

Silver Triflate/*p*-TSA Co-Catalysed Synthesis of 3-Substituted Isocoumarins from 2-Alkynylbenzoates

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General experimental details: All the reactions, that involve the use of reagents sensitive to oxygen or hydrolysis, were carried out under inert atmosphere. The glassware was previously dried in an oven at 110 °C and set with cycles of vacuum and nitrogen. Also syringes, used to transfer reagents and solvents, were previously set under nitrogen atmosphere. All chemicals and solvents are commercially available and were used without further purification. The chromatographic column separations were performed by flash technique, using silica gel (pore size 60Å, particle size 230-400 mesh, Merck Grade 9385). For thin-layer chromatography (TLC), Silica on TLC Alu foils with fluorescent indicator (254 nm) was employed and the detection was performed by irradiation with UV light ($\lambda = 254$ nm and/or 366 nm). ^1H NMR analysis were performed with 300 MHz and 500 MHz spectrometers at room temperature. The coupling constants (J) are expressed in Hertz (Hz), the chemical shifts (δ) in ppm. The multiplicity of the proton spectra were described by the following abbreviations: s (singlet), d (doublet), t (triplet), q (quartet), dt (double triplet), dd (double doublet), td (triple doublet), m (multiplet), br (broad), ps (pseudo). ^{13}C NMR analysis were performed with the same instruments at 75 MHz and 125 MHz; APT sequence was used to distinguish the methine and methyl carbon signals from those arising from methylene and quaternary carbon atoms. All ^{13}C NMR spectra were recorded with complete proton decoupling. Low resolution MS spectra were recorded with an electrospray/ion trap instrument, using a syringe pump device to directly inject sample solutions. The values are expressed as mass-charge ratio and the relative intensities of the most significant peaks are shown in brackets. Infrared spectra were recorded using discs of NaCl for liquid samples and KBr tablets for solid samples. The absorbance is reported in wavenumbers (cm^{-1}) with values between 4000 and 400 cm^{-1} . High resolution MS spectra were recorded with a ICR-FTMS electrospray equipped instrument. The melting points are uncorrected.

General procedure for the synthesis of methyl 2-halo(hetero)arylcarboxylates: The proper 2-haloarylcarboxylic acid (12 mmol) was dissolved in 60 mL of methanol. To the stirred reaction mixture 7.7 mL (12 eq) of concentrated sulfuric acid were then added dropwise. The reaction mixture was stirred at reflux until no more starting product was detected by TLC analysis. The reaction mixture was then cooled to rt and concentrated under reduced pressure. The residue was diluted with EtOAc (20 mL) and washed with saturated aqueous NaHCO_3 (30×3 mL). The organic phase was dried over Na_2SO_4 , filtered and the solvent was removed at reduced pressure.

Methyl 2-iodobenzoate: Reaction time: 3.0 h; Colorless oil. Yield 99% (3.14 g). ^1H NMR (300 MHz, CDCl_3): $\delta = 7.99$ (d, $J = 7.9$ Hz, 1H, arom), 7.80 (d, $J = 7.4$ Hz, 1H, arom), 7.40 (t, $J = 7.5$ Hz, 1H, arom), 7.15 (t, $J = 7.4$ Hz, 1H, arom), 3.93 (s, 3H, CH_3). Spectral data are in good agreement with literature values.¹

Methyl 3-bromothiophene-2-carboxylate: Reaction time: 5.5 h; White solid. Yield 99% (2.65 g); mp 46-48 °C (lit. 47-48 °C). ¹H NMR (300 MHz, CDCl₃): δ = 7.47 (d, *J* = 5.2 Hz, 1H, arom), 7.10 (d, *J* = 5.2 Hz, 1H, arom), 3.90 (s, 3H, CH₃). Spectral data are in good agreement with literature values.²

General procedure for the synthesis of methyl 2-alkynyl(hetero)arylcarboxylates. Method A:

Under a nitrogen atmosphere, to a stirred solution of the proper methyl 2-haloarylcarboxylate (0,5 mmol) in anhydrous TEA (2 mL) the appropriate alkyne (0,6 mmol, 1.2 equiv) and trans-dichlorobis-(triphenylphosphine)palladium(II) (2 mol%) were added. The reaction was stirred at rt for 10 min, and then CuI (1 mol%) was added. The reaction mixture was stirred at 50 °C until no more starting product was detected by TLC analysis. The reaction mixture was filtered on Celite and the solvent was removed at reduced pressure. The crude material was purified by flash column chromatography over silica gel. **Method B:** Under a nitrogen atmosphere, to a stirred solution of the proper methyl 2-haloarylcarboxylate (0,5 mmol) in anhydrous DMF (2 mL) the appropriate alkyne (0,6 mmol, 1.2 equiv), trans-dichlorobis-(triphenylphosphine)palladium(II) (2 mol%) and K₂CO₃ (2,5 mmol, 5 equiv) were added. The reaction was stirred at rt for 10 min, and then CuI (1 mol%) was added. The reaction mixture was stirred at 50 °C until no more starting product was detected by TLC analysis. The reaction mixture was diluted with water (50 mL) and extracted with ethyl acetate (15 mL × 3). The organic layer was dried on Na₂SO₄ and then evaporated under reduced pressure. The crude material was purified by flash column chromatography over silica gel.

Methyl 2-(p-tolylolethynyl)benzoate (1a): Method A. Reaction time: 1.5 h. Eluent for chromatography: hexane/EtOAc 95:5. Colorless oil. Yield 95% (119 mg). ¹H NMR (300 MHz, CDCl₃): δ = 7.97 (dd, *J* = 7.8, 1.4 Hz, 1H, arom), 7.64 (dd, *J* = 7.8, 1.3 Hz, 1H, arom), 7.49 (dd, *J* = 12.0, 4.7 Hz, 3H, arom), 7.37 (td, *J* = 7.6, 1.4 Hz, 1H, arom), 7.17 (d, *J* = 7.8 Hz, 2H, arom), 3.96 (s, 3H, -OCH₃), 2.38 (s, 3H, CH₃). Spectral data are in good agreement with literature values.³

Methyl 2-(phenylethynyl)benzoate (1b): Method A. Reaction time: 1 h. Eluent for chromatography: hexane/EtOAc 9:1. Yellow oil. Yield 89% (105 mg). ¹H NMR (300 MHz, CDCl₃): δ = 8.01 – 7.95 (m, 1H, arom), 7.65 (dd, *J* = 7.7, 0.9 Hz, 1H, arom), 7.61 – 7.55 (m, 2H, arom), 7.50 (td, *J* = 7.6, 1.4 Hz, 1H, arom), 7.43 – 7.31 (m, 4H, arom), 3.97 (s, 3H, CH₃). Spectral data are in good agreement with literature values.³

Methyl 2-((4-methoxyphenyl)ethynyl)benzoate (1c): Method A. Reaction time: 3 h. Eluent for chromatography: hexane/EtOAc 9:1. Colorless oil. Yield 99% (133 mg). ¹H NMR (300 MHz, CDCl₃): δ = 7.96 (d, *J* = 7.8 Hz, 1H, arom), 7.62 (d, *J* = 7.7 Hz, 1H, arom), 7.49 (dd, *J* = 16.3, 8.1

Hz, 3H, arom), 7.35 (t, $J = 7.6$ Hz, 1H, arom), 6.89 (d, $J = 8.5$ Hz, 2H, arom), 3.96 (s, 3H, -COOCH₃), 3.83 (s, 3H, -OCH₃). Spectral data are in good agreement with literature values.⁴

Methyl 2-((2-methoxyphenyl)ethynyl)benzoate (1d): Method A. Reaction time: 1 h. Eluent for chromatography: hexane/EtOAc 95:5. Yellow oil. Yield 99% (133 mg). **¹H NMR** (300 MHz, CDCl₃): $\delta = 7.97$ (dd, $J = 7.8, 1.3$ Hz, 1H, arom), 7.68 (dd, $J = 7.8, 1.2$ Hz, 1H, arom), 7.55 (dd, $J = 7.6, 1.7$ Hz, 1H, arom), 7.48 (td, $J = 7.6, 1.4$ Hz, 1H, arom), 7.41 – 7.27 (m, 2H, arom), 6.95 (dt, $J = 16.3, 4.8$ Hz, 2H, arom), 3.97 (s, 3H, -COOCH₃), 3.93 (s, 3H, -OCH₃). Spectral data are in good agreement with literature values.⁵

Methyl 2-((2-hydroxyphenyl)ethynyl)benzoate (1e): Method A. Reaction time: 1 h. Eluent for chromatography: hexane/EtOAc 3:1. Orange solid. Yields 97% (122 mg); mp 65-66 °C. **¹H NMR** (300 MHz, CDCl₃): $\delta = 7.97$ (dd, $J = 7.9, 0.6$ Hz, 1H, arom), 7.64 (d, $J = 7.7$ Hz, 1H, arom), 7.49 (td, $J = 7.3, 0.9$ Hz, 1H, arom), 7.44 – 7.34 (m, 1H, arom), 7.21 (t, $J = 7.8$ Hz, 1H, arom), 7.14 (d, $J = 7.6$ Hz, 1H, arom), 7.05 (s, 1H, arom), 6.84 (dd, $J = 7.9, 2.5$ Hz, 1H, arom), 5.25 (s, 1H, -OH), 3.96 (s, 3H, CH₃). **¹³C NMR** (75 MHz, CDCl₃): $\delta = 166.8$ (C=O), 155.4 (C-OH), 134.0 (CH, arom), 131.8 (C, arom), 131.7 (CH, arom), 130.5 (CH, arom), 129.6 (CH, arom), 127.9 (CH, arom), 124.43 (C, arom), 124.36 (CH, arom), 123.61 (C, arom), 118.3 (CH, arom), 116.0 (CH, arom), 94.0 (C sp), 88.11 (C sp), 52.26 (CH₃). **MS** ESI (+): m/z (%) = 275 [M+Na]⁺ (100), 253 [M+1]⁺ (30); C₁₆H₁₂O₃ [252.26]. **IR** (KBr): $\nu_{\max} = 3401, 2212, 1712, 1591, 1302, 1131$ cm⁻¹. **HRMS** ESI (M+1)⁺ calculated for C₁₆H₁₃O₃ 253.0859, found 253.0863.

Methyl 2-((4-chlorophenyl)ethynyl)benzoate (1f): Method A. Reaction time: 1 h. Eluent for chromatography: hexane/EtOAc 98:2. Yellow oil. Yield 99% (135 mg). **¹H NMR** (300 MHz, CDCl₃): $\delta = 7.99$ (dd, $J = 7.8, 1.4$ Hz, 1H, arom), 7.67 – 7.61 (m, 1H, arom), 7.55 – 7.46 (m, 3H, arom), 7.40 (td, $J = 7.6, 1.3$ Hz, 1H, arom), 7.37 – 7.31 (m, 2H, arom), 3.96 (s, 3H, -CH₃). Spectral data are in good agreement with literature values.⁴

Methyl 2-((4-cyanophenyl)ethynyl)benzoate (1g): Method B. Reaction time: 5 h. Eluent for chromatography: hexane/EtOAc 8:2. Yellow solid. Yield 91% (119 mg); mp 81-82 °C. **¹H NMR** (300 MHz, CDCl₃): $\delta = 8.02$ (dd, $J = 7.8, 0.9$ Hz, 1H, arom), 7.66 (d, $J = 5.5$ Hz, 5H, arom), 7.49 (dtd, $J = 28.0, 7.5, 1.4$ Hz, 2H, arom), 3.96 (s, 3H, CH₃). **¹³C NMR** (75 MHz, CDCl₃): $\delta = 166.2$ (C=O), 134.1 (CH, arom), 132.2 (CH, arom, 2C), 132.02 (CH, arom, 2C), 131.98 (C, arom), 131.85 (CH, arom), 130.6 (CH, arom), 128.7 (CH, arom), 128.3 (C, arom), 122.8 (C, arom), 118.5 (CN), 111.7 (C, arom), 92.5 (C sp), 92.3 (C sp), 52.3 (CH₃). **MS** ESI (+): m/z (%) = 262 [M+1]⁺ (100); C₁₇H₁₁NO₂ [261.27]. **IR** (KBr): $\nu_{\max} = 2223, 1706, 1604, 1296, 1125$ cm⁻¹. **HRMS** ESI (M+1)⁺ calculated for C₁₇H₁₂NO₂ 262.0863, found 262.0855.

Methyl 2-((4-(trifluoromethyl)phenyl)ethynyl)benzoate (1h): Method A. Reaction time: 1 h. Eluent for chromatography: hexane/EtOAc 95:5. Yellow oil. Yield 87% (132 mg). **¹H NMR** (300 MHz, CDCl₃): δ = 8.09 – 7.92 (m, 1H, arom), 7.66 (ddt, *J* = 15.9, 15.1, 4.6 Hz, 5H, arom), 7.52 (td, *J* = 7.6, 1.5 Hz, 1H, arom), 7.42 (td, *J* = 7.7, 1.4 Hz, 1H, arom), 3.96 (s, 3H, CH₃). **¹³C NMR** (75 MHz, CDCl₃): δ = 166.4 (C=O), 134.1 (CH, arom), 131.94 (C, arom), 131.91 (CH, 2C, arom), 131.8 (CH, arom), 130.6 (CH, arom), 130.1 (q, ²*J*_(C,F) = 32 Hz, 1C, C-CF₃), 128.5 (CH, arom), 127.1 (C, arom), 125.3 (q, ³*J*_(C,F) = 4 Hz, 2C, CH-C-CF₃), 123.0 (C, arom), 123.9 (q, ¹*J*_(C,F) = 272 Hz, 1C, CF₃), 92.7 (C sp), 90.5 (C sp), 52.3 (CH₃). **MS** ESI (+): *m/z* (%) = 305 [M+1]⁺ (100), 327 [M+Na]⁺ (20); C₁₇H₁₁F₃O₂ [304.26]. **IR** (NaCl): ν_{max} = 1726, 1610, 1321, 1257, 1163 cm⁻¹. **HRMS** ESI (M+1)⁺ calculated for C₁₇H₁₂F₃O₂ 305.0784, found 305.0802.

Methyl 2-((3-(trifluoromethyl)phenyl)ethynyl)benzoate (1i): Method A. Reaction time: 1.5 h. Eluent for chromatography: hexane/EtOAc 95:5. Colorless oil. Yield 77% (117 mg). **¹H NMR** (300 MHz, CDCl₃): δ = 8.01 (dd, *J* = 7.8, 0.8 Hz, 1H, arom), 7.83 (s, 1H, arom), 7.75 (d, *J* = 7.7 Hz, 1H, arom), 7.66 (d, *J* = 7.7 Hz, 1H, arom), 7.59 (d, *J* = 7.9 Hz, 1H, arom), 7.50 (dt, *J* = 11.1, 7.1 Hz, 2H, arom), 7.42 (td, *J* = 7.7, 1.2 Hz, 1H, arom), 3.97 (s, 3H, CH₃). **¹³C NMR** (75 MHz, CDCl₃): δ = 166.4 (C=O), 134.8 (CH, arom), 134.1 (CH, arom), 131.9 (C, arom), 131.8 (CH, arom), 131.0 (q, ²*J*_(C,F) = 32 Hz, 1C, C-CF₃), 130.6 (CH, arom), 128.9 (CH, arom), 128.42 (q, ³*J*_(C,F) = 4 Hz, 1C, CH-C-CF₃), 128.36 (CH, arom), 125.0 (q, ³*J*_(C,F) = 4 Hz, 1C, CH-C-CF₃), 124.3 (C, arom), 123.7 (q, ¹*J*_(C,F) = 272 Hz, 1C, CF₃), 123.1 (C, arom), 92.5 (C sp), 89.7 (C sp), 52.2 (CH₃). **MS** ESI (+): *m/z* (%) = 305 [M+1]⁺ (100), 367 [M+Na]⁺ (80); C₁₇H₁₁F₃O₂ [304.26]. **IR** (NaCl): ν_{max} = 1730, 1657, 1340, 1255, 1128 cm⁻¹. **HRMS** ESI (M+1)⁺ calculated for C₁₇H₁₂F₃O₂ 305.0784, found 305.0795.

Methyl 2-((4-nitrophenyl)ethynyl)benzoate (1j): Method B. Reaction time: 2 h. Eluent for chromatography: hexane/EtOAc 9:1. Yellow solid. Yield 95% (120 mg); mp 119-120 °C. **¹H NMR** (300 MHz, CDCl₃): δ = 8.26 – 8.21 (m, 2H, arom), 8.03 (dd, *J* = 7.8, 1.4 Hz, 1H, arom), 7.75 – 7.69 (m, 2H, arom), 7.68 (dd, *J* = 7.7, 1.3 Hz, 1H, arom), 7.55 (td, *J* = 7.6, 1.4 Hz, 1H, arom), 7.46 (td, *J* = 7.6, 1.4 Hz, 1H, arom), 3.97 (s, 3H, CH₃). **¹³C NMR** (75 MHz, CDCl₃): δ = 166.2 (C=O), 147.2 (C, arom), 134.2 (CH, arom), 132.43 (CH, arom), 132.4 (CH, arom), 132.0 (C, arom), 131.9 (CH, arom), 130.7 (CH, arom), 130.3 (C, arom), 128.9 (CH, arom), 123.64 (CH, arom), 123.61 (CH, arom), 122.7 (C, arom), 93.4 (C sp), 92.1 (C sp), 52.3 (CH₃). **MS** ESI (+): *m/z* (%) = 282 [M+1]⁺ (100), 304 [M+Na]⁺ (20); C₁₆H₁₁NO₄ [281.26]. **IR** (KBr): ν_{max} = 2217, 1710, 1590, 1513, 1346, 1301 cm⁻¹. **HRMS** ESI (M+1)⁺ calculated for C₁₆H₁₂NO₄ 282.0761, found 282.0775.

Methyl 2-((2-nitrophenyl)ethynyl)benzoate (1k): Method A. Reaction time: 3 h. Eluent for chromatography: hexane/EtOAc 8:2. Green solid. Yield 69% (97 mg); mp 90-91 °C. **¹H NMR** (300

MHz, CDCl₃): δ = 8.07 (ddd, J = 25.4, 8.0, 1.1 Hz, 2H, arom), 7.80 (ddd, J = 20.0, 7.7, 1.1 Hz, 2H, arom), 7.64 (td, J = 7.6, 1.2 Hz, 1H, arom), 7.50 (dddd, J = 15.2, 11.8, 7.6, 1.3 Hz, 3H, arom), 3.99 (s, 3H, CH₃). **¹³C NMR** (75 MHz, CDCl₃): δ = 166.8 (C=O), 149.82 (C, arom), 135.4 (CH, arom), 135.1 (CH, arom), 133.3 (CH, arom), 132.4 (C, arom), 132.3 (CH, arom), 131.0 (CH, arom), 129.3 (CH, arom), 129.2 (CH, arom), 125.1 (CH, arom), 123.3 (C, arom), 119.3 (C, arom), 96.2 (C sp), 89.8 (C sp), 52.7 (CH₃). **MS** ESI (+): m/z (%) = 304 [M+Na]⁺ (100), 282 [M+1]⁺ (50); C₁₆H₁₁NO₄ [281.26]. **IR** (KBr): ν_{\max} = 2217, 1720, 1607, 1517, 1341, 1301, 113 cm⁻¹. **HRMS** ESI (M+1)⁺ calculated for C₁₆H₁₂NO₄ 282.0761, found 282.0758.

Methyl 2-(3,3-diethoxyprop-1-yn-1-yl)benzoate (1l): Method A. Reaction time: 4 h. Eluent for chromatography: hexane/EtOAc 9:1. Green oil. Yield 96% (126 mg). **¹H NMR** (300 MHz, CDCl₃): δ = 7.93 (dd, J = 7.7, 1.1 Hz, 1H, arom), 7.59 (dd, J = 7.6, 1.1 Hz, 1H, arom), 7.42 (dtd, J = 22.4, 7.5, 1.5 Hz, 2H, arom), 5.53 (s, 1H, -CHO₂-), 3.91 (s, 3H, -OCH₃), 3.89 – 3.60 (m, 4H, -CH₂-CH₃), 1.28 (t, J = 7.1 Hz, 6H, -CH₂-CH₃). **¹³C NMR** (75 MHz, CDCl₃): δ = 166.4 (C=O), 134.4 (CH, arom), 132.3 (C, arom), 131.6 (CH, arom), 130.3 (CH, arom), 128.4 (CH, arom), 122.3 (C, arom), 91.9 (CH sp³), 89.4 (C sp), 83.7 (C sp), 61.0 (-CH₂-CH₃, 2C), 52.1 (CH₃), 15.1 (-CH₂-CH₃, 2C). **MS** ESI (+): m/z (%) = 203 [M - C₂H₅O - CH₃]⁺ (100), 189 [aldehyde+1]⁺ (96), 285 [M+Na]⁺ (48), 217 [M - C₂H₅O]⁺ (46), 249 [M - CH₃]⁺ (3); C₁₅H₁₈O₄ [262.30]. **IR** (NaCl): ν_{\max} = 2236, 1702, 1596 cm⁻¹. **HRMS** ESI (M+1)⁺ calculated for C₁₅H₁₉O₄ 263.1278, found 263.1269.

Methyl 2-(pent-1-yn-1-yl)benzoate (1m): Method A. Reaction time: 17.5 h. Eluent for chromatography: hexane/EtOAc 98:2. Colorless oil. Yield 81% (83 mg). **¹H NMR** (300 MHz, CDCl₃): δ = 7.88 (dd, J = 1.2 Hz, 1H, arom), 7.50 (dd, J = 7.6, 1.2 Hz 1H, arom), 7.42 (td, J = 7.6, 1.2 Hz, 1H, arom), 7.29 (td, J = 7.6, 1.2 Hz, 1H, arom), 3.91 (s, 3H, -OCH₃), 2.45 (t, J = 7.2 Hz, 2H, -CH₂-), 1.66 (sex, J = 7.2 Hz, 2H, -CH₂-), 1.05 (t, J = 7.2 Hz, 3H, -CH₃). Spectral data are in good agreement with literature values.⁶

Methyl 2-(non-1-yn-1-yl)benzoate (1n): Method A. Reaction time: 24 h. Eluent for chromatography: hexane/EtOAc 98:2. Yellow oil. Yield 56% (72 mg). **¹H NMR** (300 MHz, CDCl₃): δ = 7.92 – 7.85 (m, 1H, arom), 7.50 (d, J = 7.7 Hz, 1H, arom), 7.42 (td, J = 7.6, 1.1 Hz, 1H, arom), 7.30 (td, J = 7.6, 1.1 Hz, 1H, arom), 3.91 (s, 3H, -OCH₃), 2.47 (t, J = 7.1 Hz, 2H, -CH₂-), 1.72 – 1.56 (m, 3H, -CH₂-), 1.39 – 1.24 (m, 7H, -CH₂-), 0.89 (t, J = 6.7 Hz, 3H, -CH₂-CH₃). **¹³C NMR** (75 MHz, CDCl₃): δ = 167.0 (C=O), 134.2 (CH, arom), 132.0 (C, arom), 131.4 (CH, arom), 130.1 (CH, arom), 127.1 (CH, arom), 124.5 (C, arom), 96.1 (C sp), 79.2 (C sp), 52.0 (-COOCH₃), 31.8, 28.92, 28.86, 28.72, 22.6, 19.8 (-CH₂-), 14.1 (-CH₂-CH₃). **MS** ESI (+): m/z (%) = 259 [M+1]⁺ (100), 281 [M+Na]⁺ (85);

C₁₇H₂₂O₂ [258.36]. **IR** (NaCl): ν_{\max} = 2928, 1718, 1597, 1293, 1083 cm⁻¹ **HRMS** ESI (M+1)⁺ calculated for C₁₇H₂₃O₂ 259.1693, found 259.1684.

Methyl 2-((trimethylsilyl)ethynyl)benzoate (1o): Method A. Reaction time: 21.5 h. Eluent for chromatography: hexane/EtOAc 95:5. Colorless oil. Yield 66% (77 mg). **¹H NMR** (300 MHz, CDCl₃): δ = 7.90 (dd, J = 7.8, 1.0 Hz, 1H, arom), 7.58 (dd, J = 7.6, 1.0 Hz, 1H, arom), 7.44 (td, J = 7.6, 1.5 Hz, 1H, arom), 7.36 (td, J = 7.6, 1.4 Hz, 1H, arom), 3.92 (s, 3H, -OCH₃), 0.27 (s, 9H, -Si(CH₃)₃). Spectral data are in good agreement with literature values.⁶

Methyl 2-(thiophen-3-ylethynyl)benzoate (1p): Method A. Reaction time: 1.5 h. Eluent for chromatography: hexane/EtOAc 9:1. Yellow oil. Yield 96% (116 mg). **¹H NMR** (300 MHz, CDCl₃): δ = 7.97 (d, J = 7.8 Hz, 1H, arom), 7.63 (d, J = 7.7 Hz, 1H, arom), 7.59 – 7.55 (m, 1H, arom), 7.49 (td, J = 7.6, 1.2 Hz, 1H, arom), 7.38 (td, J = 7.8, 1.1 Hz, 1H, arom), 7.31 (dd, J = 4.9, 3.0 Hz, 1H, arom), 7.24 (dd, J = 5.0, 0.8 Hz, 1H, arom), 3.96 (s, 3H, CH₃). Spectral data are in good agreement with literature values.⁷

Methyl 3-((4-chlorophenyl)ethynyl)thiophene-2-carboxylate (1q): Method A. Reaction time: 24 h. Eluent for chromatography: hexane/EtOAc 97:3. Orange solid. Yield 76% (105 mg); mp 75-76 °C. **¹H NMR** (300 MHz, CDCl₃): δ = 7.55 – 7.48 (m, 2H, arom), 7.47 (d, J = 5.1 Hz, 1H, arom), 7.37 – 7.30 (m, 2H, arom), 7.20 (d, J = 5.1 Hz, 1H, arom), 3.93 (s, 3H, -CH₃). **¹³C NMR** (75 MHz, CDCl₃): δ = 161.7 (C=O), 134.8 (C, arom), 133.6 (C, arom), 133.0 (CH, arom, 2C), 132.0 (CH, arom), 130.5 (CH, arom), 128.8 (CH, arom, 2C), 127.1 (C, arom), 121.5 (C, arom), 94.1 (C sp), 84.8 (C sp), 52.2 (CH₃). **MS** ESI (+) (+ AcOH): m/z (%) = 245 [M(³⁵Cl)-CH₃O]⁺ (100), 247 [M(³⁷Cl)-CH₃O]⁺ (51); C₁₄H₉ClO₂S [276.74]. **IR** (KBr): ν_{\max} = 3092, 2919, 2023, 1710, 1592, 1301, 1096, 774, 524 cm⁻¹. **HRMS** ESI (M+1)⁺ calculated for C₁₄H₁₀ClO₂S 277.0085, found 277.0076.

Methyl 3-((4-methoxyphenyl)ethynyl)thiophene-2-carboxylate (1r): Method A. Reaction time: 8 h. Eluent for chromatography: hexane/EtOAc 9:1. Yellow solid. Yield 85% (116 mg); mp 95-97 °C. **¹H NMR** (300 MHz, CDCl₃): δ = 7.61 – 7.49 (m, 2H, arom), 7.46 (d, J = 5.1 Hz, 1H, arom), 7.19 (d, J = 5.1 Hz, 1H, arom), 6.97 – 6.77 (m, 2H, arom), 3.93 (s, 3H, -COOCH₃), 3.83 (s, 3H, -OCH₃). Spectral data are in good agreement with literature values.⁸

Methyl 2-((4-methoxyphenyl)ethynyl)nicotinate (1s): Method A. Reaction time: 2.5 h. Eluent for chromatography: hexane/EtOAc 7:3. Orange oil. Yield 99% (134 mg). **¹H NMR** (300 MHz, CDCl₃): δ = 7.873 (dd, J = 4.8, 1.8 Hz, 1H, arom), 8.27 (dd, J = 8.0, 1.8 Hz, 1H, arom), 7.67 – 7.52 (m, 2H, arom), 7.31 (dd, J = 8.0, 4.8 Hz, 1H, arom), 6.97 – 6.84 (m, 2H, arom), 4.00 (s, 3H, -COOCH₃), 3.84 (s, 3H, -OCH₃). Spectral data are in good agreement with literature values.⁴

Methyl 2-(pyridin-2-ylethynyl)benzoate (1t): Method A. Reaction time: 3 h. Eluent for chromatography: hexane/EtOAc 6:4. Yellow oil. Yield 74% (88 mg). ¹H NMR (300 MHz, CDCl₃): δ = 8.64 (d, *J* = 4.5 Hz, 1H, arom), 8.01 (dd, *J* = 7.8, 1.0 Hz, 1H), 7.71 (ddd, *J* = 16.5, 7.7, 1.4 Hz, 2H, arom), 7.60 (d, *J* = 7.8 Hz, 1H, arom), 7.52 (td, *J* = 7.6, 1.4 Hz, 1H, arom), 7.43 (td, *J* = 7.7, 1.3 Hz, 1H, arom), 7.29 – 7.21 (m, 1H, arom), 3.97 (s, 3H, CH₃). Spectral data are in good agreement with literature values.⁶

Methyl 5-nitro-2-((4-(trifluoromethyl)phenyl)ethynyl)benzoate (1u): Method B. Reaction time: 3 h. Eluent for chromatography: hexane/EtOAc 9:1. Orange solid. Yield 86% (175 mg); mp 114-116 °C. ¹H NMR (300 MHz, CDCl₃): δ = 8.88 (d, *J* = 2.4 Hz, 1H, arom), 8.38 (dd, *J* = 8.6, 2.4 Hz, 1H, arom), 7.84 (d, *J* = 8.6 Hz, 1H, arom), 7.71 (dd, *J* = 19.9, 8.3 Hz, 4H, arom), 4.04 (s, 3H, CH₃). ¹³C NMR (75 MHz, CDCl₃): δ = 164.3 (C=O), 146.8 (C, arom), 135.05 (CH, arom), 133.1 (C, arom), 132.3 (CH, arom, 2C), 131.1 (q, ²*J*_(C,F) = 32 Hz, 1C, C-CF₃), 129.5 (C, arom), 126.2 (CH, arom), 126.0 (C, arom), 125.9 (CH, arom), 125.5 (q, ³*J*_(C,F) = 4 Hz, 2C, CH-C-CF₃) 123.8 (q, ¹*J*_(C,F) = 272 Hz, 1C, CF₃), 98.2 (C sp), 88.8 (C sp), 52.9 (CH₃). **MS ESI (+)**: *m/z* (%) = 350 [M+1]⁺ (100), 372 [M+Na]⁺ (15); C₁₇H₁₀F₃NO₄ [349.26]. **IR** (KBr): *v*_{max} = 2955, 2220, 1735, 1606, 1522, 1341, 1324, 1255, 1063 cm⁻¹. **¹HRMS ESI (M+1)⁺** calculated for C₁₇H₁₁F₃NO₄ 350.0635, found 350.0622.

Methyl 2-((4-chlorophenyl)ethynyl)-5-methoxybenzoate (1v): Method A. Reaction time: 24 h. Eluent for chromatography: hexane/EtOAc 95:5. Dark orange oil. Yield 61% (92 mg – 20% s.m. recovered). ¹H NMR (300 MHz, CDCl₃): δ = 7.55 (1H, d, *J* = 8.6 Hz, arom), 7.50 – 7.44 (3H, m, arom), 7.31 (2H, d, *J* = 8.8, Hz, arom), 7.03 (1H, dd, *J* = 8.6, 2.8 Hz, arom), 3.95 (3H, s, CH₃), 3.86 (3 H, s, CH₃). ¹³C NMR (75 MHz, CDCl₃): δ = 166.4 (C=O), 159.2 (C arom), 135.3 (CH arom), 134.1 (C arom), 133.2 (C arom), 132.7 (CH arom), 128.6 (CH arom), 122.2 (C arom), 118.3 (CH arom), 115.6 (C arom), 115.2 (CH arom), 91.4 (C sp), 89.2 (C sp), 55.5 (CH₃), 52.2 (CH₃). **MS ESI (+)**: *m/z* (%) = 301 [M+1]⁺ (100), 323 [M+Na]⁺ (10); C₁₇H₁₃ClO₃ [300.74]. **HRMS ESI (M+1)⁺** calculated for C₁₇H₁₄ClO₃ 301.0626, found 301.0635.

Methyl 2-(3-hydroxy-3-methylbut-1-yn-1-yl)benzoate (1w): Method A. Reaction time: 24 h. Eluent for chromatography: hexane/EtOAc 6:4. Yellow oil. Yield 62% (68 mg). ¹H NMR (300 MHz, CDCl₃): δ = 7.97 – 7.88 (m, 1H, arom), 7.55 – 7.49 (m, 1H, arom), 7.45 (td, *J* = 7.5, 1.5 Hz, 1H, arom), 7.40 – 7.30 (m, 1H, arom), 3.92 (s, 3H, -COOCH₃), 2.06 (s, 1H, -OH), 1.64 (s, 6H, CH₃). Spectral data are in good agreement with literature values.⁹

General procedure for the synthesis of isocoumarins and thienopyranones: Under a nitrogen atmosphere, to a solution of the appropriate methyl 2-arylalkynylbenzoate (0.4 mmol) in dichloroethane (1.6 mL) AgOTf (1 mol%) and *p*-TSA·H₂O (0.12 mmol, 30 mol%) were added. The reaction was stirred at 60 °C until no more starting product was detected by TLC. The reaction mixture was then concentrated under reduced pressure, diluted with EtOAc (15 mL) and washed with saturated aqueous NaHCO₃ (15 mL × 2) and brine (15 mL × 2). The organic phase was dried over Na₂SO₄, filtered and the solvent was removed at reduced pressure. The crude material was purified by flash column chromatography over silica gel.

3-(*p*-Tolyl)-1*H*-isochromen-1-one (2a): Reaction time: 2.5 h. Eluent for chromatography: hexane/EtOAc 95:5. White solid. Yield 85% (80 mg); mp 113-115 °C (lit. 108-110 °C). **¹H NMR** (300 MHz, CDCl₃): δ = 8.30 (dd, *J* = 8.1, 0.7 Hz, 1H, arom), 7.78 (d, *J* = 8.3 Hz, 2H, arom), 7.71 (td, *J* = 7.4, 1.3 Hz, 1H, arom), 7.53 – 7.41 (m, 2H, arom), 7.27 (d, *J* = 7.9 Hz, 3H, arom), 6.91 (s, 1H, arom), 2.41 (s, 3H, CH₃). **¹³C NMR** (75 MHz, CDCl₃): δ = 162.4 (C=O), 153.9 (C, arom), 140.3 (C, arom), 137.7 (C, arom), 134.8 (CH, arom), 129.6 (CH, arom), 129.5 (CH, arom, 2C), 129.2 (C, arom), 127.9 (CH, arom), 125.8 (CH, arom), 125.2 (CH, arom, 2C), 120.4 (C, arom), 101.1 (CH, arom), 21.4 (CH₃). **MS** ESI (+): *m/z* (%) = 259 [M+Na]⁺ (100), 237 [M+1]⁺ (35); C₆H₁₂O₂ [236.27]. **IR** (KBr): *v*_{max} = 3032, 2918, 1730, 1603, 1307, 1182 cm⁻¹. Spectral data are in good agreement with literature values.¹⁰

3-Phenyl-1*H*-isochromen-1-one (2b): Reaction time: 3 h. Eluent for chromatography: hexane/EtOAc 8:2. White solid. Yield 96% (85 mg); mp 81-83 °C (lit. 87-89 °C). **¹H NMR** (300 MHz, CDCl₃): δ = 8.33 (d, *J* = 8.2 Hz, 1H, arom), 7.90 (dd, *J* = 7.9, 1.7 Hz, 2H, arom), 7.74 (t, *J* = 8.1 Hz, 1H, arom), 7.57 – 7.43 (m, 5H, arom), 6.97 (s, 1H, arom). **¹³C NMR** (75 MHz, CDCl₃): δ = 162.7 (C=O), 154.1 (C, arom), 137.9 (C, arom), 135.3 (CH, arom), 132.4 (C, arom), 130.4 (CH, arom), 130.3 (CH, arom), 130.1 (CH, arom), 129.2 (CH, arom), 128.6 (CH, arom), 128.5 (CH, arom), 126.4 (CH, arom), 125.7 (CH, arom), 121.0 (C, arom), 102.2 (CH, arom). **MS** ESI (+): *m/z* (%) = 223 [M+1]⁺ (100), 245 [M+Na]⁺ (20); C₁₅H₁₀O₂ [222.24]. **IR** (KBr): *v*_{max} = 3102, 1721, 1610, 1239, 1071 cm⁻¹. Spectral data are in good agreement with literature values.¹⁰

3-(4-Methoxyphenyl)-1*H*-isochromen-1-one (2c): Reaction time: 4 h. Eluent for chromatography: hexane/EtOAc 8:2. White solid. Yield 86% (87 mg); mp 110-114 °C (lit. 120-122). **¹H NMR** (300 MHz, CDCl₃): δ = 8.27 (d, *J* = 8.4 Hz, 1H, arom), 7.84 – 7.77 (m, 2H, arom), 7.68 (td, *J* = 7.4, 1.3 Hz, 1H, arom), 7.49 – 7.40 (m, 2H, arom), 6.96 (d, *J* = 9.0 Hz, 2H, arom), 6.81 (s, 1H, arom), 3.85 (s, 3H, CH₃). **¹³C NMR** (75 MHz, CDCl₃): δ = 162.4 (C=O), 161.1 (C, arom), 153.7 (C, arom), 137.9 (C, arom), 134.8 (CH, arom), 129.8 (CH, arom), 129.6 (CH, arom), 128.0 (CH, arom), 127.6 (CH,

arom), 126.8 (CH, arom), 125.7 (CH, arom), 124.5 (C, arom), 120.1 (C, arom), 114.2 (CH, arom), 100.2 (CH, arom), 55.4 (-OCH₃). **MS** ESI (+): *m/z* (%) = 275 [M+Na]⁺ (100), 253 [M+1]⁺ (20); C₁₆H₁₂O₃ [252.26]. **IR** (KBr): ν_{\max} = 3001, 2925, 1717, 1603, 1350, 1262, 1118, 1069 cm⁻¹. Spectral data are in good agreement with literature values.⁶

3-(2-Methoxyphenyl)-1H-isochromen-1-one (2d): Reaction time: 4.5 h. Eluent for chromatography: hexane/EtOAc 9:1. White solid. Yield 82% (83 mg); mp 113-115 °C (lit. 115-117 °C). **¹H NMR** (300 MHz, CDCl₃): δ = 8.29 (dd, *J* = 7.8, 0.6 Hz, 1H, arom), 7.96 (dd, *J* = 7.9, 1.7 Hz, 1H, arom), 7.72 – 7.66 (m, 1H, arom), 7.51 – 7.43 (m, 2H, arom), 7.41 – 7.32 (m, 2H, arom), 7.06 (td, *J* = 7.6, 1.1 Hz, 1H, arom), 7.00 (d, *J* = 8.3 Hz, 1H, arom), 3.95 (s, 3H, CH₃). **¹³C NMR** (75 MHz, CDCl₃): δ = 162.6 (C=O), 157.2 (C, arom), 150.4 (C, arom), 138.0 (C, arom), 134.6 (CH, arom), 130.7 (CH, arom), 129.3 (CH, arom), 128.8 (CH, arom), 127.9 (CH, arom), 126.3 (CH, arom), 120.8 (CH, arom), 120.7 (C, arom), 120.6 (C, arom), 111.3 (CH, arom), 107.0 (CH, arom), 55.6 (-OCH₃). **MS** ESI (+): *m/z* (%) = 253 [M+1]⁺ (100), 275 [M+Na]⁺ (50); C₁₆H₁₂O₃ [252.26]. **IR** (KBr): ν_{\max} = 3011, 2925, 1719, 1596, 1253, 1179 cm⁻¹. Spectral data are in good agreement with literature values.¹¹

3-(3-Hydroxyphenyl)-1H-isochromen-1-one (2e): Reaction time: 5.0 h. Eluent for chromatography: hexane/EtOAc 6:4. Red solid. Yield 89% (85 mg); mp 179-181 °C. **¹H NMR** (300 MHz, d₆-acetone): δ = 8.66 (s, 1H, -OH), 8.22 (dd, *J* = 7.9, 0.6 Hz, 1H, arom), 7.89 – 7.75 (m, 1H, arom), 7.68 (d, *J* = 7.7 Hz, 1H, arom), 7.63 – 7.53 (m, 1H, arom), 7.45 – 7.39 (m, 2H, arom), 7.35 (dd, *J* = 11.7, 4.5 Hz, 1H, arom), 7.28 (s, 1H, arom), 7.00 – 6.91 (m, 1H, arom). **¹³C NMR** (75 MHz, d₆-acetone): δ = 161.3 (C=O), 157.9 (C, arom), 153.2 (C, arom), 137.7 (C, arom), 135.0 (CH, arom), 133.6 (C, arom), 130.0 (CH, arom), 129.0 (CH, arom), 128.2 (CH, arom), 126.4 (CH, arom), 120.5 (C, arom), 117.0 (CH, arom), 116.3 (CH, arom), 111.8 (CH, arom), 101.8 (CH, arom). **MS** ESI (+): *m/z* (%) = 261 [M+Na]⁺ (100), 239 [M+1]⁺ (35); C₁₅H₁₀O₃ [238.24]. **IR** (KBr): ν_{\max} = 3301, 1717, 1602, 1332, 1256, 1184 cm⁻¹. **HRMS** ESI (M+1)⁺ calculated for C₁₅H₁₁O₃ 239.0703, found 239.0721.

3-(4-Chlorophenyl)-1H-isochromen-1-one (2f): Reaction time: 7.0 h. Eluent for chromatography: hexane/EtOAc 9:1. White solid. Yield 84% (86 mg); mp 143-145 °C (lit. 144-146 °C). **¹H NMR** (300 MHz, CDCl₃): δ = 8.30 (d, *J* = 7.8 Hz, 1H, arom), 7.87 – 7.78 (m, 2H, arom), 7.73 (td, *J* = 7.6, 1.2 Hz, 1H, arom), 7.51 (t, *J* = 7.7 Hz, 2H, arom), 7.47 – 7.40 (m, 2H, arom), 6.93 (s, 1H, arom). **¹³C NMR** (75 MHz, CDCl₃): δ = 162.0 (C=O), 152.5 (C, arom), 137.2 (C, arom), 136.0 (C, arom), 135.0 (CH, arom), 130.4 (C, arom), 129.7 (CH, arom), 129.1 (CH, arom, 2C), 128.4 (CH, arom), 126.5 (CH, arom, 2C), 126.0 (CH, arom), 120.6 (C, arom), 102.1 (CH, arom). **MS** ESI (+): *m/z* (%) = 257 [M(³⁵Cl)+H]⁺ (100), 259 [M(³⁷Cl)+H]⁺ (50), 279 [M(³⁵Cl)+Na]⁺ (40), 281 [M(³⁷Cl)+Na]⁺ (15);

C₁₅H₉ClO₂ [256.68]. **IR** (KBr): ν_{\max} = 3100, 1726, 1603, 1486, 1071, 529 cm⁻¹. Spectral data are in good agreement with literature values.¹⁰

4-(1-Oxo-1H-isochromen-3-yl)benzotrile (2g): Reaction time: 5.5 h. Eluent for chromatography: hexane/EtOAc 8:2. White solid. Yield 82% (81 mg); mp 208-210 °C. **¹H NMR** (300 MHz, d₆-DMSO): δ = 8.17 (d, J = 7.9 Hz, 1H, arom), 8.02 (dd, J = 28.6, 8.7 Hz, 4H, arom), 7.92 – 7.84 (m, 1H, arom), 7.72 (d, J = 4.6 Hz, 2H, arom), 7.67 – 7.59 (m, 1H, arom). **¹³C NMR** (75 MHz, d₆-DMSO): δ = 161.3 (C=O), 150.9 (C, arom), 137.1 (C, arom), 136.3 (C, arom), 136.0 (CH, arom), 133.4 (CH, 2C, arom), 129.8 (CH, arom), 129.4 (CH, arom), 127.5 (CH, arom), 126.0 (CH, 2C, arom), 120.8 (C, arom), 118.9 (CN), 112.4 (C, arom), 105.3 (CH, arom). **MS** ESI (+): m/z (%) = 248 [M+1]⁺ (100); C₁₆H₉NO₂ [247.25]. **IR** (KBr): ν_{\max} = 3099, 2227, 1723, 1607 cm⁻¹. **HRMS** ESI (M+1)⁺ calculated for C₁₆H₁₀NO₂ 248.0706, found 248.0703.

3-[4-(Trifluoromethyl)phenyl]-1H-isochromen-1-one (2h): Reaction time: 5.0 h. Eluent for chromatography: hexane/EtOAc 95:5. White solid. Yield 84% (98 mg); mp 178-184 °C (lit. 151-154 °C). **¹H NMR** (300 MHz, CDCl₃): δ = 8.35 (d, J = 7.7 Hz, 1H, arom), 8.02 (d, J = 8.3 Hz, 2H, arom), 7.84 – 7.70 (m, 3H, arom), 7.57 (t, J = 7.6 Hz, 2H, arom), 7.06 (s, 1H, arom). **¹³C NMR** (75 MHz, CDCl₃): δ = 161.8 (C=O), 152.0 (C, arom), 136.9 (C, arom), 135.3 (C, arom), 135.1 (CH, arom), 131.6 (q, $^2J_{(C,F)}$ = 32 Hz, 1C, C-CF₃), 129.2 (CH, arom), 128.9 (CH, arom), 126.3 (CH, arom), 125.9 (q, $^3J_{(C,F)}$ = 4 Hz, 2C, CH-C-CF₃), 125.5 (CH, 2C, arom), 123.8 (q, $^1J_{(C,F)}$ = 272 Hz, 1C, CF₃), 120.9 (C, arom), 103.4 (CH, arom). **MS** ESI (+): m/z (%) = 291 [M+1]⁺ (100); C₁₆H₉F₃O₂ [290.24]. **IR** (KBr): ν_{\max} = 3094, 1722, 1640, 1328, 1111 cm⁻¹. Spectral data are in good agreement with literature values.¹²

3-[3-(Trifluoromethyl)phenyl]-1H-isochromen-1-one (2i): Reaction time: 4 h. Eluent for chromatography: hexane/EtOAc 8:2. White solid. Yield 91% (106 mg); mp 149-150 °C (lit. 100-102). **¹H NMR** (300 MHz, CDCl₃): δ = 8.32 (d, J = 7.7 Hz, 1H, arom), 8.12 (s, 1H, arom), 8.06 (d, J = 7.8 Hz, 1H, arom), 7.75 (t, J = 7.6 Hz, 1H, arom), 7.68 (d, J = 7.7 Hz, 1H, arom), 7.61 (d, J = 7.8 Hz, 1H, arom), 7.54 (dd, J = 7.6, 5.6 Hz, 2H, arom), 7.03 (s, 1H, arom). **¹³C NMR** (75 MHz, CDCl₃): δ = 161.8 (C=O), 152.0 (C, arom), 136.9 (C, arom), 135.1 (CH, arom), 132.8 (C, arom), 131.4 (q, $^2J_{(C,F)}$ = 32 Hz, 1C, C-CF₃), 129.8 (CH, arom), 129.4 (CH, arom), 128.7 (CH, arom), 128.3 (CH, arom), 126.4 (q, $^3J_{(C,F)}$ = 4 Hz, 1C, CH-C-CF₃), 126.2 (CH, arom), 123.8 (q, $^1J_{(C,F)}$ = 272 Hz, 1C, CF₃), 122.0 (q, $^3J_{(C,F)}$ = 4 Hz, 1C, CH-C-CF₃), 120.8 (C, arom), 102.9 (CH, arom). **MS** ESI (+): m/z (%) = 291 [M+1]⁺ (100), 313 [M+Na]⁺ (55); C₁₆H₉F₃O₂ [290.24]. **IR** (KBr): ν_{\max} = 3101, 1730, 1605, 1334, 1230, 1108 cm⁻¹. Spectral data are in good agreement with literature values.¹⁰

3-(4-Nitrophenyl)-1H-isochromen-1-one (2j): Reaction time: 6.0 h. Eluent for chromatography: hexane/EtOAc 8:2. Yellow solid. Yield 89% (95 mg); mp 219-221 °C (lit. 227-229 °C). **¹H NMR** (300 MHz, CDCl₃): δ = 8.39 – 8.25 (m, 3H, arom), 8.04 (d, *J* = 8.8 Hz, 2H, arom), 7.68 (dt, *J* = 15.9, 7.6 Hz, 3H, arom), 7.12 (s, 1H, arom). **¹³C NMR** (75 MHz, CDCl₃): δ = 161.4 (C=O), 151.0 (C, arom), 148.3 (C, arom), 137.7 (C, arom), 136.5 (C, arom), 135.21 (CH, arom), 129.9 (CH, arom), 129.4 (CH, arom), 126.6 (CH, arom), 125.9 (CH, 2C, arom), 124.2 (CH, 2C, arom), 121.0 (C, arom), 104.8 (CH, arom). **MS** ESI (+): *m/z* (%) = 268 [M+1]⁺ (100); C₁₅H₉NO₄ [267.24]. **IR** (KBr): *v*_{max} = 3016, 1721, 1602, 1517, 1349, 1106 cm⁻¹. Spectral data are in good agreement with literature values.¹²

3-(2-Nitrophenyl)-1H-isochromen-1-one (2k): Reaction time: 24 h. Eluent for chromatography: hexane/EtOAc 8:2. Yellow solid. Yield 41% (44 mg); mp 149-154 °C. **¹H NMR** (300 MHz, CDCl₃): δ = 8.31 (d, *J* = 7.9 Hz, 1H, arom), 8.00 (d, *J* = 8.0 Hz, 1H, arom), 7.79 – 7.44 (m, 6H, arom), 6.70 (s, 1H, arom). **¹³C NMR** (75 MHz, CDCl₃): δ = 161.4 (C=O), 151.3 (C, arom), 148.2 (C, arom), 136.7 (C, arom), 135.0 (CH, arom), 133.0 (CH, arom), 131.0 (CH, arom), 130.8 (CH, arom), 129.8 (CH, arom), 129.0 (CH, arom), 127.9 (C, arom), 126.1 (CH, arom), 124.8 (CH, arom), 120.7 (C, arom), 105.9 (CH, arom). **MS** ESI (+): *m/z* (%) = 290 [M+Na]⁺ (100), 268 [M+H]⁺ (95); C₁₅H₉NO₄ [267.24]. **IR** (KBr): *v*_{max} = 3068, 1735, 1608, 1530, 1345, 1055 cm⁻¹. **HRMS** ESI (M+1)⁺ calculated for C₁₅H₁₀NO₄ 268.0604, found 268.0611.

1-Oxo-1H-isochromene-3-carbaldehyde (2l): Reaction time: 4 h. Eluent for chromatography: hexane/EtOAc 7:3. Yellow solid. Yield 44% (31 mg); mp 163-164 °C. **¹H NMR** (300 MHz, CDCl₃): δ = 9.60 (s, 1H, -CHO), 8.37 (d, *J* = 7.9 Hz, 1H, arom), 7.83 (dd, *J* = 7.5, 1.2 Hz, 1H, arom), 7.71 (dd, *J* = 13.7, 7.3 Hz, 2H, arom), 7.30 (s, 1H, arom). **¹³C NMR** (75 MHz, CDCl₃): δ = 183.3 (-CHO), 160.1 (C=O), 149.4 (C, arom), 135.3 (CH, arom), 134.4 (C, arom), 131.7 (CH, arom), 130.3 (CH, arom), 128.2 (CH, arom), 123.4 (C, arom), 115.3 (CH, arom). **MS** ESI (+): *m/z* (%) = 175 [M+H]⁺ (100); C₁₀H₆O₃ [174.15]. **IR** (KBr): *v*_{max} = 3096, 2852, 1727, 1693, 1599, 1291, 1110 cm⁻¹. **HRMS** ESI (M+1)⁺ calculated for C₁₀H₇O₃ 175.0390, found 175.0398.

3-Propyl-1H-isochromen-1-one (2m): Reaction time: 2 h. Eluent for chromatography: hexane/EtOAc 95:5. Colorless oil. Yield 65% (49 mg). **¹H NMR** (300 MHz, CDCl₃): δ = 8.28 – 8.18 (m, 1H, arom), 7.65 (ddd, *J* = 7.8, 7.4, 1.4 Hz, 1H, arom), 7.47 – 7.39 (m, 1H, arom, arom), 7.34 (d, *J* = 7.8 Hz, 1H, arom), 6.24 (s, 1H), arom, 2.49 (t, *J* = 7.5 Hz, 2H, -CH₂-CH₂-CH₃), 1.73 (sex, *J* = 7.8 Hz, 2H, -CH₂-CH₂-CH₃), 0.98 (t, *J* = 7.4 Hz, 3H, -CH₂-CH₂-CH₃). **¹³C NMR** (75 MHz, CDCl₃): δ = 163.1 (C=O), 158.0 (C, arom), 137.6 (C, arom), 134.7 (CH, arom), 129.4 (CH, arom), 127.5 (CH, arom), 125.0 (CH, arom), 120.1 (C, arom), 103.0 (CH, arom), 35.4 (-CH₂-CH₂-CH₃), 20.2 (-CH₂-CH₂-CH₃), 13.5

(-CH₂-CH₂-CH₃). **MS** ESI (+): *m/z* (%) = 189 [M+1]⁺ (100); C₁₂H₁₂O₂ [188.22]. **IR** (NaCl): ν_{\max} = 2963, 2874, 1728, 1607, 1292, 1097 cm⁻¹. Spectral data are in good agreement with literature values.⁶

3-Heptyl-1H-isochromen-1-one (2n): Reaction time: 1 h. Eluent for chromatography: hexane/EtOAc 97:3. Colorless oil. Yield 77% (75 mg). **¹H NMR** (300 MHz, CDCl₃): δ = 8.25 (dd, *J* = 8.0, 0.5 Hz, 1H, arom), 7.67 (td, *J* = 7.8, 1.3 Hz, 1H, arom), 7.44 (t, *J* = 7.6 Hz, 1H, arom), 7.35 (d, *J* = 7.9 Hz, 1H, arom), 6.25 (s, 1H, arom), 2.52 (t, *J* = 7.6 Hz, 2H, -CH₂-), 1.50 – 1.10 (m, 10H, -CH₂-), 0.88 (t, *J* = 6.7 Hz, 3H, -CH₃). **¹³C NMR** (75 MHz, CDCl₃): δ = 163.1 (C=O), 158.4 (C, arom), 137.6 (C, arom), 134.6 (CH, arom), 129.5 (CH, arom), 127.5 (CH, arom), 125.0 (CH, arom), 120.1 (C, arom), 102.8 (CH, arom), 33.5 (CH₂), 31.7 (CH₂), 29.7 (CH₂), 29.0 (CH₂), 26.9 (CH₂), 22.6 (CH₂), 14.0 (CH₃). **MS** ESI (+): *m/z* (%) = 267 [M+Na]⁺ (100), 245 [M+1]⁺ (35); C₁₆H₂₀O₂ [244.33]. **IR** (NaCl): ν_{\max} = 3069, 2928, 1732, 1607, 1327, 1107 cm⁻¹. Spectral data are in good agreement with literature values.¹³

3-(Thiophen-3-yl)-1H-isochromen-1-one (2p): Reaction time: 6 h. Eluent for chromatography: hexane/EtOAc 9:1. White solid. Yield 99% (90 mg); mp 111-112 °C (lit. 110-112 °C). **¹H NMR** (300 MHz, CDCl₃): δ = 8.30 (d, *J* = 7.4 Hz, 1H, arom), 7.89 (dd, *J* = 2.9, 1.3 Hz, 1H, arom), 7.72 (td, *J* = 7.7, 1.3 Hz, 1H, arom), 7.55 – 7.37 (m, 4H, arom), 6.79 (s, 1H, arom). **¹³C NMR** (75 MHz, CDCl₃): δ = 162.1 (C=O), 150.4 (C, arom), 137.6 (C, arom), 134.9 (CH, arom), 134.3 (C, arom), 129.8 (CH, arom), 127.9 (CH, arom), 126.9 (CH, arom), 125.8 (CH, arom), 124.3 (CH, arom), 124.1 (CH, arom), 120.5 (C, arom), 101.4 (CH, arom). **MS** ESI (+): *m/z* (%) = 175 [M+Na]⁺ (100), 229 [M+H]⁺ (65); C₁₃H₈O₂S [228.27]. **IR** (KBr): ν_{\max} = 3122, 3101, 1723, 1604, 1333, 1072, 749 cm⁻¹. Spectral data are in good agreement with literature values.¹⁰

5-(4-Chlorophenyl)-7H-thieno[2,3-*c*]pyran-7-one (2q): Reaction time: 2 h. Eluent for chromatography: hexane/EtOAc 9:1. White solid. Yield 95% (99 mg); mp 180-182 °C. **¹H NMR** (300 MHz, CDCl₃): δ = 7.84 (d, *J* = 5.1 Hz, 1H, arom), 7.78 (d, *J* = 8.6 Hz, 2H, arom), 7.41 (d, *J* = 8.6 Hz, 2H, arom), 7.23 (d, *J* = 5.1 Hz, 1H, arom), 7.09 (s, 1H, arom). **¹³C NMR** (75 MHz, CDCl₃): δ = 157.9 (C=O), 155.2 (C, arom), 147.2 (C, arom), 136.9 (CH, arom), 136.1 (C, arom), 130.3 (C, arom), 129.2 (CH, arom, 2C), 126.6 (CH, arom, 2C), 124.7 (CH, arom), 123.1 (C, arom), 99.2 (CH, arom). **MS** ESI (+): *m/z* (%) = 285 [M(³⁵Cl)+Na]⁺ (100), 287 [M(³⁷Cl)+Na]⁺ (40); C₁₃H₇ClO₂S [262.71]. **IR** (KBr): ν_{\max} = 3123, 1714, 1606, 1414, 1089, 619 cm⁻¹. **HRMS** ESI (M+1)⁺ calculated for C₁₃H₈ClO₂S 262.9928, found 262.9932.

5-(4-Methoxyphenyl)-7H-thieno[2,3-*c*]pyran-7-one (2r): Reaction time: 1 h. Eluent for chromatography: hexane/EtOAc 8:2. Pale green solid. Yield 93% (96 mg); mp 143-145 °C. **¹H NMR** (300 MHz, CDCl₃): δ = 7.85 – 7.77 (m, 3H, arom), 7.20 (d, *J* = 5.1 Hz, 1H, arom), 6.99 (s, 1H, arom),

6.99 – 6.92 (m, 2H, arom), 3.86 (s, 3H, CH₃). **¹³C NMR** (75 MHz, CDCl₃): δ = 161.2 (C=O), 158.4 (C, arom), 156.6 (C, arom), 147.8 (C, arom), 136.6 (CH, arom), 126.9 (CH, arom, 2C), 124.5 (CH, arom), 124.4 (C, arom), 122.1 (C, arom), 114.3 (CH, arom, 2C), 97.6 (CH, arom), 55.4 (CH₃). **MS** ESI (+): m/z (%) = 281 [M+Na]⁺ (100); C₁₄H₁₀O₃S [258.29]. **IR** (KBr): ν_{max} = 3085, 1713, 1608, 1336, 1263, 1114, 1020 cm⁻¹. **HRMS** ESI (M+1)⁺ calculated for C₁₄H₁₁O₃S 259.0423, found 259.0436.

7-nitro-3-(4-(trifluoromethyl)phenyl)-1H-isochromen-1-one (**2u**): Reaction time: 24 h. Recrystallized from CH₃CN. Pale green solid. Yield 67% (90 mg); mp 223-225 °C. **¹H NMR** (300 MHz, d₆-DMSO): δ = 8.78 (d, *J* = 2.3 Hz, 1H, arom), 8.62 (dd, *J* = 8.7, 2.4 Hz, 1H, arom), 8.14 (d, *J* = 8.2 Hz, 2H, arom), 7.93 (t, *J* = 8.3 Hz, 3H, arom), 7.85 (s, 1H, arom). **¹³C NMR** (75 MHz, d₆-DMSO): δ = 160.3 (C=O), 154.2 (C, arom), 147.2 (C, arom), 142.4 (C, arom), 135.2 (C, arom), 131.0 (q, ²*J*_(C,F) = 32 Hz, 1C, C-CF₃), 129.8 (CH, arom), 129.2 (CH, arom), 126.6 (CH, arom, 2C), 126.5 (q, ³*J*_(C,F) = 4 Hz, 2C, CH-C-CF₃), 124.7 (CH, arom), 124.3 (q, ¹*J*_(C,F) = 272 Hz, 1C, CF₃), 121.3 (C, arom), 103.8 (CH, arom). **MS** ESI (+): m/z (%) = 331 [M-CO+Na]⁺ (100), 359 [M+Na]⁺ (90), 381 [M+2Na]⁺ (45); C₁₆H₈F₃NO₄ [335.23]. **IR** (KBr): ν_{max} = 3089, 1754, 1609, 1522, 1336, 1323, 1115, 1010 cm⁻¹. **HRMS** ESI (M+1)⁺ calculated for C₁₆H₉F₃NO₄ 336.0478, found 336.0463.

3-(4-chlorophenyl)-7-methoxy-1H-isochromen-1-one (**2v**): Reaction time: 24 h. Eluent for chromatography: hexane/EtOAc 85:15. White solid. Yield 70% (84 mg); mp 151-153 °C. **¹H NMR** (300 MHz, CD₂Cl₂): δ = 7.80 (2H, d, *J* = 8.7 Hz, arom), 7.70 (1H, d, *J* = 2.5 Hz, arom), 7.47 (3H, m, arom), 7.35 (1 H, dd, *J* = 8.6, 2.7), 6.95 (1 H, s, arom), 3.94 (3H, s, CH₃). **¹³C NMR** (75 MHz, d₆-CD₂Cl₂): δ = 161.7 (C, arom), 159.8 (C, arom), 150.4 (C, arom), 135.2 (C, arom), 130.82 (C, arom), 130.80 (C, arom), 129.0 (CH, arom), 127.7 (CH, arom), 126.1 (CH, arom), 124.3 (CH, arom), 121.8 (C, arom), 110.2 (CH, arom), 101.9 (CH, arom), 55.8 (CH₃). **MS** ESI (+): m/z (%) = 287 [M(³⁵Cl)+1]⁺ (96), 289 [M(³⁷Cl)+1]⁺ (38), 309 [M(³⁵Cl)+Na]⁺ (100), 311 [M(³⁷Cl)+Na]⁺ (42); C₁₆H₁₁ClO₃ [286.71]. **HRMS** ESI (M+1)⁺ calculated for C₁₆H₁₂ClO₃ 287.0469, found 287.0478.

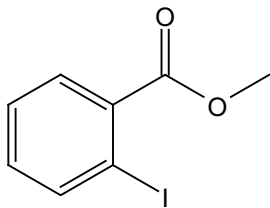
Methyl 2-(3-methylbut-2-enoyl)benzoate (**3a**): Reaction time: 2 h. Eluent for chromatography: hexane/EtOAc 9:1. Yellow oil. Yield 30% (26 mg). **¹H NMR** (300 MHz, CDCl₃): δ = 7.85 (dd, *J* = 7.6, 1.2 Hz, 1H, arom), 7.51 (dddd, *J* = 23.6, 8.7, 7.4, 1.3 Hz, 3H, arom), 6.40 – 6.27 (m, 1H, CH sp²), 3.86 (s, 3H, -COOCH₃), 2.20 (d, *J* = 1.1 Hz, 3H, -CH₃), 1.98 (d, *J* = 1.1 Hz, 3H, -CH₃). **¹³C NMR** (75 MHz, CDCl₃): δ = 194.7 (C=O ketone), 167.7 (C=O ester), 156.4 (C, arom), 143.9 (C, arom), 131.8 (CH, arom), 129.7 (CH, arom), 129.6 (CH, arom), 129.4 (C sp²), 127.0 (CH, arom), 123.9 (CH sp²), 52.4 (-OCH₃), 27.9 (-CH₃), 21.0 (-CH₃). **MS** ESI (+): m/z (%) = 459 [2M+Na]⁺ (100),

241 [M+Na]⁺ (10); C₁₃H₁₄O₃ [218.25]. **IR** (NaCl): ν_{\max} = 2917, 1727, 1668, 1613, 1288, 1196 cm⁻¹. **HRMS** ESI (M+1)⁺ calculated for C₁₃H₁₅O₃ 219.1016, found 219.1029.

Procedure for the deuteration of *p*-TSA: 100 mg of *p*-TSA·H₂O (0.5 mmol) were dissolved in 500 μ L of D₂O (28 mmol, 53 equiv). The reaction mixture was stirred at reflux for one hour, then the solvent was removed under reduced pressure. This sequence was repeated three times to give quantitatively a white solid. The percentage of deuteration (\approx 81% d) was determined by comparison of the ¹H-NMR spectra of the product obtained with a pure sample of *p*-TSA·H₂O using a mixture of CD₂Cl₂/d₆-DMSO (v/v 95:5) as solvent and a prolonged delay time (d1 = 10 s).

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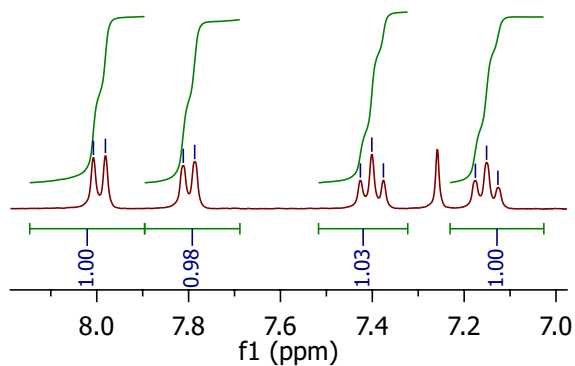
Methyl 2-iodobenzoate

$^1\text{H-NMR}$, 300 MHz, CDCl_3

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7.13

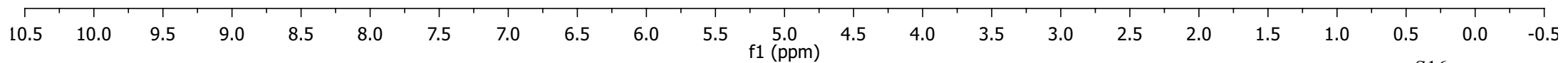
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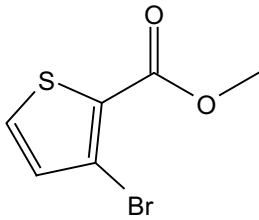
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7.15
7.13



1.00
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1.03
1.00

3.27

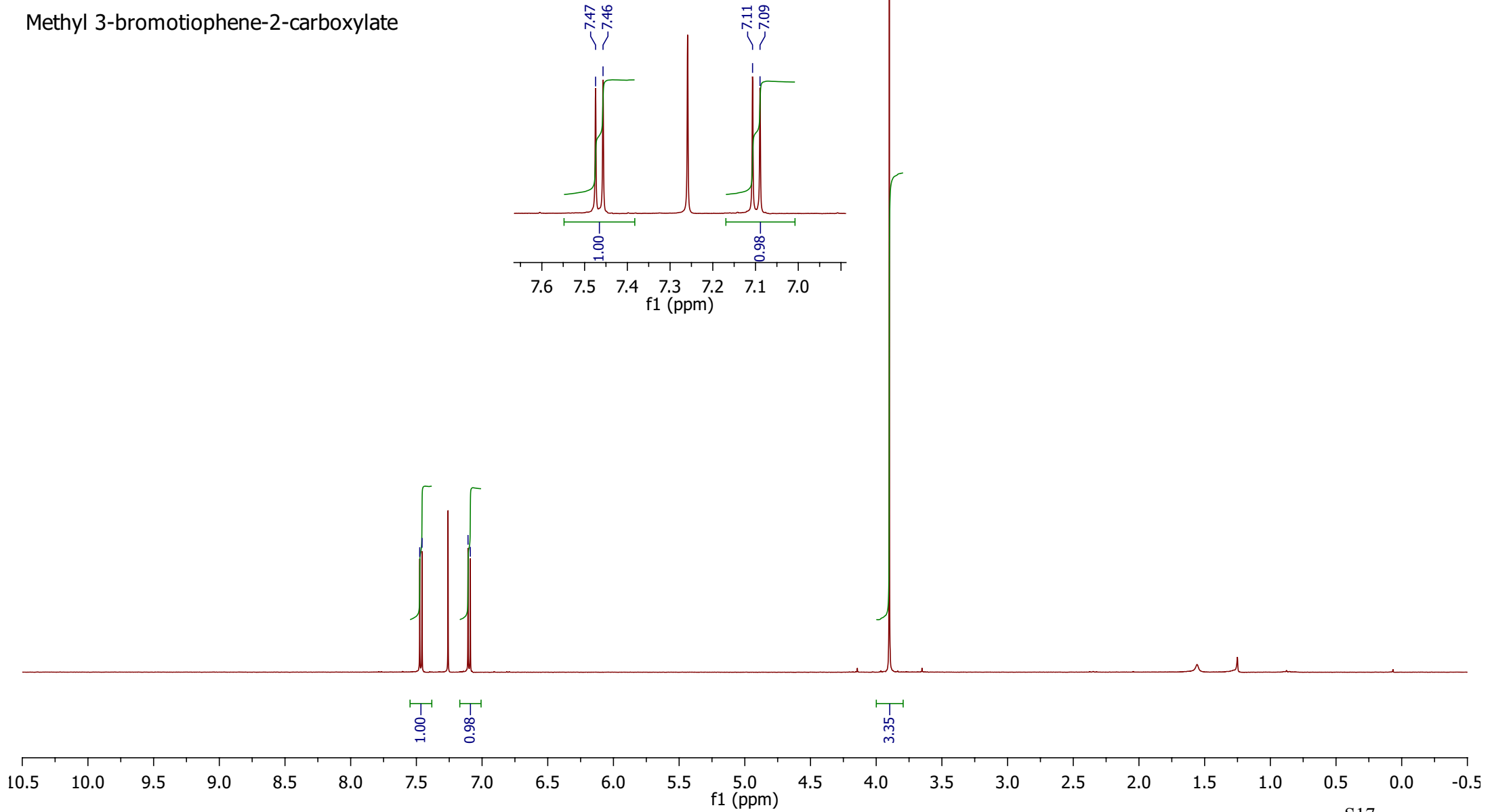


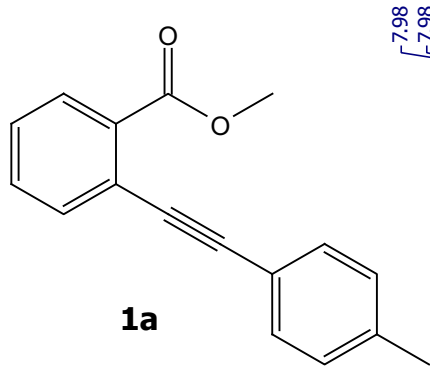


7.47
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¹H-NMR, 300 MHz, CDCl₃

Methyl 3-bromothiophene-2-carboxylate



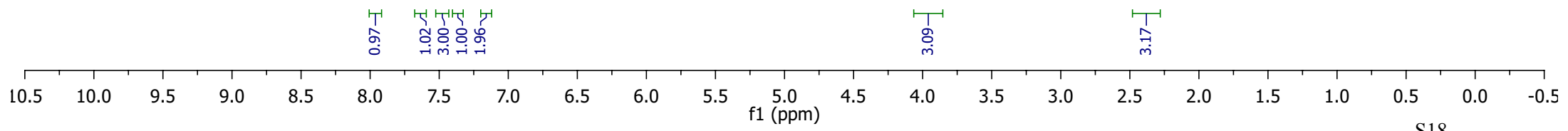
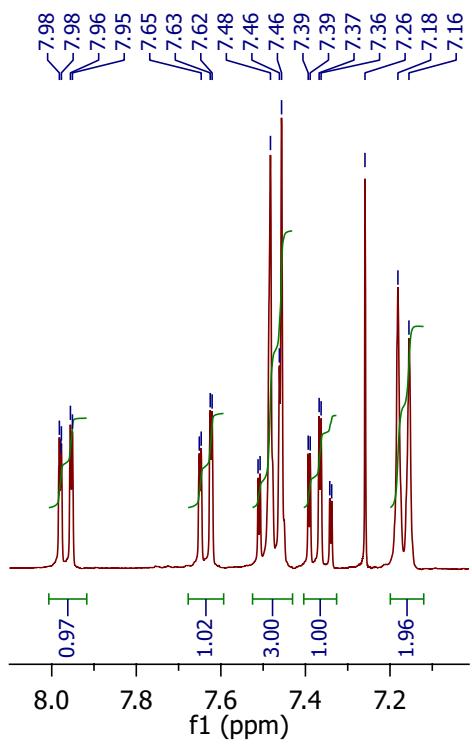


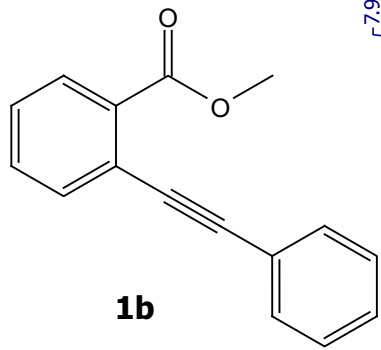
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7.34
7.18
7.16

¹H-NMR, 300 MHz, CDCl₃

3.96

2.38

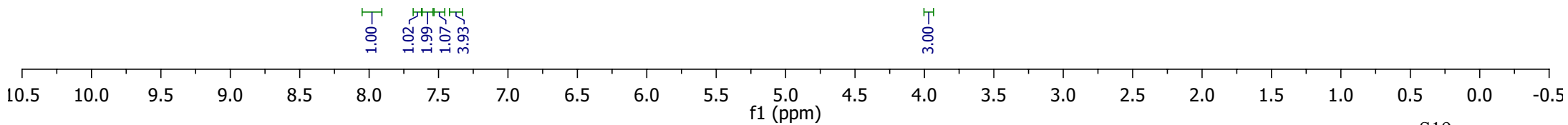
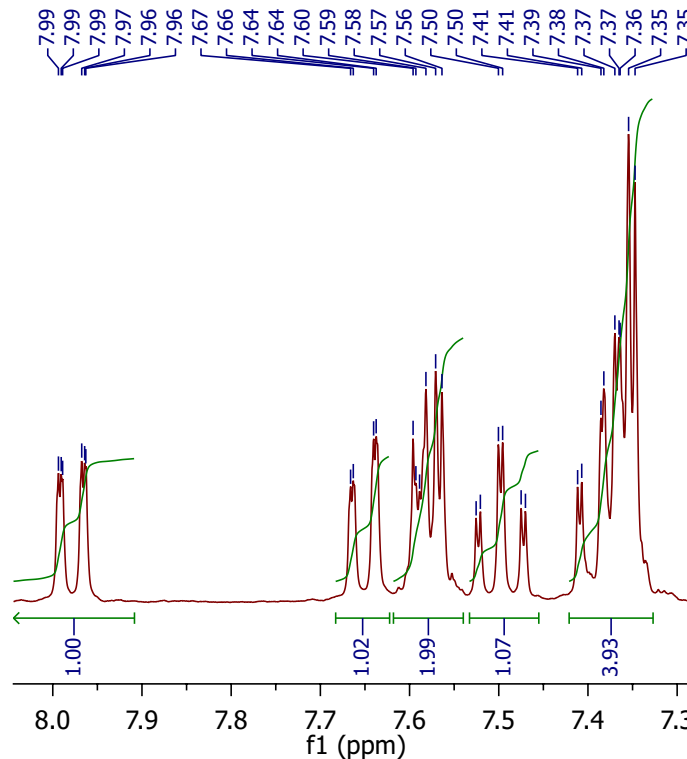


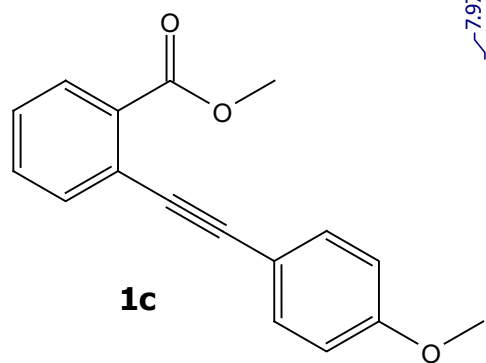


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3.97

¹H-NMR, 300 MHz, CDCl₃

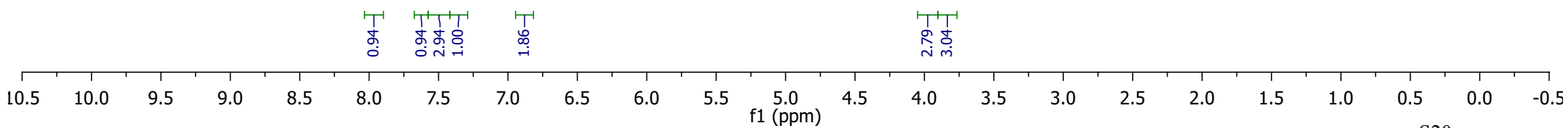
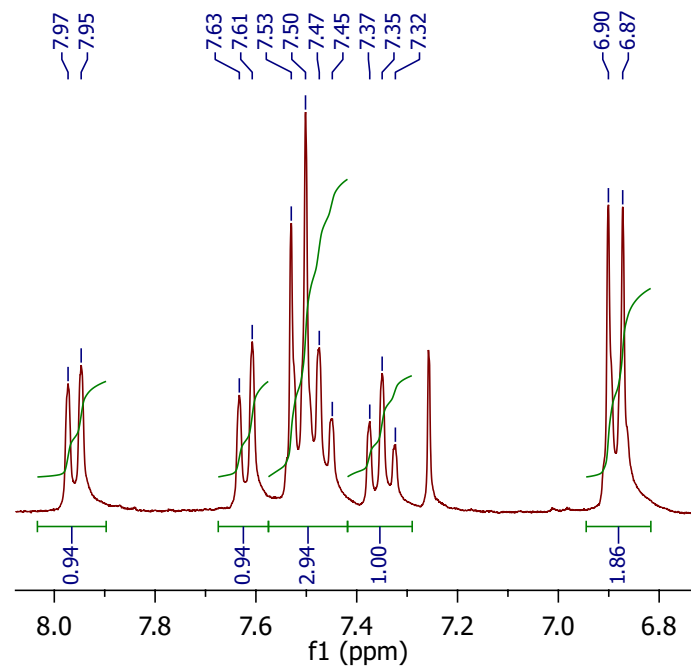




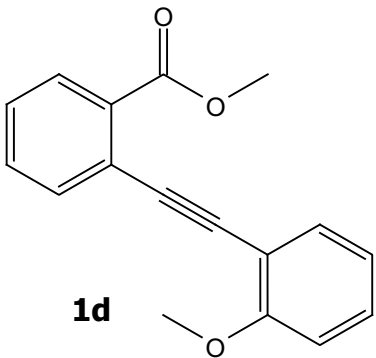
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6.87

3.96
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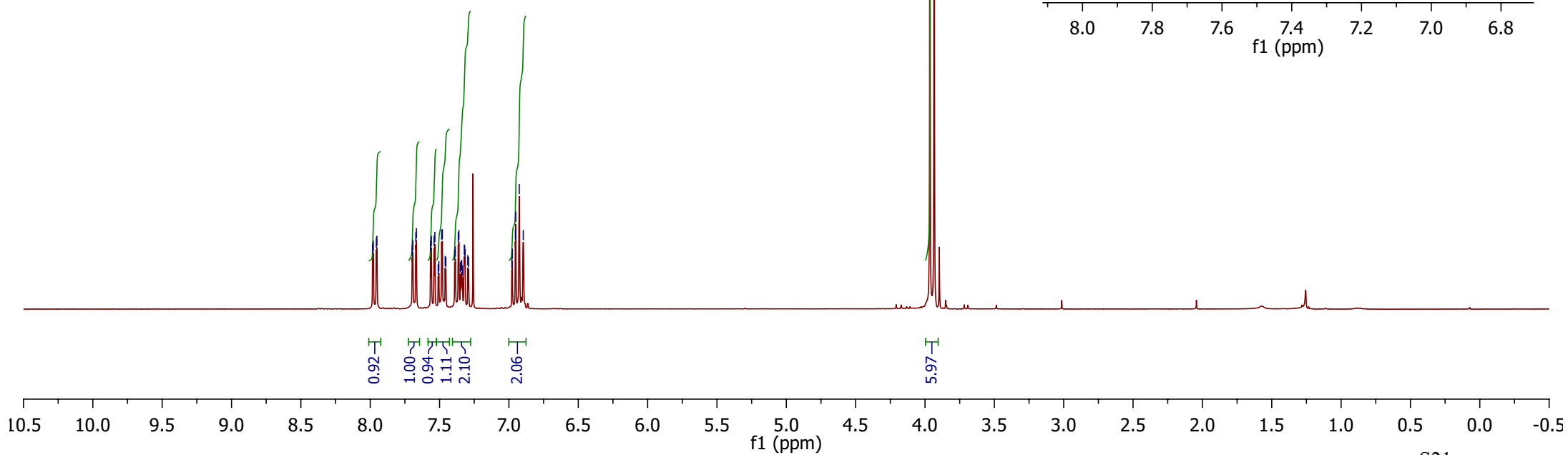
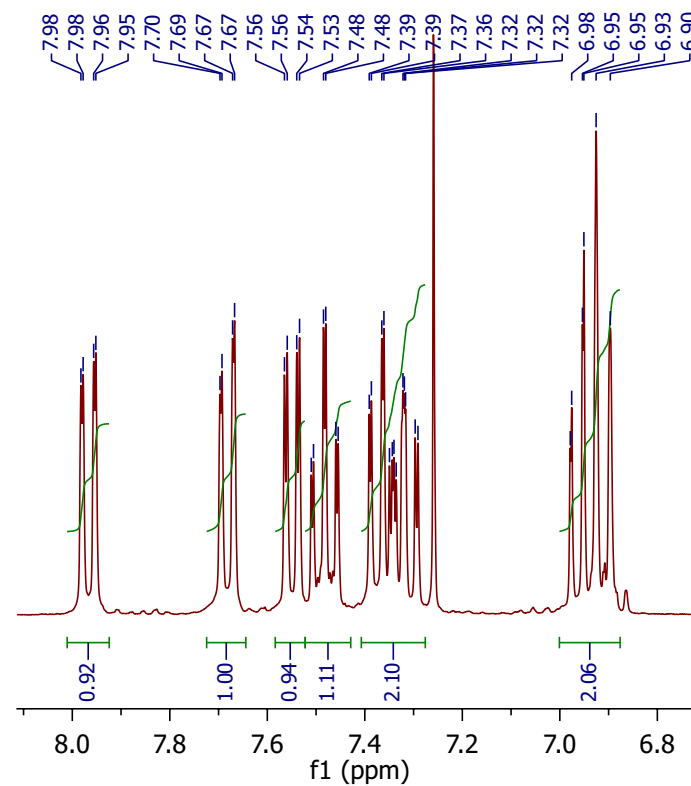
¹H-NMR, 300 MHz, CDCl₃

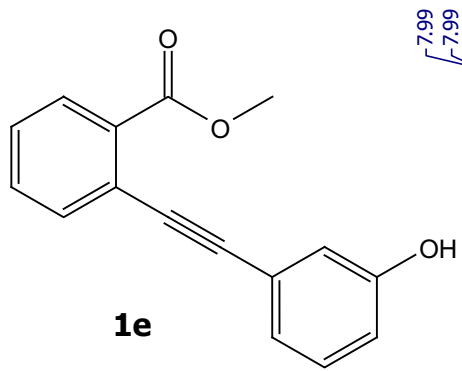


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6.93
6.90



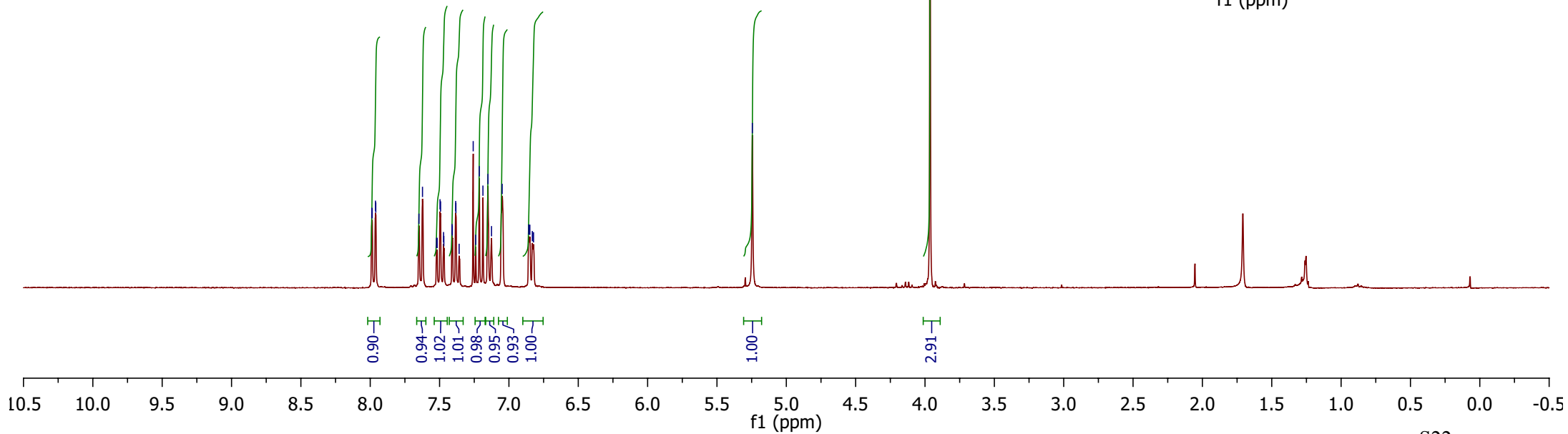
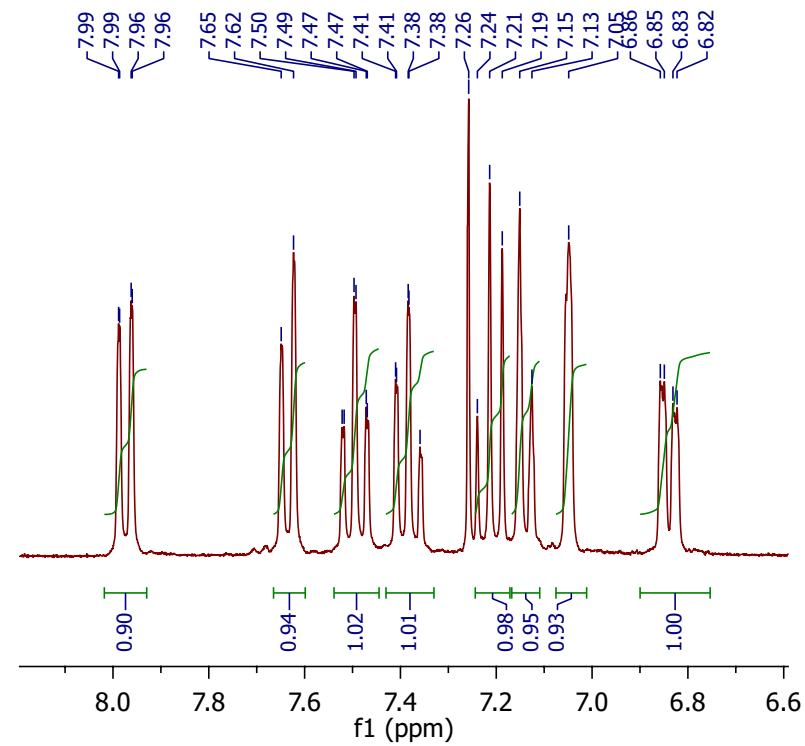
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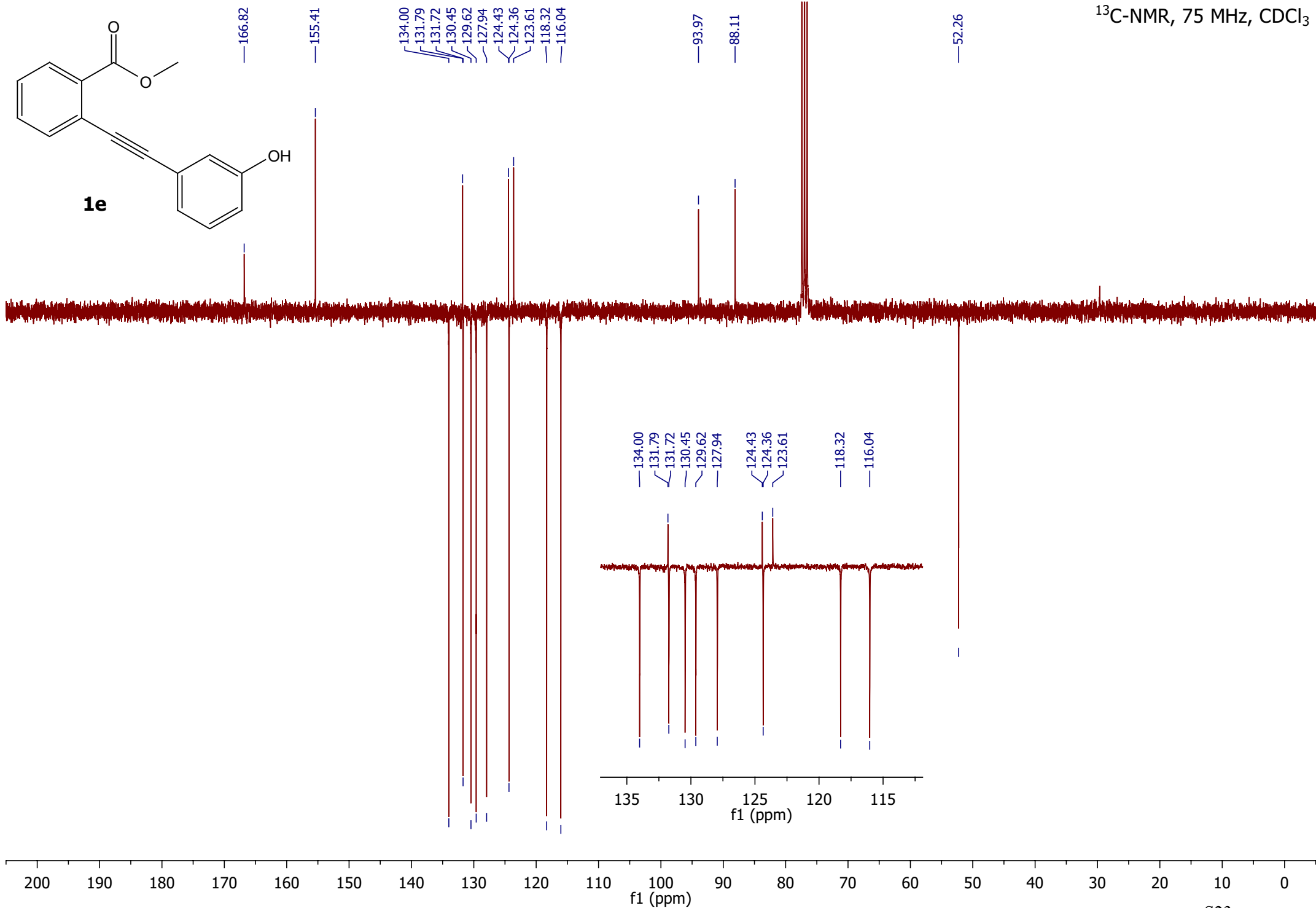


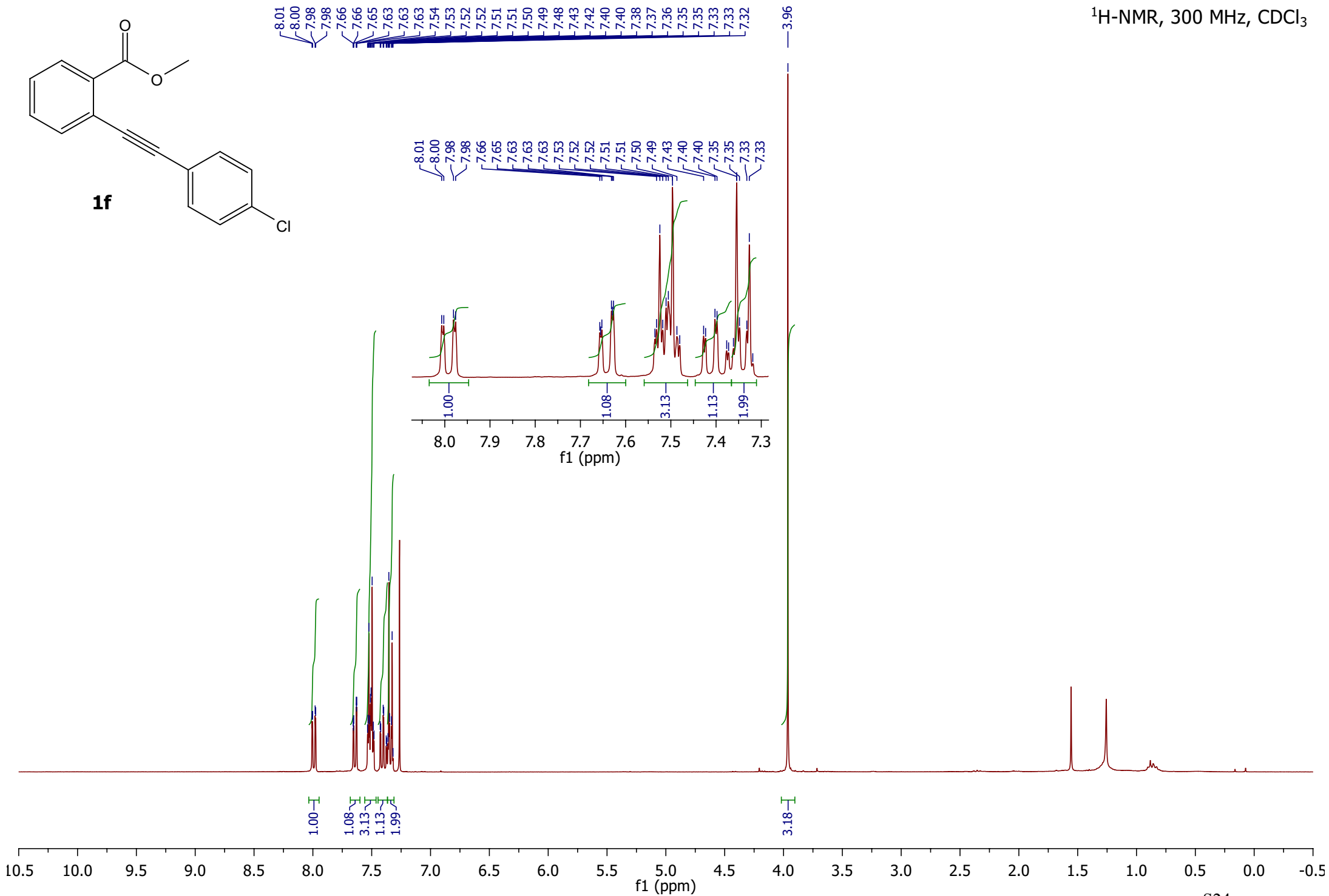
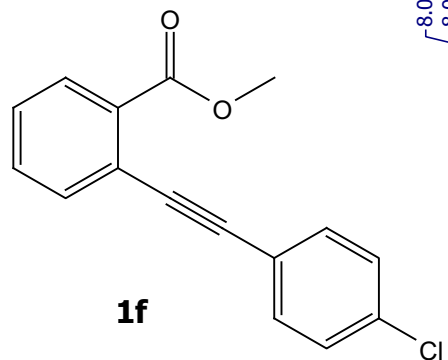


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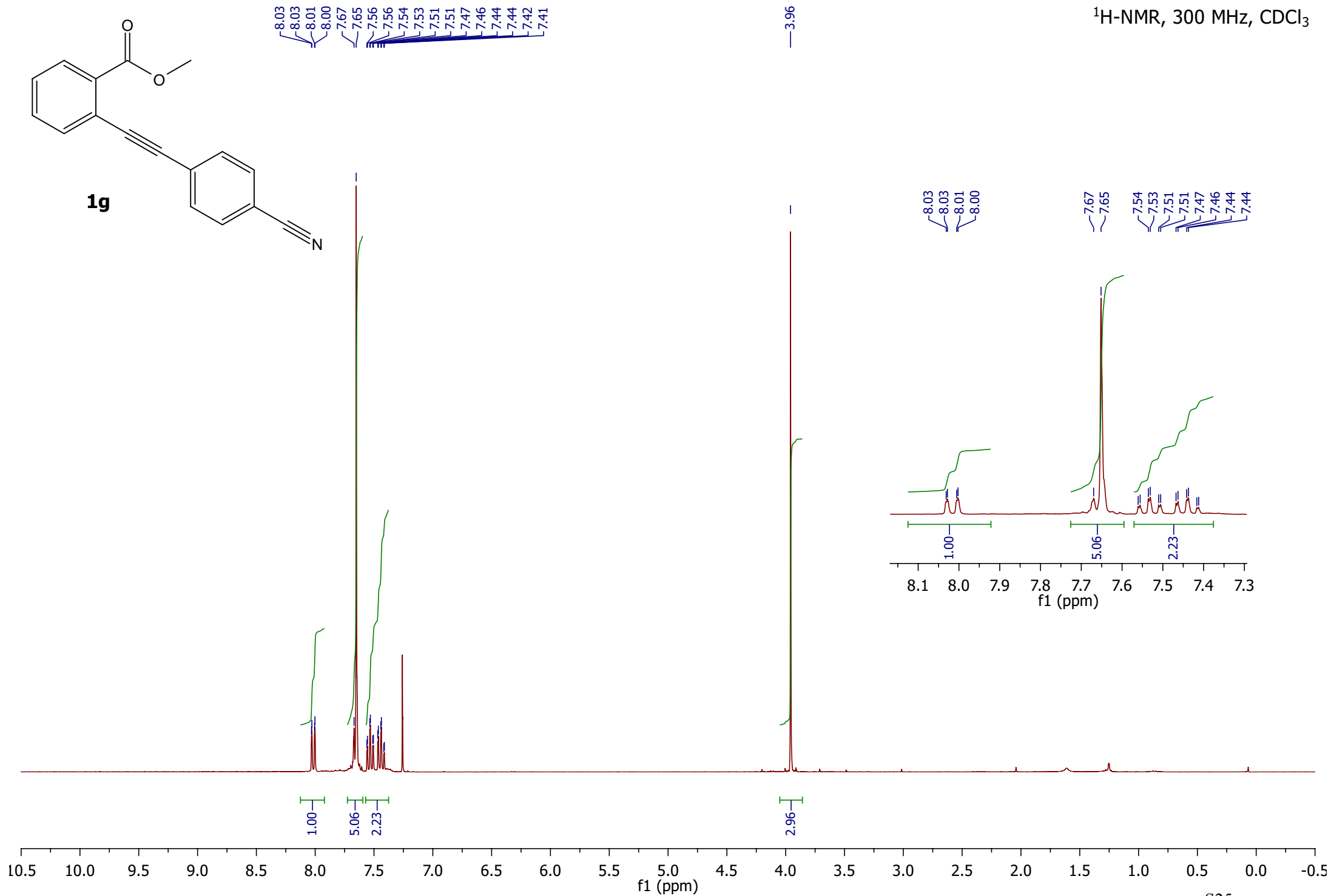
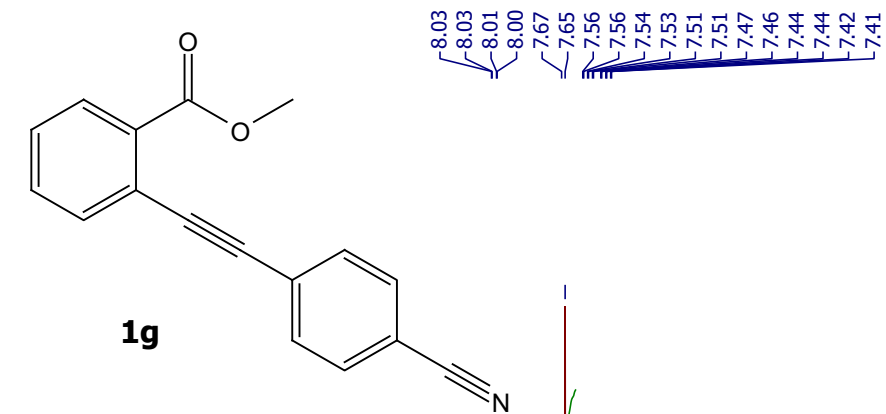
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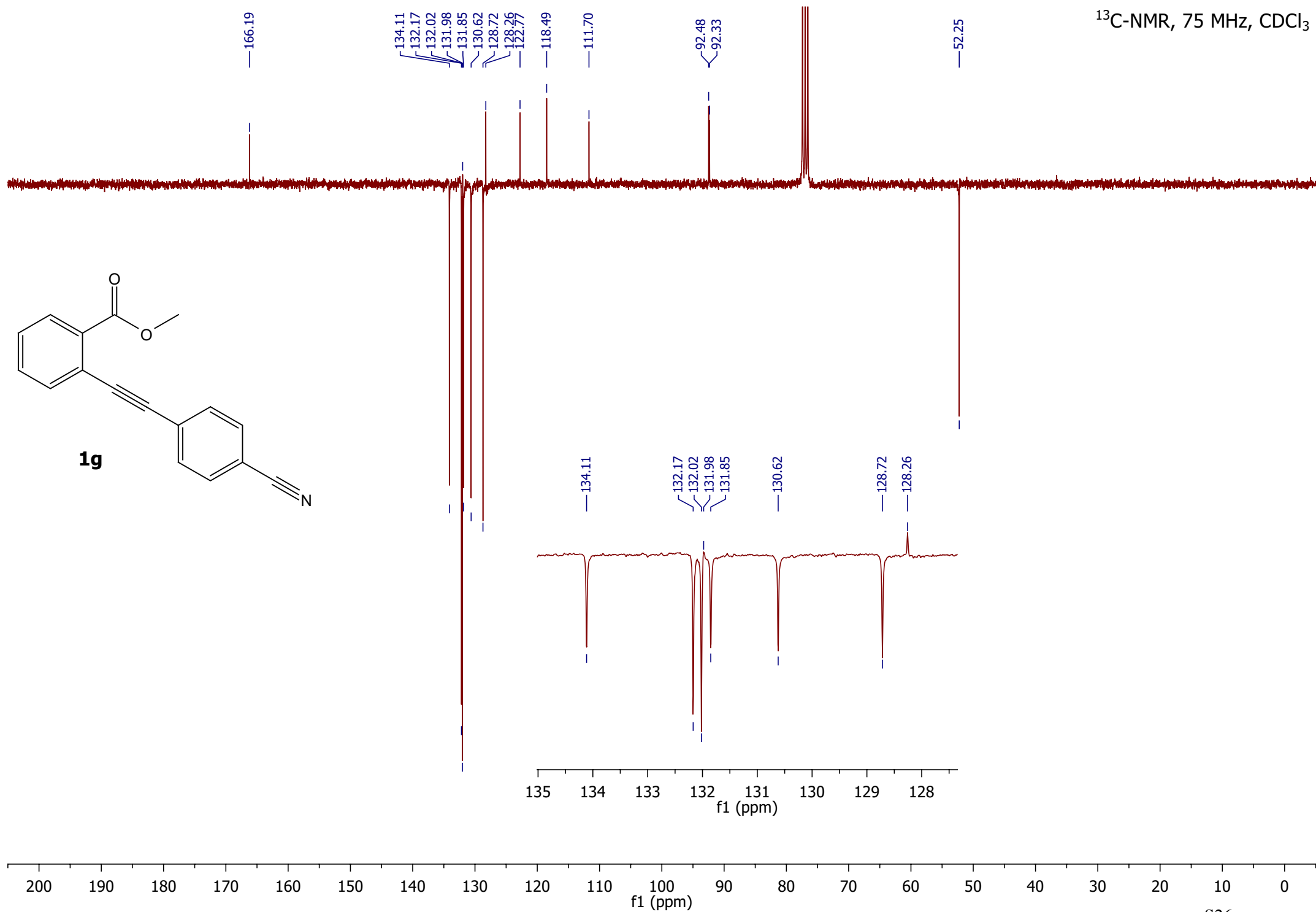
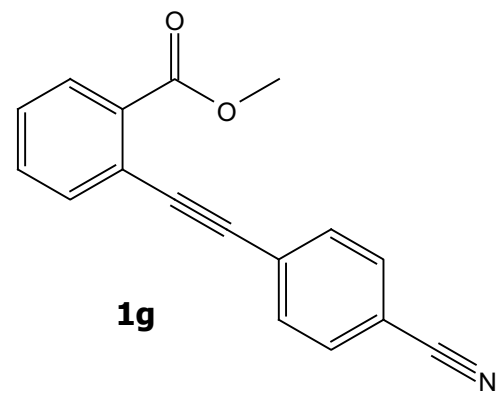


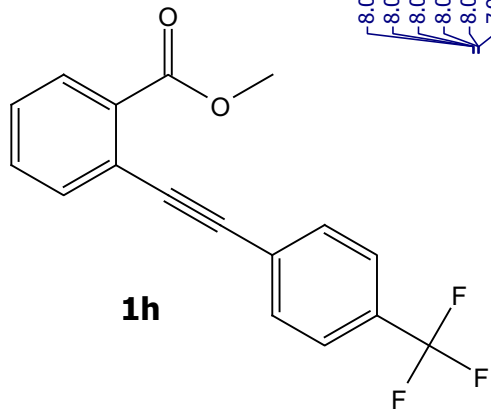




¹H-NMR, 300 MHz, CDCl₃

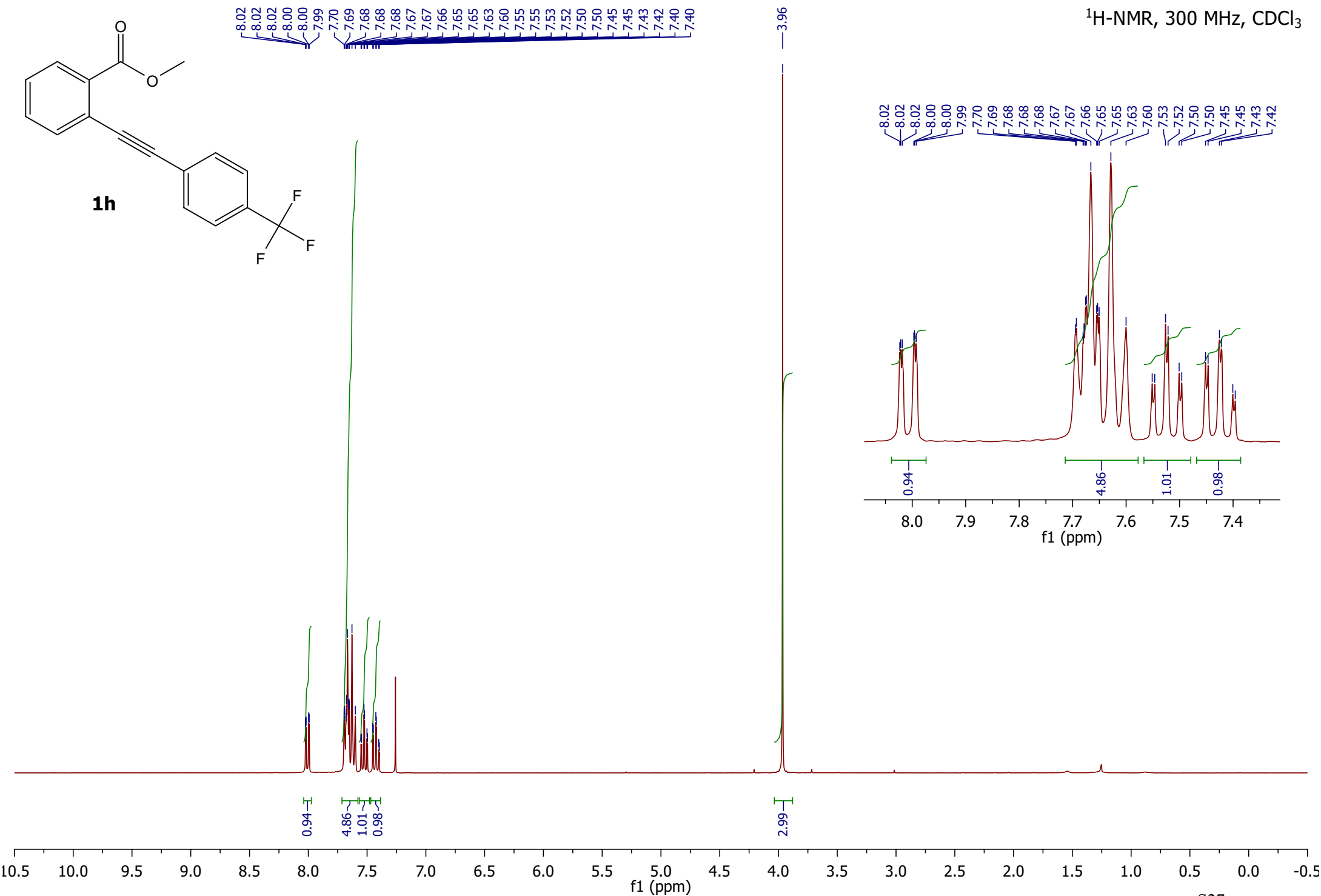
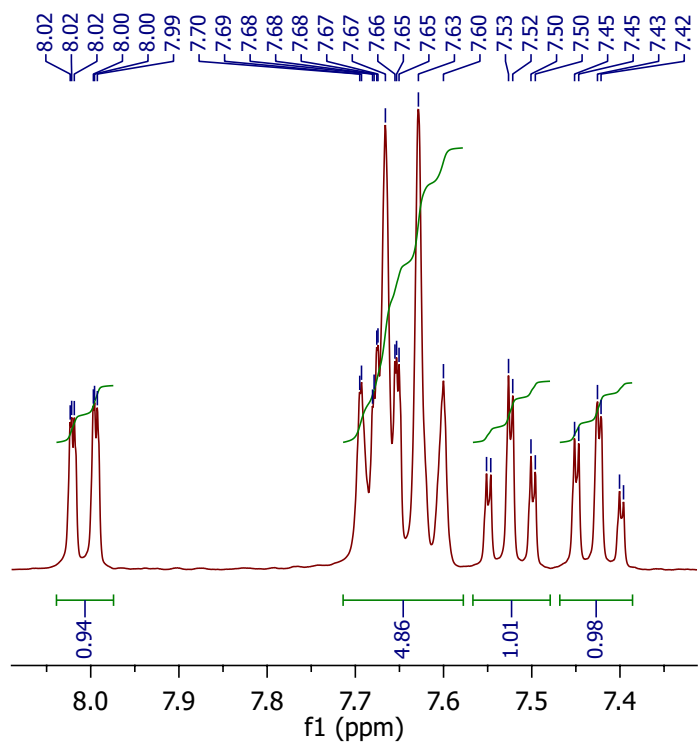


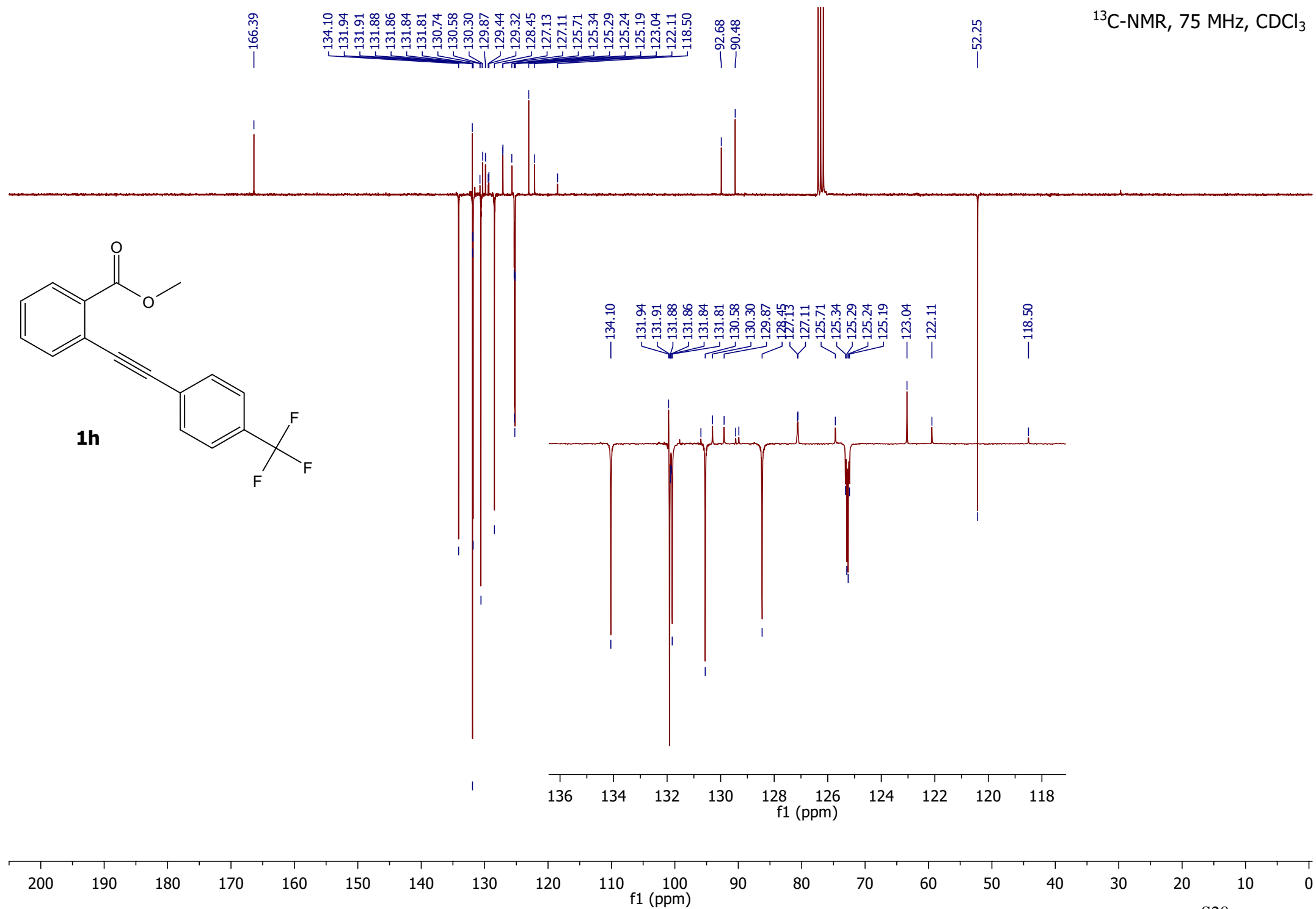
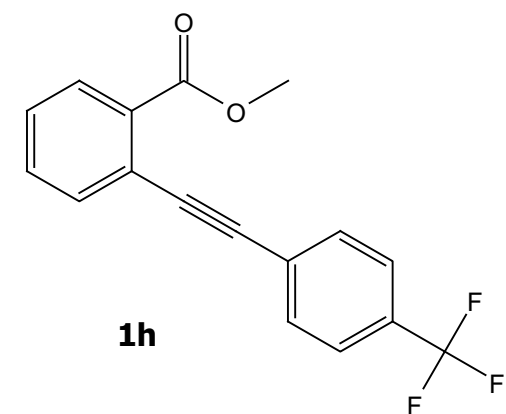


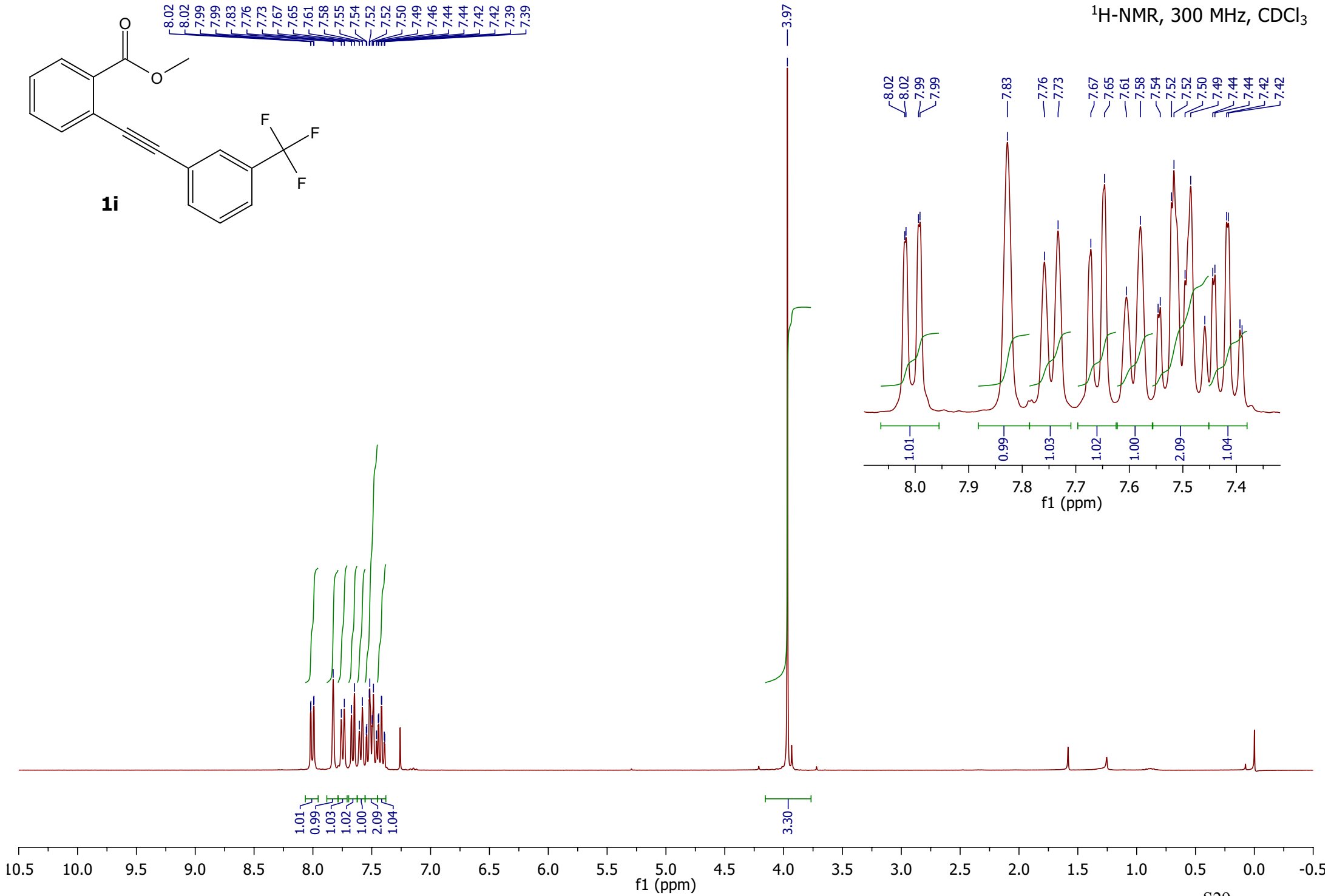
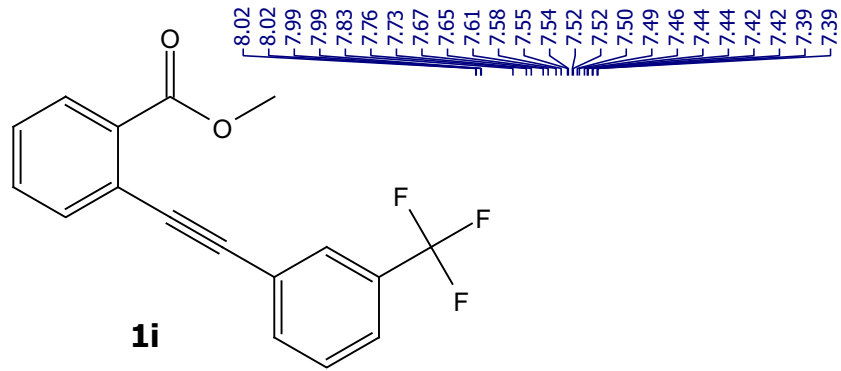


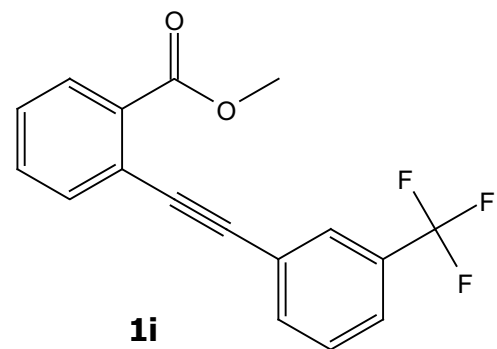
8.02
8.02
8.02
8.00
8.00
7.99
7.70
7.69
7.68
7.68
7.68
7.67
7.67
7.66
7.65
7.65
7.63
7.60
7.55
7.55
7.53
7.52
7.50
7.50
7.45
7.45
7.43
7.42
7.40
7.40

¹H-NMR, 300 MHz, CDCl₃



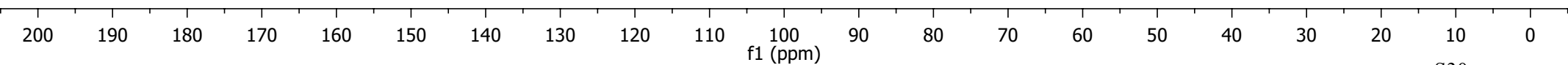


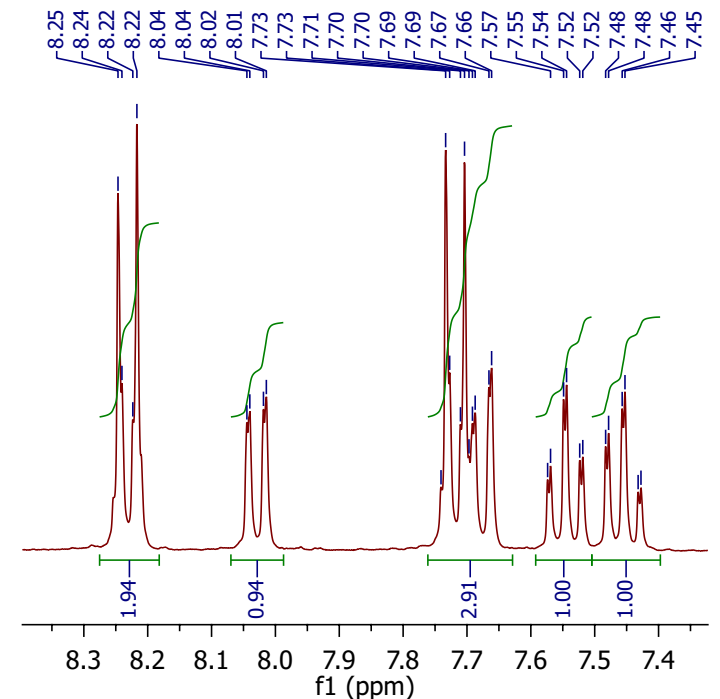
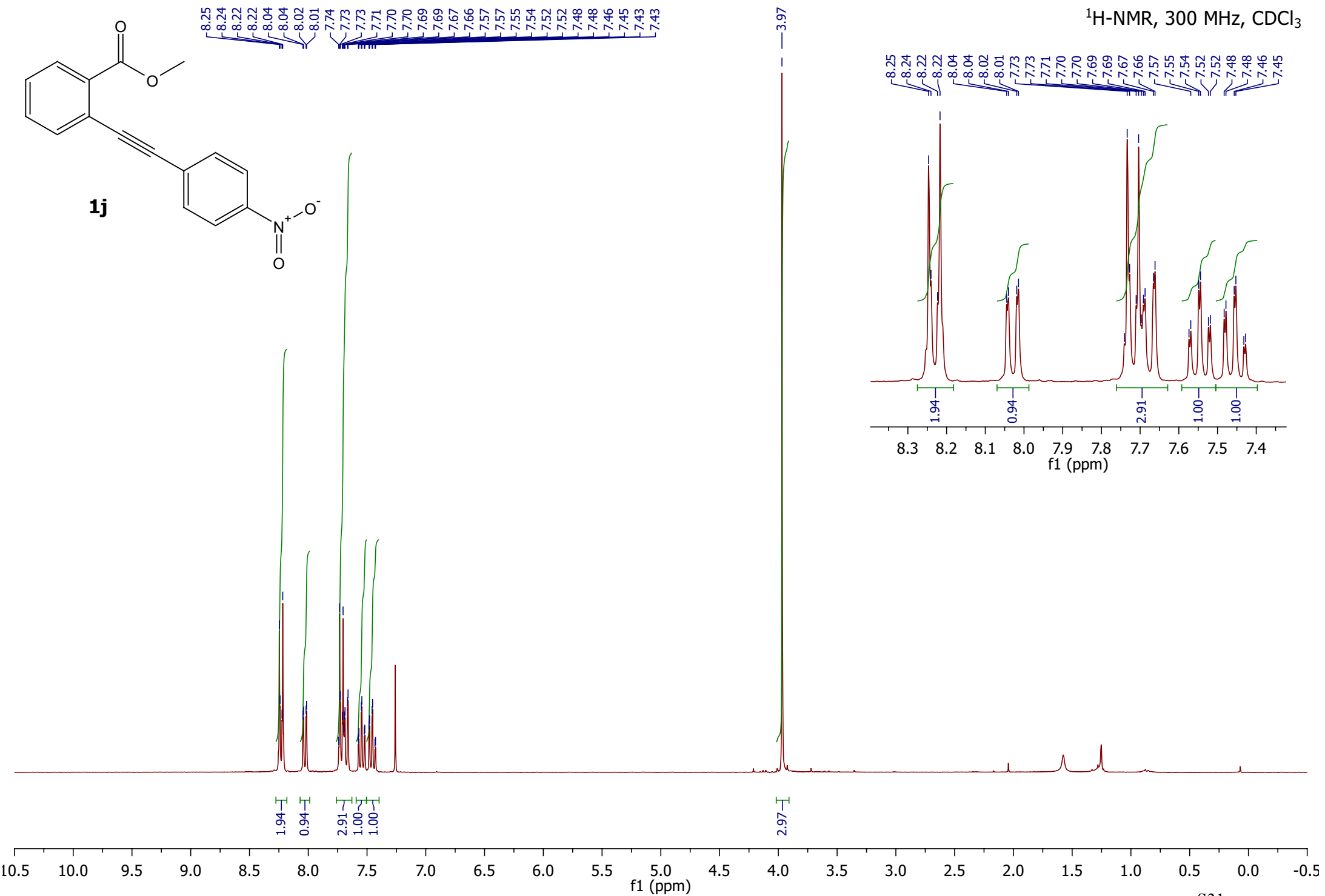
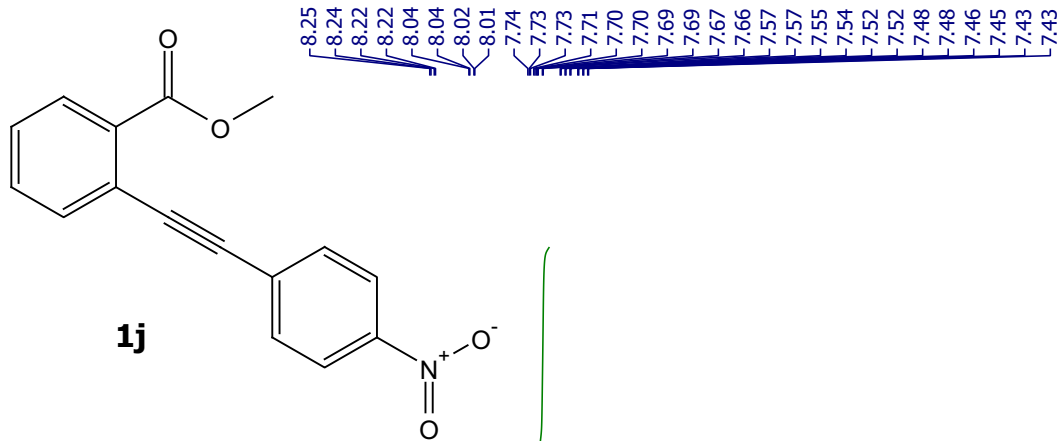


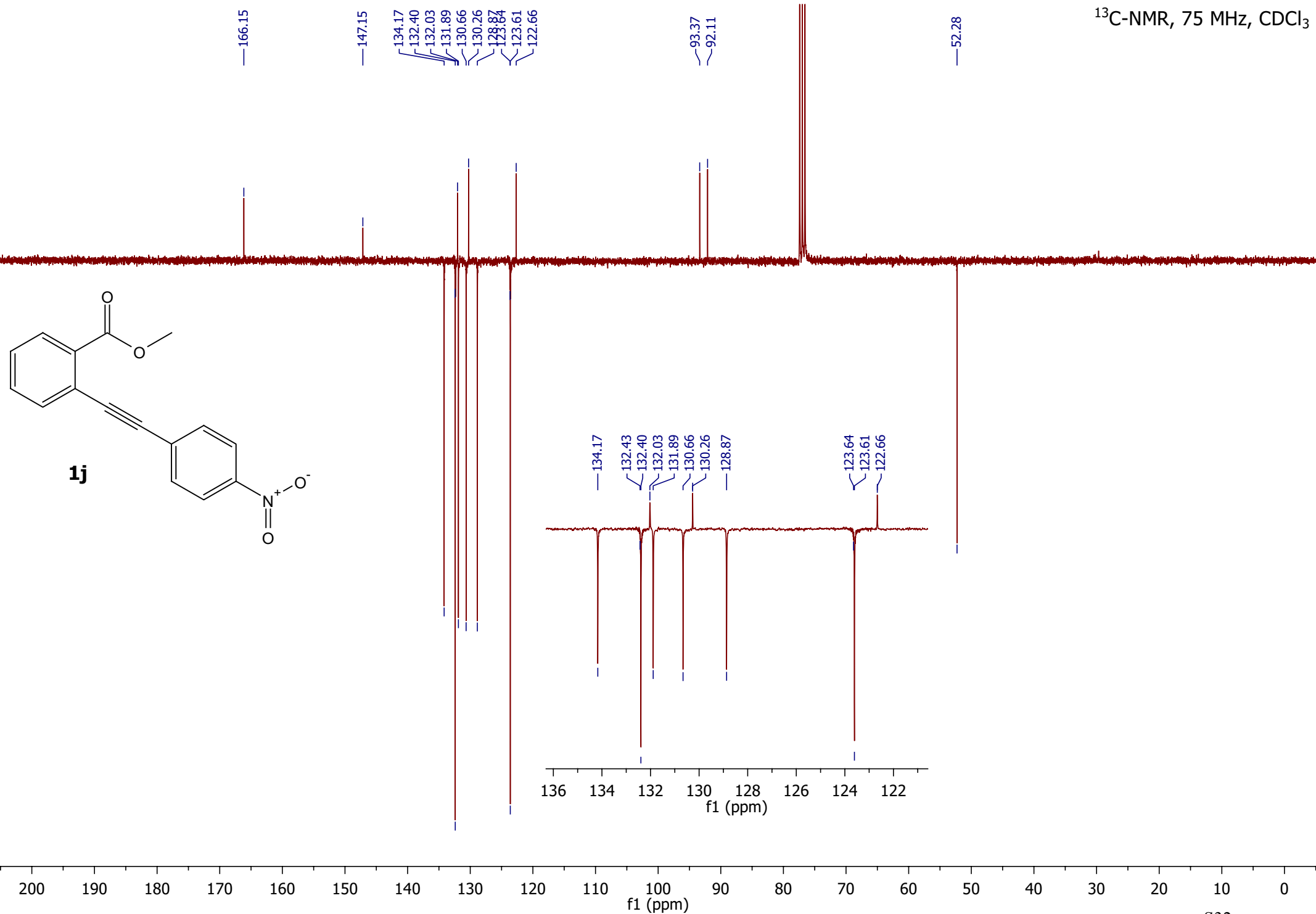


166.39
134.79
134.78
134.08
131.91
131.79
131.61
131.18
130.75
130.56
130.32
129.12
128.86
128.50
128.44
128.39
128.36
125.51
125.05
125.00
124.95
124.90
124.27
123.09
121.90
118.29
92.54
89.65
52.22

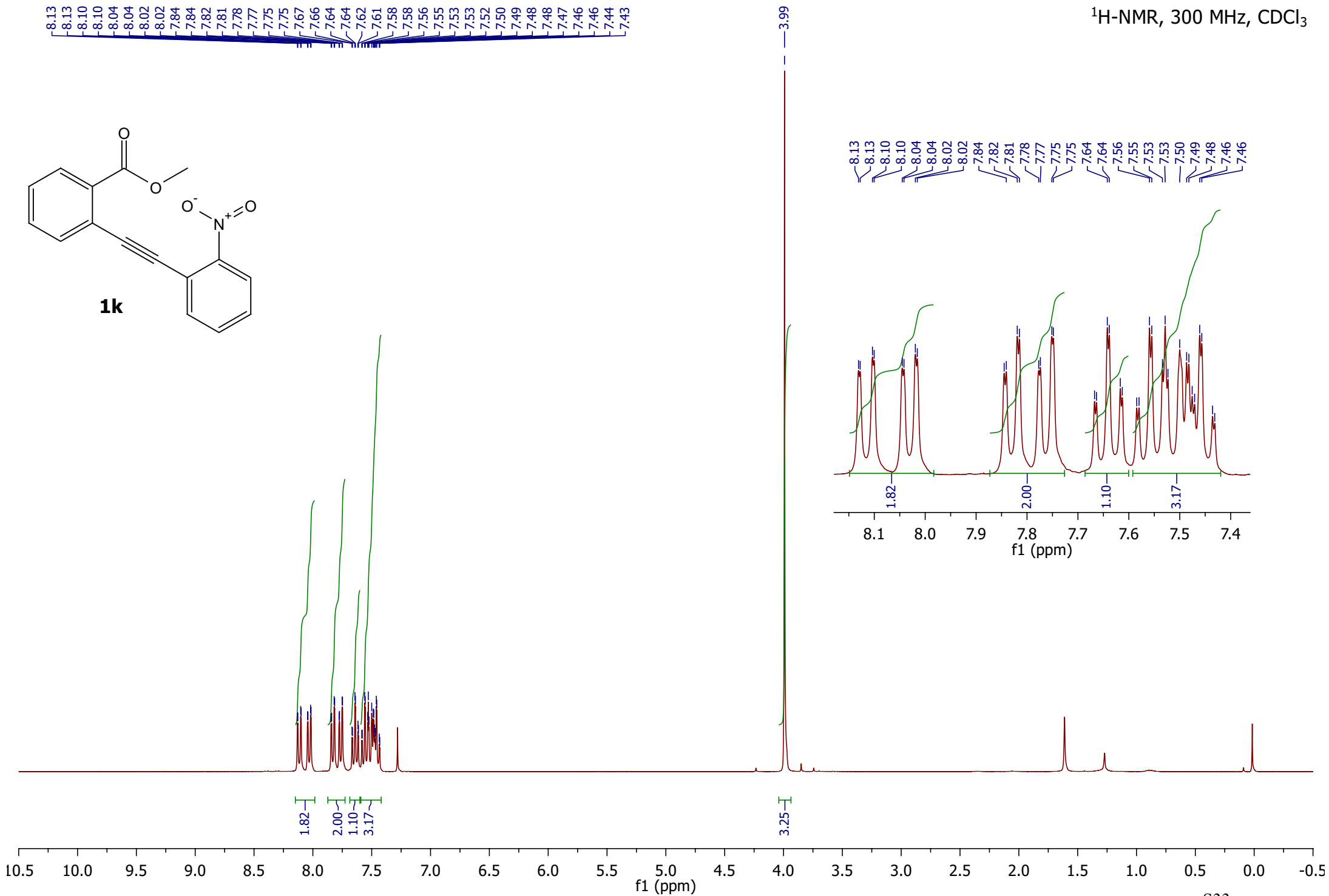
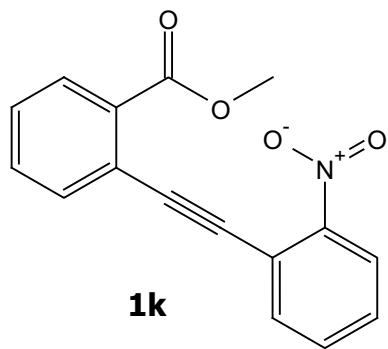
134.79
134.78
134.08
131.91
131.79
131.61
131.18
130.75
130.56
130.32
128.86
128.50
128.44
128.39
128.36
125.05
125.00
124.95
124.90
124.27
123.09
121.90

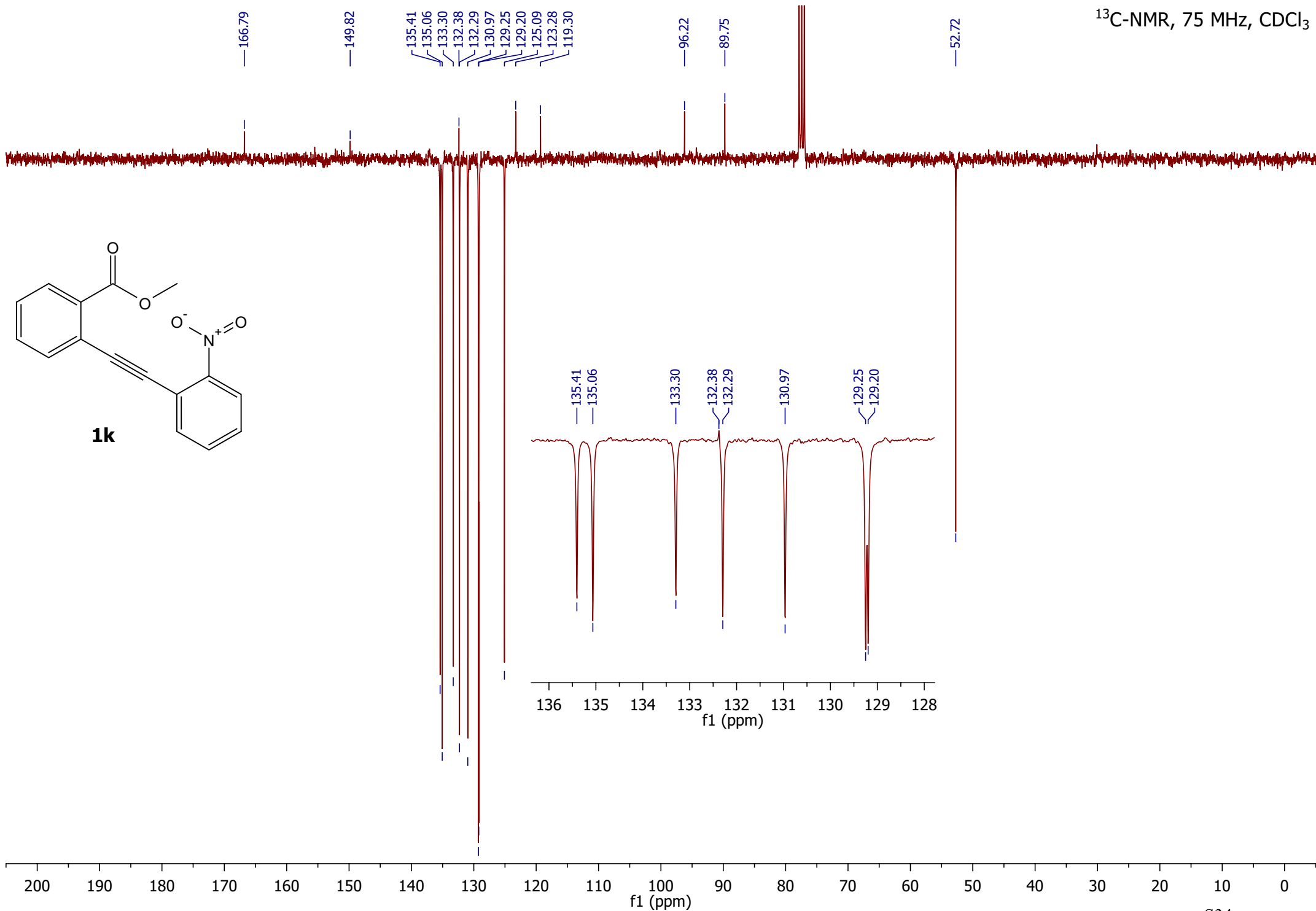


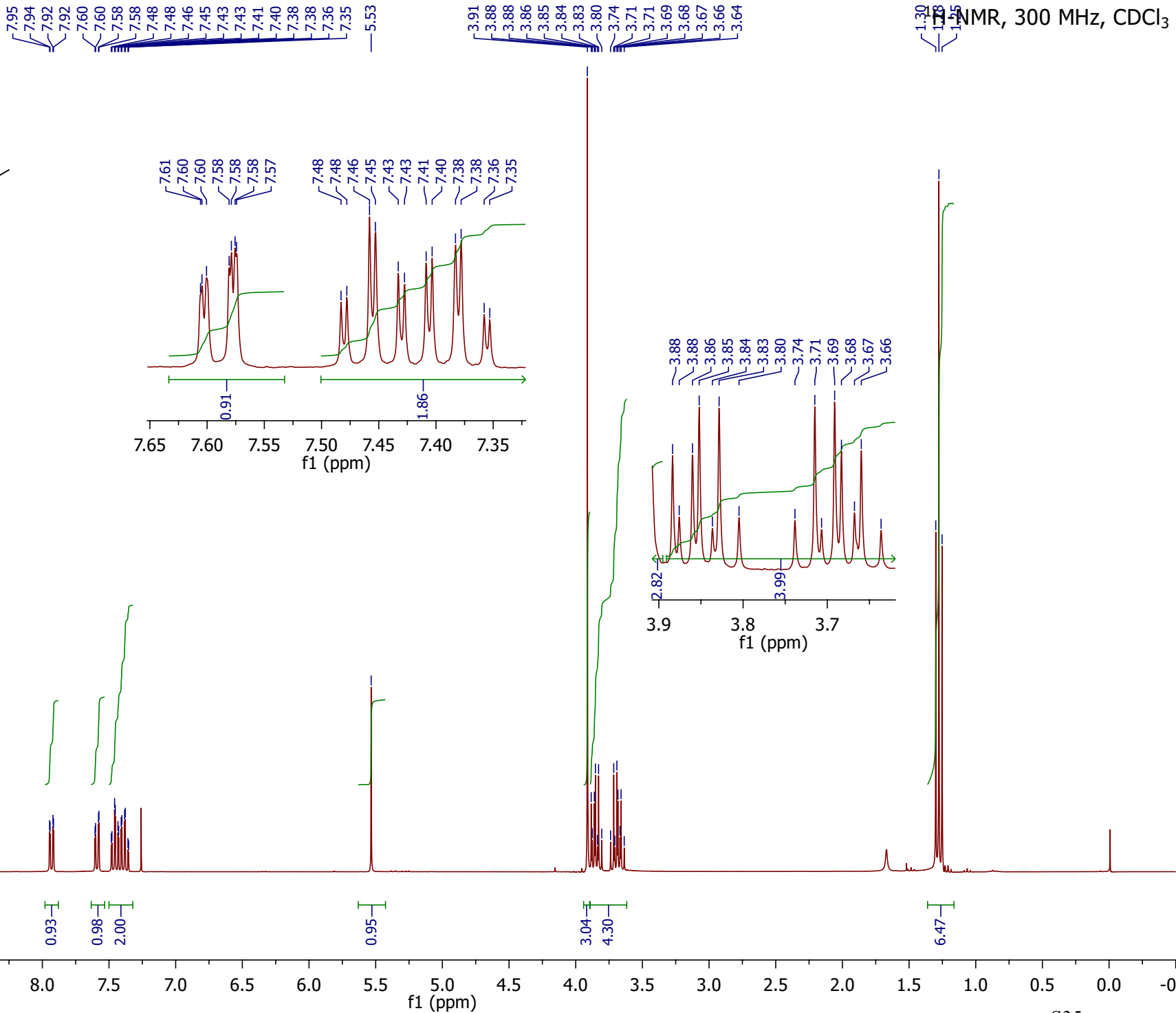
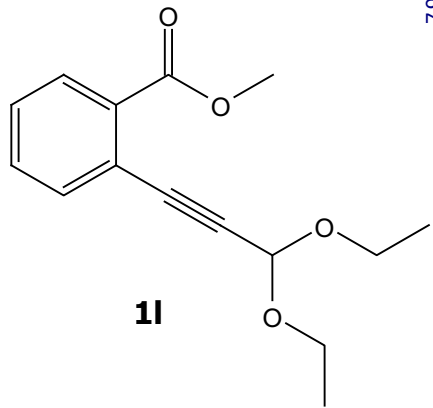




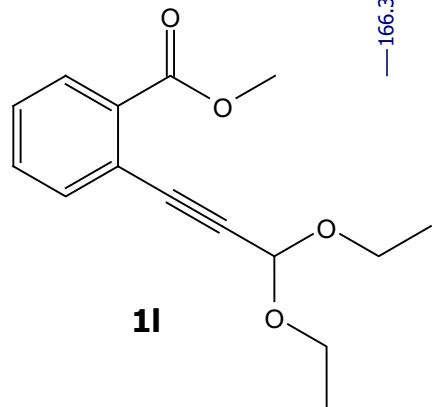
¹H-NMR, 300 MHz, CDCl₃







¹³C-NMR, 75 MHz, CDCl₃



166.39

134.43

132.34

131.55

130.32

128.42

122.34

91.89

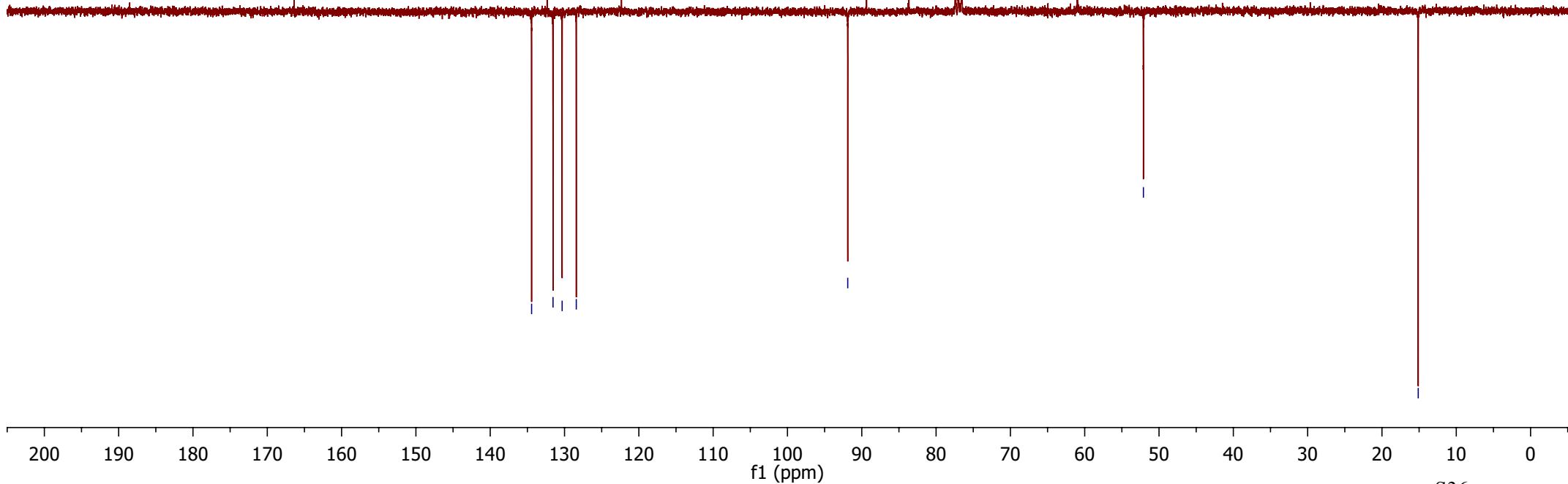
89.37

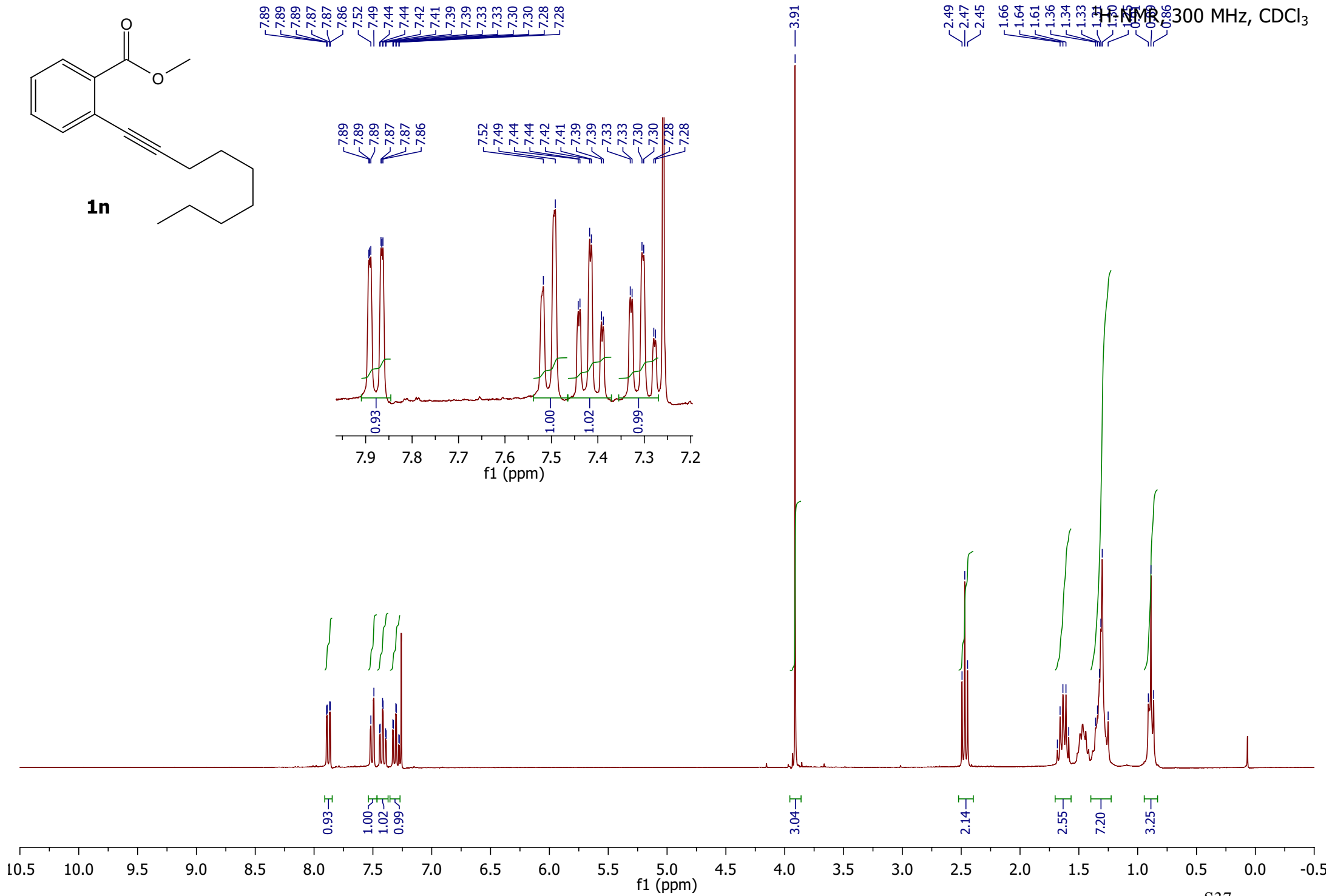
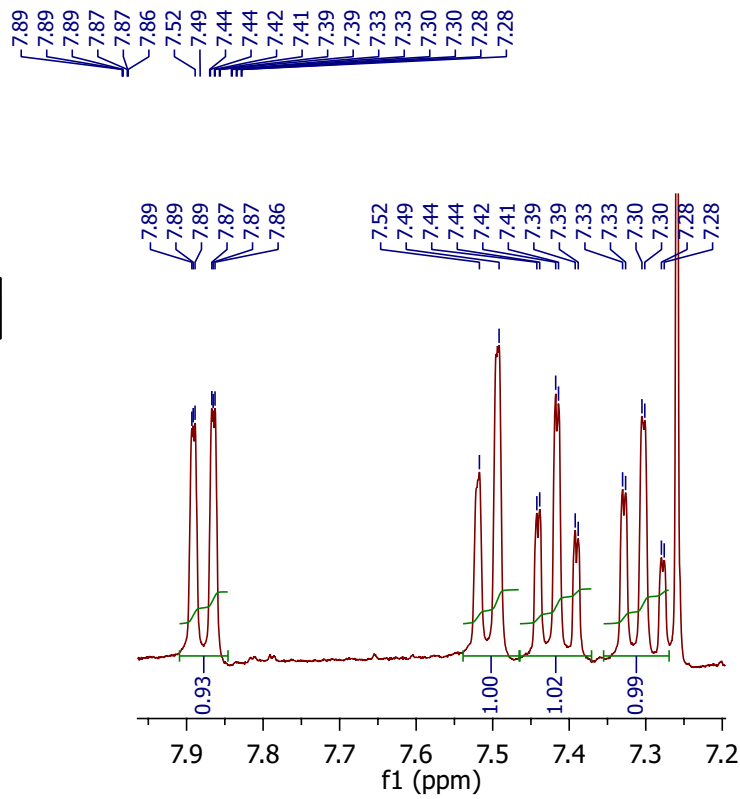
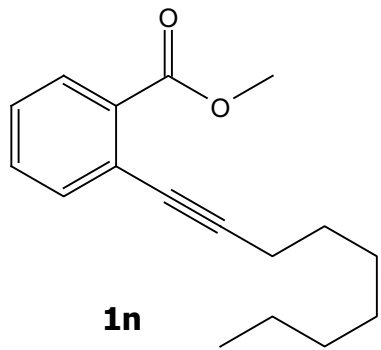
83.65

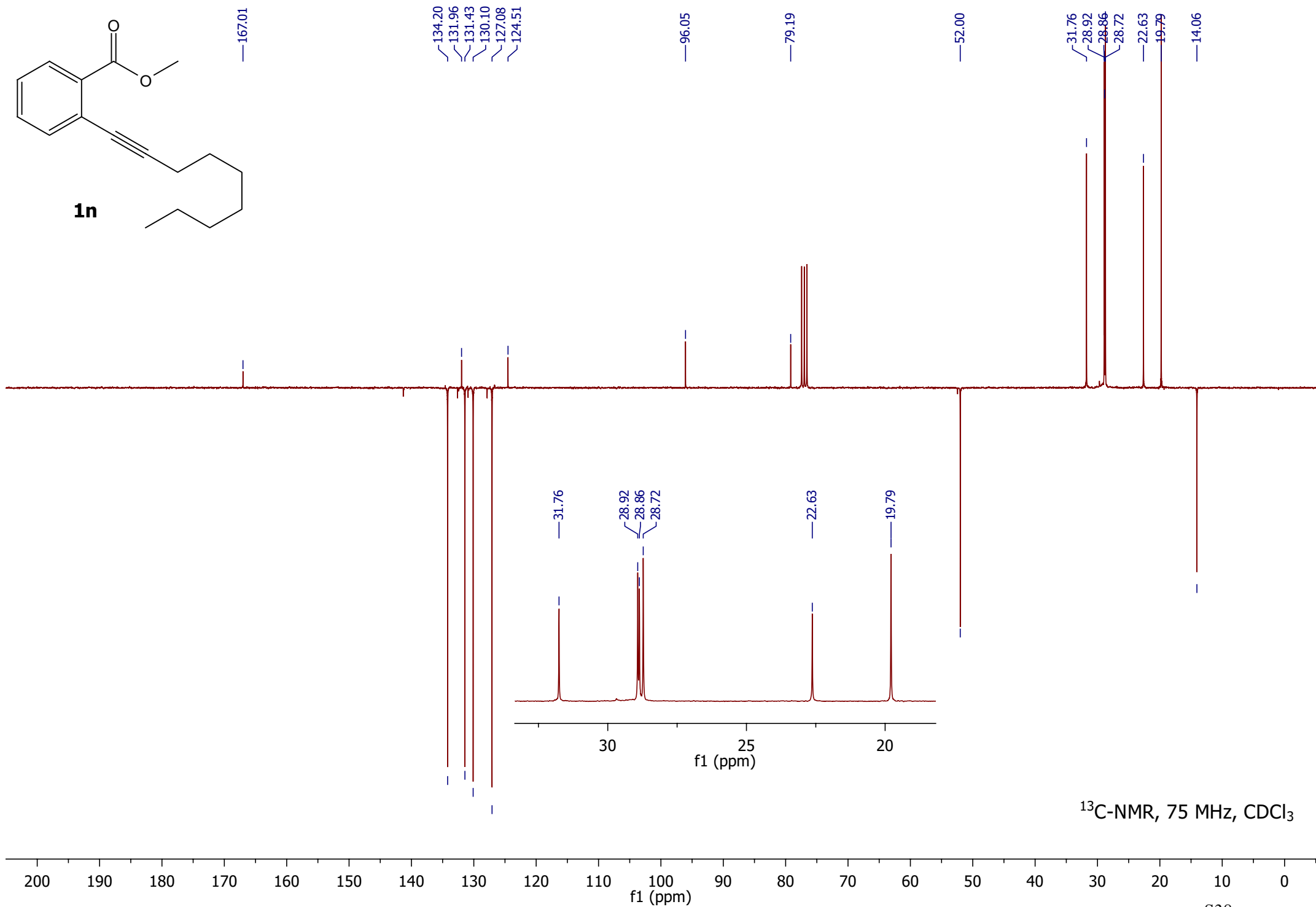
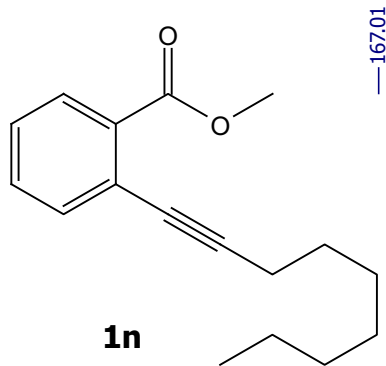
60.99

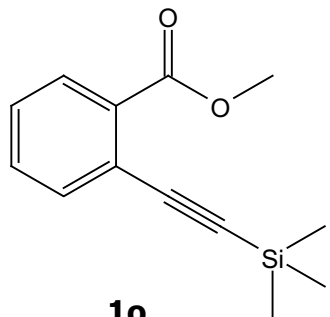
52.10

15.12



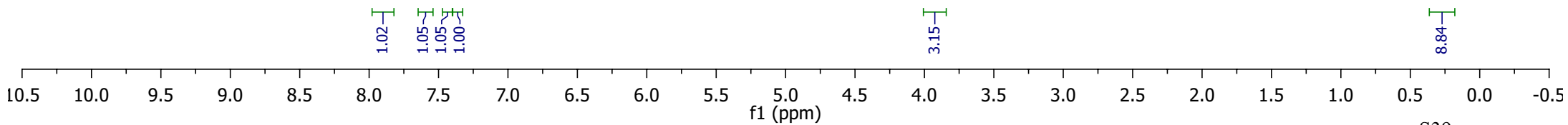
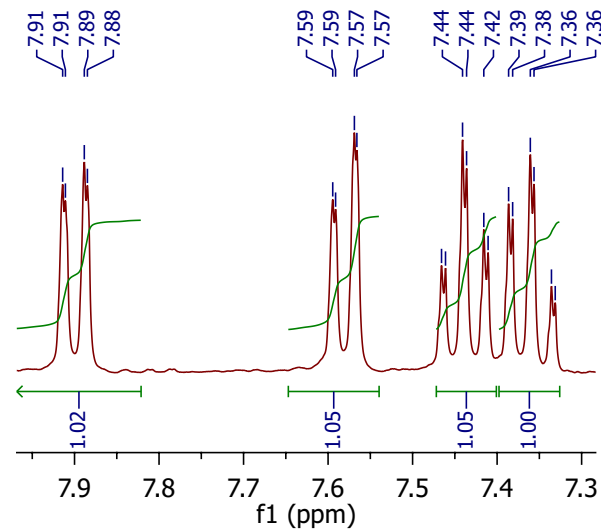




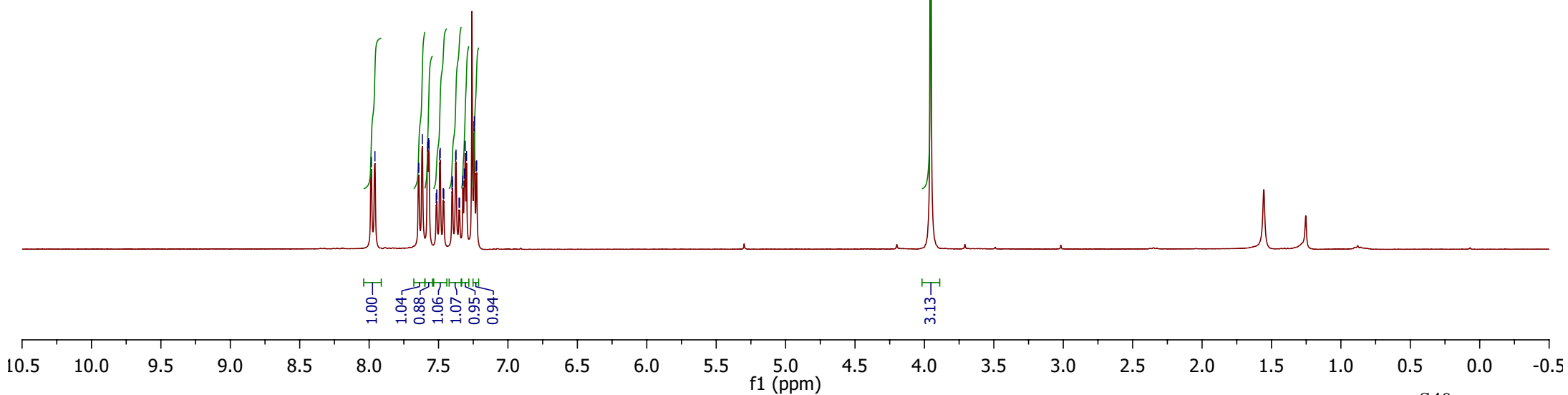
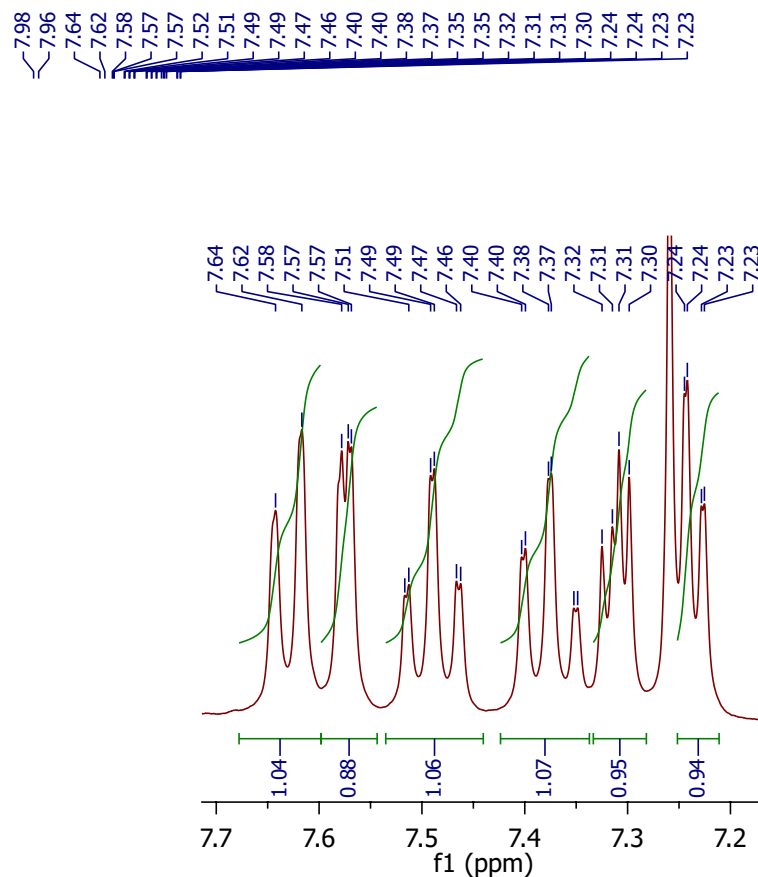
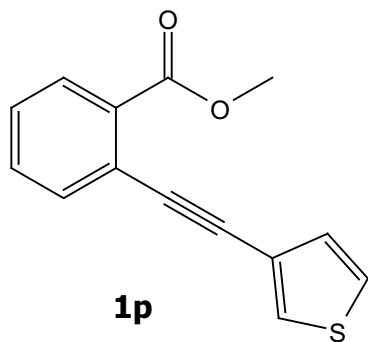


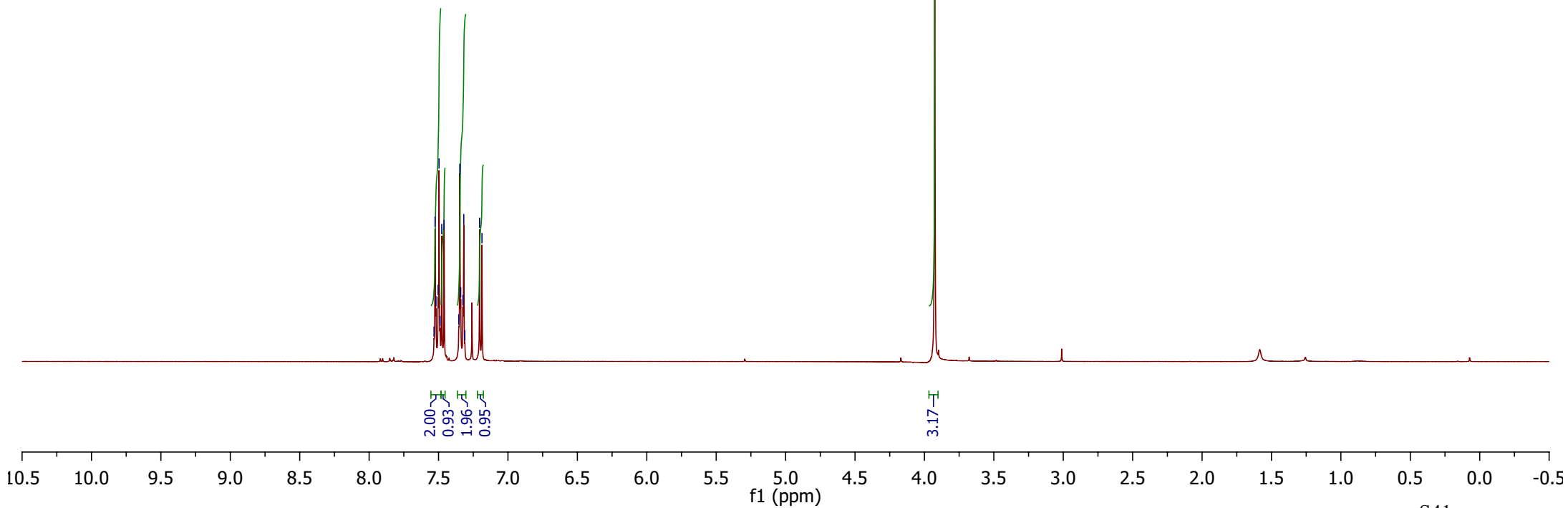
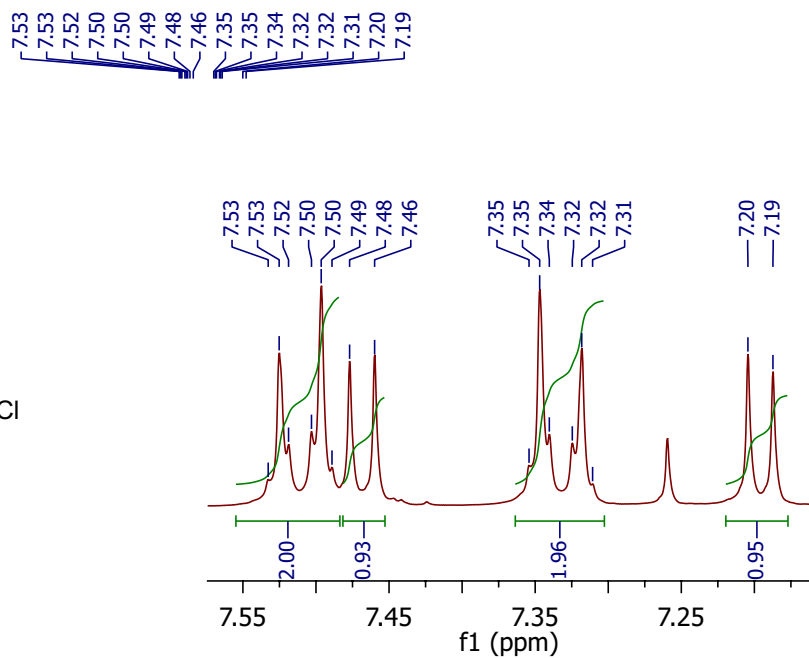
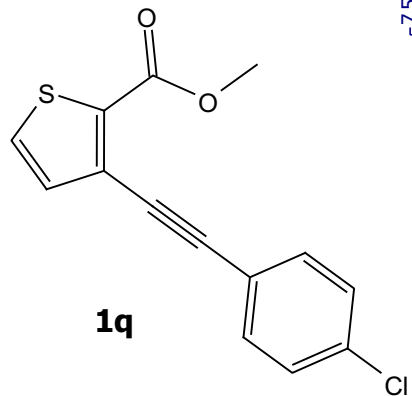
7.91
7.91
7.89
7.88
7.59
7.59
7.57
7.57
7.47
7.46
7.44
7.44
7.42
7.41
7.39
7.38
7.36
7.36
7.34
7.33

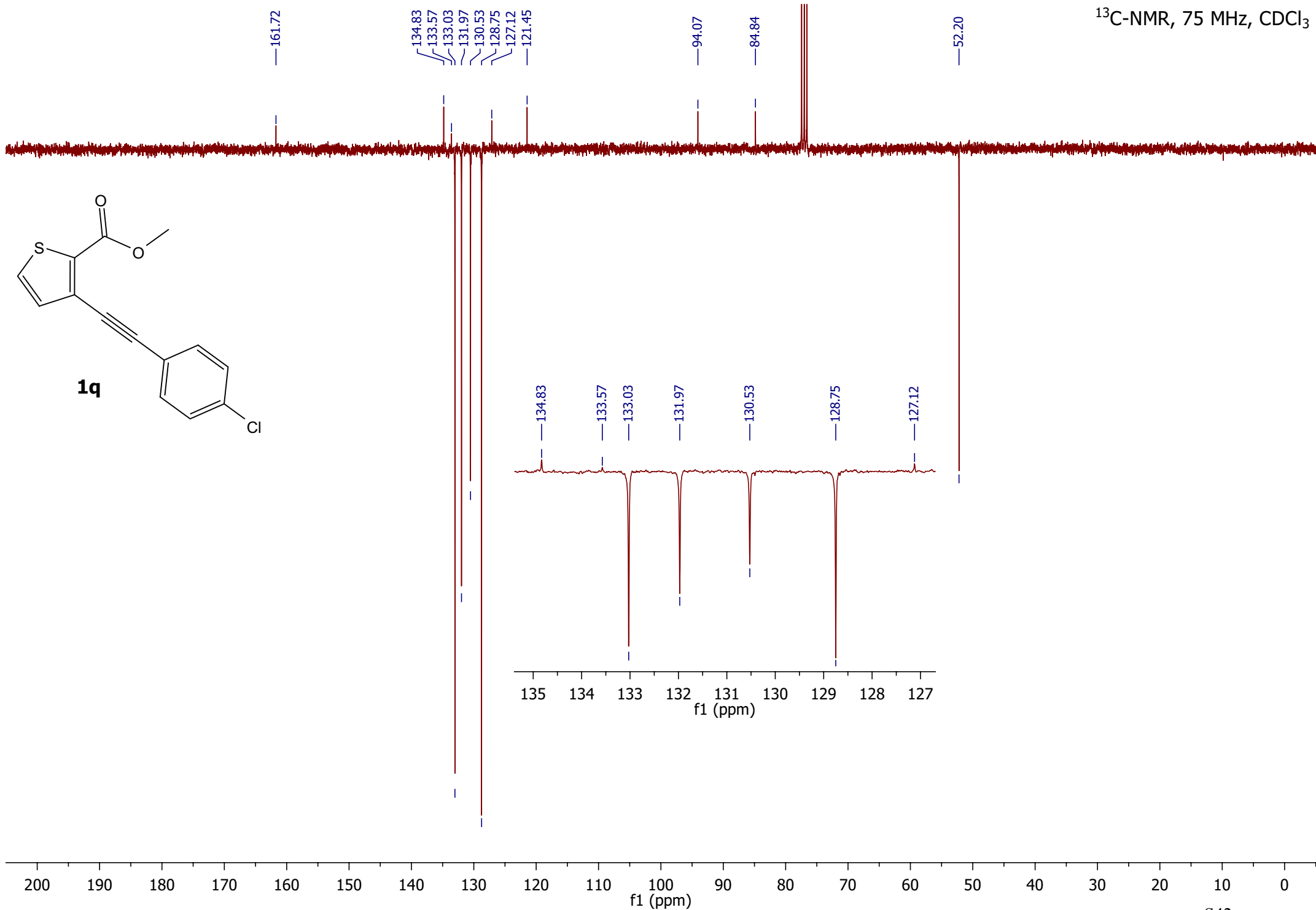
¹H-NMR, 300 MHz, CDCl₃



S39

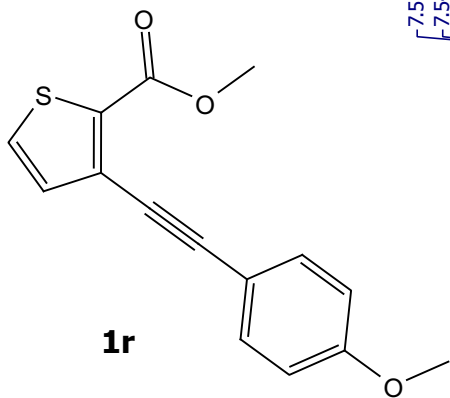






¹H-NMR, 300 MHz, CDCl₃

7.55
7.54
7.54
7.52
7.51
7.50
7.46
7.45
7.20
7.18
6.91
6.90
6.89
6.88
6.87
6.86



3.93
3.83

7.55
7.54
7.54
7.52
7.51
7.50
7.46
7.45

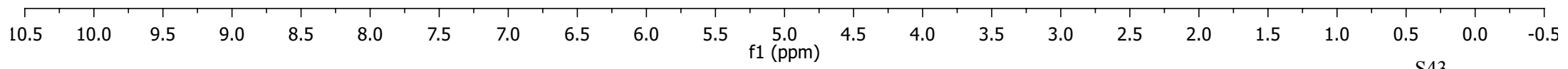
7.20
7.18

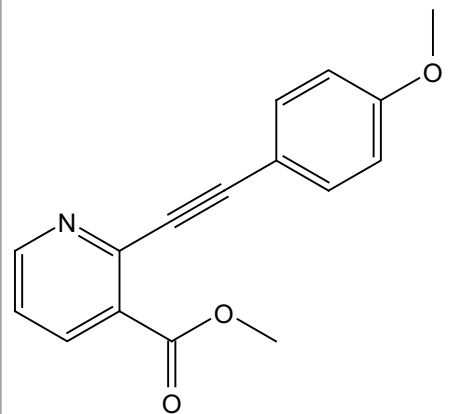
6.91
6.90
6.89
6.88
6.87
6.86

2.05
1.00
0.97
2.10

2.05
1.00
0.97
2.10

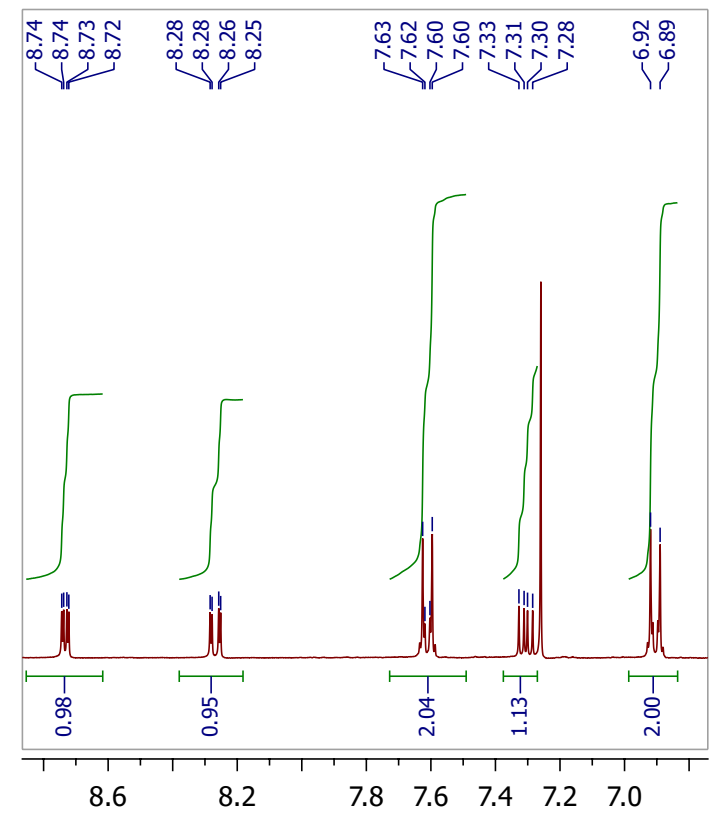
3.11
3.28





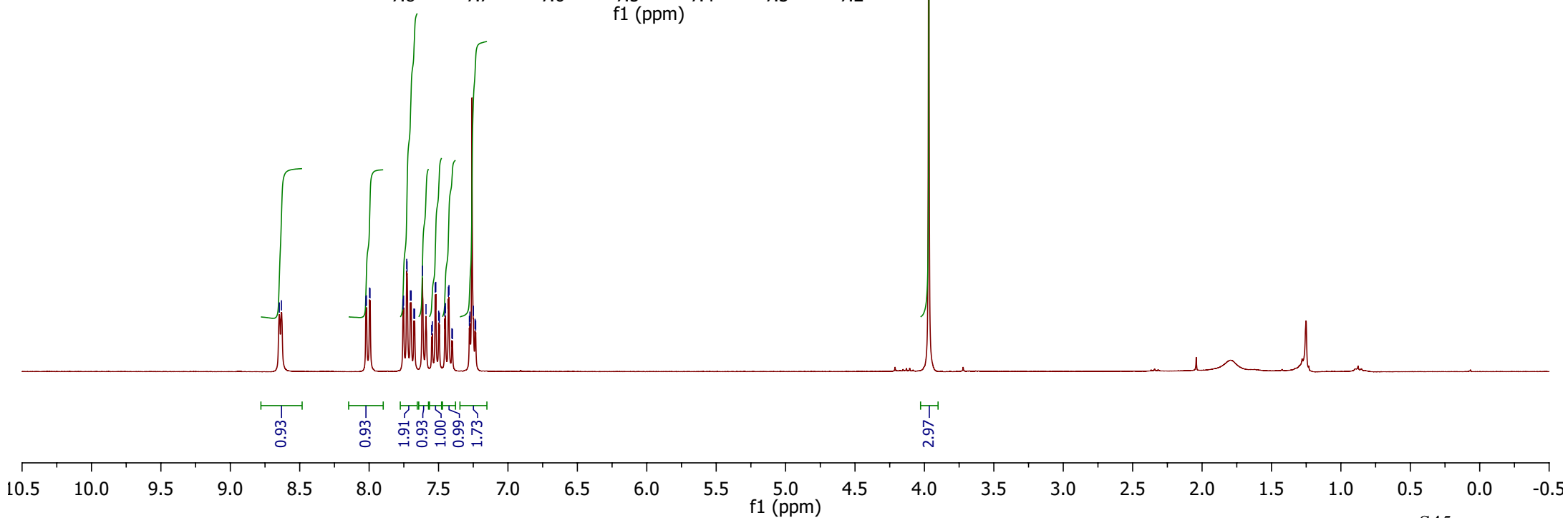
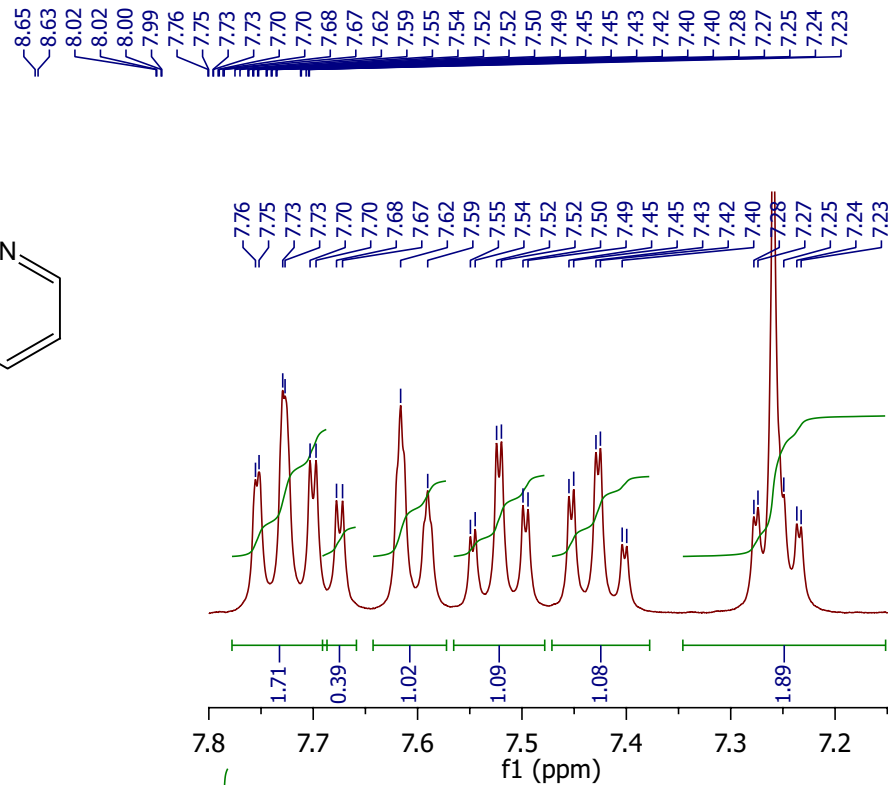
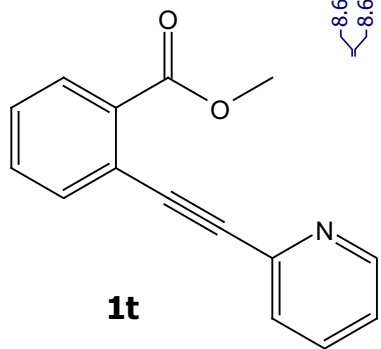
8.74
8.74
8.73
8.72
8.28
8.28
8.26
8.25
7.63
7.60
7.33
7.31
7.30
7.28
6.92
6.89

4.00
3.84

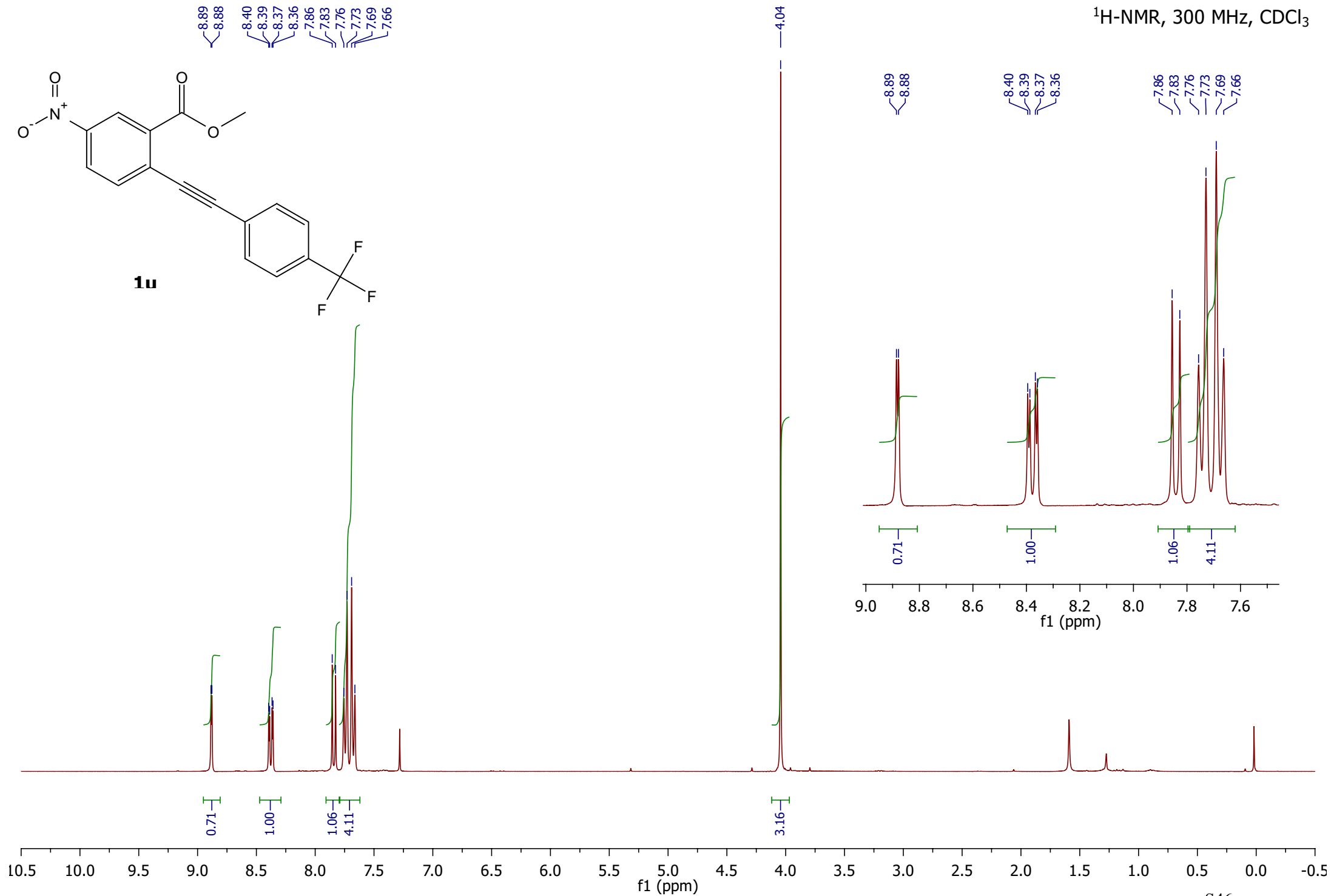
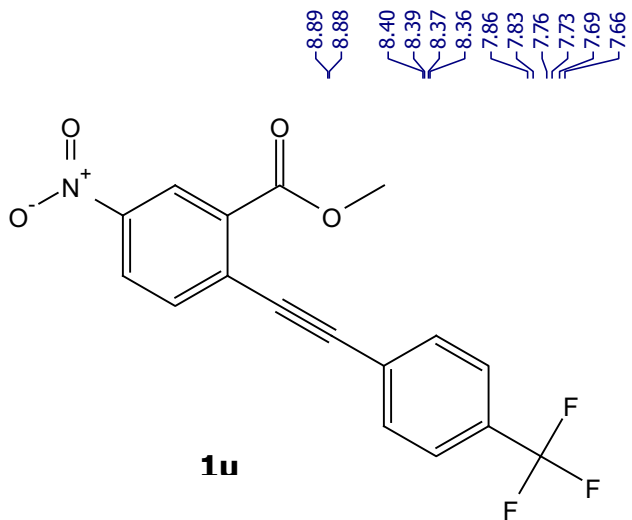


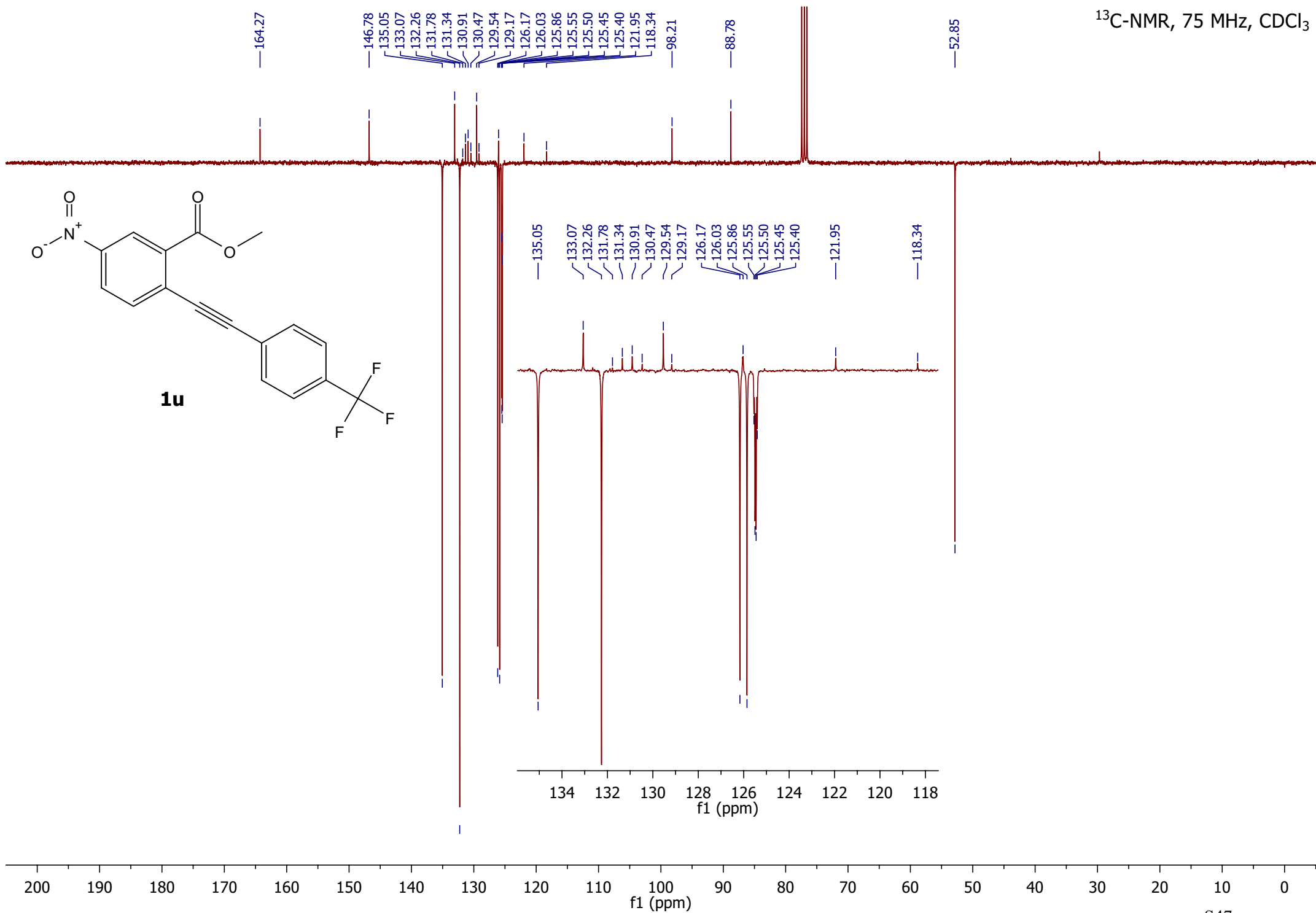
0.98
0.95
2.04
1.13
2.00
2.92
3.30

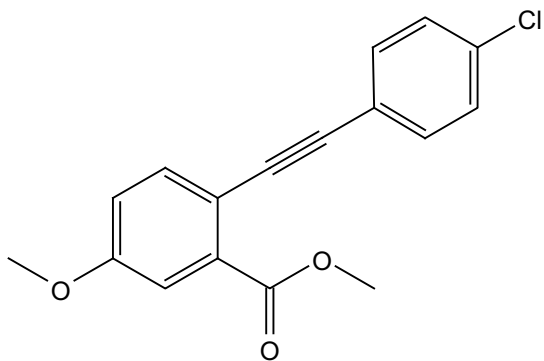
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5



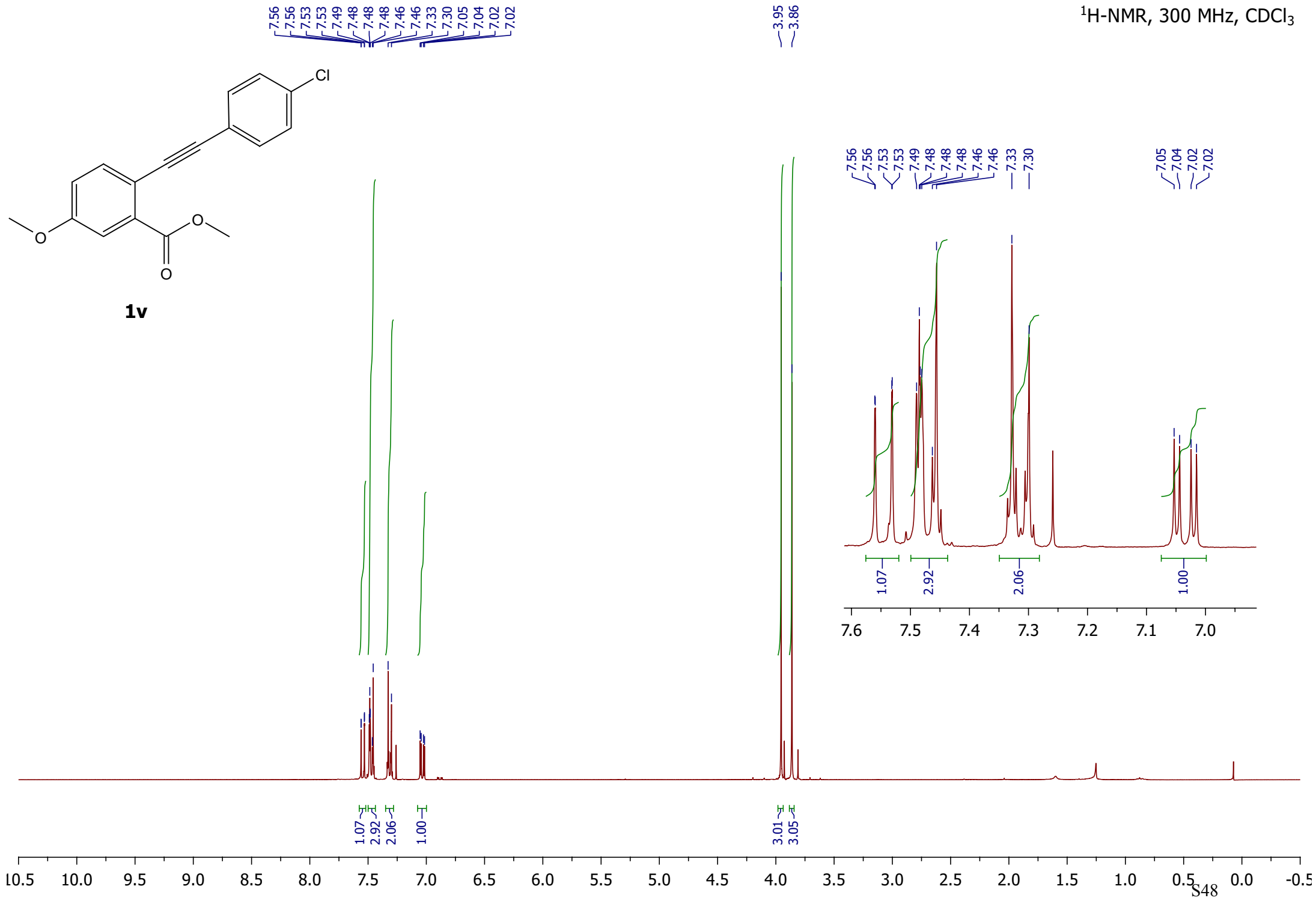
¹H-NMR, 300 MHz, CDCl₃



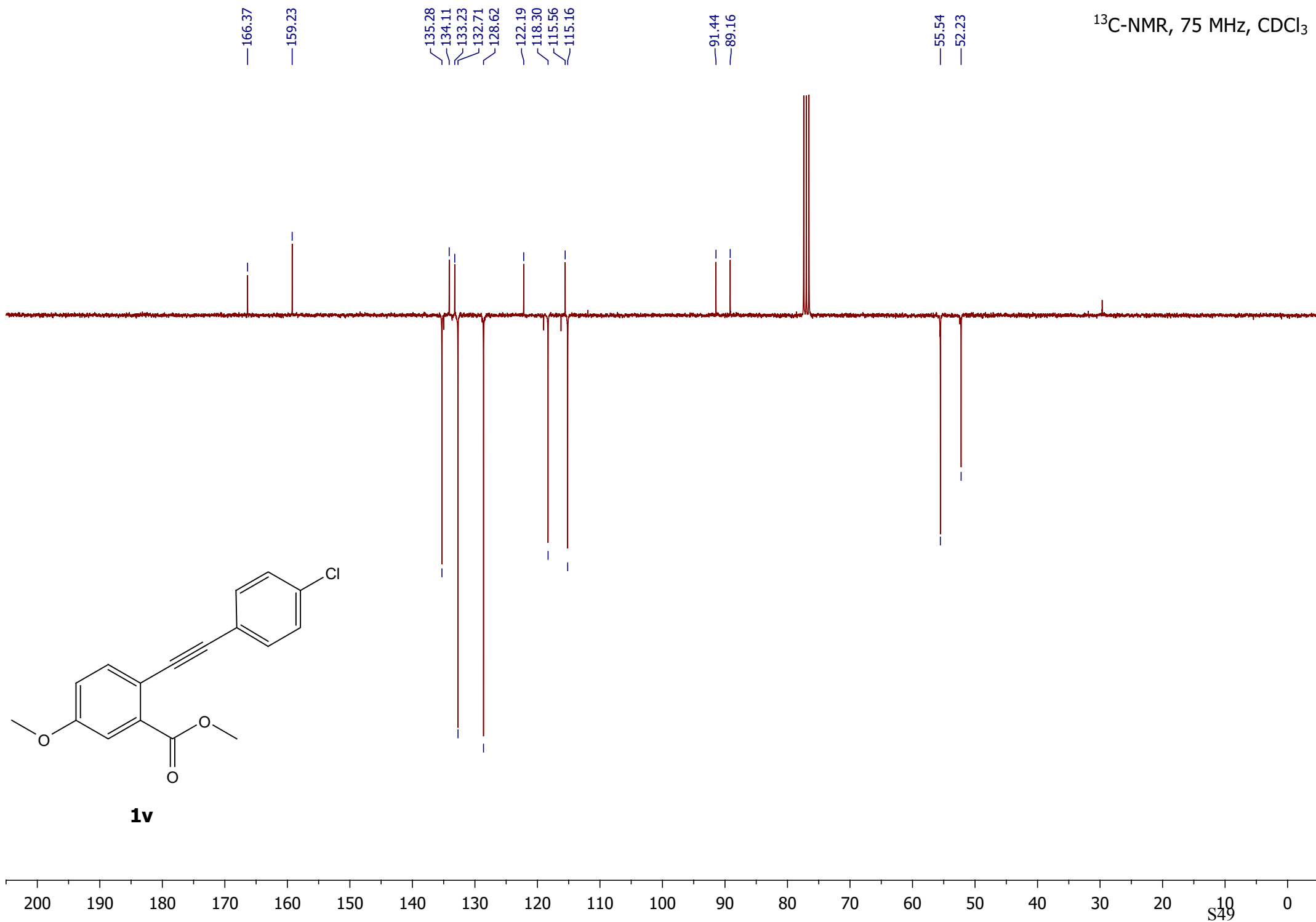


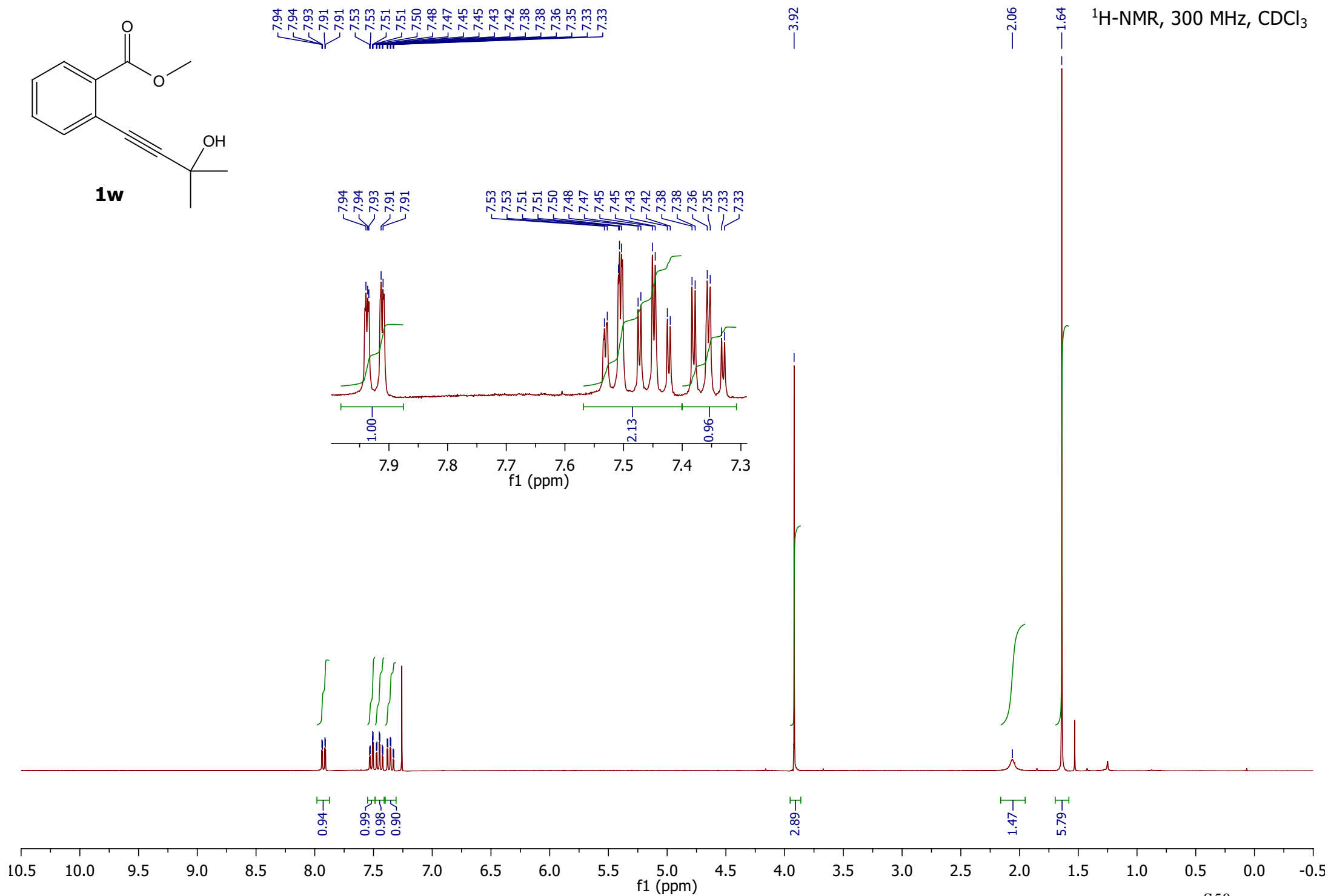
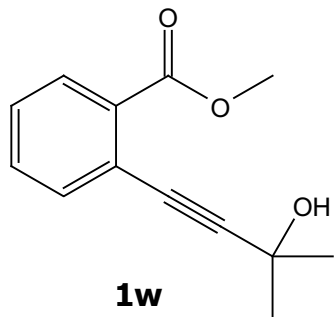


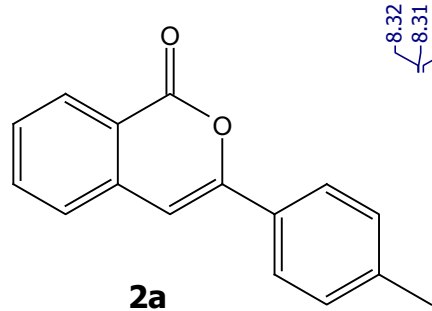
1v



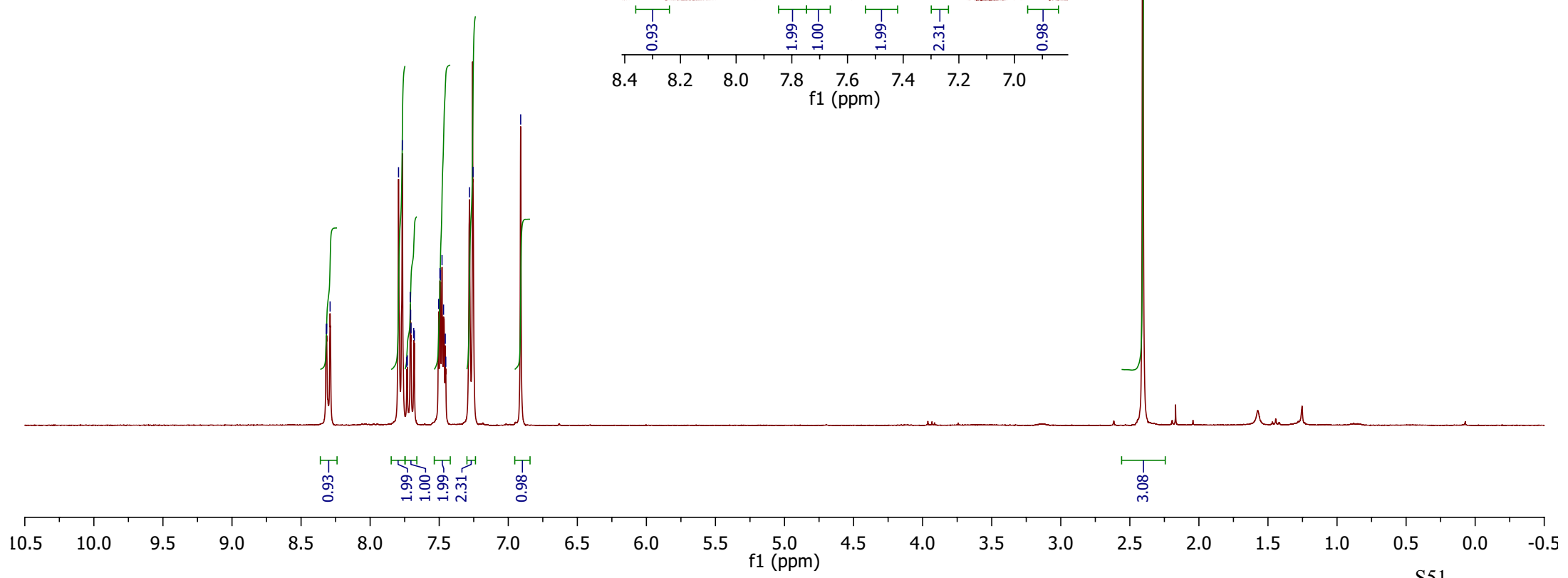
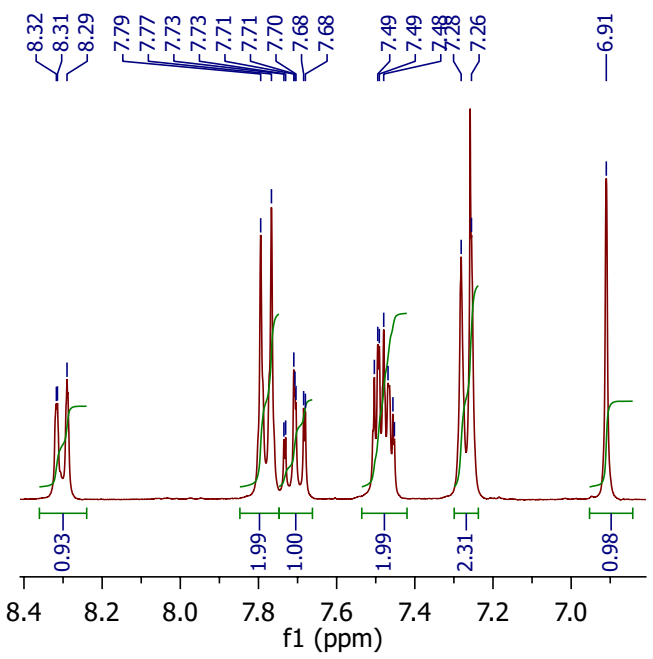
$^{13}\text{C-NMR}$, 75 MHz, CDCl_3



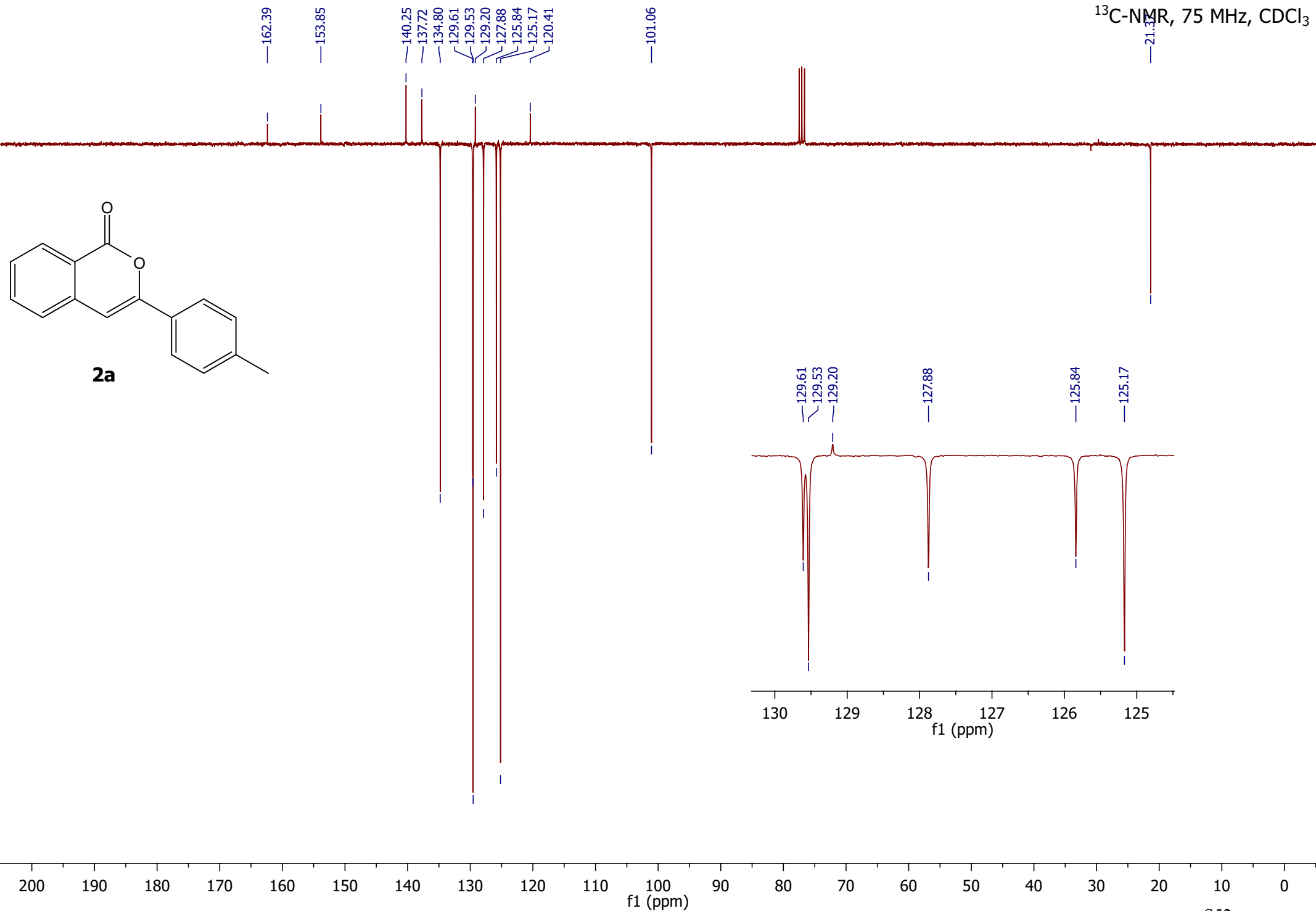


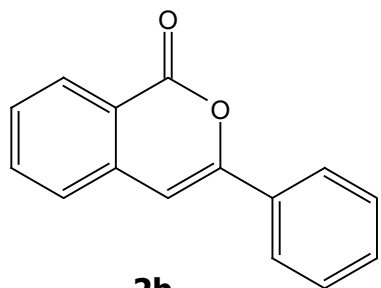


8.32
8.31
8.29
7.79
7.77
7.71
7.49
7.49
7.48
7.28
6.99



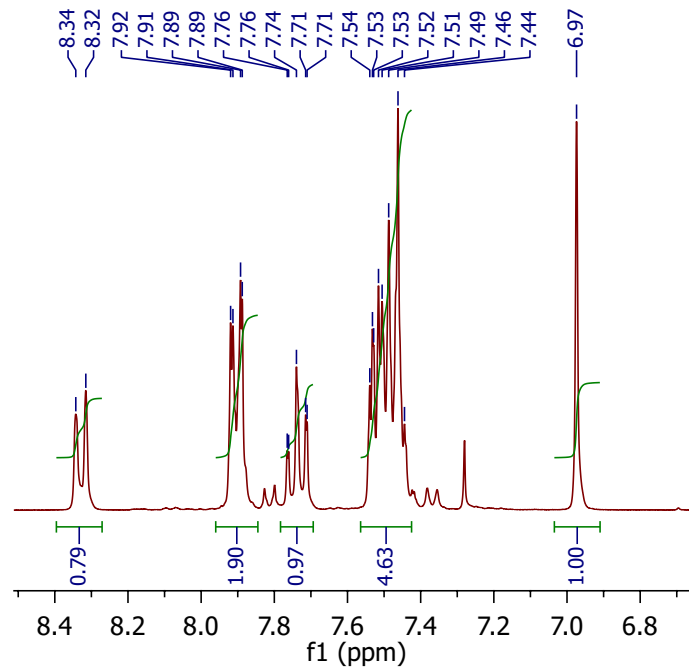
¹³C-NMR, 75 MHz, CDCl₃



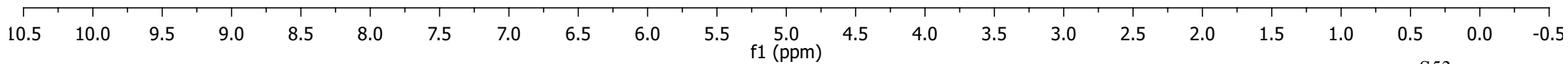


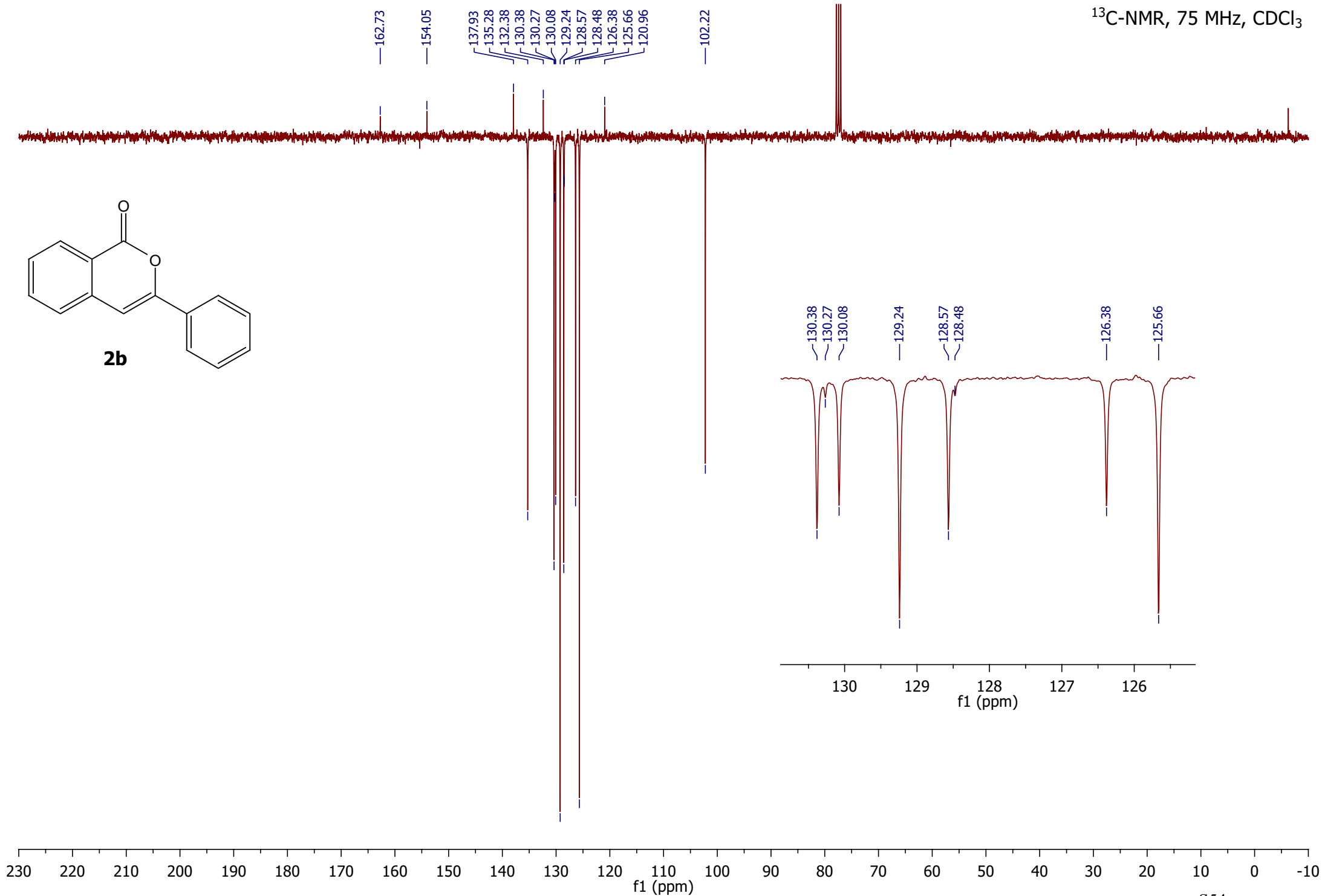
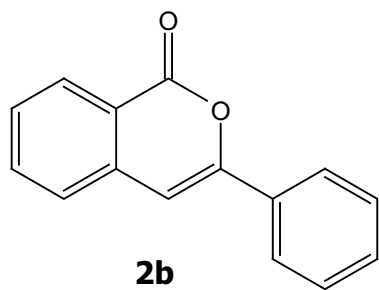
8.34
8.32
7.92
7.91
7.89
7.89
7.52
7.51
7.49
7.46

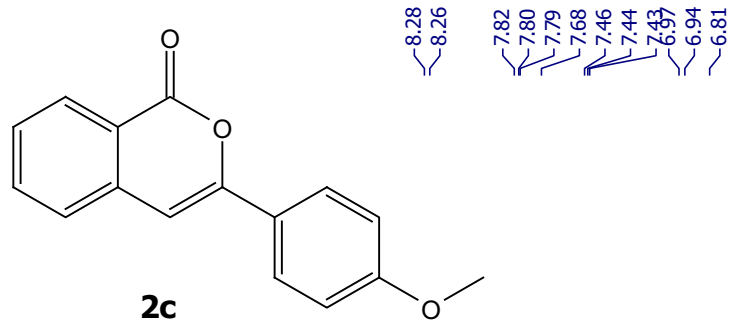
8.34
8.32
7.92
7.89
7.89
7.76
7.76
7.74
7.71
7.71
7.54
7.53
7.53
7.52
7.51
7.49
7.46
7.44
6.97



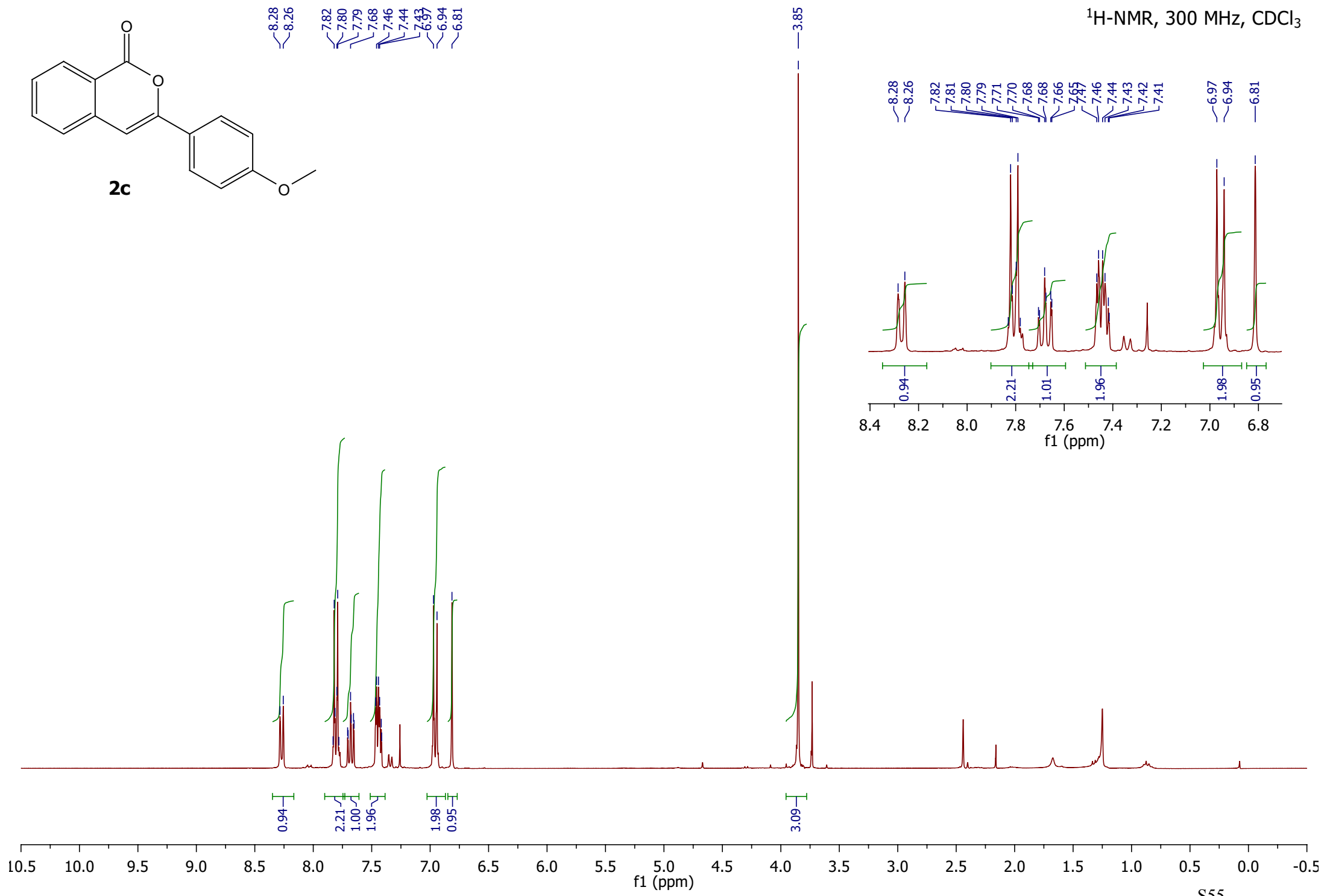
0.79
1.90
0.97
4.63
1.00

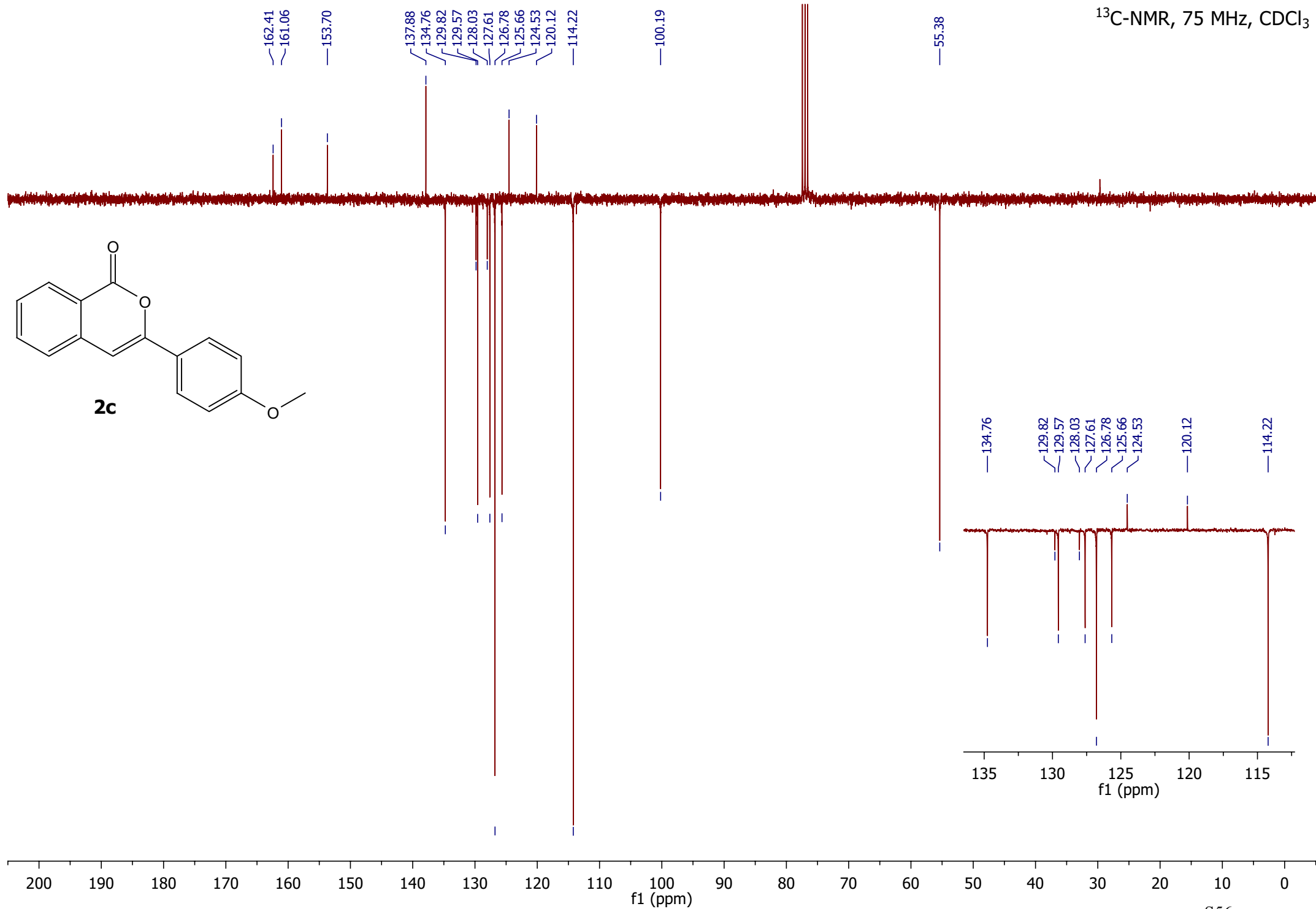
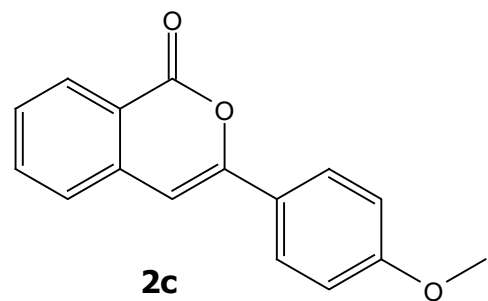


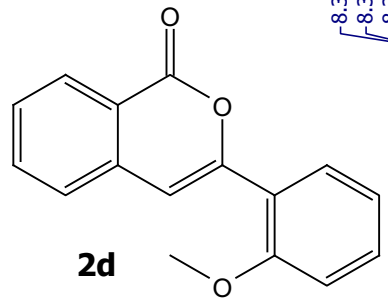




¹H-NMR, 300 MHz, CDCl₃

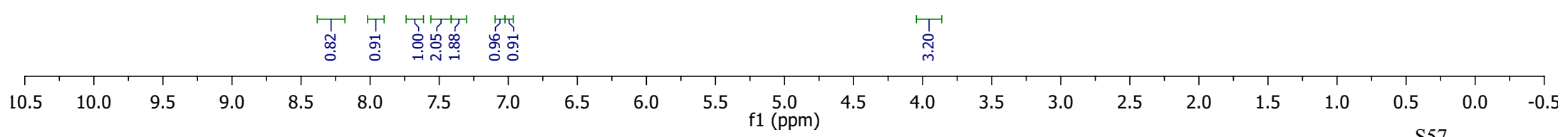
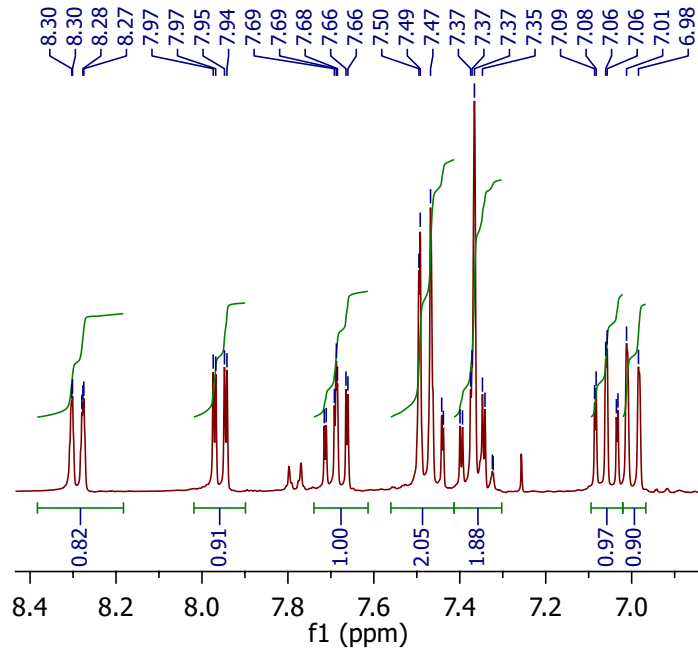


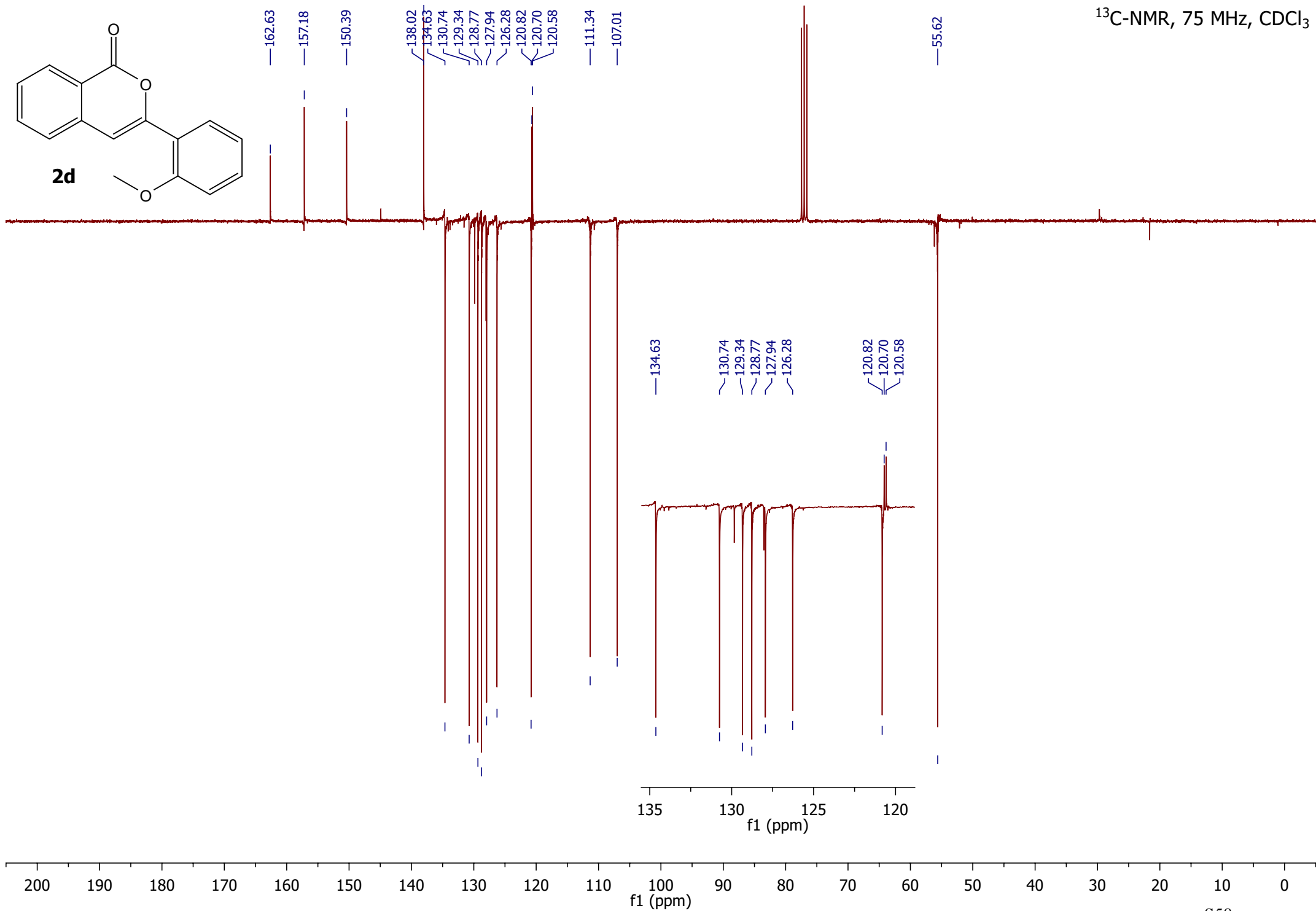
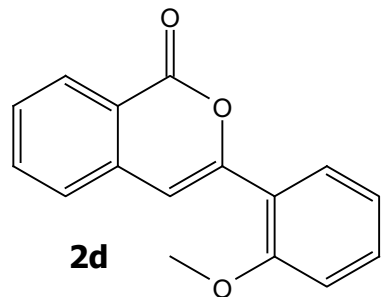


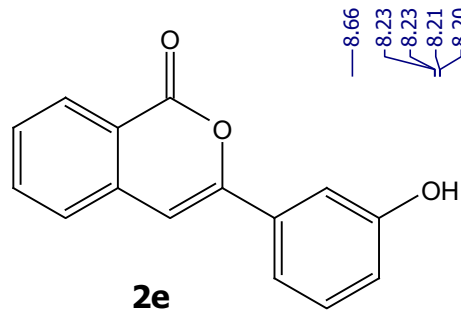


8.30
8.30
8.28
8.28
8.27
7.97
7.97
7.95
7.94
7.72
7.71
7.69
7.69
7.68
7.66
7.66
7.50
7.49
7.47
7.44
7.44
7.40
7.39
7.37
7.37
7.37
7.35
7.34
7.09
7.08
7.06
7.06
7.04
7.03
7.01
6.95

¹H-NMR, 300 MHz, CDCl₃

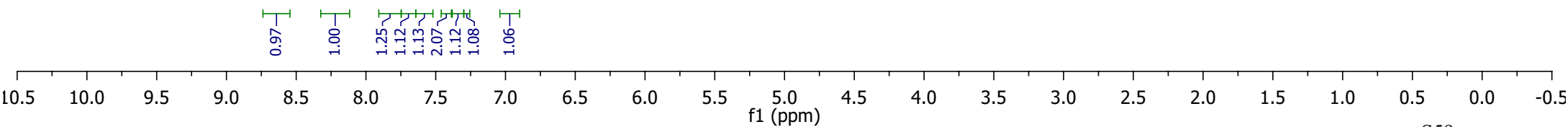
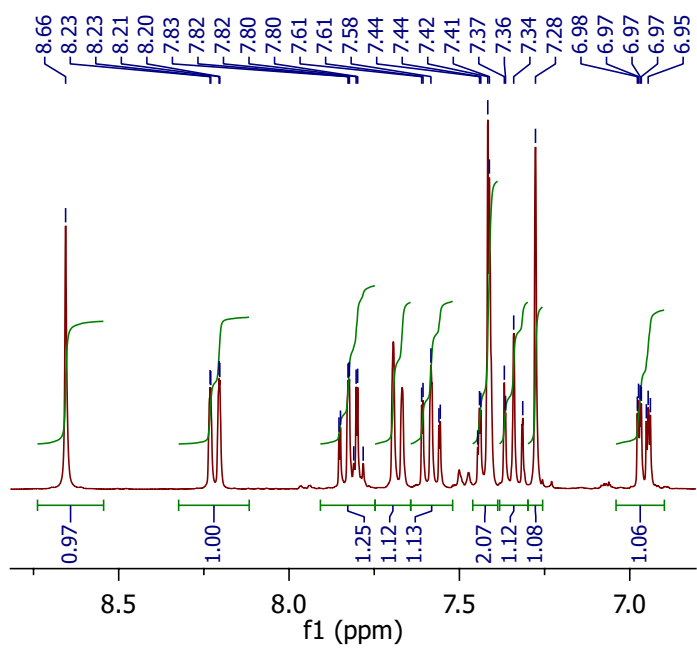


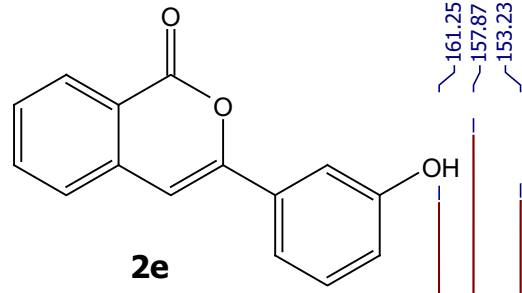




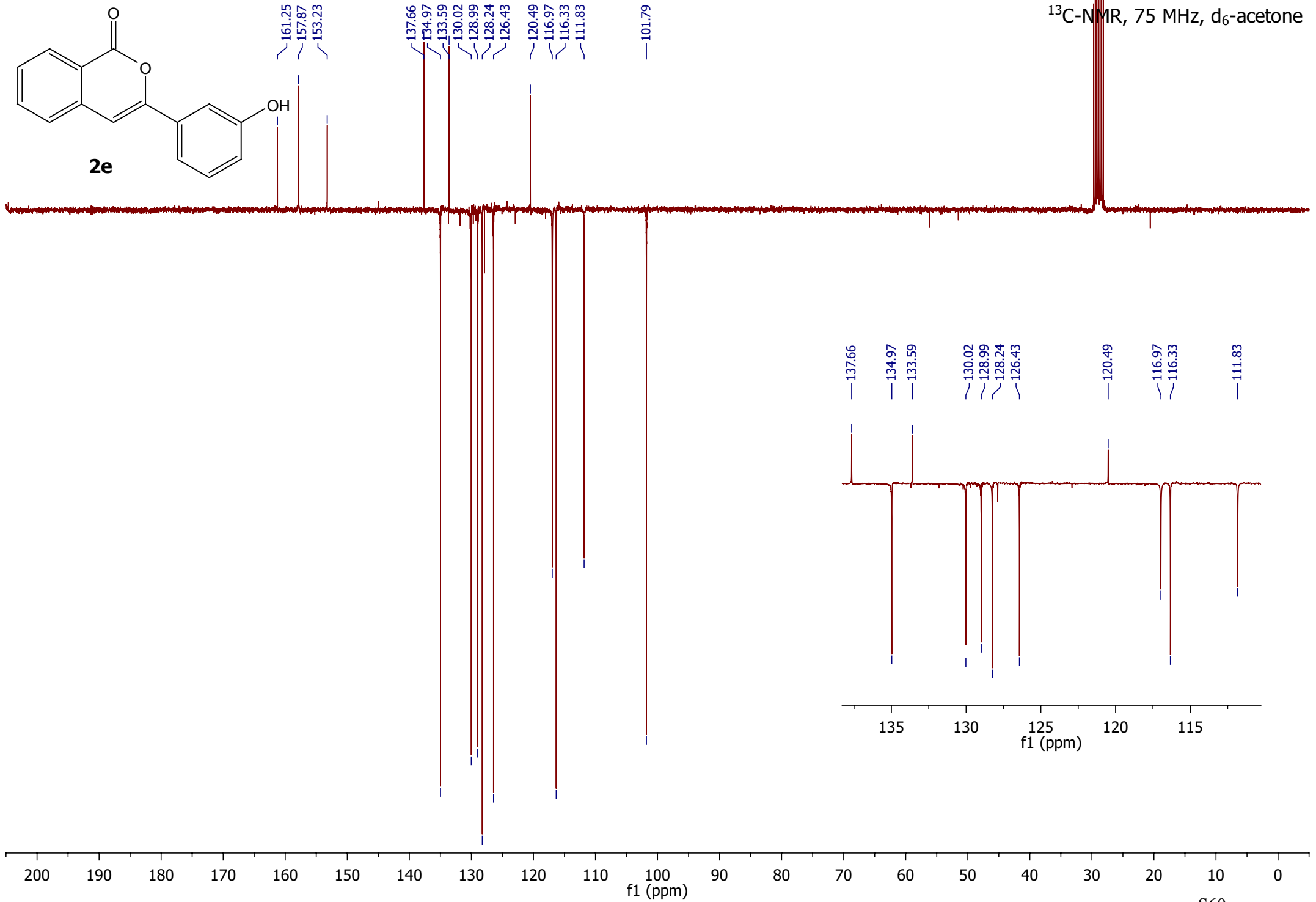
8.66
8.23
8.23
8.21
8.20
7.82
7.58
7.42
7.41
7.34
7.38
6.97
6.97
6.97
6.95
6.95
6.94

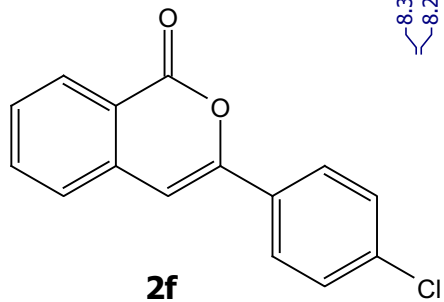
2.99





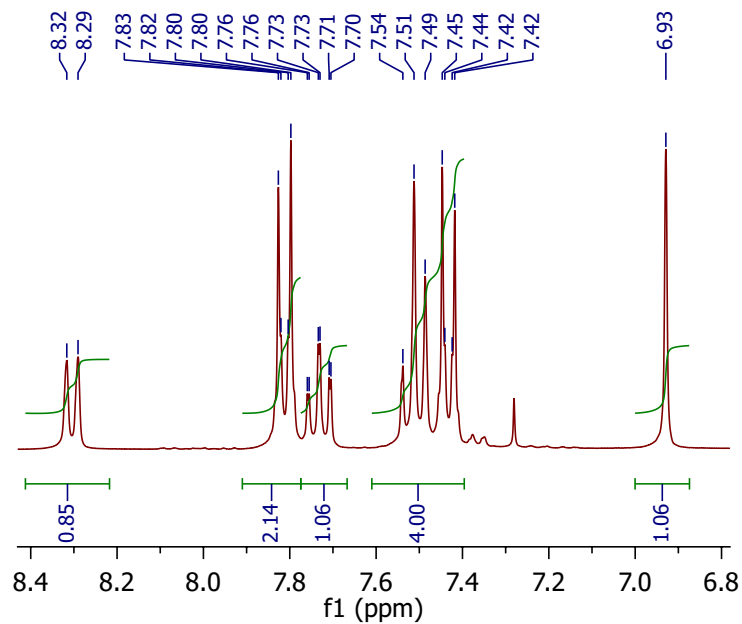
¹³C-NMR, 75 MHz, d₆-acetone





8.32
8.29

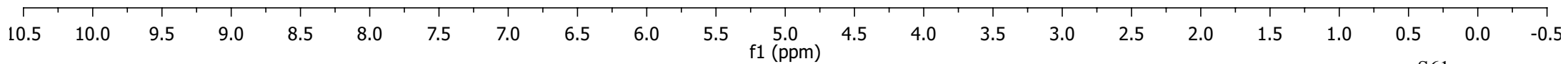
7.83
7.82
7.80
7.80
7.51
7.49
7.45
7.43

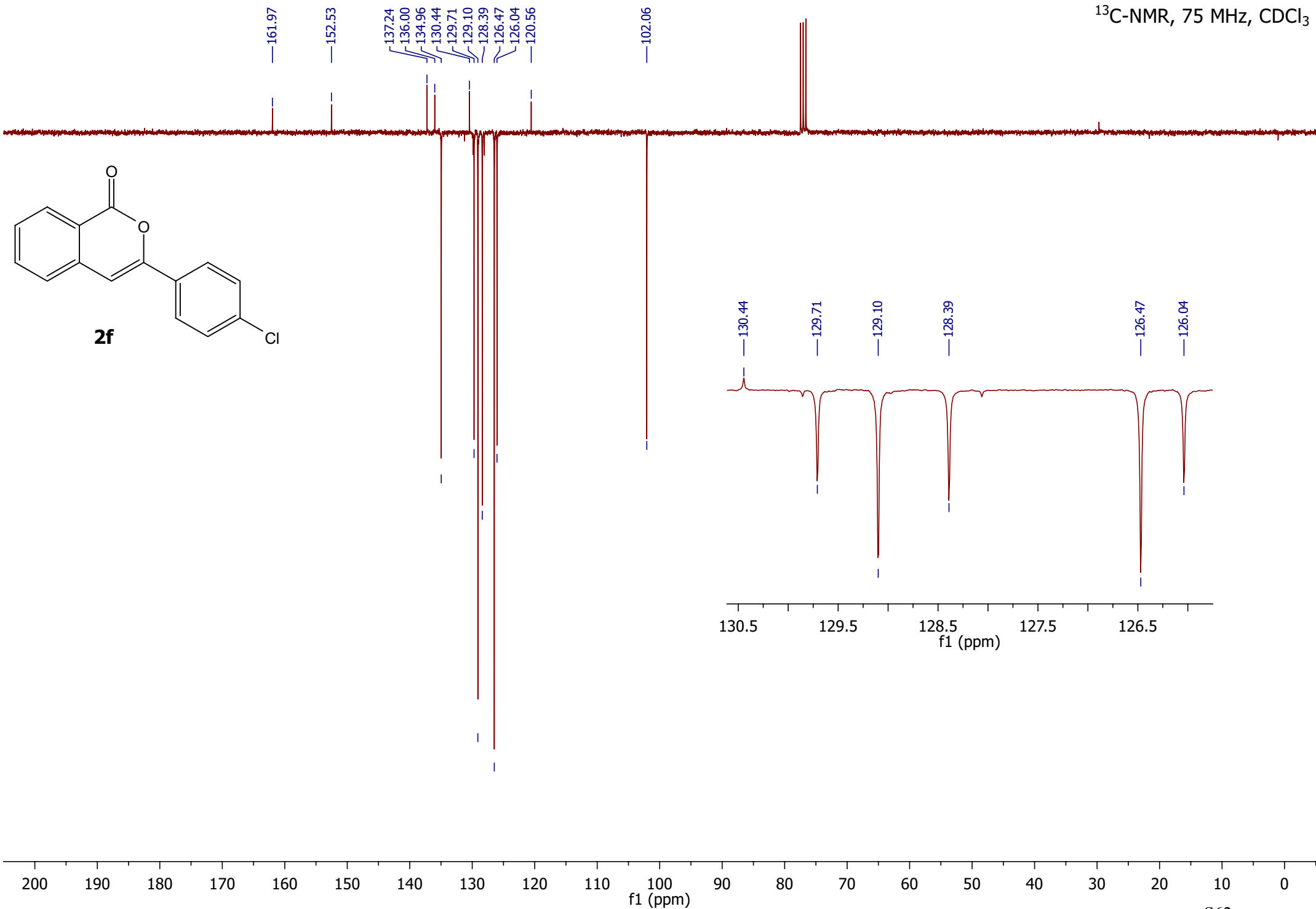


0.85

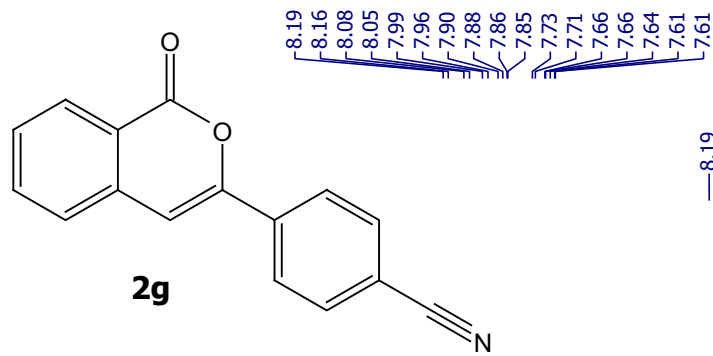
2.14
1.06
2.12
1.86

1.06

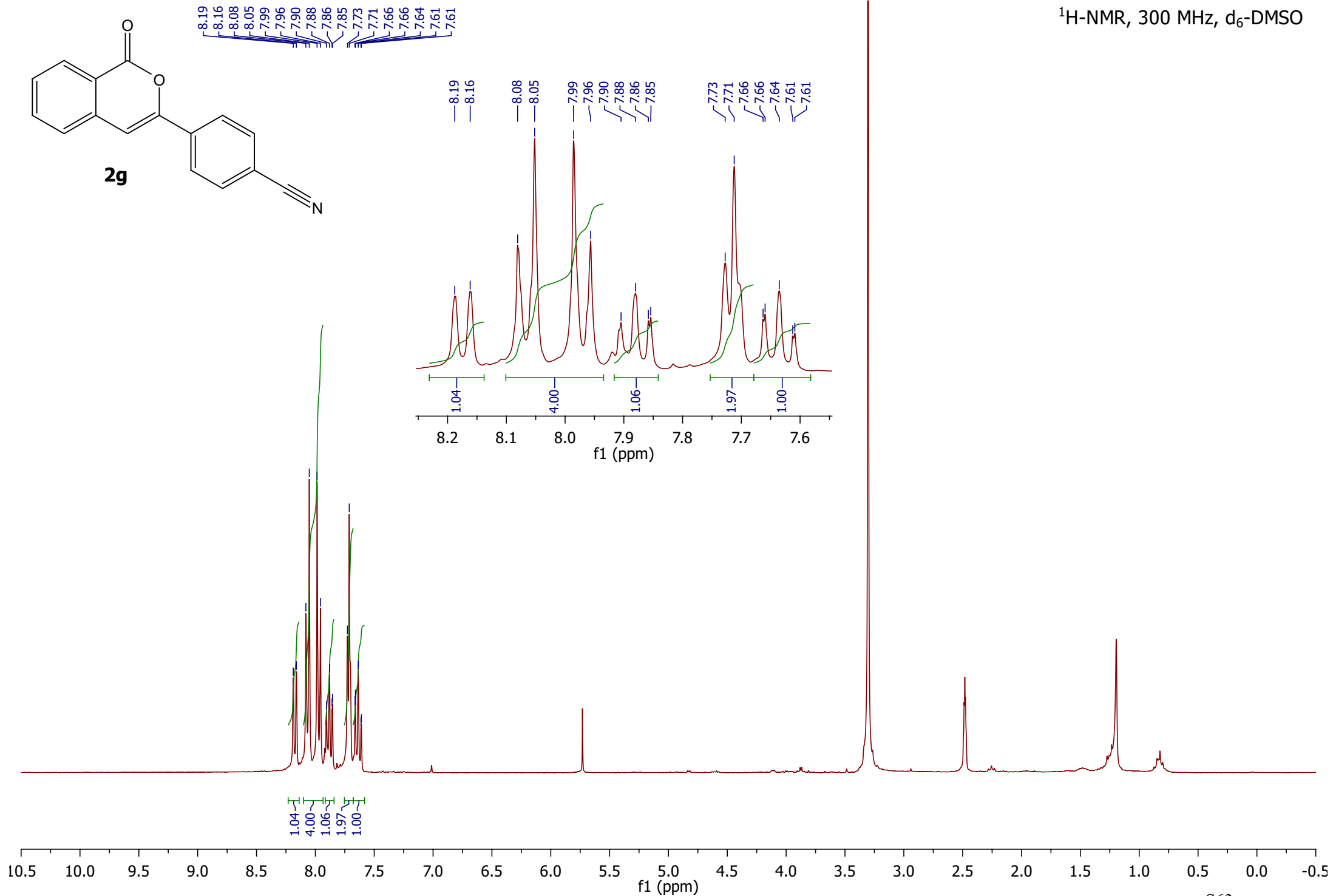
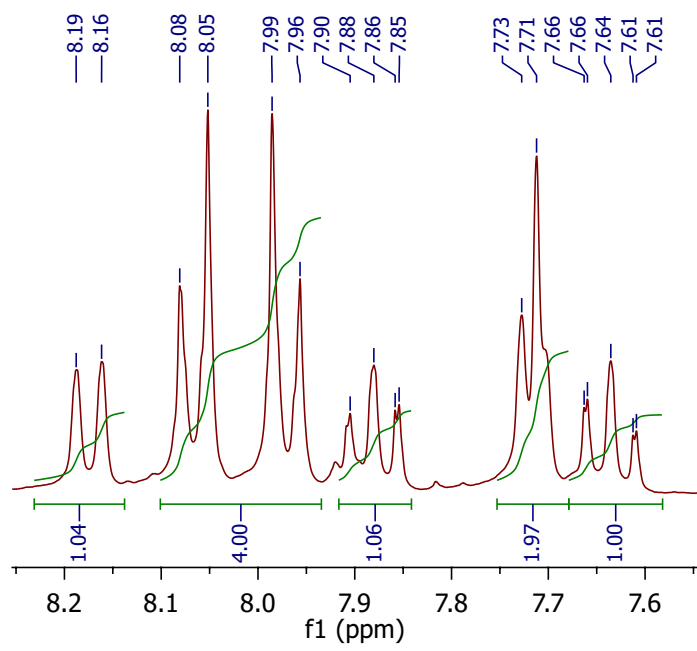


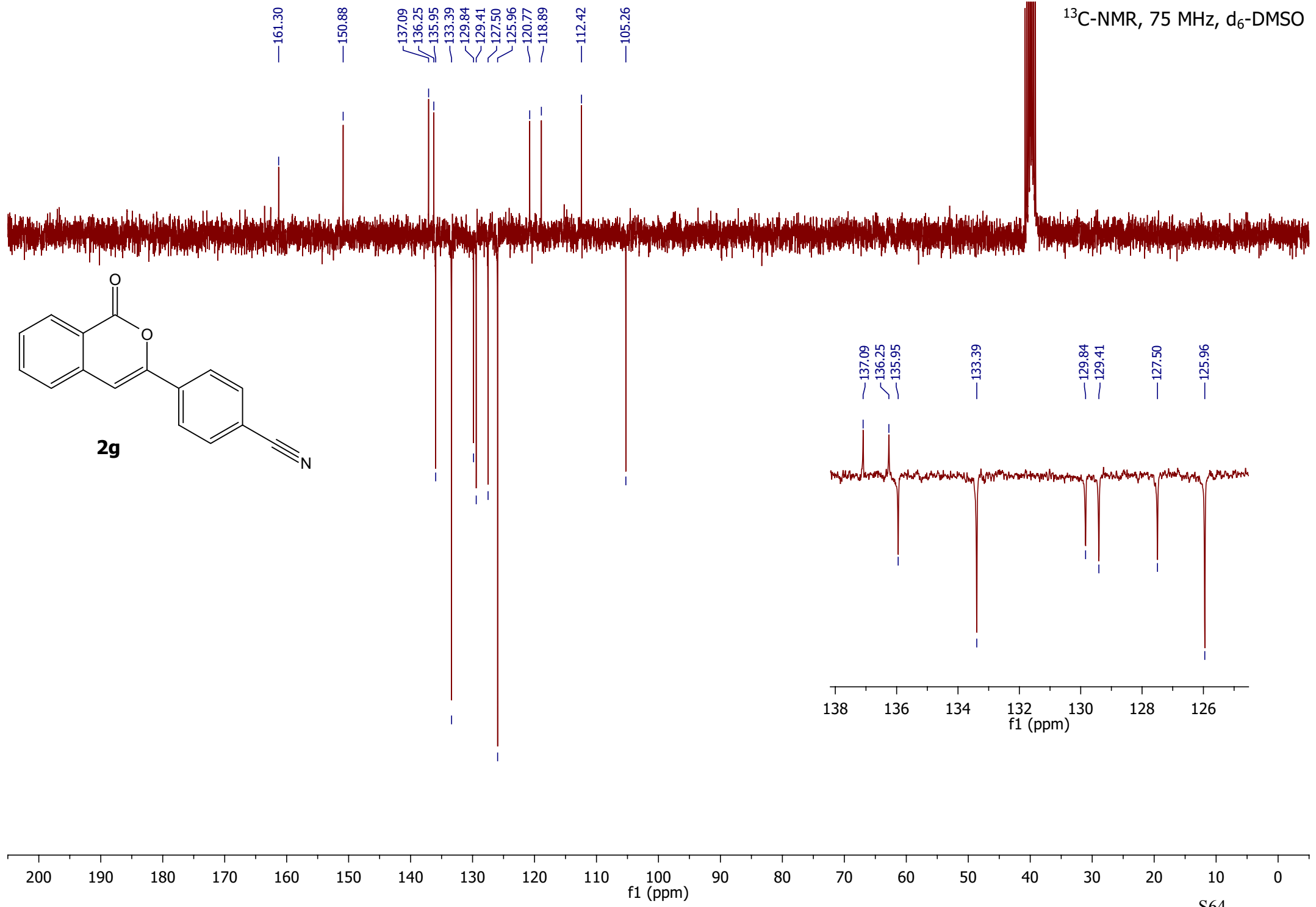


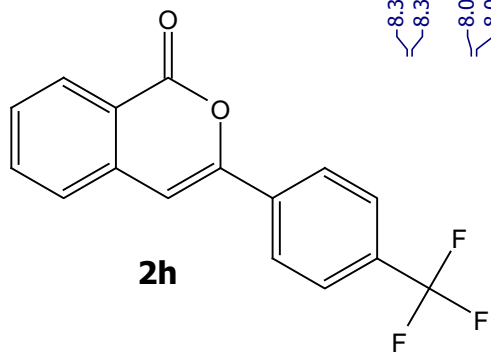
¹H-NMR, 300 MHz, d₆-DMSO



8.19
8.16
8.08
8.05
7.99
7.96
7.90
7.88
7.86
7.85
7.73
7.71
7.66
7.66
7.64
7.61
7.61

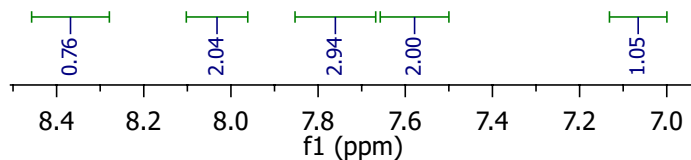




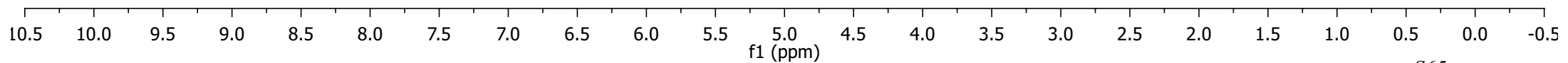


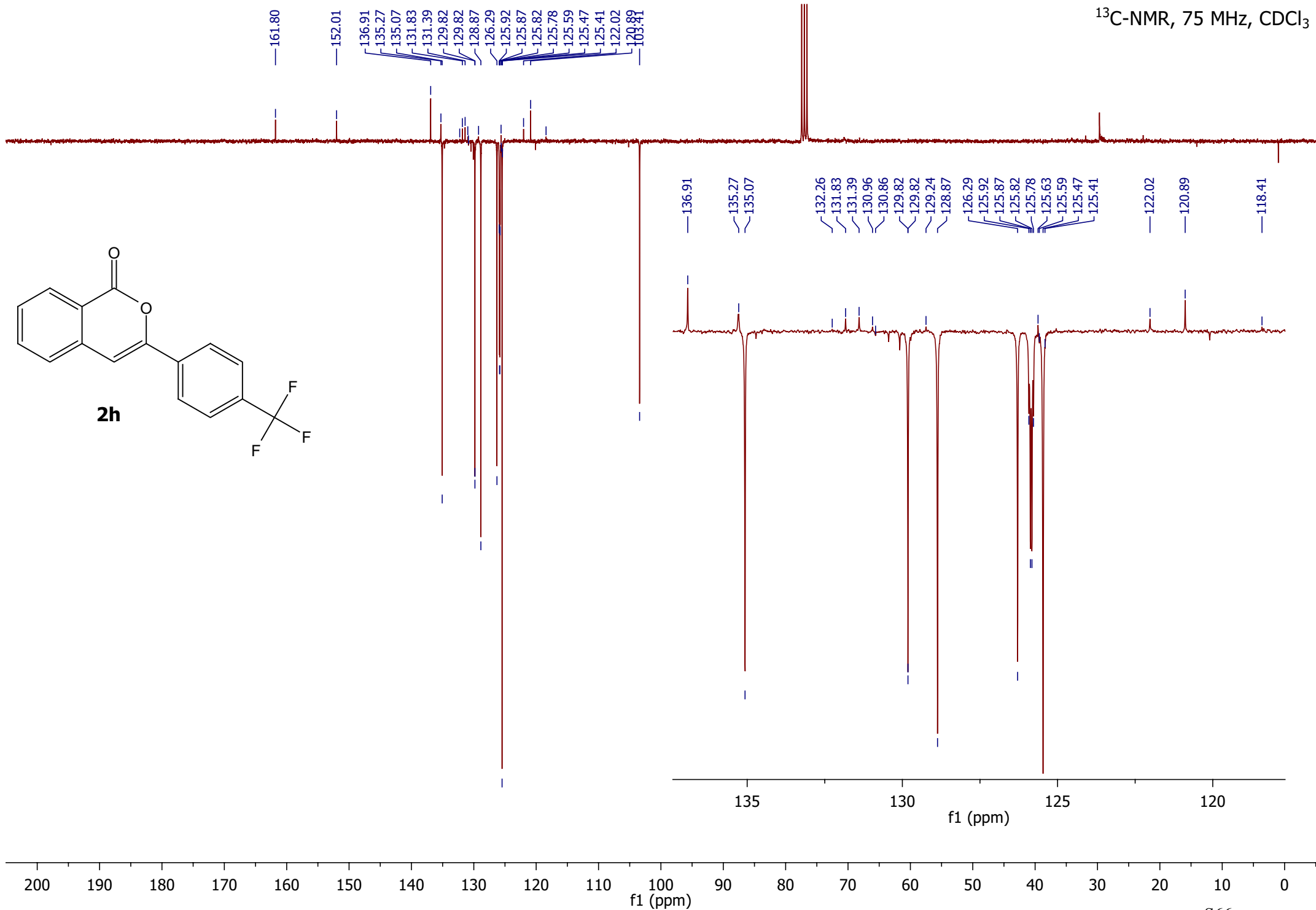
8.36
8.34
8.03
8.00
7.78
7.75
7.73
7.60
7.57
7.55
7.06

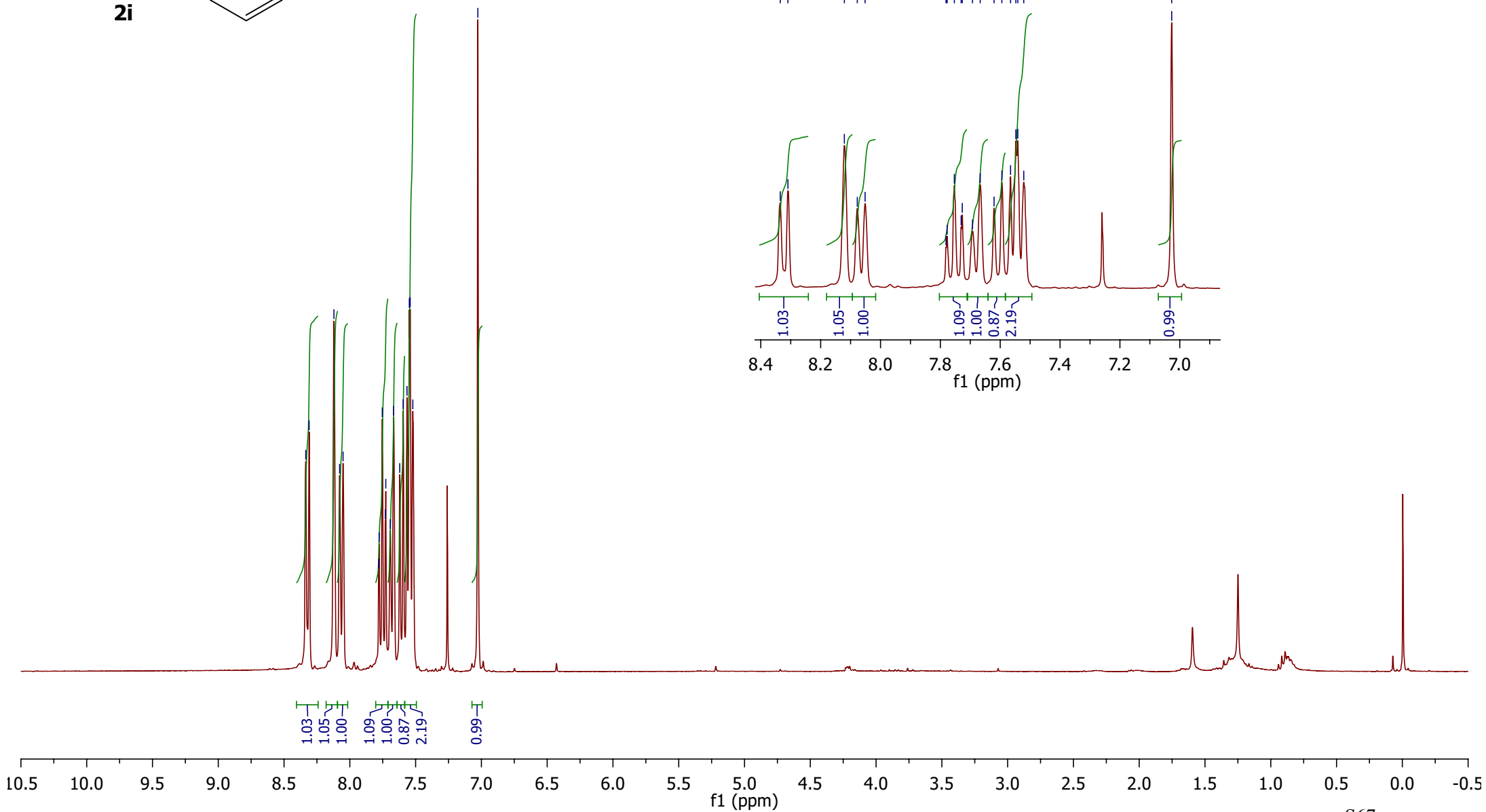
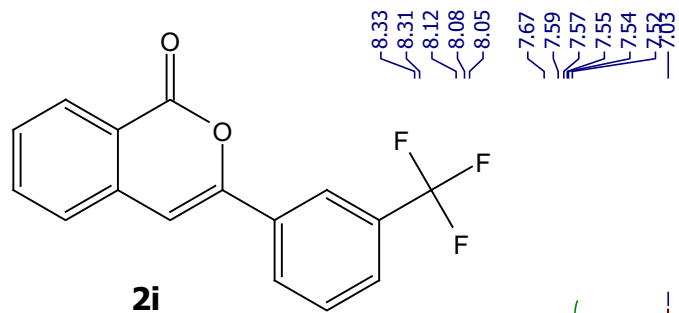
8.36
8.34
8.03
8.00
7.81
7.80
7.78
7.75
7.73
7.60
7.57
7.55
7.06



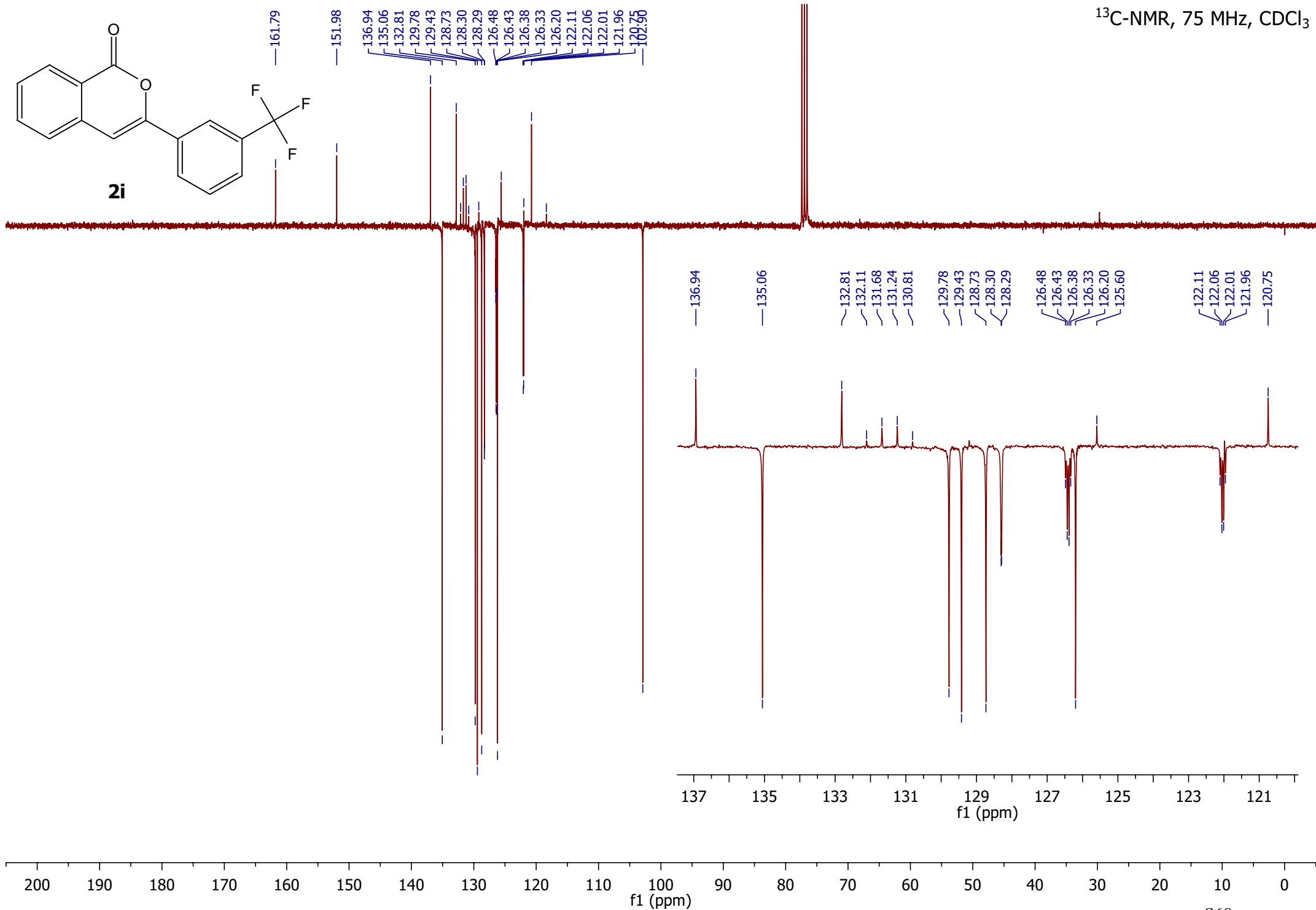
0.76
2.04
2.94
2.00
1.05

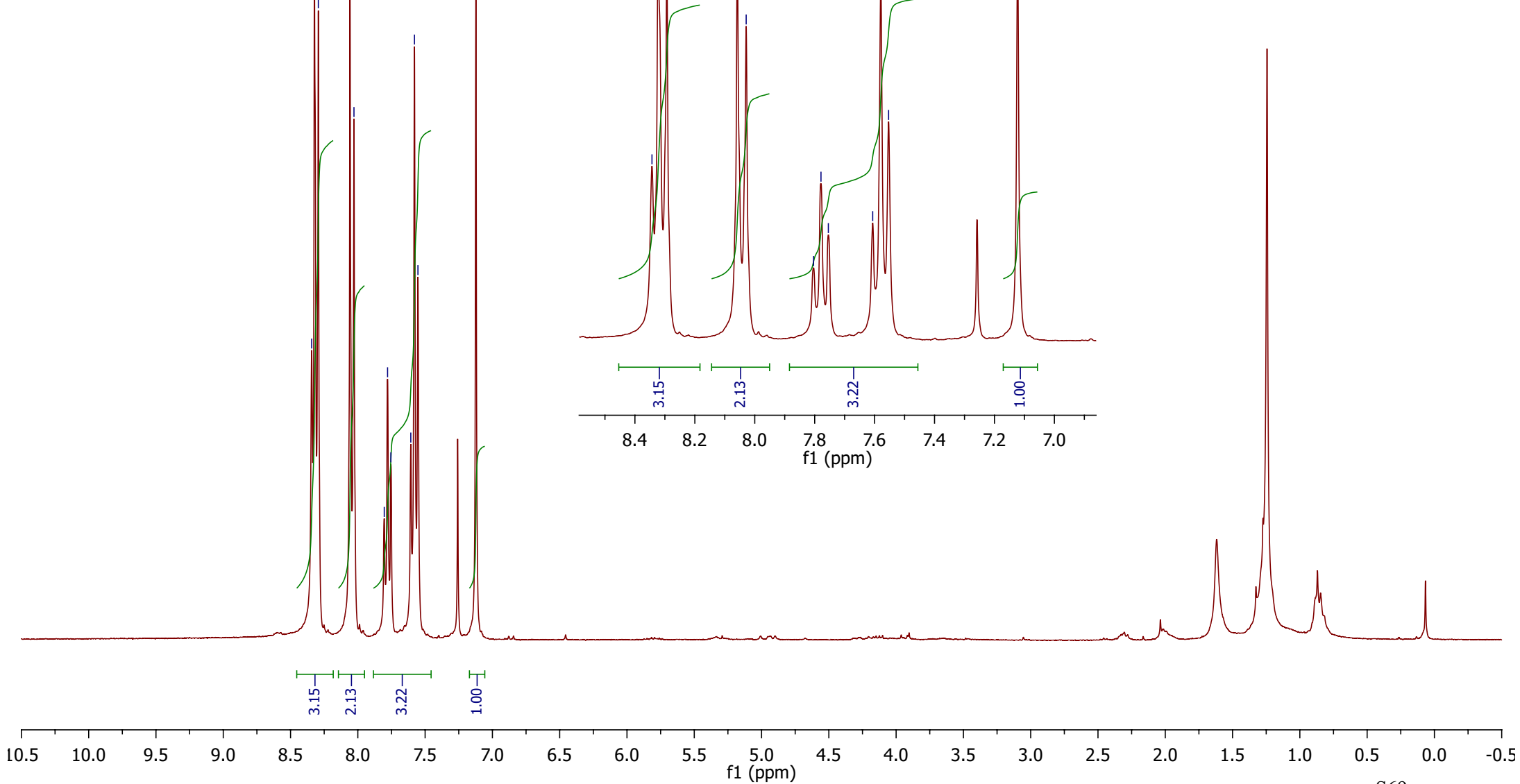
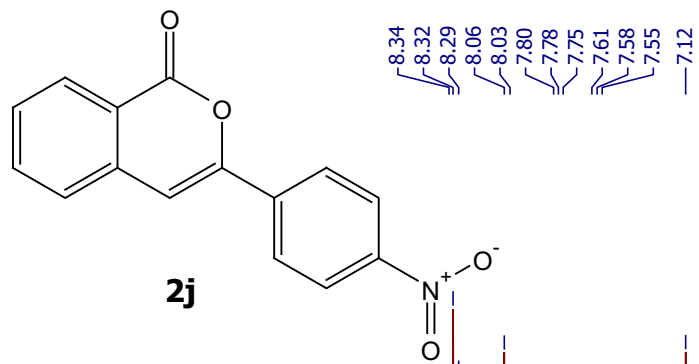




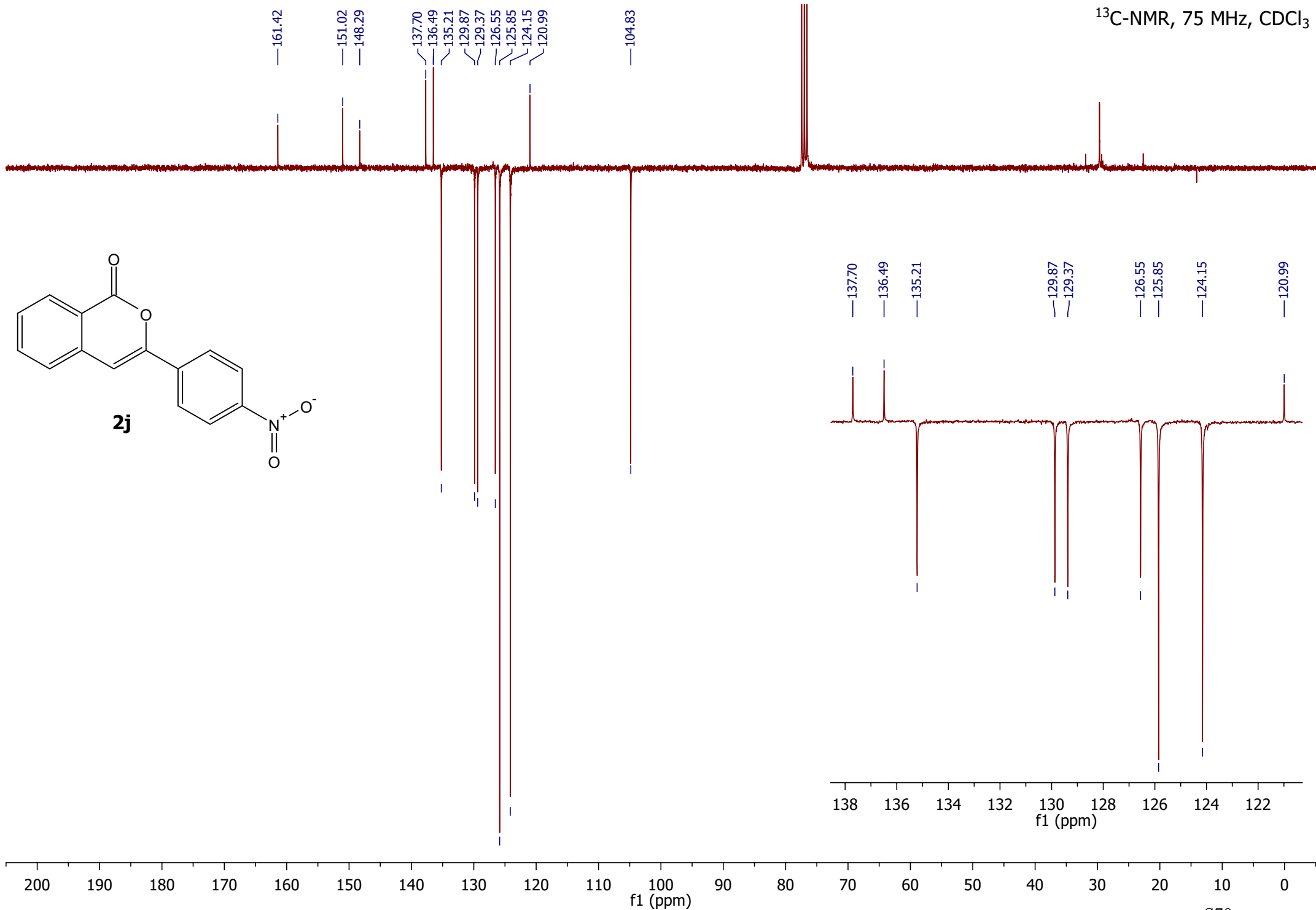


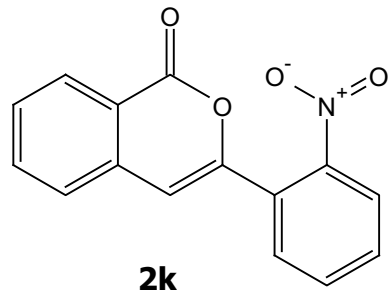
¹³C-NMR, 75 MHz, CDCl₃





¹³C-NMR, 75 MHz, CDCl₃

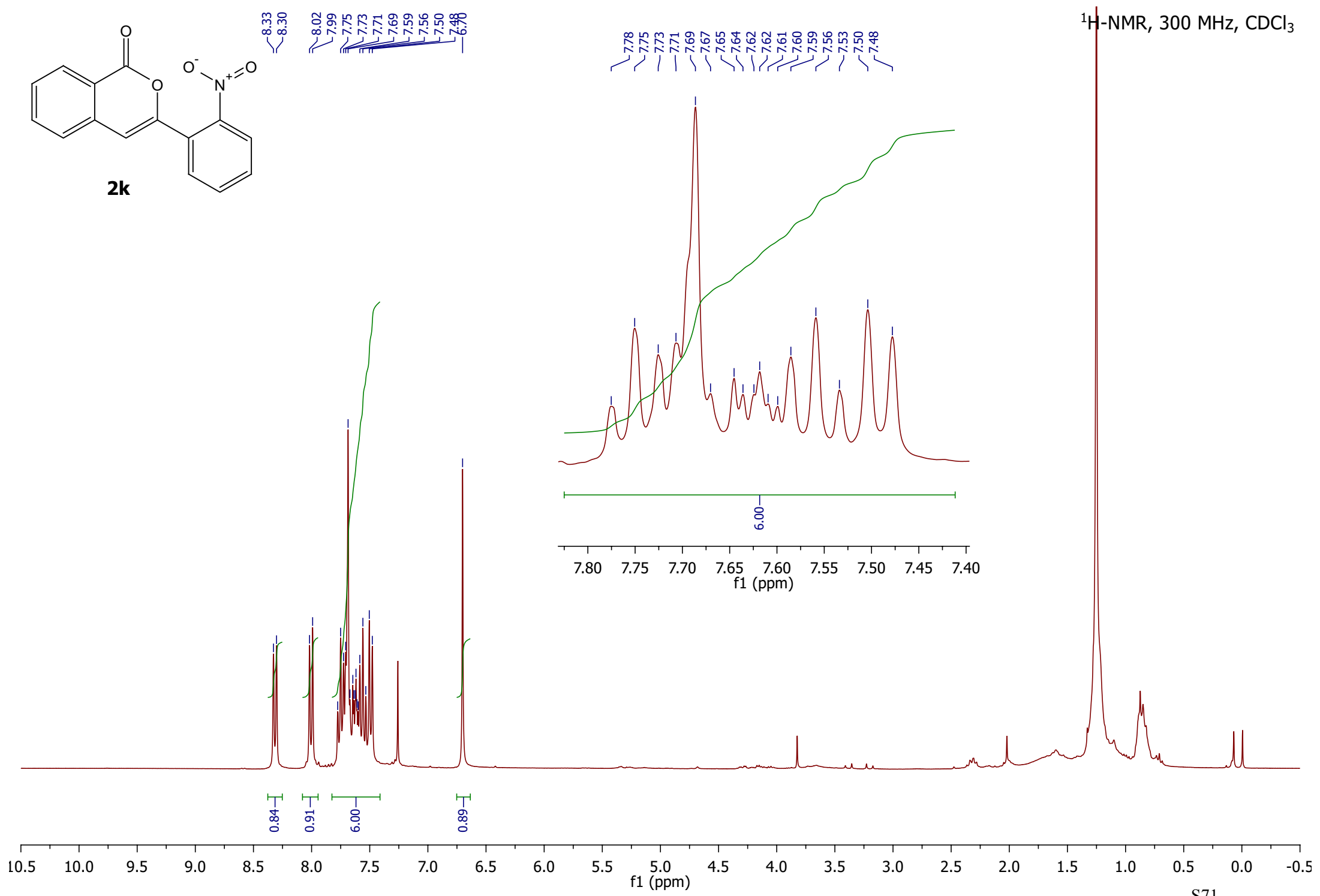


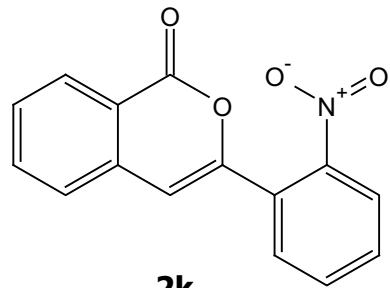


8.33
8.30
8.02
7.99
7.75
7.73
7.71
7.69
7.59
7.56
7.50
7.48

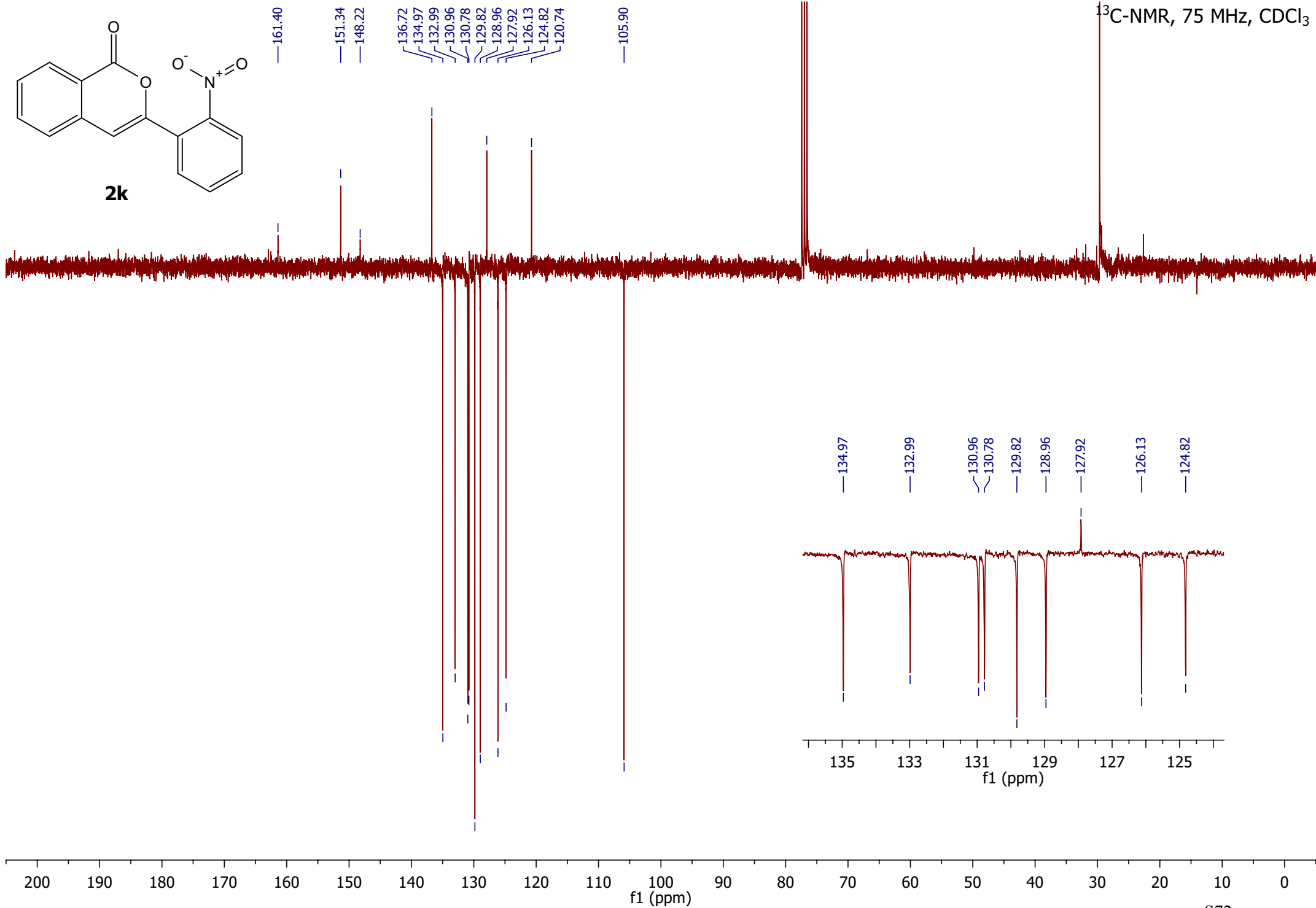
7.78
7.75
7.73
7.71
7.69
7.67
7.65
7.64
7.62
7.62
7.61
7.60
7.59
7.56
7.53
7.50
7.48

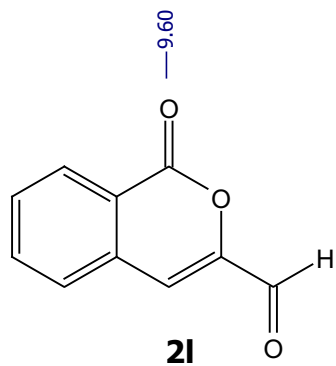
¹H-NMR, 300 MHz, CDCl₃





2k



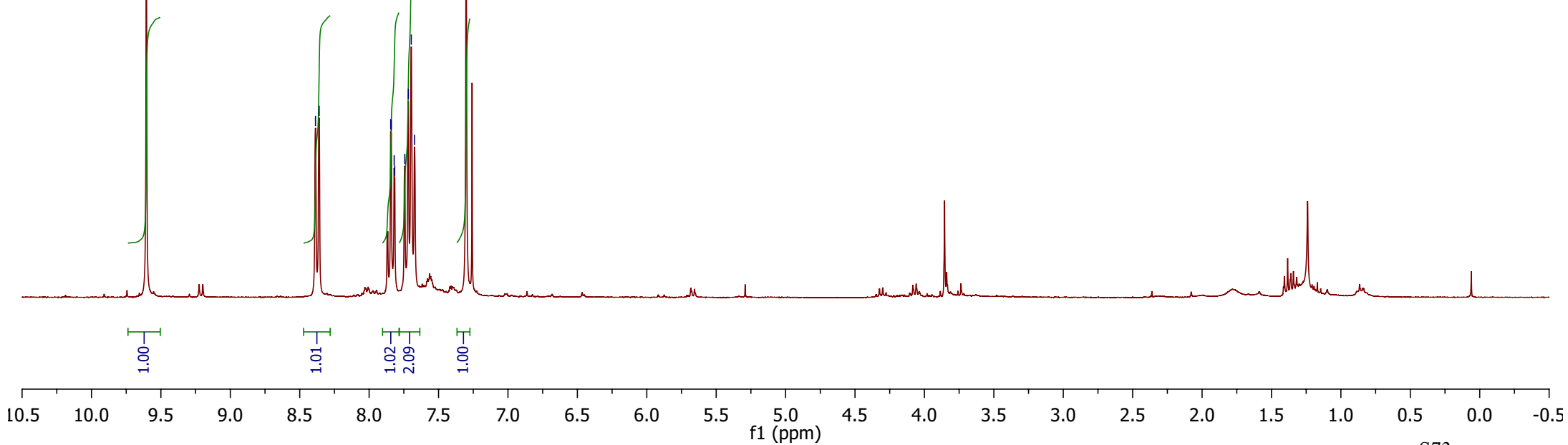
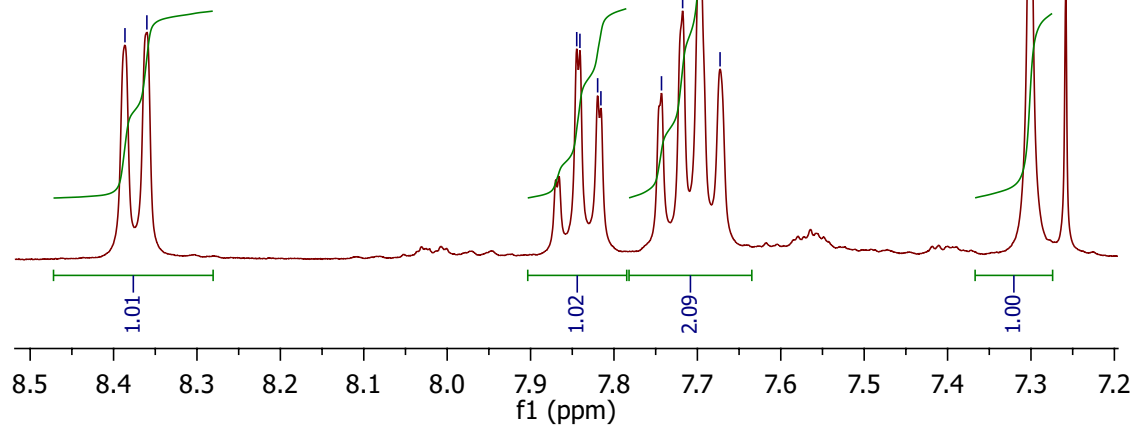


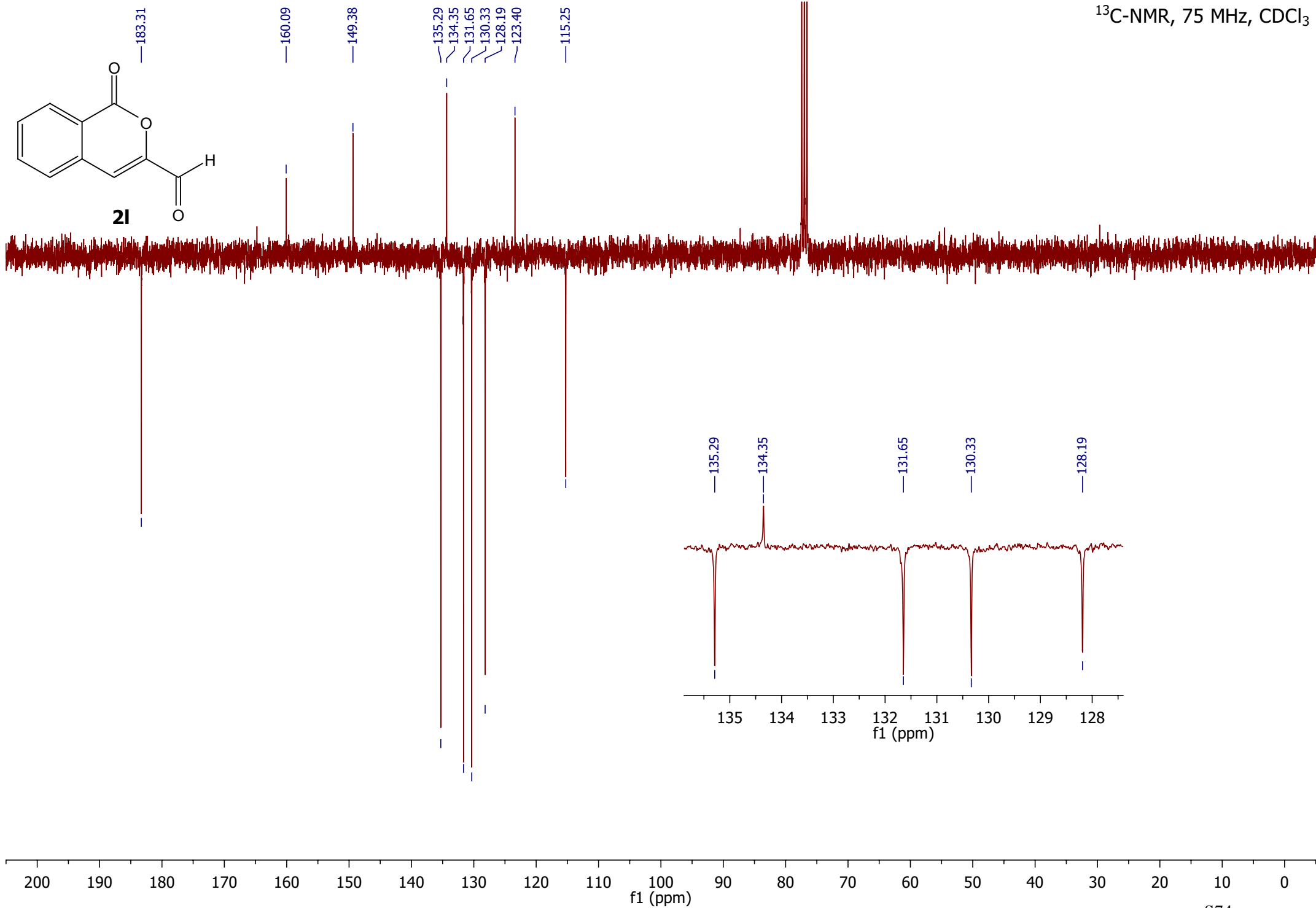
8.39
8.36
7.84
7.84
7.74
7.72
7.70
7.67

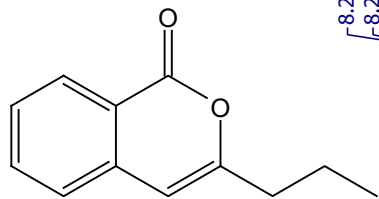
8.39
8.36

7.84
7.84
7.82
7.74
7.72
7.70
7.67

7.30







2m

8.25
8.24
8.24
8.22
8.22
8.21

7.65
7.65
7.65
7.63
7.62
7.43
7.42
7.42
7.35
7.32
6.24
6.24

8.25
8.24
8.24
8.22
8.21

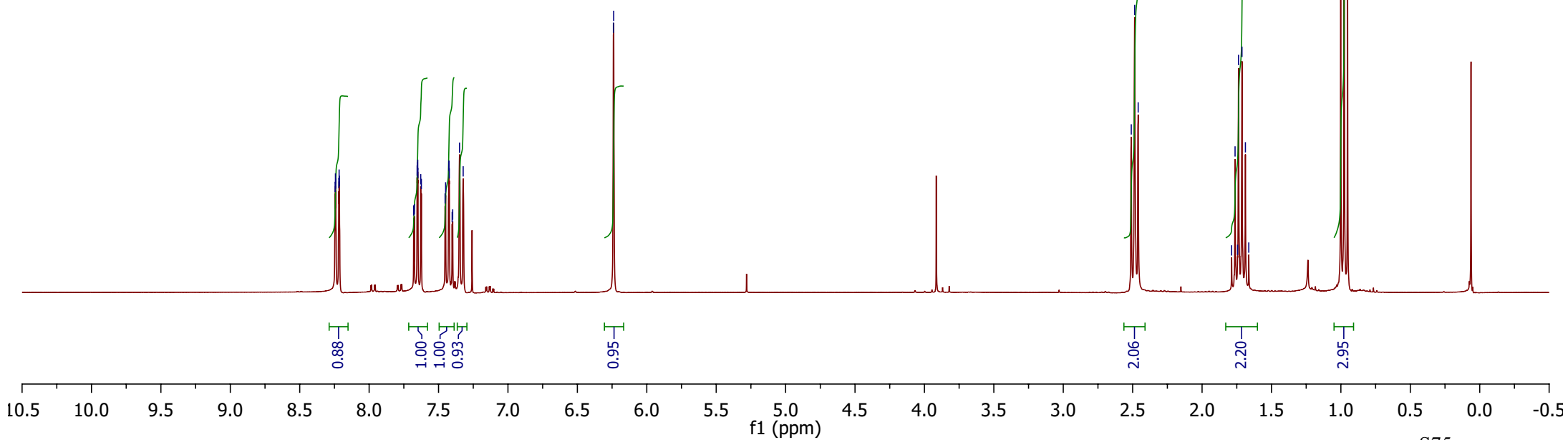
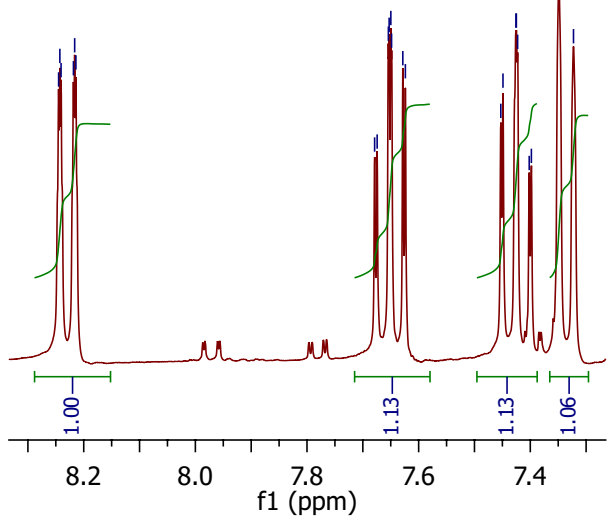
7.68
7.67
7.65
7.65
7.65
7.63
7.62

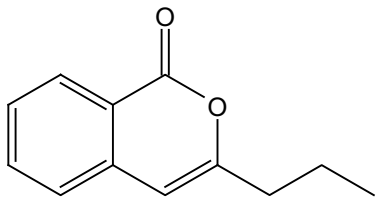
7.43
7.42
7.42
7.35
7.32

2.51
2.49
2.46

1.79
1.76
1.74
1.74
1.71
1.69
1.66
1.66
1.00
0.98
0.95

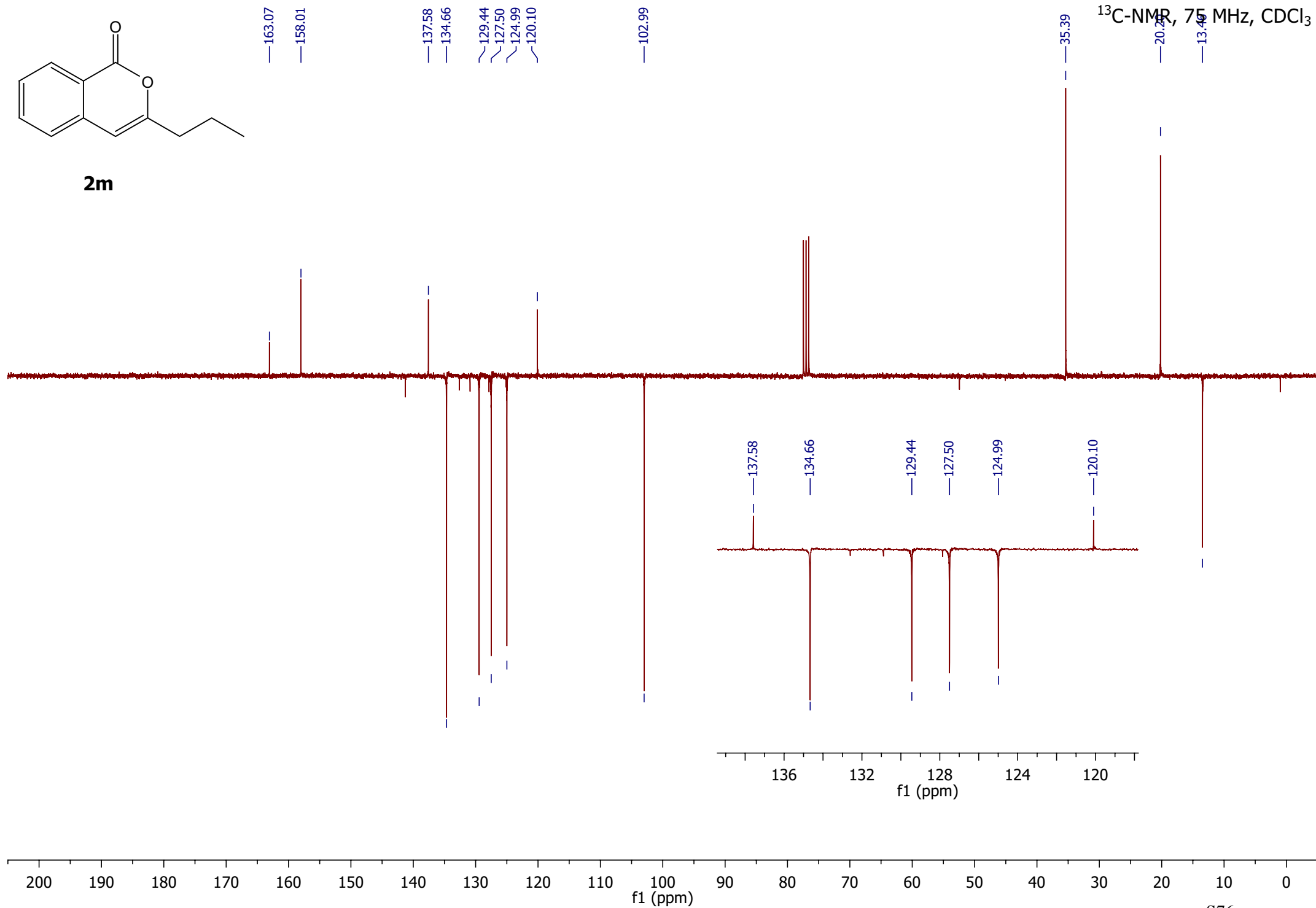
CDCl₃, 300 MHz, CDCl₃

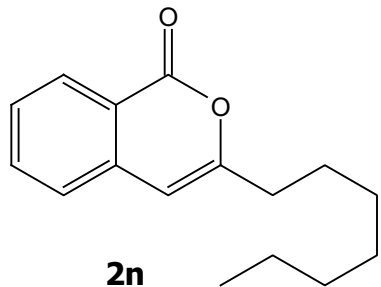




2m

$^{13}\text{C-NMR}$, 75 MHz, CDCl_3



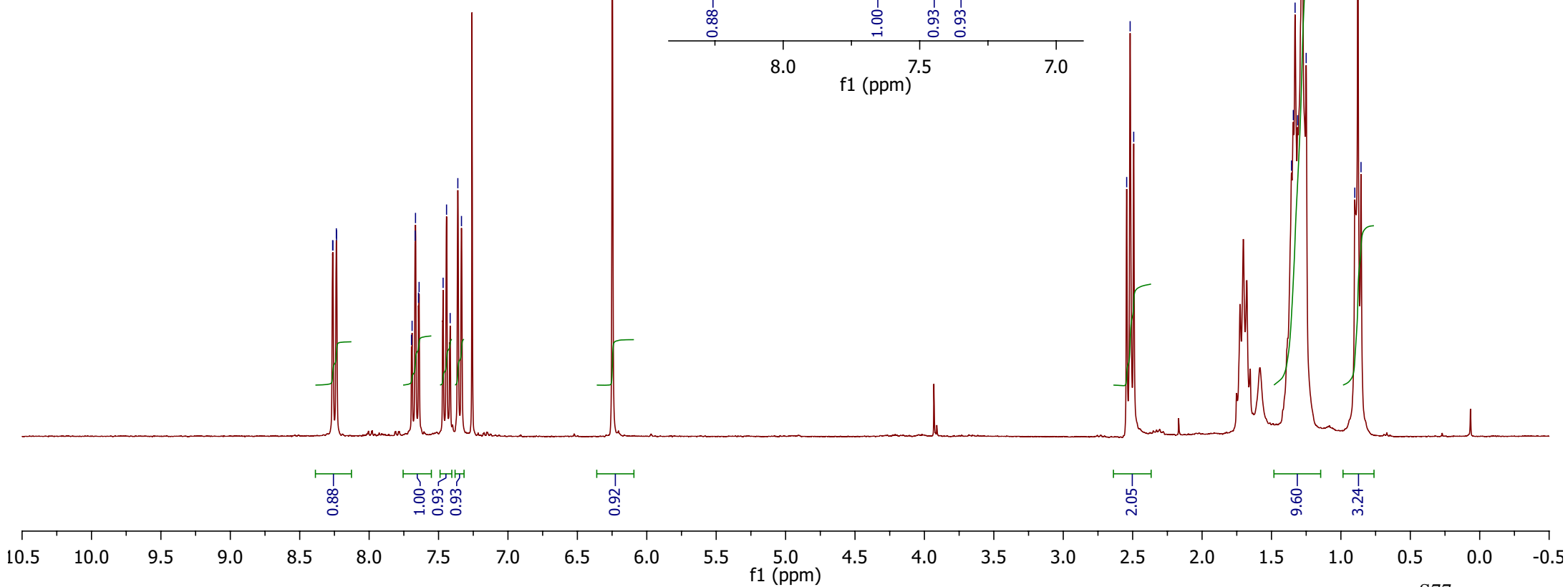
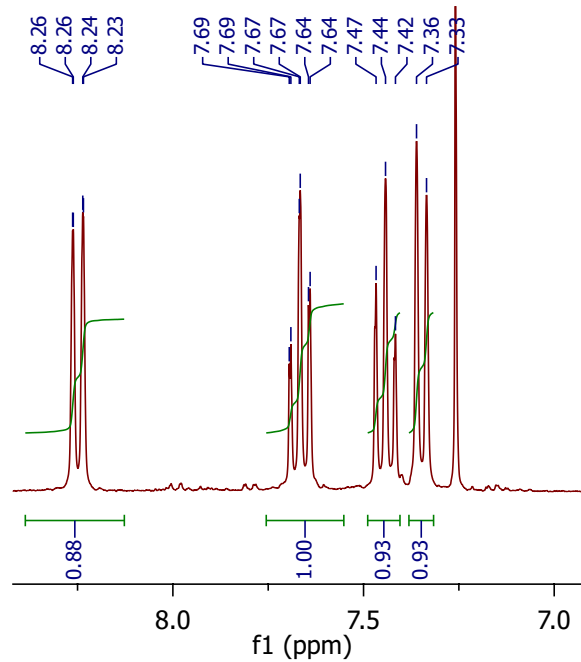


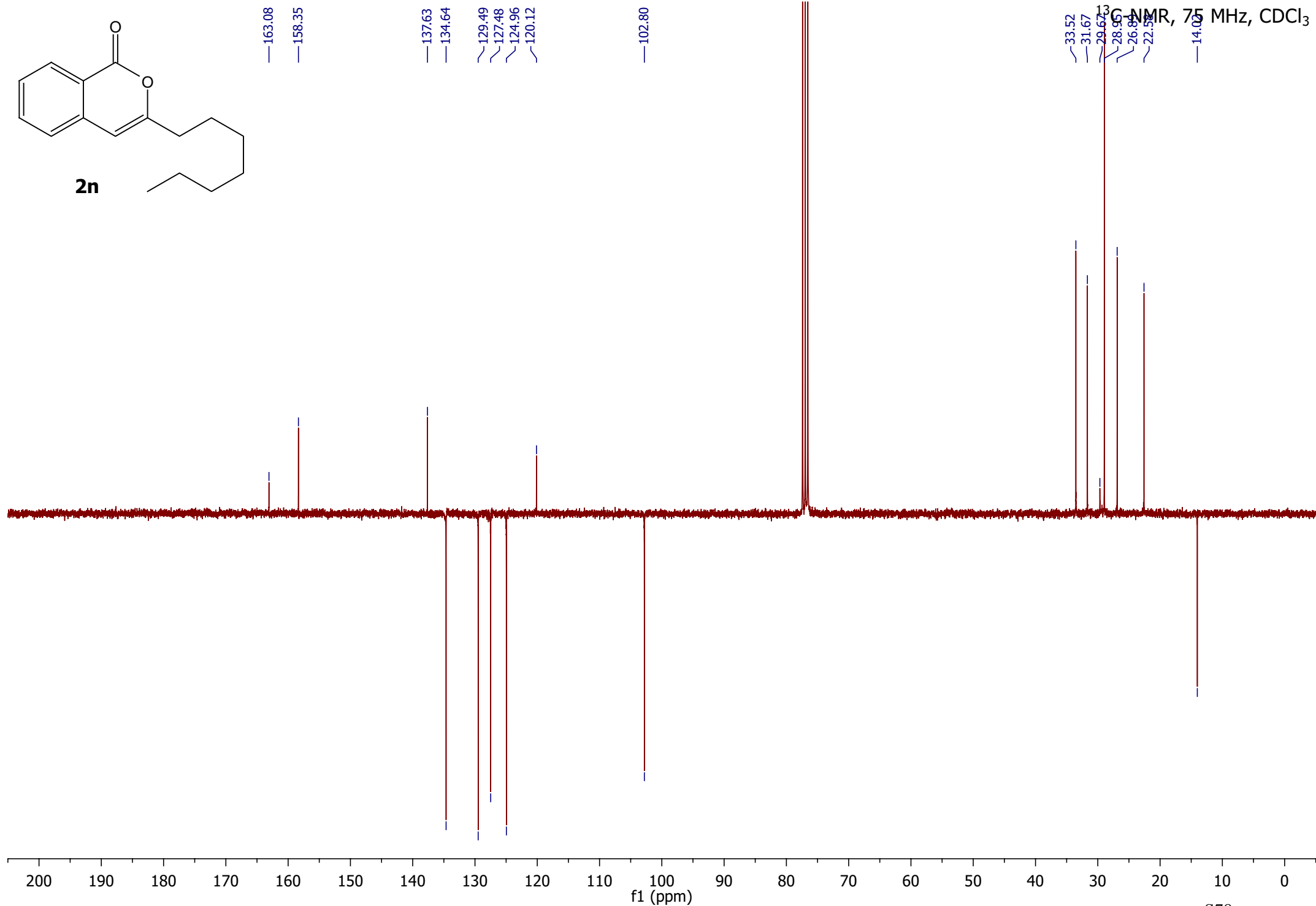
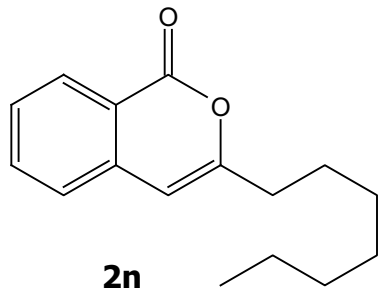
8.26
8.26
8.24
8.23
7.69
7.67
7.67
7.64
7.64
7.47
7.44
7.42
7.36
7.33
6.25

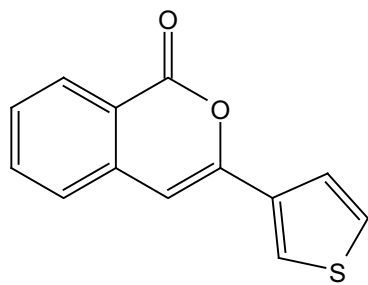
2.54
2.52
2.49

1.36
1.34
1.33
1.31
1.29
1.25
0.90
0.88
0.86

¹H-NMR, 300 MHz, CDCl₃







2p

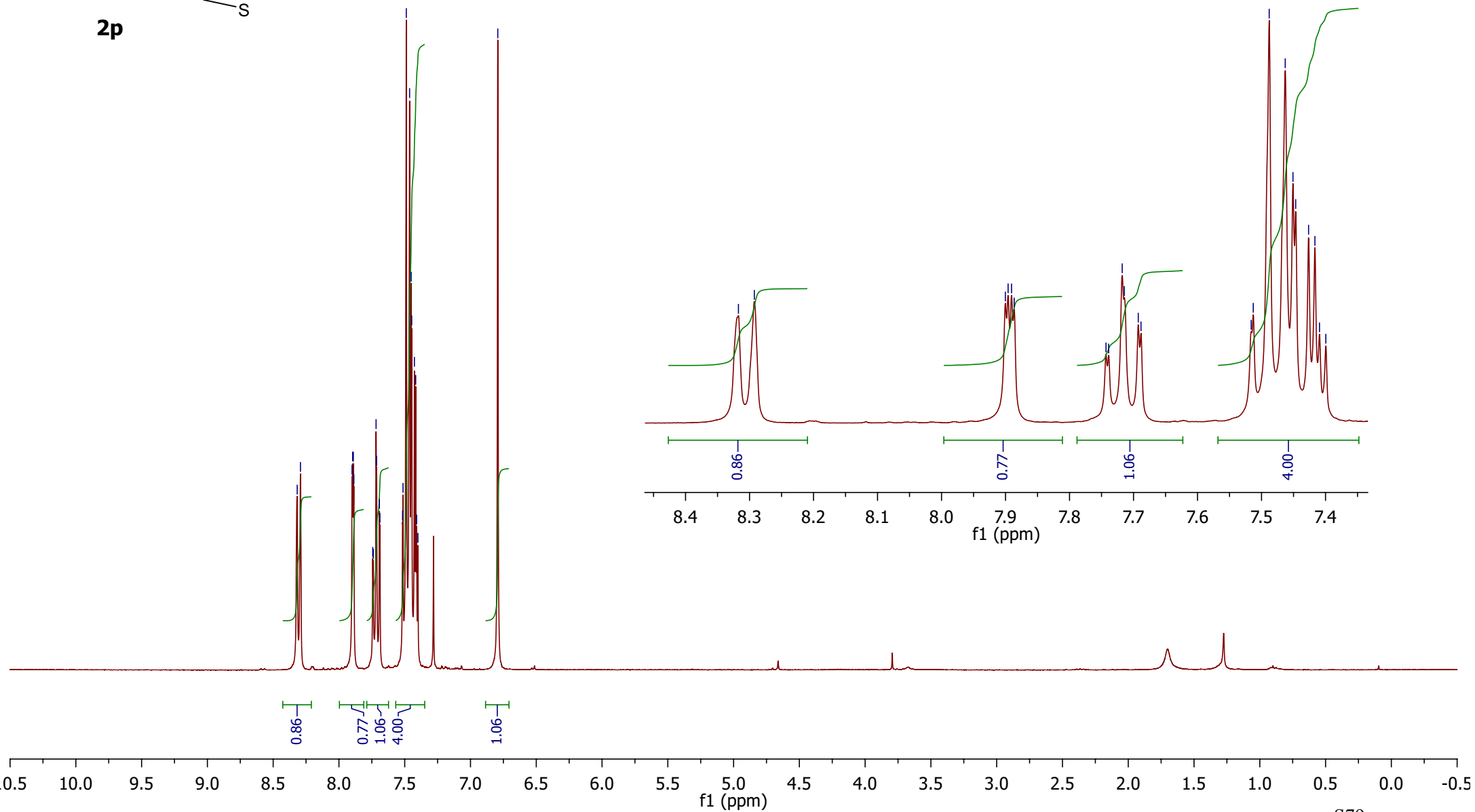
8.32
8.29
7.90
7.89
7.72
7.49
7.46
7.45
7.45
7.43
7.42

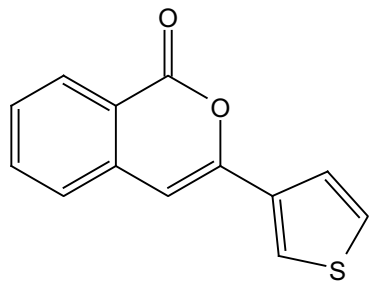
8.32
8.29

7.90
7.89
7.89

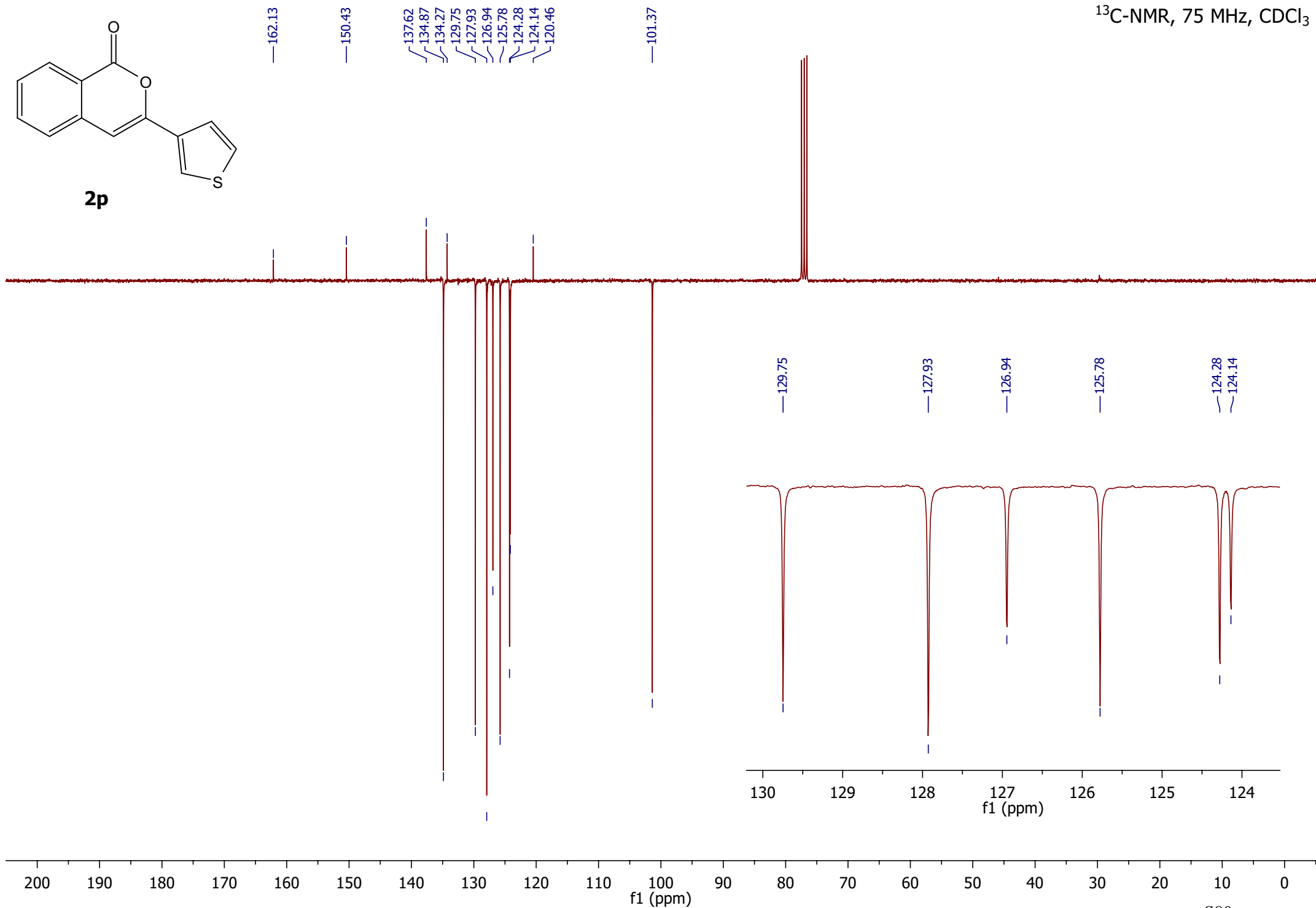
7.74
7.74
7.72
7.71
7.69
7.69

7.52
7.51
7.49
7.46
7.45
7.45
7.43
7.42
7.41
7.40

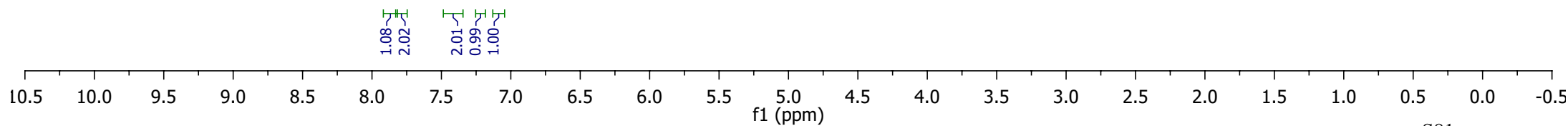
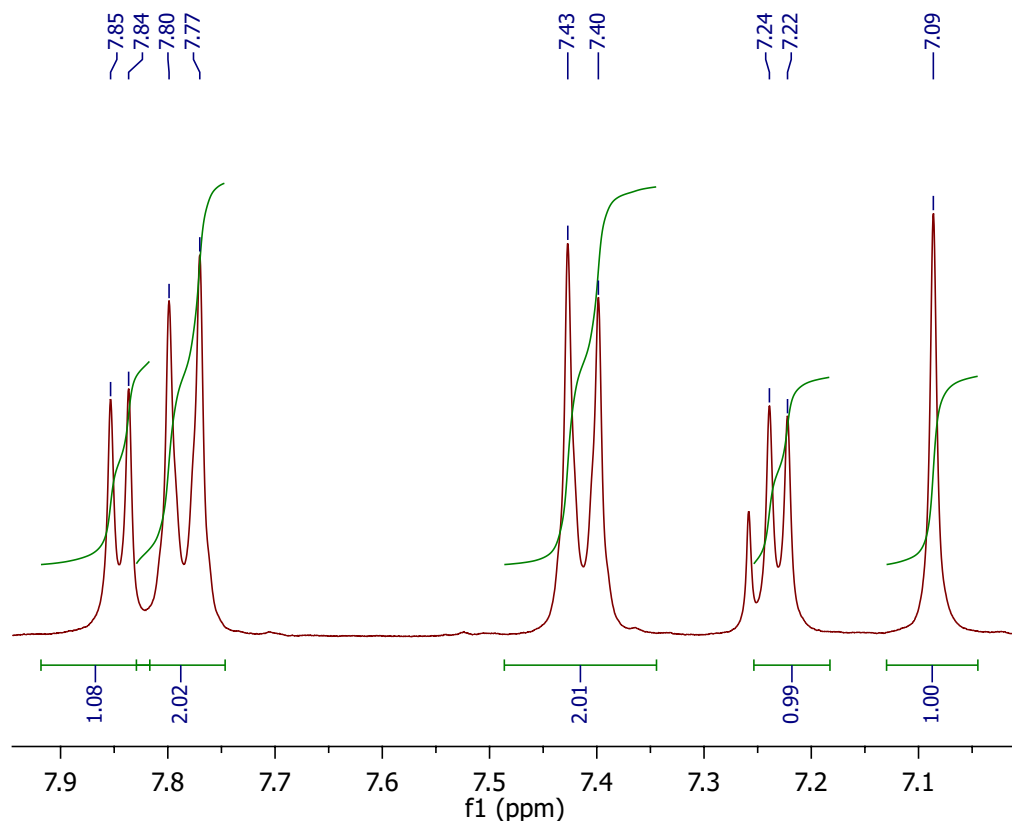
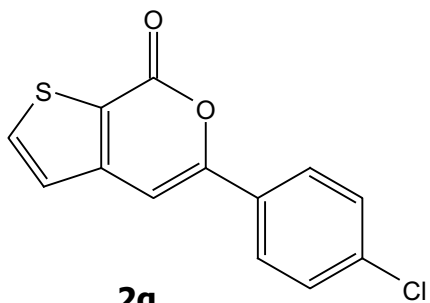


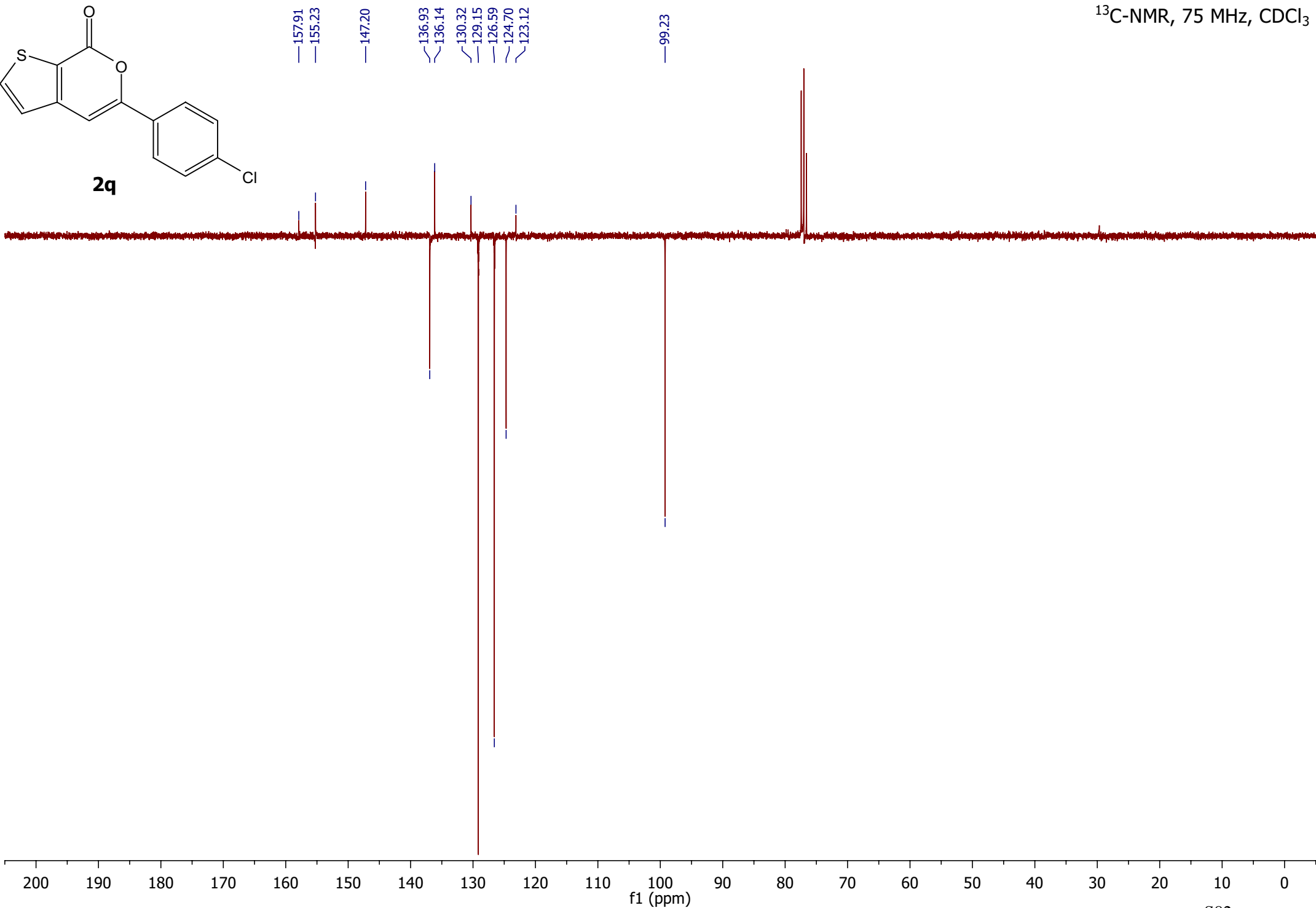
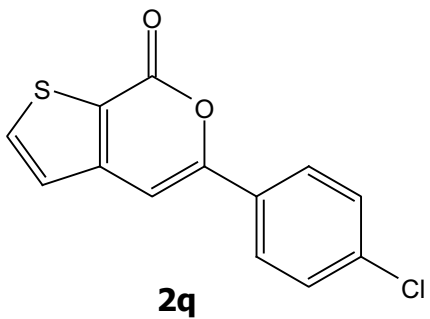


2p



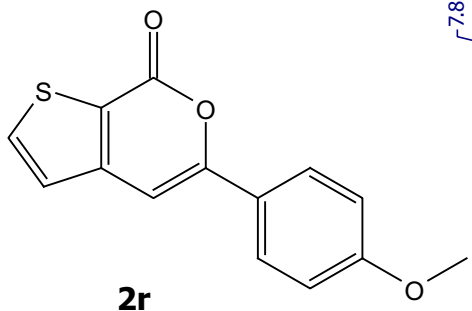
7.85
7.84
7.80
7.77
7.43
7.40
7.24
7.22
7.09





¹H-NMR, 300 MHz, CDCl₃

7.82
7.81
7.80
7.79
7.79
7.21
7.19
6.99
6.98
6.97
6.97
6.95
6.94
6.93

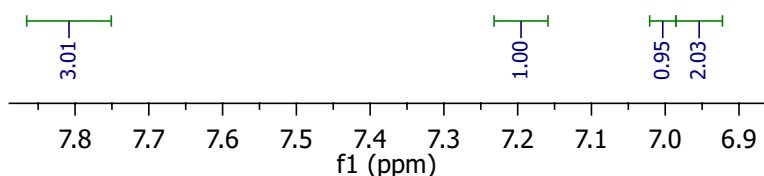


7.82
7.81
7.80
7.79

7.21
7.19

6.99
6.98
6.97
6.97
6.95
6.94
6.93

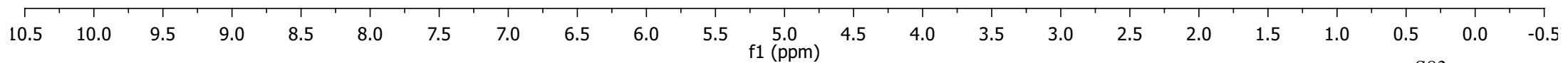
3.86

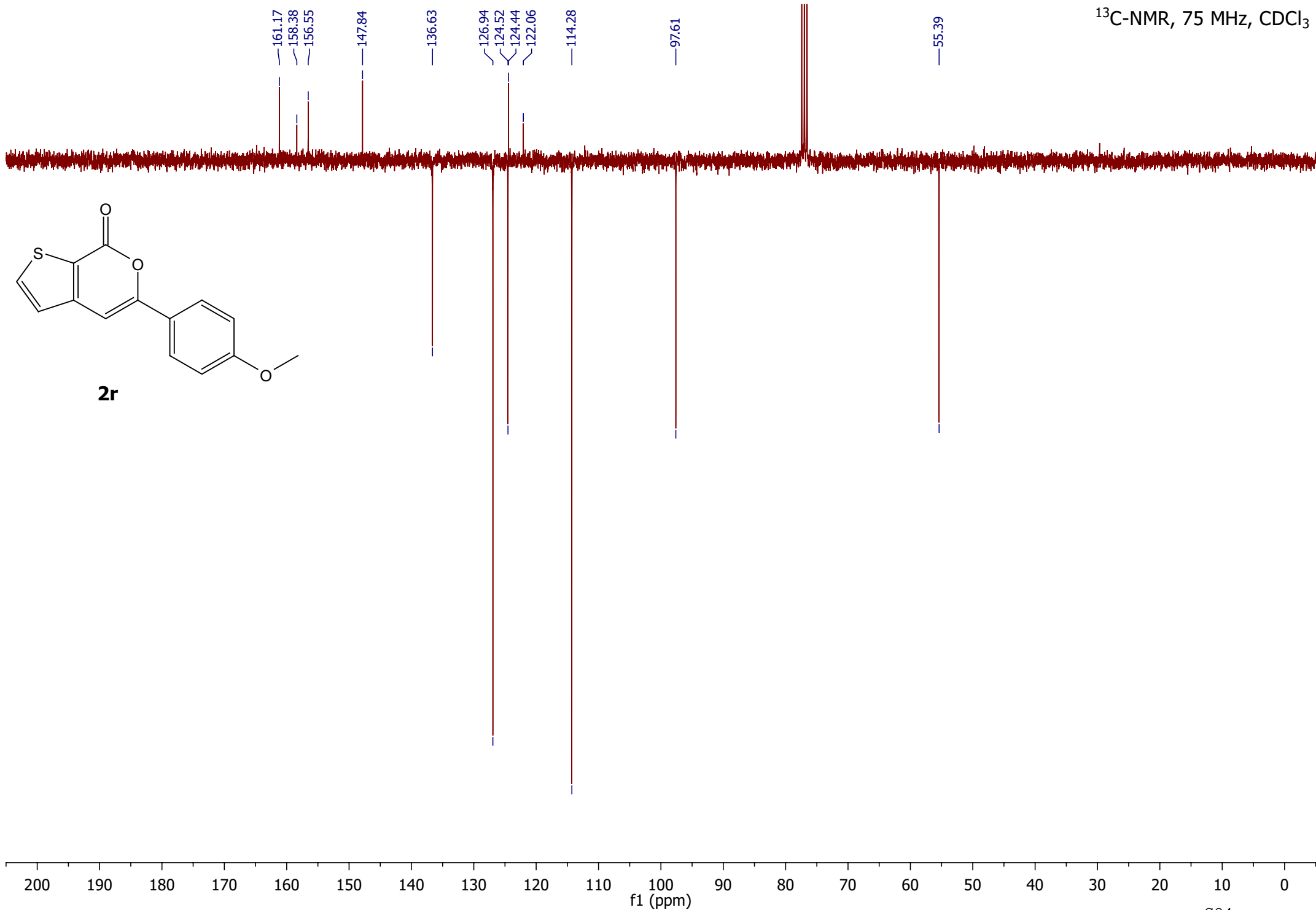


3.01

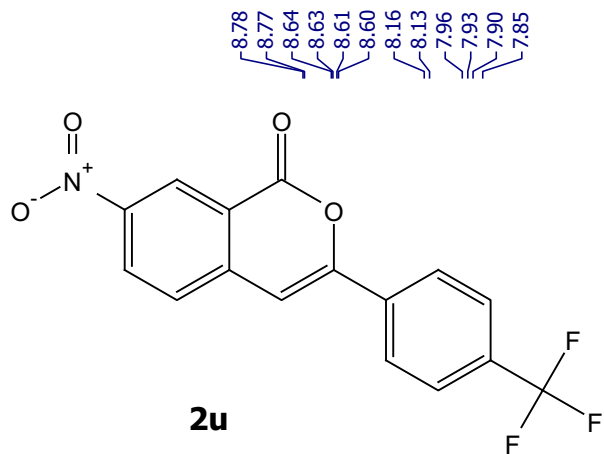
1.00
0.95
2.03

3.08





¹H-NMR, 300 MHz, d₆-DMSO



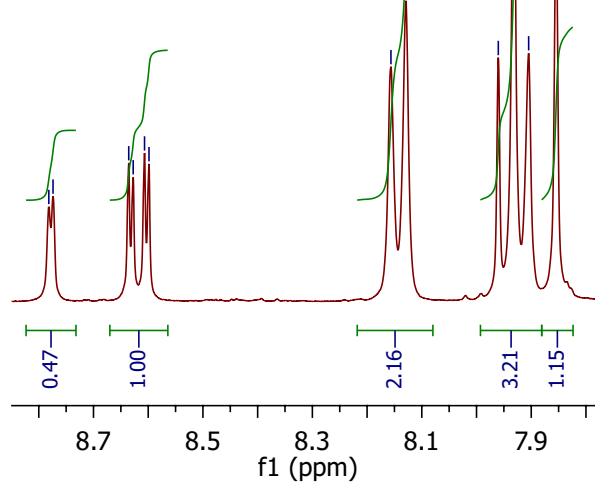
8.78
8.77
8.64
8.63
8.61
8.60
8.16
8.13
7.96
7.93
7.90
7.85

8.78
8.77
8.64
8.63
8.61
8.60

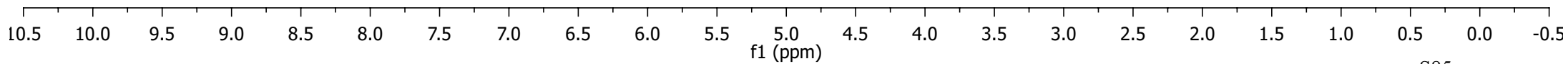
8.16
8.13

7.96
7.93
7.90
7.85

2u

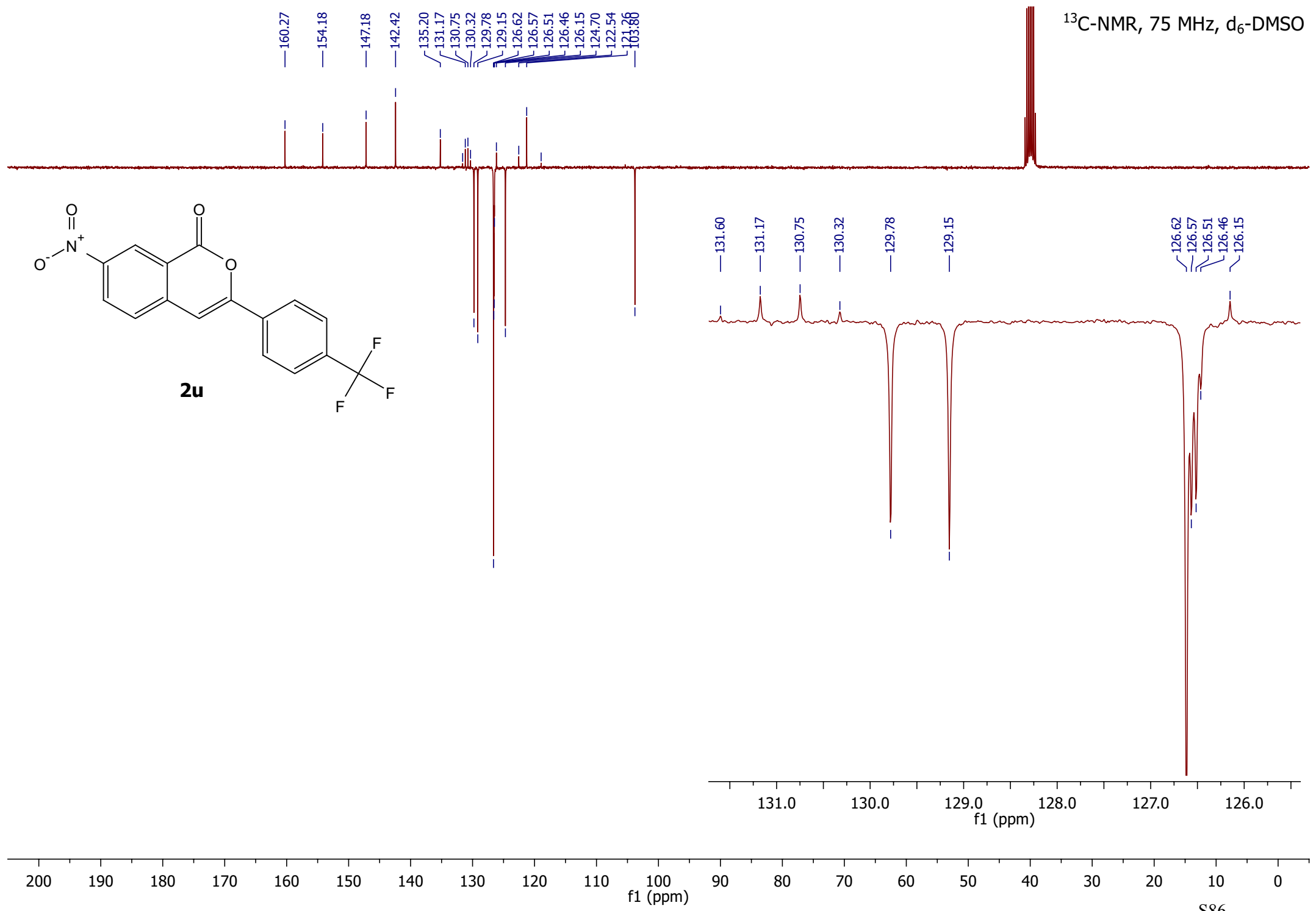
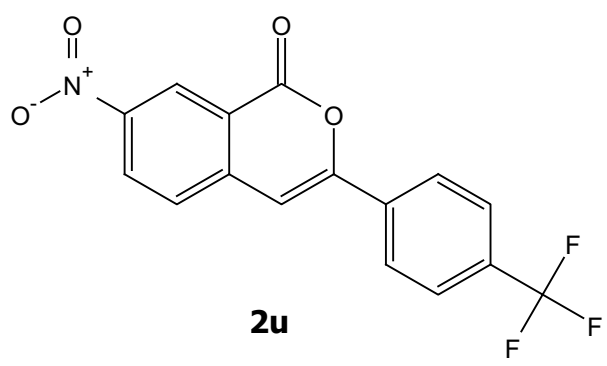


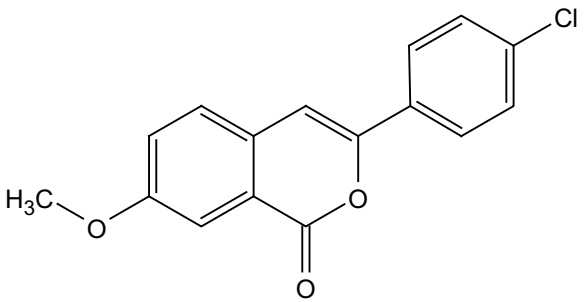
0.47
1.00
2.16
3.21
1.15



S85

¹³C-NMR, 75 MHz, d₆-DMSO

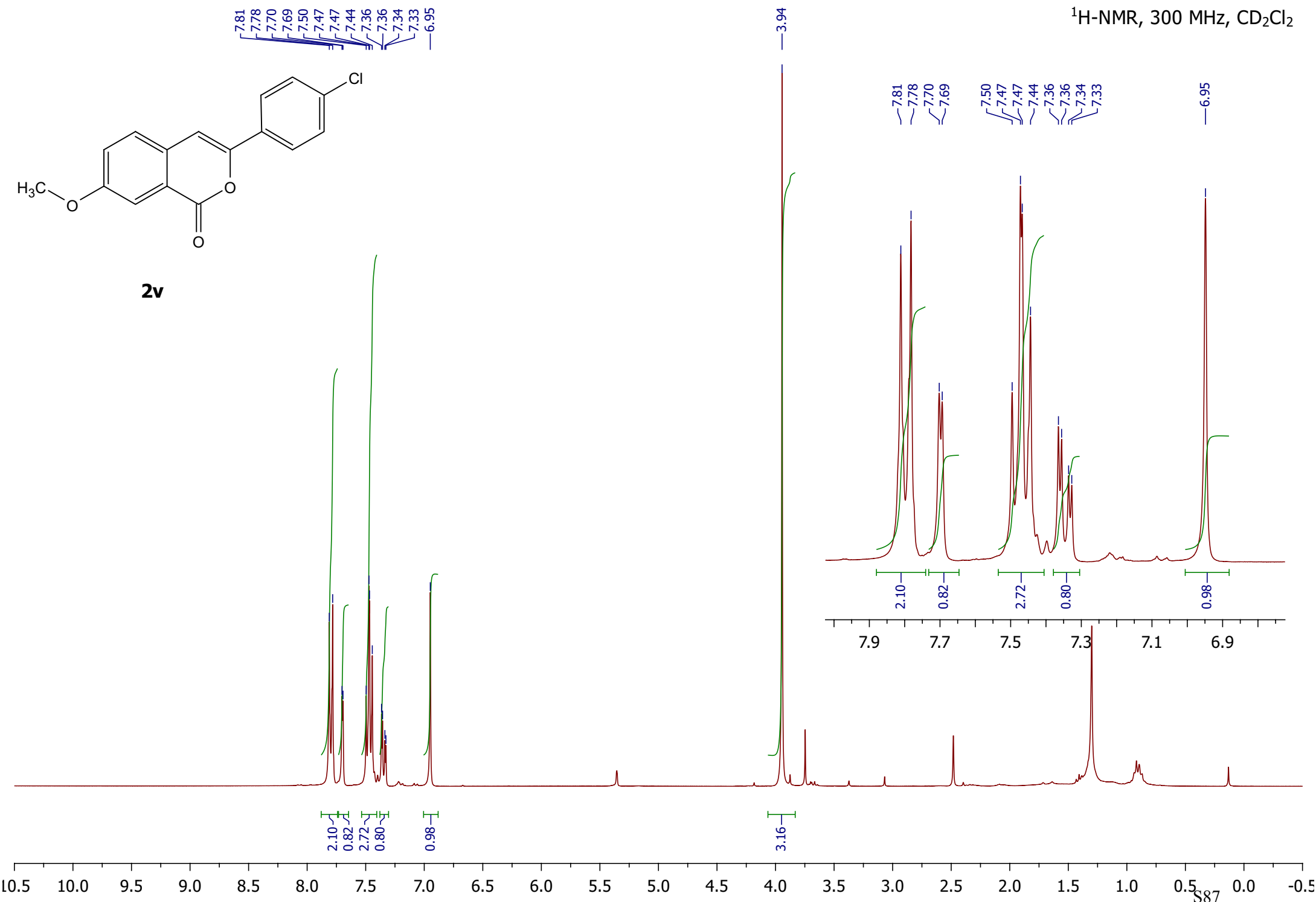


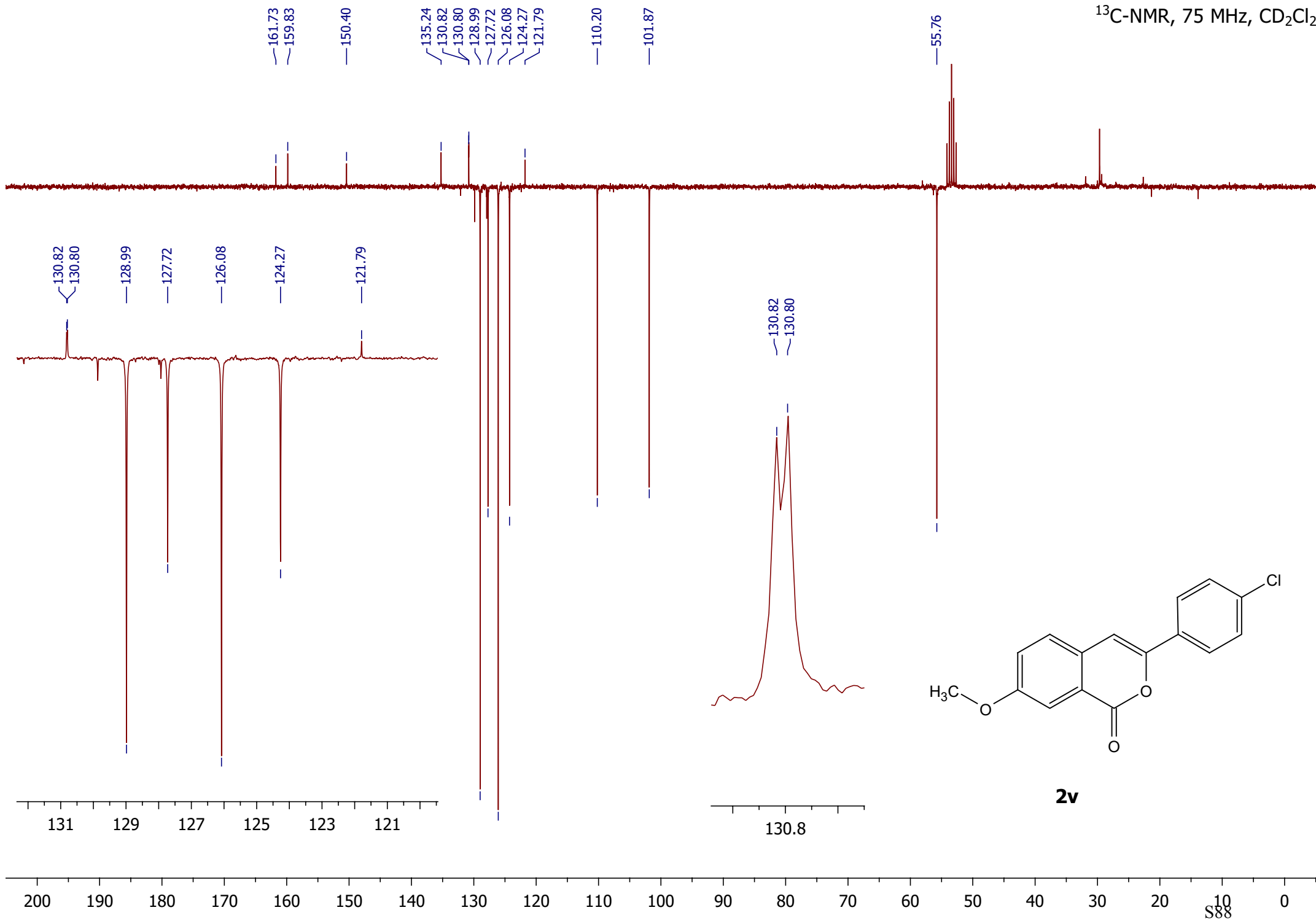


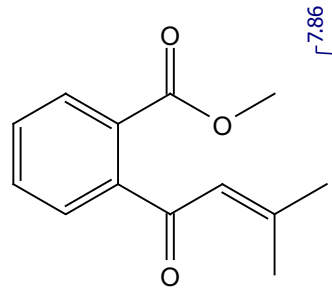
2v

7.81
7.78
7.70
7.69
7.50
7.47
7.47
7.44
7.36
7.36
7.34
7.33
6.95

7.81
7.78
7.70
7.69
7.50
7.47
7.47
7.44
7.36
7.36
7.34
7.33
6.95

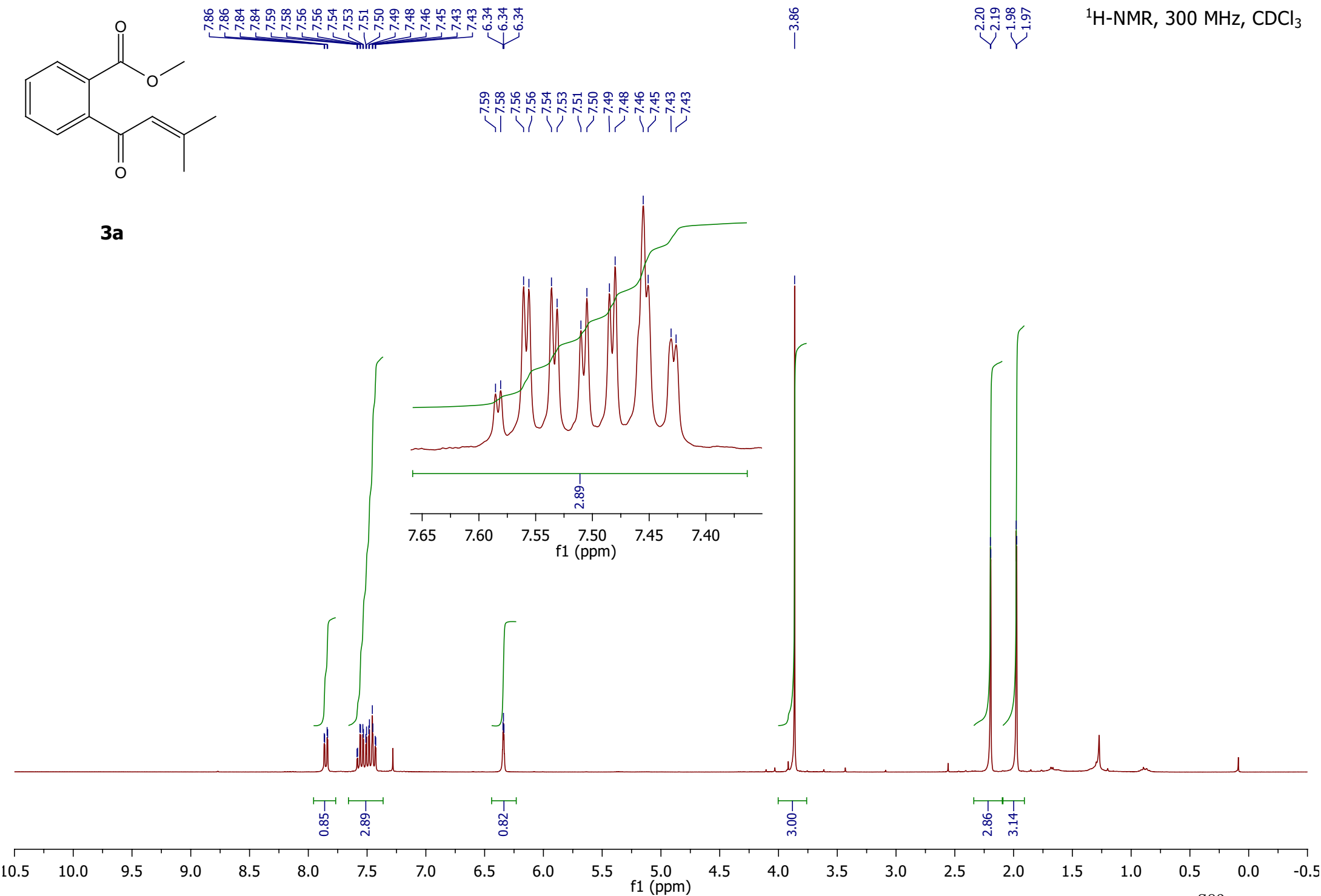


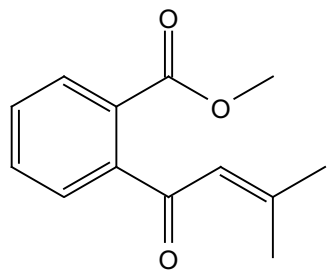




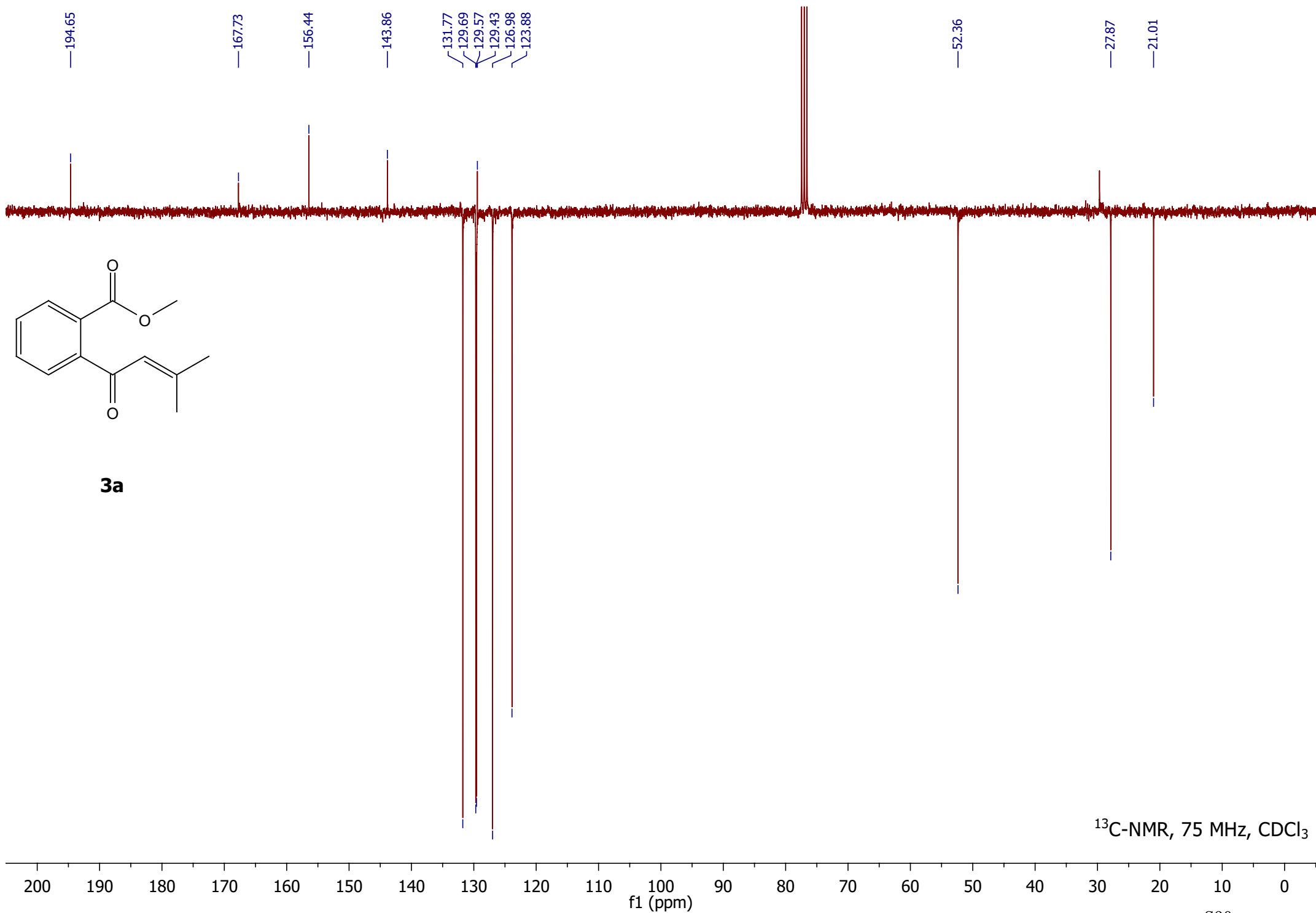
¹H-NMR, 300 MHz, CDCl₃

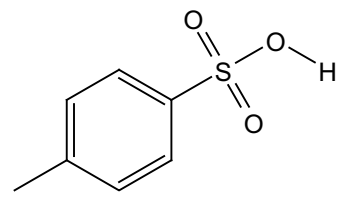
3a





3a

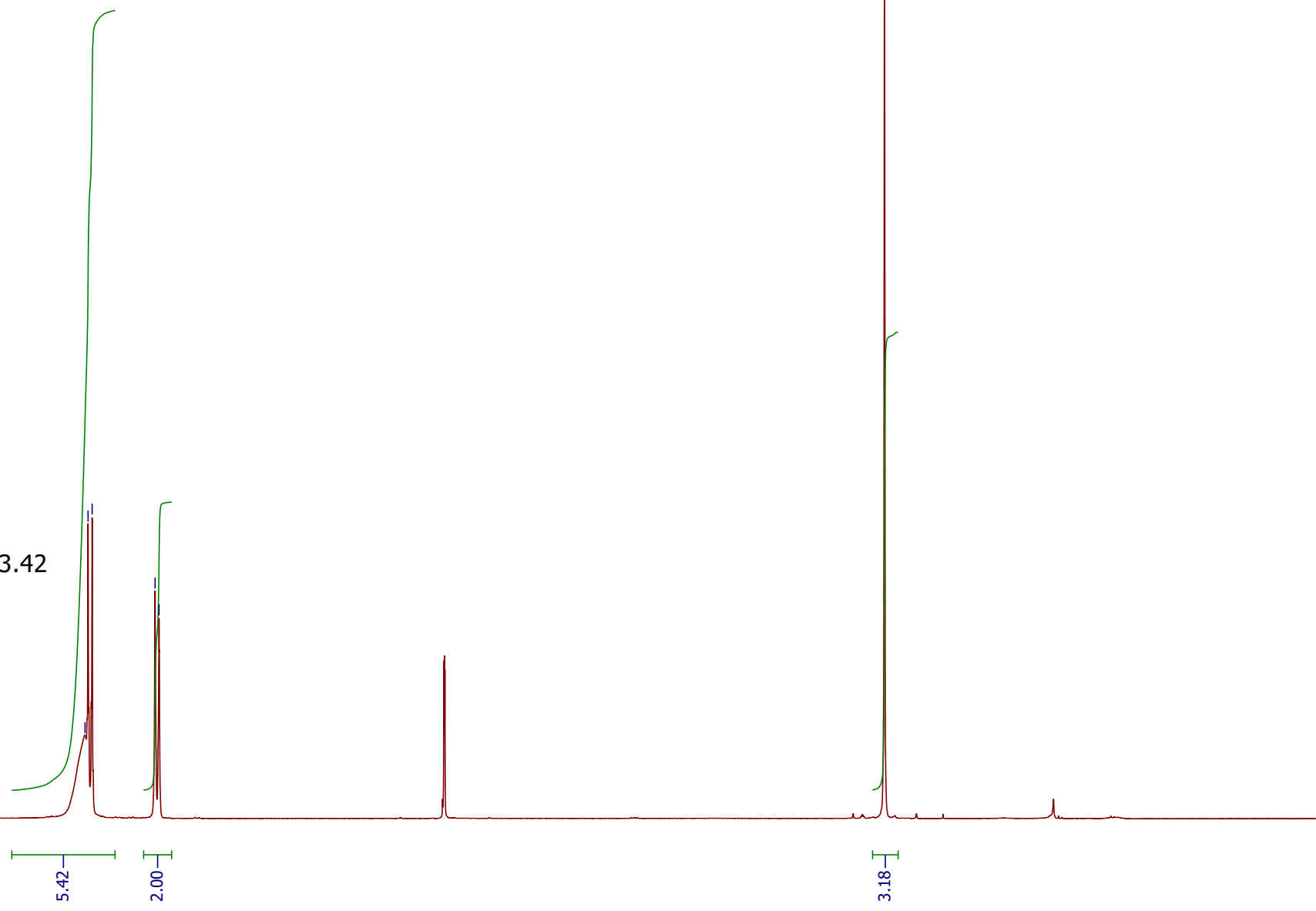




7.74
7.72
7.69
7.27
7.24

2.39

Integral of total mobile protons = 3.42



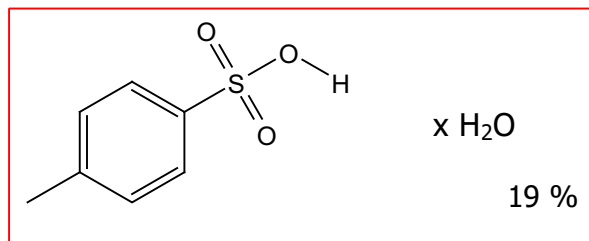
5.42
2.00

3.18

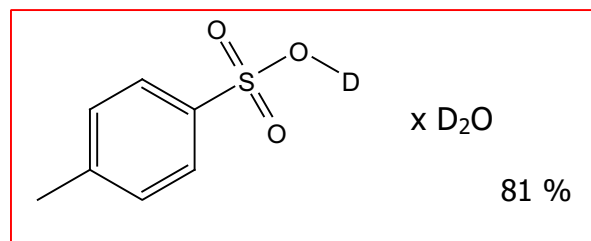
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0

¹H-NMR, 300 MHz, CD₂Cl₂

8.23
7.72
7.72
7.70
7.70
7.28
7.28
7.25
7.25



+



2.39

Integral of total mobile protons = 0.64

0.64 : 3.42 x 100 = 18.7
% of d ≈ 81%

