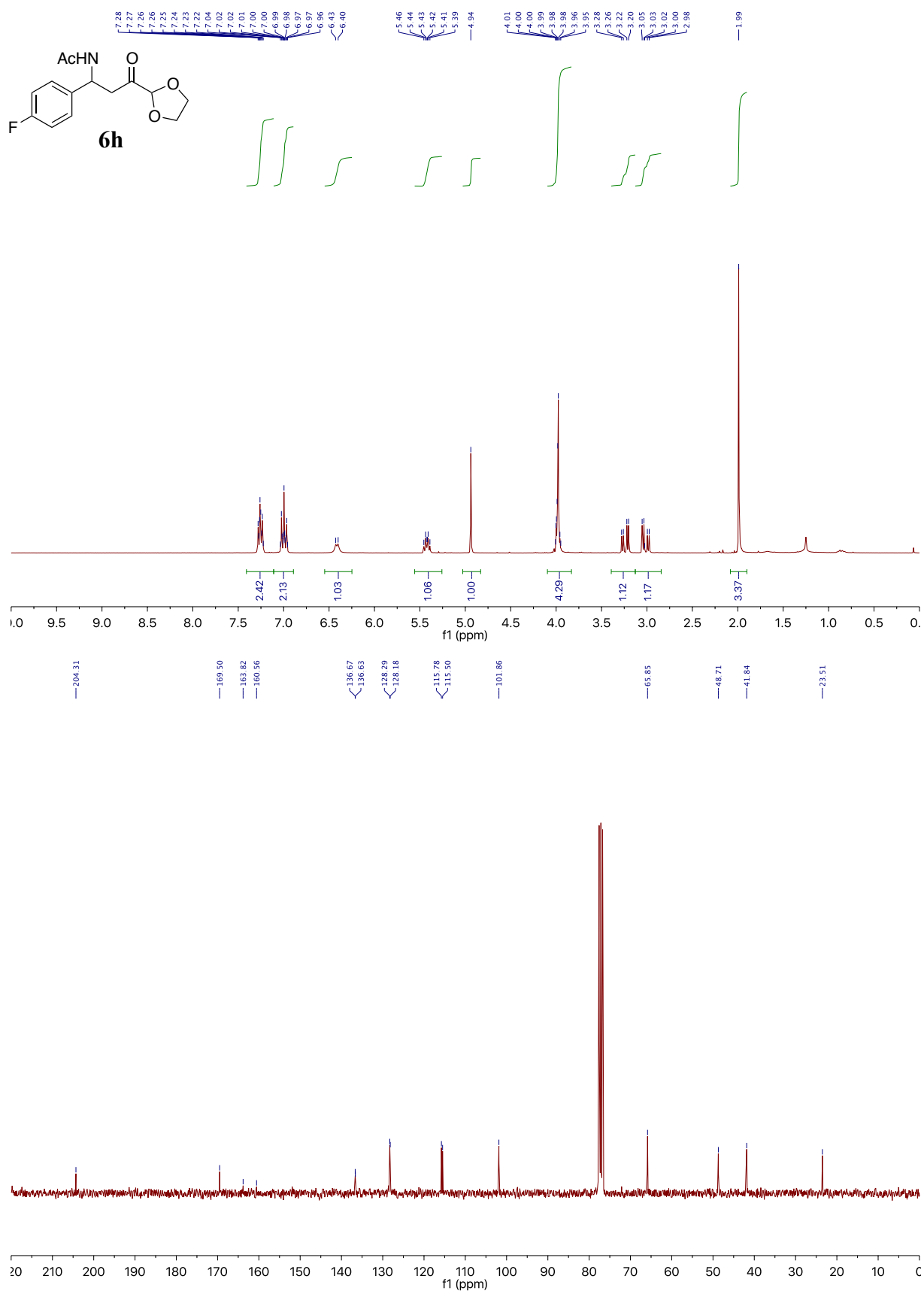
Results Table:

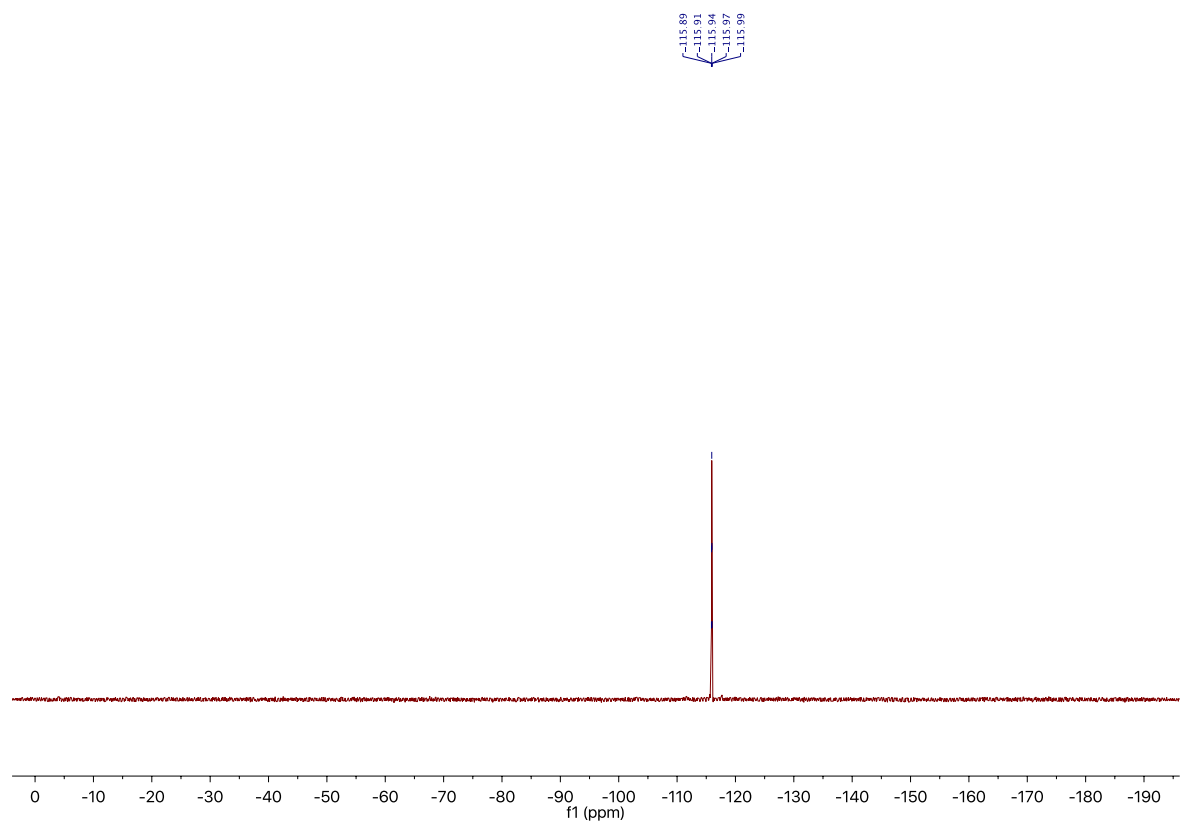
Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[μV]	[μV.Min]	[%]
1	UNKNOWN	10.48	11.60	13.06	0.00	49.38	360.9	230.6	49.383
2	UNKNOWN	13.84	14.79	17.25	0.00	50.62	241.1	236.3	50.617
Total						100.00	602.0	466.9	100.000

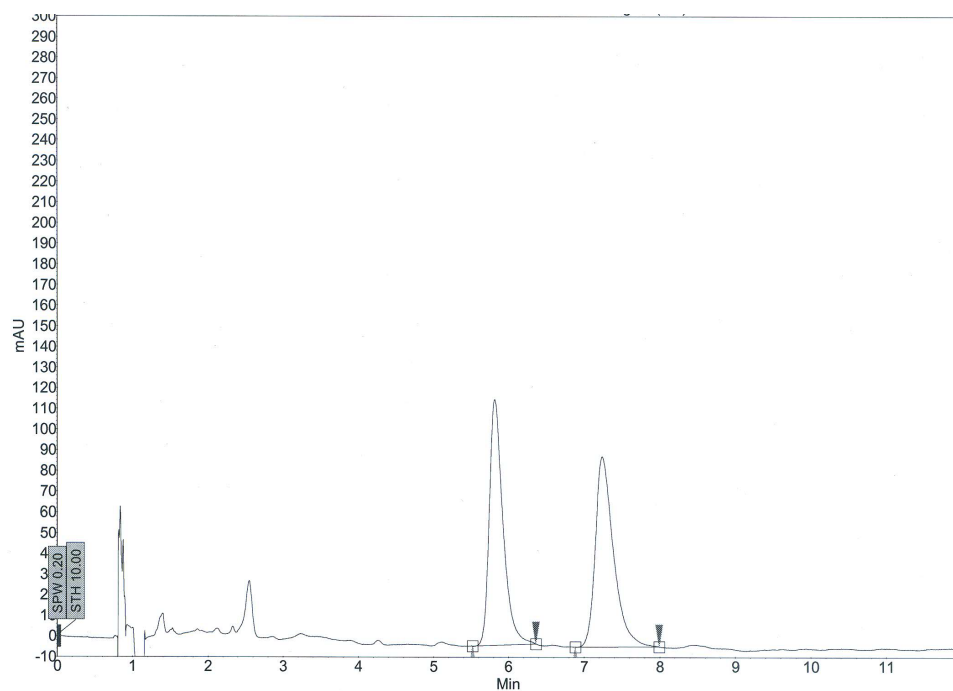


Results Table:

Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[μV]	[μV.Min]	[%]
1	UNKNOWN	11.29	11.92	12.59	0.00	2.32	5.0	2.8	2.317
2	UNKNOWN	13.74	14.92	17.87	0.00	97.68	122.5	117.1	97.683
Total						100.00	127.6	119.8	100.000

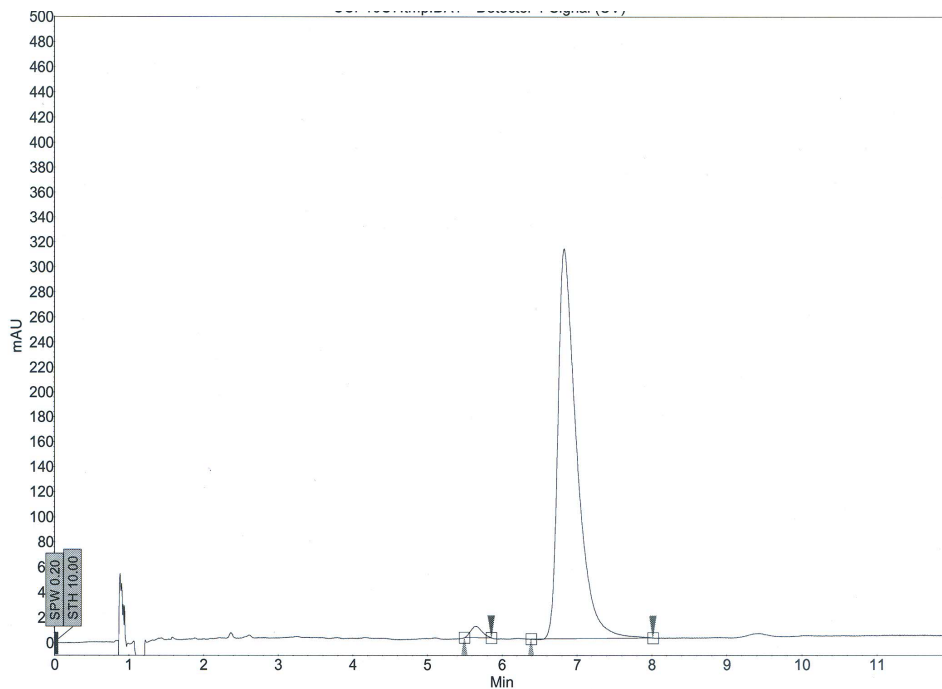






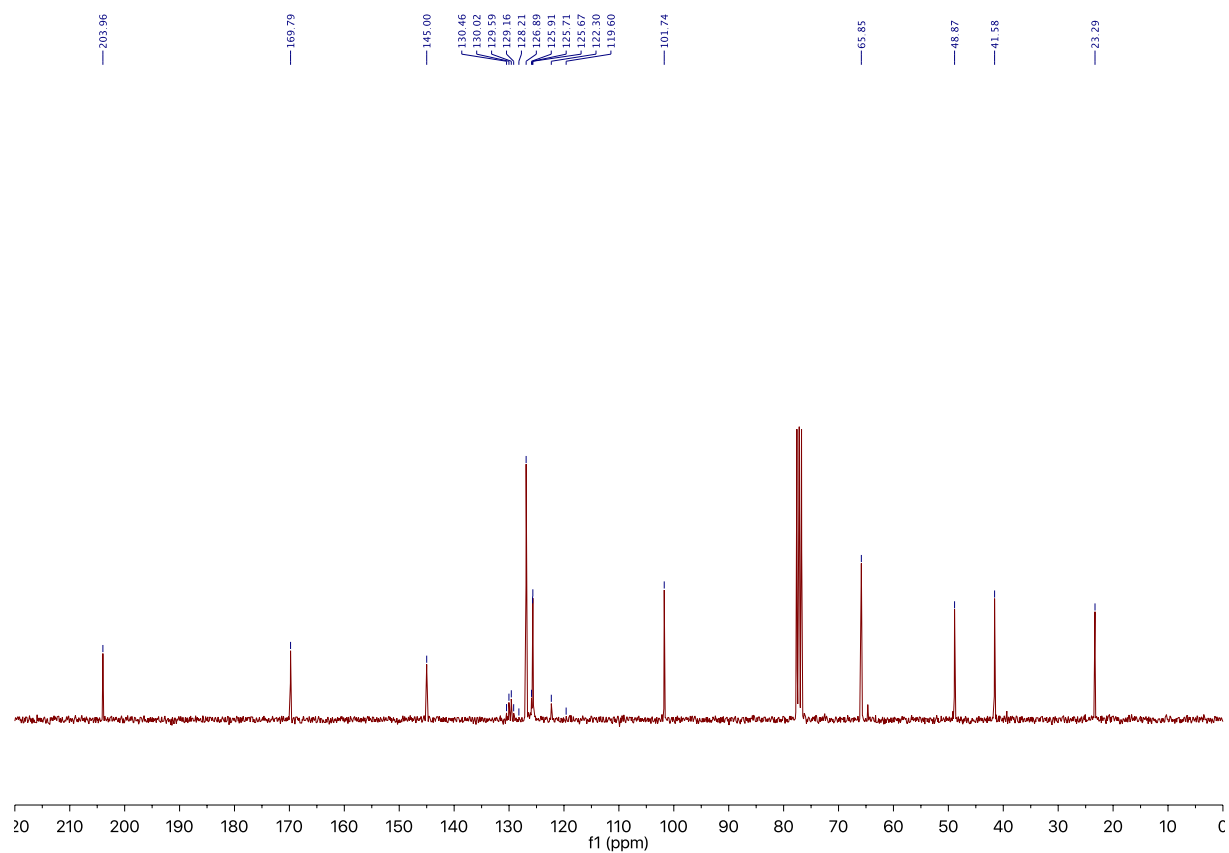
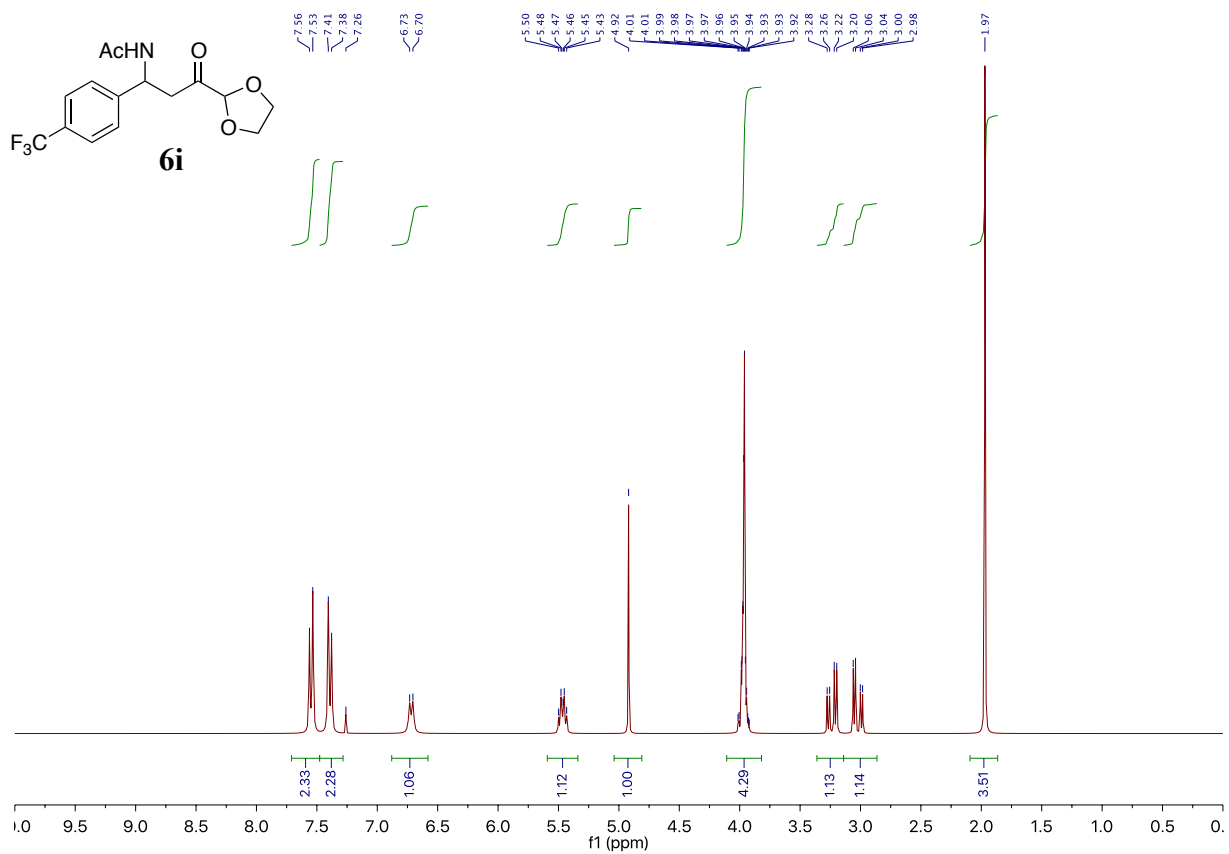
Results Table:

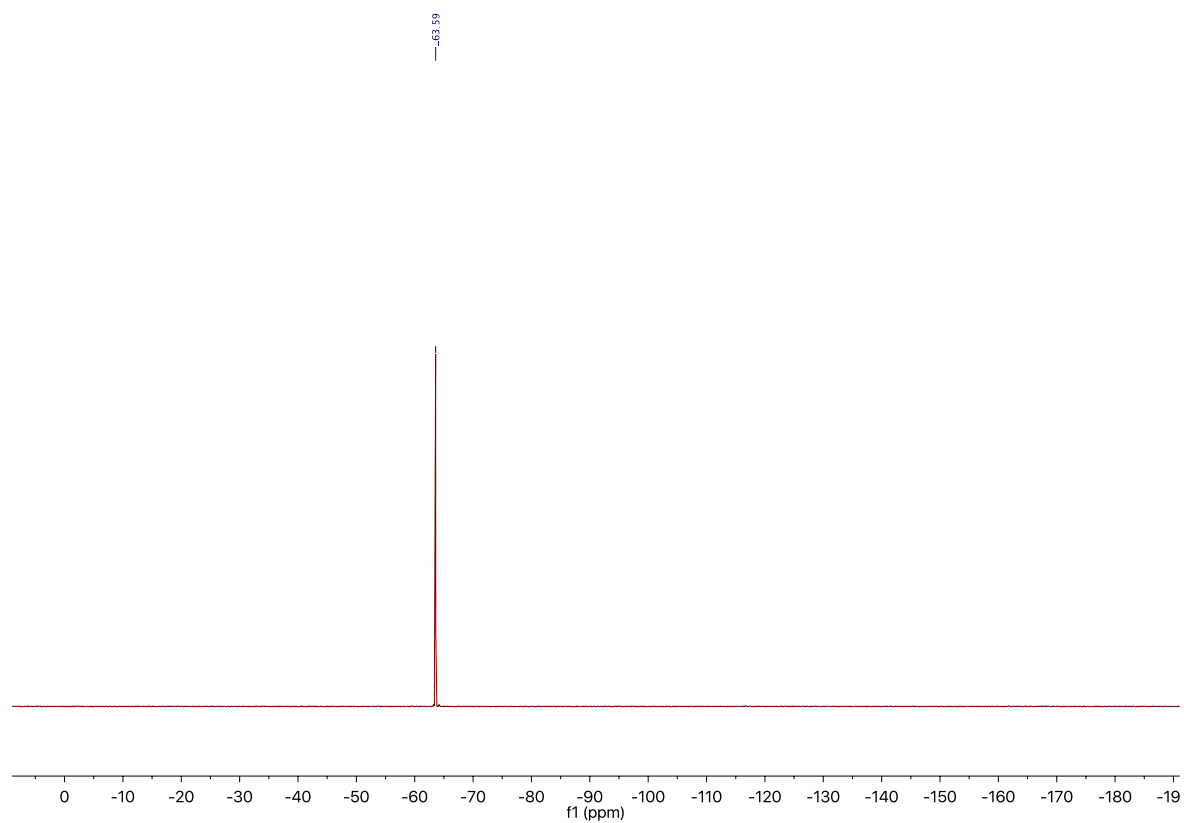
Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[μ V]	[μ V.Min]	[%]
1	UNKNOWN	5.52	5.82	6.36	0.00	49.60	118.7	25.2	49.600
2	UNKNOWN	6.89	7.24	7.99	0.00	50.40	91.9	25.6	50.400
Total						100.00	210.6	50.8	100.000

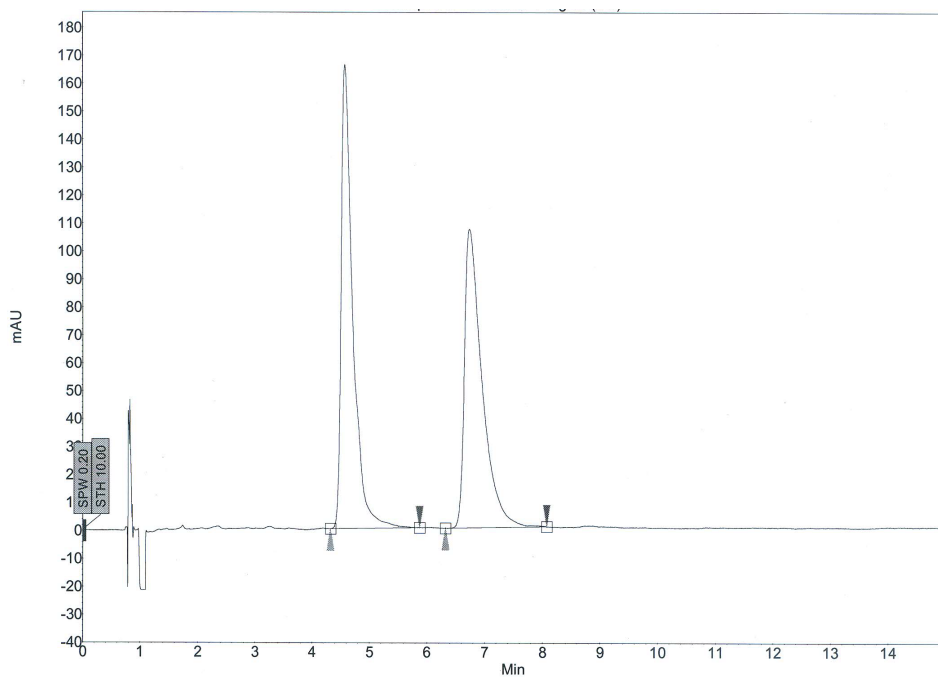


Results Table:

Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[μ V]	[μ V.Min]	[%]
1	UNKNOWN	5.50	5.65	5.86	0.00	1.72	8.9	1.6	1.722
2	UNKNOWN	6.39	6.83	8.01	0.00	98.28	311.3	90.0	98.278
Total						100.00	320.2	91.5	100.000

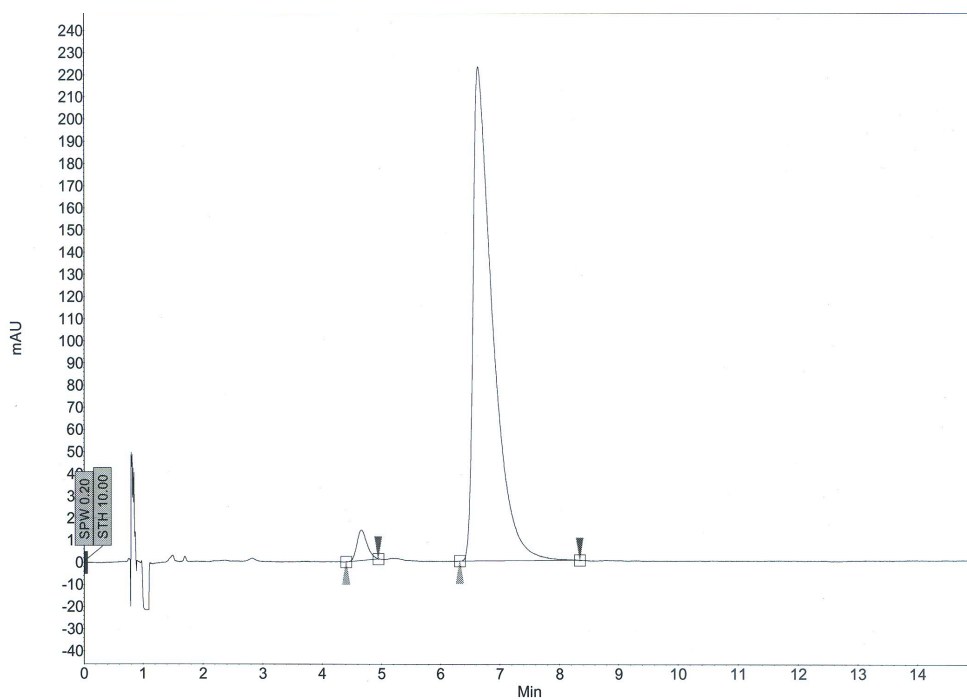






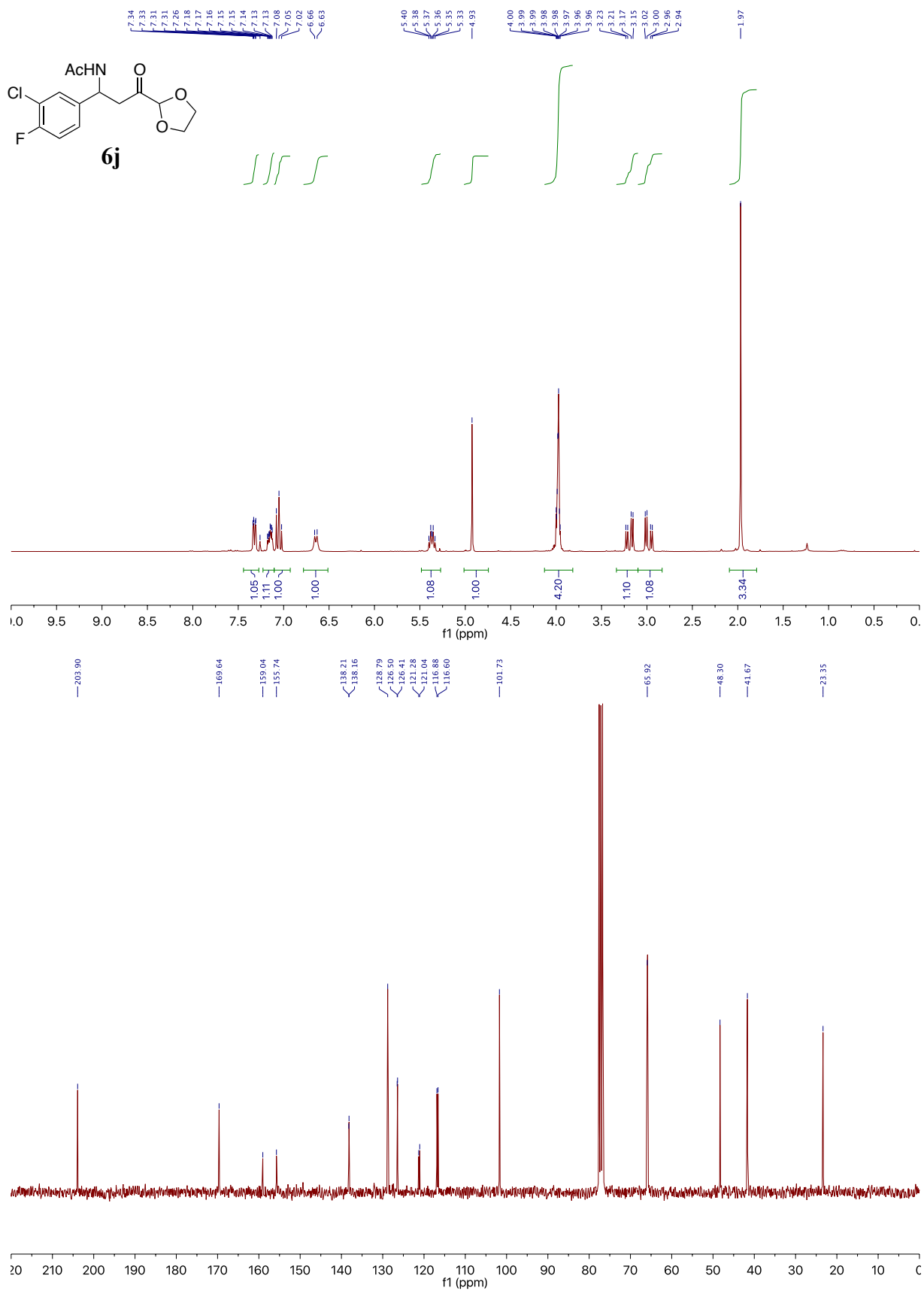
Results Table:

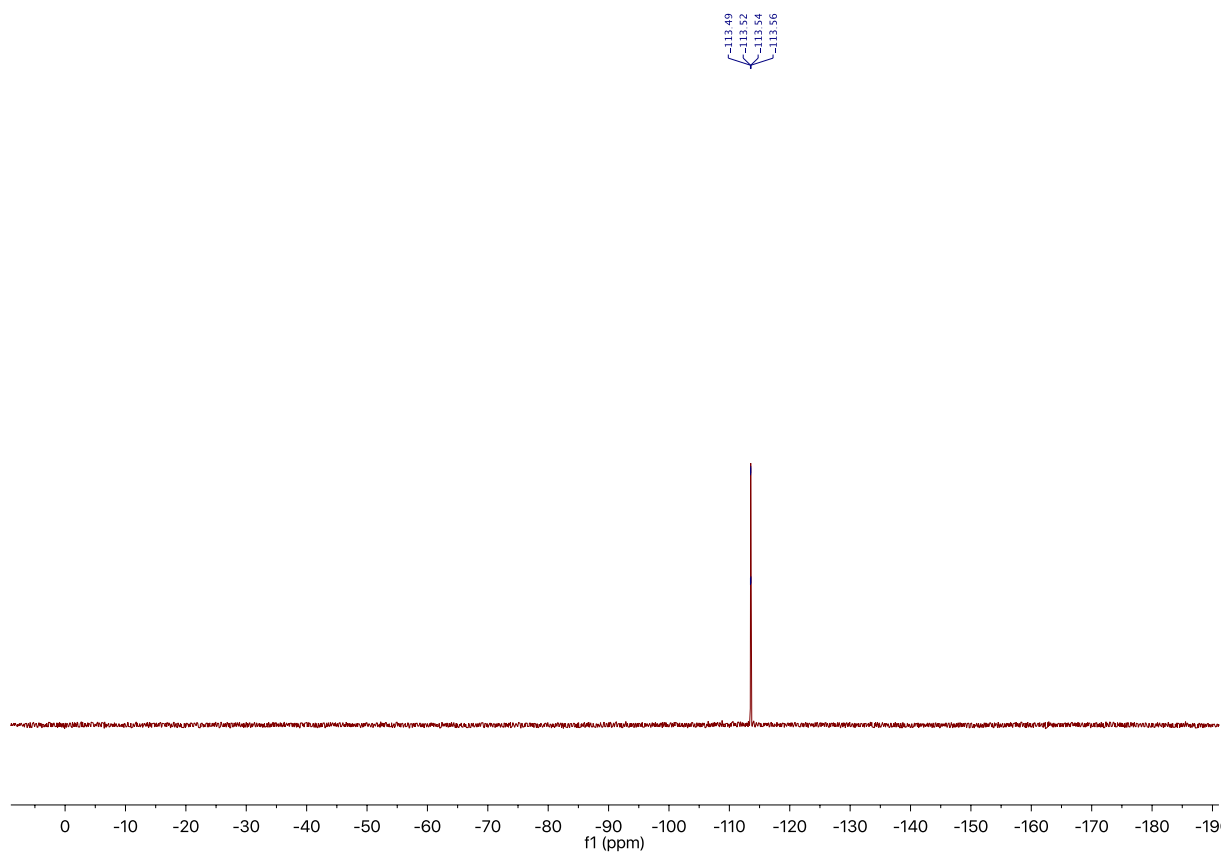
Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[μV]	[μV.Min]	[%]
1	UNKNOWN	4.33	4.58	5.88	0.00	50.71	166.0	38.8	50.711
2	UNKNOWN	6.33	6.74	8.08	0.00	49.29	106.9	37.7	49.289
Total						100.00	272.8	76.4	100.000

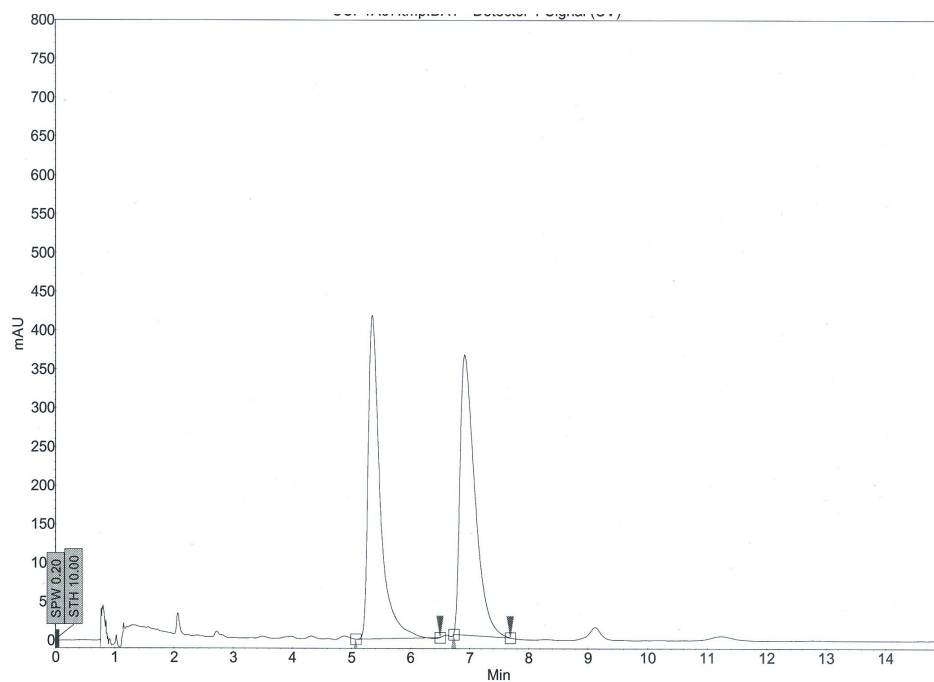


Results Table:

Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[μV]	[μV.Min]	[%]
2	UNKNOWN	4.40	4.66	4.95	0.00	3.10	13.8	2.7	3.101
1	UNKNOWN	6.33	6.63	8.34	0.00	96.90	223.0	84.3	96.899
Total						100.00	236.8	87.0	100.000

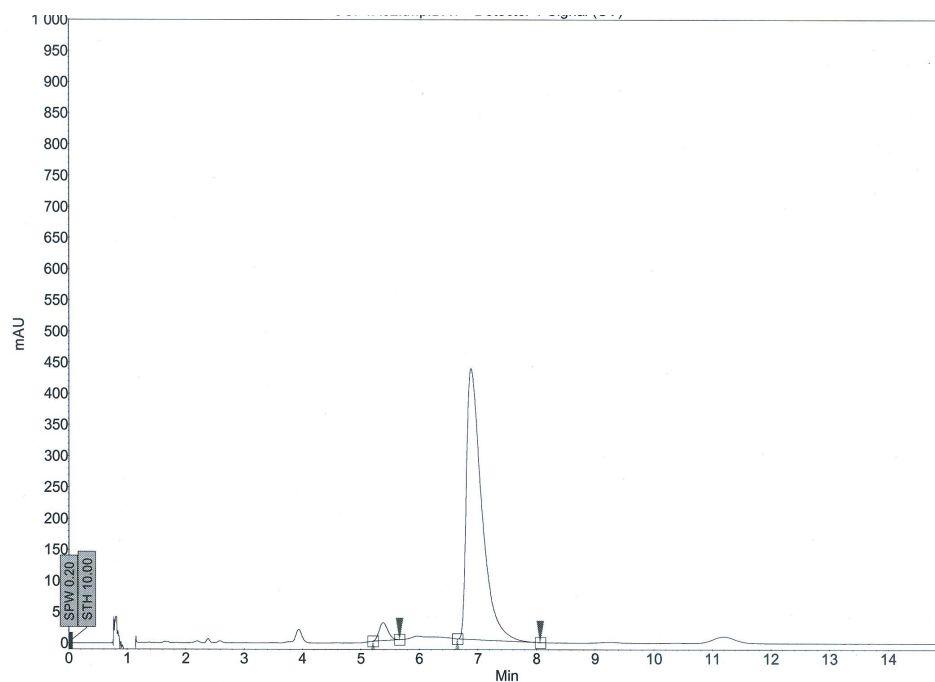






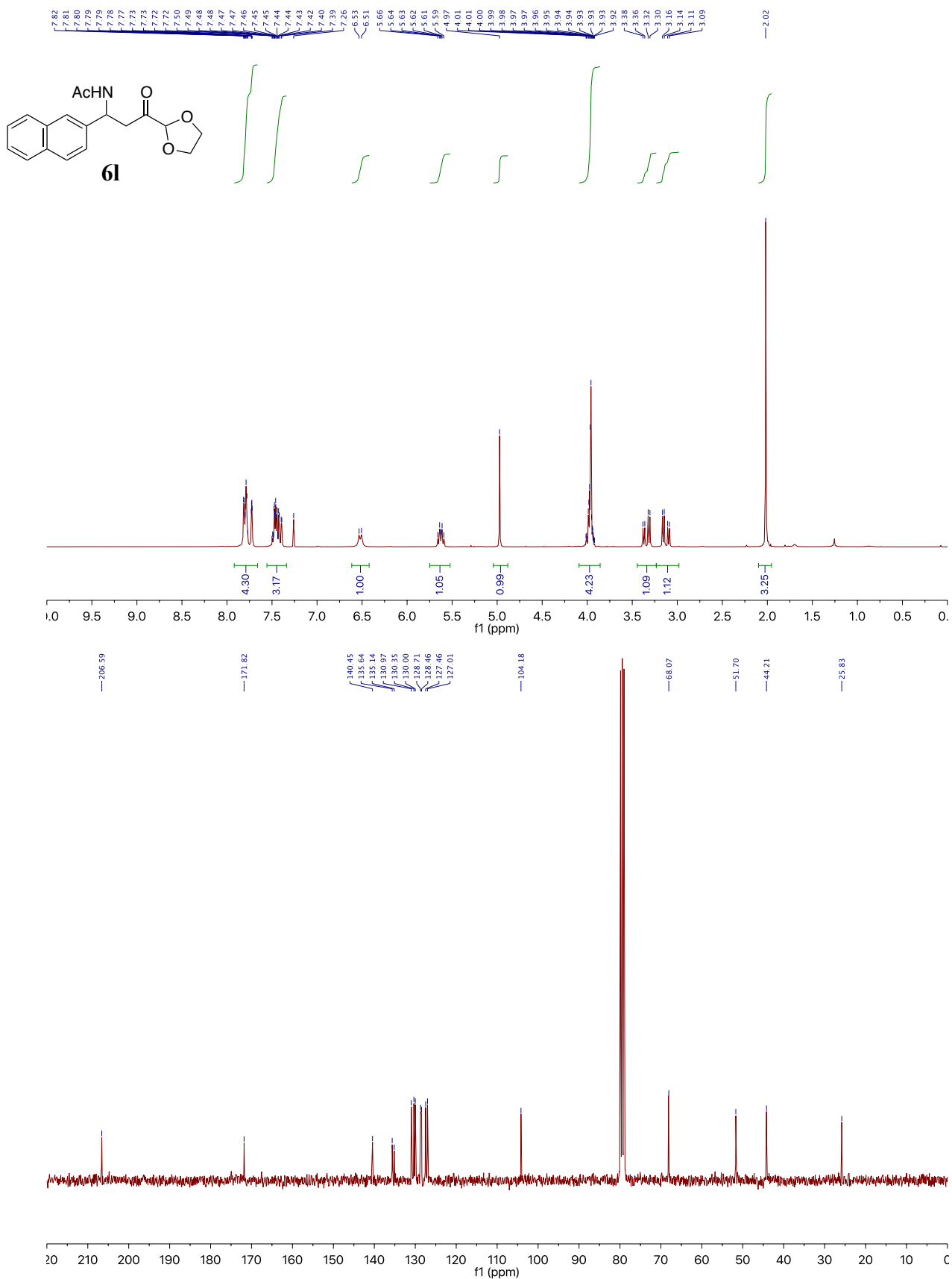
Results Table:

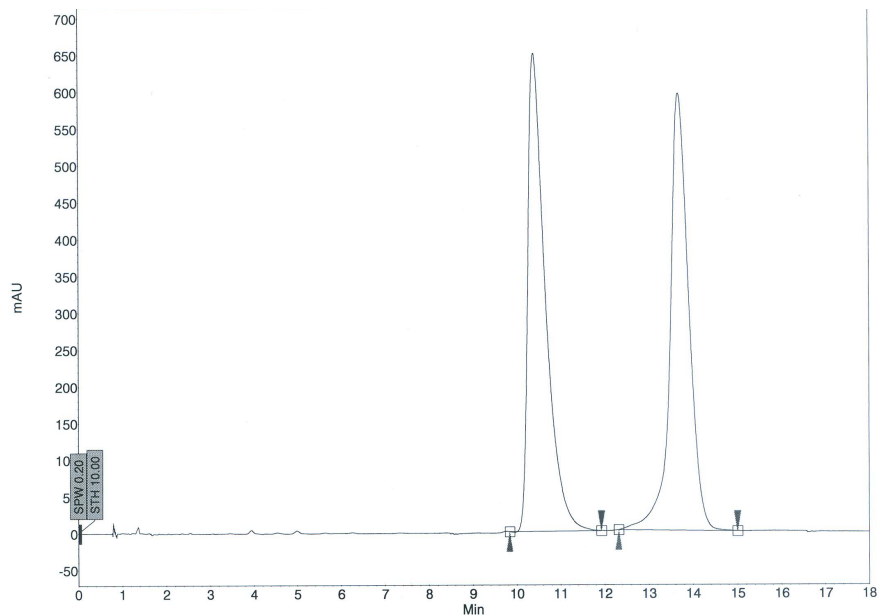
Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[μV]	[μV.Min]	[%]
1	UNKNOWN	5.07	5.35	6.50	0.00	47.99	417.0	97.5	47.987
2	UNKNOWN	6.73	6.92	7.69	0.00	52.01	361.4	105.7	52.013
Total						100.00	778.4	203.1	100.000



Results Table:

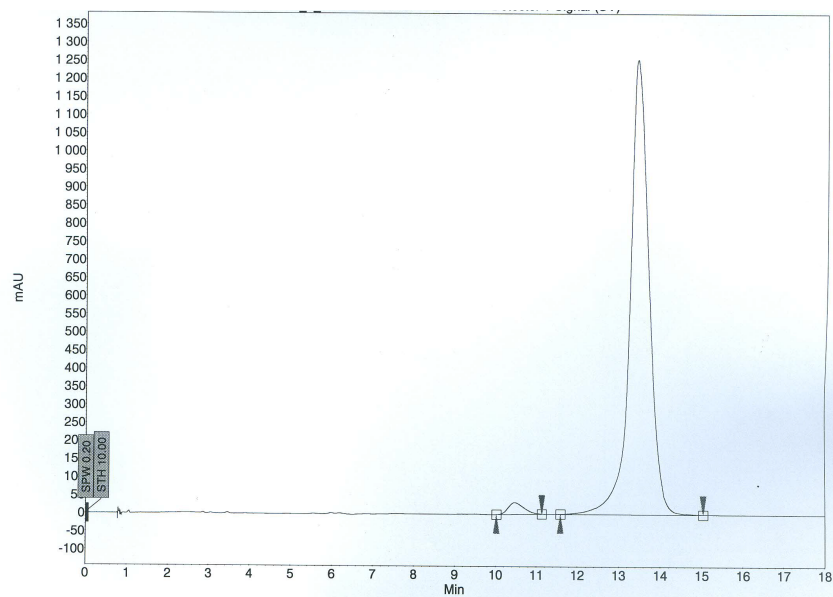
Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[μV]	[μV.Min]	[%]
1	UNKNOWN	5.21	5.38	5.66	0.00	3.69	28.5	5.0	3.688
2	UNKNOWN	6.65	6.89	8.06	0.00	96.31	434.1	131.2	96.312
Total						100.00	462.7	136.3	100.000





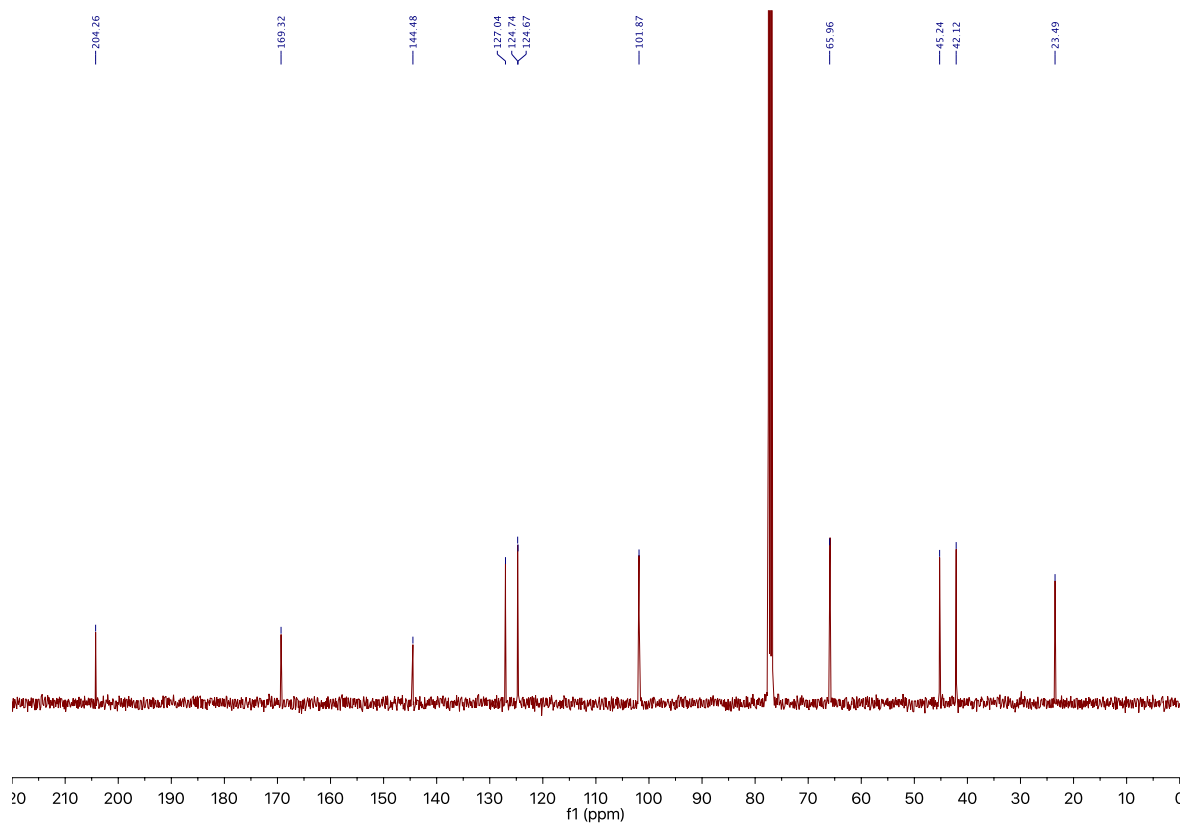
Results Table:

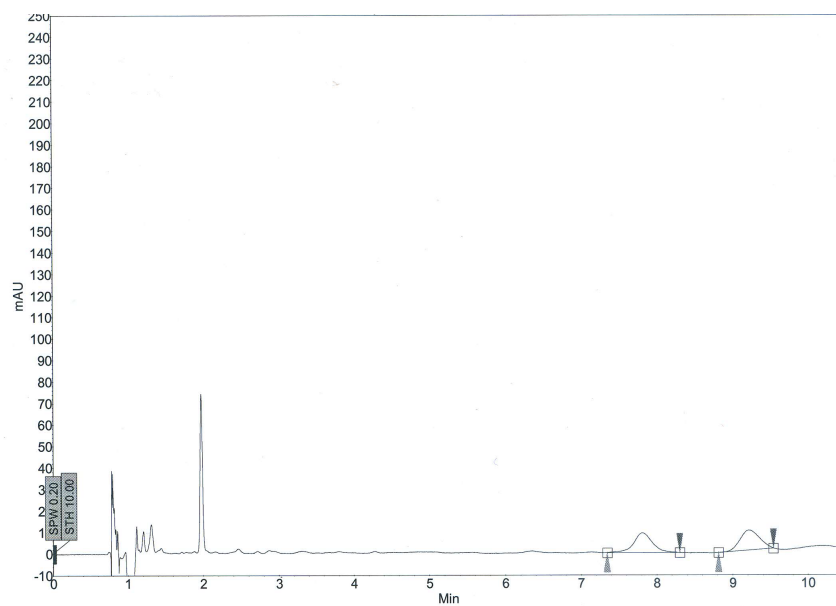
Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[μ V]	[μ V.Min]	[%]
1	UNKNOWN	9.83	10.40	11.93	0.00	50.72	648.9	301.7	50.724
2	UNKNOWN	12.32	13.68	15.00	0.00	49.28	592.7	293.0	49.276
Total						100.00	1241.6	594.7	100.000



Results Table:

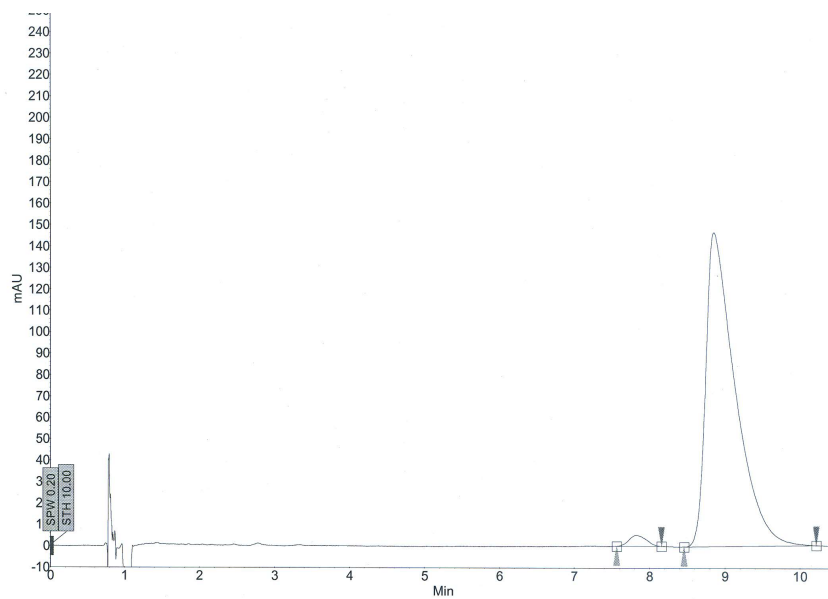
Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[μ V]	[μ V.Min]	[%]
1	UNKNOWN	10.02	10.46	11.13	0.00	2.13	32.6	14.6	2.127
2	UNKNOWN	11.59	13.40	15.04	0.00	97.87	1253.3	672.7	97.873
Total						100.00	1286.0	687.4	100.000





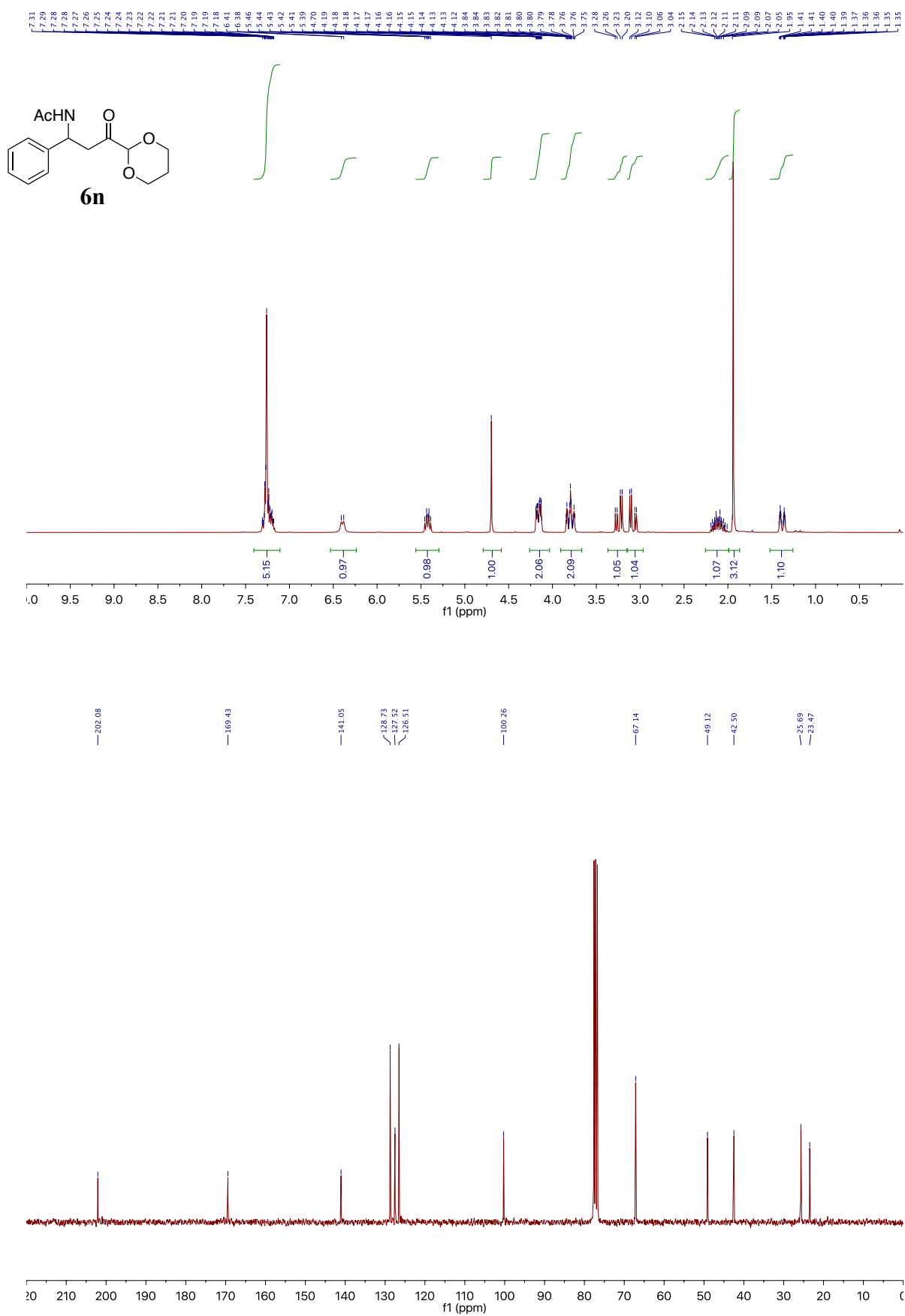
Results Table:

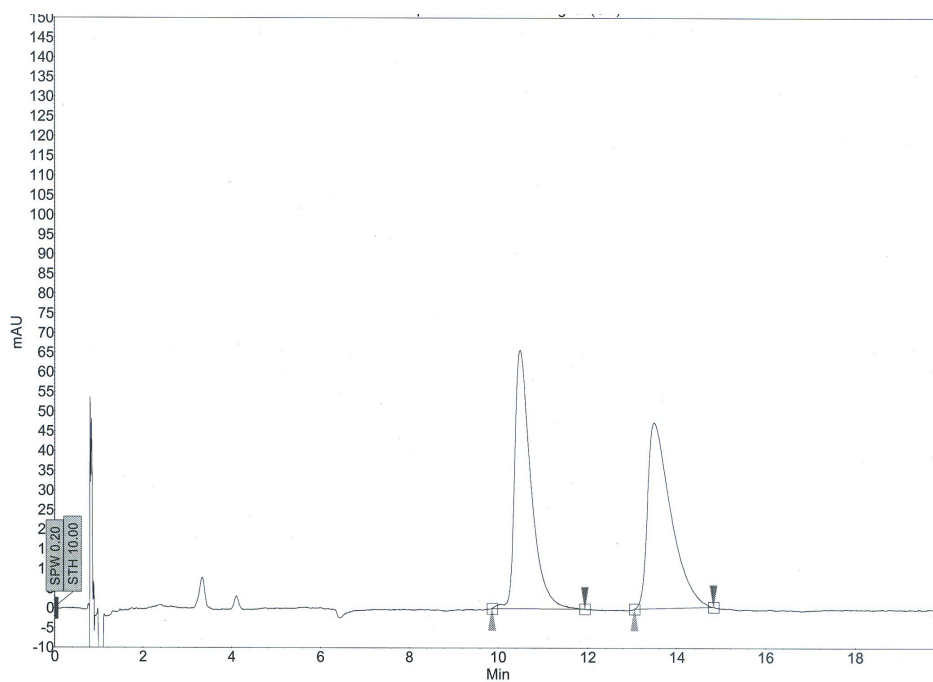
Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[μV]	[μV.Min]	[%]
1	UNKNOWN	7.34	7.81	8.30	0.00	49.00	9.2	2.6	48.999
2	UNKNOWN	8.81	9.21	9.54	0.00	51.00	9.3	2.8	51.001
Total						100.00	18.5	5.4	100.000



Results Table:

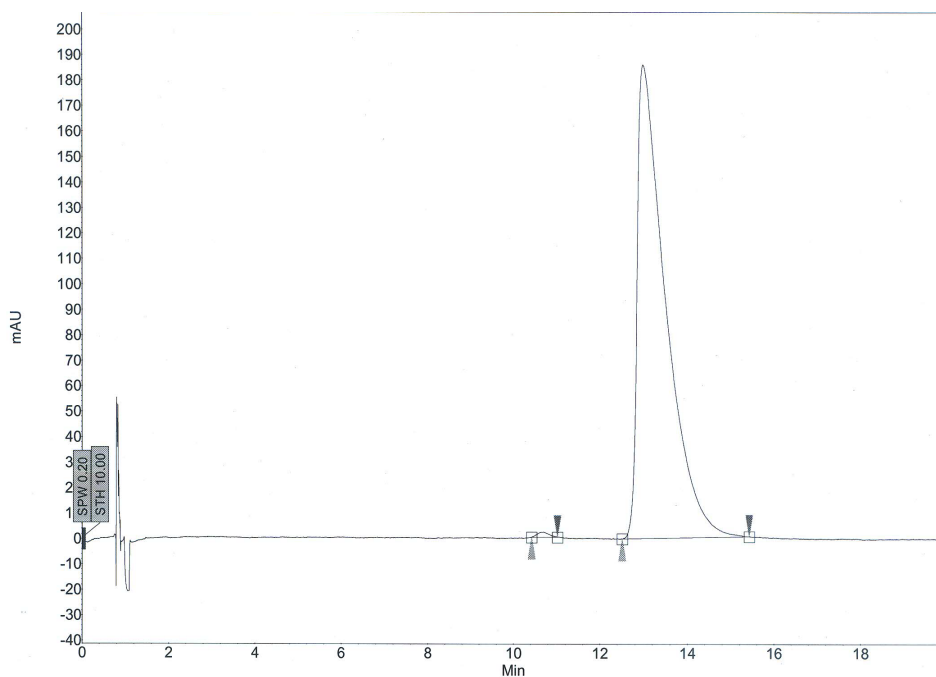
Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[μV]	[μV.Min]	[%]
1	UNKNOWN	7.57	7.83	8.16	0.00	2.02	5.1	1.4	2.022
2	UNKNOWN	8.46	8.85	10.22	0.00	97.98	146.6	66.3	97.978
Total						100.00	151.7	67.6	100.000





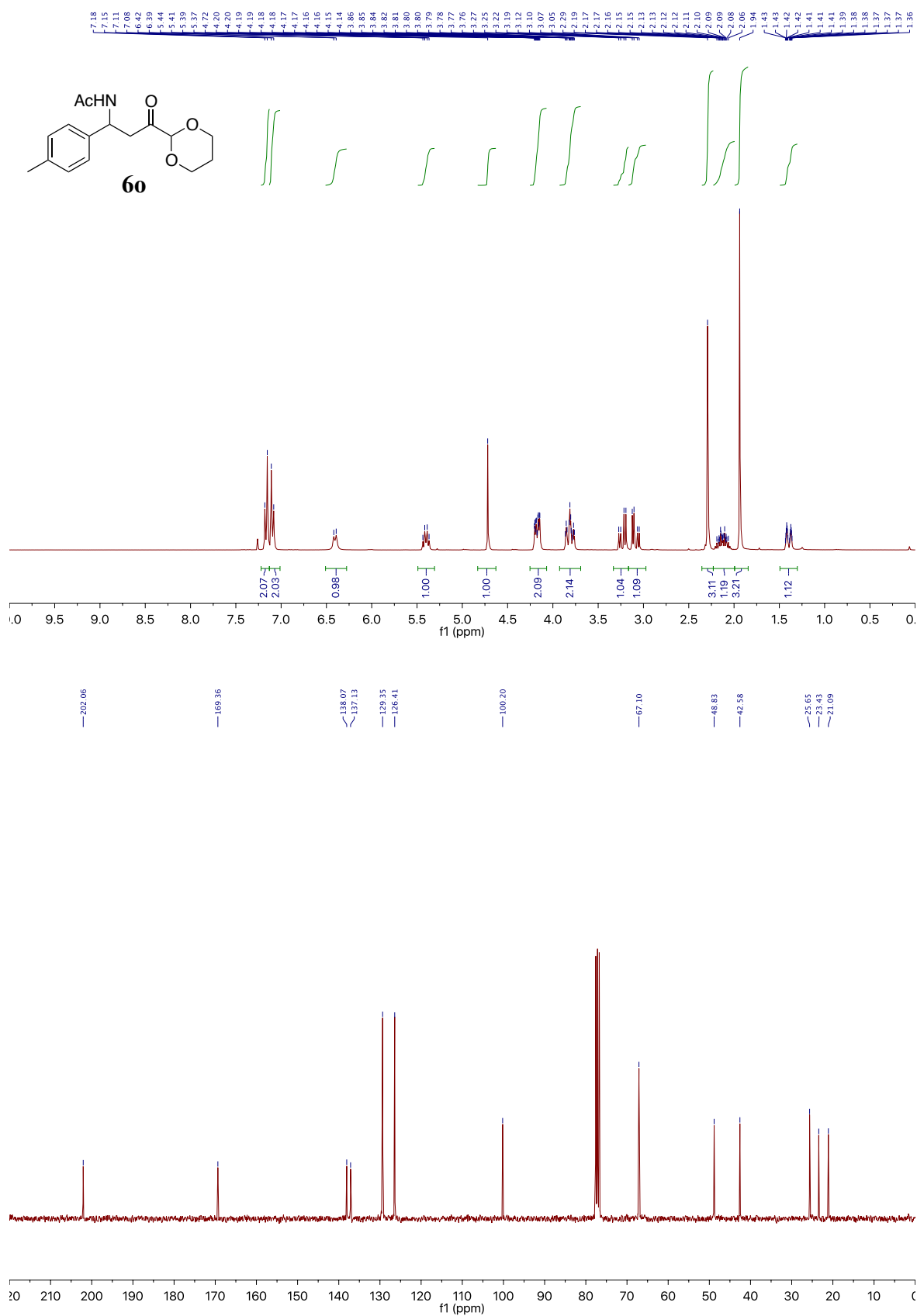
Results Table:

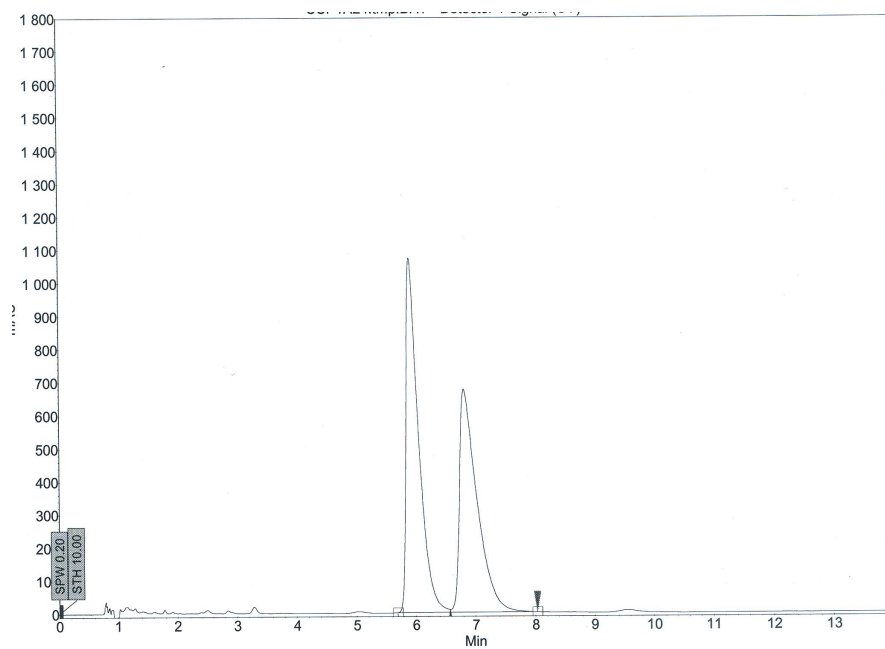
Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[μV]	[μV.Min]	[%]
2	UNKNOWN	9.86	10.49	11.93	0.00	48.98	65.6	27.6	48.982
1	UNKNOWN	13.05	13.48	14.83	0.00	51.02	47.2	28.8	51.018
Total						100.00	112.8	56.4	100.000



Results Table:

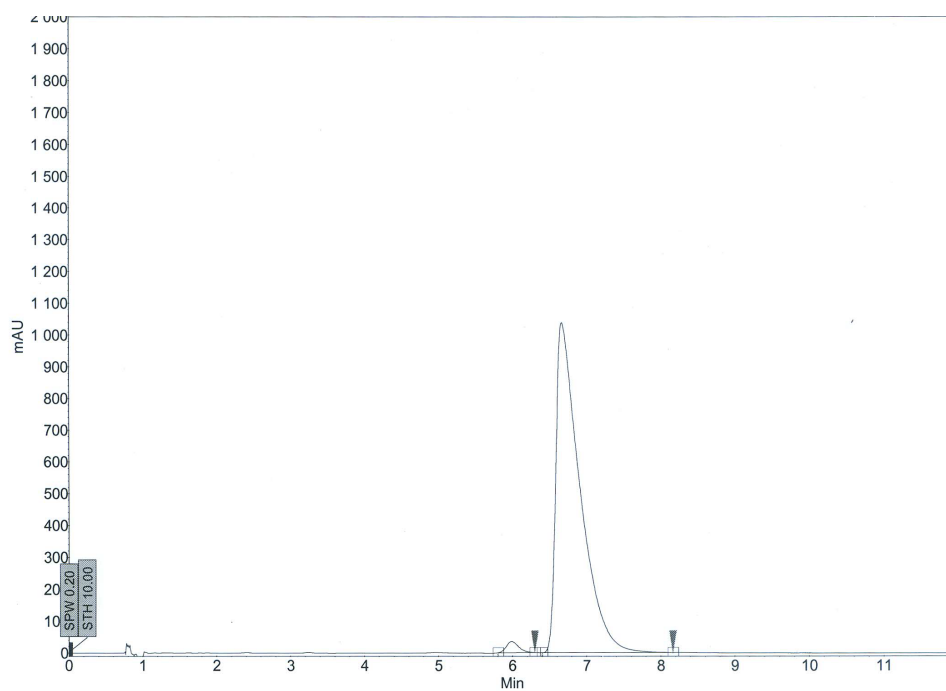
Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[μV]	[μV.Min]	[%]
1	UNKNOWN	10.42	10.70	11.02	0.00	0.45	2.0	0.6	0.446
2	UNKNOWN	12.51	12.99	15.43	0.00	99.55	186.0	139.3	99.554
Total						100.00	188.0	139.9	100.000





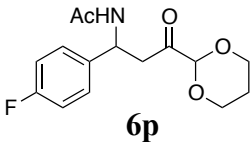
Results Table:

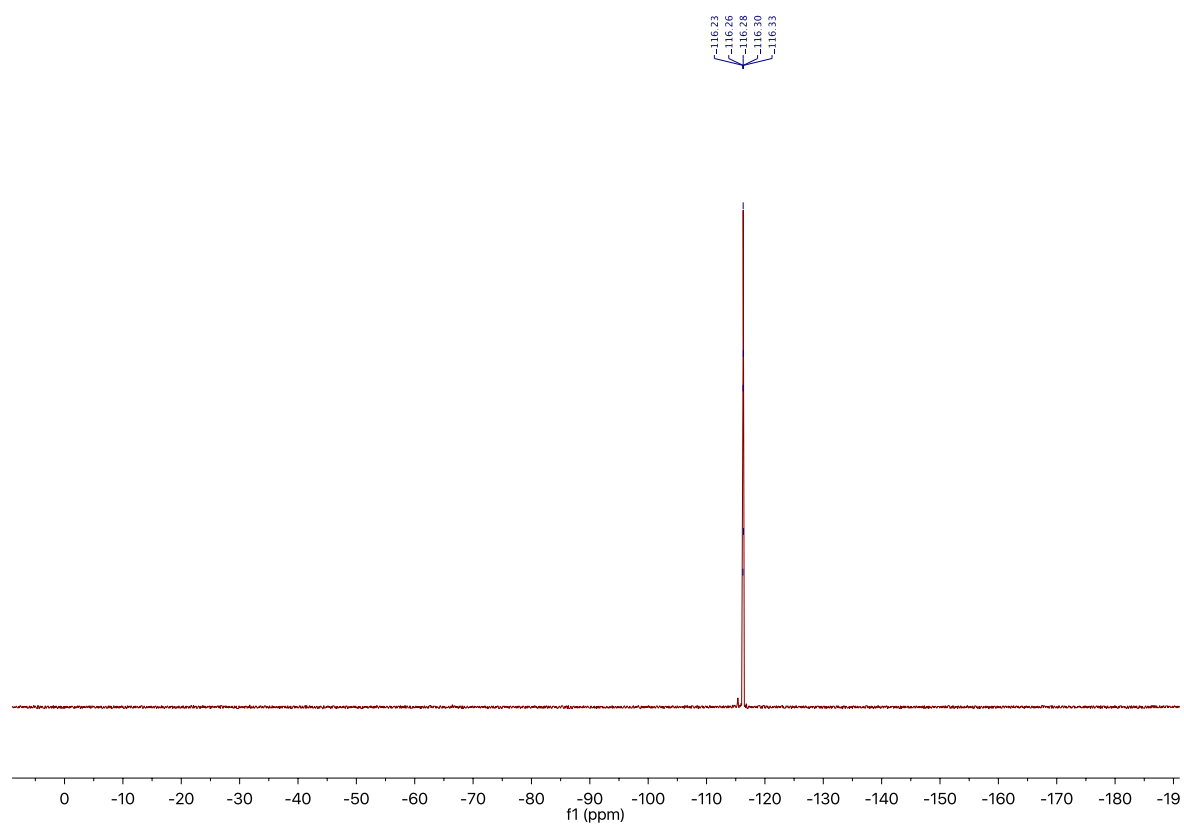
Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[μV]	[μV.Min]	[%]
1	UNKNOWN	5.44	5.79	6.53	0.00	49.04	1075.5	272.1	49.038
2	UNKNOWN	6.53	6.77	8.10	0.00	50.96	751.3	282.8	50.962
Total						100.00	1826.7	554.9	100.000

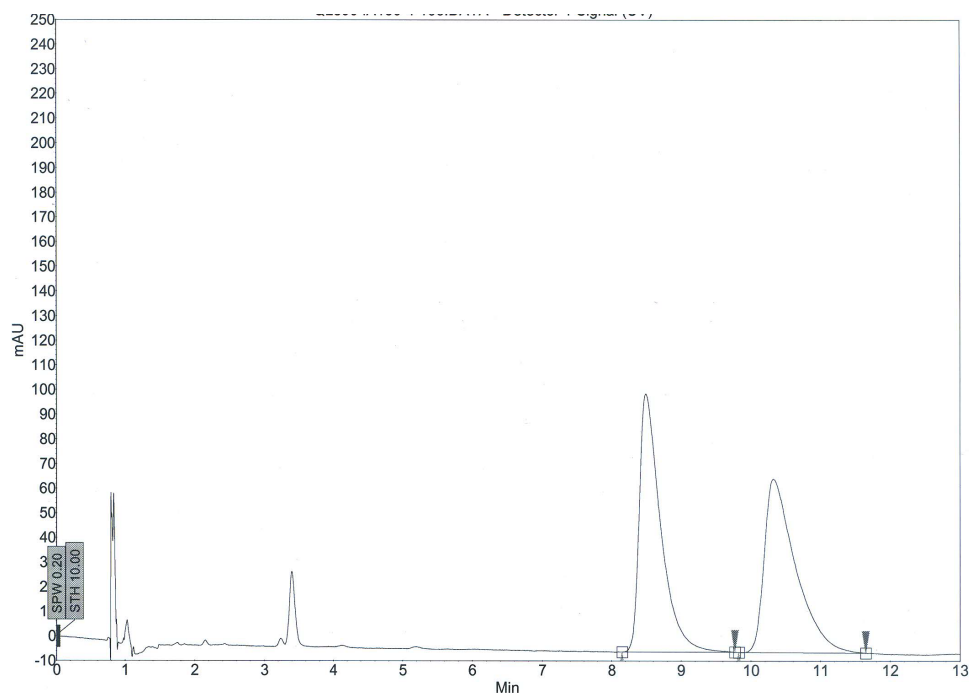


Results Table:

Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[μV]	[μV.Min]	[%]
1	UNKNOWN	5.81	5.99	6.30	0.00	1.71	34.9	6.7	1.708
2	UNKNOWN	6.40	6.67	8.16	0.00	98.29	1037.1	388.2	98.292
Total						100.00	1072.1	394.9	100.000

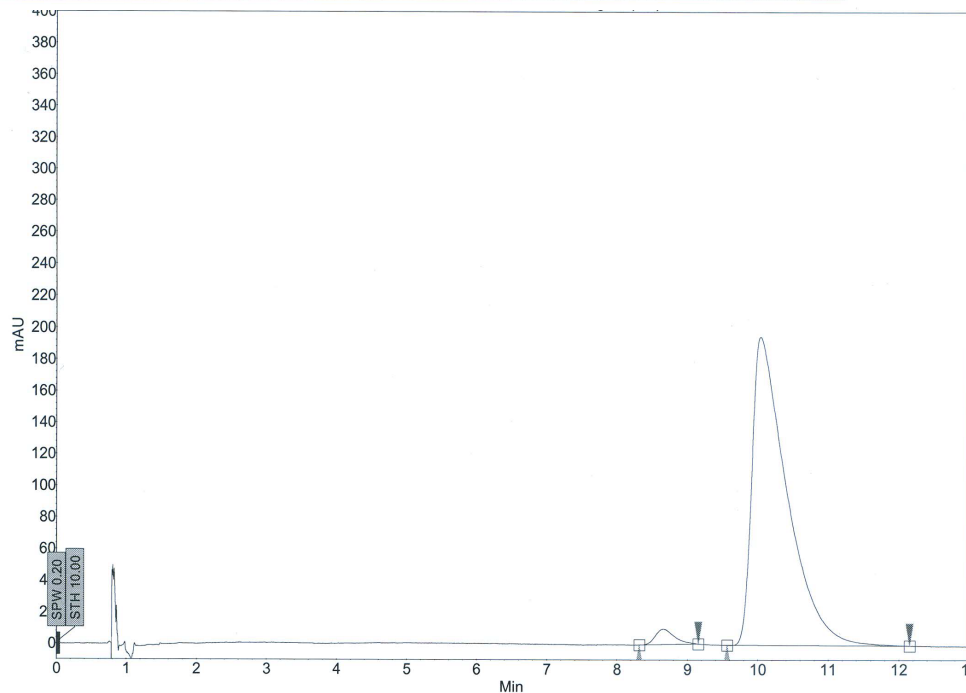






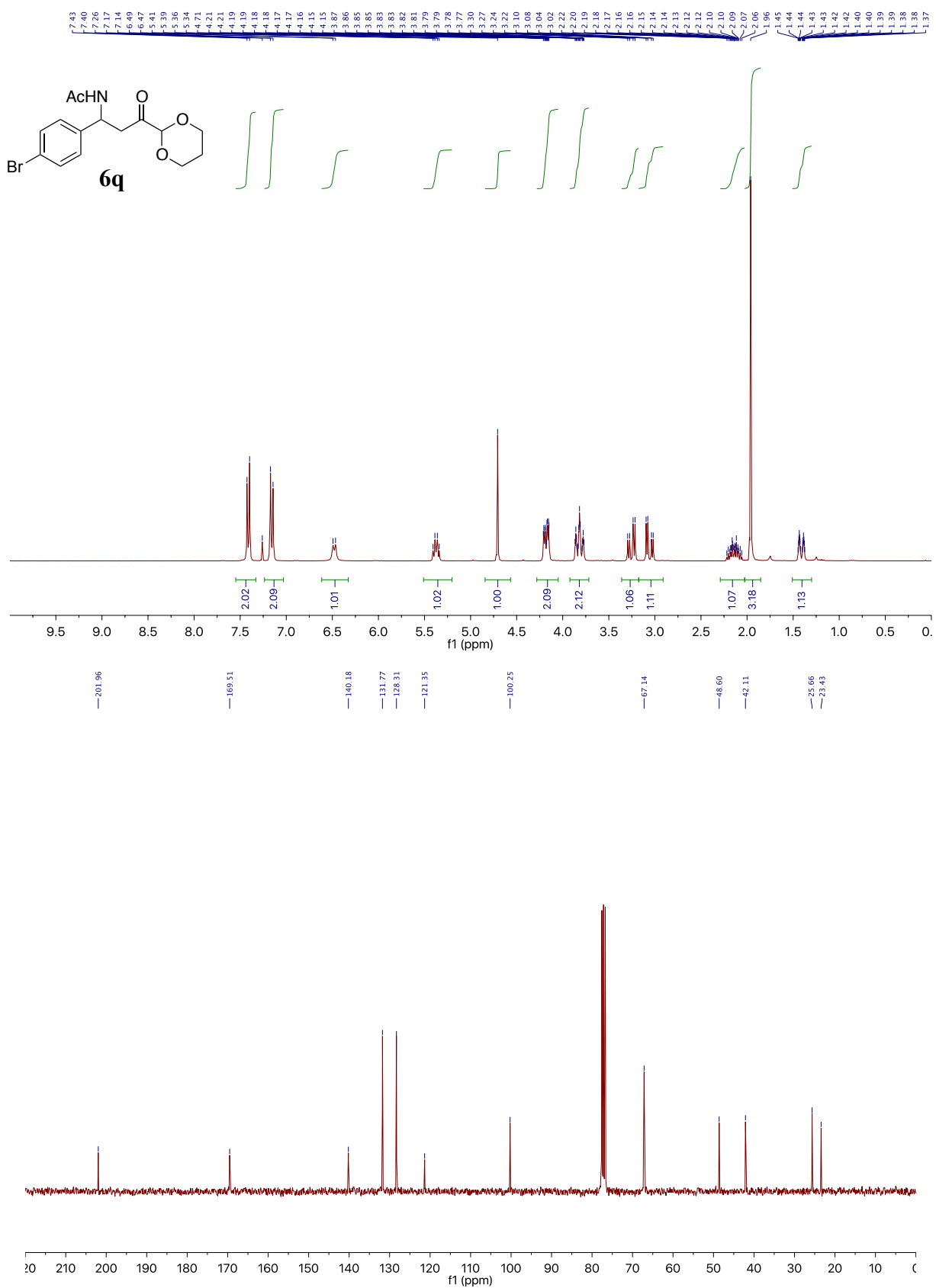
Results Table:

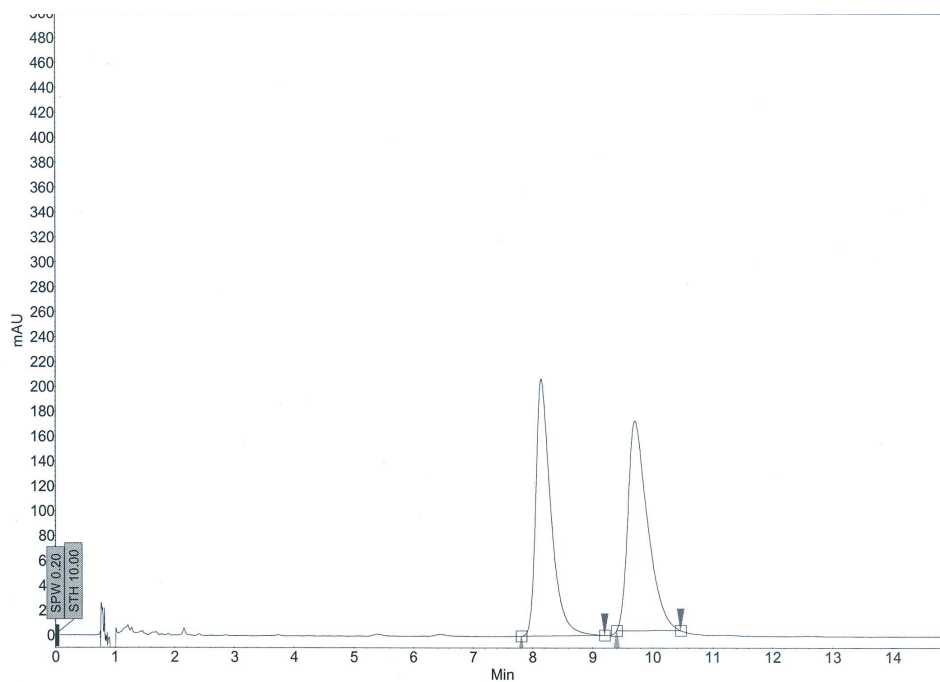
Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[μV]	[μV.Min]	[%]
1	UNKNOWN	8.15	8.50	9.77	0.00	50.57	104.8	37.3	50.572
2	UNKNOWN	9.83	10.32	11.65	0.00	49.43	70.4	36.5	49.428
Total						100.00	175.2	73.8	100.000



Results Table:

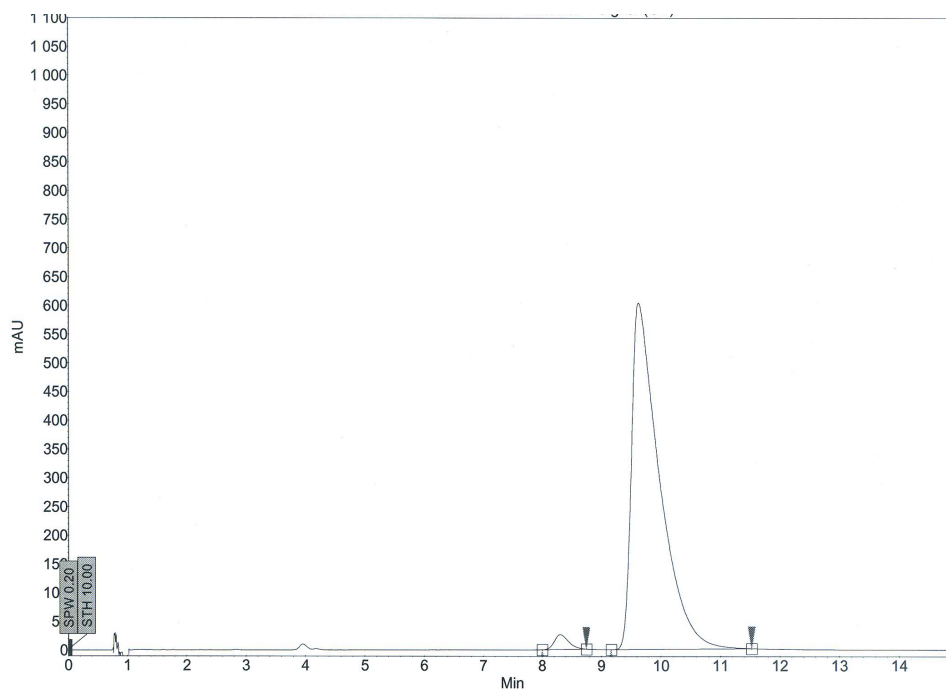
Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[μV]	[μV.Min]	[%]
1	UNKNOWN	8.32	8.66	9.16	0.00	2.68	9.8	3.1	2.677
2	UNKNOWN	9.57	10.04	12.15	0.00	97.32	195.0	111.7	97.323
Total						100.00	204.8	114.8	100.000





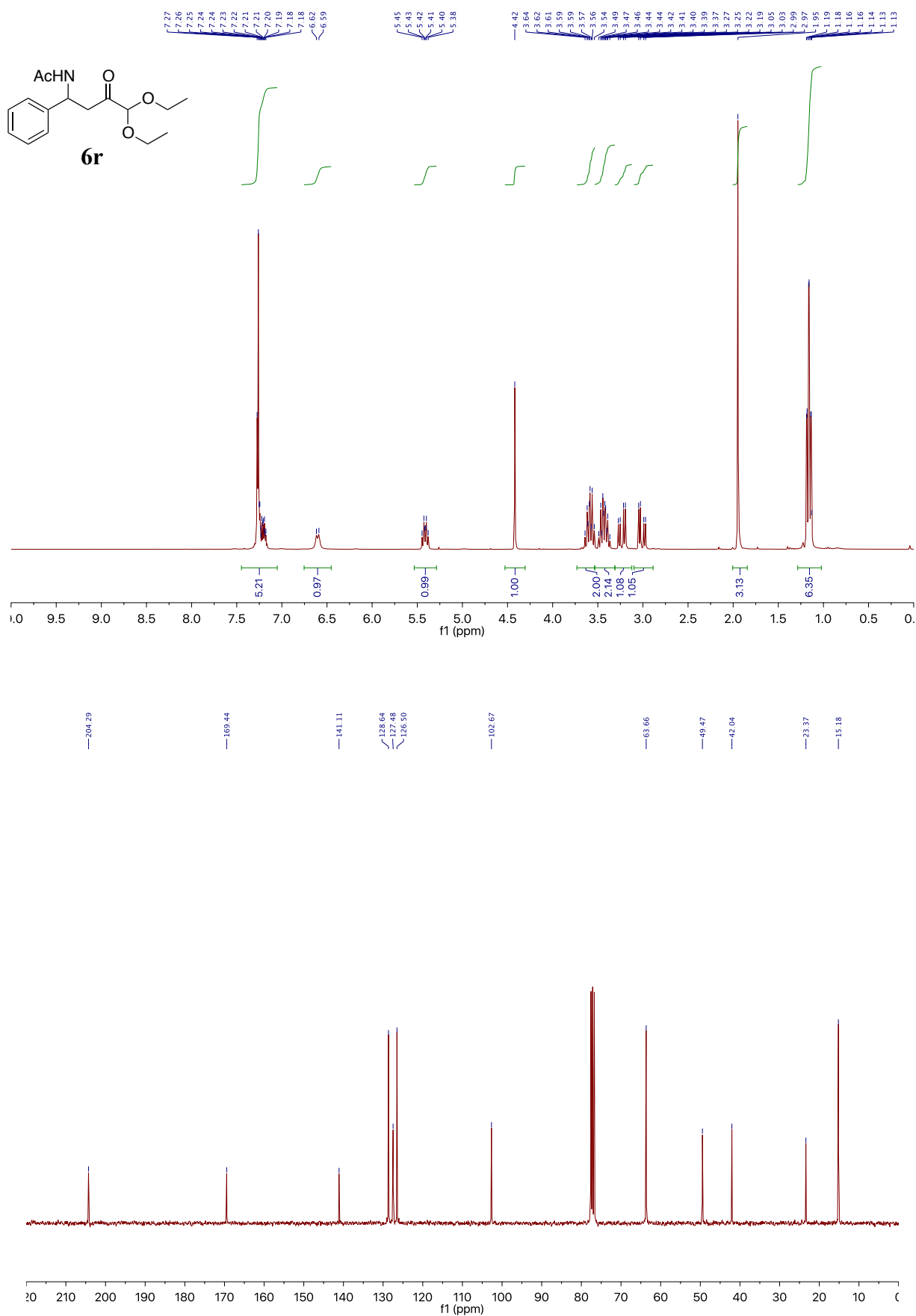
Results Table:

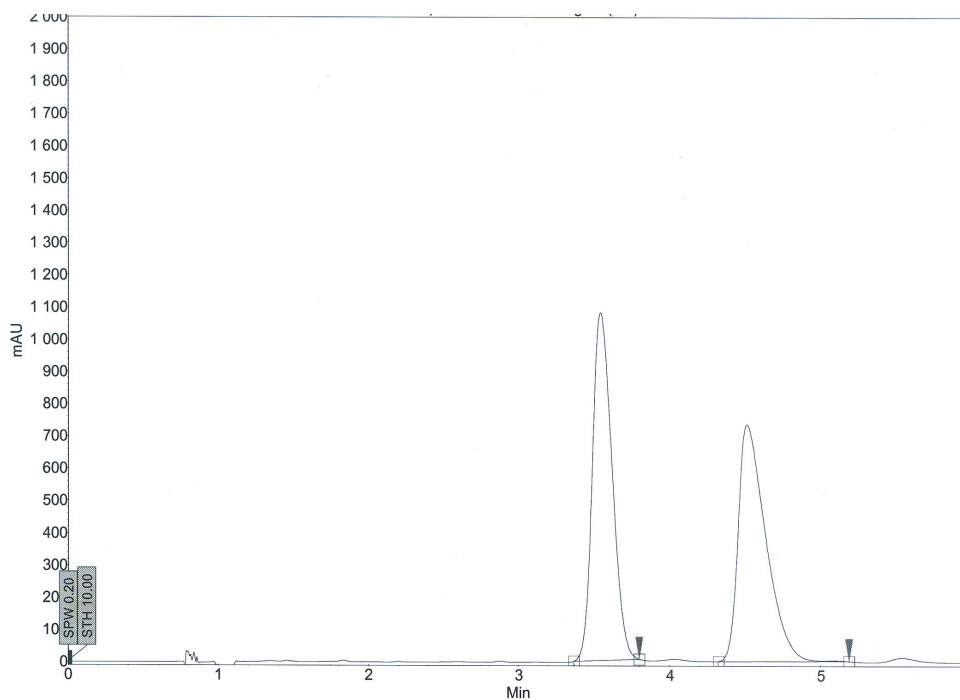
Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[μ V]	[μ V.Min]	[%]
1	UNKNOWN	7.82	8.14	9.20	0.00	48.55	206.8	60.3	48.546
2	UNKNOWN	9.40	9.70	10.46	0.00	51.45	168.7	63.9	51.454
Total						100.00	375.5	124.3	100.000



Results Table:

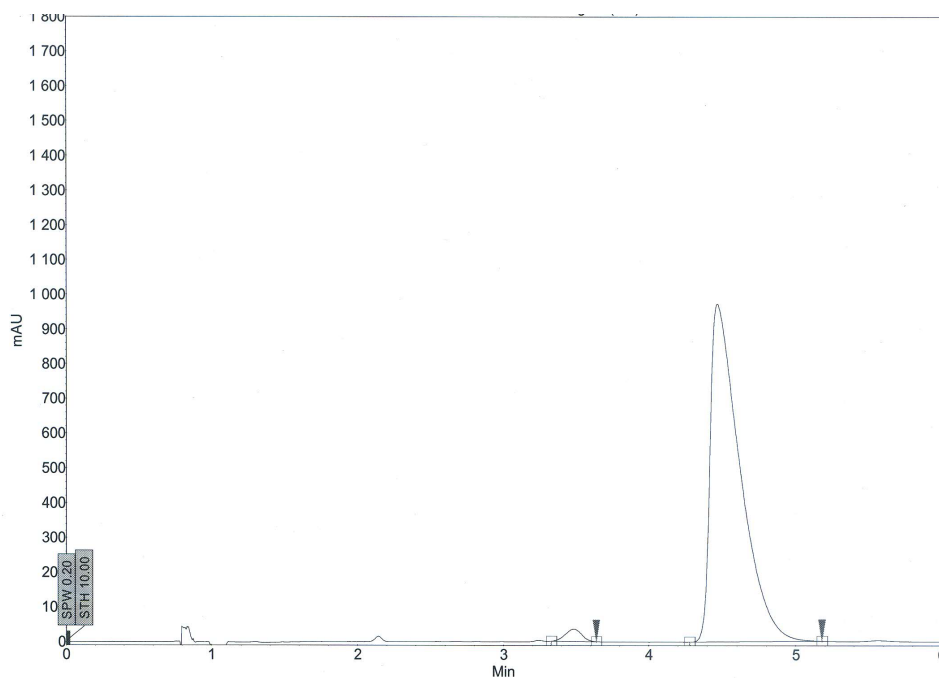
Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[μ V]	[μ V.Min]	[%]
1	UNKNOWN	8.00	8.31	8.75	0.00	2.16	26.0	7.2	2.159
2	UNKNOWN	9.17	9.63	11.52	0.00	97.84	602.8	326.2	97.841
Total						100.00	628.8	333.4	100.000





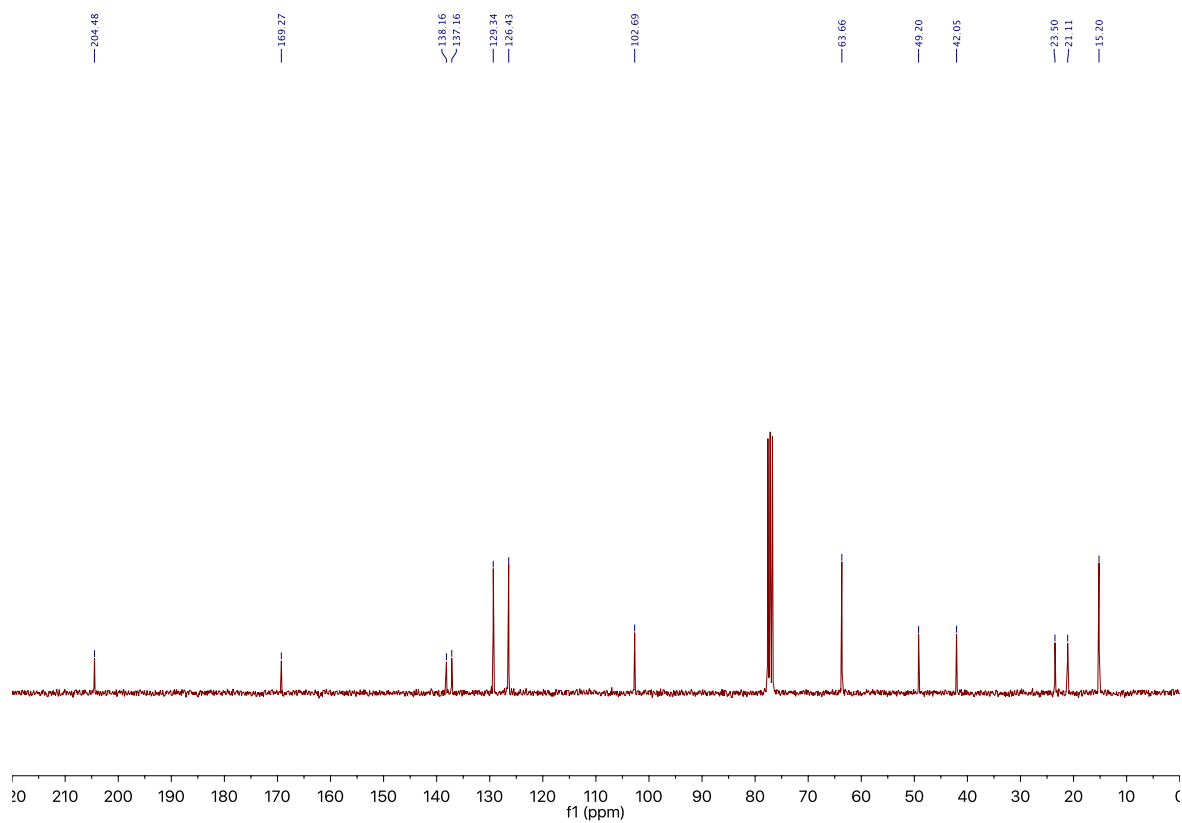
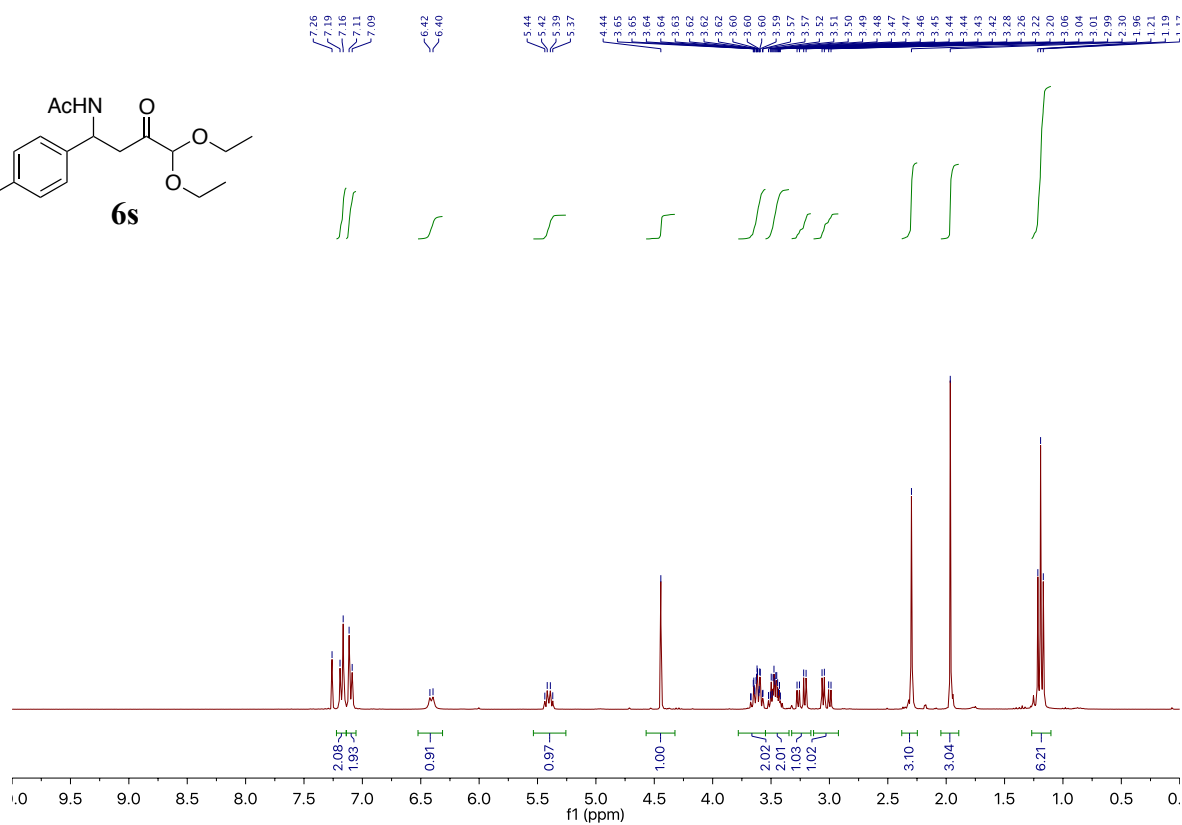
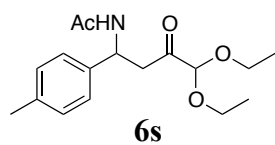
Results Table:

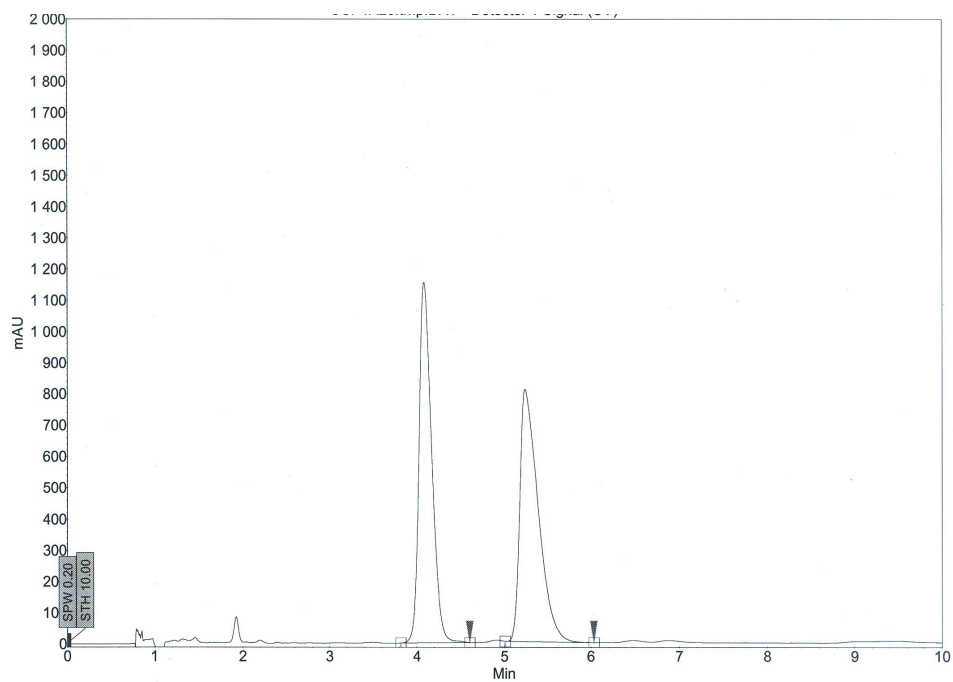
Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[μV]	[μV.Min]	[%]
1	UNKNOWN	3.36	3.54	3.80	0.00	51.04	1078.0	161.7	51.038
2	UNKNOWN	4.32	4.51	5.19	0.00	48.96	733.0	155.2	48.962
Total						100.00	1811.0	316.9	100.000



Results Table:

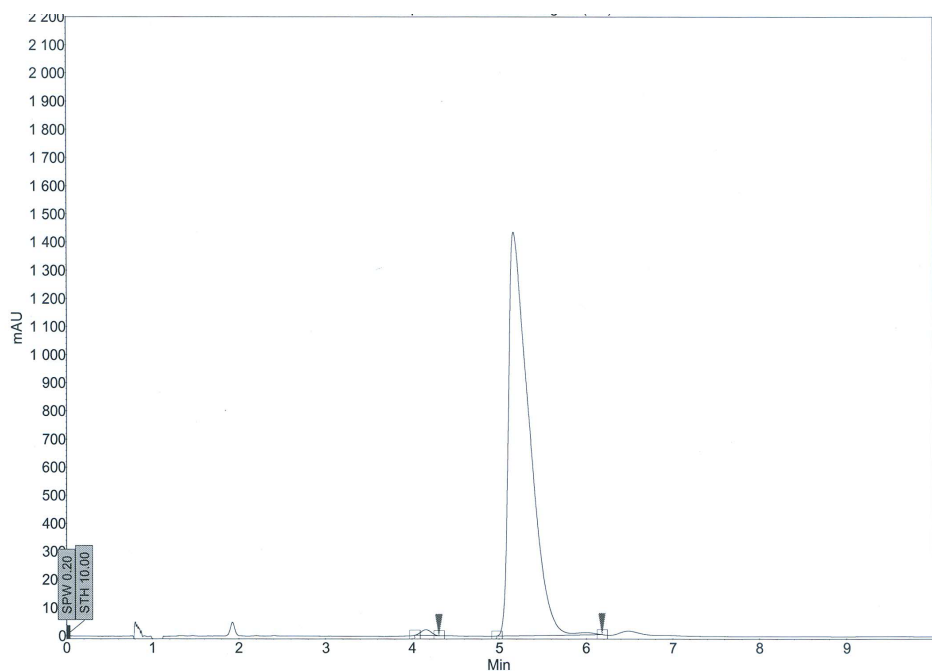
Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[μV]	[μV.Min]	[%]
1	UNKNOWN	3.33	3.48	3.64	0.00	2.00	35.4	4.6	2.004
2	UNKNOWN	4.28	4.47	5.18	0.00	98.00	971.9	226.4	97.996
Total						100.00	1007.3	231.1	100.000





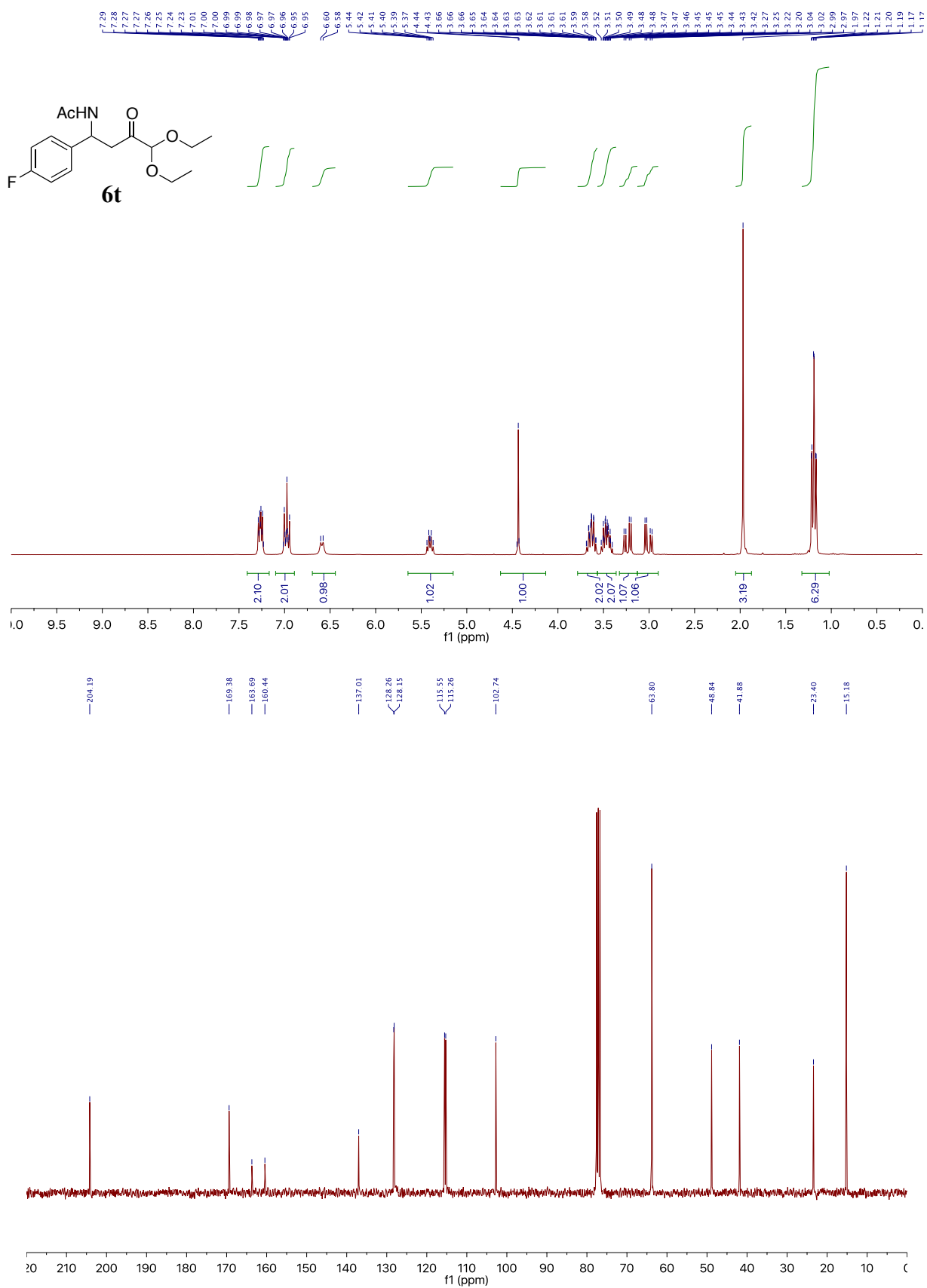
Results Table:

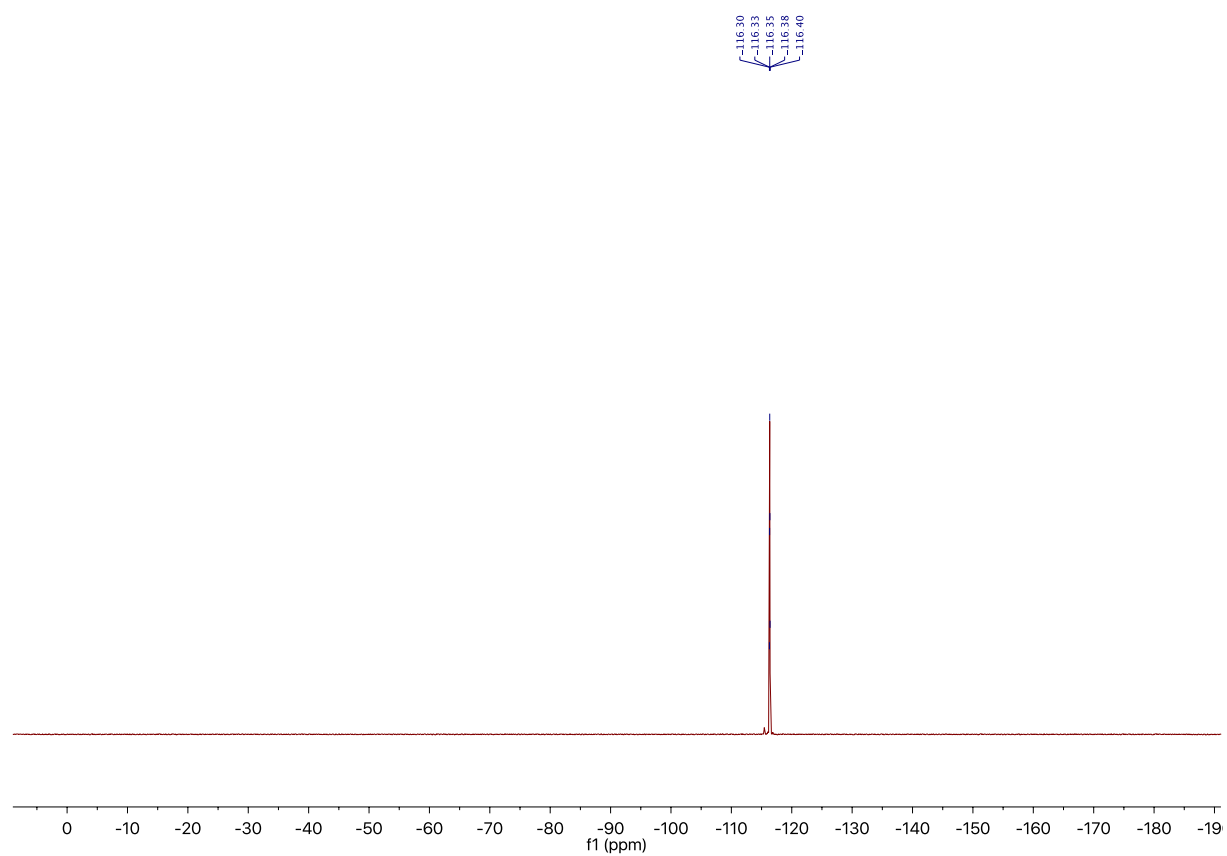
Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[μ V]	[μ V.Min]	[%]
2	UNKNOWN	3.82	4.09	4.61	0.00	49.32	1152.8	192.5	49.319
1	UNKNOWN	5.01	5.24	6.03	0.00	50.68	806.2	197.8	50.681
Total						100.00	1958.9	390.2	100.000

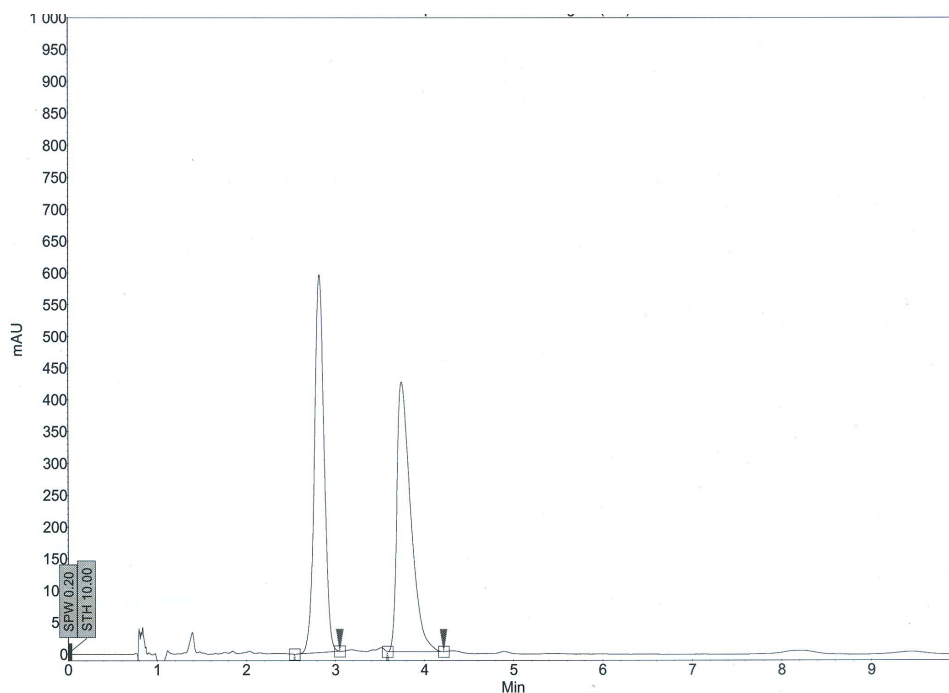


Results Table:

Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[μ V]	[μ V.Min]	[%]
1	UNKNOWN	4.03	4.16	4.31	0.00	0.68	20.1	2.7	0.677
2	UNKNOWN	4.97	5.17	6.18	0.00	99.32	1434.2	389.7	99.323
Total						100.00	1454.3	392.4	100.000

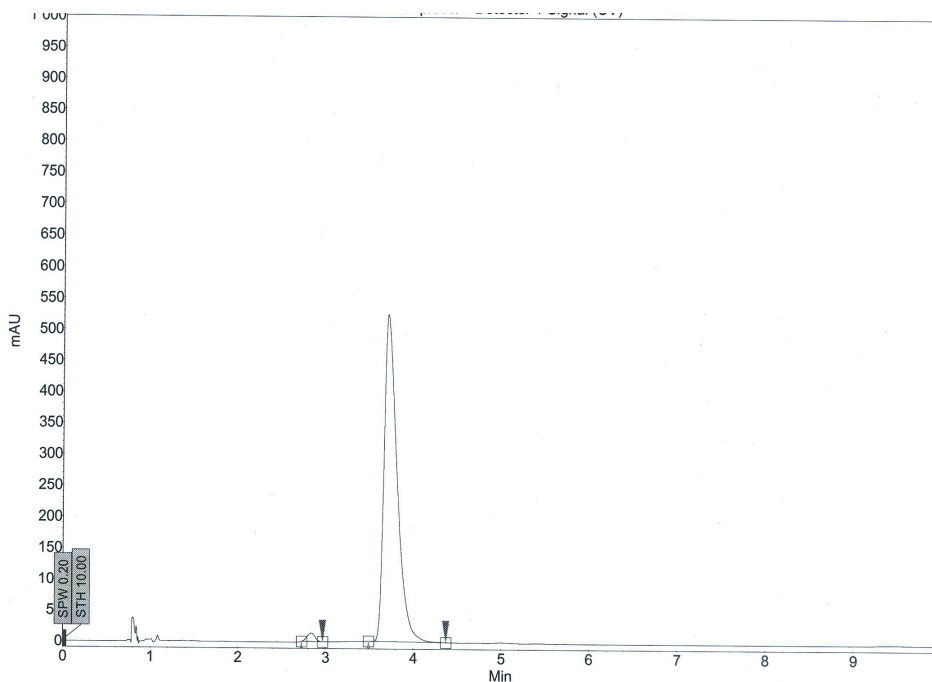






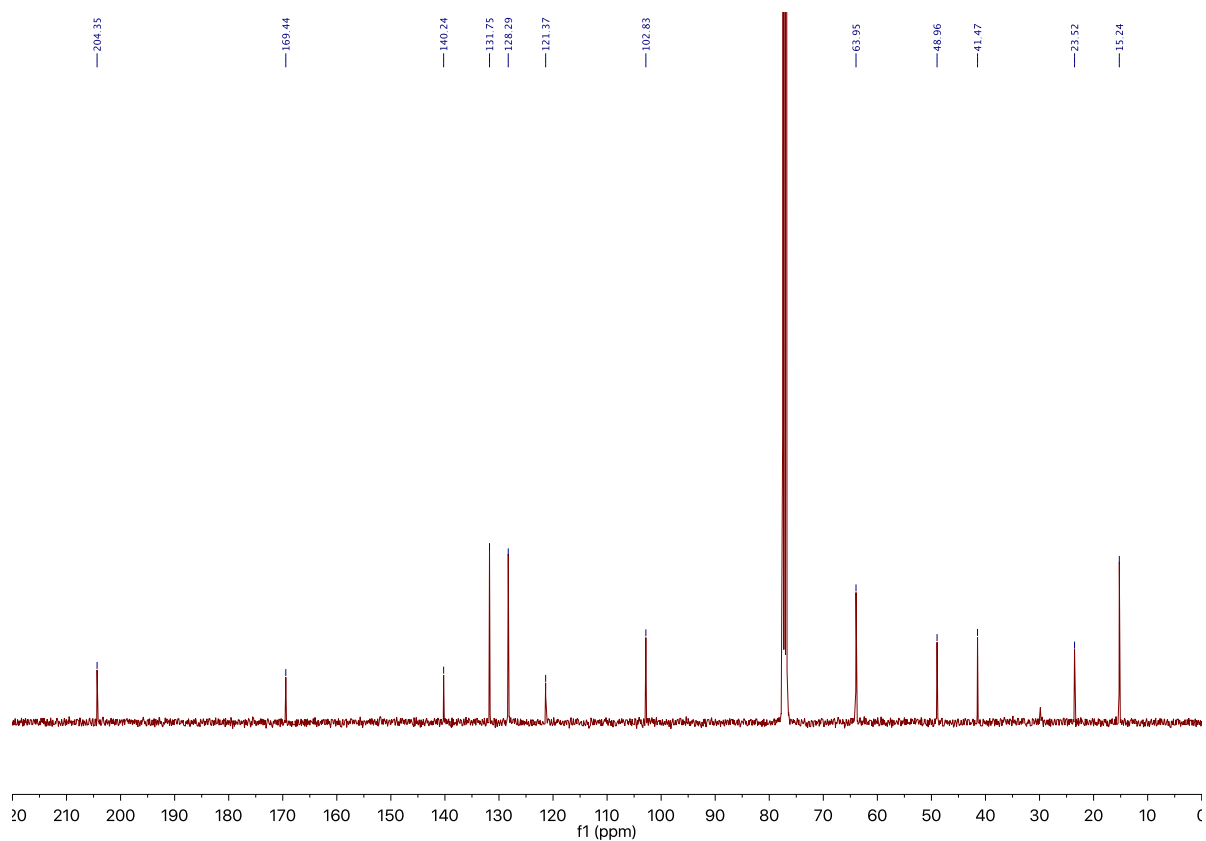
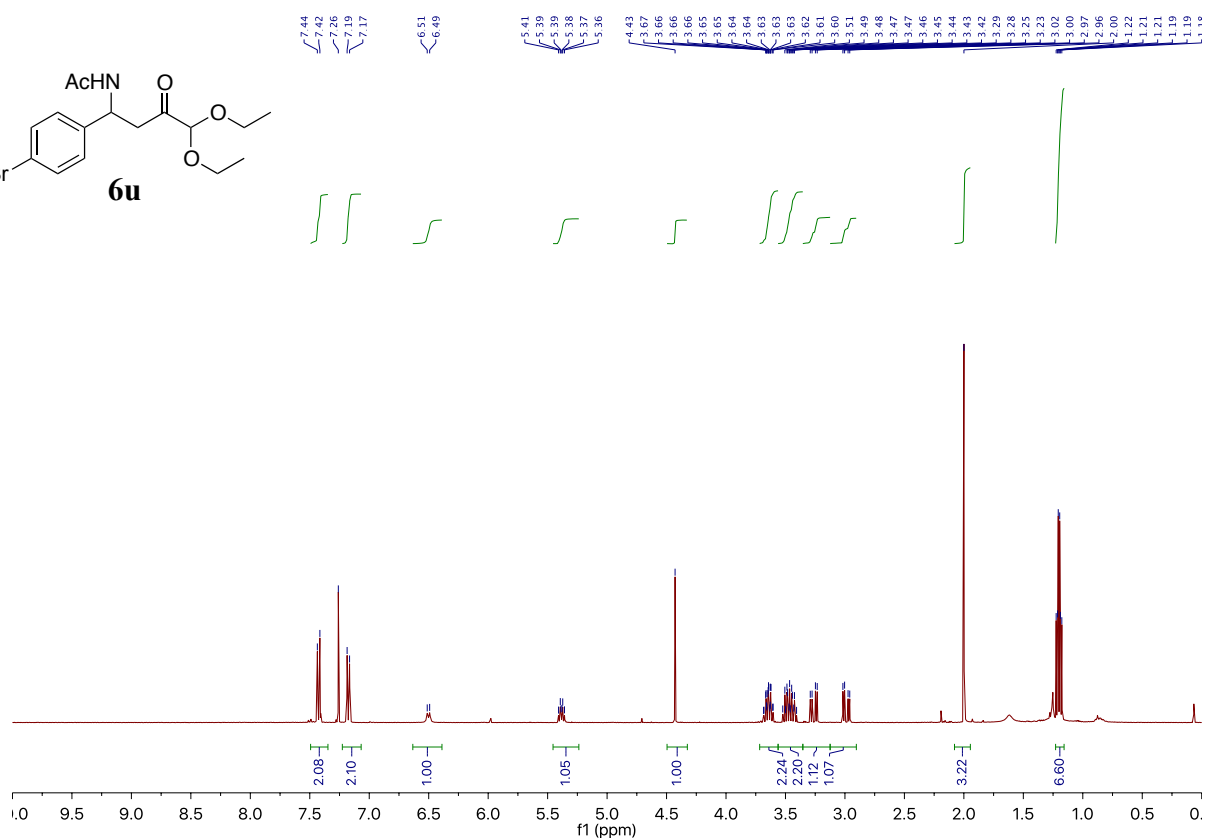
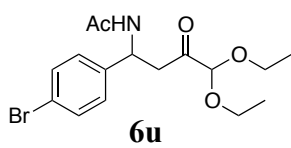
Results Table:

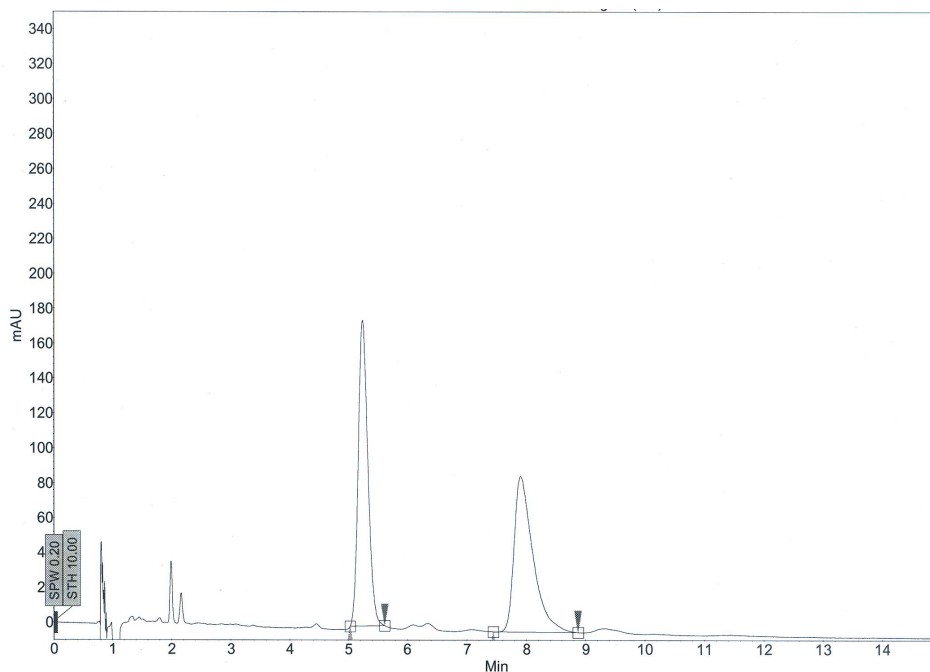
Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[μ V]	[μ V.Min]	[%]
1	UNKNOWN	2.54	2.82	3.05	0.00	49.68	594.6	75.2	49.685
2	UNKNOWN	3.59	3.75	4.22	0.00	50.32	423.7	76.2	50.315
Total						100.00	1018.2	151.4	100.000



Results Table:

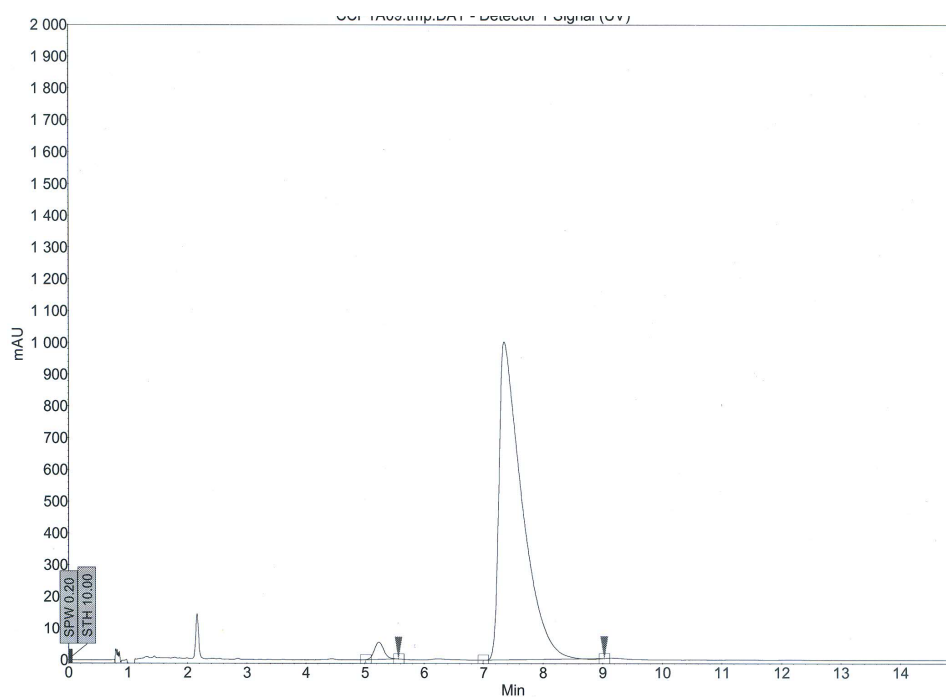
Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[μ V]	[μ V.Min]	[%]
2	UNKNOWN	2.73	2.84	2.97	0.00	1.57	13.6	1.4	1.573
1	UNKNOWN	3.49	3.70	4.37	0.00	98.43	523.7	90.2	98.427
Total						100.00	537.3	91.7	100.000





Results Table:

Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[μV]	[μV.Min]	[%]
2	UNKNOWN	5.02	5.24	5.61	0.00	50.40	175.4	33.3	50.402
1	UNKNOWN	7.44	7.90	8.87	0.00	49.60	89.3	32.8	49.598
Total						100.00	264.7	66.1	100.000

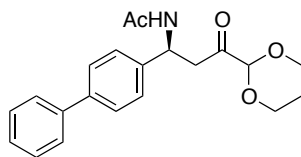


Results Table:

Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[μV]	[μV.Min]	[%]
1	UNKNOWN	5.01	5.24	5.57	0.00	2.22	54.3	10.1	2.224
2	UNKNOWN	6.99	7.35	9.03	0.00	97.78	1001.1	442.9	97.776
Total						100.00	1055.4	453.0	100.000

10. Analytical data for compound 7

(*S*)-*N*-(1-([1,1'-biphenyl]-4-yl)-3-(1,3-dioxan-2-yl)-3-oxopropyl)acetamide 7



In a sealed tube under argon were introduced **6r** (50 mg, 0.14 mmol, 1.0 equiv.), PhB(OH)₂ (25.4 mg, 0.21 mmol, 1.3 equiv.), Pd(PPh₃)₄ (9.24 mg, 0.008 mmol, 5 mol%), K₂CO₃ (48.5 mg, 0.35 mmol, 2.2 equiv.), toluene (2 mL) and deionized water (0.1 mL). The resulting mixture was stirred during 48 h under reflux, then hydrolyzed with a saturated NaHCO₃ aqueous solution. The aqueous layer was extracted with CH₂Cl₂, combined organic layers were dried over MgSO₄ and concentrated *in vacuo*. The resulting crude product was purified by silica gel chromatography (EtOAc) to afford the pure product as a white solid (43 mg, 87%, mp = 186 – 188 °C).

Chemical Formula: C₂₁H₂₃NO₄

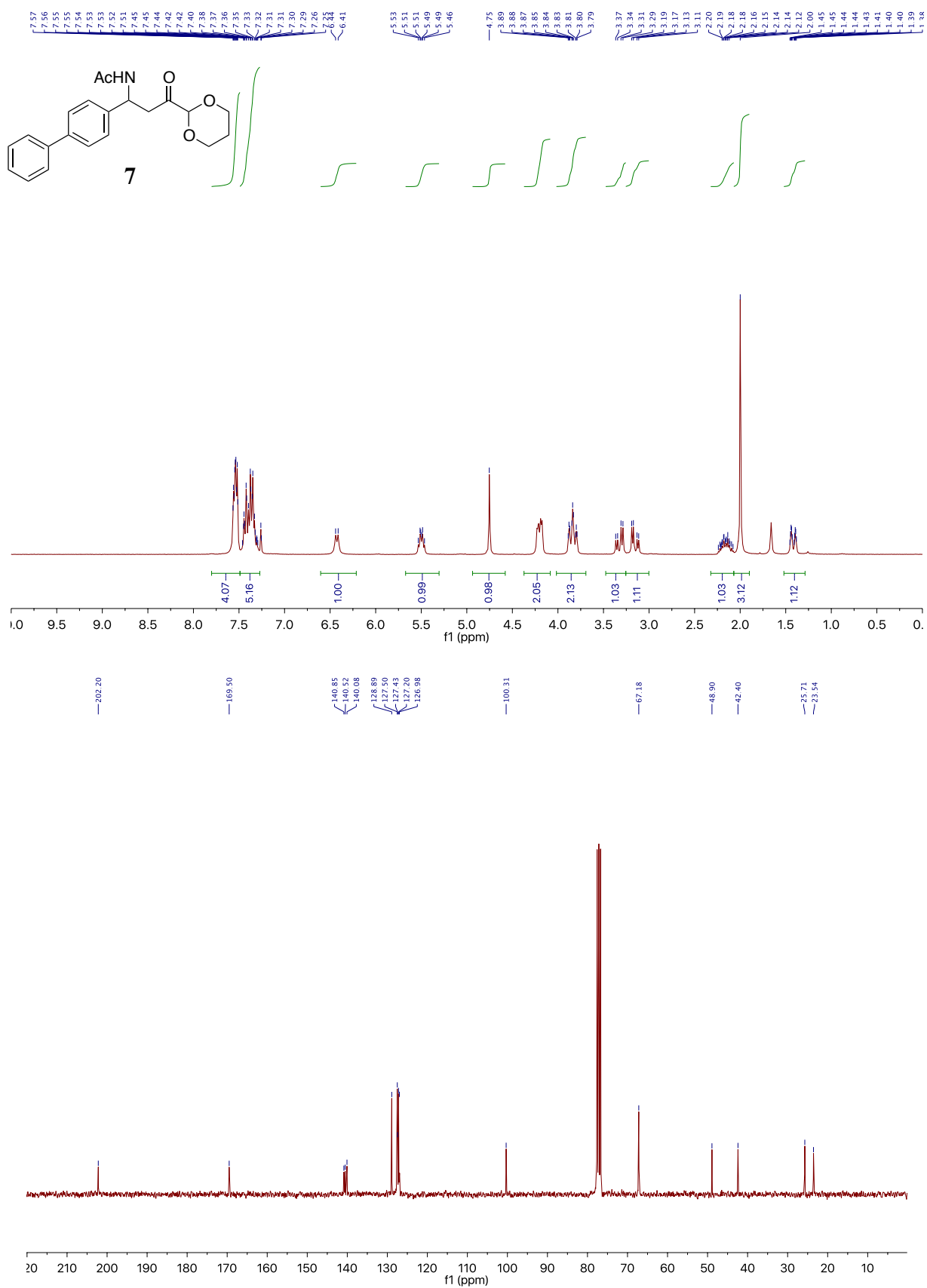
¹H NMR (300 MHz, CDCl₃) δ 7.57 – 7.51 (m, 4H), 7.49 – 7.27 (m, 5H), 6.43 (brd, *J* = 8.5 Hz, 1H), 5.50 (dt, *J* = 8.5, 6.0 Hz, 1H), 4.75 (s, 1H), 4.37 – 4.08 (m, 2H), 4.02 – 3.69 (m, 2H), 3.33 (dd, *J* = 17.5, 6.0 Hz, 1H), 3.15 (dd, *J* = 17.5, 6.0 Hz, 1H), 2.32 – 2.07 (m, 1H), 2.00 (s, 3H), 1.52 – 1.29 (m, 1H).

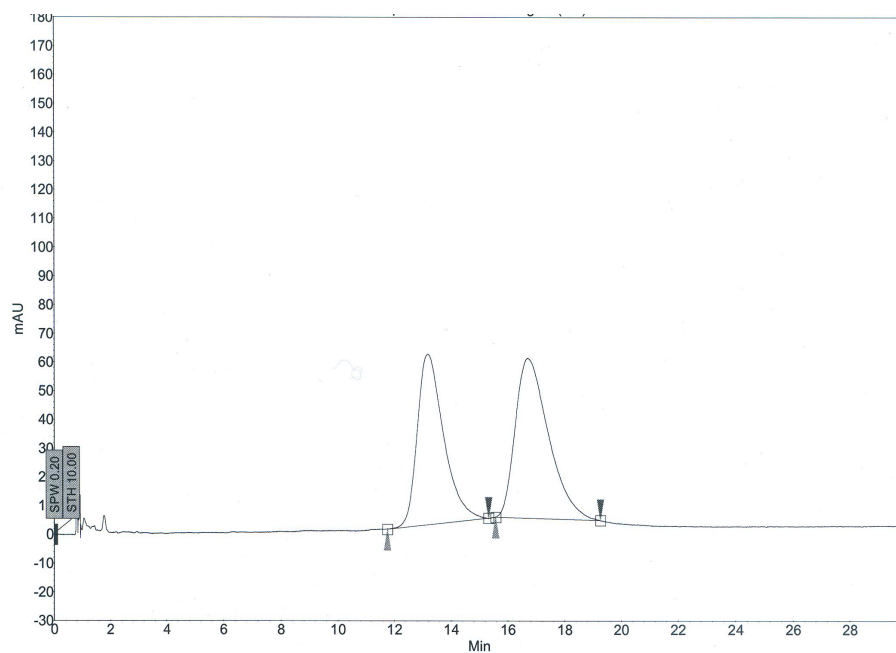
¹³C NMR (75 MHz, CDCl₃) δ 202.2, 169.5, 140.9, 140.5, 140.1, 128.9, 127.5, 127.4, 127.2, 126.9, 100.3, 67.2, 48.9, 42.4, 25.7, 23.5.

Mass (ESI) MH⁺ 353

HRMS (ESI): *m/z* [M+Na]⁺ calcd for C₂₁H₂₃NNaO₄: 376.1519, found : 376.1526

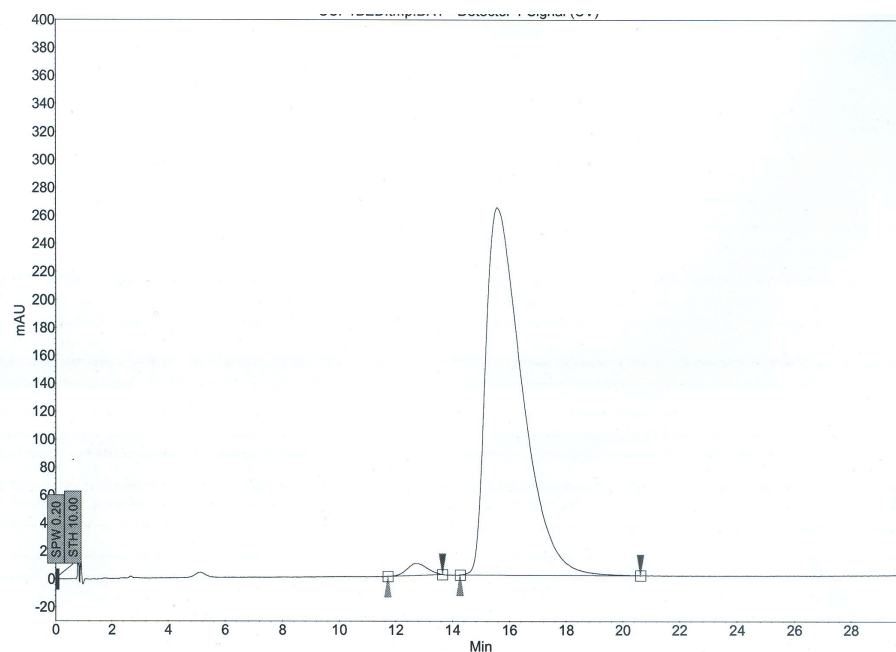
SFC: CHIRALPAK AS-H, scCO₂/iPrOH (90:10), 4 mL/min, P = 150 bar, λ = 215 nm; *t*_R [minor] = 12.74 min, *t*_R [major] = 15.58 min.





Results Table:

Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[μ V]	[μ V.Min]	[%]
1	UNKNOWN	11.76	13.19	15.32	0.00	45.82	59.3	64.1	45.823
2	UNKNOWN	15.57	16.71	19.26	0.00	54.18	55.7	75.7	54.177
Total						100.00	115.1	139.8	100.000

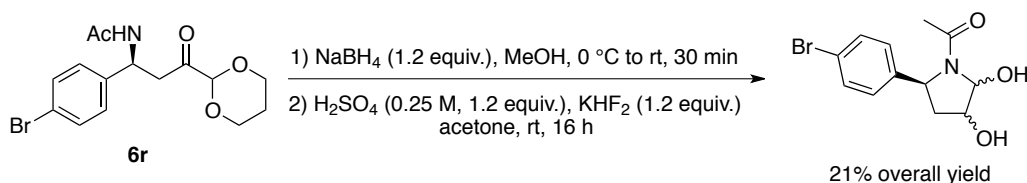


Results Table:

Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[μ V]	[μ V.Min]	[%]
2	UNKNOWN	11.73	12.74	13.65	0.00	1.77	8.4	7.0	1.771
1	UNKNOWN	14.27	15.58	20.63	0.00	98.23	262.7	387.7	98.229
Total						100.00	271.1	394.7	100.000

11. Post-functionalization of compound 6v

1-((5*S*)-(4-bromophenyl)-2,3-dihydroxypyrrolidin-1-yl)ethanone



In a round bottom flask under argon were introduced **6r** (50 mg, 0.14 mmol, 1.0 equiv.) and methanol (1.0 mL). NaBH₄ (6.3 mg, 0.17 mmol, 1.2 equiv.) was added at 0 °C. The resulting mixture was stirred at room temperature for 30 min and then hydrolyzed with water. The aqueous layer was extracted with EtOAc, combined organic layers were dried over MgSO₄ and concentrated *in vacuo*. The crude product was dissolved in acetone (1 mL) and diluted H₂SO₄ (0.25 M, 0.64 mL, 0.17 mmol, 1.2 equiv.) and KHF₂ (13.4 mg, 0.17 mmol, 1.2 equiv.) were added at room temperature. The resulting mixture were stirred for 16 h at this temperature and then hydrolyzed with water. The aqueous layer was extracted with CH₂Cl₂, combined organic layers were dried over MgSO₄ and concentrated *in vacuo*. The resulting crude product was purified by silica gel chromatography (CH₂Cl₂/MeOH 95:5) to afford the pure product as a yellow oil (7 mg, 21% overall yield) as a mixture of 4 diastereoisomers.

Description of the major diastereoisomer

Chemical Formula: C₁₂H₁₄BrNO₃

¹H NMR (400 MHz, CDCl₃) δ 7.47 (d, *J* = 8.5 Hz, 2H), 7.24 (d, *J* = 8.5 Hz, 2H), 5.72 (d, *J* = 3.0 Hz, 1H), 4.81 (s, 1H), 4.72 (t, *J* = 7.5 Hz, 1H), 4.26 – 4.14 (m, 1H), 2.75 (d, *J* = 7.5 Hz, 1H), 2.08 – 1.93 (m, 2H), 1.72 (s, 3H).

¹³C NMR (101 MHz, CDCl₃) δ 172.9, 141.9, 132.3, 127.9, 121.6, 80.4, 69.8, 60.6, 42.3, 22.6.

HRMS (ESI): *m/z* [M+Na]⁺ calcd for C₁₂H₁₄BrNO₃Na: 322.0049, found: 322.0040

